TCTAP 2019

Role of External Stents for SVG in 2019:

Update for Cardiologists

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Professor of Cardiovascular Surgery, University of Oxford

Conflicts of Interest:
Commercial: Research Funding, Speaking and Travelling Fees and Share Options from Vascular Graft Solutions

The NEW ENGLAND JOURNAL of MEDICINE

[May 2018]

ORIGINAL ARTICLE

Radial-Artery or Saphenous-Vein Grafts in Coronary-Artery Bypass Surgery

Mario Gaudino, M.D., Umberto Benedetto, M.D., Stephen Fremes, M.D., Giuseppe Biondi-Zoccai, M.D., M.Stat., Art Sedrakyan, M.D., Ph.D., John D. Puskas, M.D., Gianni D. Angelini, M.D., Brian Buxton, M.D., Giacomo Frati, M.D., David L. Hare, M.D., Philip Hayward, M.D., Giuseppe Nasso, M.D., Neil Moat, M.D., Miodrag Peric, M.D., Kyung J. Yoo, M.D., Giuseppe Speziale, M.D., Leonard N. Girardi, M.D., and David P. Taggart, M.D., for the RADIAL Investigators*

Table 3. Main Outcomes.* 5 years: SVG Failure Similar to Historic Studies

Outcome	Radial-Artery Group (N=534)		Saphenous-Vein Group (N=502)		Treatment Effect†	
	No. of Events (%)	Events per 1000 Patient-Yr‡	No. of Events (%)	Events per 1000 Patient-Yr‡	Hazard Ratio (95% CI)	P Value
Death, myocardial infarction, or repeat revascularization	67 (12.5)	25	94 (18.7)	39	0.67 (0.49–0.90)	0.01
Death	40 (7.5)	15	42 (8.4)	17	0.90 (0.59–1.41)	0.68
Myocardial infarction	16 (3.0)	6	21 (4.2)	9	0.72 (0.53–0.99)	0.04
Repeat revascularization	23 (4.3)	9	43 (8.6)	17	0.50 (0.40–0.63)	<0.001
Graft occlusion§	28/345 (8.1)	19	61/307 (19.9)	46	0.44 (0.28–0.70)	<0.001

RADIAL ARTERY: CARDIOLOGISTS TO THE RIGHT and SURGEONS TO THE LEFT !!

European Journal of Cardio-Thoracic Surgery 53 (2018) 1127–1134
doi:10.1093/ejcts/ezx432 Advance Access publication 8 December 2017

REVIEW

Cite this article as: Mawhinney JA, Mounsey CA, Taggart DP. The potential role of external venous supports in coronary artery bypass graft surgery. Eur J Cardiothorac Surg 2018;53:1127–34.

The potential role of external venous supports in coronary artery bypass graft surgery†

Jamie A. Mawhinney[a,*], Craig A. Mounsey[a] and David P. Taggart[b]

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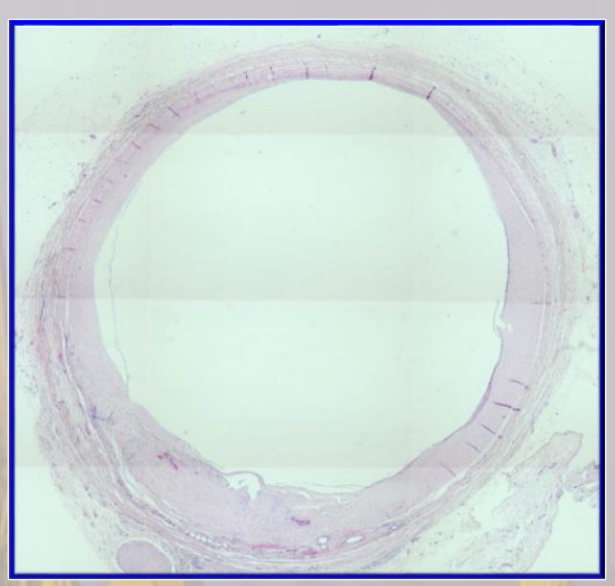
80% of CABG Grafts are SVG: ¾ occluded or diseased by 10 yrs

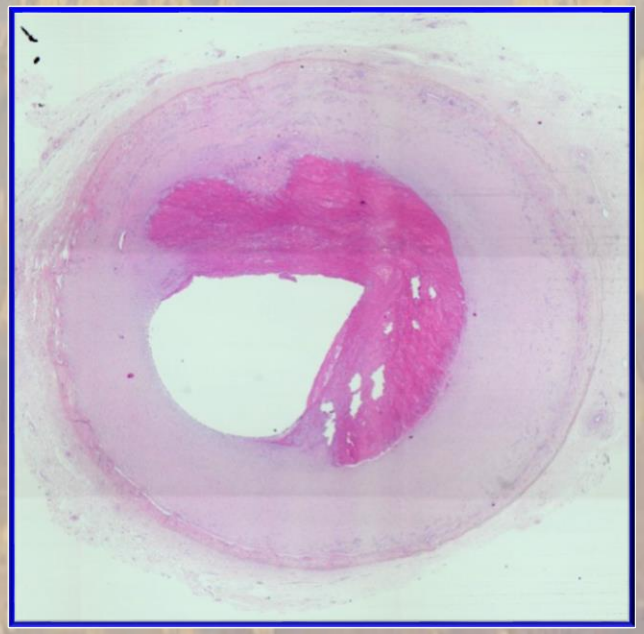
Vein Graft Remodeling: 2 Distinct Phases

- ✓EARLY
- ✓shear induced remodeling → luminal enlargement



- ✓LATE

wall tension induced remodeling →
wall thickening and stiffening
intimal hyperplasia
atherosclerosis



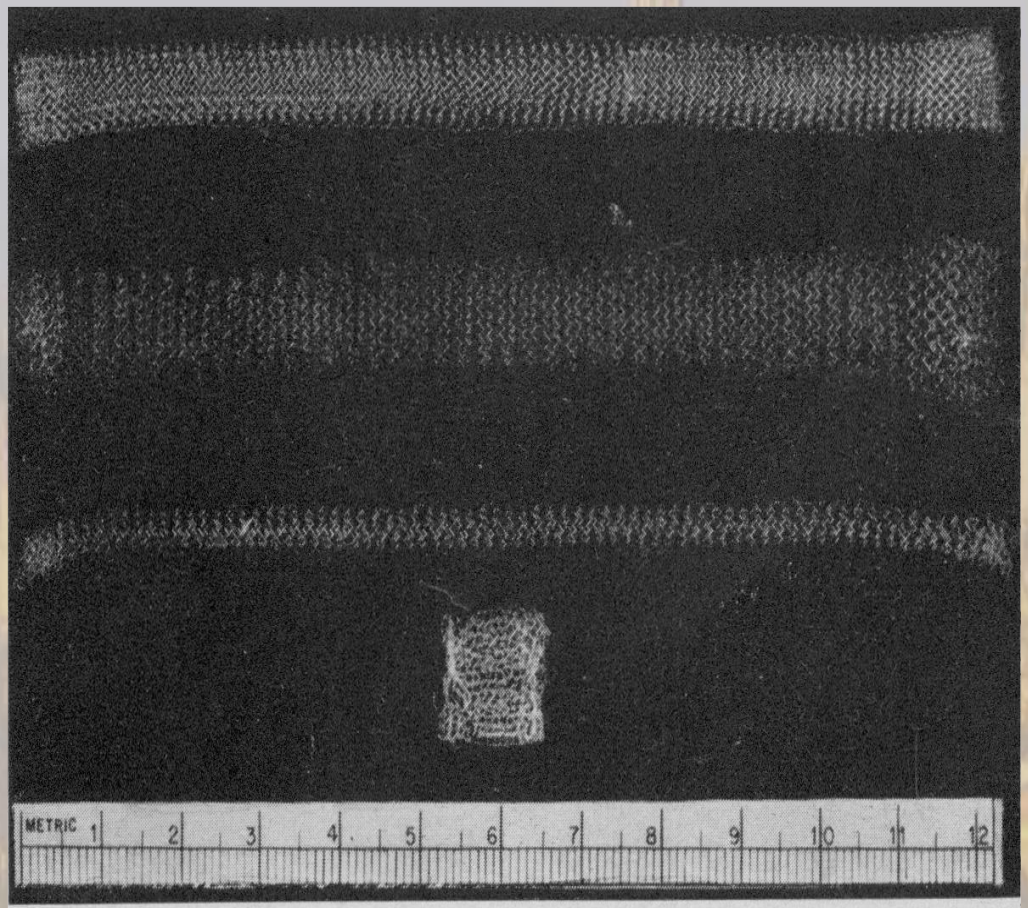
New Stent for Support of Veins in Arterial Grafts

[ARCH SURG 1963]

VICTOR PARSONNET MD, A.ATTAI LARI MD, I.H. SHAH MD

EXTERNAL STENTING OF SVG PROPOSED >50 YEARS AGO

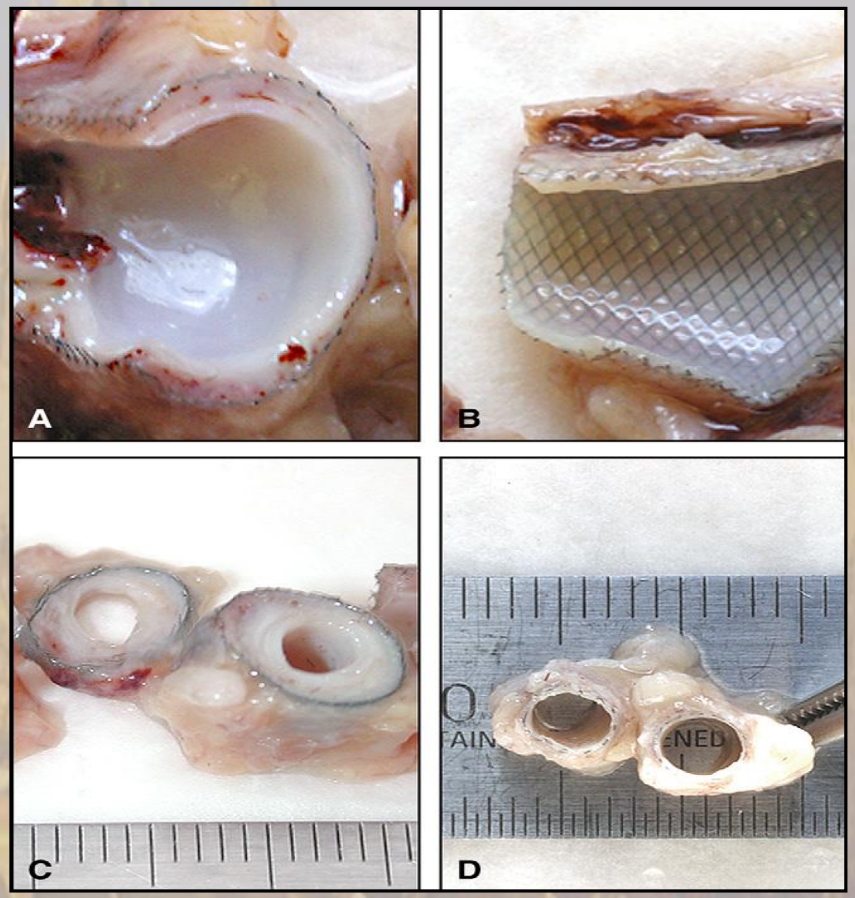
- Extensive animal (femoral/carotid) testing successful
- BUT NO CABG model



Zilla et al JTCVS 2008

Constrictive external nitinol meshes inhibit vein graft intimal hyperplasia in nonhuman primates

Peter Zilla, MD, PhD,[a] Paul Human, PhD,[a] Michael Wolf, BSc,[b] Wilhelm Lichtenberg, MB ChB,[a] Nasser Rafiee, BSc,[c] Deon Bezuidenhout, PhD,[a] Nazlia Samodien, BTechHons,[a] Christian Schmidt, MD,[a] and Thomas Franz, PhD[a]



Early Stent RCTs in CABG: Very Poor Patency (0-30% @ 1 year)

A randomized trial of an external Dacron sheath for the prevention of vein graft disease: The Extent study

JTCVS 2007

Gavin J. Murphy, MD, FRCS, Andrew C. Newby, BA, PhD, Jamie Y. Jeremy, PhD, Andreas Baumbach, MD, FRCP, and Gianni D. Angelini, MD, FRCS, Bristol, United Kingdom

- 20 SVG knitted polyester stents: patency 0% at 6 months

Highly flexible nitinol mesh to encase aortocoronary saphenous vein grafts: first clinical experiences and angiographic results nine months postoperatively☆

