

**SCIENZIATI DI IMPATTO – FARE
RICERCA ALTAMENTE CITATA IN
ITALIA**

Antonio Colombo

*Centro Cuore Columbus and
S. Raffaele Scientific Institute, Milan, Italy*

Be inspired by:

Problem solving

The long term outcome of what you do

The legacy you leave to young colleagues and students

The people helping you:
without them you may have gone nowhere

AND

Never look for your Impact Factor: Let Others do that

PROBLEM SOLVING

Clinical research should be directed to solve problems

There is no need to publish an additional paper
unless we increase our understanding of the
reality and contribute to solve a problem

February 10-12, 2011

Rome, Italy

At that time an unresolved problem was a coronary dissection. The treatment was a prolonged balloon inflation (perfusion balloons) with unpredictable success

OR

Emergency by-pass surgery

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Ulrich Sigwart



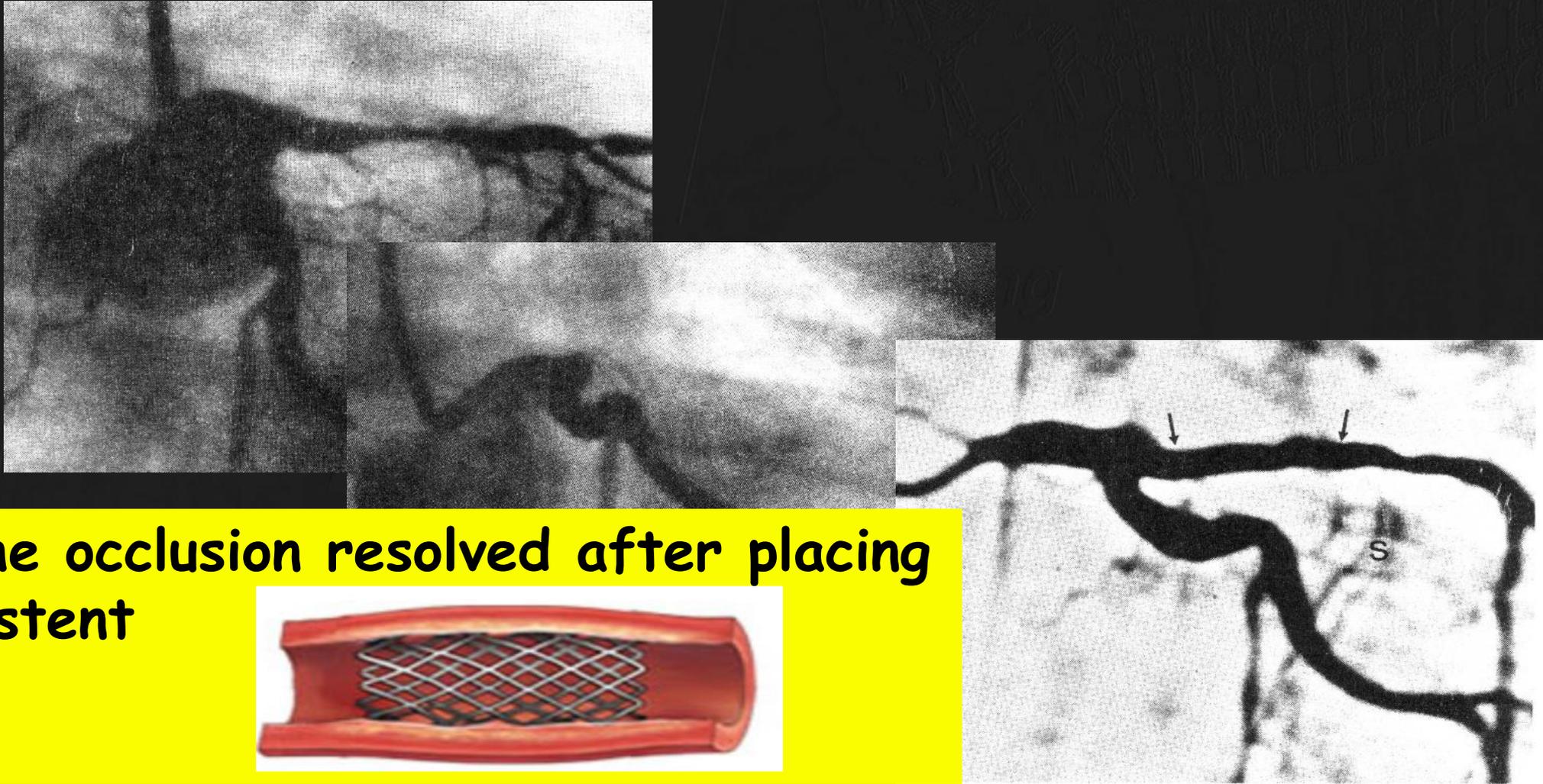
Gary Roubin



Rome, Italy

International meeting

« Proof of Concept » June 1986: stents came about to treat PTCA complications not to prevent restenosis



Problems associated with Stents

Stent Thrombosis leading to myocardial infarction and sometimes to death

Joint Interventional meeting

Hemorrhagic complications as a consequence of Intense Anticoagulation to prevent Stent Thrombosis

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Rome, Italy

International meeting

STENT THROMBOSIS

NEJM 1991

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.

Therapy: aspirin+dypiridamole +subacute heparin for 6 weeks

117 patients:

21 stent occlusions within 14 days, 8 deaths in the first year

Hemorrhagic Complication Rate

Palmaz-Schatz Stent

Values are %

Author (year)	Pts	Groin	Gastro-int.	Total
Sigwart (1988)	11	9.1	0	9.1
Schatz (1991)	226	3.1	0.1	3.2
Haude (1991)	50	6.0	3.0	9.0
de Scheerder(1992)	69	26.0	2.9	28.9
Roubin (1992)	115	6.1	3.5	9.6
Herrman (1992)	56	8.9	5.4	14.3
Benestent I(1994)	259	6.0	4.0	10.0
Total	783	9.3	2.7	12.0

