ICCA STROKE 2019

WIST

UPDATE ON CAROTID STENT TRIALS

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DISCLOSURE STATEMENT OF FINANCIAL INTEREST

Within the past 12 months, I or my spouse/ partner have not had a financial interest/ arrangement or affiliation with any organization

AFFILIATION/FINANCIAL RELATIONSHIP	COMPANY
• Grant/Research Support	• None
• Consulting Fees/Honoraria	
• Major Stock Shareholder/Equity	
• Royalty Income	
• Ownership/Founder	
• Intellectual Property Rights	
• Other Financial Benefit	

DISCLOSURE STATEMENT OF FINANCIAL INTEREST

I, (Kavita Vani) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Why do we need any more trials?

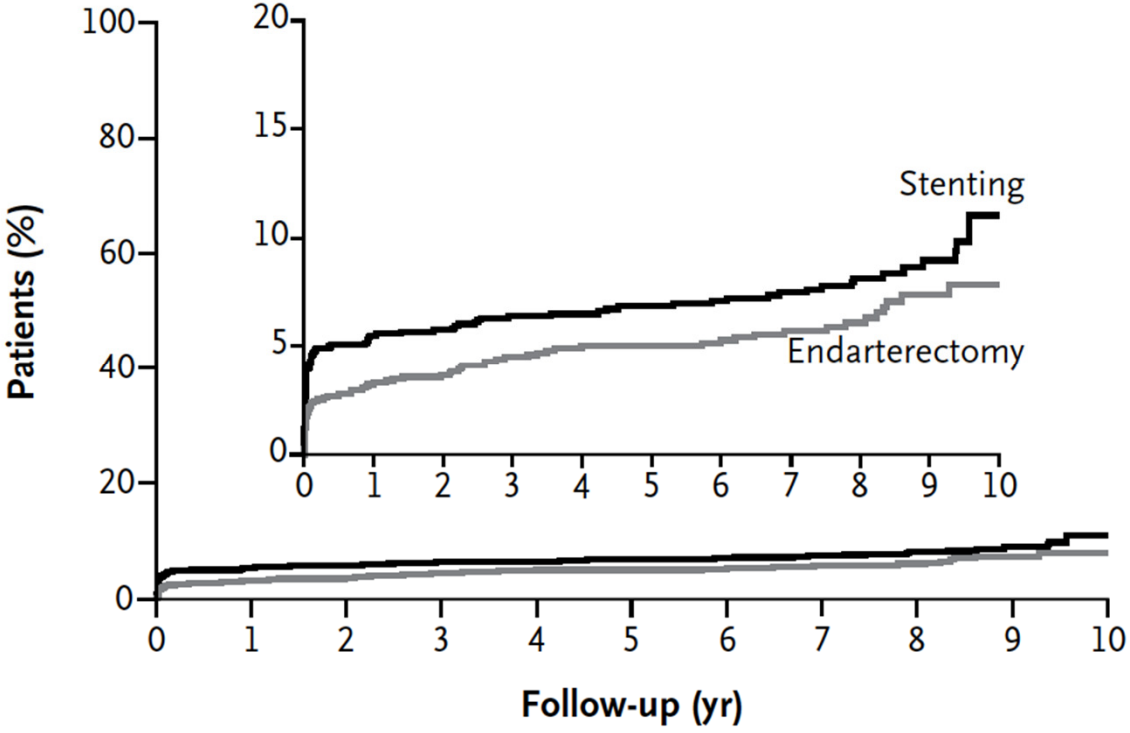
Question

- At *10-year* follow-up in CREST, the combined *stroke and death* rate was:
  - A. Significantly *lower in the CEA* compared to the CAS group
  - B. The *same* in the CAS and CEA group
  - C. Significantly *higher in the CEA* compared to the CAS group

  - Ans: A

CREST

- Periprocedural stroke or death and subsequent ipsilateral stroke
  - 11.9% versus 7.9% (HR 1.37 p=0.04)



Rosenfield et al. NEJM March 2016 Vol 374 No. 11

Question

- In CREST, at *latest reported follow-up*, compared with CEA, the MI rate with CAS was:

- Ans LOWER

CREST: Initial follow-up

End Point	Periprocedural Period				
	CAS (N=1262)	CEA (N=1240)	Absolute Treatment Effect of CAS vs. CEA (95% CI)	Hazard Ratio for CAS vs. CEA (95% CI)	P Value
	no. of patients (% ±SE)		*percentage points*		
Death	9 (0.7±0.2)	4 (0.3±0.2)	0.4 (−0.2 to 1.0)	2.25 (0.69 to 7.30)†	0.18†
Stroke					
Any	52 (4.1±0.6)	29 (2.3±0.4)	1.8 (0.4 to 3.2)	1.79 (1.14 to 2.82)	0.01
Major ipsilateral	11 (0.9±0.3)	4 (0.3±0.2)	0.5 (−0.1 to 1.2)	2.67 (0.85 to 8.40)	0.09
Major nonipsilateral‡	0	4 (0.3±0.2)	NA	NA	NA
Minor ipsilateral	37 (2.9±0.5)	17 (1.4±0.3)	1.6 (0.4 to 2.7)	2.16 (1.22 to 3.83)	0.009
Minor nonipsilateral	4 (0.3±0.2)	4 (0.3±0.2)	0.0 (−0.4 to 0.4)	1.02 (0.25 to 4.07)	0.98†
Myocardial infarction	14 (1.1±0.3)	28 (2.3±0.4)	−1.1 (−2.2 to −0.1)	0.50 (0.26 to 0.94)	0.03

Brott et al. N Engl J Med 2010;363:11-23.

CREST data is not unique…

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Carotid Artery Stenting Versus Endarterectomy for Stroke Prevention

A Meta-Analysis of Clinical Trials

Partha Sardar, MD,[a] Saurav Chatterjee, MD,[b] Herbert D. Aronow, MD,[c] Amartya Kundu, MD,[d] Preethi Ramchand, MD,[e] Debabrata Mukherjee, MD,[f] Ramez Nairooz, MD,[g] William A. Gray, MD,[h] Christopher J. White, MD,[i] Michael R. Jaff, DO,[j] Kenneth Rosenfield, MD,[j] Jay Giri, MD[k,l]

Sardar et al. JACC 2017

JACC 2017 meta-analysis

Trials	Total Patients (CAS/CEA)*	Follow-Up Duration (Median yrs)	Recruitment Period	Use of EPD (%)	Asymptomatic Patients (%)
ACT I 2016	1,089/364	5.0	2005–2013	Yes (97.8)	100.0
CREST 2010 and 2016†	1,262/1,240	7.4	2000–2008	Yes (96.1)	47.2
EVA-3S 2006 and 2014	265/262	7.1	2000–2005	Yes (91.9)	0.0
ICSS 2010 and 2015‡	853/857	4.2	2001–2008	Yes (70.7)	0.0
SAPPHIRE 2004 and 2008	167/167	3.0	2000–2002	Yes (95.6)	72.3

Sardar et al. JACC 2017

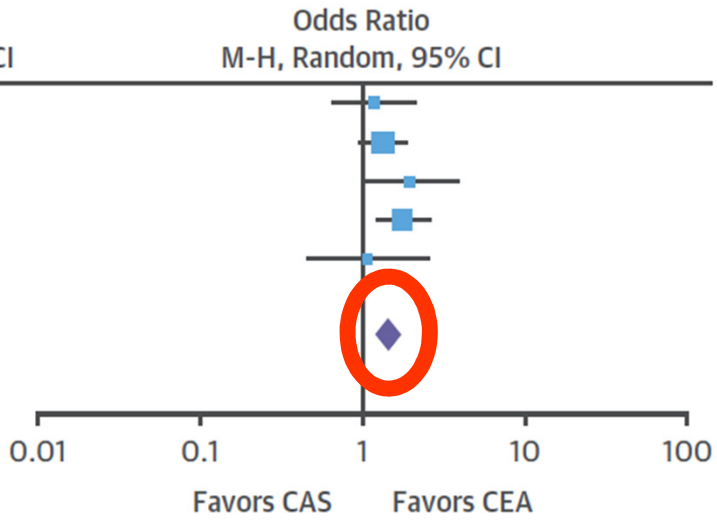
JACC 2017 meta-analysis

Risk of stroke

Study or Subgroup	CAS Events	CAS Total	CEA Events	CEA Total	Weight	Odds Ratio M-H, Random, 95% CI
ACT I 2016	54	1089	15	364	12.1%	1.21 [0.68, 2.18]
CREST 2016	94	1262	70	1240	40.6%	1.35 [0.98, 1.85]
EVA-3S 2014	29	265	15	262	9.9%	2.02 [1.06, 3.87]
ICSS 2015	86	853	50	857	31.6%	1.81 [1.26, 2.60]
SAPPHIRE 2008	12	167	11	167	5.8%	1.10 [0.47, 2.56]
Total (95% CI)		3636		2890	100.0%	1.50 [1.22, 1.84]
Total events	275		161			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.32$, df = 4 (P = 0.51); $I^2 = 0\%$

Test for overall effect: Z = 3.91 (P < 0.0001)



Sardar et al. JACC 2017

JACC 2017 meta-analysis

TABLE 3 Absolute Risk Metrics of Outcomes of Major Interest

Outcome of Interest	Number of Events/Patients (Absolute Event Rate, %)		NNT/NNH for CAS	p Value
	CAS Group	CEA Group		
Aggregate efficacy/safety outcome*	295/3,636 (8.1)	218/2,890 (7.5)	–	0.14
Periprocedural any stroke + nonperiprocedural ipsilateral stroke	275/3,636 (7.6)	161/2,890 (5.6)	50 (NNH)	<0.001
Periprocedural any stroke	169/3,636 (4.6)	73/2,890 (2.5)	47 (NNH)	<0.001
Periprocedural minor stroke	124/3,636 (3.4)	44/2,890 (1.5)	52 (NNH)	<0.001
Periprocedural death	26/3,636 (0.7)	16/2,890 (0.5)	–	0.48
Periprocedural MI	24/3,636 (0.6)	48/2,890 (1.6)	99 (NNT)	0.002
Periprocedural CN palsy	9/3,636 (0.2)	135/2,890 (4.7)	22 (NNT)	<0.001
Periprocedural neurological injury	178/3,636 (4.9)	208/2,890 (7.2)	43 (NNT)	0.02
Periprocedural neck hematoma	20/3,469 (0.6)	53/2,723 (1.9)	73 (NNT)	<0.001
Composite periprocedural safety outcome†	224/3,636 (6.2)	263/2,890 (9.1)	34 (NNT)	0.008
Long-term stroke in any territory (includes periprocedural stroke)	305/3,636 (8.4)	200/2,890 (6.9)	68 (NNH)	<0.001
Long-term death	429/3,636 (11.8)	357/2,890 (12.3)	–	0.18

Sardar et al. JACC 2017

CREST data is not unique…

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Carotid Artery Stenting Versus

CONCLUSIONS CAS and CEA were associated with similar rates of a composite of periprocedural death, stroke, MI, or nonperiprocedural ipsilateral stroke. The risk of long-term overall stroke was significantly higher with CAS and was mostly attributed to periprocedural minor stroke. CAS was associated with lower rates of periprocedural MI and cranial nerve palsy than CEA. (J Am Coll Cardiol 2017;69:2266–75) © 2017 by the American College of Cardiology Foundation.

