

The long and winding historical route of interventional cardiology All you ever wanted to know

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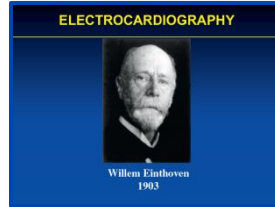


The ten advances that have defined modern cardiology

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Electrocardiography



Cholesterol and atherosclerosis

This truly seminal paper led ultimately to the cholesterol theory of atherogenesis, which in turn resulted in successful attempts to lower serum cholesterol in order to reverse, prevent, or at least retard the development of atherosclerosis and its complications.

Anitschkow: Zentralblf. Allg. Pathol. Anat. 1913;24:1

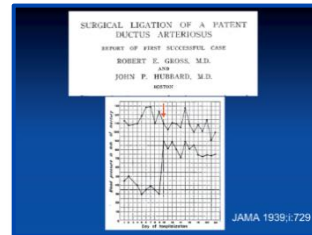


Cardiac catheterization

First carried out by Forssmann in 1929, a urologist, won the Nobel Prize

Cardiovascular surgery

The first cardiovascular operation in 1939, ligation of a patent ductus arteriosus in a seven and a half-year old girl



Coronary angiography and percutaneous coronary angioplasty

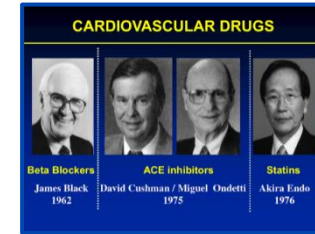
In 1958, while performing an angiogram of the aortic root, the tip of the catheter accidentally slipped into the ostium of the right coronary artery.

Sones et al: Circulation 20:773, 1959

The coronary care unit

In 1961, Desmond Julian, a registrar (fellow/resident) in cardiology at the Royal Infirmary in Edinburgh, wrote a brief paper describing the coronary care unit that was published in Lancet, in which he stated:

Cardiovascular drugs



Preventive cardiology

Kannel et al: The Framingham study Ann Intern Med 55:33, 1961

Cardiac imaging: Echocardiography

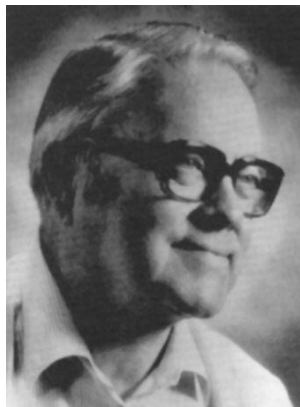
During World War II, ultrasound was widely used to detect submarines and to track torpedoes. The collaboration between two brilliant Norwegians, an emeritus Professor of Cardiology, Inge Edler, and an engineer, Helmut Hertz, led to the development of echocardiography. Edler and Hertz: Kungl Fysiogr Sallsk Lund Forth24, 1954

Cardiac pacemakers and defibrillation

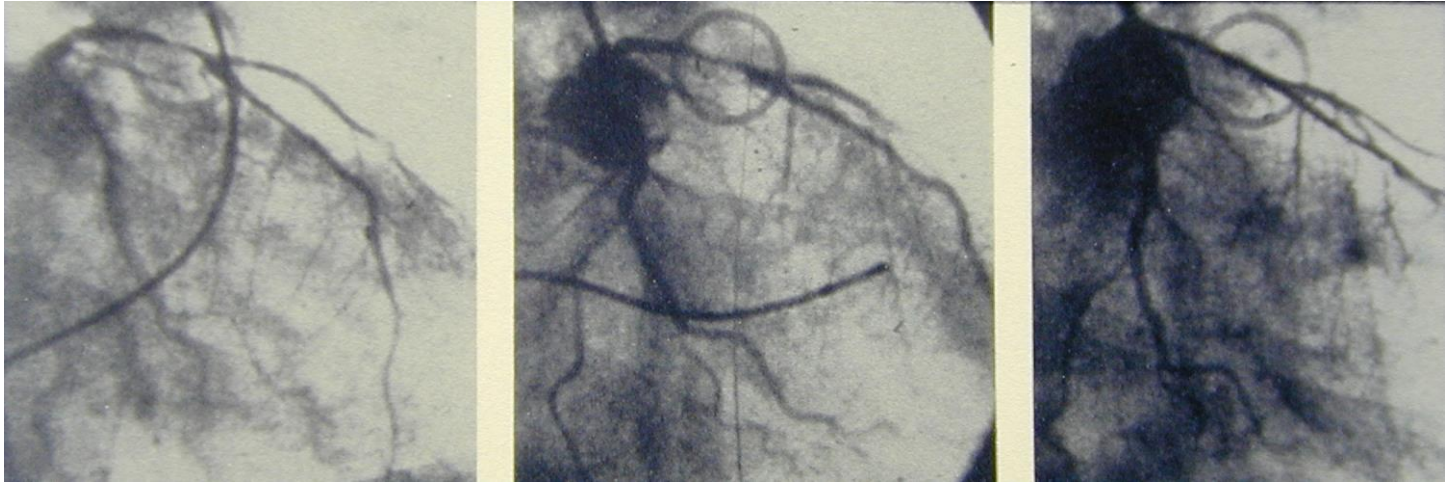
Mirowski et al: N Engl J Med 303:322, 2008

Outline

- **From balloon angioplasty (PCTA) to stent to scaffold, a history of trends, technology and techniques**
- From luminology to physiology (& advanced invasive imaging)
- New trends, technologies & techniques for the years ahead

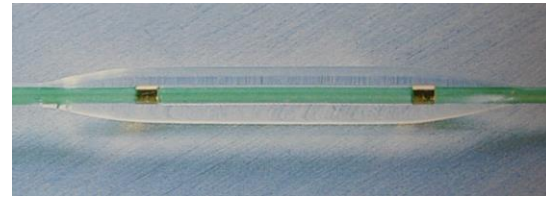
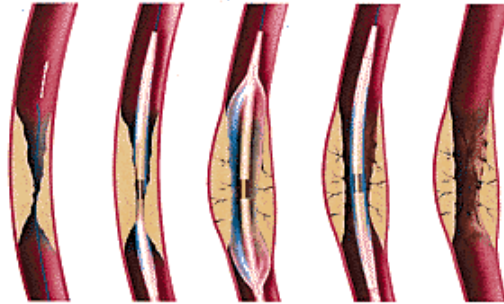


Coronary angioplasty



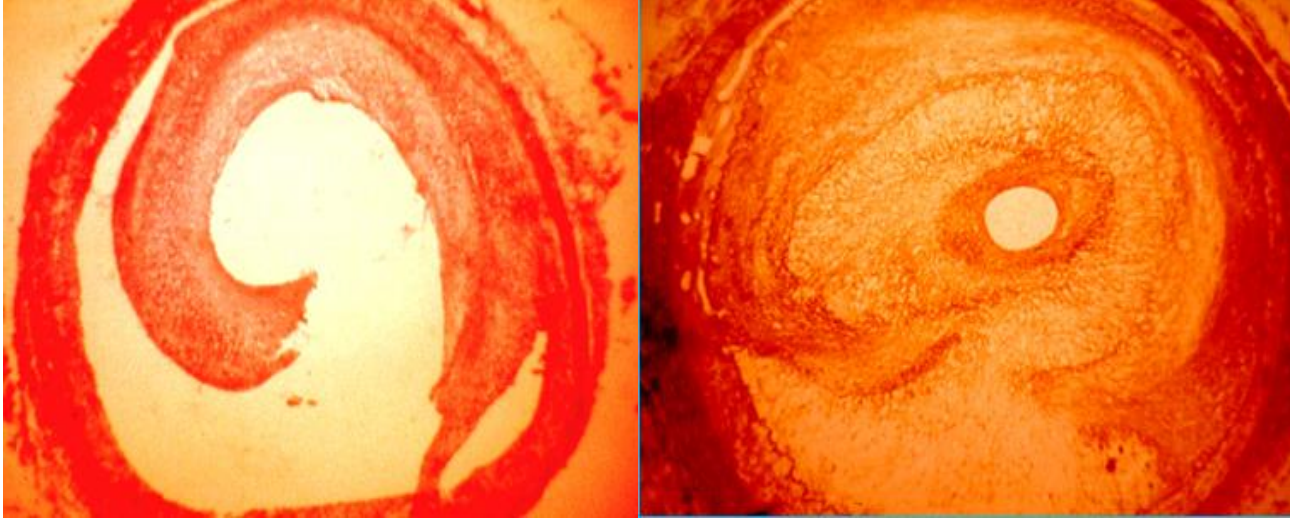
Zürich 1977

Coronary angioplasty





Coronary angioplasty



Daily interventional practice in the 80's

- Toxic contrast medium
- Immediate images unreliable
- High X-ray doses – ignorance about radiation danger
- PTCA only – restenosis rates around 30%
- Suboptimal visualisation during intervention
- Issues with vascular access management
- Pharmacological gap (DAPT, statins, ACE-inhibitors)

Fighting restenosis

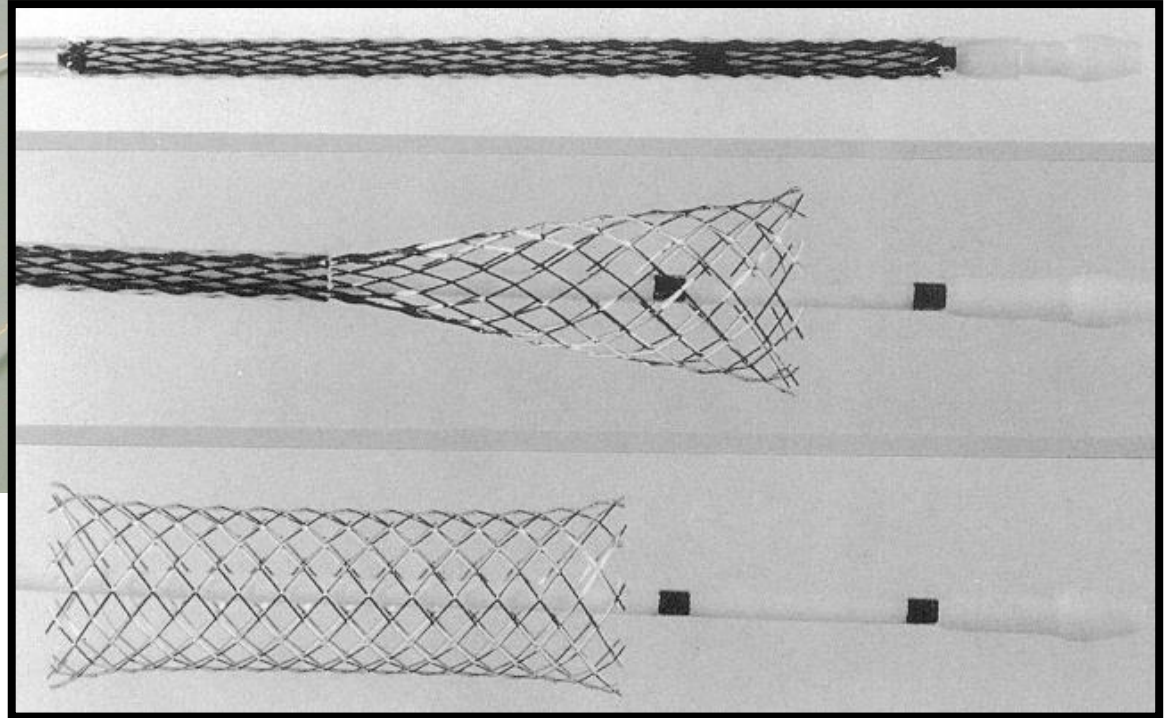
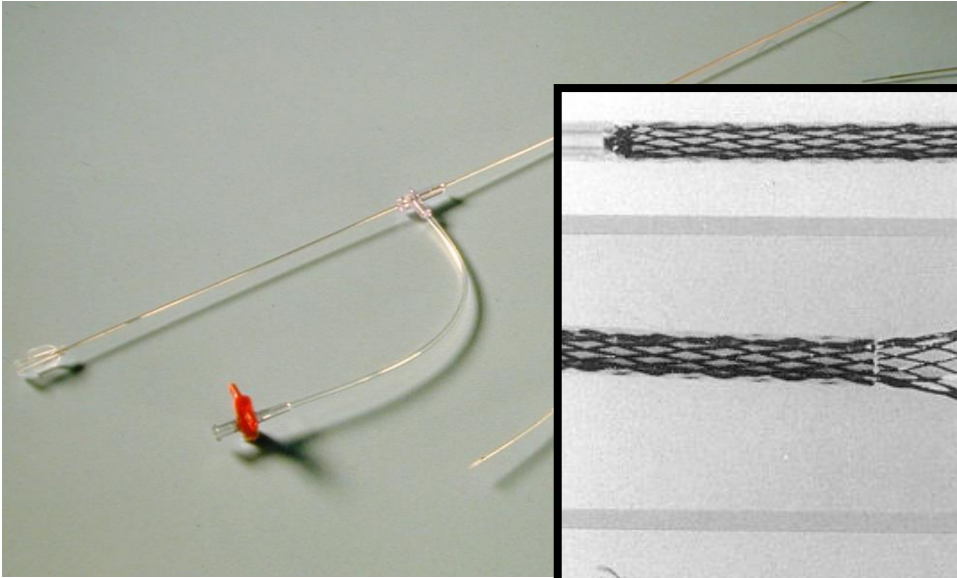
1991 Carport	(Tx A2-rptr antagonist) Circulation
1992 Mercator	(Cilazapril) Circulation
1993 Park	(Ketanserin) Circulation
1993 Marcator	(Cilazapril) Circulation
1995 Helvetica	(Hirudin) NEJM
1999 Flare	(Fluvastatin) European Heart J
2000 Eurocare	(Carvedilol) European Heart J
2001 Trapist	(Trapidil) European Heart J
2002 Presto	(Tranilast) Circulation
2002 Italics	(Antisense) JACC
2002 LIPS	(Fluvastatin) JAMA

The stent

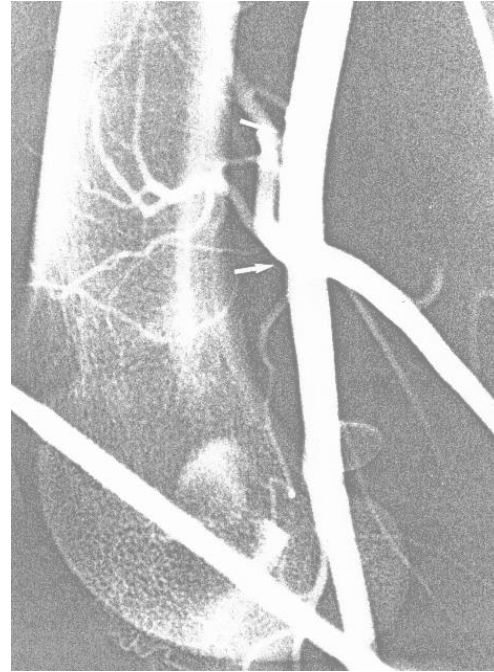
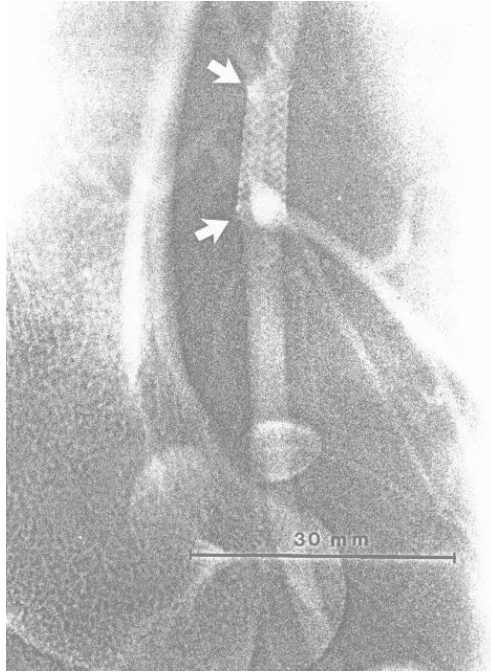


“Wallsten was a Swedish engineer who, in the early 1960s, invented a system to print out both sides of a newspaper page simultaneously. As a result of this quite revolutionary invention he quickly made a fortune and early in his career decided to retreat to the country of retired millionaires: Switzerland. At a social party in 1980 he met one of his compatriots, Senning, a prominent surgeon working in Zurich (the father of the so-called “Senning operation” for congenital heart disease). Senning was concerned by the high mortality of acute surgery in patients suffering acute dissection of the ascending and descending aorta. Wallsten proposed an ingenious mechanical device which could be introduced percutaneously and would scaffold the dissection flap in the aorta.”