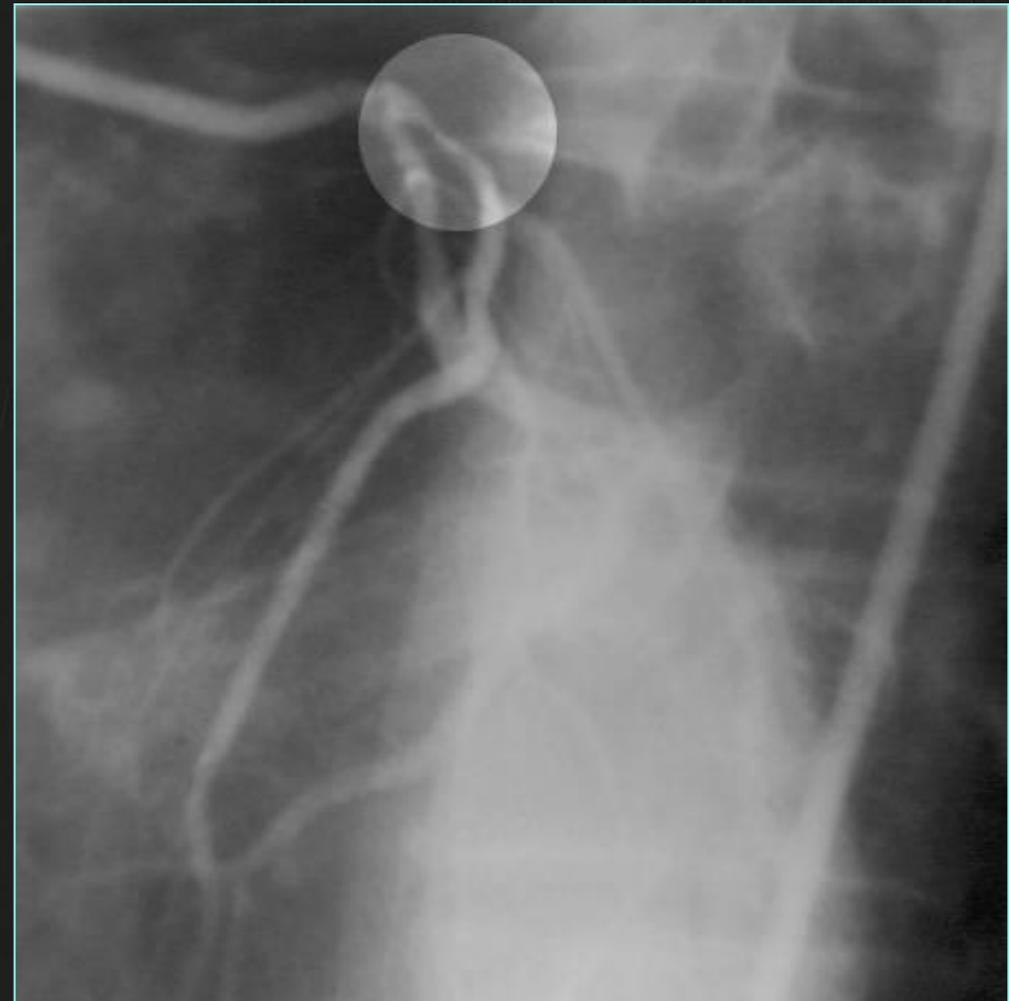
I experienced the problem of Stent
Thrombosis quite early:
My second Stent implantation

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My first case of stent thrombosis

January 1990, unstable angina with **LAD restenosis** following PTCA

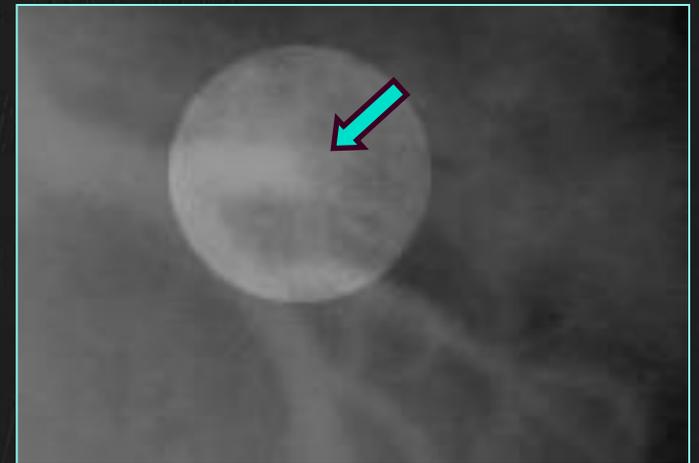


Baseline

My first case of stent thrombosis

Two days later while patient on heparin infusion just started oral anticoagulants, dypiridamole and aspirin

Sudden chest pain and ST elevation



Stent thrombosis
and Ventricular
Fibrillation

I wrote a letter to dr. Richard Schatz pioneer of stenting

Richard A. Schatz, MD, FACC
Director,
Research and Education

January 25, 1990

Richard Schatz Answer

January 25, 1990

Dr. Antonio Colombo
Casa Di Cura "Columbus"
20145 Milano
via Michelangelo Buonarroti,
ITALY

RE: [REDACTED]

Dear Antonio:

Thank you very much for sending the film on the above patient for my review. I am vitally interested in every complication that occurs so that I can continue to learn from every case. In the United States, as you know, we have had only one case of thrombosis on

Thank you very for sending the film.... I am vitally interested in every complication so I can continue to learn from every case

If I have to point out few things that may have contributed: the omission of Persantine prior to the procedure, inflow obstruction and underdilatation of the stent were factors.....**this could be a stroke of bad luck**

congratulate you on the good work you are doing there as reported

Don't be discouraged by this one set back. **I believe these thrombosis are rare occurrences.....**

Richard A. Schatz, M.D.

Richard A. Schatz, M.D.

RAS/meg
Enclosure

What happened was not “a stroke of bad luck”

Be strict to accept “outliers” as exceptions to the rule.

Do not accept a rule which cannot fully explain outliers.