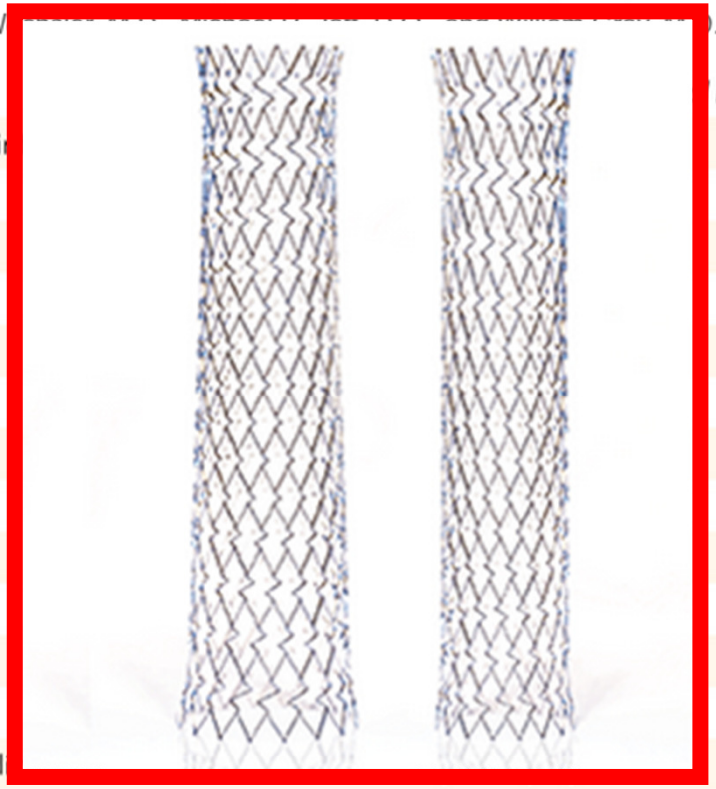
Preethi Ramchand, MD,[e] Debabrata Mukherjee, MD,[f] Ramez Nairooz, MD,[g] William A. Gray, MD,[h]
Christopher J. White, MD,[i] Michael R. Jaff, DO,[j] Kenneth Rosenfield, MD,[j] Jay Giri, MD[k,l]

Sardar et al. JACC 2017

ORIGINAL ARTICLE

Randomized Trial of Stent versus Surgery for Asymptomatic Carotid Stenosis

Kenneth Rosenfield, M.D., M.H.C.D.S., Jon S. Matsumura, M.D., Seemant Chaturvedi, M.D., Tom Riles, M.D., Gary M. Ansel, M.D., D. Chris Metzger, M.D., Lawrence W[illegible]. for the ACT I Investigators*



		no. (%)	
Death, stroke, or myocardial i[illegible]		9/348 (2.6)	0.60
Death or stroke		6/348 (1.7)	0.33
Death or major stroke		2/348 (0.6)	1.00
Death		1/348 (0.3)	0.43
All stroke		5/348 (1.4)	0.23
Major stroke		1/348 (0.3)	1.00
Ipsilateral		1/348 (0.3)	1.00
Nonipsilateral		0/348	1.00
Minor stroke		4/348 (1.1)	0.20
Ipsilateral		4/348 (1.1)	0.36
Nonipsilateral		0/348	0.58
Myocardial infarction		3/348 (0.9)	0.41
Composite measure of compl[illegible]		17/364 (4.7)	0.13
Cranial-nerve injury	1/1089 (0.1)	[illegible]	
Peripheral-nerve injury	0/1089		
Vascular injury	8/1089 (0.7)		
Noncerebral bleeding	21/1089 (1.9)		
Endarterectomy incision or puncture-site bleeding	3/1089 (0.3)		
Other complications	0/1089		

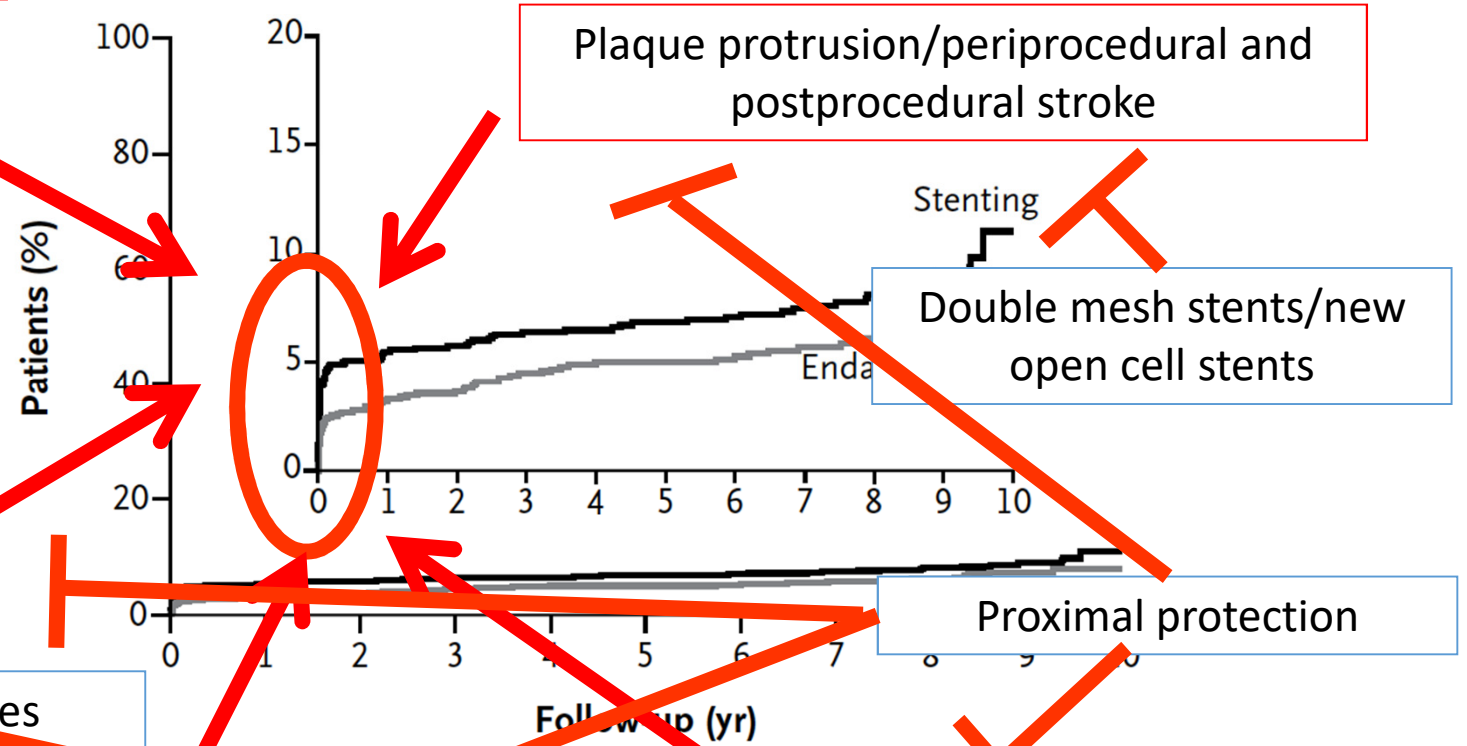
Why do we need any more trials?
Because
we can and must do better!
If we want to perform acute stroke intervention which has a demonstrated dramatic effect on neurologic outcome we need to become proficient with a procedure (CAS) the benefit of which compared to alternative (CEA) has not been conclusively shown

What prevents the more widespread use of carotid stenting?