IJCTVS 2011

Jan Schoettler[a,*], Jill Jussli-Melchers[a], Christina Grothusen[a], Lars Stracke[b], Felix Schoeneich[a], Simon Stohn[a], Grischa Hoffmann[a], Jochen Cremer[a]

- 25 SVG KIPSBAY (nitinol mesh+glue): patency 28% at 9 months

Saphenous Vein Graft Wrapping by Nitinol Mesh: A Word of Caution

IJCTVS 2014

Giuseppe Rescigno[1] Carlo Aratari[1] Sacha Marco Matteucci[1] Rosario Parisi[2] Giulia Gironi[1] Niccolò Schicchi[3] Alessandro D'Alfonso[1] Valentina Cola[4] Lucia Torracca[1]

- 25 SVG KIPSBAY (nitinol mesh+glue): patency 34% at 1 yr

2007

Knitted Polyester Stent

6 month patency 0%

2008

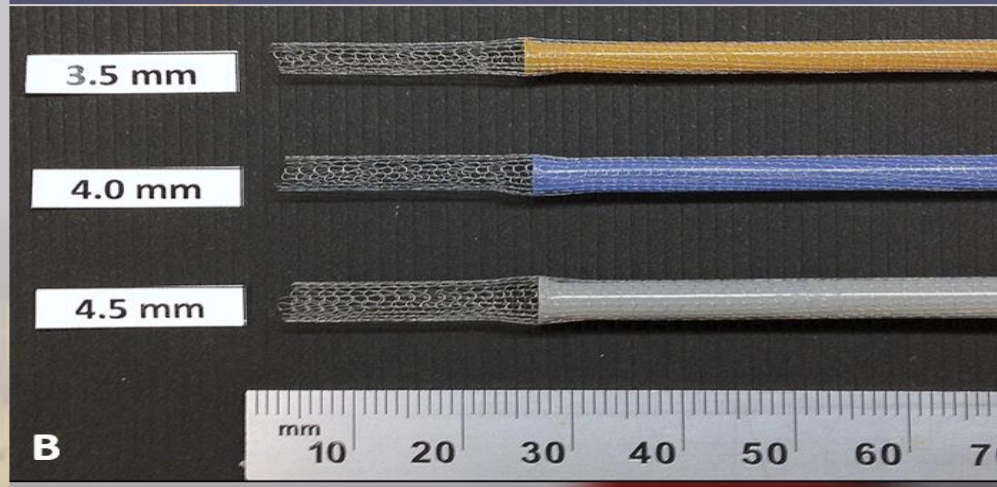
Kipsbay: nitinol mesh + glue

1 year patency 30%

2017

VEST: cobalt chromium alloy

6 month patency 90%



The *VEST* External Stent for SVG

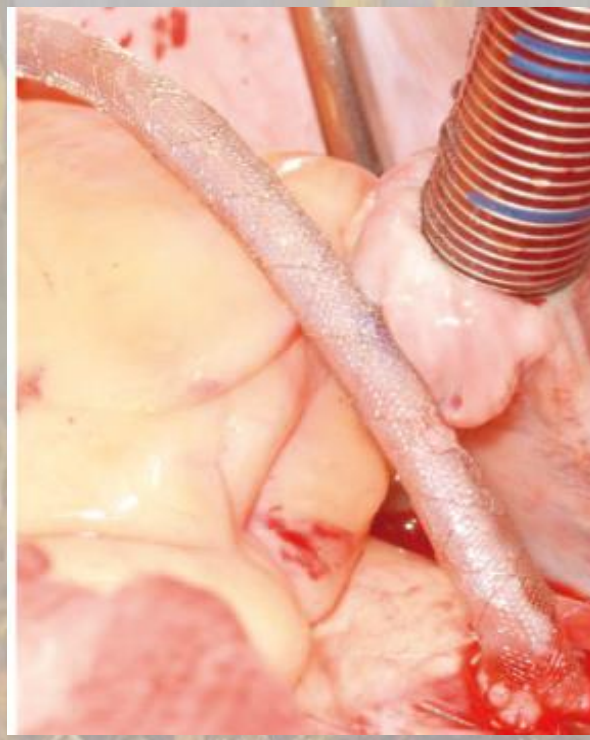
(Successful Testing in Sheep CABG Model 2011-13)

Mechanical Properties:

- ✓Cobalt Chromium Alloy
- ✓Radial Elasticity (Kink and Crush resistant)
- ✓Axial Plasticity (adjust from 3-6 cm to 10-22 cm)
- ✓Maintains its in situ configuration without fixation

Effects of VEST Stent on Vein:

- ✓REDUCES diameter by around 10%
- ✓REDUCES lumen irregularities and flow discrepancies
- ✓REDUCES wall tension
- ✓REDUCES size mismatch vs native coronary artery
- ✓Prevents vein dilatation post implantation



One minute to implant and no other change in technique needed

A Randomized Trial of External Stenting for Saphenous Vein Grafts in Coronary Artery Bypass Grafting

VEST I

[ATS 2015]

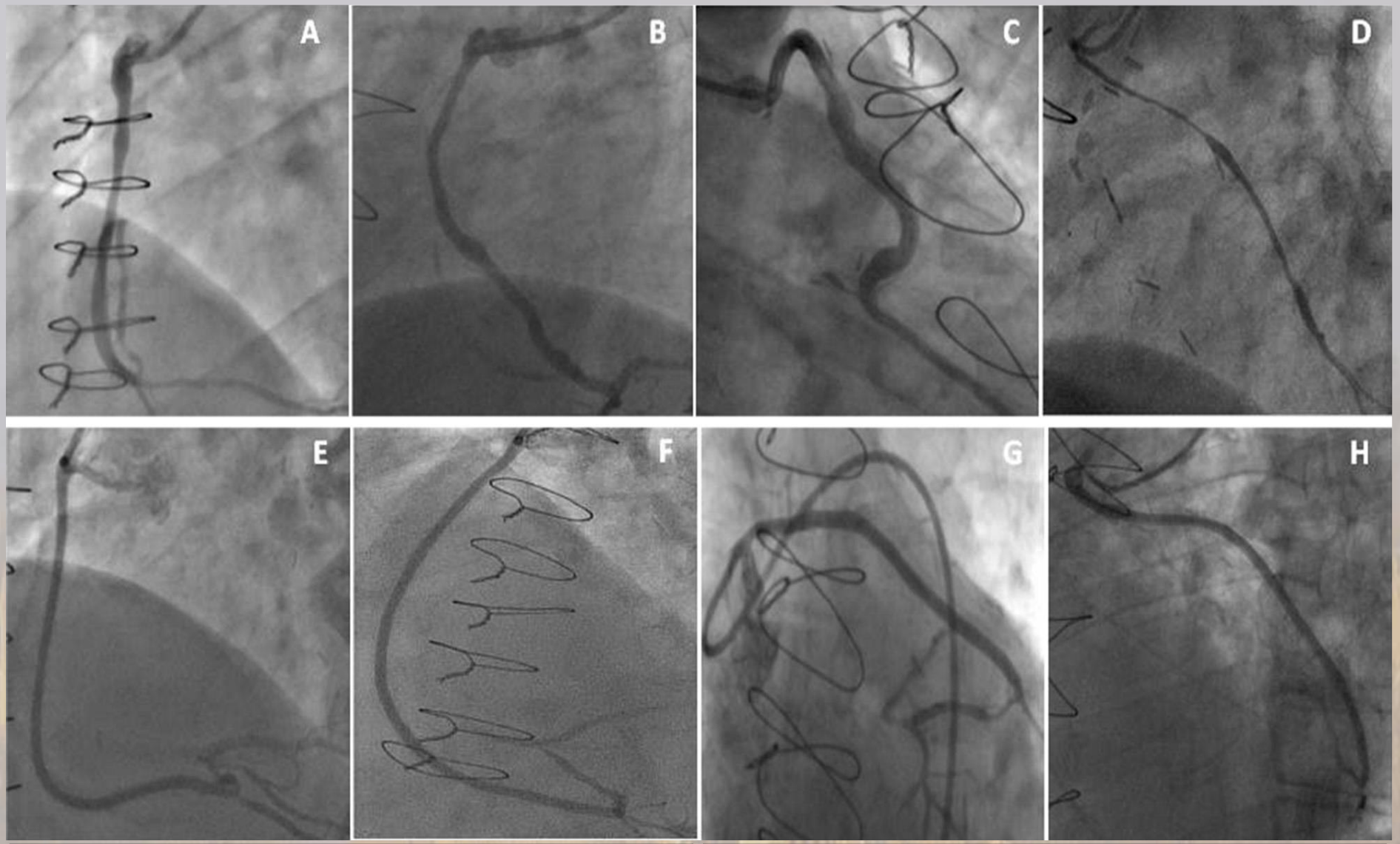
David P. Taggart, MD, PhD, Yanai Ben Gal, MD, Belinda Lees, PhD, Niket Patel, MD, Carolyn Webb, PhD, Syed M. Rehman, MD, Anthony Desouza, MD, Rashmi Yadav, MD, Fabio De Robertis, MD, Miles Dalby, MD, Adrian Banning, MD, Keith M. Channon, MD, Carlo Di Mario, MD, and Eyal Orion, MD

- RCT of 30 patients undergoing CABG x 3 (IMA + SVG x2)
- One SVG randomized to **Stent**, one SVG as **Control**
- **All grafts had excellent flow (TTFM) prior to chest closure**
- 1 year angio: IMA 100% patent
- SVG Angio Failure (occlusion or stenoses >50%)
- **Control** SVG: 28% (7% RCA and 25% Cx)
- **Stented** SVG: 30% (46% RCA and 18% Cx)
- Highest failure rate for Stented grafts (i) metallic clips used inside stent (ii) fixation of proximal/distal anastomoses (especially on right)
- **SVG Perfect Patency: 81% STENTS vs 48% CONTROL**
- **INTIMAL HYPERPLASIA:** significant reduction in **Stents**

VEST I

1 Year RCA: NO STENT

1 Year OM: NO STENT



1 Year RCA: STENT

1 Year OM: STENT

VEST I: Intimal Hyperplasia (IVUS): Primary Endpoint

Variable	Stented (n = 21)	Nonstented (n = 23)	Percent Difference	*p* Value
All saphenous vein grafts				
Plaque area, mm^2	4.37 ± 1.40	5.12 ± 1.35	−14.6	0.04
Plaque thickness, mm	0.37 ± 0.10	0.42 ± 0.10	−11.9	0.06
Average lumen diameter, mm	3.36 ± 0.57	3.42 ± 0.53	−1.0	0.60
Effect of SB ligation method on intimal hyperplasia				
Plaque area, mm^2				
SB ligated with metal clips	5.01 ± 1.23 (n = 11)	5.25 ± 1.42 (n = 13)	−4.6	0.33
SB ligated with sutures	3.59 ± 1.22 (n = 9)	4.95 ± 1.32 (n = 10)	−27.4	0.05
Plaque thickness, mm				
SB ligated with metal clips	0.41 ± 0.10 (n = 11)	0.42 ± 0.10 (n = 13)	−2.4	0.60
SB ligated with sutures	0.32 ± 0.09 (n = 9)	0.42 ± 0.10 (n = 10)	−23.8	0.04

- STENTS Overall reduction in SVG plaque area (15%) and thickness (12%)
- BUT much greater reduction in SVG plaque area (27%) and thickness (24%) when SB ligated rather than occluded with metallic clips