The study of “outliers” is an important source of knowledge leading to better understanding the real concept

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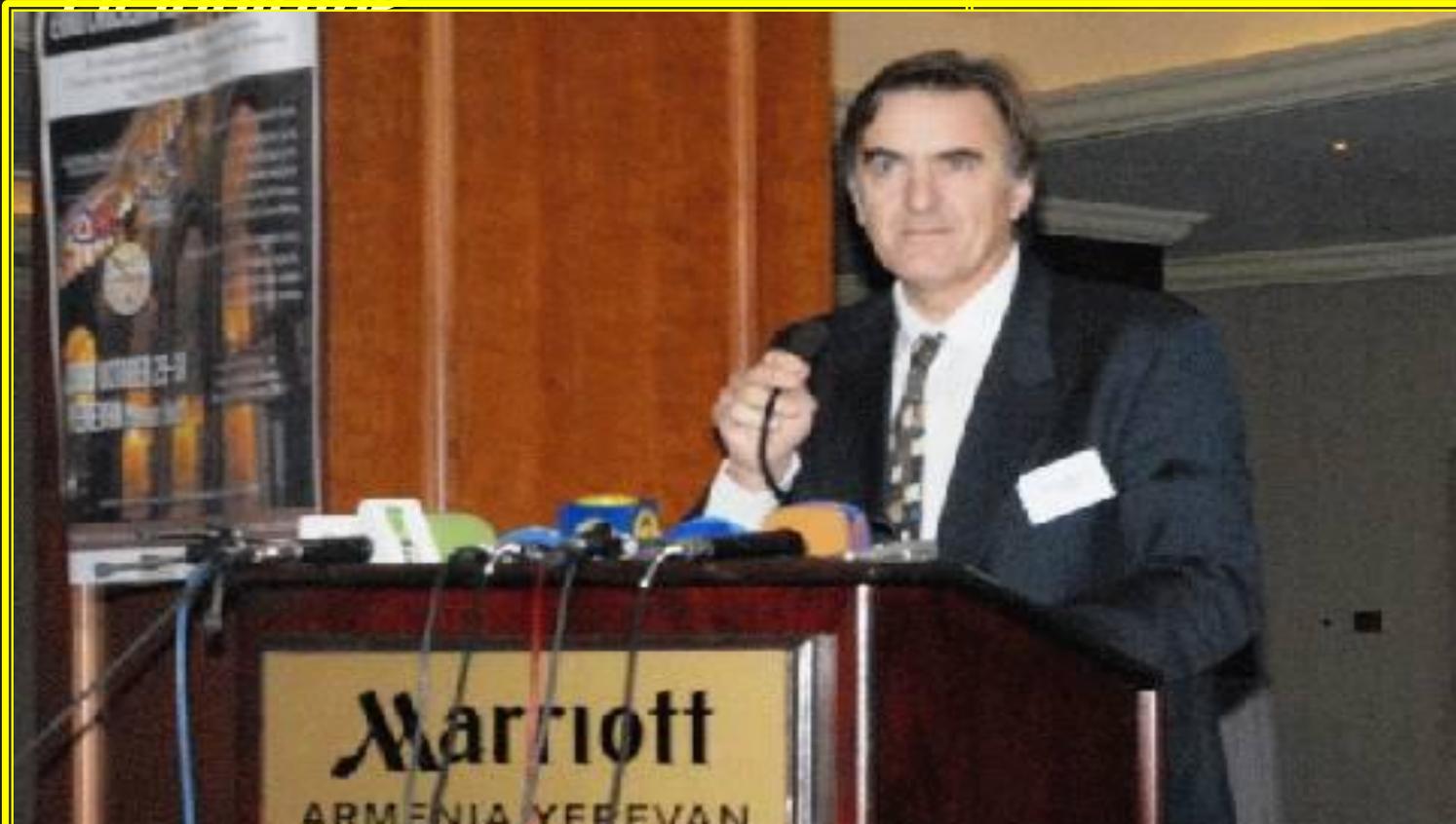
International meeting

I hypothesized

- Heparin or systemic anticoagulation were not the answer
- Platelets cannot be “tranquilized” only with aspirin. A better antiplatelet drug having synergy with aspirin was needed
- Better stent expansion

Why did I pursue Ticlopidine?

Dr. Paul Barraghan: "If you start
A cardiac surgeon: "There is no question that
Ticlopidine few days before PTCA and
Ticlopidine causes a malignant bleeding. I will
continue you will have less dissections
not operate on any patient who is receiveing
which will occlude".
Ticlopidine"



The association of Aspirin with
Ticlopidine (later Clopidogrel) gave
birth to Dual Anti Platelet Therapy

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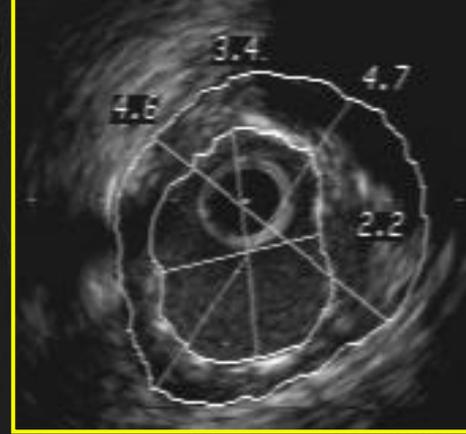
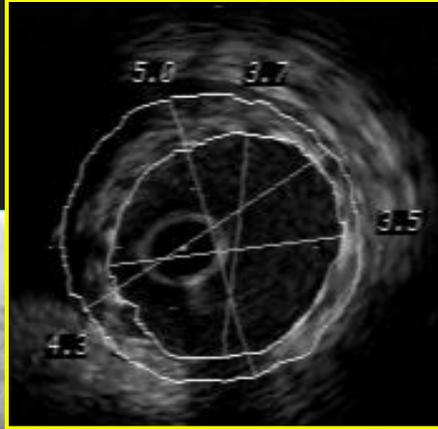
Rome, Italy