Transcervical carotid access/radial access

Aortic arch manipulation

Plaque protrusion/periprocedural and postprocedural stroke



Double mesh stents/new open cell stents

Lesion crossing

Proximal protection

Smaller filter pores

Postdilatation

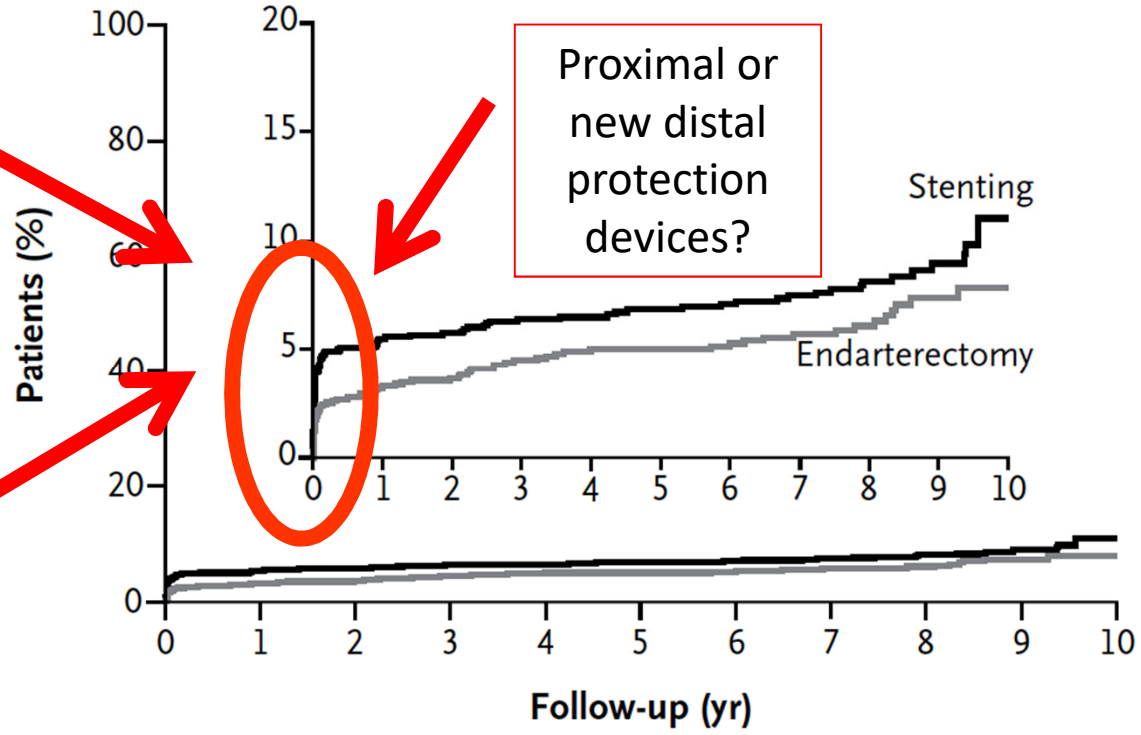
Filter pore size

What prevents the more widespread use of carotid stenting?

New stent design?

Proximal or new distal protection devices?

Antiplatelet therapy and high dose statins/PCSK 9?



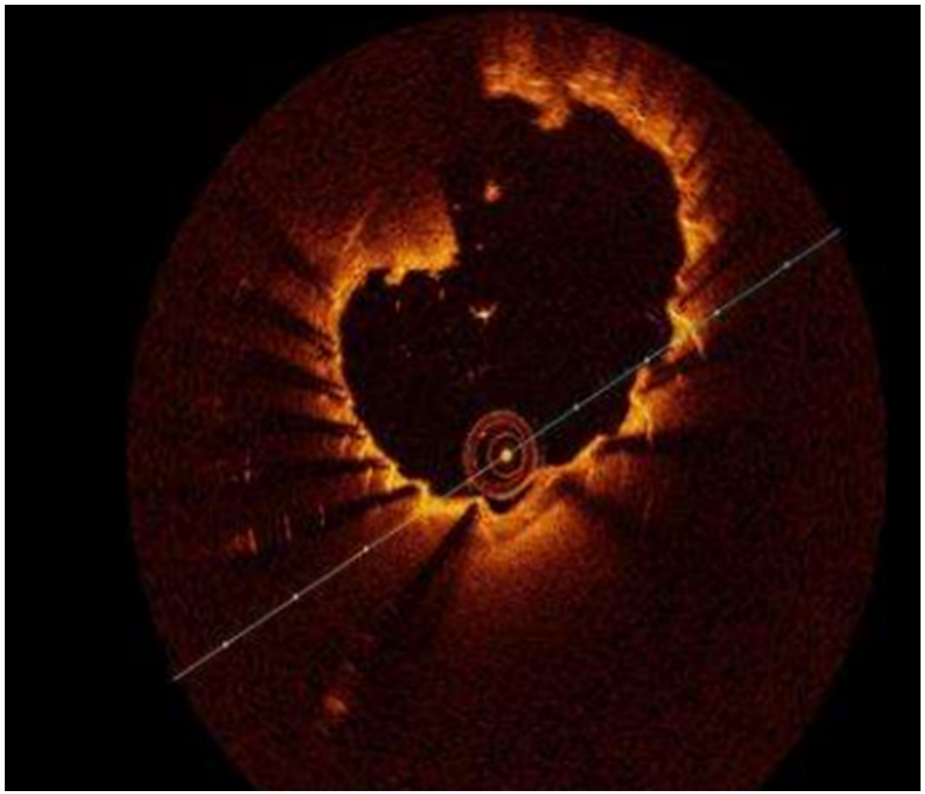
What causes periprocedural strokes?

- Plaque embolization during arch manipulation
  - Direct carotid access
  - Radial access (right)
  - Operator experience
- Plaque embolization during lesion crossing
  - Proximal protection
- Plaque embolization during balloon inflation and stent deployment
  - Stent design
  - Proximal and distal protection
- Plaque protrusion and embolization and thrombus formation after completion of the procedure
  - Stent design Open cell area >7.5mm^2 , timing
  - Antiplatelet therapy

Open cell design

- SPACE-1
- ICSS

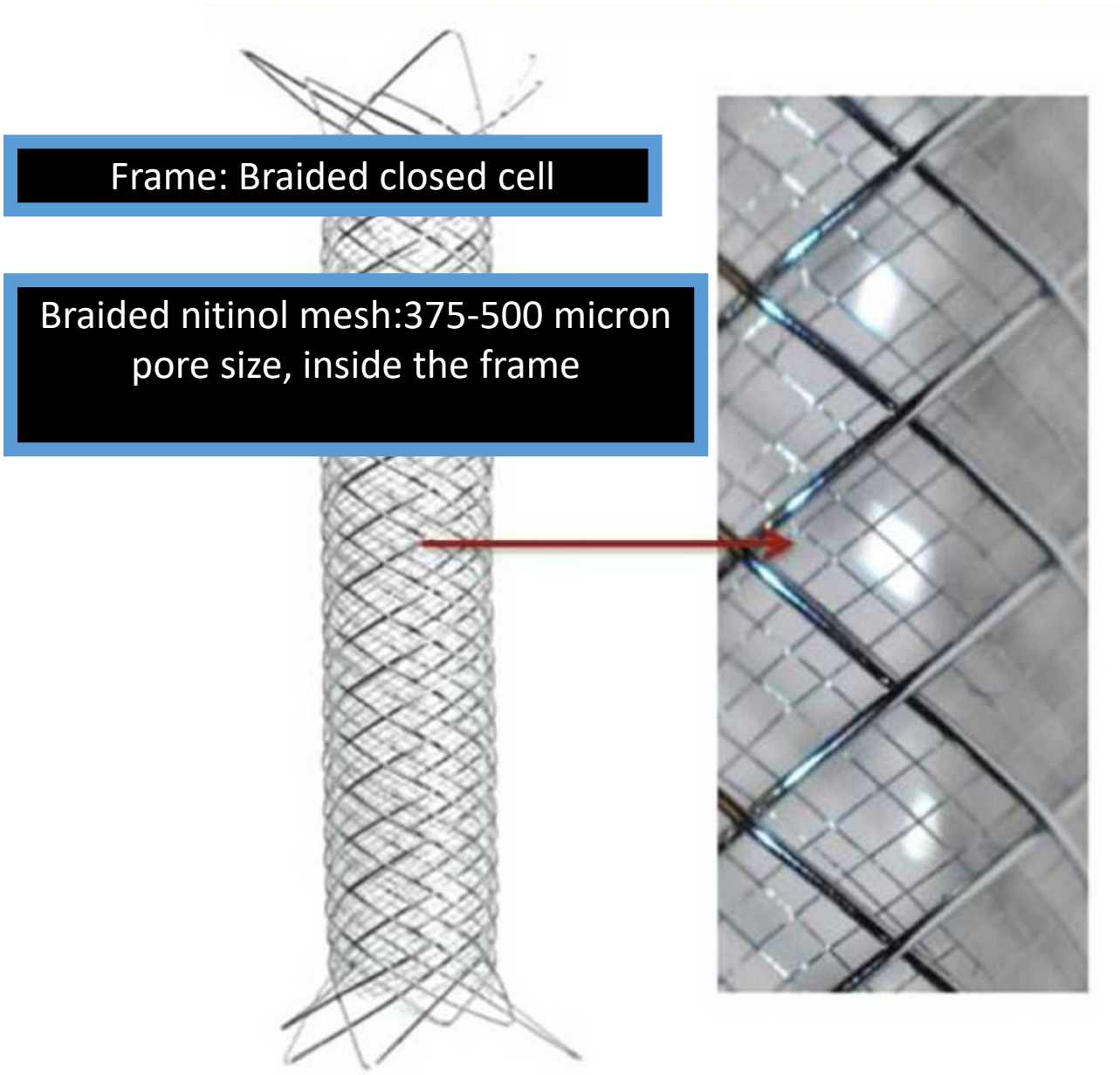
Plaque protrusion



Trials with new stent technology

- CAS with double layer stents
  - Roadsaver (Terumo)
  - CGUARD (InspireMD)
  - Gore Carotid stent (Gore)
- Open cell design with small cell area (MER-stent)
- CAS with hybrid stents
  - Cristallo Ideale (Medtronic)

Roadsaver


Frame: Braided closed cell
Braided nitinol mesh:375-500 micron pore size, inside the frame

Roadsaver

The CLEAR-ROAD study: evaluation of a new dual layer micromesh stent system for the carotid artery

Marc Bosiers[1]*, MD; Koen Deloose[1], MD; Giovanni Torsello[2], MD; Dierk Scheinert[3], MD; Lieven Maene[4], MD; Patrick Peeters[5], MD; Stefan Müller-Hülsbeck[6], MD, PhD; Horst Sievert[7], MD; Ralf Langhoff[8], MD; Michel Bosiers[2], MD; Carlo Setacci[9], MD