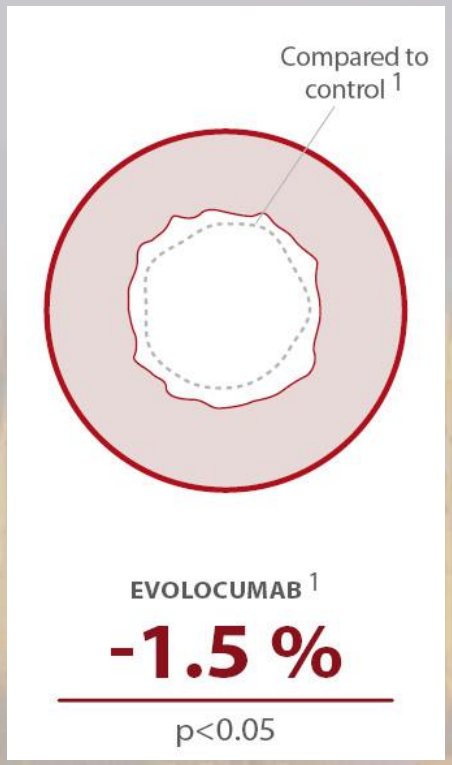
Research

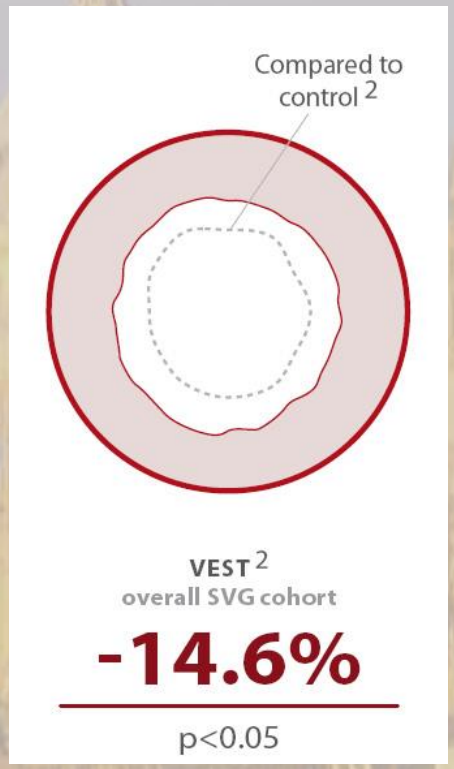
JAMA | Original Investigation

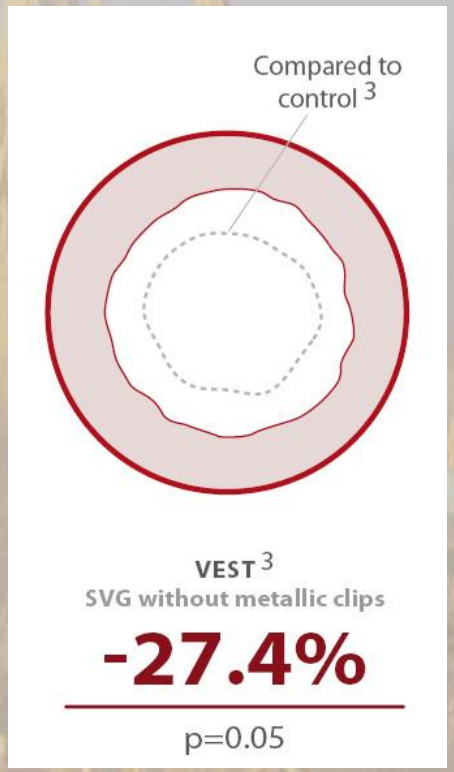
Effect of Evolocumab on Progression of Coronary Disease in Statin-Treated Patients
The GLAGOV Randomized Clinical Trial

[JAMA 2016]

Stephen J. Nicholls, MBBS, PhD; Rishi Puri, MBBS, PhD; Todd Anderson, MD; Christie M. Ballantyne, MD; Leslie Cho, MD; John J. P. Kastelein, MD, PhD; Wolfgang Koenig, MD; Ransi Somaratne, MD; Helina Kassahun, MD; Jingyuan Yang, PhD; Scott M. Wasserman, MD; Robert Scott, MD; Imre Ungi, MD, PhD; Jakub Podolec, MD, PhD; Antonius Oude Ophuis, MD, PhD; Jan H. Cornel, MD, PhD; Marilyn Borgman, RN, BSN; Danielle M. Brennan, MS; Steven E. Nissen, MD







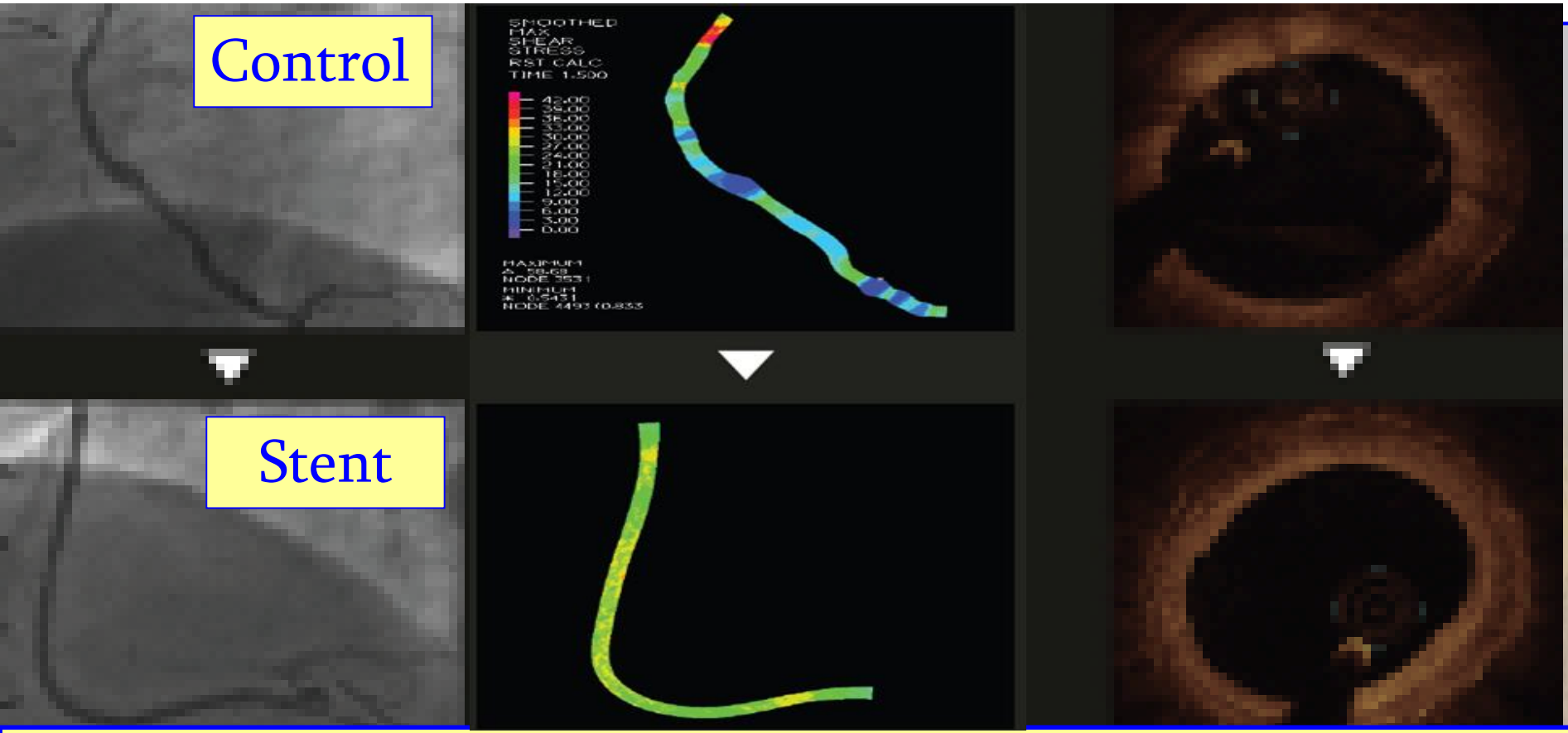
Evolocumab costs $14,000/year vs $1000 for VEST stent

VEST I

Flow patterns in externally stented saphenous vein grafts and development of intimal hyperplasia

[JTCVS 2015]

Tomer Meirson, BS,[a] Eyal Orion, MD, MBA,[b] Carlo Di Mario, MD, PhD,[c] Carolyn Webb, PhD,[c,d] Niket Patel, MD,[e] Keith M. Channon, MD,[e] Yanai Ben Gal, MD,[f] and David P. Taggart, MD, PhD[g]



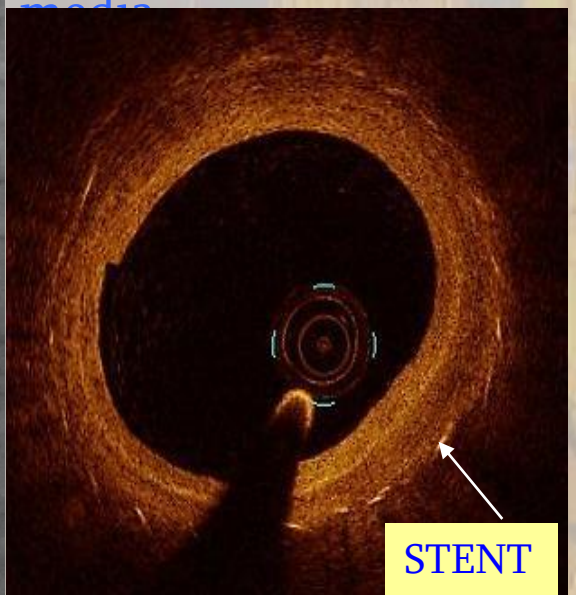
- Stent results in less turbulent flow (significantly lower oscillatory shear index (OSI))
- OSI (and not wall shear stress) is the major determinant of development of intimal hyperplasia (first description of this in SVG)

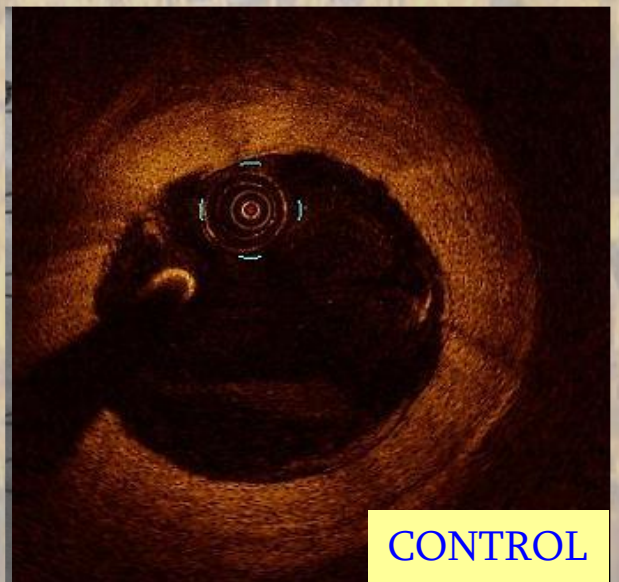
OCT Imaging of Aorto-Coronary Vein Graft Pathology Modified By External Stenting One year Post Surgery [EHJ Cardiovasc Imaging 2015]

Carolyn Webb, Eyal Orion, David P Taggart, Keith M Channon, Carlo di Mario

VEST I	Control (23)	Stent (20)	p
Cross Sectional Area (mm)	8.4 (3)	7.6 (2.7)	**0.005**
Homogeneity (max-min lumen) mm	0.33 (0.23)	0.28 (0.19)	**0.06**
Eccentricity (loss of 'circularity')	0.10 (0.06)	0.08(0.06)	**0.019**
Thrombus present	3 (13%)	0	

SENTS Significantly better SVG lumen regularity, smaller smoother intima and media





A prospective study of external stenting of saphenous vein grafts to the right coronary artery: the VEST II study

VEST II

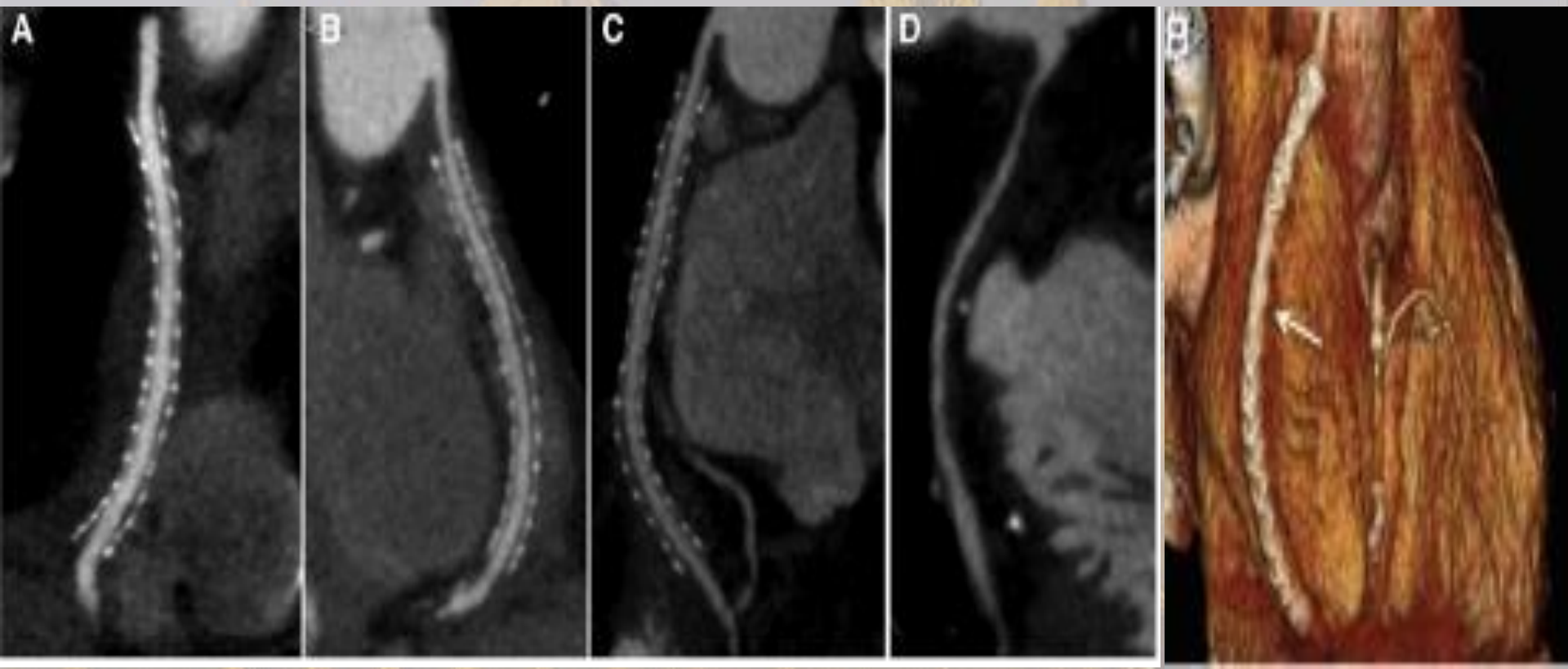
[EJCTS 2017]