The stent

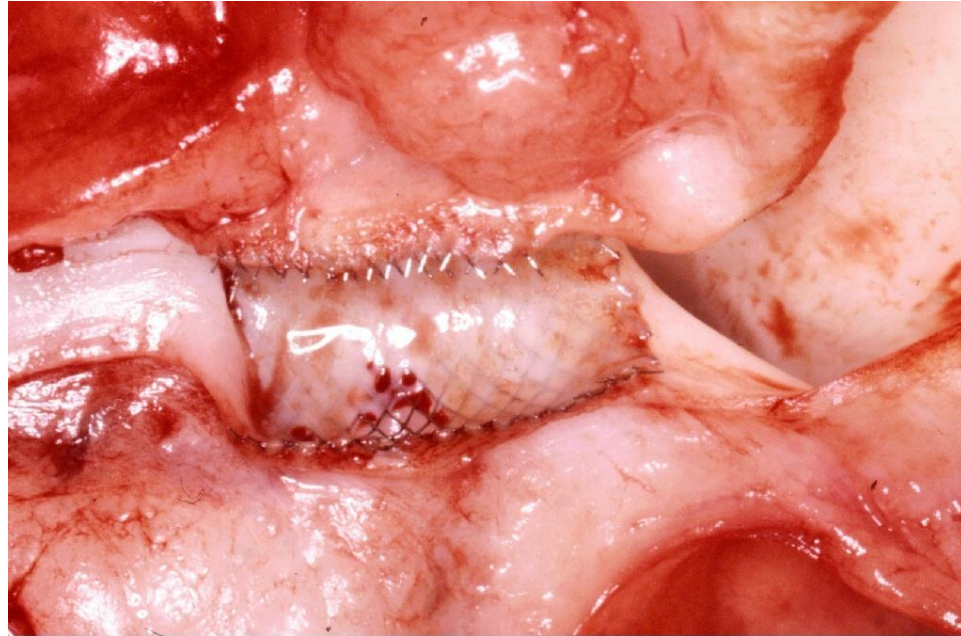


The stent



U. Sigwart (1985): first stent implant in canine artery

The stent



The stent

The first stent
in a human being
28.03.1986
J. Puel
Toulouse



From 1986-1990: infancy and growing pains "the Wallstent's time"

"In February 1986 I met Jacques Puel in Toulouse during one of the numerous cardiology meetings, and at that particular meeting he told me about one of his new endeavours ("implantation of metallic, self-expanding prostheses in the femoral arteries of goats").

At about the same time I found a leaflet on my desk announcing an angioplasty course in Lausanne, organized by Ulrich Sigwart and the topic of stented angioplasty was indicated on the programme."



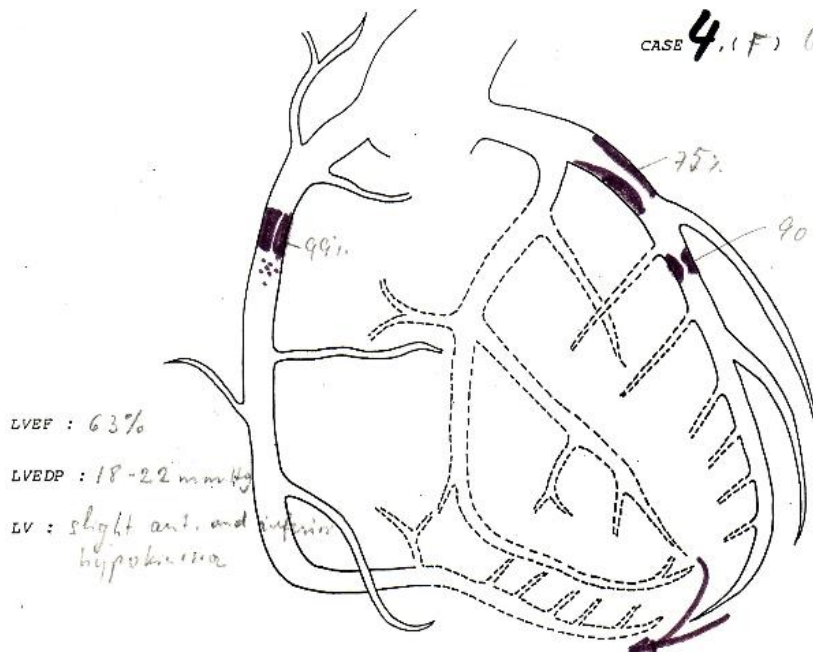
June 13, 1986

CH-1011 Lausanne, Switzerland

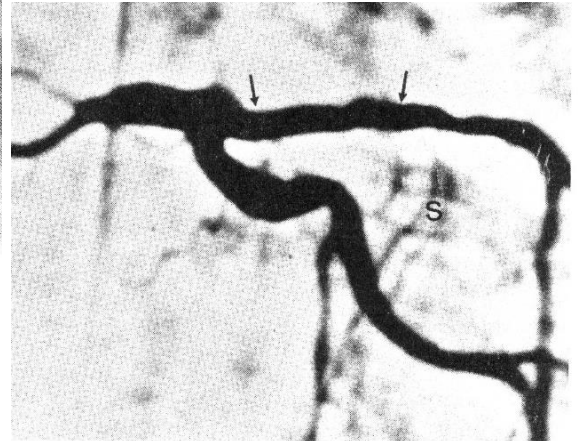
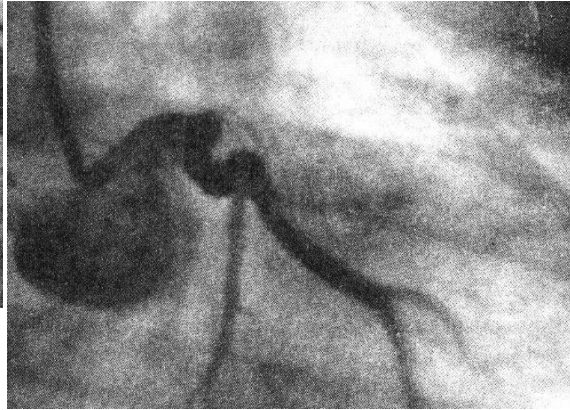
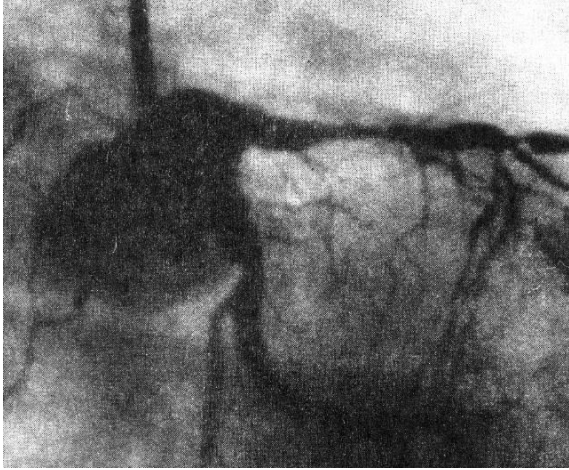
Limited Participation

Program

CASE 4, (F) G.D.,



The stent



The stent

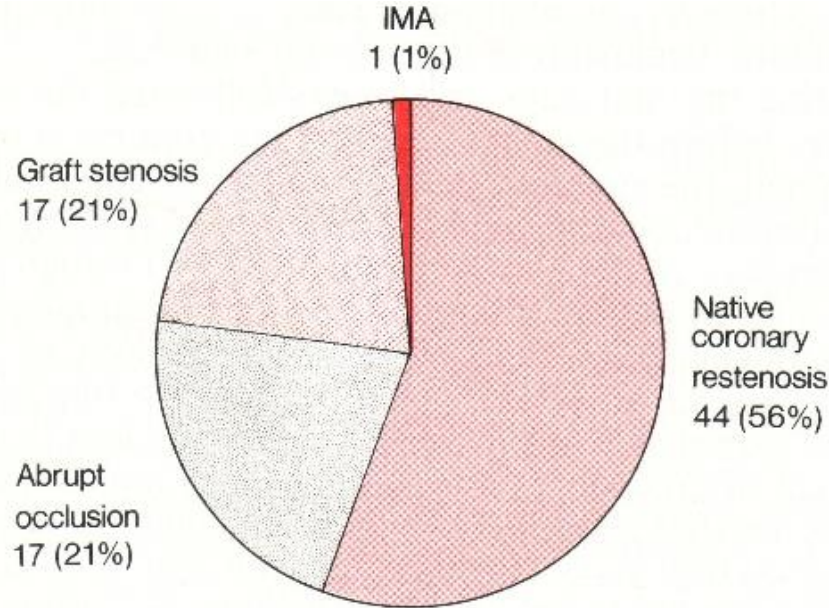


FIGURE 11. Indications for stenting during the first 2 years of clinical use in Lausanne, Switzerland (79 procedures). (IMA = Internal mammary artery stenosis.)

The stent

Diagnostic anatomo-pathologique:

Infarctus aigu apico-basal antéro-septal du myocarde (env. 40%).

Nécrose fraîche des piliers postérieurs de la mitrale.

Plaque d'artériosclérose sur l'IVA à 1,5 cm de son départ.

Status 3 jours après dilatation de l'IVA et mise en place d'une prothèse endoluminale.

Thrombose très récente dans la lumière de la prothèse.

25.04.1986 – U. Sigwart - Lausanne



The stent

ANGIOGRAPHIC FOLLOW-UP AFTER PLACEMENT OF A SELF-EXPANDING CORONARY-ARTERY STENT

PATRICK W. SERRUYS, M.D., BRADLEY H. STRAUSS, M.D., KEVIN J. BEATT, M.B., B.S.,
MICHEL E. BERTRAND, M.D., JACQUES PUEL, M.D., ANTHONY F. RICKARDS, M.B., B.S.,
BERNHARD MEIER, M.D., JEAN-JACQUES GOY, M.D., PIERRE VOGT, M.D., LUKAS KAPPENBERGER, M.D.,
AND ULRICH SIGWART, M.D.

Abstract *Background.* The placement of stents in coronary arteries after coronary angioplasty has been investigated as a way of treating abrupt coronary-artery occlusion related to the angioplasty and of reducing the late intimal hyperplasia responsible for gradual restenosis of the dilated lesion.

Methods. From March 1986 to January 1988, we implanted 117 self-expanding, stainless-steel endovascular stents (Wallstent) in the native coronary arteries (94 stents) or saphenous-vein bypass grafts (23 stents) of 105 patients. Angiograms were obtained immediately before and after placement of the stent and at follow-up at least one month later (unless symptoms required angiography sooner). The mortality after one year was 7.6 percent (8 patients). Follow-up angiograms (after a mean [\pm SD] of 5.7 ± 4.4 months) were obtained in 95 patients with 105 stents and were analyzed quantitatively by a computer-assisted system of cardiovascular angiographic analysis. The 10 patients without follow-up angiograms included 4 who died.

Results. Complete occlusion occurred in 27 stents in

25 patients (24 percent). 21 occlusions were documented within the first 14 days after implantation. Overall, immediately after placement of the stent there was a significant increase in the minimal luminal diameter and a significant decrease in the percentage of the diameter with stenosis (changing from a mean [\pm SD] of 1.88 ± 0.43 to 2.48 ± 0.51 mm and from 37 ± 12 to 21 ± 10 percent, respectively; $P<0.0001$). Later, however, there was a significant decrease in the minimal luminal diameter and a significant increase in the stenosis of the segment with the stent (1.68 ± 1.78 mm and 48 ± 34 percent at follow-up). Significant restenosis, as indicated by a reduction of 0.72 mm in the minimal luminal diameter or by an increase in the percentage of stenosis to ≥ 50 percent, occurred in 32 percent and 14 percent of patent stents, respectively.

Conclusions. Early occlusion remains an important limitation of this coronary-artery stent. Even when the early effects are beneficial there are frequently late occlusions or restenosis. The place of this form of treatment for coronary artery disease remains to be determined. (N Engl J Med 1991; 324:13-7.)

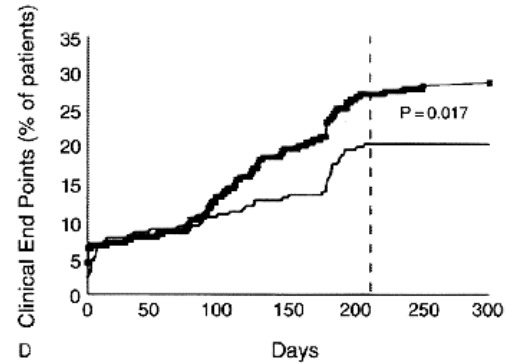
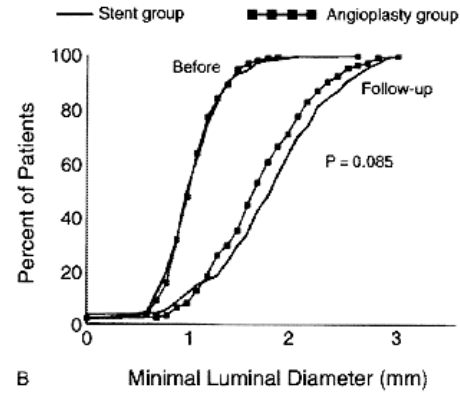
Late loss : 0.8mm, restenosis rate : 14%

The stent

BENESTENT I

STRESS I

NEJM 1994

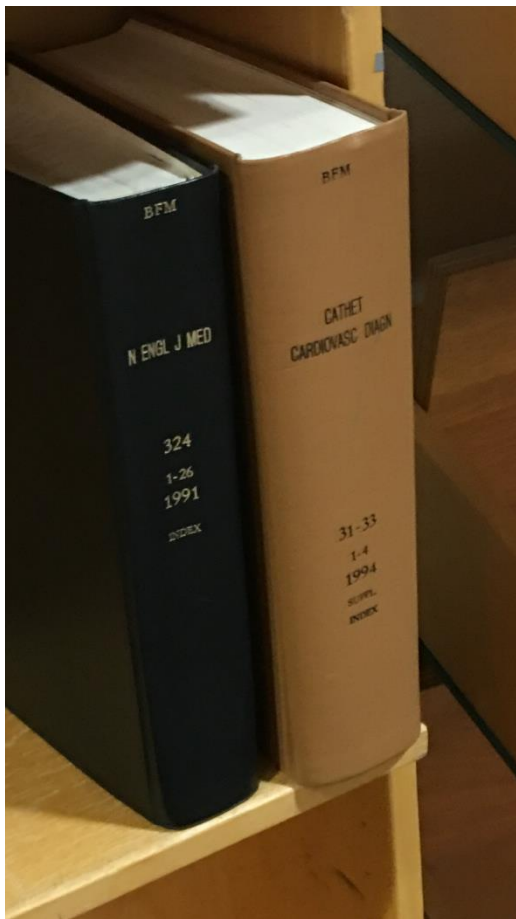


EVENT	ANGIOPLASTY	STENT	RELATIVE RISK (95% CI)	VARIABLE†	ANGIOPLASTY	STENT	P VALUE
	(N = 257)	(N = 259)			(N = 240)	(N = 237)	
	number (percent)				mean ±SD		
Death				Reference diameter (mm)			
In hospital	0	0	—	Before	3.01±0.46	2.99±0.45	NS
At 7 mo	1 (0.4)	2 (0.8)	1.98 (0.18–21.75)	After	3.09±0.44	3.16±0.43	0.045
All events	1 (0.4)	2 (0.8)	1.98 (0.18–21.75)	Follow-up	3.05±0.49	2.96±0.48	0.04
Cerebrovascular accident				Minimal luminal diameter (mm)			
In hospital	1 (0.4)	0	—	Before	1.08±0.31	1.07±0.33	NS
At 7 mo	2 (0.8)	0	—	After	2.05±0.33	2.48±0.39	<0.001
All events	2 (0.8)	0	—	Follow-up	1.73±0.55	1.82±0.64	0.09‡
Q-wave MI				Stenosis (%)			
In hospital	2 (0.8)	5 (1.9)	2.48 (0.49–12.67)	Before	64±10	64±10	NS
At 7 mo	4 (1.6)	7 (2.7)	1.74 (0.51–5.86)	After	33±8	22±8	<0.001
All events	5 (1.9)	7 (2.7)	1.39 (0.45–4.32)	Follow-up	43±16	38±18	0.003
Non-Q-wave MI				Restenosis rate (%)	32	22	0.02
In hospital	6 (2.3)	4 (1.5)	0.66 (0.19–2.32)	Gain (mm)	0.97±0.39	1.40±0.44	<0.001
At 7 mo	6 (2.3)	4 (1.5)	0.66 (0.19–2.32)	Loss (mm)	0.32±0.47	0.65±0.57	<0.001
All events	7 (2.7)	4 (1.5)	0.57 (0.17–1.91)	Net gain (mm)	0.65±0.59	0.75±0.66	0.09
Urgent CABG							
In hospital	4 (1.6)	5 (1.9)	1.24 (0.34–4.57)				
At 7 mo	4 (1.6)	5 (1.9)	1.24 (0.34–4.57)				
All events	5 (1.9)	6 (2.3)	1.19 (0.37–3.85)				
Elective CABG							
In hospital	0	3 (1.2)	—				
At 7 mo	6 (2.3)	8 (3.1)	1.32 (0.47–3.76)				
All events	6 (2.3)	10 (3.9)	1.65 (0.61–4.48)				
Repeat PTCA							
In hospital	3 (1.2)	1 (0.4)	0.33 (0.03–3.16)				
At 7 mo	53 (20.6)	26 (10.0)	0.49 (0.32–0.75)				
All events	60 (23.3)	35 (13.5)	0.58 (0.40–0.85)				
Any event							
In hospital	16 (6.2)	18 (6.9)	1.12 (0.58–2.14)				
At 7 mo	76 (29.6)	52 (20.1)	0.68 (0.50–0.92)				

**All events" refers to the total count of events at seven months (i.e., if a patient required repeat angioplasty and later coronary-artery bypass grafting, the total count at seven months would reflect both events, not just the first that occurred). CI denotes confidence interval, MI myocardial infarction, CABG coronary-artery bypass graft, PTCA percutaneous transluminal coronary angioplasty, and NS not significant.

†Reference values are the interpolated diameters of normal vessels; gain, the minimal luminal diameter after the procedure minus the value obtained before the procedure; loss, the minimal luminal diameter after the procedure minus the follow-up value; and net gain, the minimal luminal diameter at follow-up minus the value obtained before the procedure.

‡P = 0.08 and P = 0.03 for the difference in minimal luminal diameter between the two study groups at follow-up when the pre-intervention lumen and vessel size, respectively, were used as covariates.