EuroIntervention 2016;11

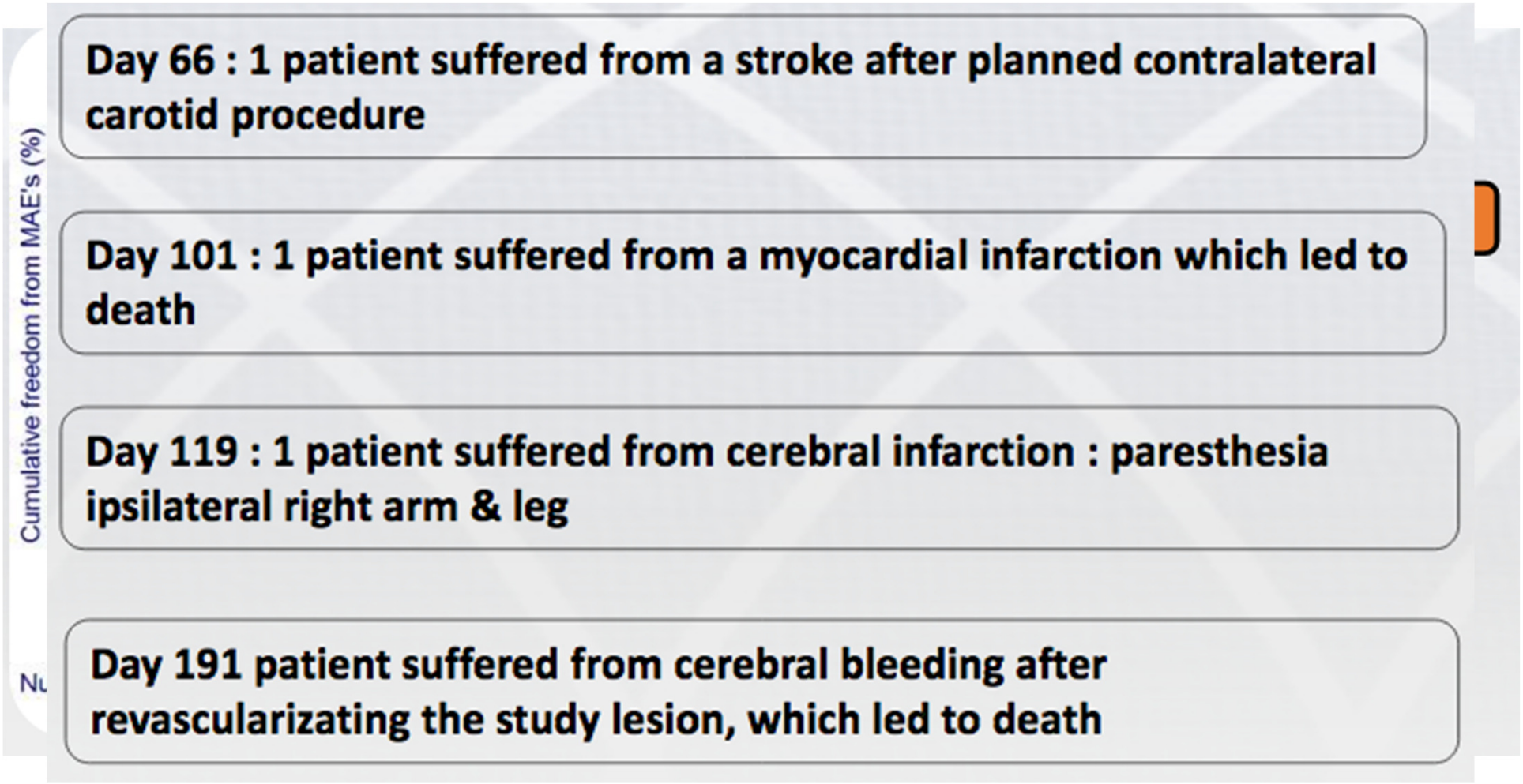
Trials with new technology

- Roadsaver
  - Prospective study
    - 100 pts, 31% symptomatic
    - EPD 58%
    - 30-day MAE 2.1% (1 MI->death, 1 [minor] stroke)

	N=100
Male *(%)*	70 *(70.0%)*
Age *(min – max; ±SD)*	73.44 *(47.78 – 89.12 ±9.55)*
Neurological Status: - Symptomatic (%) - Asymptomatic (%)	 31 *(31.0%)* 69 *(69.0%)*
Nicotine abuse* *(%) *former & current*	67 *(67.0%)*
Hypertension *(%)*	**80 *(80.0%)***
Diabetes mellitus *(%)*	31 *(31.0%)*
Hypercholesterolemia *(%)*	**74 *(74.0%)***
Obesity *(%)*	28 *(28.0%)*
Cerebrovascular disease *(%)*	24 *(24.0%)*

EuroIntervention 2016;11

CLEAR ROAD



Peters LINC 2017

Roadsaver

- Multicenter trial (3 centers in Italy)
- N=150
- Proximal protection 41%, distal protection 59%
- Technical success 100%
- 30-day stroke rate: 0%
- Plaque prolapse detected in 7.7% of patients
- Stent patency at 30 days by ultrasound 100%

Carotid artery stenting with a new-generation double-mesh stent in three high-volume Italian centres: clinical results of a multidisciplinary approach

Roberto Nerla[1]*, MD; Fausto Castriota[1], MD; Antonio Micari[1], MD, PhD;
Paolo Sbarzaglia[1], MD; Gioel Gabrio Secco[2], MD; Maria Antonella Ruffino[3], MD;
Gianmarco de Donato[4], MD; Carlo Setacci[4], MD; Alberto Cremonesi[1], MD

Eurointervention 2016;12:e677-683

Roadsaver

Mesh-covered (Roadsaver) stent as a new treatment modality for symptomatic or high-risk carotid stenosis

Roman Machnik[1], Piotr Paluszek[1], Łukasz Tekieli[2], Karolina Dzierwa[2], Damian Maciejewski[2], Mariusz Trystuła[1], Andrzej Brzychczy[1], Krzysztof Banaszkiewicz[3], Robert Musiał[4], Piotr Pieniążek[1]

- Single center study
- N=40
- Symptomatic stenosis in all
- Proximal protection in 27, distal in 14
- Technical success 100%
- One minor stroke (after carotid artery engagement)
- One TIA

Machnik et al. Adv Interv Cardiol 2017; 13, 2 (48): 130–134

Trials with new technology

Incidence of New Ischaemic Brain Lesions After Carotid Artery Stenting with the Micromesh Roadsaver Carotid Artery Stent: A Prospective Single-Centre Study

Maria Antonella Ruffino[1] · Riccardo Faletti[2] · Laura Bergamasco[3] · Paolo Fonio[2] · Dorico Righi[1]

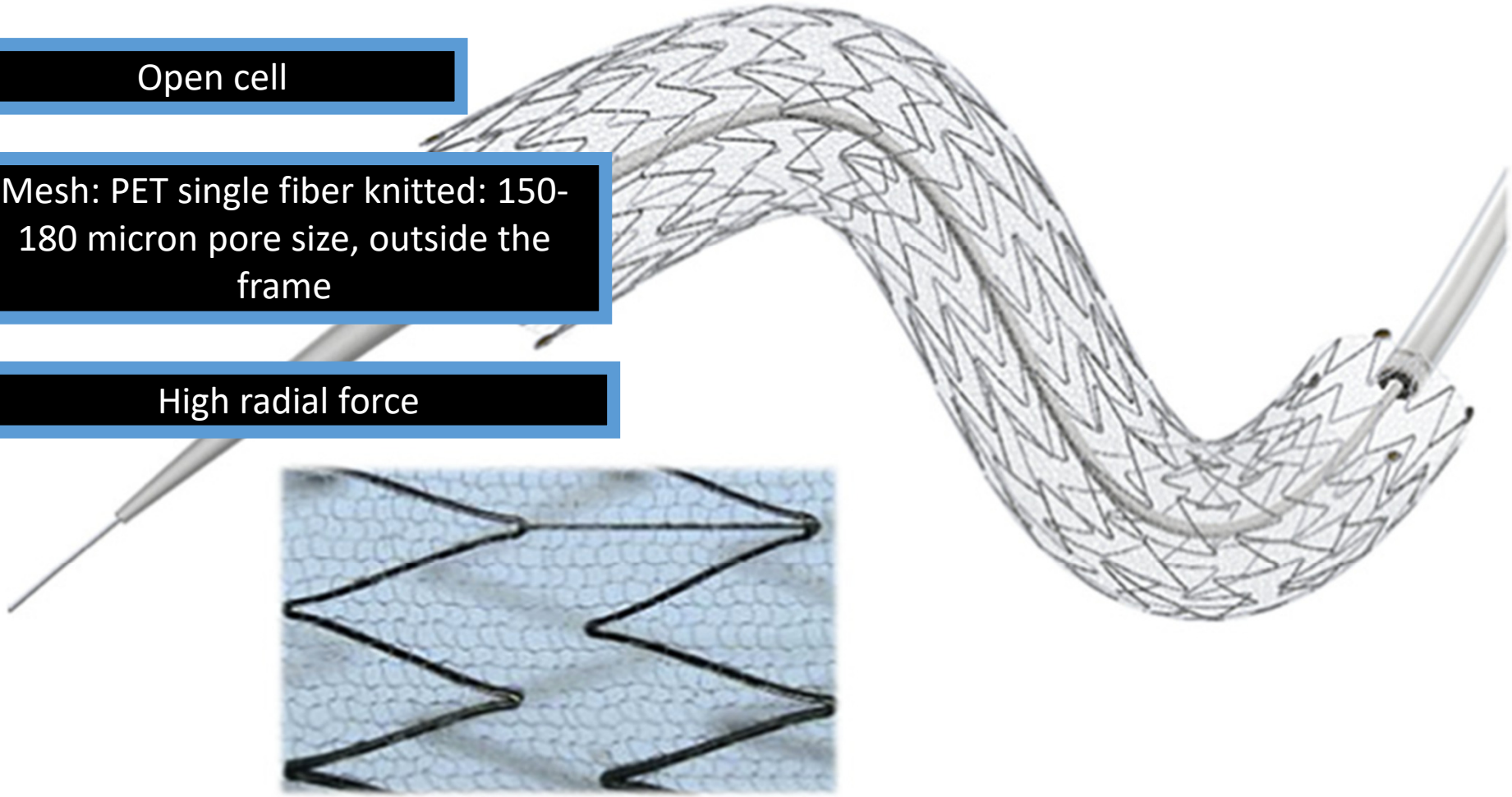
Ruffino et al. Cardiovasc Intervent Radiol (2016) 39:1541–1549