International meeting

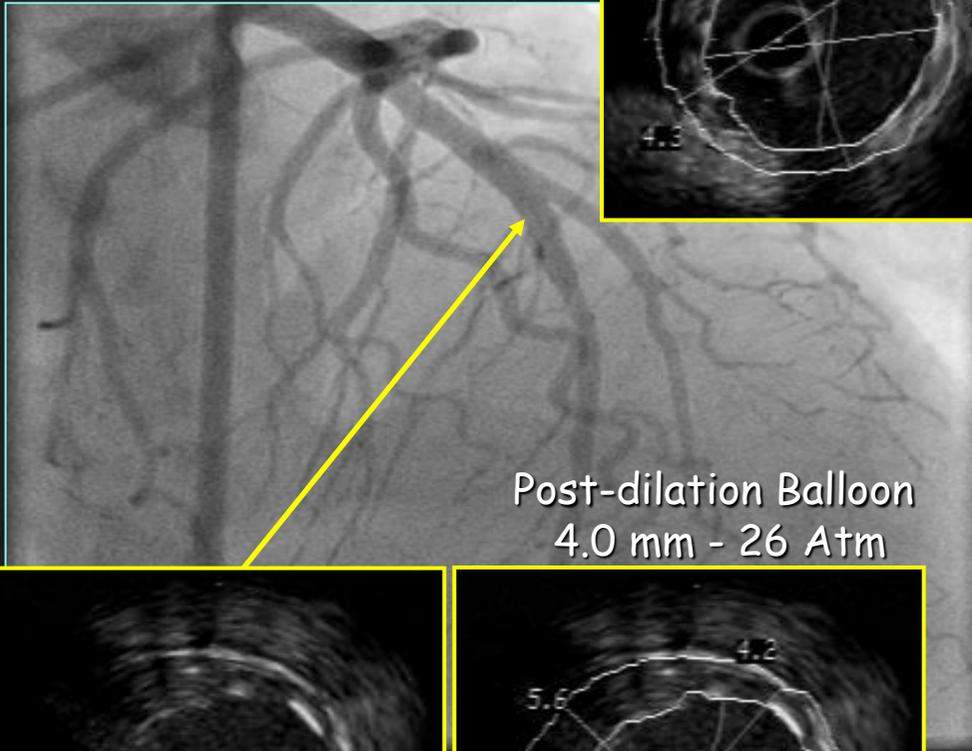
IVUS guided stent optimization



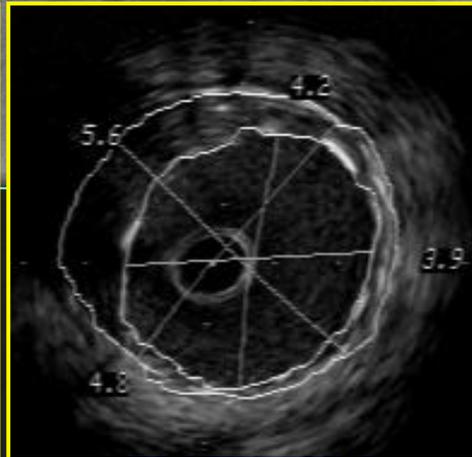
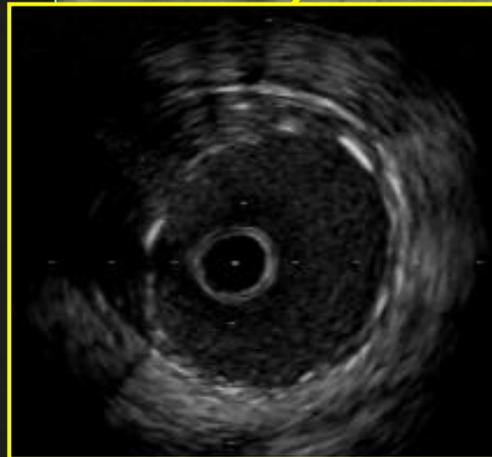
Thanks to Jonathan Tobis MD



After stent
implantation



Post-dilation Balloon
4.0 mm - 26 Atm



IVUS guidance leads to
better stent expansion with
a larger final stent cross
sectional area

Final Result after IVUS
optimization

These evaluations made me ready to:

- Challenge established and “PROVEN” current knowledge
- Build theories based on intuition
- Sometimes the correct explanation comes later
- Survive critiques and demolitions

Among various attributes the one I found of outmost importance was: PERSISTENCE

**PERSISTENCE CAN BE MORE
VALUABLE THAN INTELLIGENCE**

Joint Interventional meeting

It may be more important to be:
Very Persistent rather than very Intelligent !

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A Registry: Not a Randomized Study

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

(Circulation. 1995;91:1676-1688.)

1995

Coronary stenting without anticoagulation

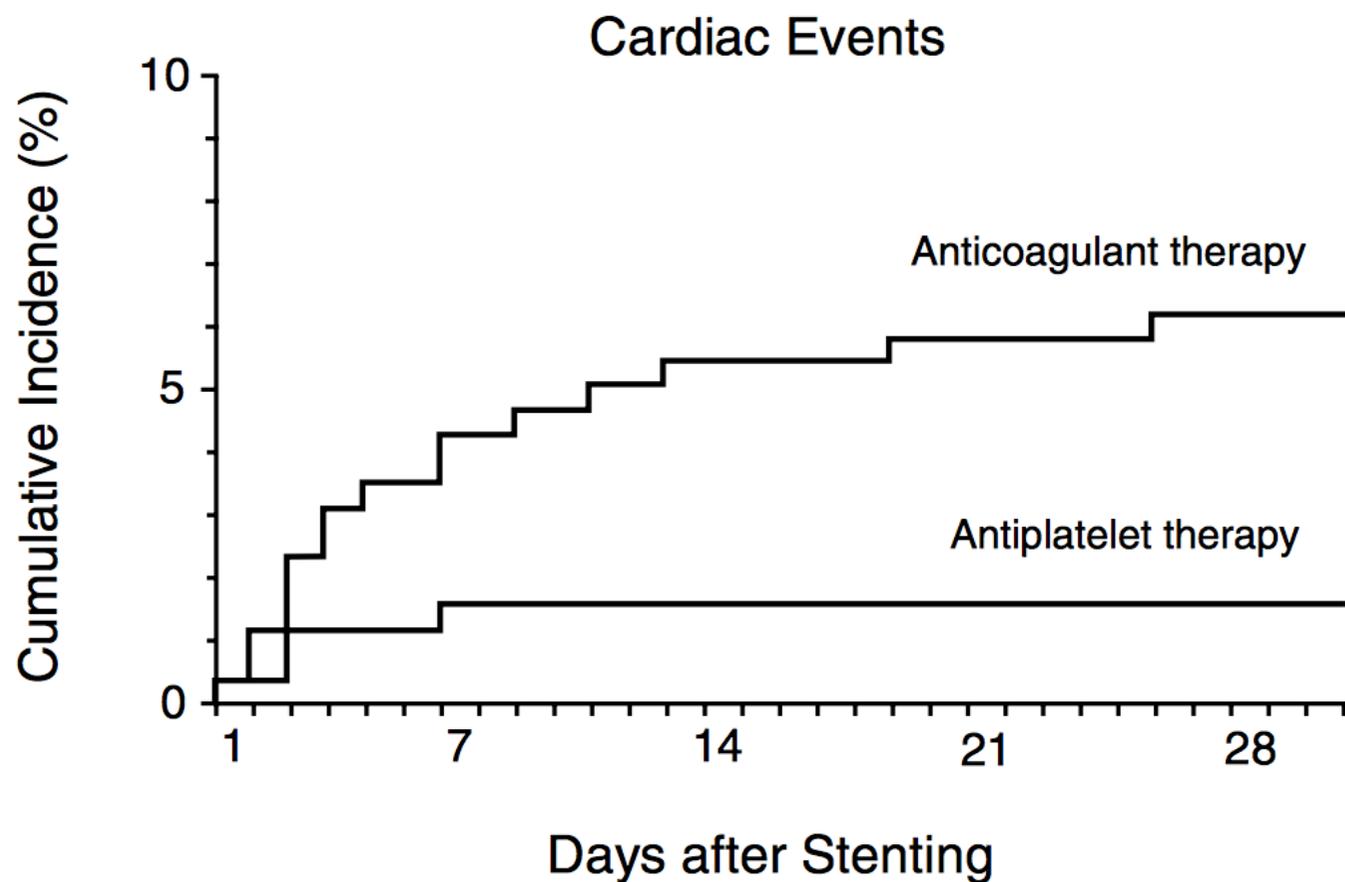
359 patients on Aspirin + Ticlopidine+ IVUS evaluation