David P. Taggart[a,b], Sanaz Amin[a,b,*], Jasmina Djordjevic[b], Evangelos K. Oikonomou[c], Sheena Thomas[c], Anna-Maria Kampoli[d], Nikant Sabharwal[a,c], Charalambos Antoniades[a,c] and George Krasopoulos[a,b]

30 patients with SVG to RCA

No anastomotic fixation or metallic clips:

6 month patency 86% (previously 54% in VEST I)



Taggart *et al. Journal of Cardiothoracic Surgery* (2018) 13:117
https://doi.org/10.1186/s13019-018-0803-9

Journal of Cardiothoracic Surgery

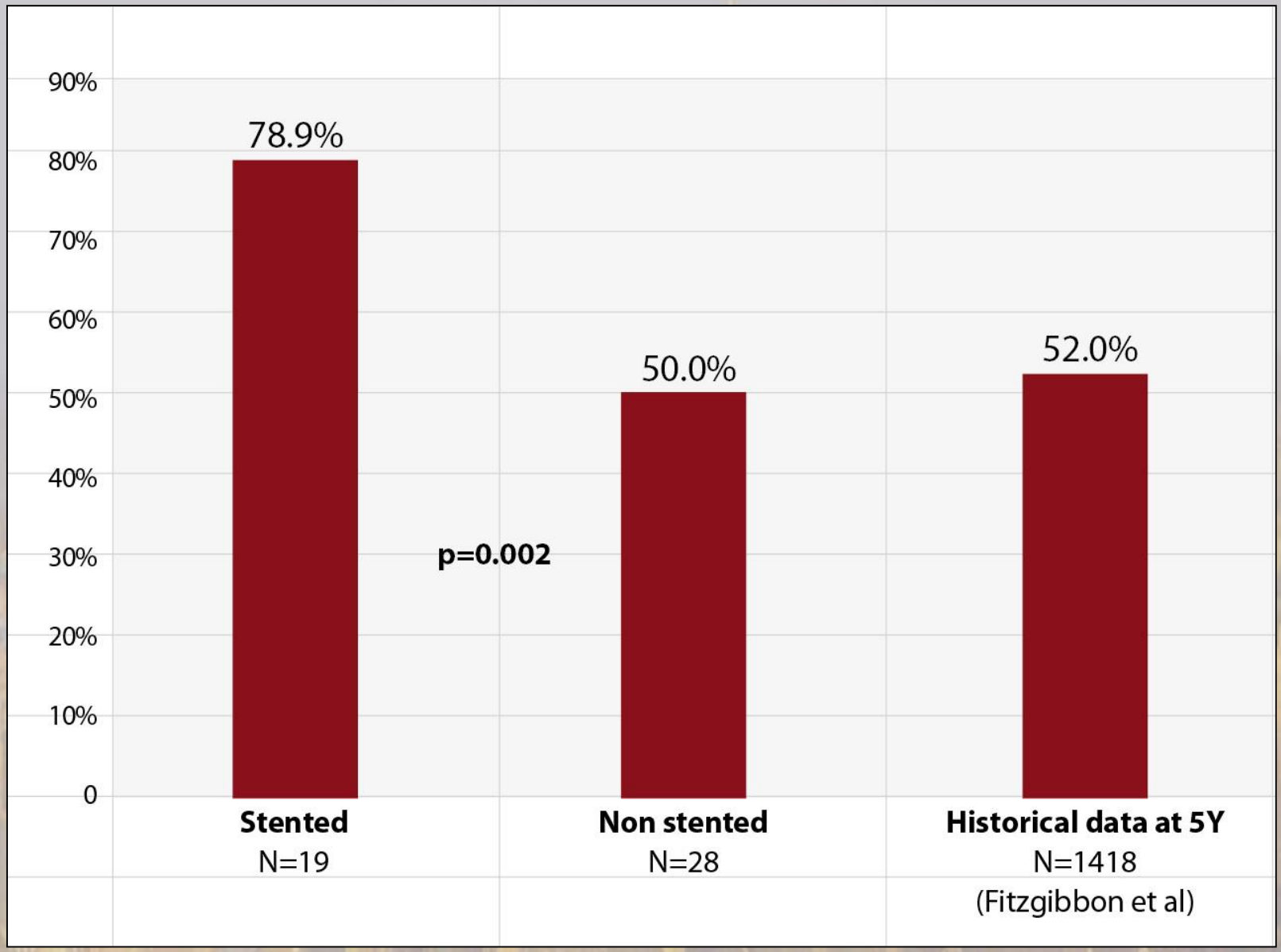
RESEARCH ARTICLE Open Access

Long-term performance of an external stent for saphenous vein grafts: the VEST IV trial

David P. Taggart[1†], Carolyn M. Webb[2,3*†], Anthony Desouza[4], Rashmi Yadav[4], Keith M. Channon[5], Fabio De Robertis[6] and Carlo Di Mario[3]

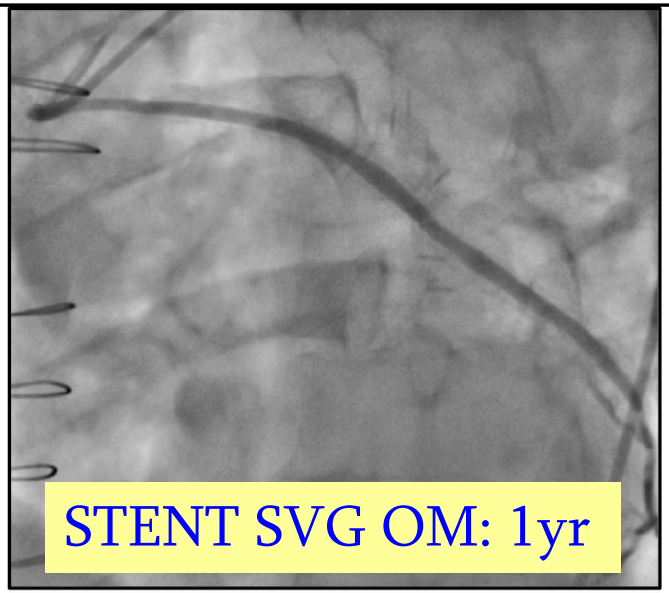
VEST IV (VEST I patients who returned at 5 years)

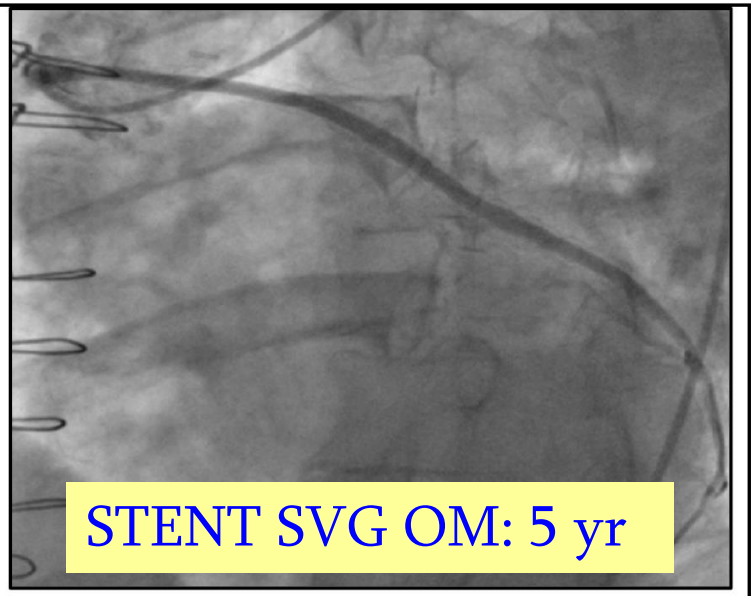
Fitzgibbon Perfect Patency at 5 years

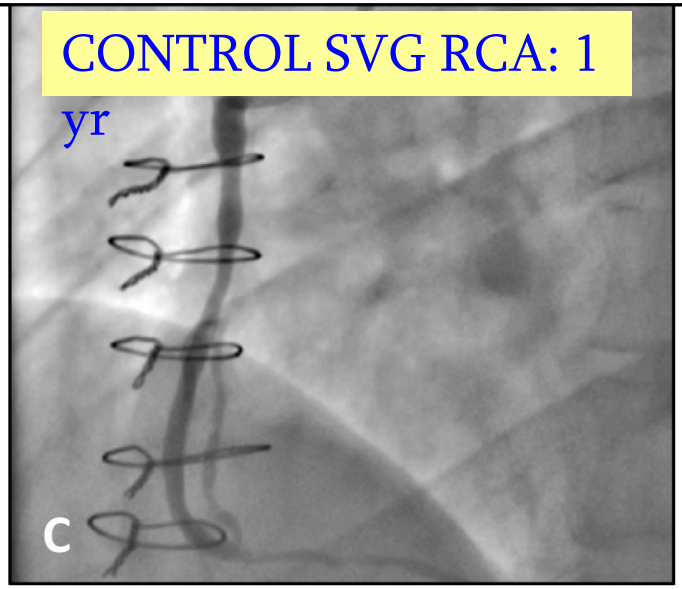


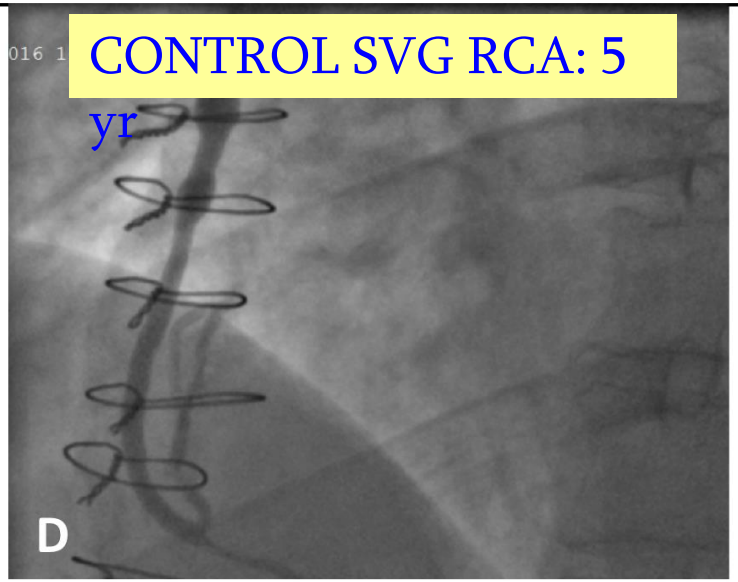
VEST IV (VEST I @ 5 Years)