C-Guard

Open cell

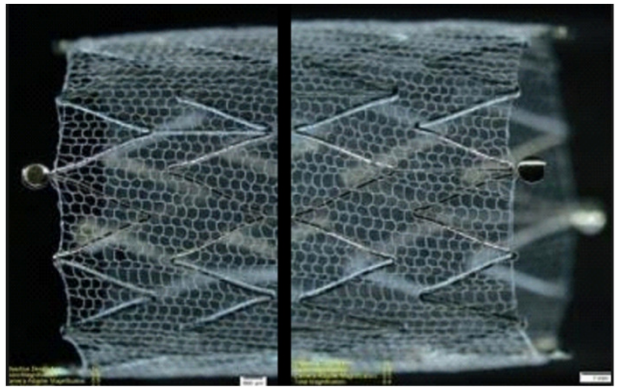
Mesh: PET single fiber knitted: 150-180 micron pore size, outside the frame

High radial force



Trials with new technology

- CGUARD (InspireMD, Boston, MA, USA)
  - Inner open cell nitinol
  - Outer closed cell PET
    - Initial experience (N=30)
      - Symptomatic patients
      - No stroke up to 6 months
    - CARENET trial
      - Multicenter non-randomized study
      - N=30
      - No stroke at 30 days
      - 48 hour new ipsilateral ischemic lesions in 37% MRI
      - At 30 days all but one resolved (one new)



PERIPHERAL

A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent

The CGuard CARENET Trial (Carotid Embolic Protection Using MicroNet)

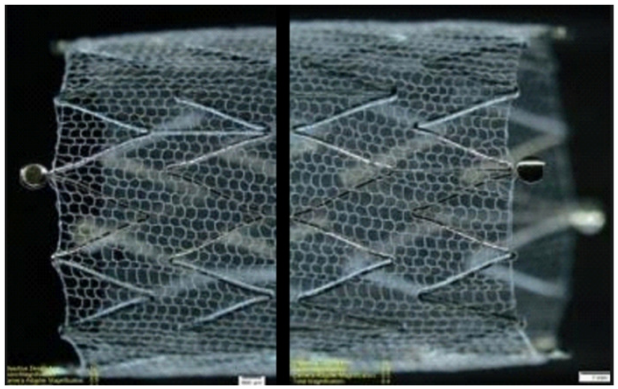
Joachim Schofer, MD,* Piotr Musiałek, MD, DPHIL,† Klaudija Bijuklic, MD,* Ralf Kolvenbach, MD,‡ Mariusz Trystula, MD,† Zbigniew Siudak, MD,†§ Horst Sievert, MD‖

Am Coll Cardiol Intv 2015;8:1229–34

Trials with new technology

Novel PARADIGM in carotid revascularisation: Prospective evaluation of All-comer peRcutaneous cArotiD revascularisation in symptomatic and Increased-risk asymptomatic carotid artery stenosis using CGuard™ MicroNet-covered embolic prevention stent system

Piotr Musialek[1]*, MD, DPhil; Adam Mazurek[1], MD; Mariusz Trystula[2], MD, PhD; Anna Borratynska[3], MD, PhD; Agata Lesniak-Sobelga[1], MD, PhD; Malgorzata Urbanczyk[4], MD; R. Pawel Banys[4], MSc; Andrzej Brzychczy[2], MD, PhD; Wojciech Zajdel[5], MD, PhD; Lukasz Partyka[6], MD, PhD; Krzysztof Zmudka[5], MD, PhD; Piotr Podolec[1], MD, PhD



Eurointervention 2016;12:e658-670

C-Guard IRON-Guard Study

Thirty-day results from prospective multi-specialty evaluation of carotid artery stenting using the CGuard MicroNet-covered Embolic Prevention System in real-world multicentre clinical practice: the IRON-Guard study

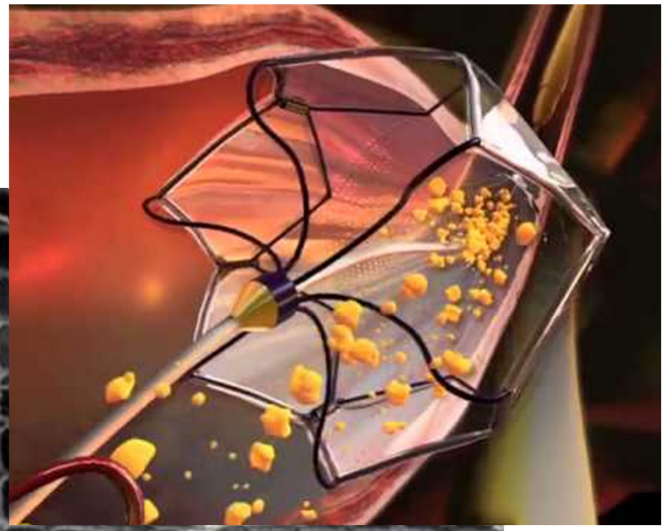
Francesco Speziale[1], MD; Laura Capoccia[1]*, MD; Pasqualino Sirignano[1], MD; Wassim Mansour[1], MD; Chiara Pranteda[1], MD; Renato Casana[2], MD; Carlo Setacci[3], MD; Federico Accrocca[4], MD; Domenico Alberti[5], MD; Gianmarco de Donato[3], MD; Michelangelo Ferri[6], MD; Andrea Gaggiano[7], MD; Giuseppe Galzerano[3], MD; Arnaldo Ippoliti[8], MD; Nicola Mangialardi[9], MD; Giovanni Pratesi[8], MD; Sonia Ronchey[9], MD; Maria Antonella Ruffino[10], MD; Andrea Siani[4], MD; Angelo Spinazzola[11], MD; Massimo Sponza[12], MD

Eurointervention 2018;13:1774-1720

C-Guard IRON-Guard Study

- Prospective multicenter study
- 200 consecutive patients
- Distal embolic protection 91%
- Technical success 100%
- No periprocedural death, MI or major stroke
- 2 TIAs and 5 periprocedural minor strokes (2.5%)
- No external carotid occlusion
- New postprocedural DW-MRI defects in 19.6%

Eurointervention 2018;13:1774-1720



Open Cell nitinol frame and 500 micron PTFE lattice, coating with CBAS bioactive heparin coating

Gray LINC 2018

SCAFFOLD

	N=312
Male, n (%)	202 (64.7%)
White, n (%)	299 (95.8%)
Age, mean (SD)	73.2 (8.8)
Symptomatic, n (%)	40 (12.8%)
Diabetes, n (%)	125 (40.1%)
HTN, n (%)	291 (93.3%)
H/O CAD, n (%)	196 (62.8%)

Gray LINC 2018

SCAFFOLD

Number of subjects	312
Gore carotid stent successfully implanted	100% (312/312)
Gore embolic filter successfully deployed	94.6% (295/312)
Additional EPD used	4.5% (14/312)

Gray LINC 2018

Meta-analysis double layered stent

Double layered stents for carotid angioplasty: A meta-analysis of available clinical data

Anna Sannino, MD[1,2*] | Giuseppe Giugliano, MD, PhD[1,2*] | Evelina Toscano, MD[1,2] | Gabriele G. Schiattarella, MD[1,2] | Anna Franzone, MD, PhD[1,2] | Tullio Tesorio, MD[3] | Bruno Trimarco, MD[1,2] | Giovanni Esposito, MD, PhD[1,2] | Eugenio Stabile, MD, PhD[1,2]

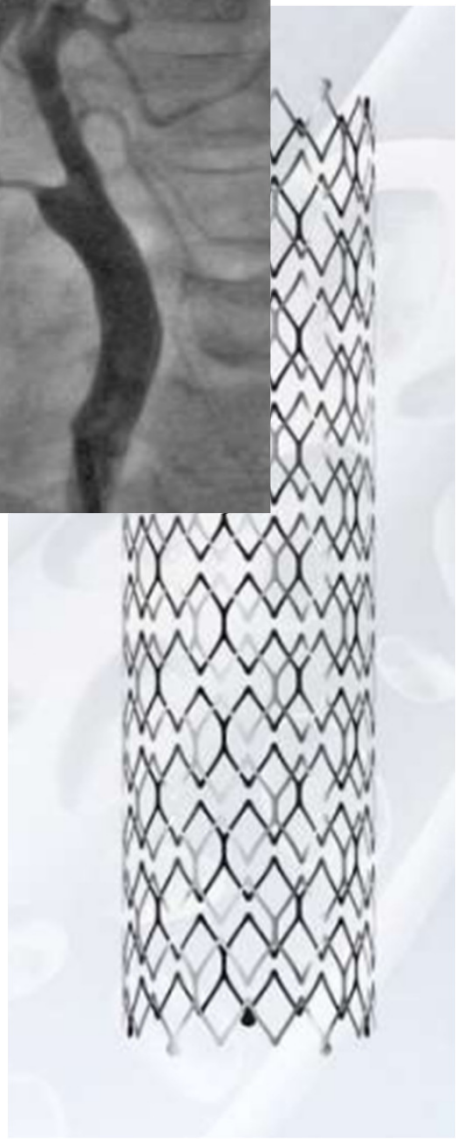
Catheter Cardiovasc Interv. 2018;91:751–757