Catheterization and Cardiovascular Diagnosis 32:133–138 (1994)

Ticlopidine and Subcutaneous Heparin as an Alternative Regimen Following Coronary Stenting

P. Barragan, MD, J. Sainsous, MD, M. Silvestri, MD, J.L. Bouvier, MD, B. Comet, MD, J.B. Siméoni, MD, C. Charmasson, MD, and M. Bremondry, MD

Subacute thrombosis of coronary stents may occur up to the end of the first month after their implantation and remains the major problem associated with the technique. A cohort of 238 patients with placement of one or more stents in 244 arteries was monitored for this period. All patients were given 500 mg/day of ticlopidine (started 3 days before) and a push dose of 10,000 IU of heparin during the procedure, then 1,000–1,500 IU/hr for 20 hr. Following removal of the arterial introducer, they were kept on subcutaneous heparin for 1 week and ticlopidine (500 mg/day) for 3–6 months. Nine patients (3.8%) showed evidence of thrombosis at 7 days. The overall thrombosis rate at 30 days was 4.2% (3.5% for elective stents, as compared with 7.9% associated with occlusive dissections). Emergency treatment by further angioplasty (8 cases) and intracoronary thrombolysis (5 cases) was undertaken. Complications were as follows: 5 deaths (2%), 3 MI (1.2%), 2 non-Q MI (1.7%). Three predictive factors for subacute thrombosis were identified: age <70 ($p = 0.00006$), unstable angina ($p = 0.006$) and arterial diameter less than 3 mm ($p = 0.043$). The peripheral vascular complication rate was 4.6%. This study suggests that preventive treatment with ticlopidine appears to reduce the incidence of subacute thrombosis of stents in patients >70 years of age. Furthermore, the combination of ticlopidine and heparin facilitates laboratory monitoring after stenting. Stenting is thought to represent definitive treatment in situations where placement for occlusive dissection is the indication. © 1994 Wiley-Liss, Inc.

Key words: subacute thrombosis, stents, ticlopidine

The stent

Intracoronary Stenting Without Anticoagulation Accomplished With Intravascular Ultrasound Guidance

Antonio Colombo, MD; Patrick Hall, MD; Shigeru Nakamura, MD; Yaron Almagor, MD;
Luigi Maiello, MD; Giovanni Martini, CCP; Antonio Gaglione, MD;
Steven L. Goldberg, MD; Jonathan M. Tobis, MD

Background The placement of stents in coronary arteries has been shown to reduce restenosis in comparison to balloon angioplasty. However, clinical use of intracoronary stents is impeded by the risk of subacute stent thrombosis and complications associated with the anticoagulant regimen. To reduce these complications, the hypothesis that systemic anticoagulation is not necessary when adequate stent expansion is achieved was prospectively evaluated on a consecutive series of patients who received intracoronary stents.

Methods and Results From March 1993 to January 1994, 359 patients underwent Palmaz-Schatz coronary stent insertion. After an initial successful angiographic result with <20% stenosis by visual estimation had been achieved, intravascular ultrasound imaging was performed. Further balloon dilatation of the stent was guided by observation of the intravascular ultrasound images. All patients with adequate stent expansion confirmed by ultrasound were treated only with antiplatelet therapy (either ticlopidine for 1 month with short-term aspirin for 5 days or only aspirin) after the procedure. Clinical success (procedure success without early postprocedural events) at 2 months was achieved in 338 patients (94%). With an inflation pressure of 14.9 ± 3.0 atm and a balloon-to-vessel ratio of 1.17 ± 0.19 , optimal stent expansion was achieved in 321 of the 334 patients (96%) who underwent intravascular ultrasound evaluation, with these patients receiving only antiplatelet therapy after the procedure. Despite the absence of anticoagulation, there were only two acute stent thromboses (0.6%) and one subacute stent thrombosis (0.3%) at 2-month clinical follow-up. Follow-up angiography at 3 to 6 months docu-


mented two additional occlusions (0.6%) at the stent site. A 6-month clinical follow-up, angiographically documented stenosis had occurred in 5 patients (1.6%). At 6-month clinical follow-up, there was a 5.7% incidence of myocardial infarction, a 6.4% rate of coronary bypass surgery, and a 1.9% incidence of death. Emergency intervention (emergency angioplasty or bailout stent) for a stent thrombosis event was performed in 3 patients (0.8%). The overall event rate was relatively high because of intraprocedural complications that occurred in 16 patients (4.5%). Intraprocedural complications however, decreased to 1% when angiographically appropriately sized balloons were used for final stent dilations. There was one ischemic vascular complication that occurred at the time of the procedure and one ischemic vascular complication that occurred at the time of angiographic follow-up. By 6 months repeat angioplasty for symptomatic restenosis was performed in 47 patients (13.1%).

Conclusions The Palmaz-Schatz stent can be safely inserted in coronary arteries without subsequent anticoagulation provided that stent expansion is adequate and there are no other flow-limiting lesions present. The use of high-pressure final balloon dilatations and confirmation of adequate stent expansion by intravascular ultrasound provide assurance that anticoagulation therapy can be safely omitted. This technique significantly reduces hospital time and vascular complications and has a low stent thrombosis rate. (*Circulation*. 1995;91:1676-1688.)

Key Words • stents • ultrasonics • balloon • platelets

The stent

stent thrombosis (unless specified otherwise)



Trial	No pts	ASA & thienopyridine	ASA & warfarin	Characteristic
ISAR*	517	0.8%	5.4%	
FANTASTIC [°]	473	0.4%	3.5%	Subacute thrombosis
STARS**	1096	0.5%	2.7%	Angiographic thrombosis
MATTIS ^{°°}	350	5.6%	11%	Composite end point

*Schomig et al, NEJM 1996 - ° Bertrand et al, Circulation 1998

** Leon et al, NEJM 1998 - °° Urban et al, Circulation 1998

The stent

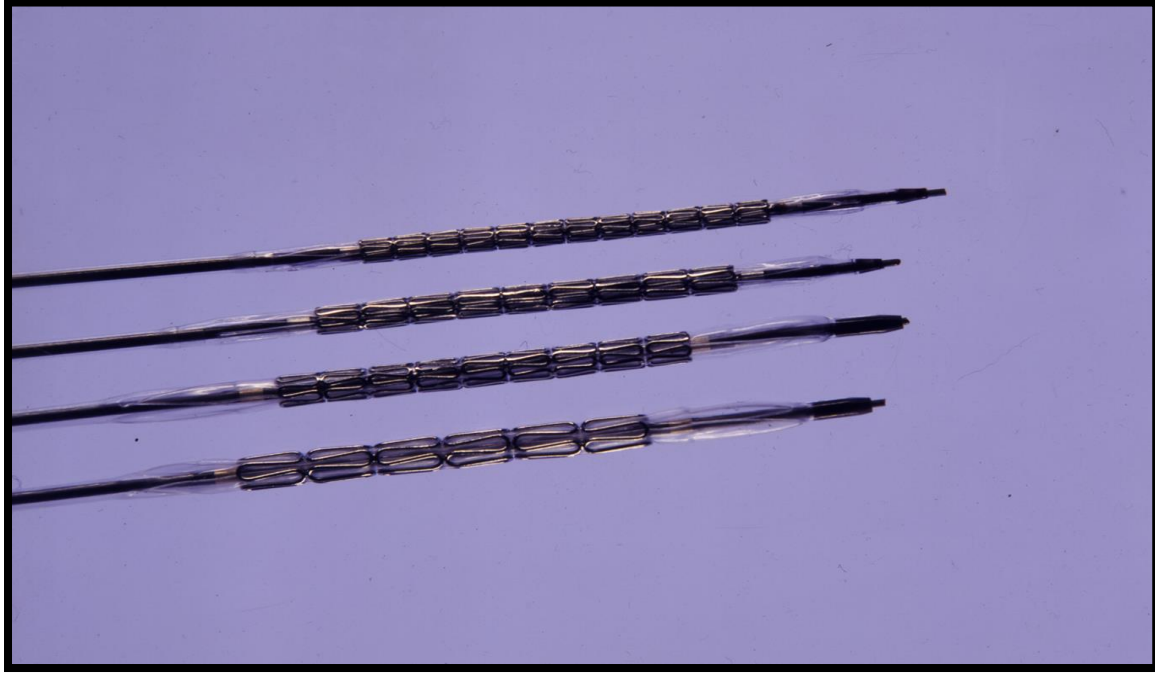
CLASSICS – Bertrand et al, Circulation 2000

	Clopidogrel 300mg loading & ASA 325mg	Clopidogrel 75mg loading & ASA 325mg	Ticlopidine 500mg & ASA 325mg
Safety end point*	2.9%	6.3%	9.1%
Efficacy end point**	1.2%	1.5%	0.9%

*Major bleeding – neutropenia – thrombocytopenia – early study drug discontinuation

** Cardiac death – myocardial infarction – target lesion revascularization

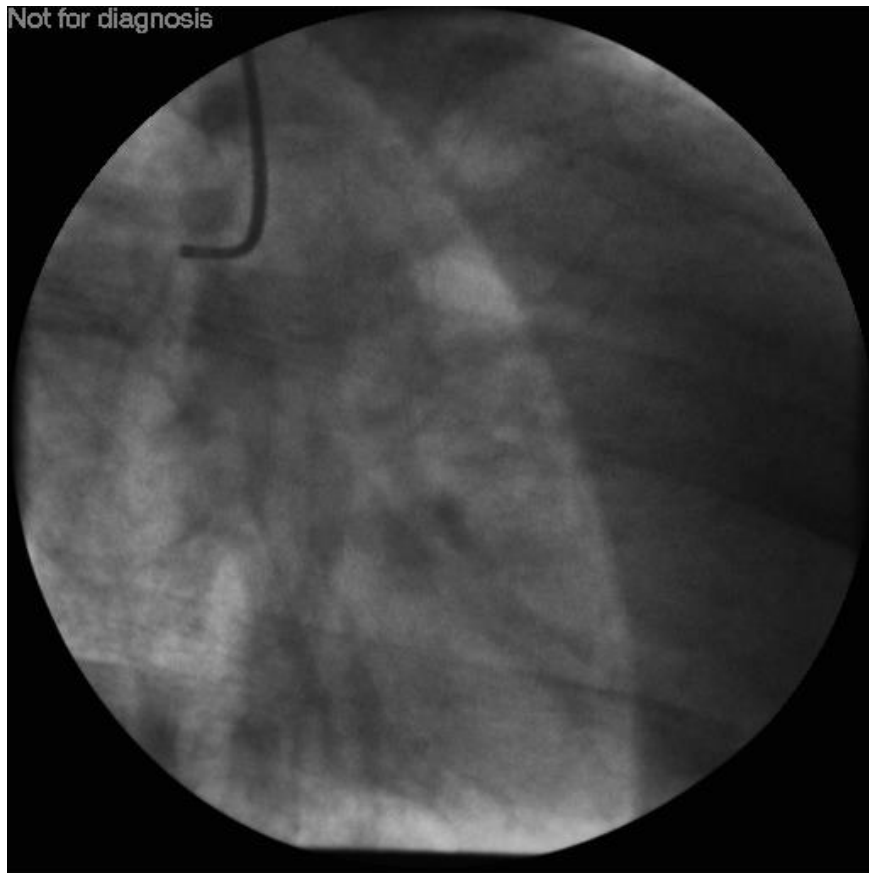
The stent



Clinical case (I)

- 2001 : just prior to Christmas
- 42-year old man, in instance of divorce
- Never seen a “doctor”
- Routine check-up for atypical chest pain
- Exercise test by his cardiologist
It was about 3pm on a week day

Not for diagnosis



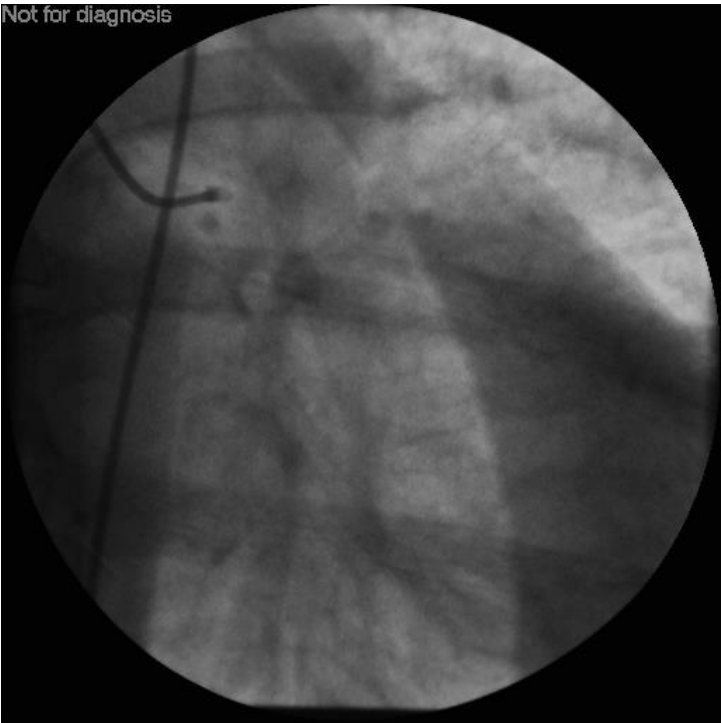
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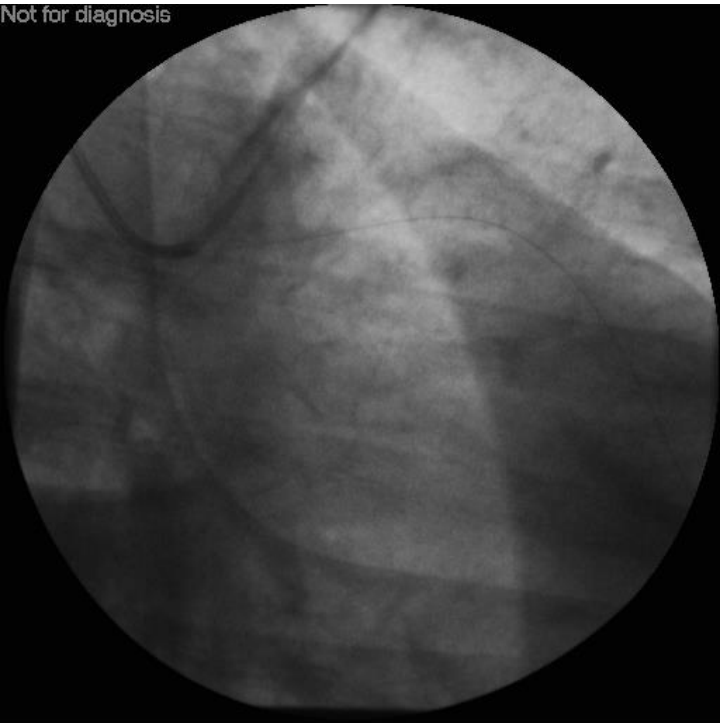
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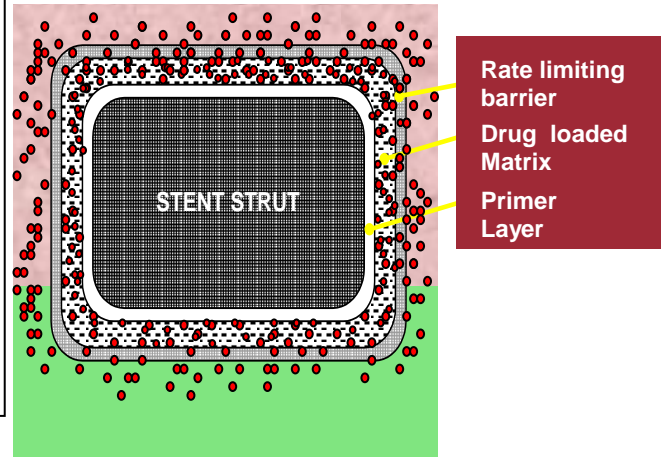
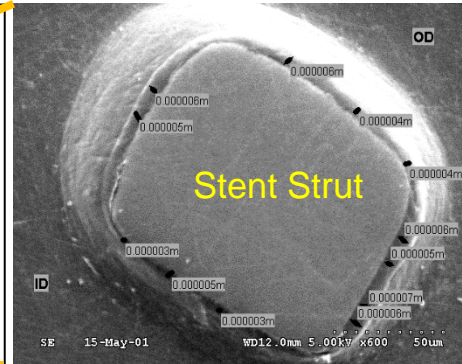
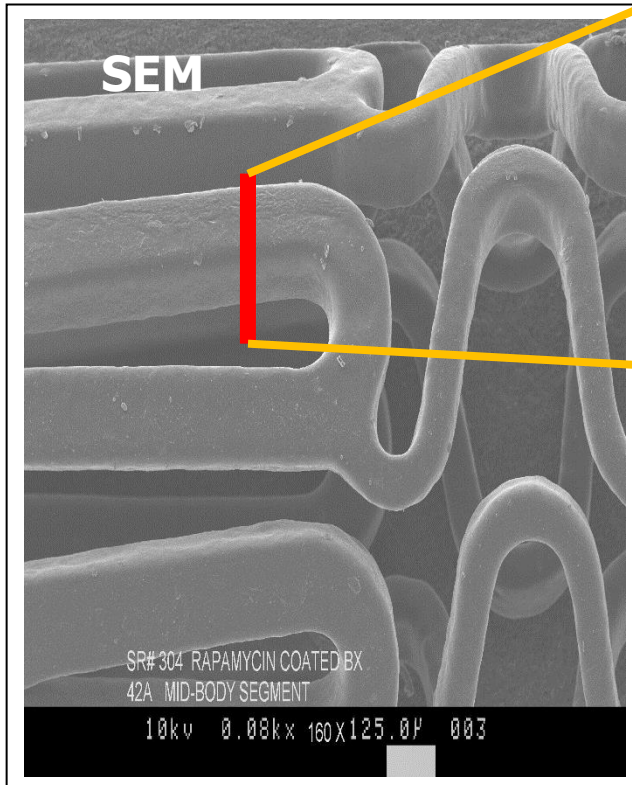