- ➔ Aspirin + Ticlopidine in most pts
- ➔ Average balloon pressure 14.9 atm
- ➔ Balloon artery ratio 1.17
- ➔ Thrombosis 0.9%

Colombo et al Circulation 1995

International meeting

A RANDOMIZED COMPARISON OF ANTIPLATELET AND ANTICOAGULANT THERAPY AFTER THE PLACEMENT OF CORONARY-ARTERY STENTS



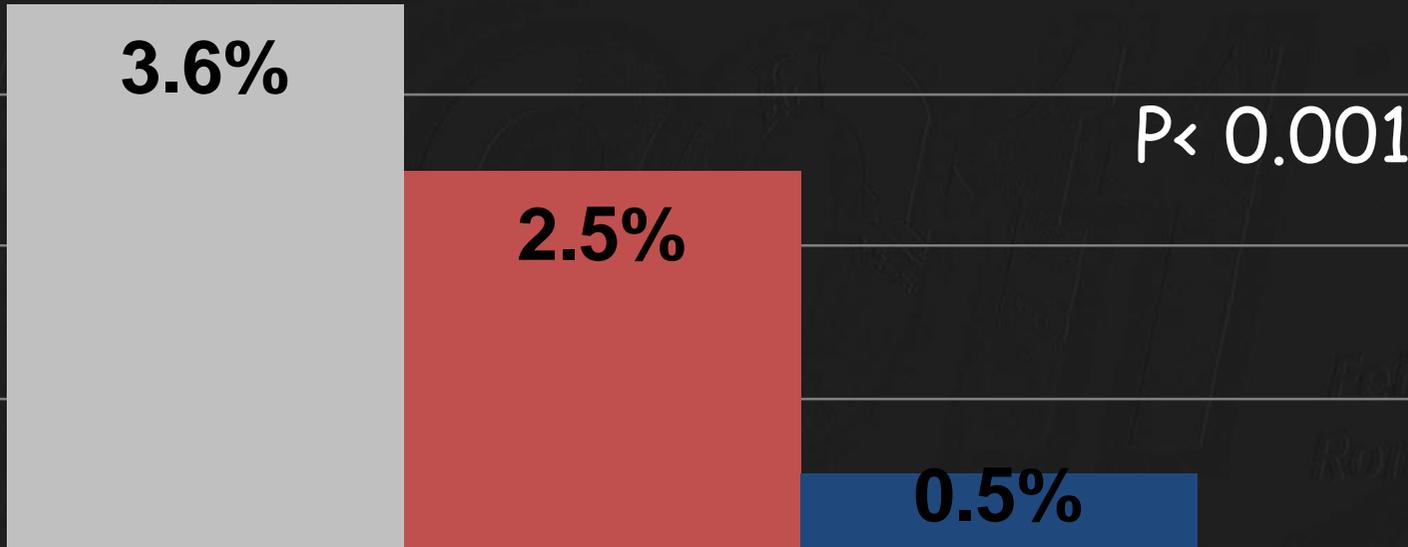
1996

STARS Trial, in 1998

The antithrombotic effect of adding ticlopidine to aspirin

- Aspirin alone (N=557)
- Aspirin+Warfarin (N=550)
- Aspirin+Ticlopidine (N=546)