Meta-analysis double layered stent

Authors (Ref. #)	Year	Stent type	*n*	Primary outcome			Secondary outcome
				30-Day stroke and mortality (%)	30-Day stroke (%)	30-Day mortality (%)	Procedural unsuccess (%)
Bosiers et al. [11]	2016	Roadsaver	100	2.1	1.0	1.0	0
Castagno et al. [12]	2016	Roadsaver	4	0	0	0	0
Kedev et al [13]	2015	Roadsaver	10	0	0	0	0
Mazzaccaro et al. [14]	2016	C-Guard	5	0	0	0	0
Musialek et al. [9]	2016	C-Guard	101	0	0	0	0.9
Nerla et al. [10]	2016	Roadsaver	150	0	0	0	0
Ruffino et al. [16]	2017	Roadsaver	23	2.0	1.0	1.0	3.0
Schofer et al. [8]	2015	C-Guard	30	0	0	0	0
Speziale et al. [17]	2017	C-Guard	200	2.5	2.5	0	0
Wissgott et al. [15]	2015	Roadsaver	12	0	0	0	0

Catheter Cardiovasc Interv. 2018;91:751–757

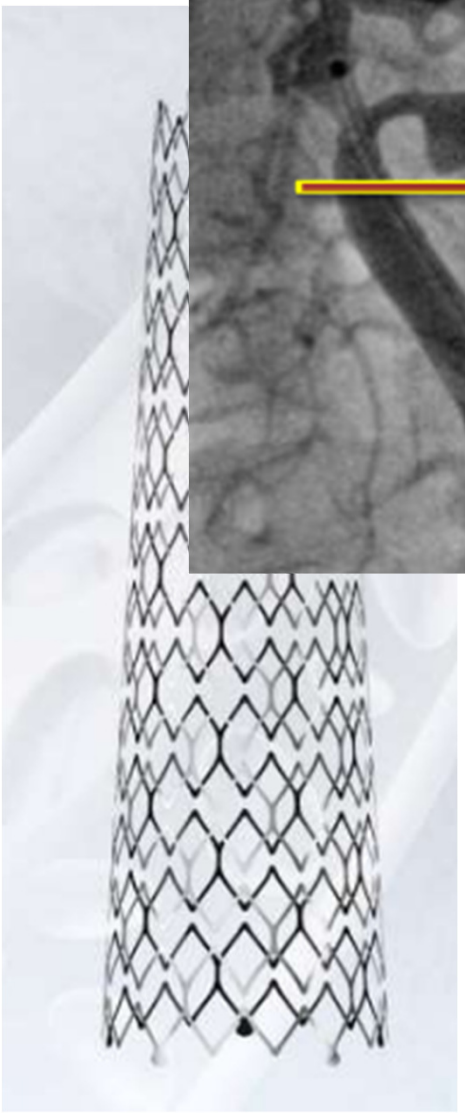
SMALL CELL OPEN CELL (MER-) STENT OCEANUUS



?

MEI

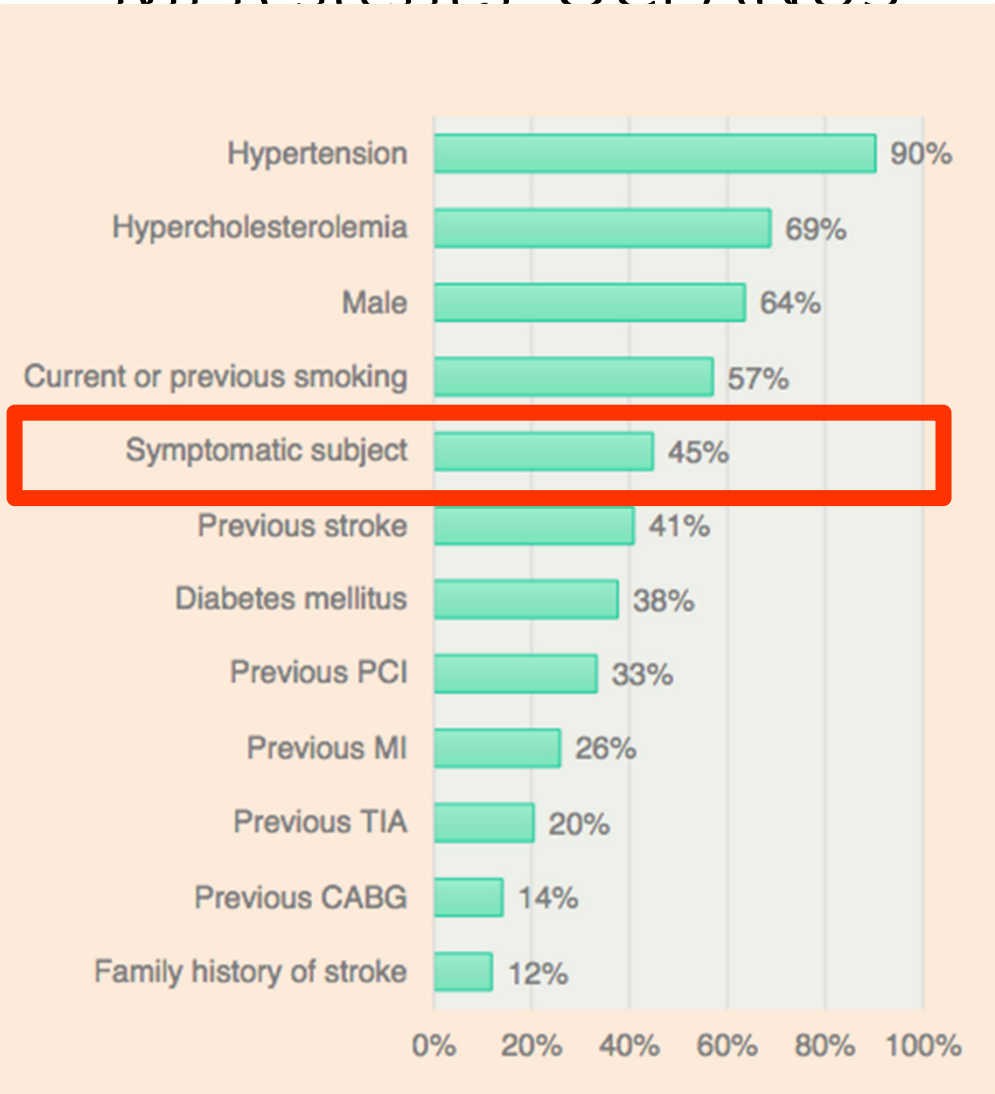
BALTON®



CELL AREA (6.2 mm2)

Pienziazek LINC 2018

MER stent:I. OCEANUS



Variable	Measure	Total
Age at enrollment, years	n	100
	Mean (±SD)	68.55 (±8.24)
	Mean 95% CI	(66.87; 70.23)
	Me (Q1; Q3)	68.00 (62.00; 75.00)
	Min/Max	51.00 / 85.00
Systolic blood pressure, mmHg	n	100
	Mean (±SD)	152.39 (±23.68)
	Mean 95% CI	(147.51; 157.26)
	Me (Q1; Q3)	152.00 (135.00; 170.00)
	Min/Max	83.00 / 213.00
Diastolic blood pressure, mmHg	n	100
	Mean (±SD)	78.41 (±11.48)
	Mean 95% CI	(76.04; 80.77)
	Me (Q1; Q3)	80.00 (70.00; 85.00)
	Min/Max	53.00 / 120.00
Diameter stenosis NASCET, %	n	100
	Mean (±SD)	76.42 (±9.79)
	Mean 95% CI	(74.40; 78.43)
	Me (Q1; Q3)	76.00 (72.00; 83.00)
	Min/Max	49.00 / 95.00