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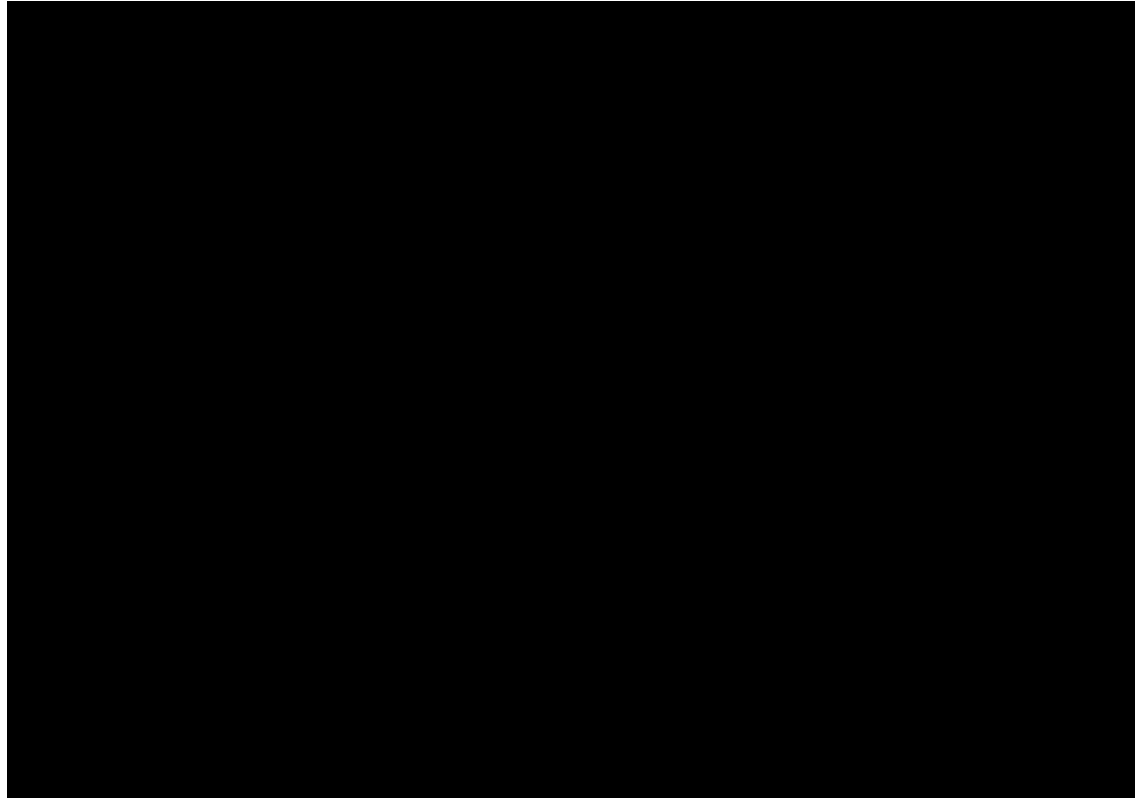


The drug-eluting stent



July 1999 : the first DES concept

The drug-eluting stent



First-In-Man study with the CYPHER stent: Sao Paulo, Dec. 2000

Robert
Falotico The
father of the
sirolimus stent




RAVEL

A **R**andomised, double-blind study with the Sirolimus-eluting Bx **VE**LOCITY™ balloon expandable stent in the treatment of patients with *de novo* native coronary artery **L**esions

Authors:

J. Fajadet, M. Perin, E. Ban Hayashi, A. Colombo,
G. Schuler, P. Barragan, C. Bode, J.E. Sousa,
M.C. Morice, P.W. Serruys



This randomized double-blind trial demonstrated complete abolition of neo-intimal proliferation at 6 months:

- MLD (2.42 mm)
remains basically unchanged compared to
- MLD post deployment (2.43 mm)
- No late loss (-0.01 mm)
- Restenosis (0%)
- No evidence of edge effect

First Four-Year Clinical Follow-Up from a Randomized Trial of a Polymer-Based, Paclitaxel-Eluting Stent: TAXUS I



Eberhard Grube^a, Sigmund Silber^b, Karl E. Hauptman^c, Mary E. Russell^d,* for the TAXUS I Investigators

^aHeart Center Siegburg, ^bCardiology Practice and Hospital, Munich ^cKrankenhaus der Barmherzigen Bruder, ^dBoston Scientific Corporation

*Employee and stockholder of Boston Scientific Corporation

Background

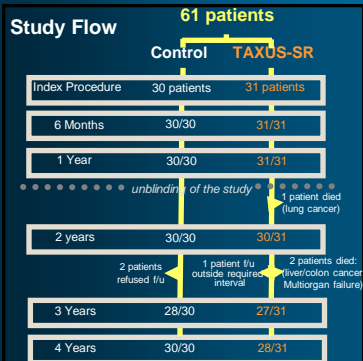
- ❖ TAXUS I is a prospective, randomized, double-blind study to evaluate safety and performance of coronary artery stenting with a paclitaxel-eluting stent (TAXUS NIRx) for the treatment of de novo and restenotic lesions.
- ❖ The first human use study evaluating the TAXUS slow-release stent showed continued safety and sustained reduction in target lesion revascularization through 3 years post implantation.
- ❖ We now present results from the first 4-year follow-up of the TAXUS NIRx stent.

Objective

To evaluate the 4-year clinical outcomes from the first human trial of a polymer-based paclitaxel-eluting stent (TAXUS NIRx™) vs a bare metal stent (NIR™)

Patient Population (Methods)

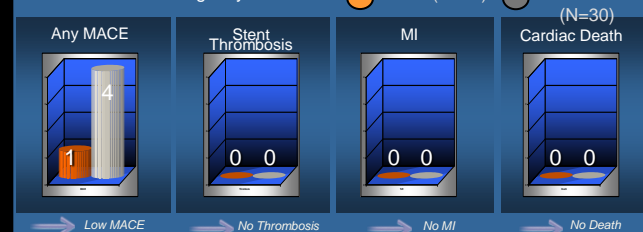
- ❖ 61 patients; 3 centers
- ❖ 1st patient enrolled Oct. 12, 2000 and last patient Mar. 1, 2001
- ❖ No statistically differences in baseline patient characteristics between groups.
- ❖ No statistically significant differences in lesion classification
- ❖ Procedural success was 100% for both study & control populations
- ❖ TAXUS slow-release (SR) stent vs. bare metal stent
- ❖ Primary endpoint: 30-day MACE (cardiac death, myocardial infarction and TVR)



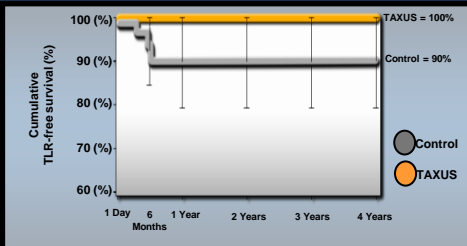
No patients lost to follow-up and no patients have withdrawn consent

Results

Patients w/events through 4 years



Freedom from TLR through 4 years



Adjudicated MACE

TAXUS: No patients w/new events from 9 months to 4 years
 Control: 1 patient with events (2) 9 months to 4 years



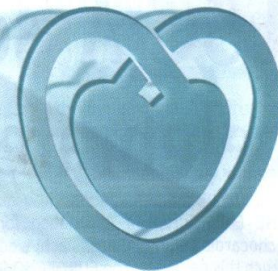
Summary

- ❖ No cases of stent thrombosis, death, or MI were reported in the TAXUS or Control groups through 4 years follow-up.
- ❖ No TLR for the TAXUS group through 4 years follow-up.
- ❖ The cumulative 4-year MACE rate was 3.57% (1/28) in the TAXUS NIRx group versus 13.33% (4/30) for the control group.
- ❖ The single MACE in TAXUS NIRx was a target vessel revascularization occurring outside the target lesion 200 days post-index procedure.
- ❖ No new MACE occurred in TAXUS between 9 months and 4 years post-index procedure.
- ❖ TAXUS NIRx is stable out to 4 years

Conclusions

- ❖ Absence of stent thrombosis through 4 years and no new MACE after 9 months post-stent implantation confirm the excellent, continued long-term safety of this polymer-based, paclitaxel-eluting stent.
- ❖ Prolonged exposure of the vessel wall to a paclitaxel-eluting stent does not result in safety concerns.
- ❖ The results of this first-in-man study indicate that the TAXUS-SR stent reduces the need for repeat revascularization and its safety profile remains durable over long periods of time.

ESC Congress News



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World Congress of Cardiology 2006

*The unique meeting of the European Society of Cardiology Congress 2006
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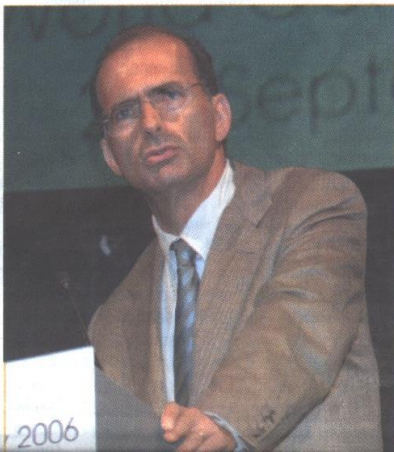


Do drug-eluting stents increase deaths?

TWO SEPARATE, independent meta-analyses, presented in Hot Line session I, suggest drug-eluting stents (DES) may increase death, Q-wave myocardial infarction (clinical surrogates of in-stent thrombosis) and cancer deaths, bringing the long-term safety of DES firmly into the spotlight. Discussant Salim Yusuf (McMaster University, Canada) hailed the data as one of the most important presentations to come out of this year's meeting.

"Six million people in the world have been implanted with DES, yet their long-term safety and efficacy is unknown," said Yusuf. "I've a feeling the data we're seeing today is only the tip of the iceberg. We need to encourage more public access to the data."

Presenter, Edoardo Camenzind (Geneva, Switzerland), said recent care reports had



obtain this data from the manufacturer," said Nordmann. He speculated that the increase in cancer might be due to a rapid impairment of the immune system.

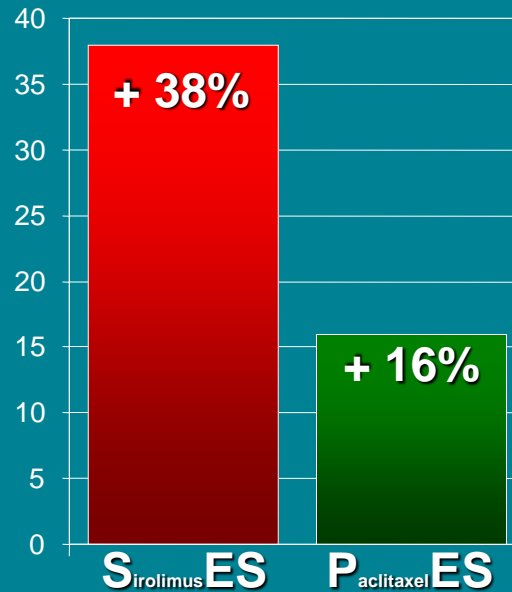
Yusuf widened the debate to include percutaneous coronary intervention (PCI). "The overuse of PCI is an insidious change in the culture of cardiology that needs to be reversed," he said. The use of PCI was established in MI, high-risk unstable angina and cardiogenic shock. However, its use in stable disease was a totally different question.

"There's no beneficial influence on mortality – PCI does nothing to prevent heart attack. All we are doing is providing short-term relief of chest pain. It's not re-stenosis that kills but the thousands of lesions you can't see. Stable disease is not treated with fully medical

Safety of DES

Meta-Analyses

Relative excess death/Q-Wave MI
of 1st generation DES vs BMS (%)



E. Camenzind, CH, 992



The DES empire strikes back

A Pooled Analysis of Data Comparing Sirolimus-Eluting Stents

Safety and Efficacy of Sirolimus-

Stent Thrombosis Redux — The FDA Perspective

Andrew Farb, M.D., and Ashley B. Boam, M.S.

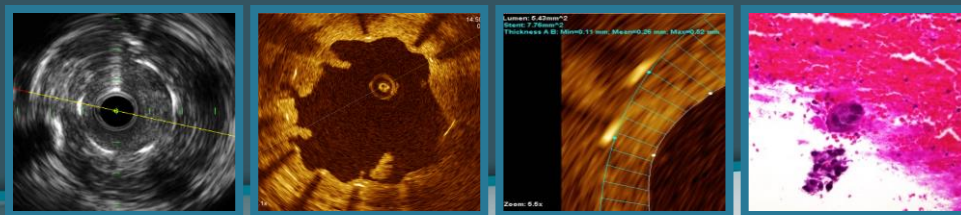
Perspective
MARCH 8, 2007

Unanswered Questions — Drug-Eluting Stents and the Risk of Late Thrombosis

William H. Maisel, M.D., M.P.H.

In-Vivo Mechanisms of Late Drug Eluting Stent Thrombosis. Optical Coherence Tomography, Intravascular Ultrasound and Thrombus Aspirated Findings

case	Positive Remodeling	Uncovered/Total Struts/section >30 %	Aggressive restenosis	Eosinophil Fraction
1	-	+	-	.05
2	-	+	-	.02
3	+	+	-	.02
4	+	+	-	.02
5	+	+	-	.21
6	+	+	-	.49
7	-	-	+	.18
8	-	-	+	.01
9	-	-	+	.04
10	-	-	-	.02



V.Sirbu, IT, 827

The Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery: The SYNTAX Study

Primary Endpoint Results at One Year in the Randomized Cohort

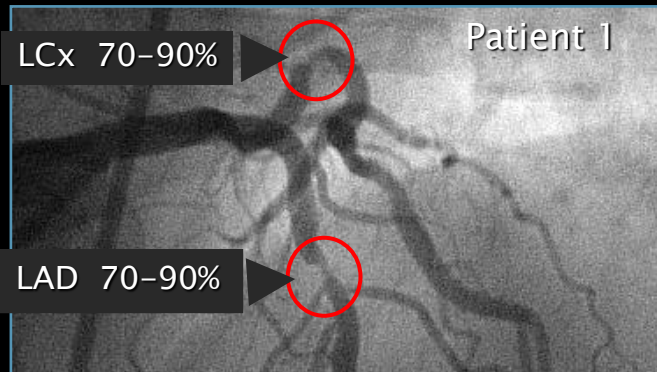
Patrick W. Serruys MD PhD
Friedrich W. Mohr MD PhD
On behalf of the SYNTAX investigators

Conflicts of Interest: None

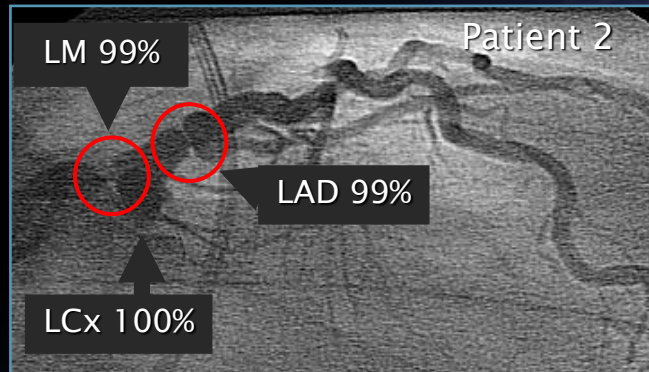


There is '3-vessel disease' and '3-vessel disease'

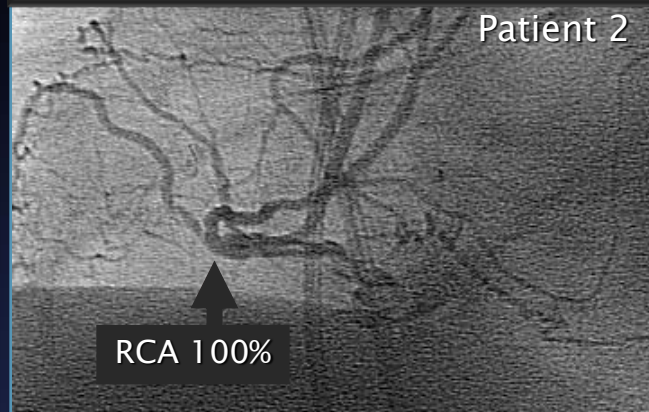
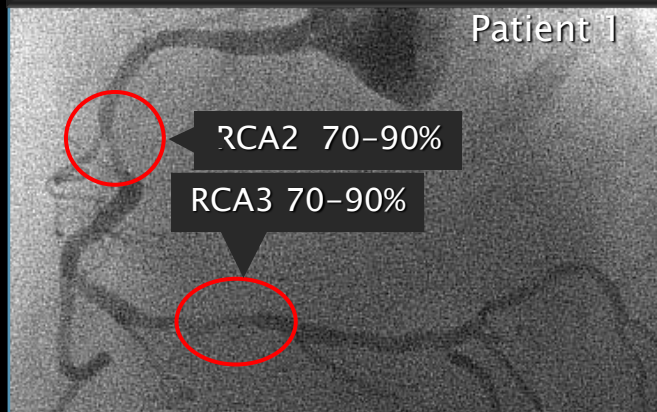
SYNTAX



SYNTAX SCORE 21



SYNTAX SCORE 52



**The XIENCE V / PROMUS Everolimus-
Eluting Stent: Comprehensive Update
of the Clinical Trial Program**

Featuring the First Presentation
of the SPIRIT III 3-Year Results

Gregg W. Stone, MD

Columbia University Medical Center
The Cardiovascular Research Foundation



TRANSCATHETER CARDIOVASCULAR THERAPEUTICS

ORIGINAL ARTICLE

Comparison of Zotarolimus-Eluting and Everolimus-Eluting Coronary Stents

Patrick W. Serruys, M.D., Ph.D., Sigmund Silber, M.D., Ph.D.,
Scot Garg, M.B., Ch.B., M.R.C.P., Robert Jan van Geuns, M.D., Ph.D.,
Gert Richardt, M.D., Pawel E. Buszman, M.D., Ph.D., Henning Kelbæk, M.D.,
Adrianus Johannes van Boven, M.D., Ph.D., Sjoerd H. Hofma, M.D., Ph.D.,
Axel Linke, M.D., Ph.D., Volker Klauss, M.D., Ph.D., William Wijns, M.D., Ph.D.,
Carlos Macaya, M.D., Ph.D., Philippe Garot, M.D., Carlo DiMario, M.D., Ph.D.,
Ganesh Manoharan, M.B., B.Ch., M.D., F.R.C.P., Ran Kornowski, M.D.,
Thomas Ischinger, M.D., Ph.D., Antonio Bartorelli, M.D., Jacintha Ronden, Ph.D.,
Marco Bressers, M.Sc., Pierre Gobbens, B.Sc., Manuela Negoita, M.D.,
Frank van Leeuwen, M.D., and Stephan Windecker, M.D.