EVENTS AT 30 DAYS

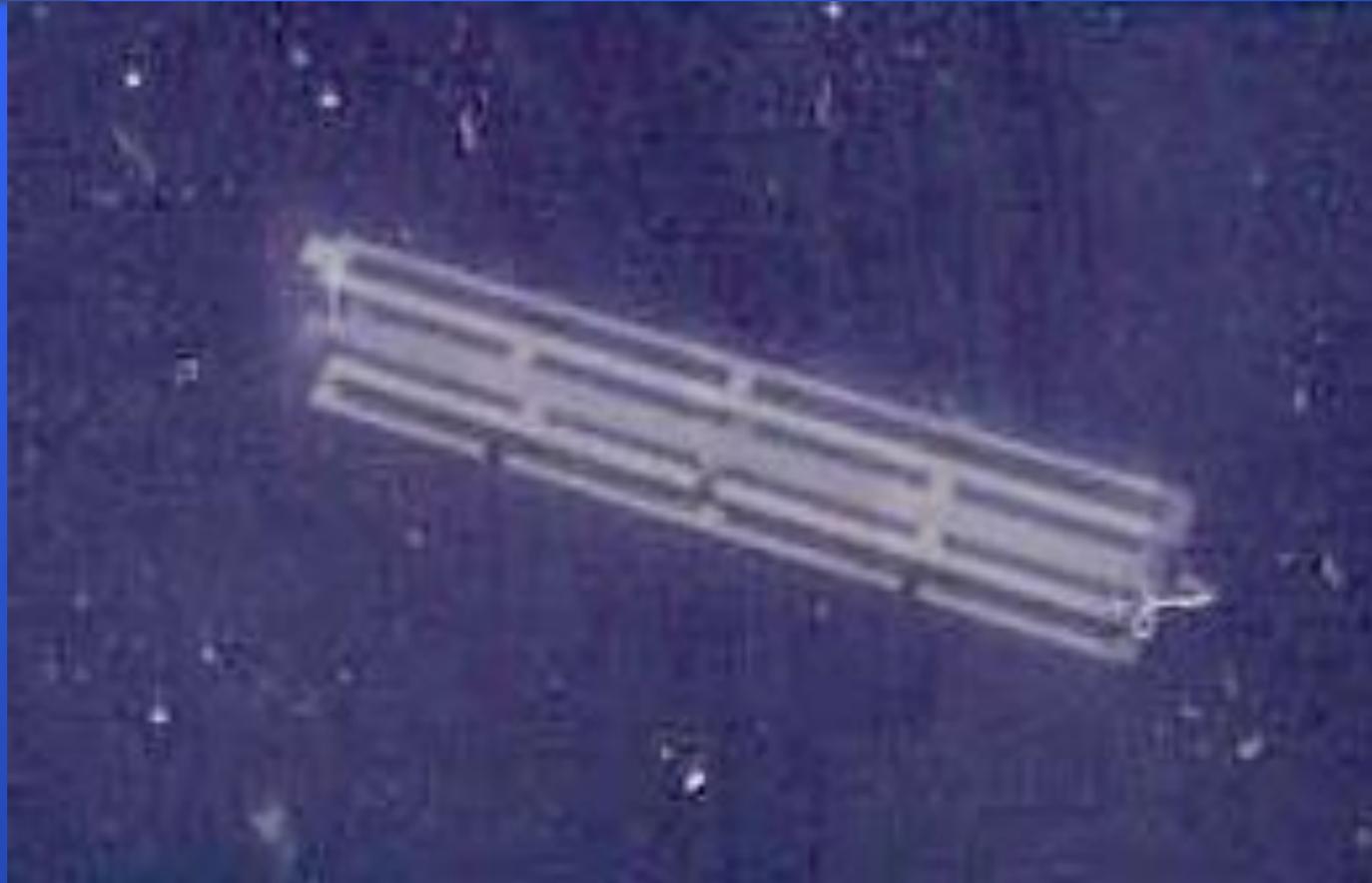


*Death, TLR, thrombus, MI

Leon MD et al N Eng J Med 1998; 339: 1665-71

1994: we felt the need for new tools

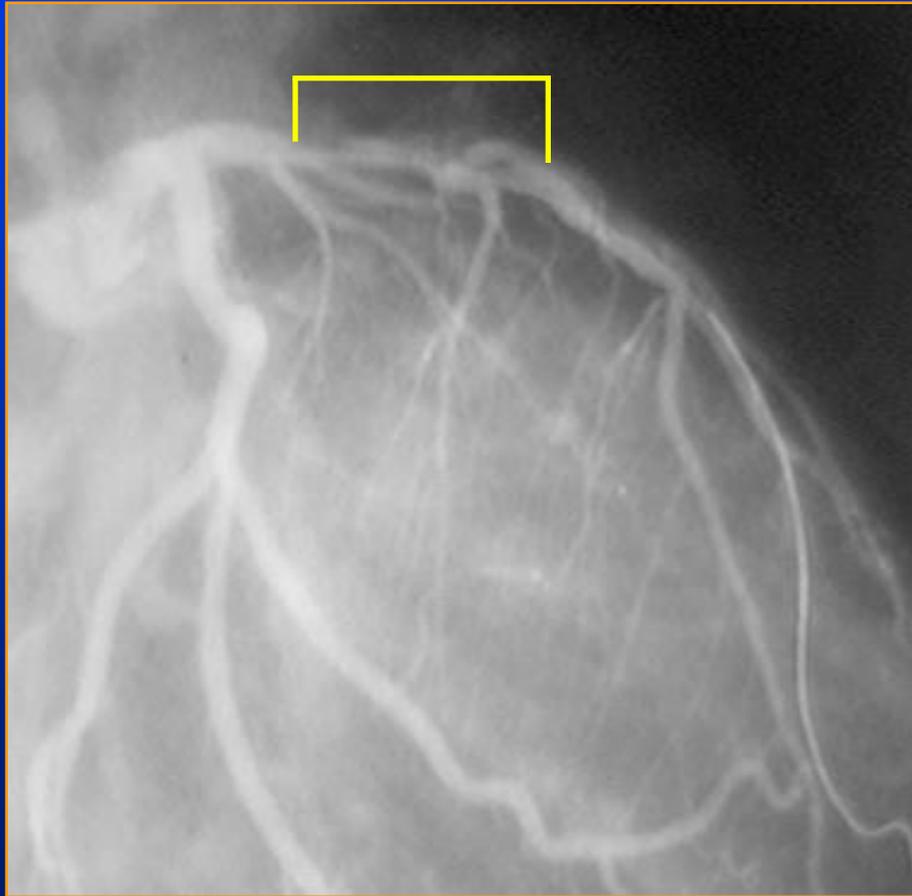
- Short and Long stents
- High pressure balloons with no compliance in order to perform safe stent post-dilatation
- Stent dedicated to bifurcation lesions