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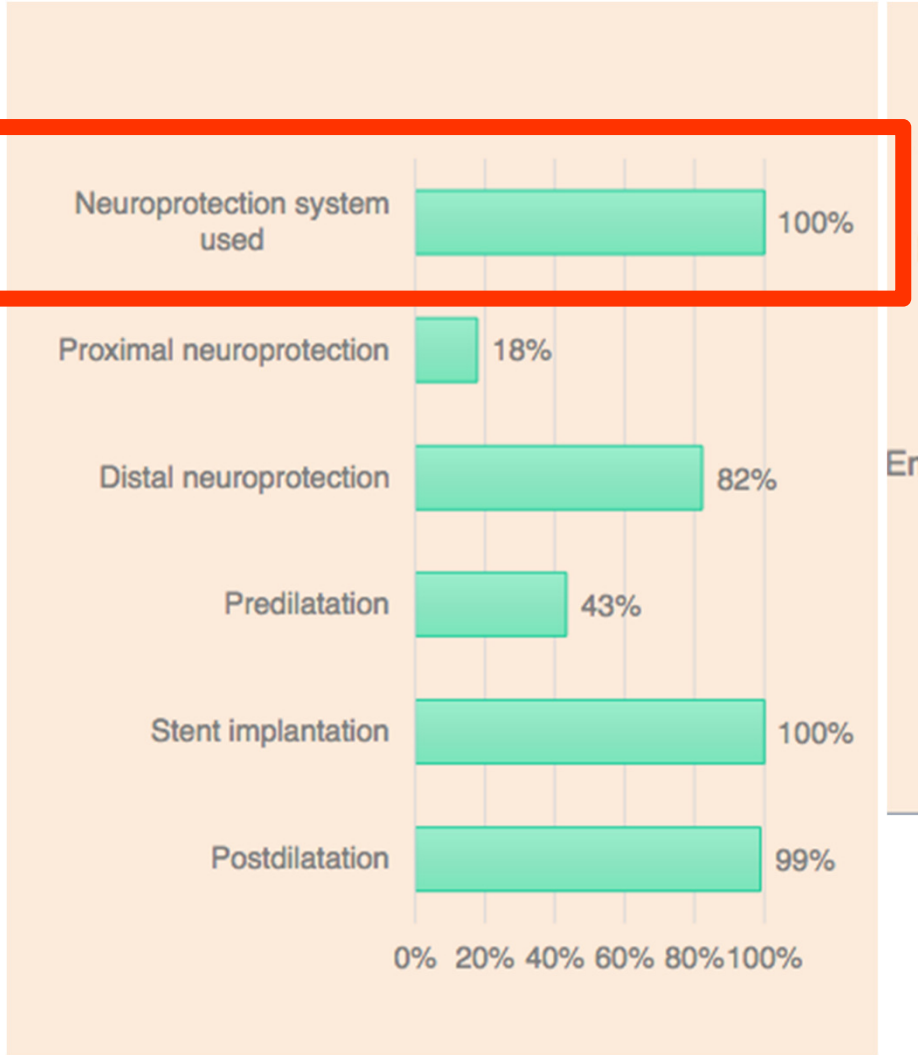
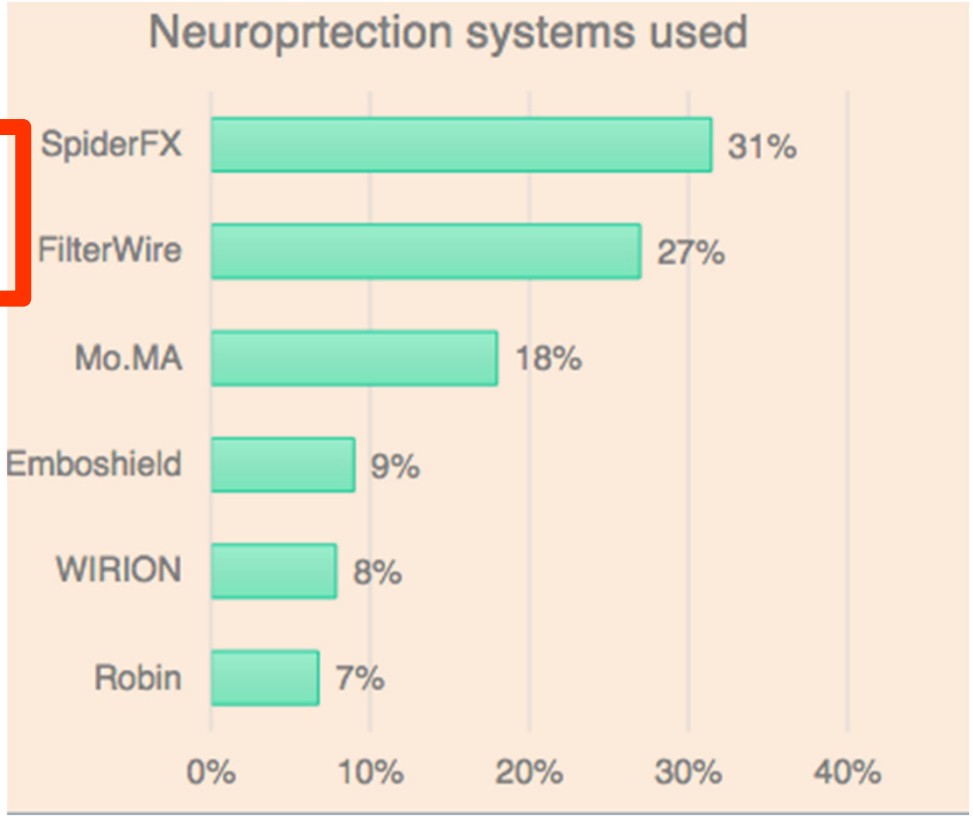
MER stent: OCEANUS





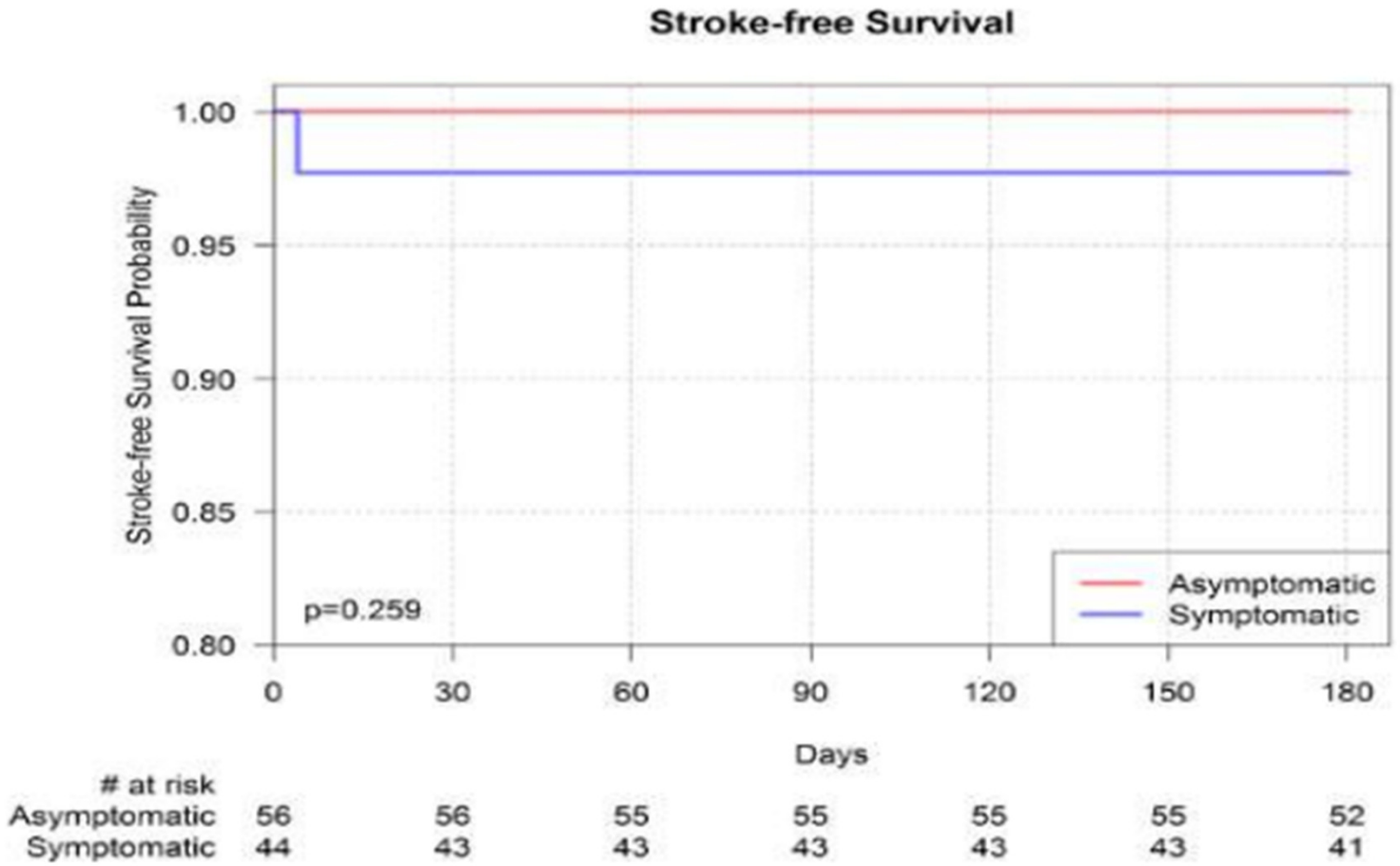
Pienziazek LINC 2018

MER-stent: OCEANUS

- N=100
- 30-day
  - 1 stroke at day 4
  - Death: 0
  - MI: 0
  - Edge dissection requiring additional stent: 1 patient