SAME PATIENT @ 1 and 5 YEARS



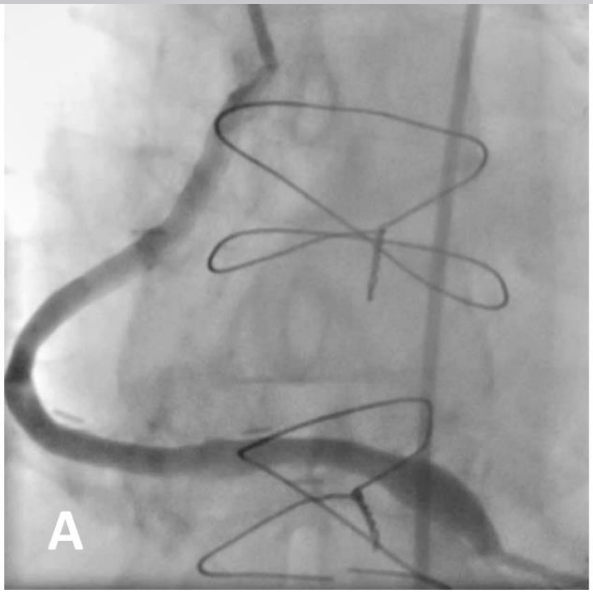




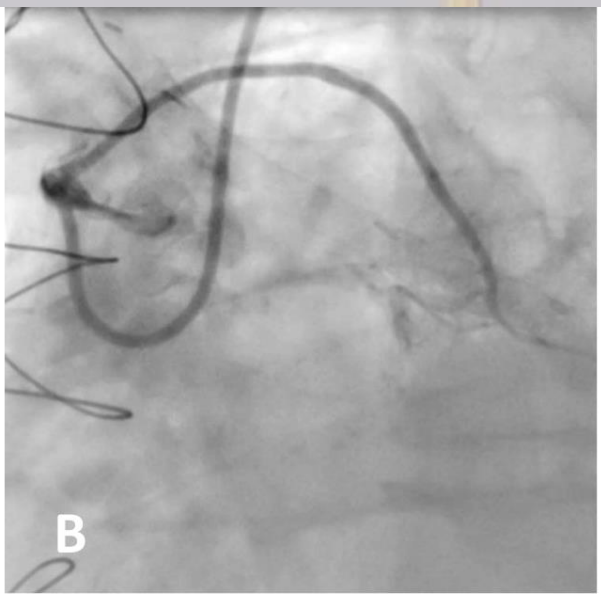


VEST IV

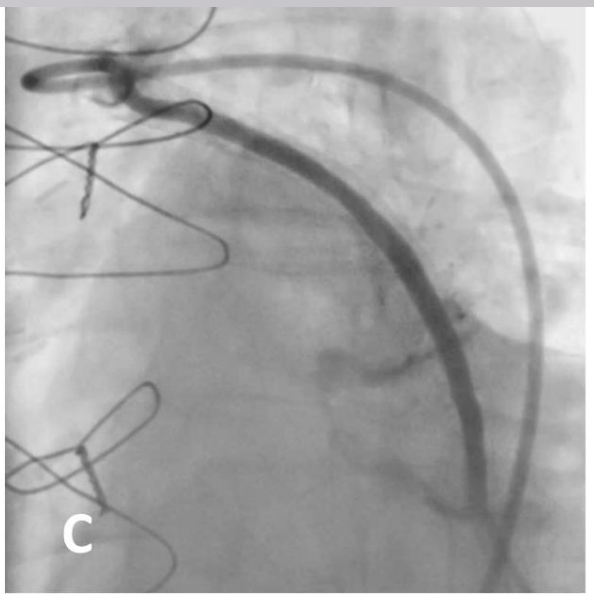
Same Patient at 5 years



CONTROL

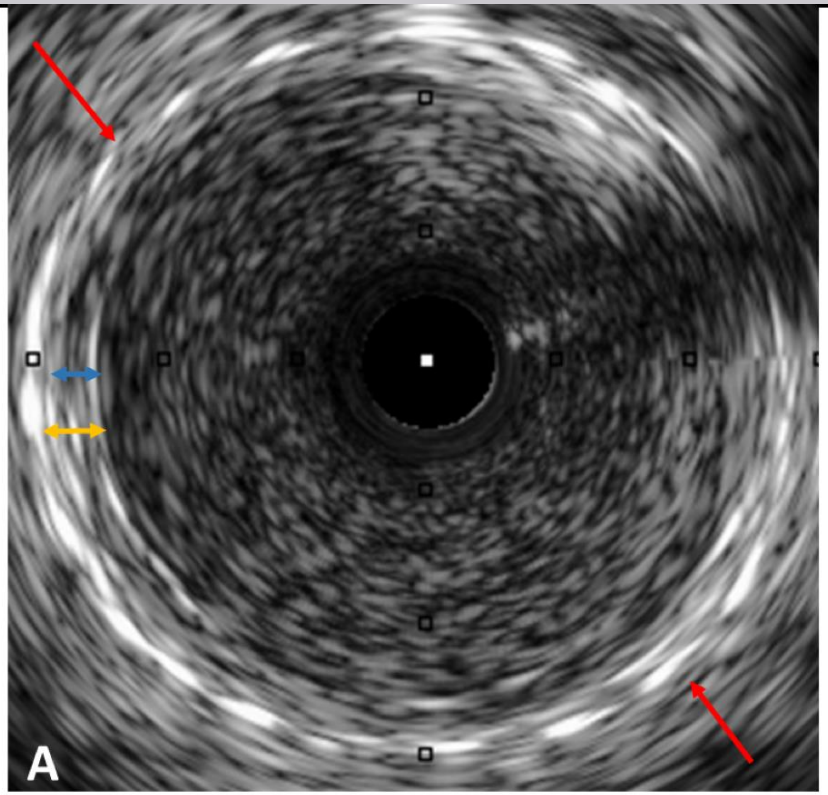


CONTROL

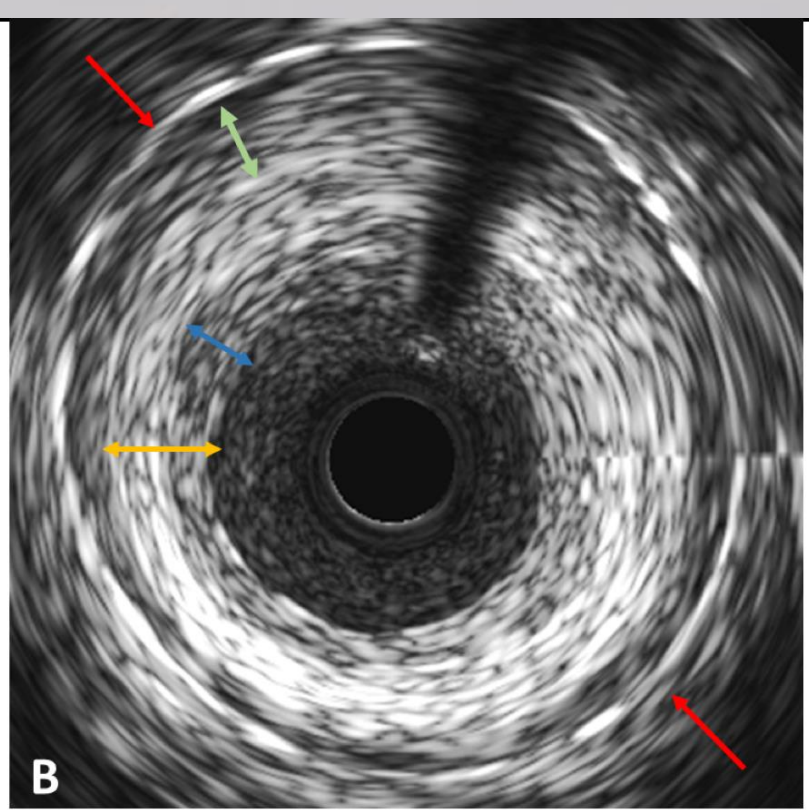


STENT

Effect of (A) constrictive versus (B) lose fitting external sten



CONSRICTIVE STENT



LOOSE FITTING STENT

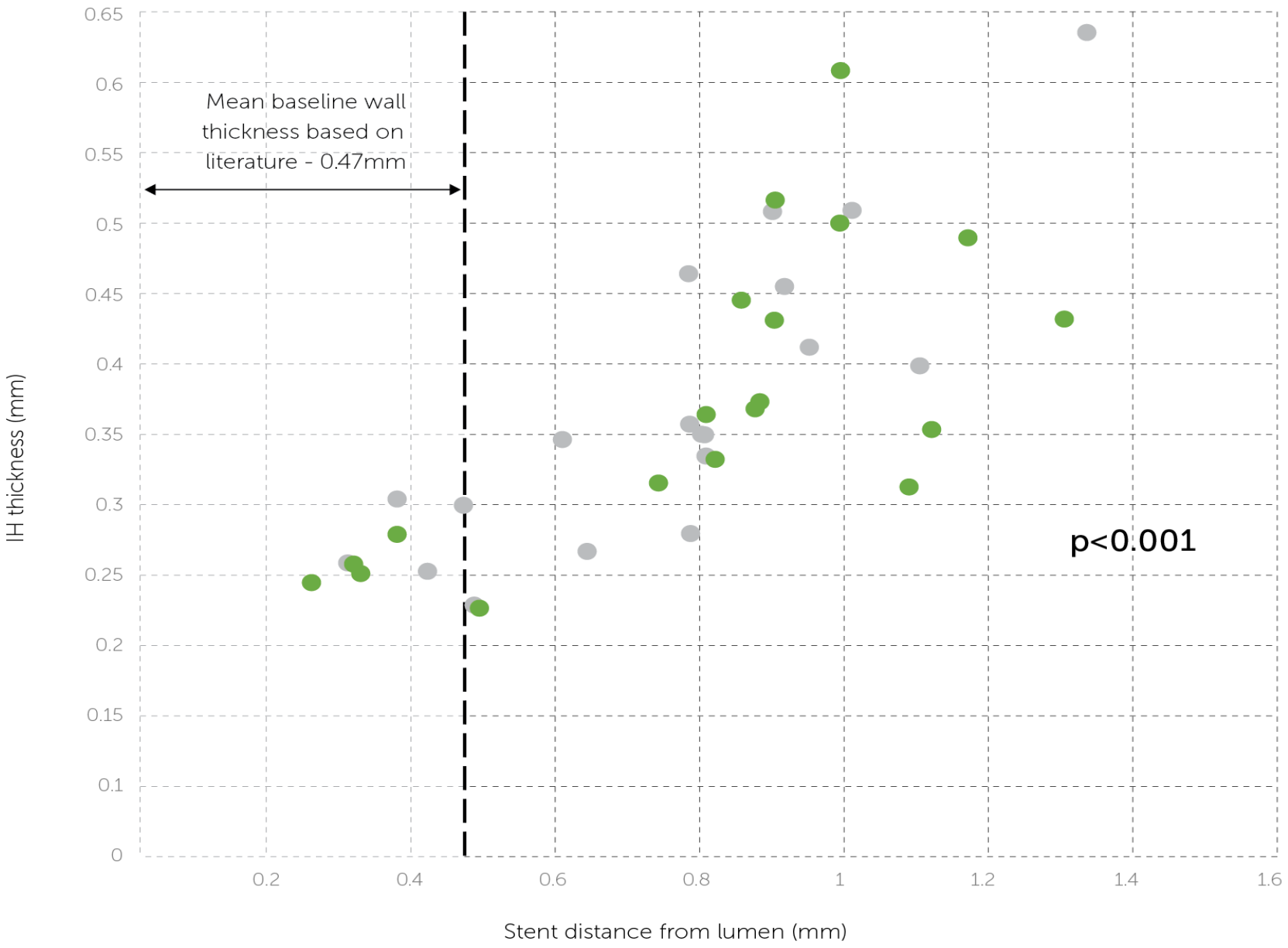
STENT: **red arrow**

INTIMA: blue

WALL THICKNESS: **yellow**

NEOADVENTITIA: **green**

VEST IV IH and WALL THICKNESS INCREASE WITH LOOSE FITTING STENTS



THE OXFORD VEST STUDIES

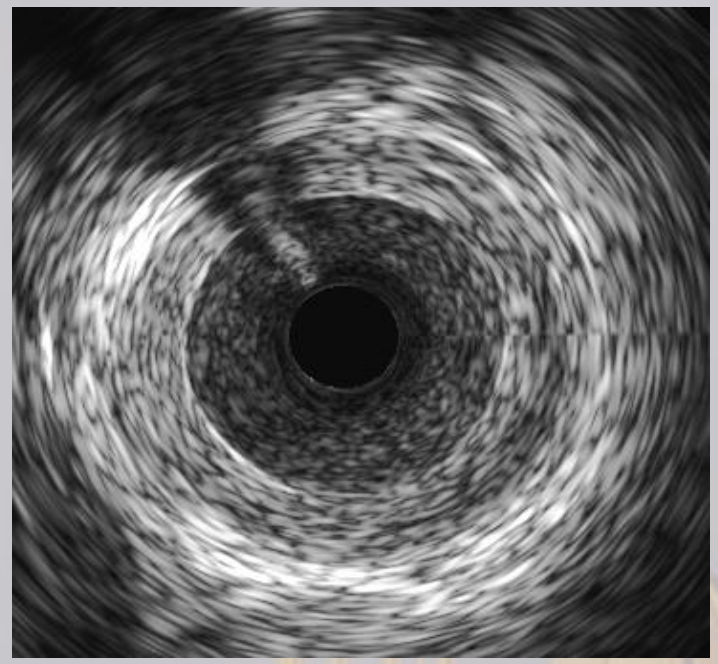
	N	STUDY	Primary Outcome	Status
VEST I	30	First in man RCT	IH, OCT, flow dynamic and patency @ 1 year	Published ATS 2015
VEST II	30	Stent patency to SVG to RCA	Patency @ 6 months	Published EJCTS 2017
VEST III	180	2nd RCT (multicentre European RCT)	Perfect patency + IVUS @ 6 months and 2 yrs	Interimanalyses AATS 2018; Final results 2020
VEST IV	21	5 year outcome of VEST I	Perfect patency on angio at 5 yrs and IH	Published JCTS 2018