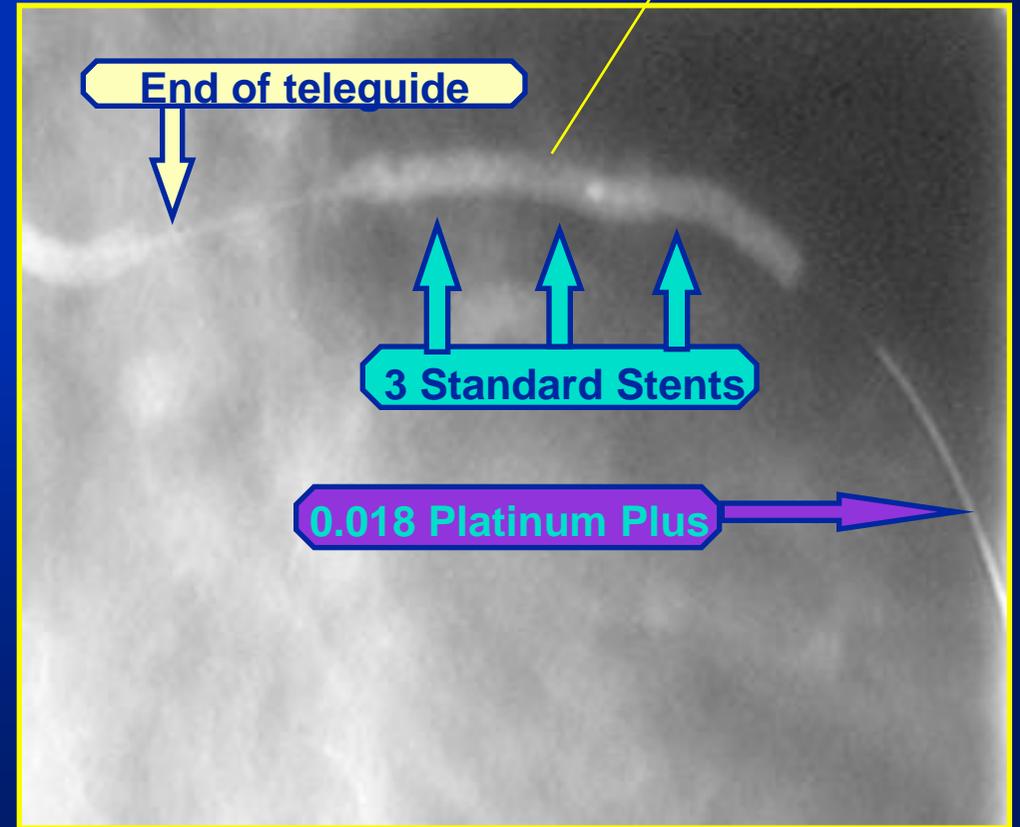
Half Palmaz-Schatz Stent

CUSTOM MADE LONG STENT

*We wish this long COBRA
had two markers !*



DISSECTION AFTER PTCA



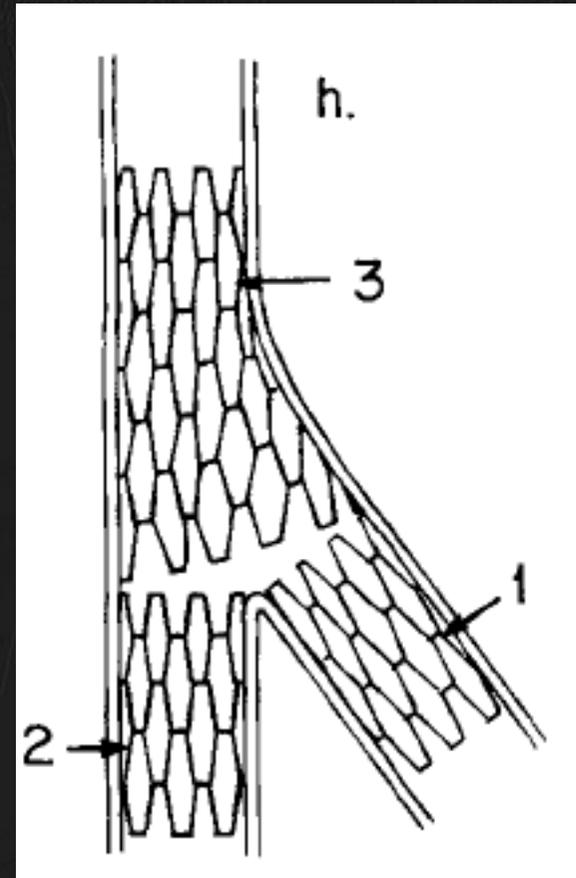
3 P-S STENTS ON A LONG BALLOON

Editorial Comment

Is Bifurcation Stenting the Answer?

Donald S. Baim, MD
Beth Israel Hospital
Boston, Massachusetts

Catheterization Cardiovascular
Diagnosis, 1996



"Trouser legs and seat" approach of Colombo (February 1995), with "touching" stents, followed by close deployment of a proximal stent crimped onto two kissing balloons and advanced to the bifurcation.

The Present:
Late and Very Late Stent Thrombosis

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The next step was to modulate tissue proliferation around the stent: drug eluting stents were then invented. This fact represents a very important link between Basic Research (anti-proliferative compounds) and Clinical Medicine

Enthusiasm was very high and we did not pay sufficient attention to possible complications: “*only placebo has almost no complications!*”

Complications were Stent Thrombosis occurring Late and Very Late after stent implantation