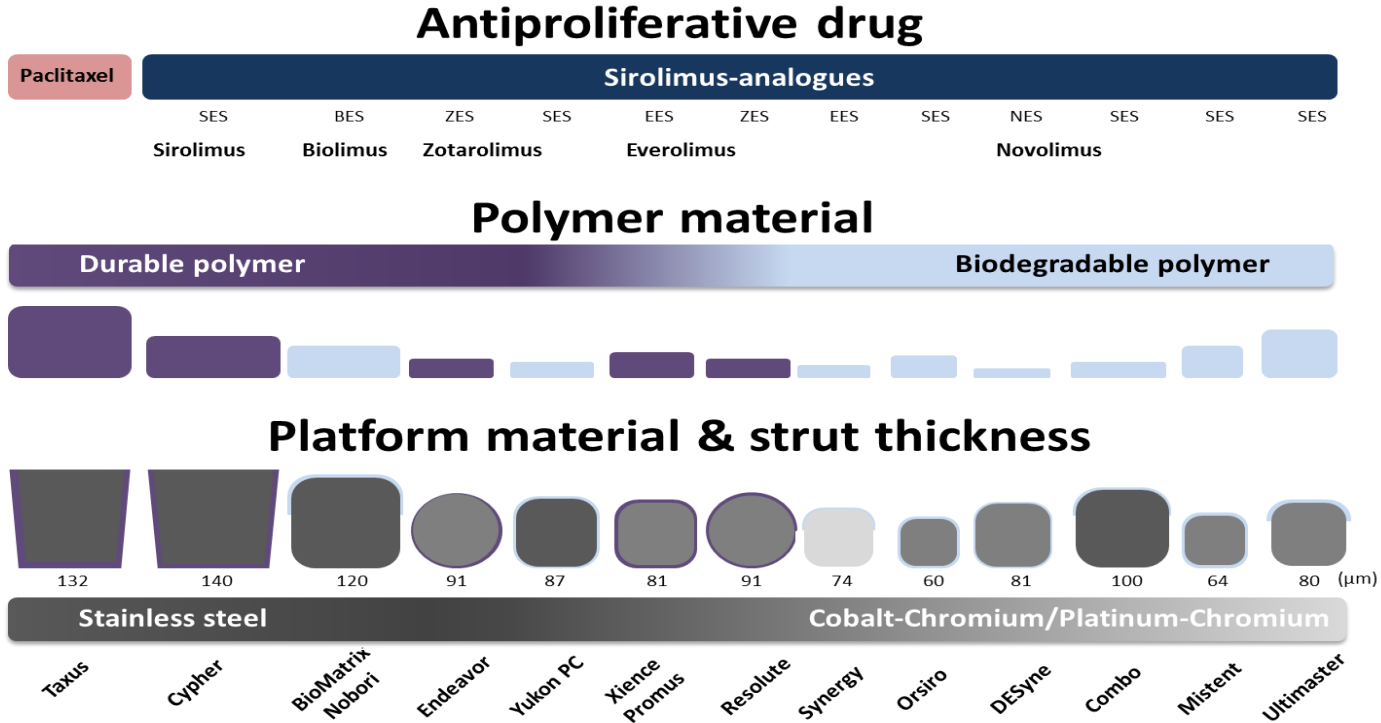
Biolimus-Eluting Stents With Biodegradable Polymer Versus Bare Metal Stents in Acute Myocardial Infarction: the COMFORTABLE AMI Trial

*Lorenz Räber, Henning Kelbæk, Miodrag Ostojic,
Andreas Baumbach, David Tüller, Clemens v. Birgelen,
Dik Heg, Marco Roffi, Aris Moschovitis, Ahmed A. Khattab,
Peter Wenaweser, Robert Bonvini, Giovanni Pedrazzini,
Ran Kornowski, Klaus Weber, Thomas F. Lüscher,
Masanori Taniwaki, Bernhard Meier,
Peter Jüni, Stephan Windecker*

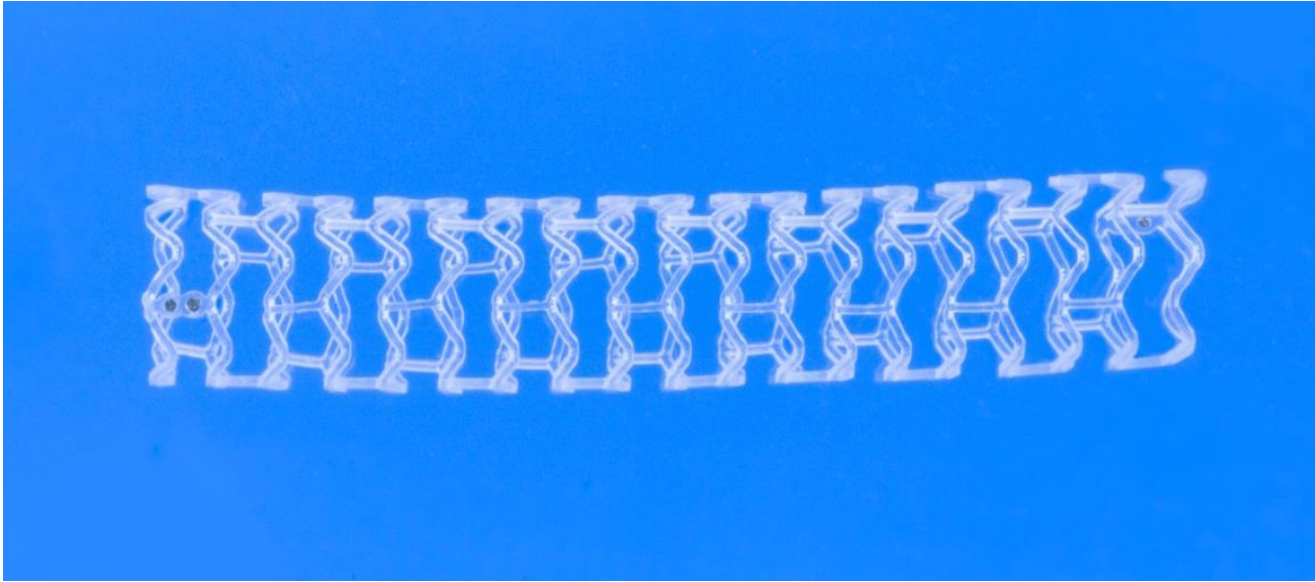
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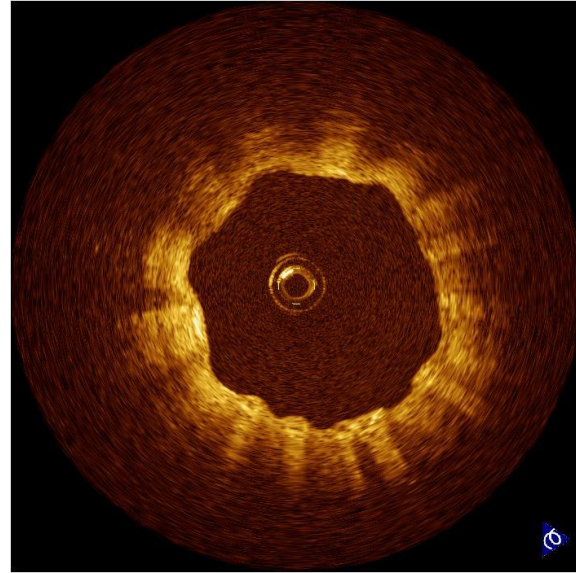
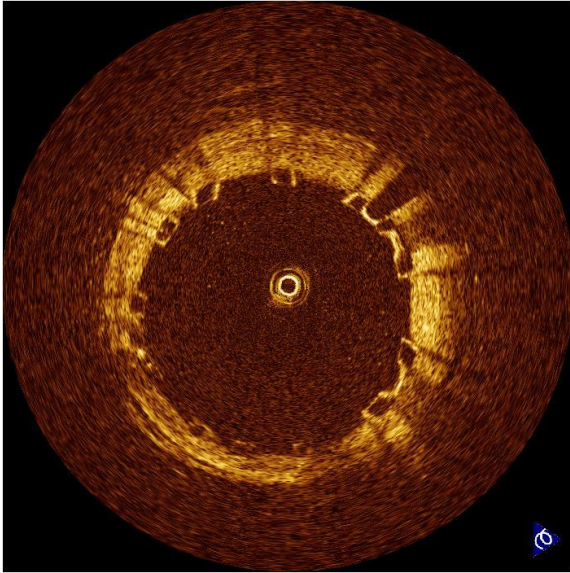
Progress with metallic drug-eluting stents



Biovascular scaffolds



Biovascular scaffolds



2006

**Six-month angiographic and IVUS results of the
first-in-man use of
the Bioabsorbable Everolimus Eluting Coronary
Stent System:
the ABSORB trial**

Patrick W. Serruys, MD, PhD and John A. Ormiston, MD

On behalf of the ABSORB Investigators

Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands

Auckland City Hospital, Auckland, New Zealand

PW Serruys declares no conflict of interest

THELANCET-D-15-06564R1

Embargo: October 12, 2015—00:01 (BST)

Articles

ZN/LP

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Safety and performance of the second-generation drug-eluting absorbable metal scaffold in patients with de-novo coronary artery lesions (BIOSOLVE-II): 6 month results of a prospective, multicentre, non-randomised, first-in-man trial



Michael Haude, Hüseyin Ince, Alexandre Abizaid, Ralph Toelg, Pedro Alves Lemos, Clemens von Birgelen, Ewald Høj Christiansen, William Wijns, Franz-Josef Neumann, Christoph Kaiser, Eric Eckhout, Soo Teik Lim, Javier Escaned, Hector M Garcia-Garcia, Ron Waksman

Summary

Background Absorbable scaffolds were designed to overcome the limitations of conventional, non-absorbable metal-based drug-eluting stents. So far, only polymeric absorbable scaffolds are commercially available. We aimed to assess the safety and performance of a novel second-generation drug-eluting absorbable metal scaffold (DREAMS 2G) in patients with de-novo coronary artery lesions.

Methods We did this prospective, multicentre, non-randomised, first-in-man trial at 13 percutaneous coronary intervention centres in Belgium, Brazil, Denmark, Germany, Singapore, Spain, Switzerland, and The Netherlands. Eligible patients had stable or unstable angina or documented silent ischaemia, and a maximum of two de-novo lesions with a reference vessel diameter between 2.2 mm and 3.7 mm. Clinical follow-up was scheduled at months 1, 6, 12, 24, and 36. Patients were scheduled for angiographic follow-up at 6 months, and a subgroup of patients was scheduled for intravascular ultrasound, optical coherence tomography, and vasomotion assessment. All patients were recommended to take dual antiplatelet treatment for at least 6 months. The primary endpoint was in-segment late lumen loss at 6 months. We did analysis by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT01960504.

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[http://dx.doi.org/10.1016/S0140-6736\(15\)00447-X](http://dx.doi.org/10.1016/S0140-6736(15)00447-X)

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[http://dx.doi.org/10.1016/S0140-6736\(15\)00447-X](http://dx.doi.org/10.1016/S0140-6736(15)00447-X)

Medical Clinic I, Städtische

Kliniken Neuss,

Lukaskrankenhaus GmbH,

Neuss, Germany

(Prof M Haude MD);

Department of Cardiology,

Vivantes Klinikum im

Friedrichshain and Am Urban,

Berlin, Germany

(Prof H Ince MD); Istituto de

Cardiologia Dante Pazzanese,

Mechanisms of Very Late Bioresorbable Scaffold Thrombosis



The INVEST Registry

Kyohei Yamaji, MD, PhD,^{a,b} Yasushi Ueki, MD,^a Geraud Souteyrand, MD, MSc,^c Joost Daemen, MD, PhD,^d Jens Wiebe, MD,^e Holger Nef, MD,^f Tom Adriaenssens, MD, PhD,^g Joshua P. Loh, MBBS,^h Benoit Lattuca, MD,ⁱ Joanna J. Wykzykowska, MD, PhD,^j Josep Gomez-Lara, MD, PhD,^k Leo Timmers, MD, PhD,^l Pascal Motreff, MD, PhD,^c Petra Hoppmann, MD,^m Mohamed Abdel-Wahab, MD,ⁿ Robert A. Byrne, MB, BCh, PhD,^e Felix Meincke, MD,^o Niklas Boeder, MD,^f Benjamin Honton, MD,^p Crochan J. O'Sullivan, MD, PhD,^q Alfonso Ielasi, MD,^r Nicolas Delarche, MD,^s Günter Christ, MD,^t Joe K.T. Lee, MD,^{u,v} Michael Lee, MD, PhD,^v Nicolas Amabile, MD, PhD,^w Alexios Karagiannis, PhD,^x Stephan Windecker, MD,^a Lorenz Räber, MD, PhD^a

ABSTRACT

BACKGROUND Very late scaffold thrombosis (VLST) occurs more frequently after bioresorbable scaffold (Absorb BVS 1.1, Abbott Vascular, Santa Clara, California) implantation than with metallic everolimus-eluting stents.

OBJECTIVES The purpose of this study was to elucidate mechanisms underlying VLST as assessed by optical coherence tomography (OCT).

METHODS The INVEST (Independent OCT Registry on Very Late Bioresorbable Scaffold Thrombosis) registry is an international consortium of investigators who used OCT to examine patients with VLST.

RESULTS Between June 2013 and May 2017, 36 patients with 38 lesions who had VLST underwent OCT at 19 centers. VLST occurred at a median of 20 months (interquartile range: 16 to 27 months) after implantation. At the time of VLST, 83% of patients received aspirin monotherapy and 17% received dual-antiplatelet therapy. The mechanisms underlying VLST were (in descending order) scaffold discontinuity (42.1%), malapposition (18.4%), neoatherosclerosis (18.4%), underexpansion or scaffold recoil (10.5%), uncovered struts (5.3%), and edge-related disease progression (2.6%). Discontinuity (odds ratio [OR]: 110; 95% confidence interval [CI]: 73.5 to 173; $p < 0.001$), malapposed struts (OR: 17.0; 95% CI: 14.8 to 19.7; $p < 0.001$), and uncovered struts (OR: 7.3; 95% CI: 6.2 to 8.8; $p < 0.001$) were more frequent in the thrombosed than the nonthrombosed scaffold regions. In 2 of 16 patients with scaffold discontinuity, intercurrent OCT before VLST provided evidence of circularly apposed scaffold struts with minimal tissue coverage.

CONCLUSIONS The leading mechanism underlying VLST was scaffold discontinuity, which suggests an unfavorable resorption-related process, followed by malapposition and neoatherosclerosis. It remains to be determined whether modifications in scaffold design and optimized implantation can mitigate the risk of VLST. (Independent OCT Registry on Very Late Bioresorbable Scaffold Thrombosis [INVEST]; [NCT03180931](https://clinicaltrials.gov/ct2/show/study/NCT03180931)) (J Am Coll Cardiol 2017;70:2330-44) © 2017 by the American College of Cardiology Foundation.

Outline

- From balloon angioplasty (PCTA) to stent to scaffold, a history of trends, technology and techniques
- **From luminology to physiology (& advanced invasive imaging)**
- New trends, technologies & techniques for the years ahead

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FIGURE 1. Doppler catheters (top 3) and Doppler angio-plasty guidewire (bottom).

velocity and volumetric flow, where

$$\text{flow} = \text{vessel area} \times \text{velocity integral} \times \text{heart rate}$$

The differences or changes in Doppler coronary flow velocities, thus, can be used to represent changes in absolute coronary flow. Assuming a constant vessel diameter, flow rate can be calculated as a product of the vessel cross-sectional area (CSA), the flow velocity integral (FVi), and the heart rate:

$$\text{flow} = \text{CSA} \times \text{FVi} \times \text{heart rate}$$

If the interrogating angle is $<20^\circ$, the velocity measurements will be within 5% of absolute values. The velocity integral can be easily measured in

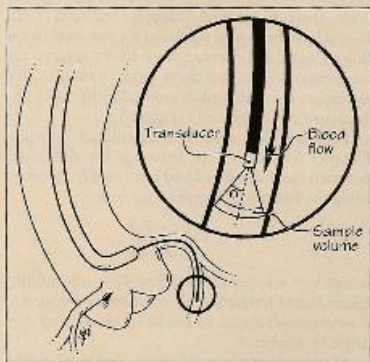


FIGURE 2. Illustration of Doppler Flowire positioned in the

a 3-mm vessel by using a broad sample volume in the presence of a parabolic flow profile.