- Currently VEST stent is CE marked and has been implanted in >2300 patients in Europe
- FDA Approved RCT in North America by CTS network: started Jan 2018 224/224 patients recruited Jan 2019 (same design as VEST I)

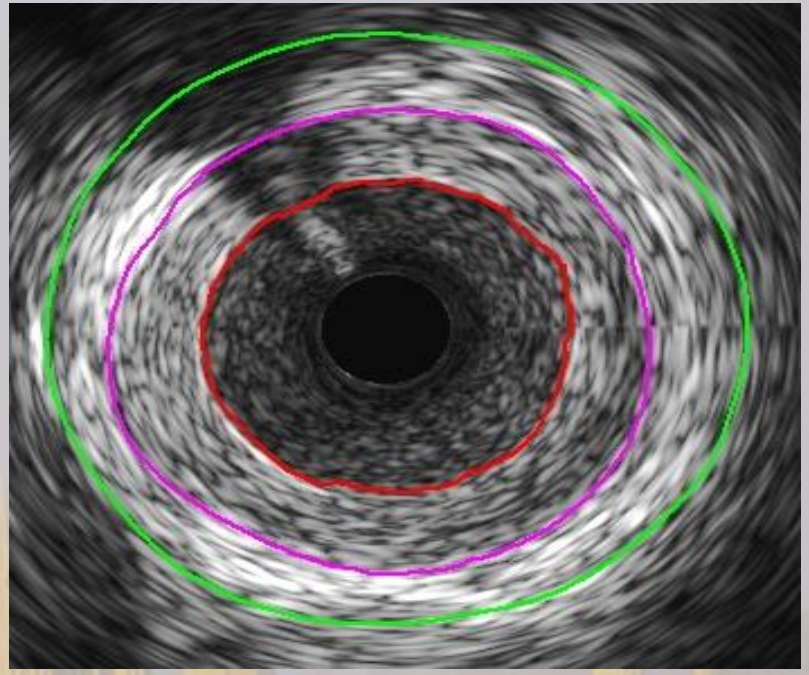
Summary and Conclusions

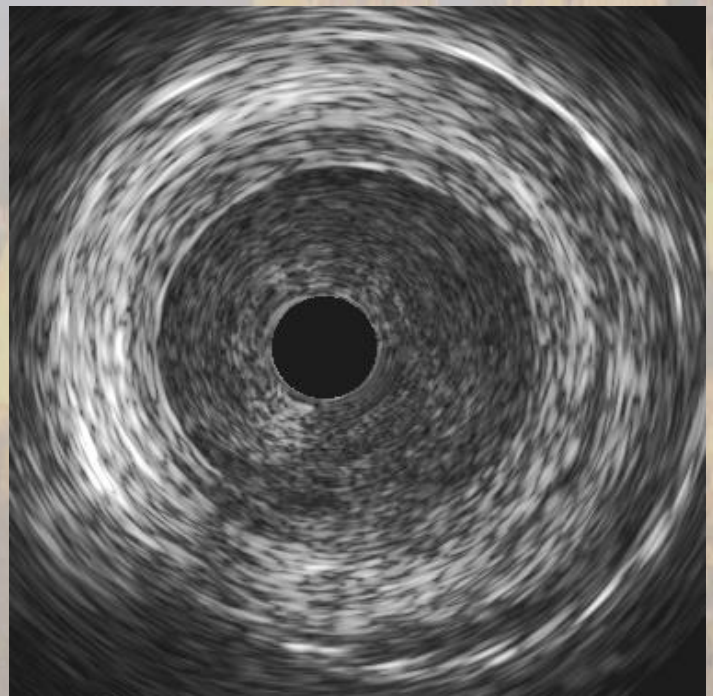
- ✓ *80% of all CABG grafts are SVG; failure is still a major limitation*
- ✓ *VEST I: Overall VEST had much superior patency to previous external stents but unexpectedly high failure rate to RCA*
- ✓ *At one year External Stenting reduces intimal hyperplasia, and improves perfect SVG patency, flow haemodynamics and OCT findings*
- ✓ *VEST II: Superior patency of SVG to RCA when NO metal clips and NO fixation of the proximal or distal anastomoses*
- ✓ *VEST III: 180 patient RCT – enrolment completed Jan 2017: interim analysis of first 90 patients showed 90% patency at 6 months*
- ✓ *VEST IV: External stent preserves perfect patency @ 5years*
- ✓ ***Can External Stenting improve SVG patency @ 10-15 years ?***

VEST IV

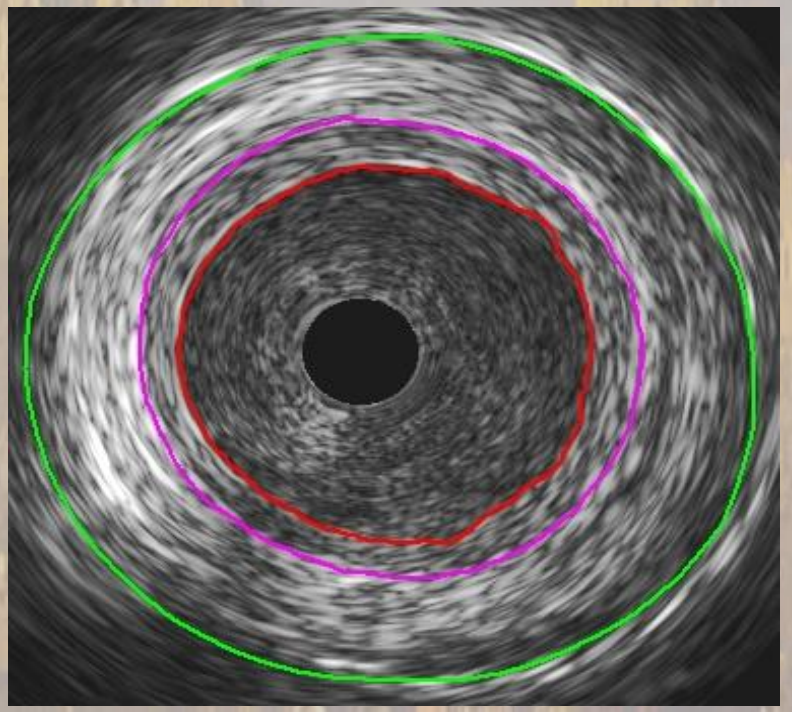


NO STENT

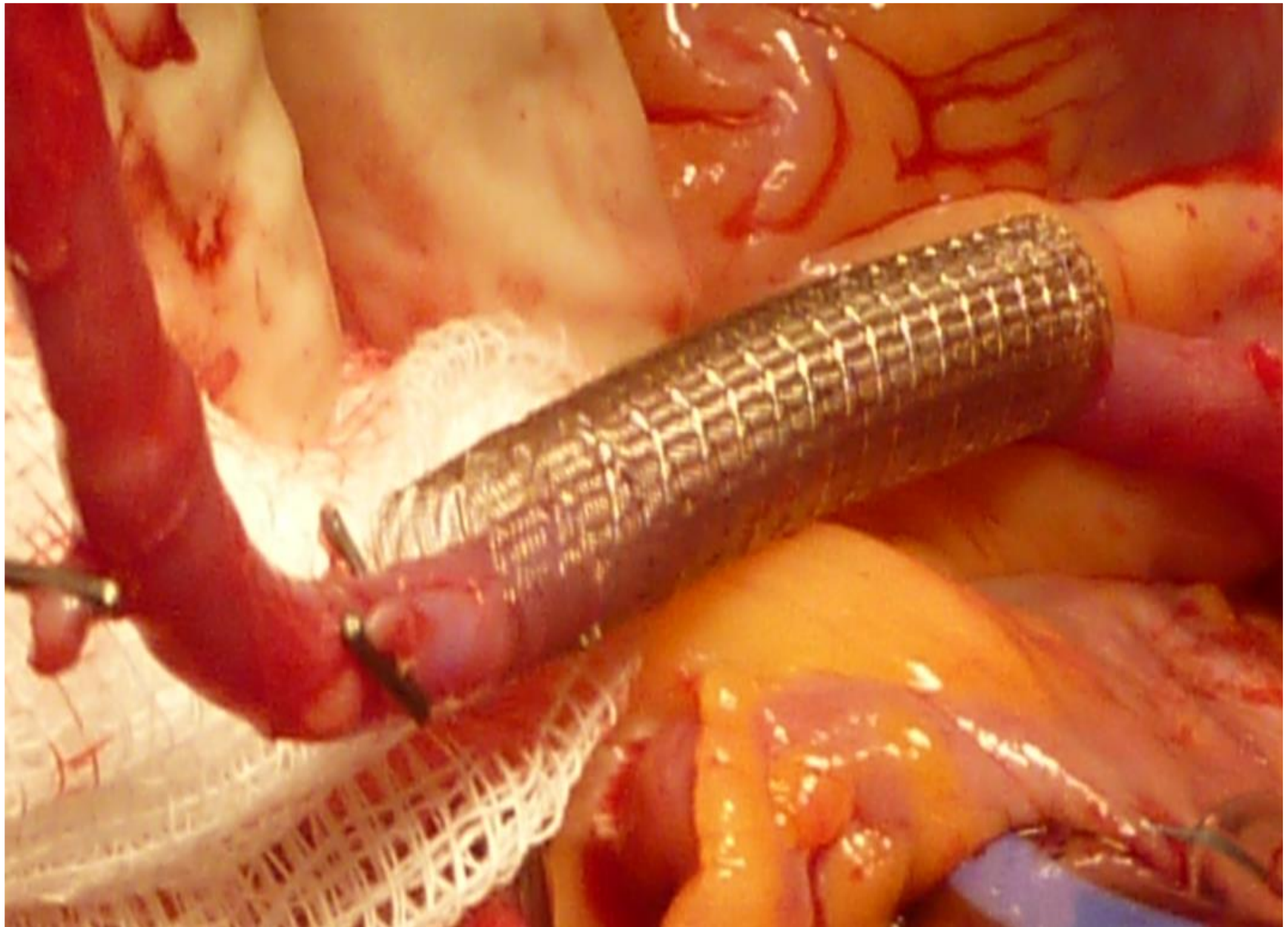




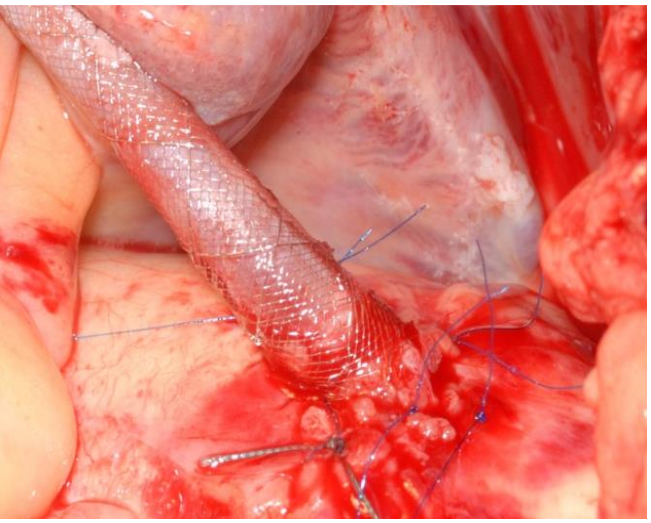
STENT

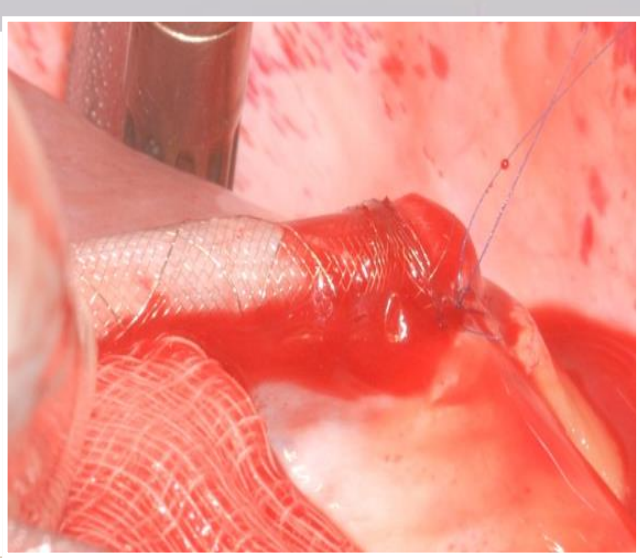


Mistake 1: Metal Clips Inside the STENT



Mistake 2
Fixating VEST to the anastomoses





Failure of stented SVG was higher on the right than left side despite excellent intraoperative flows with TTFM

Kinking of the anastomoses after chest closure ?