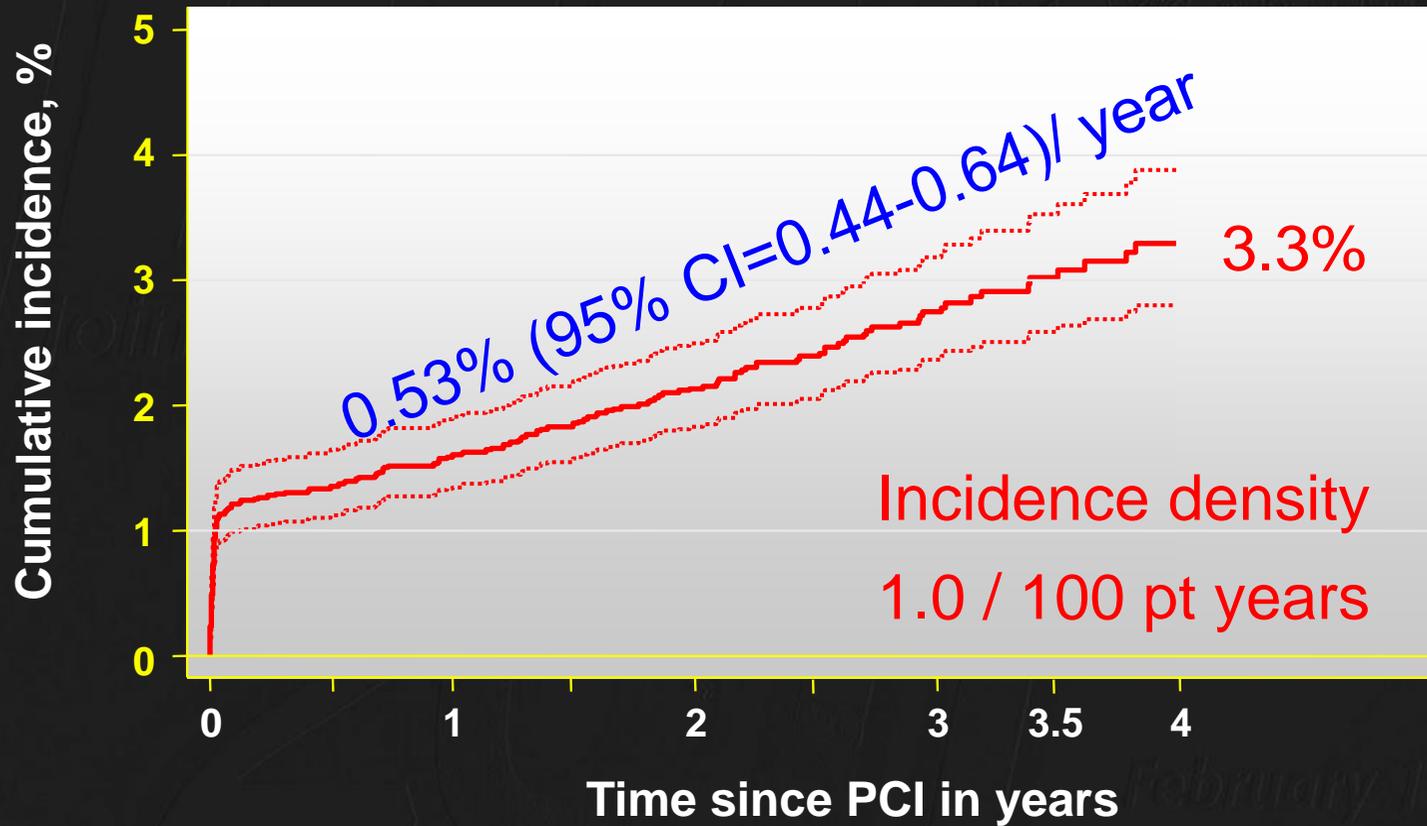
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Late and Very Late Stent Thrombosis With DES: Bern-Rotterdam Cohort Study at 4 Years

192 ST cases in a cohort of 8,146 patients



The development of New Generation Drug-
Eluting Stents and Bioresorbable Stents
"Scaffolds" became the possible answer

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Bioabsorbable Stents

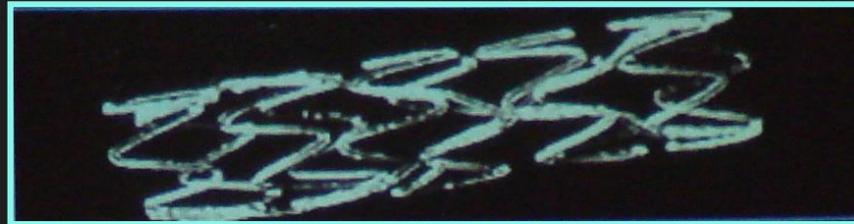
Hideo Tamai MD

1948-2009



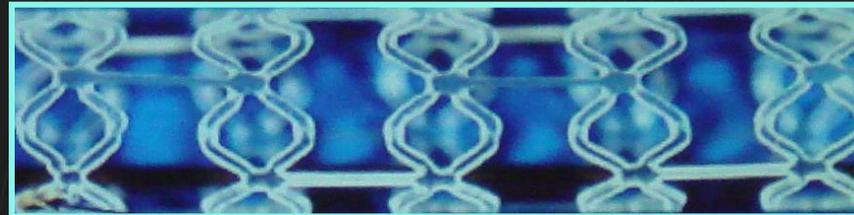
Bioresorbable stent

Igaki-Tamai



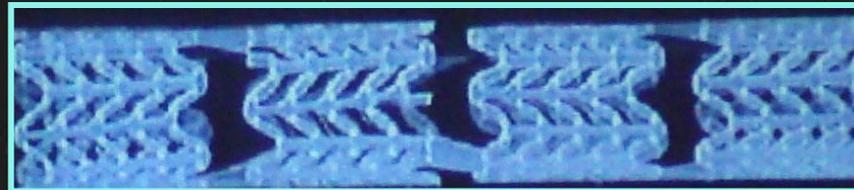
PLA

BVS



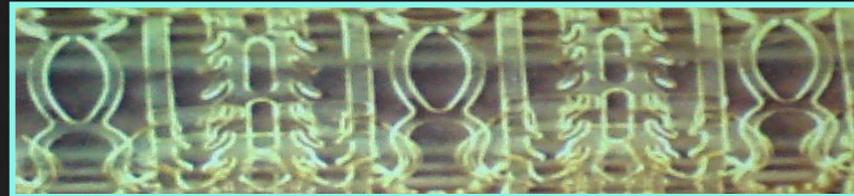
PLA

Sahajanand



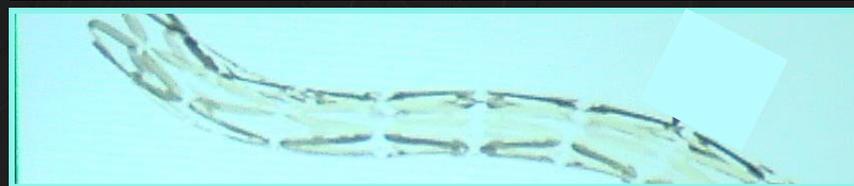
PLA

REVA



Tyrosine-
polycarbonate

BIT



PAE salicylate

Biotronik



Magnesium

Editorial

Biodegradable Stents

“Fulfilling the Mission and Stepping Away”

Antonio Colombo, MD; Evangelia Karvouni, MD

Circulation 2000;102:371-373

The complete disappearance of drug, polymer and stent may eliminate the problem of very late stent thrombosis and free the patient from the dependence on dual antiplatelet therapy preserving the possibility of vessel remodeling

JACC: CARDIOVASCULAR INTERVENTIONS

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EDITORIAL COMMENT

Who Is Thrombogenic: The Scaffold or the Doctor? Back to the Future!*



CrossMark

Antonio Colombo, MD,[†] Neil Ruparelia, MB BS, DPHIL^{†‡}

Rome, Italy

International meeting

The Long Term Outcome of what you
do is the most important and
valuable **END POINT**

joint international meeting

This has been My Operating Philosophy

February 10-12, 2011

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