DOPPLER CATHETERS AND THE DOPPLER FLOWIRE

Until recently, coronary flow velocities have been measured by Doppler catheters, the smallest being 3 F in diameter, thus limiting flow measurements to the proximal and middle coronary artery. An additional limitation of most current Doppler catheters is that velocity signals are processed by zero-crossing analysis with potential for overestimation of true peak velocities in the presence of turbulent flow or motion artifact.⁵

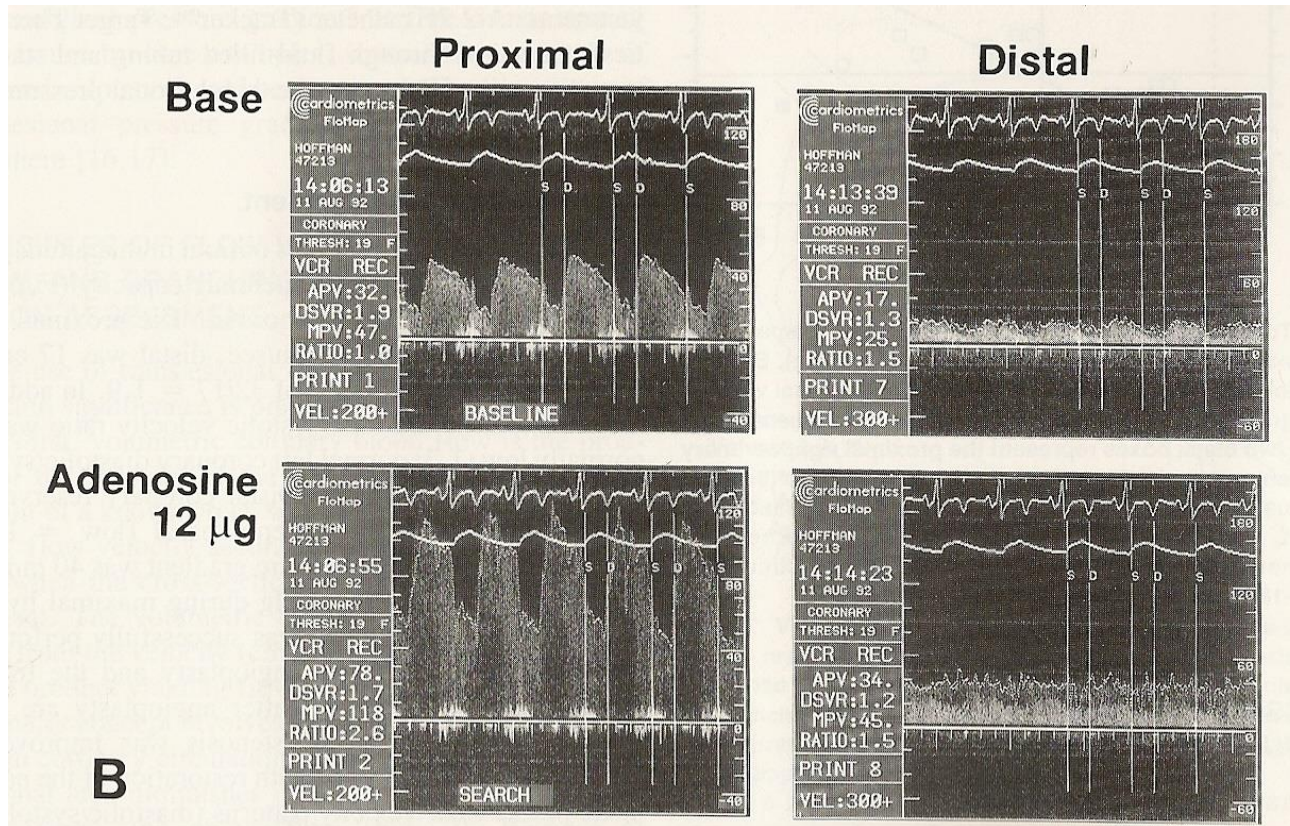
The Doppler Flowire (Cardimetrics; Mountain View, CA) is a 1/5-cm long, 0.018-in diameter steerable guidewire that has a 12 MHz transducer at its distal tip (Figure 2). The profile of the Flowire allows the device to be advanced beyond a coronary stenosis to the distal vessel, thus allowing velocity sampling.⁶ In distinction to existing catheters, velocity signals are processed on-line by fast Fourier transform with spectral display. Several velocity parameters can be calculated by analysis of the spectral waveform and have been found to correlate with absolute coronary flow measurements in both in vitro and in vivo validation studies.^{8,9} The Doppler spectrum is digitized to obtain the following: the peak diastolic velocity, peak systolic velocity, mean velocity (which is the time average of the spectral peak velocity waveform), integral of the diastolic velocity, integral of the systolic velocity, and the first 1/3 flow fraction and the first 1/2 flow fraction (Figure 3). The following ratios are also computed: the diastolic to peak systolic velocity, the diastolic to systolic velocity integral, and the proximal mean velocity to the distal mean velocity.

CORONARY FLOW VELOCITY PARAMETERS IN NORMAL, PROXIMAL, AND DISTAL CORONARY ARTERIES

It has been noted that coronary flow may be similar in normal as well as abnormal arteries in the basal state. Accordingly, several coronary vasodilating agents have been introduced to "stress" the coronary system by increasing flow and exaggerating differences in flow (and velocity) beyond stenotic lesions. The assessment of such lesions involves measurement of velocity parameters at baseline and again following maximal hyperemia provoked with intravenous or intracoronary administration of intracoronary vasodilating. Coronary vasodi-



Flow Velocity across significant Stenosis – Prox vs. Distal



TRAINING COURSE IN INTRACORONARY DIAGNOSTIC TECHNIQUES

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THE CATHARINA HOSPITAL DEPARTMENT OF CARDIOLOGY

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IN COOPERATION WITH

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AND

THE WORKING GROUP ON CORONARY CIRCULATION
OF THE EUROPEAN SOCIETY OF CARDIOLOGY

COURSE DIRECTORS:

NICO H.J. PULS, MD, PHD, BERNARD DE BRUYNE, MD, H. ROLF MICHELS, MD



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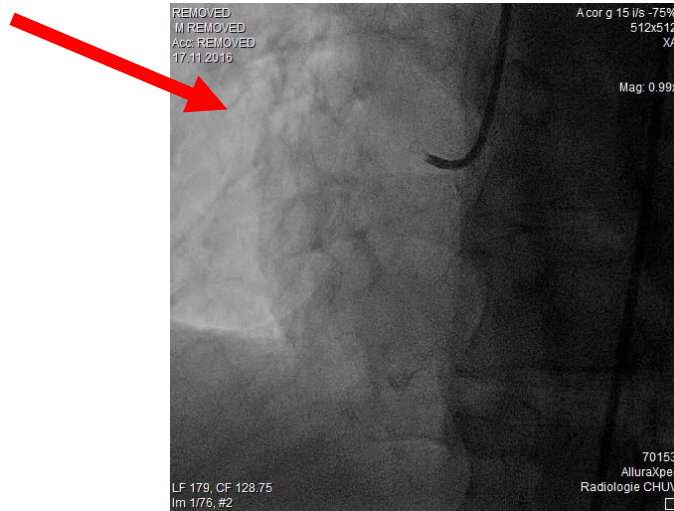
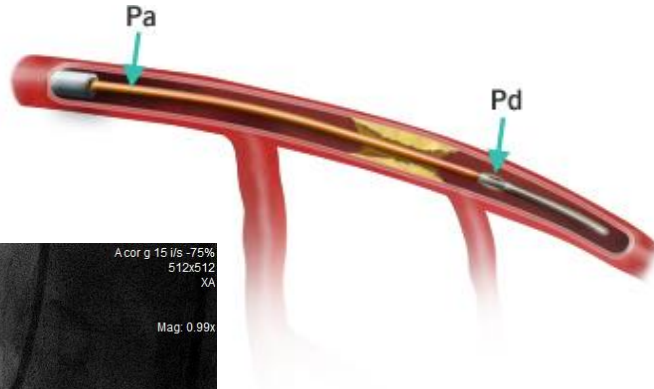


To achieve optimum training and interaction between operators and audience, the number of participants is limited to 65 trainees only. Registration will be made upon a "first come first serve basis".

The FFR principle

$$\text{FFR} = \frac{\text{Distal Coronary Pressure (Pd)}}{\text{Proximal Coronary Pressure (Pa)}}$$

(During Maximum Hyperemia)



Fractional Flow Reserve
versus

Angiography for
Multivessel
Evaluation

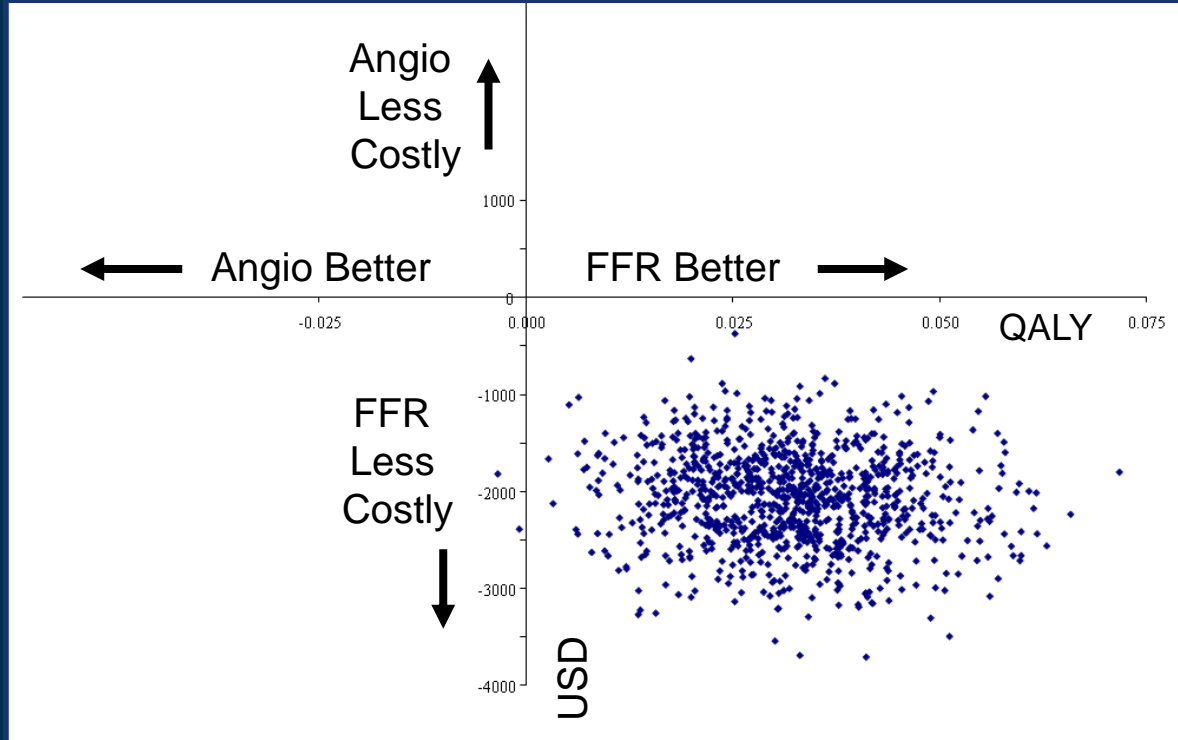


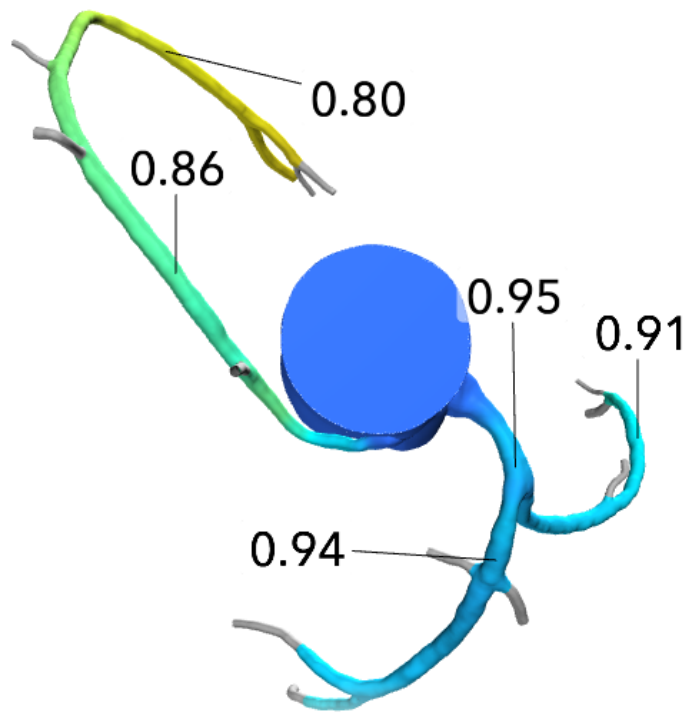
FRACTIONAL FLOW RESERVE
versus **ANGIOGRAPHY**
FOR GUIDING PCI IN PATIENTS WITH
MULTIVESSEL CORONARY ARTERY DISEASE



1 Year Economic Evaluation

Bootstrap Simulation





 Info

Patient ID A10002000812

CT Study Date 12/28/2009

Referring Physician *Not provided*

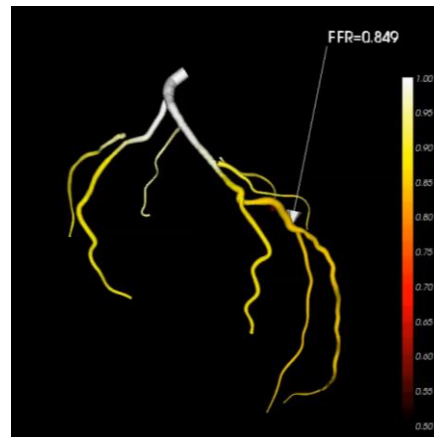
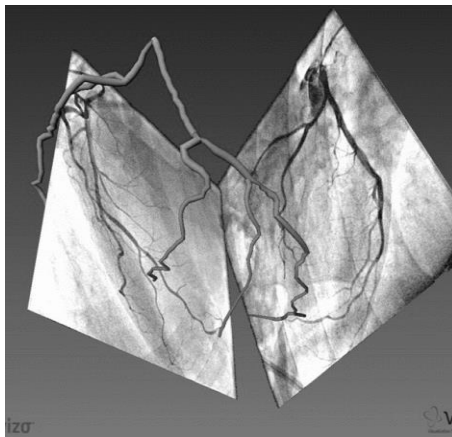
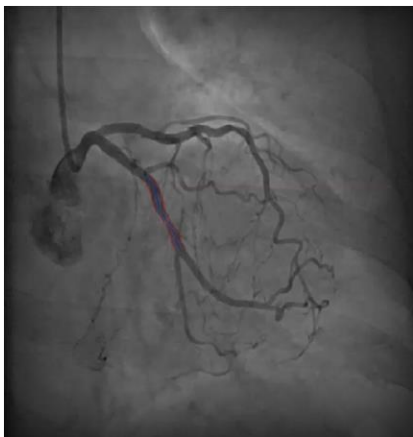
Institution Clinical - Bichat Hospital