VEST III (Interim Analysis)

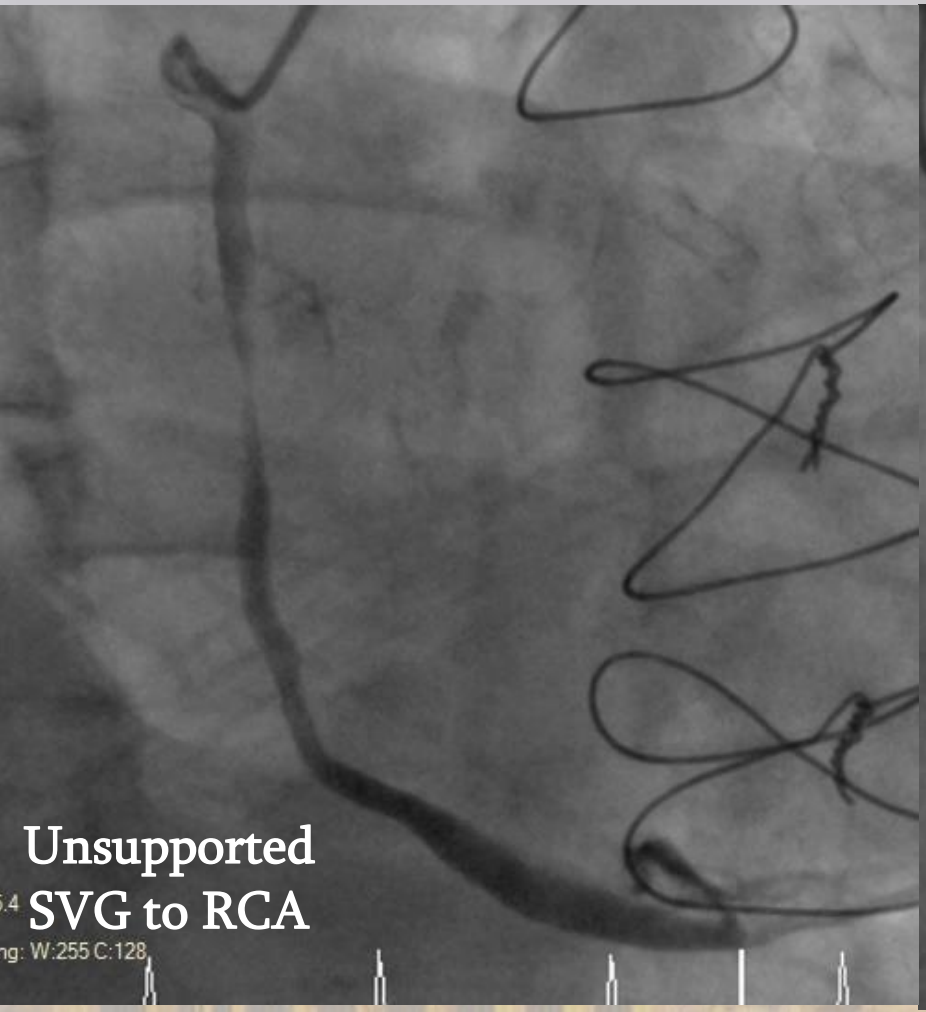
- 180 patient RCT: Enrolment Complete January 2017
- Same method as VEST I (IMA + SVG x2 (one with stent)
- Primary end point: Perfect angiographic patency at 2 years
- Secondary end point: CT angio at 6 months and IVUS at 2 yrs

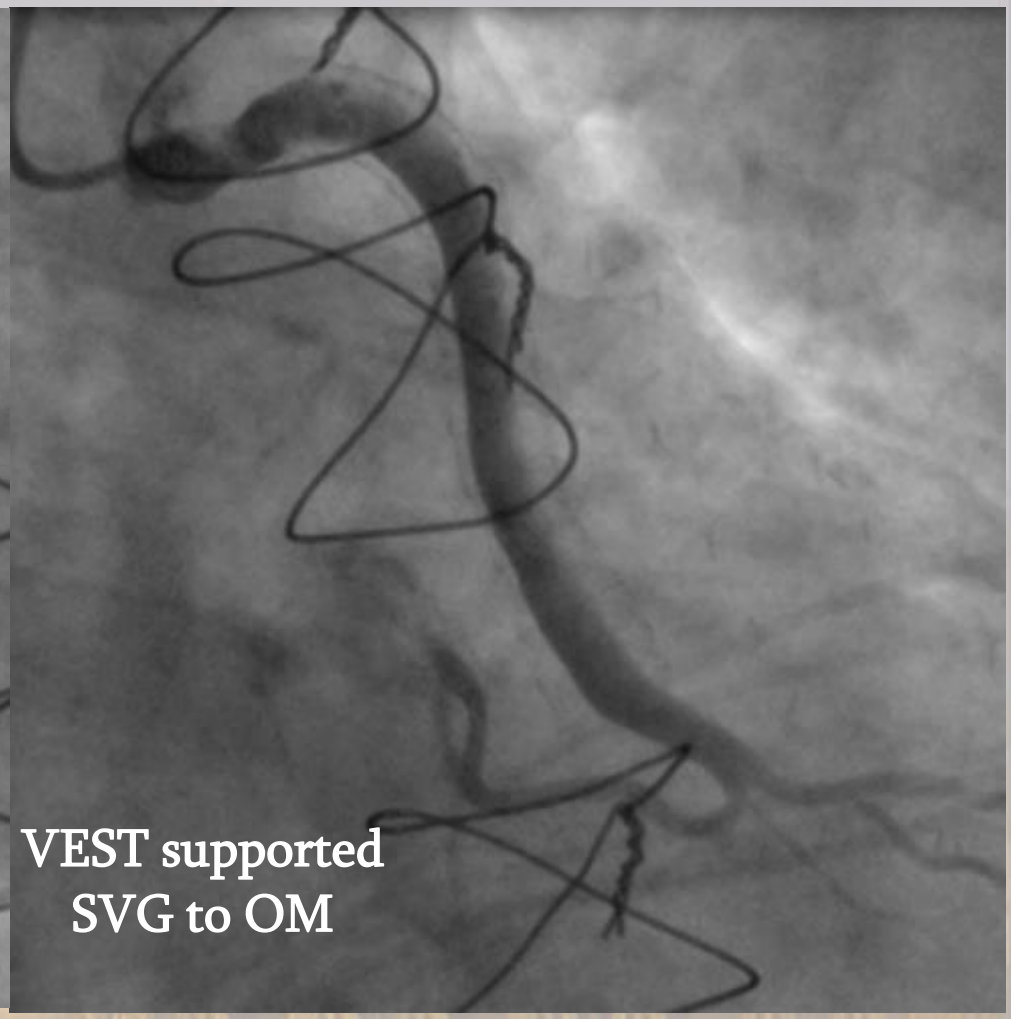
- **Interim analysis of Angiographic Patency:**
- **first 90 patients @ 6 months (AATS 2017)**
- **Patency: 90% both stented and nonstented groups**

Universitätsklinikum Essen AöR	DE
Krankenhaus der Barmherzigen Brüder Trier	DE
Universitätsklinikum Schleswig-Holstein - Campus Lübeck	DE
German Heart Centre Berlin	DE
Immanuel Klinikum Bernau Herzzentrum	DE
University Magdeburg	DE

John Radcliffe hospital	UK
Blackpool Victoria hospital	UK
Papworth hospital	UK
Bristol Heart Institute	UK
Southhampton General hospital	UK
Sheba MC	IL
Rambam MC	IL
Assuta MC	IL
Medical University of Vienna,	AS

VEST III





VEST III patient, returned with chest pain 7 months after CABG

CTSN
CARDIOTHORACIC SURGICAL TRIALS network

VGS

CD0131 VEST STUDY

DESIGNED TO SUPPORT FDA PRE MARKET APPROVAL APPLICATION

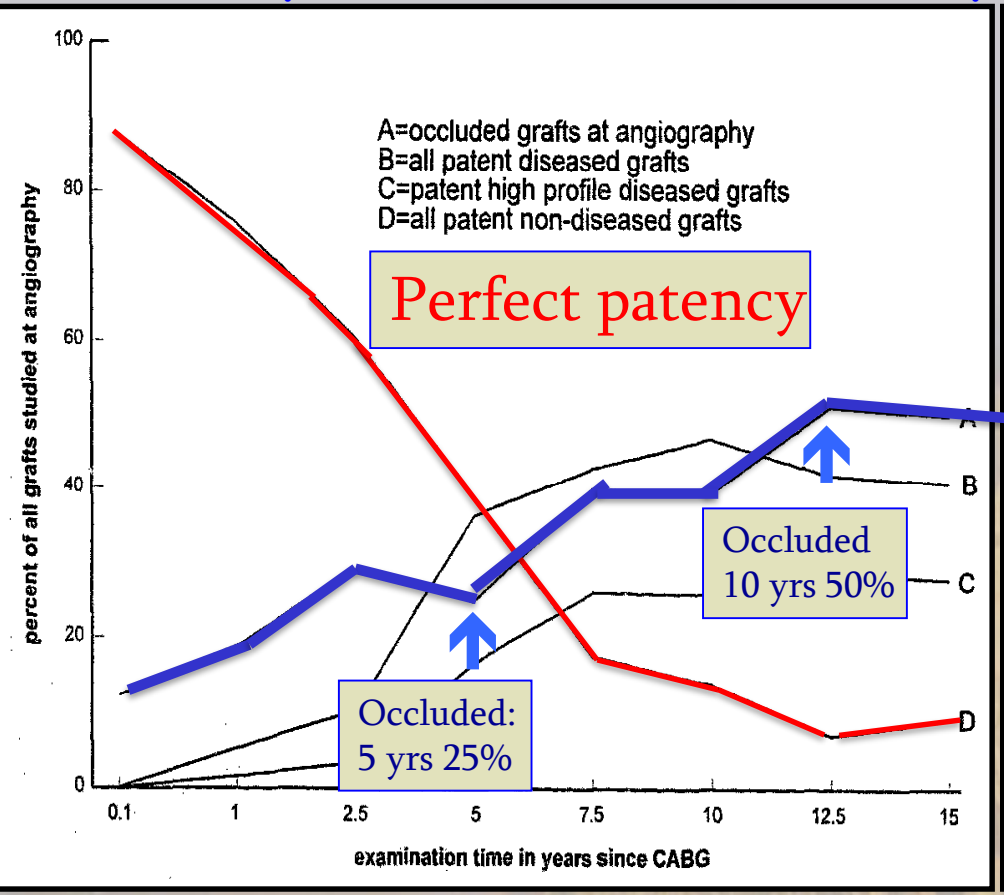
PIVOTAL TRIAL:
PIs Drs Puskas and Goldstein
224 patients
Enrolment now completed