HeartFlow ID BHH-170724-YYHW

CT Series ▶ 1

 Download Summary

 Warnings

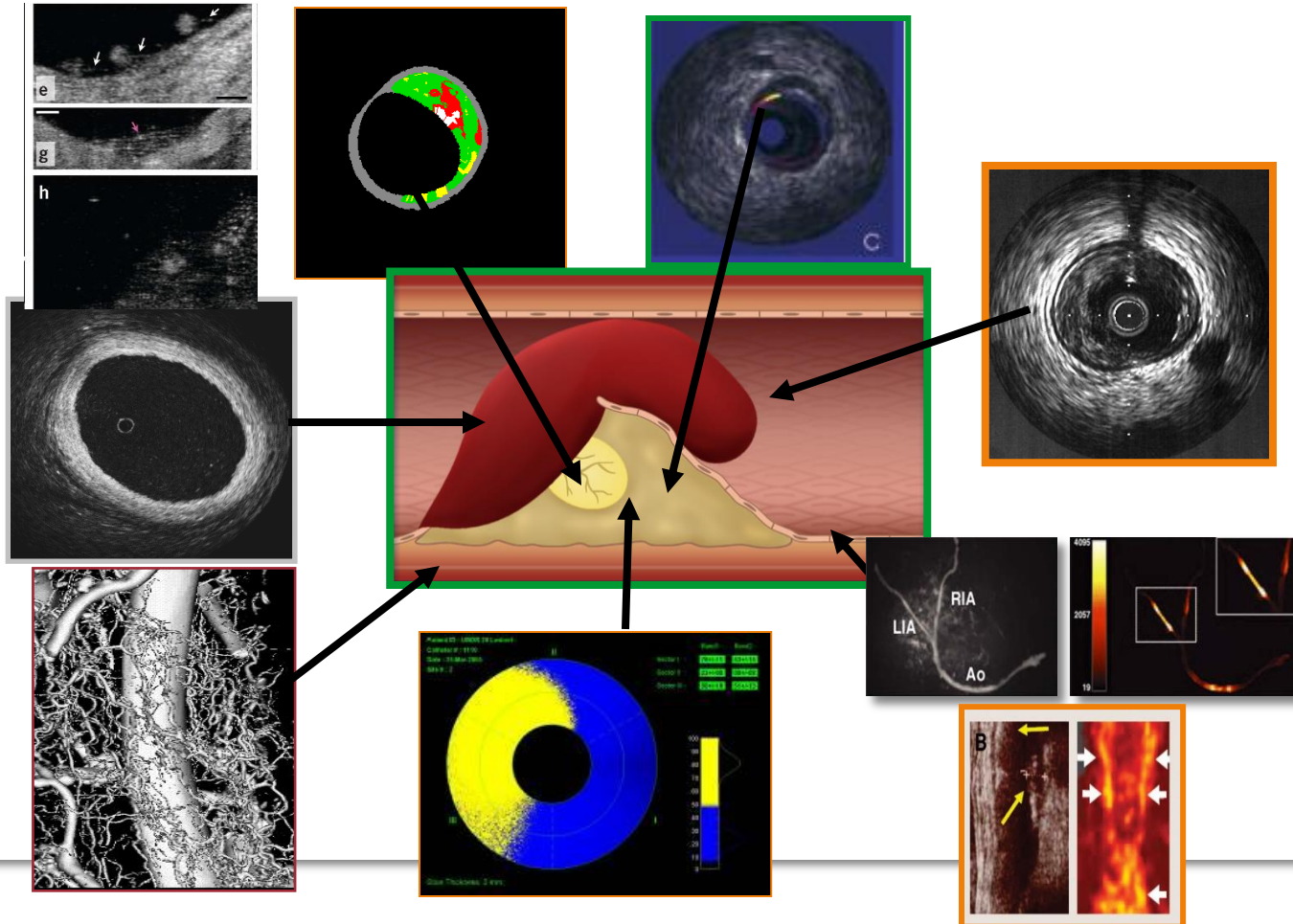


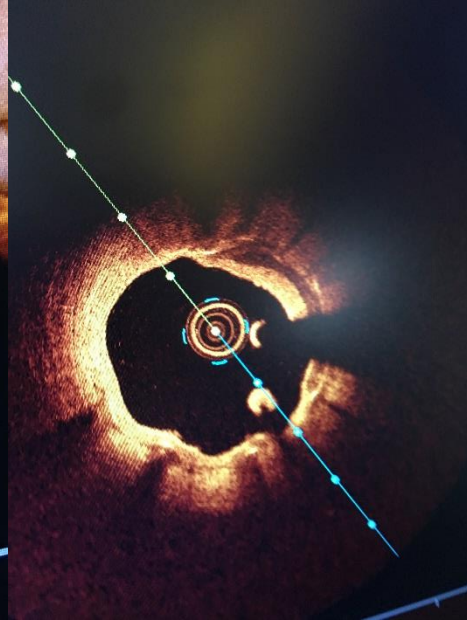
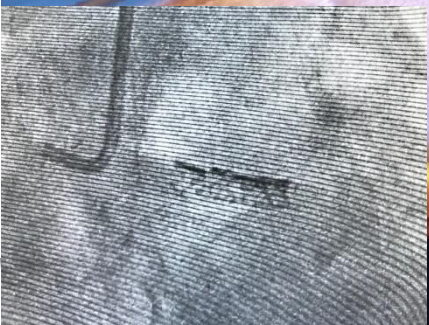
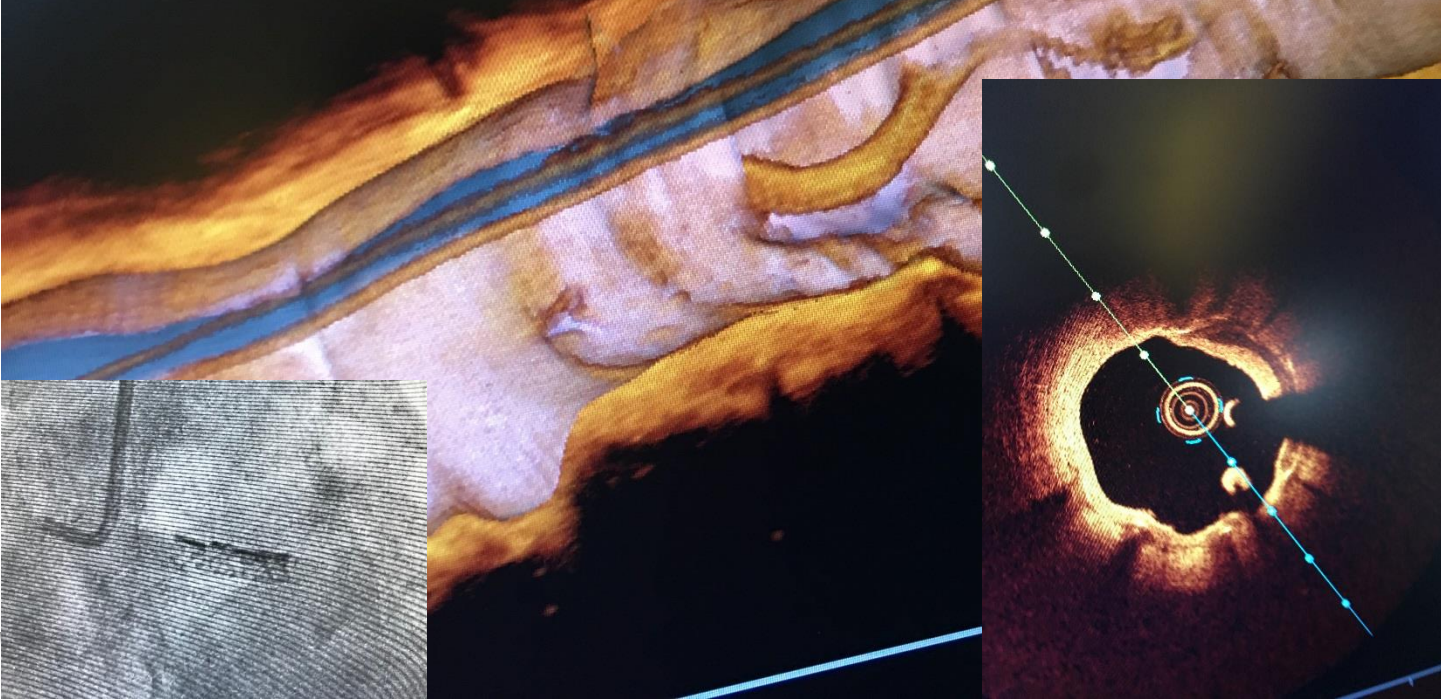
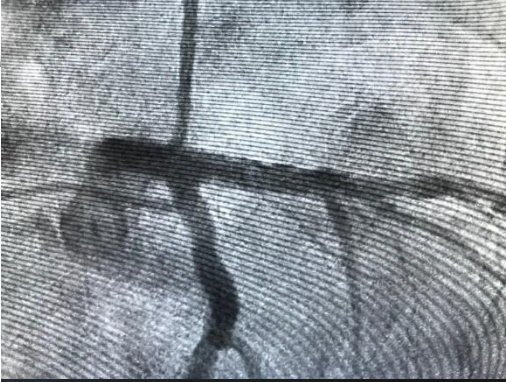
1 Routine angiograms

2 3D full tree & flow analysis

3 FFR-ratio color coded map

Invasive imaging





Clinical case (II)

- October 2015, 54 year old man
- Blanco past medical history
- Ongoing intense chest pain since 1 hour, ST depression in several leads
- Hemodynamically stable

REMOVED
M REMOVED
Acc: REMOVED
25.09.2015

A cor g 25 i/s -50% REMOVED
512x512 M REMOVED
XAcc: REMOVED
25.09.2015

A cor g 25 i/s -50%
512x512
XA

Mag: 1.00x

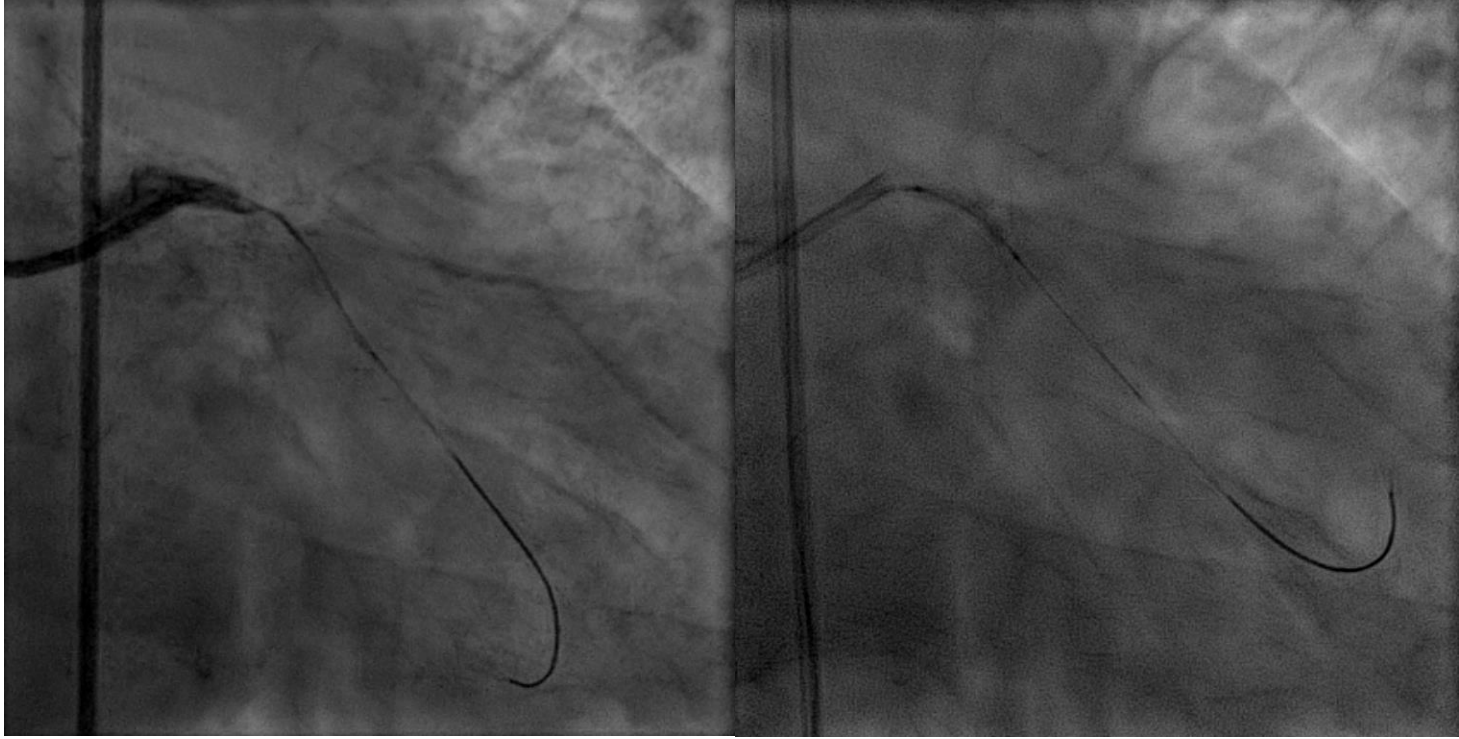
Mag: 1.00x

LF 169.50, CF 128.75
Im 1/151, #3

70151
AlluraXper
Radiologie CHUV

Im 1/59, #4

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AlluraXper
Radiologie CHUV



REMOVED
M REMOVED
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25.09.2015

A cor g 25 i/s -50% REMOVED
512x512 M REMOVED
XA Acc: REMOVED
25.09.2015

A cor g 15 i/s -50%
512x512
XA

Mag: 1.00x

Mag: 1.00x

LF 169.50, CF 128.75
Im 1/106, #7

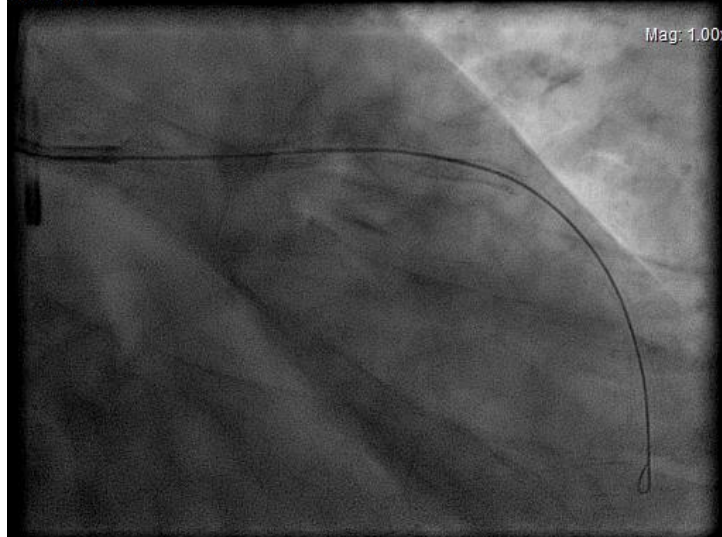
70151
AlluraXper
Radiologie CHUV
LF 150.50, CF 129
Im 1/44, #9

70151
AlluraXper
Radiologie CHUV

REMOVED
M REMOVED
Acc: REMOVED
25.09.2015

A cor g 25 i/s -50%
512x512
XA

Mag: 1.00x

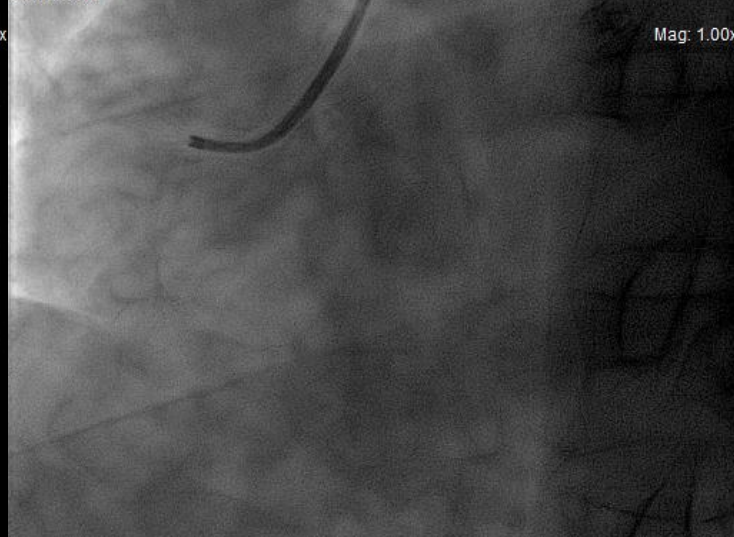


LF 169.50, CF 128.75
Im 1/136, #46

REMOVED
M REMOVED
Acc: REMOVED
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A cor g 25 i/s -50%
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XA

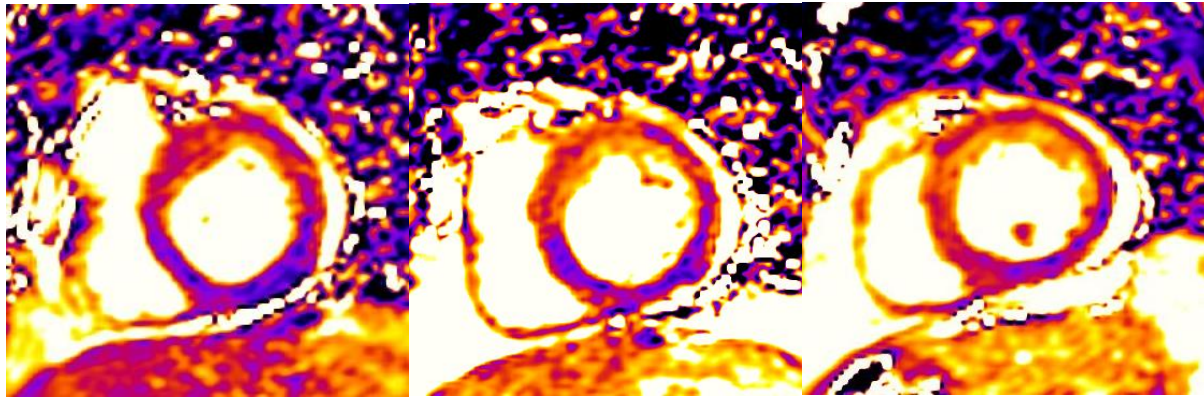
Mag: 1.00x



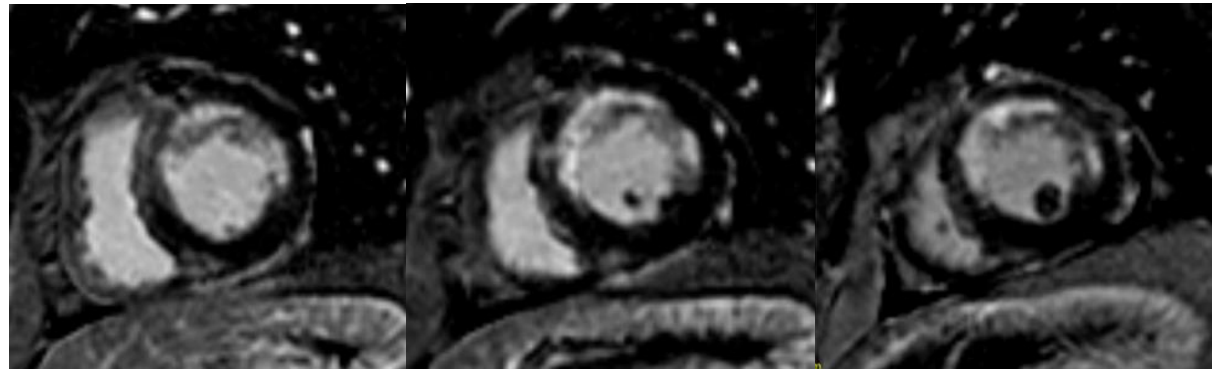
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Radiologie CHUV LF 169.50, CF 128.75
 Im 1/144, #49

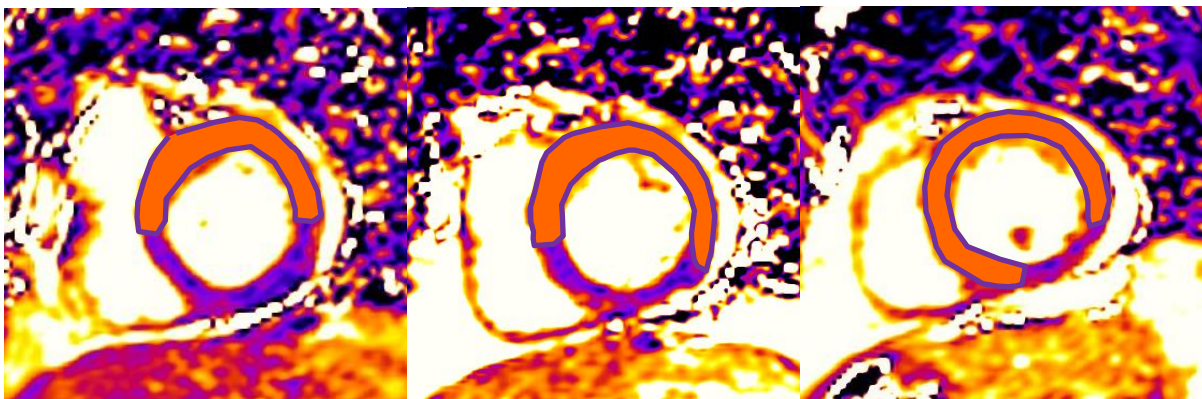
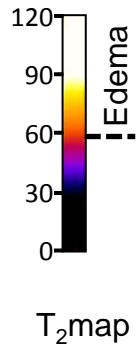
70151
AlluraXper
Radiologie CHUV

120
90
60
30
0
Edema
 T_2 map



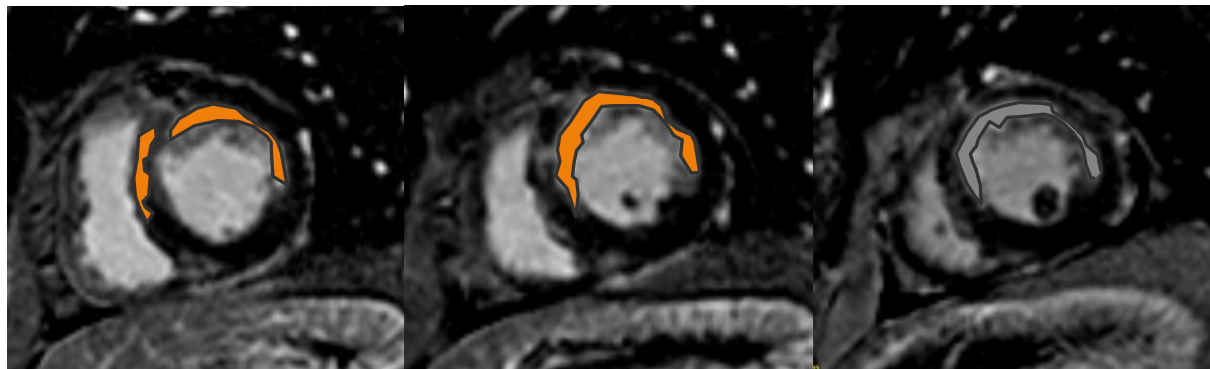
LGE

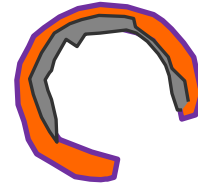
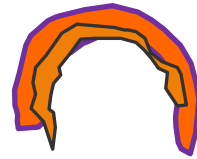
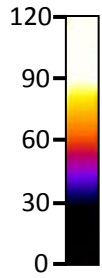




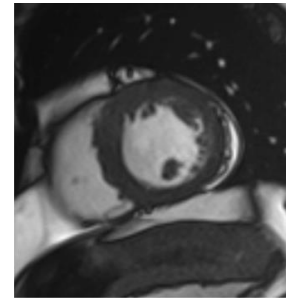
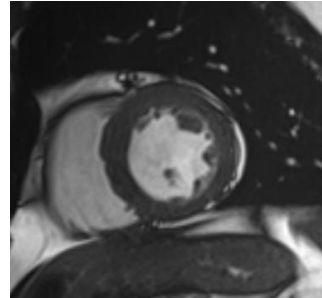
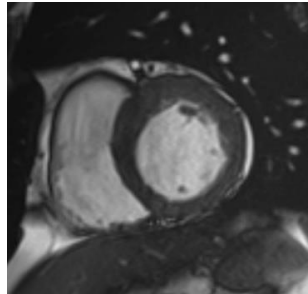
Necrosis

LGE

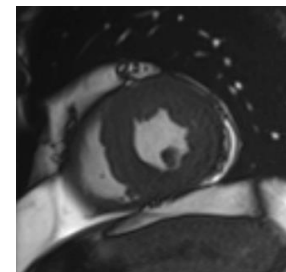
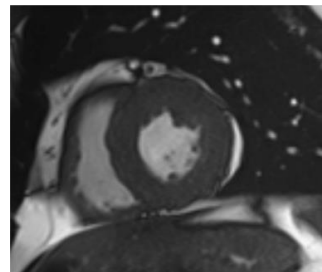
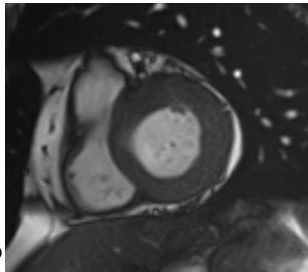




End-Diastole



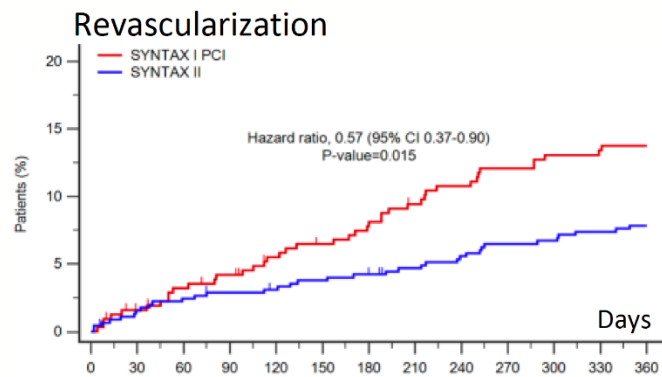
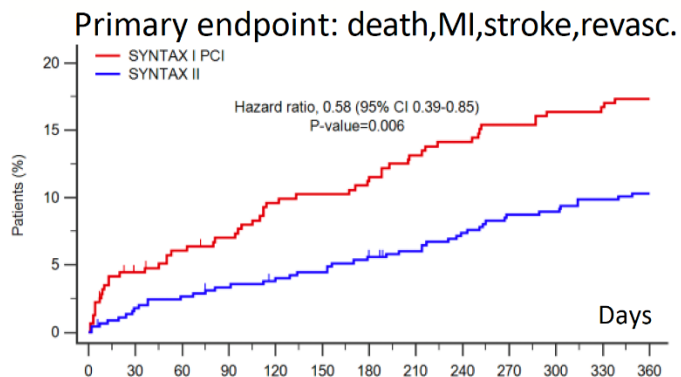
End-Systole



Cine-SSFP

PCI – current status in 2019 ?

Patients with 3-Vessel Coronary Artery Disease – SYNTAX II trial –



DES technology – heart team approach – pharmacotherapy – physiological assessment
Adjunctive invasive imaging

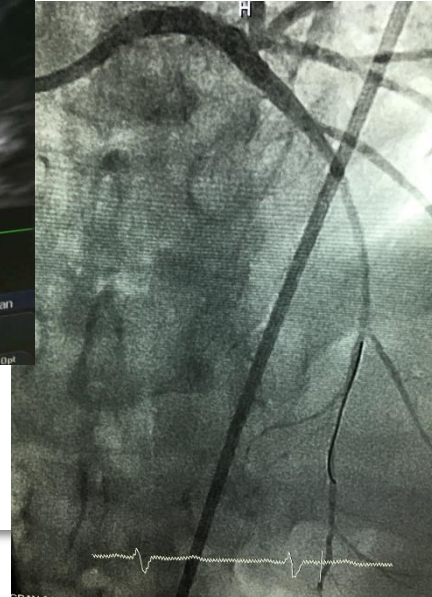
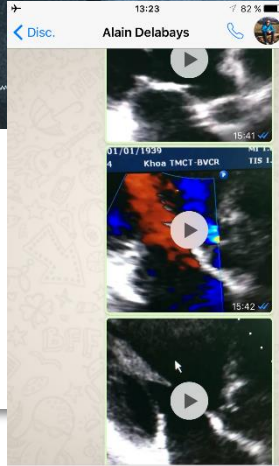
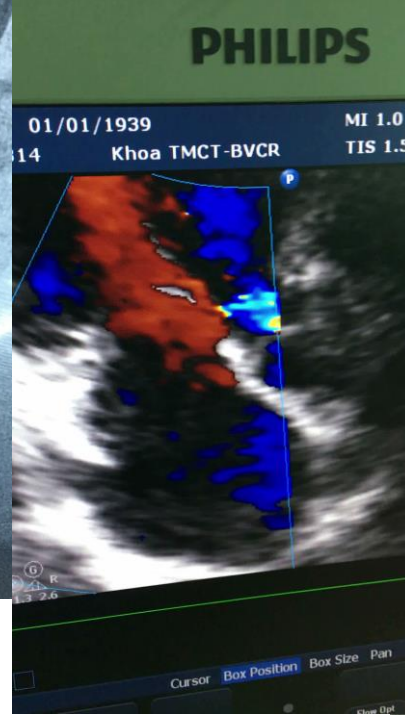
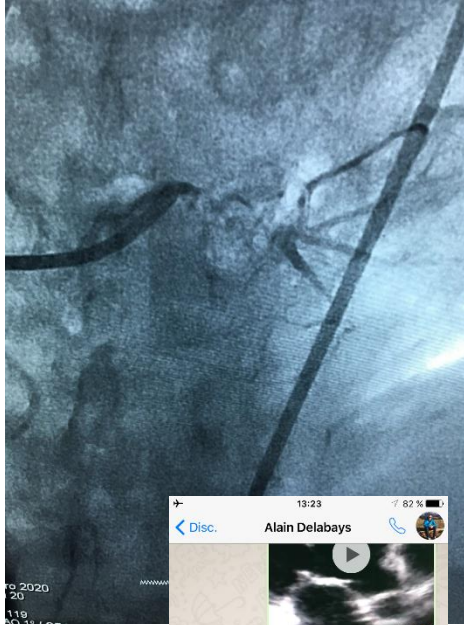
Outline

- From balloon angioplasty (PCTA) to stent to scaffold, a history of trends, technology and techniques
- From luminology to physiology (& advanced invasive imaging)
- **New trends, technologies & techniques for the years ahead**

Current daily interventional practice

- Safe contrast medium
- Digitized immediate image processing – fusion imaging
- Very low X-ray doses
- 3th or 4th generation of drug-eluting stents
- Impressive balloon & wire technology
- Booming of radial access, vascular closure devices for femoral access
- Adequate cardiovascular drugs
- Physiological lesion assessment & booming of invasive coronary imaging
- Mature technology for lesion subsets (bifurcation, left main disease, chronic total occlusions)
- The heart-team approach
- Interventional STEMI management
- Social media – robotics – the world : a village...

Ho Chi Minh City – Cho Ray Hospital – december 2015



De : [Twitter](#) >

À : [Eeckhout Eric](#) >

Masquer



Cosyns Bernard a tweeté : Post Mi VSD rupture successfully treated p...

aujourd'hui à 17:58



Vos Temps forts



Cosyns Bernard

@Cosyns

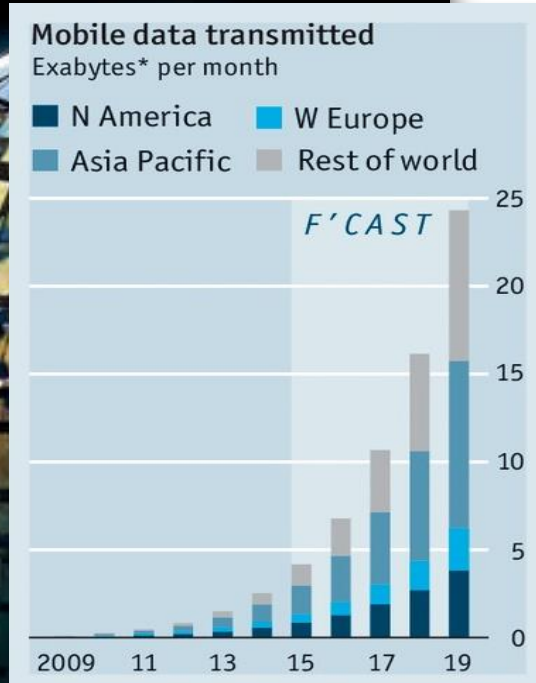
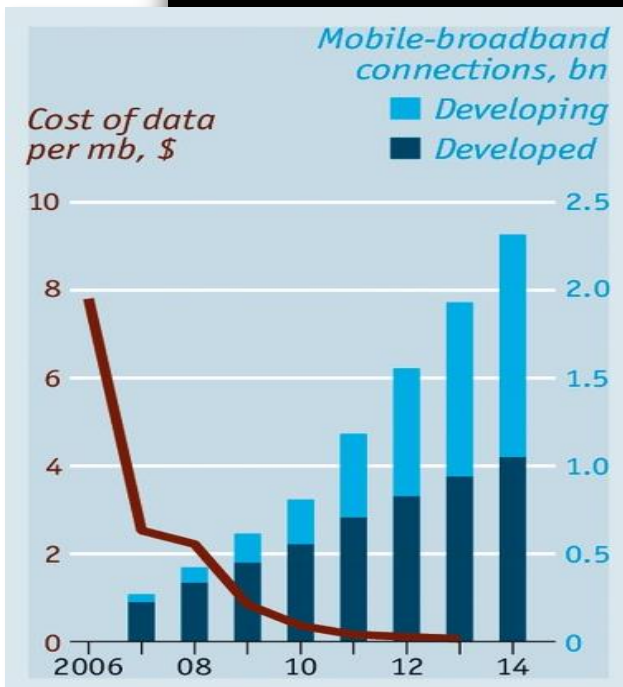
Post Mi VSD rupture successfully treated percutaneously at UZ Brussel today. @JGrapsa @ColletCarlos @ThorEdvardsen @jumagne @Steph_Achenbach @denisamuraru pic.twitter.com/FVgXAIDP8H

4

22

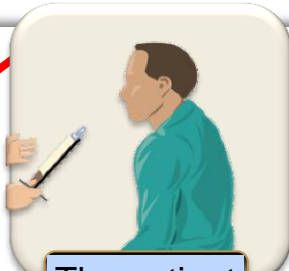
56

Planet of the phones



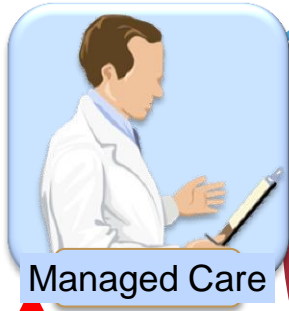


Traditional
face to face

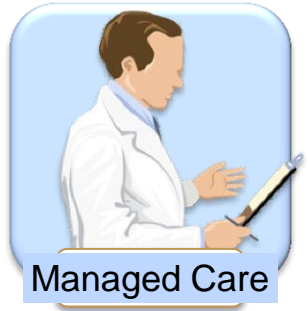


The patient

The UBERization of
medicine



Managed Care



Managed Care

External

Internal

Digital Impact on Customer Experience

Review s

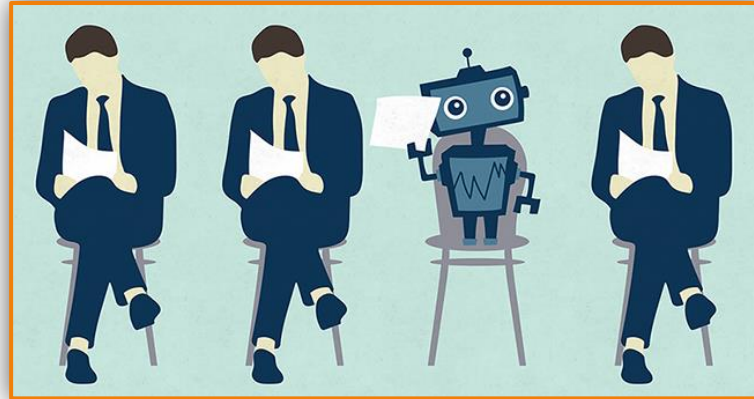
70%

Comfortable communicating with doctors via texting,
email, video instead of seeing them in person



CorPath 200 System
Control Console
Interventional Cockpit
Cockpit Monitors (Live/Reference Angio, Hemo)

Robots Threaten These Jobs



Soon you could be competing with a robot for a job

Economists are sharply divided over the exact timing of the threat from robots and other forms of futuristic technology. Some see an imminent threat, others believe it won't happen until later this century – If at all

Unmet needs & uncertainties

- Living in an interventional bubble
- Biovascular scaffolds
- The future of cardiovascular surgery in certain areas & the evolution of the heart team
- The interventional stardom & conflicts of interest
- Cardiology congresses

There is no limit...

- Knowledge, technology will further improve
- Automatisations will progress
- Preventive high-tech treatment modalities may appear
- The mindset & profile of cardiovascular caretakers is evolving and will change
- Suboptimal clinical practice will persist
- Bringing optimal cardiovascular care to the planet will remain a major issue



Protesters demanding justice for Dr Payal Tadvi outside BYL Nair Charitable Hospital in Mumbai on Tuesday. Dr Tadvi has been constantly harassed by three upper-caste senior students. PHOTO: NOLINA MINZ, ADIVASI RESURGENCE