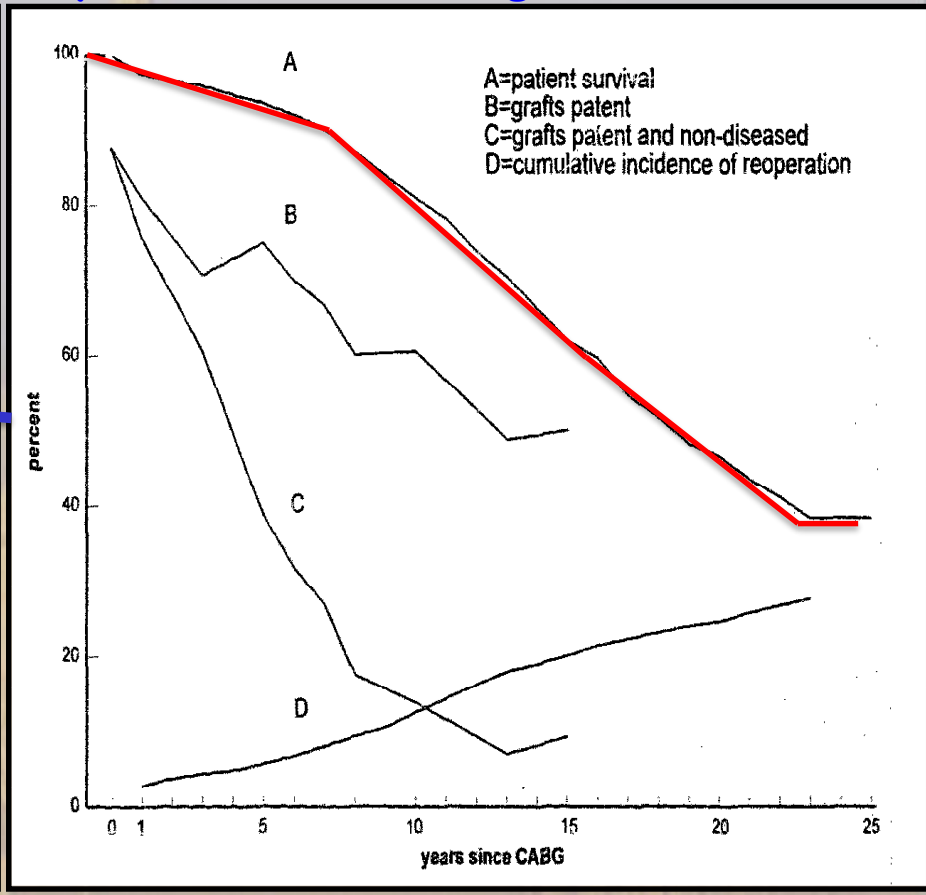
Coronary Bypass Graft Fate and Patient Outcome: Angiographic Follow-Up of 5,065 Grafts Related to Survival and Reoperation in 1,388 Patients During 25 Years

[JACC 1996]

GERALD M. FITZGIBBON, LRCP&S(IRELAND), FACC, HENRYK P. KAFKA, MD, FACC, ALAN J. LEACH, MD, FRCPC, WILBERT J. KEON, MD, FACC, G. DAVID HOOPER, MD, FACC,† JEFFREY R. BURTON, MD, FACC

In current practice of > 1 million CABG per year > 80% of all grafts are SVG





While some contemporary studies show much superior vein graft patency the largest angiographic studies (PREVENT IV, RADIAL) shows similar inferior patency

4 Promising Interventions to Improve SVG Patency

1) 'No touch' harvest technique
2) Buffered storage solutions for SVG after harvest
3) Composite SVG from ITA
4) SVG External Stents

Ben-Gal et al. Journal of Cardiothoracic Surgery 2013, 8:122
http://www.cardiothoracicsurgery.org/content/8/1/122

JOURNAL OF CARDIOTHORACIC SURGERY

RESEARCH ARTICLE Open Access

Expandable external support device to improve Saphenous Vein Graft Patency after CABG

Yanai Ben-Gal[1*], David P Taggart[2], Mathew R Williams[3], Eyal Orion[4], Gideon Uretzky[1], Rona Shofti[5], Shmuel Banai[1], Liad Yosef[4] and Gil Bolotin[5]

Abstract

Objectives: Low patency rates of saphenous vein grafts remain a major predicament in surgical revascularization. We examined a novel expandable external support device designed to mitigate causative factors for early and late graft failure.

Methods: For this study, fourteen adult sheep underwent cardiac revascularization using two vein grafts for each; one to the LAD and the other to the obtuse marginal artery. One graft was supported with the device while the other served as a control. Target vessel was alternated between consecutive cases. The animals underwent immediate and late angiography and were then sacrificed for histopathologic evaluation.

Results: Of the fourteen animals studied, three died peri-operatively (unrelated to device implanted), and ten survived the follow-up period. Among surviving animals, three grafts were thrombosed and one was occluded, all in the control group ($p = 0.043$). Quantitative angiographic evaluation revealed no difference between groups in immediate level of graft uniformity, with a coefficient-of-variance (CV%) of 7.39 in control versus 5.07 in the supported grafts, $p = 0.082$. At 12 weeks, there was a significant non-uniformity in the control grafts versus the supported grafts ($CV = 22.12$ versus 3.01, $p < 0.002$). In histopathologic evaluation, mean intimal area of the supported grafts was significantly lower than in the control grafts (11.2 mm^2 versus 23.1 mm^2 $p < 0.02$).

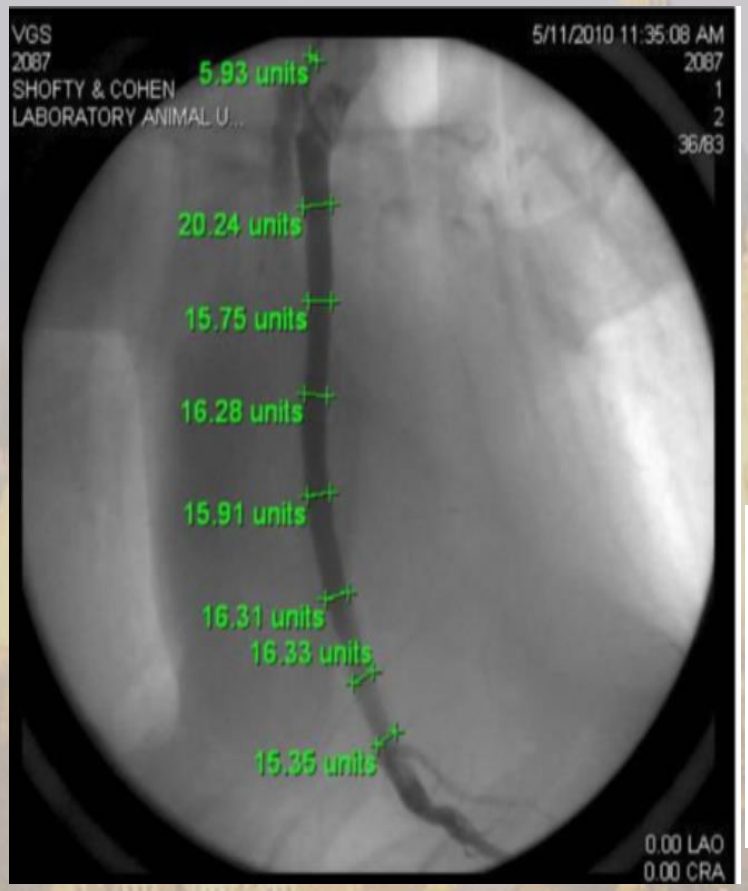
Conclusions: The expandable SVG external support system was found to be efficacious in reducing SVG's non-uniform dilatation and neointimal formation in an animal model early after CABG. This novel technology may have the potential to improve SVG patency rates after surgical myocardial revascularization.

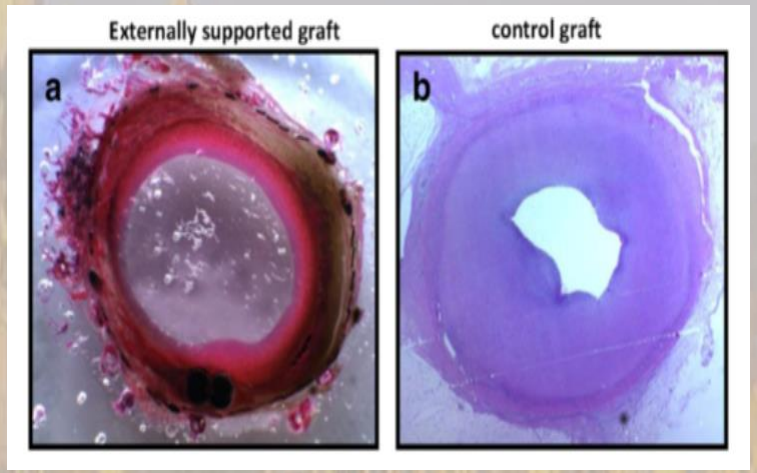
Expandable external support device to improve Saphenous Vein Graft Patency after CABG

[JCTS 2013]

Yanai Ben-Gal[1*], David P Taggart[2], Mathew R Williams[3], Eyal Orion[4], Gideon Uretzky[1], Rona Shofti[5], Shmuel Banai[1], Liad Yosef[4] and Gil Bolotin[5]

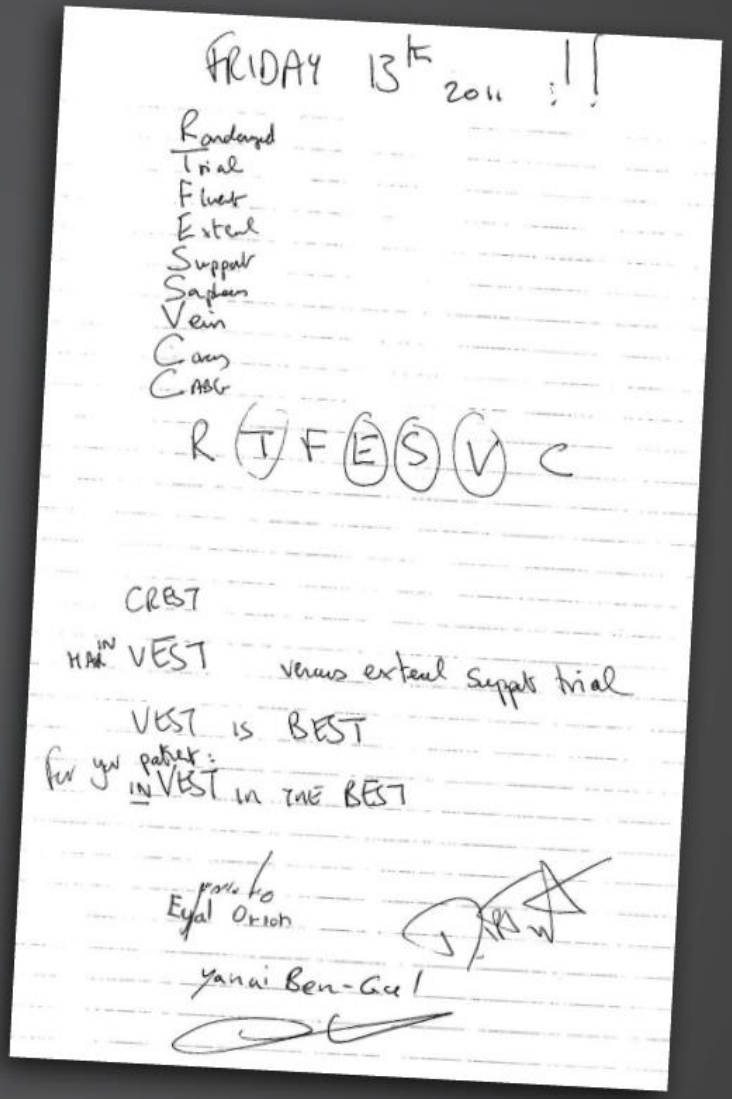
- 14 sheep implants: at 12 weeks control angiography + autopsy





- ✓ **Diameter:** Control SVG increased 200%, Stented SVG decreased 40% ($p<0.002$)
- ✓ **Neointimal Area:** 23 mm^2 control graft v 11 mm^2 supported grafts ($p<0.02$)
- ✓ **Occlusion:** 4 control grafts (3 with thrombus)

Venous External Support Trial



A Randomized Trial of External Stenting for Saphenous Vein Grafts in Coronary Artery Bypass Grafting

ADULT CARDIAC

External stenting significantly reduces intimal hyperplasia by 20%, 1 year after CABG (p<0.05)

Taggart et al. Ann Thorac Surg 2015;99:2039-45

51 YEARS AGO: First SYSTEMATIC report of SVG for CABG

Saphenous Vein Autograft Replacement of Severe Segmental Coronary Artery Occlusion

Operative Technique

ATS [Apr 1968]

Rene G. Favaloro, M.D.

CURRENT CABG

- @ 1 million CABG performed worldwide each year
- 150,000 CABG in USA (69 % of operations in STS database)
- 80% of all bypass grafts are vein grafts (despite much superior angiographic patency of arterial grafts)