Pienziazek LINC 2018

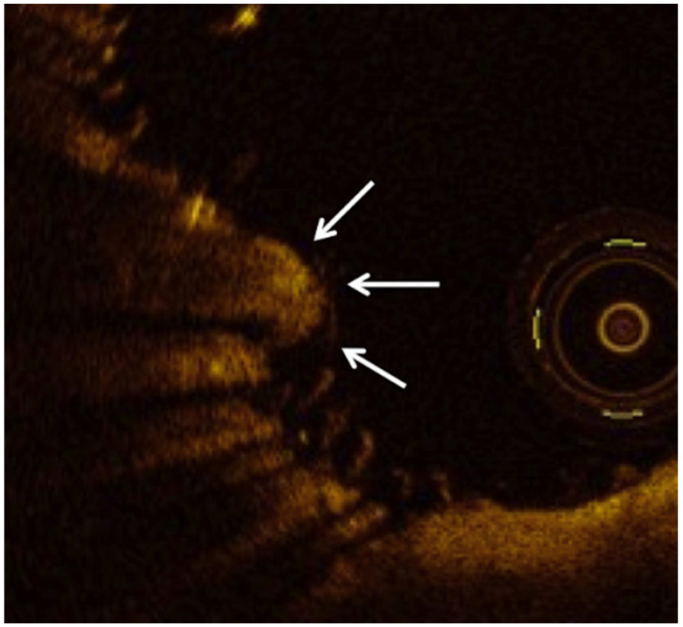
MER-stent 6 months: OCEANUS

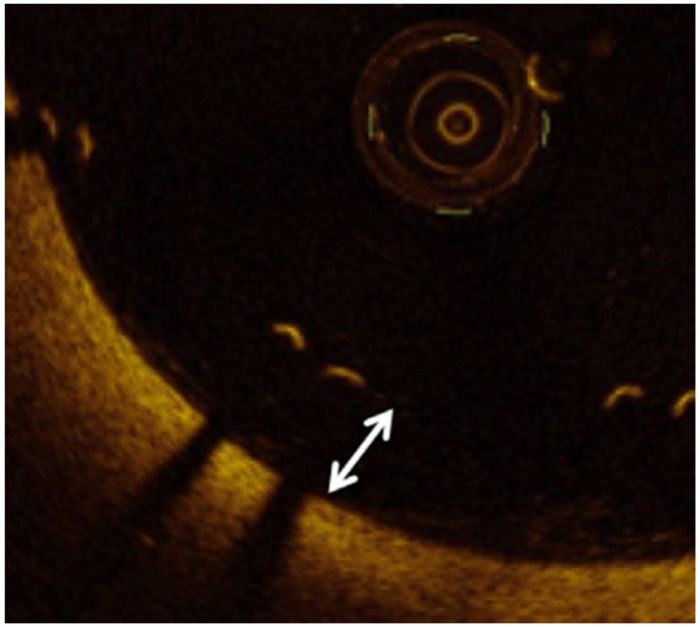


Pienziazek LINC 2018

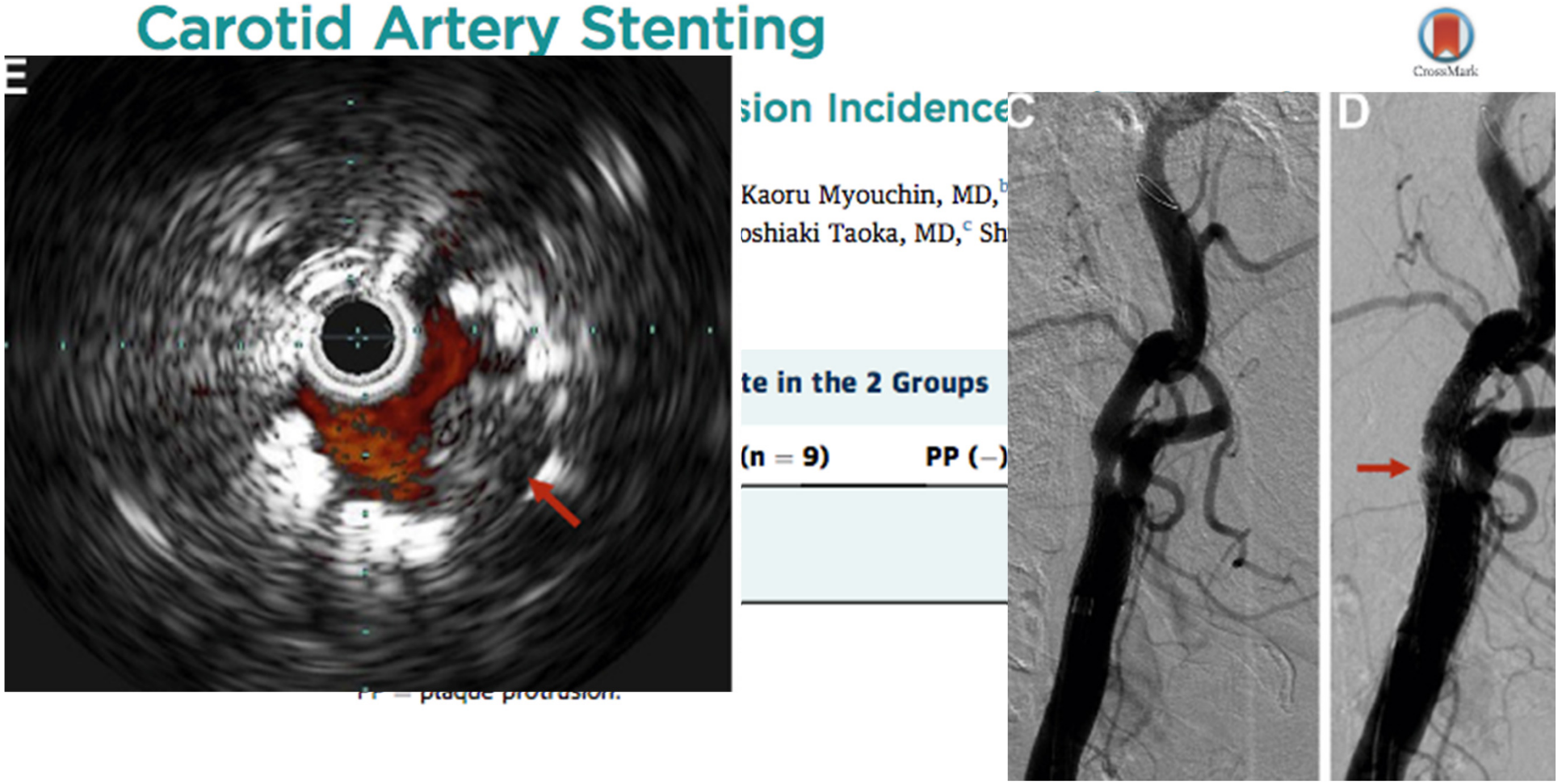
Plaque protrusion/prolapse and stent malapposition

- De Donato et al.





Plaque protrusion: does it matter?



JACC: CARDIOVASCULAR INTERVENTIONS VOL. 10, NO. 8, 2017

Plaque protrusion: does it matter?

TABLE 5 PP Incidence by Stent Design

	PP (+) Group (n = 9)	PP (−) Group (n = 345)
Open-cell stent	9	229
Closed-cell stent	0	116

Values are n. $p < 0.034$.
PP = plaque protrusion.

TABLE 6 PP Incidence by Plaque Morphology

	PP (+) Group (n = 9)	PP (−) Group (n = 326)
Stable plaque	1	193
Unstable plaque	8	133

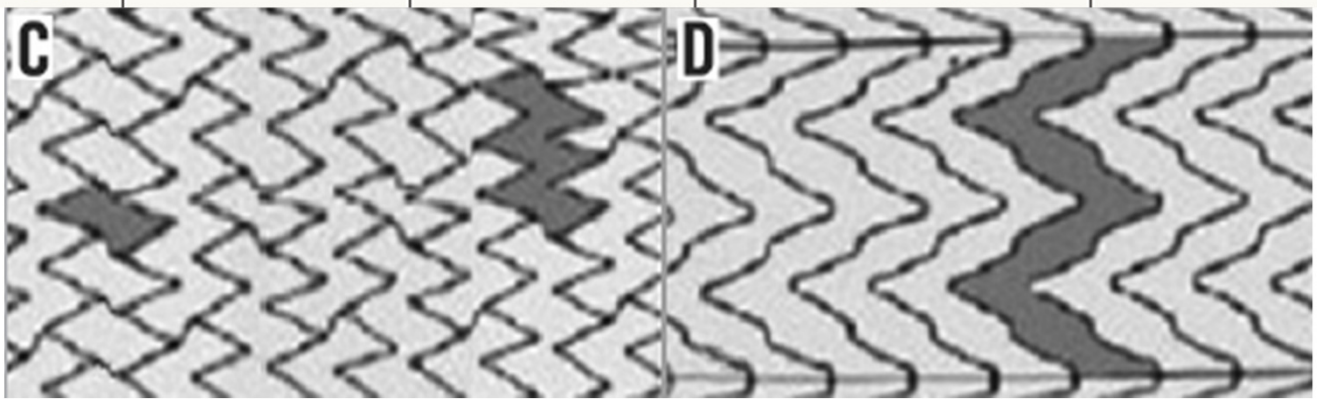
Values are n. $p < 0.004$.
PP = plaque protrusion.

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 10, NO. 8, 2017

Open versus closed cell design

Impact on outcome of different types of carotid stent: results from the European Registry of Carotid Artery Stenting

	Closed (n=713)	Hybrid (n=456)	Open with free cell area <7.5 mm² (n=238)	Open with free cell area >7.5 mm² (n=197)	*p*-value
Death, n (%)	1 (0.14)	3 (0.66)	0	0	0.213
Stroke, n (%)	8 (1.12)	2 (0.44)	3 (1.26)	6 (3.05)	0.045
Death and stroke, n (%)	8 (1.12)	5 (1.10)	3 (1.26)	6 (3.05)	0.196



EuroIntervention 2016; 12:e265-270

Proximal versus distal embolic protection meta-analysis

Cerebral Embolic Lesions Detected With Diffusion-Weighted Magnetic Resonance Imaging Following Carotid Artery Stenting

A Meta-Analysis of 8 Studies Comparing Filter Cerebral Protection and Proximal Balloon Occlusion

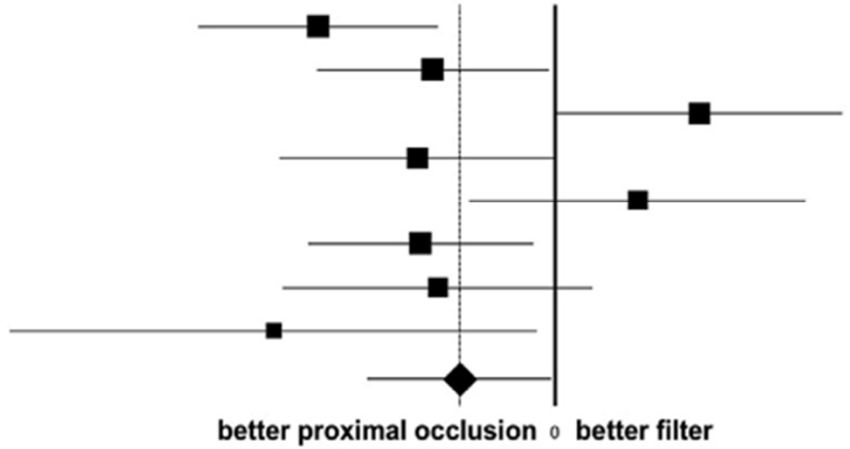
Eugenio Stabile, MD, PhD, Anna Sannino, MD, Gabriele Giacomo Schiattarella, MD, Giuseppe Gargiulo, MD, Evelina Toscano, MD, Linda Brevetti, MD, Fernando Scudiero, MD, Giuseppe Giugliano, MD, Cinzia Perrino, MD, PhD, Bruno Trimarco, MD, Giovanni Esposito, MD, PhD

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 7, NO. 10, 2014

Proximal versus distal embolic protection meta-analysis

Incidence of new (DW-MRI) ischemic brain lesions after CAS

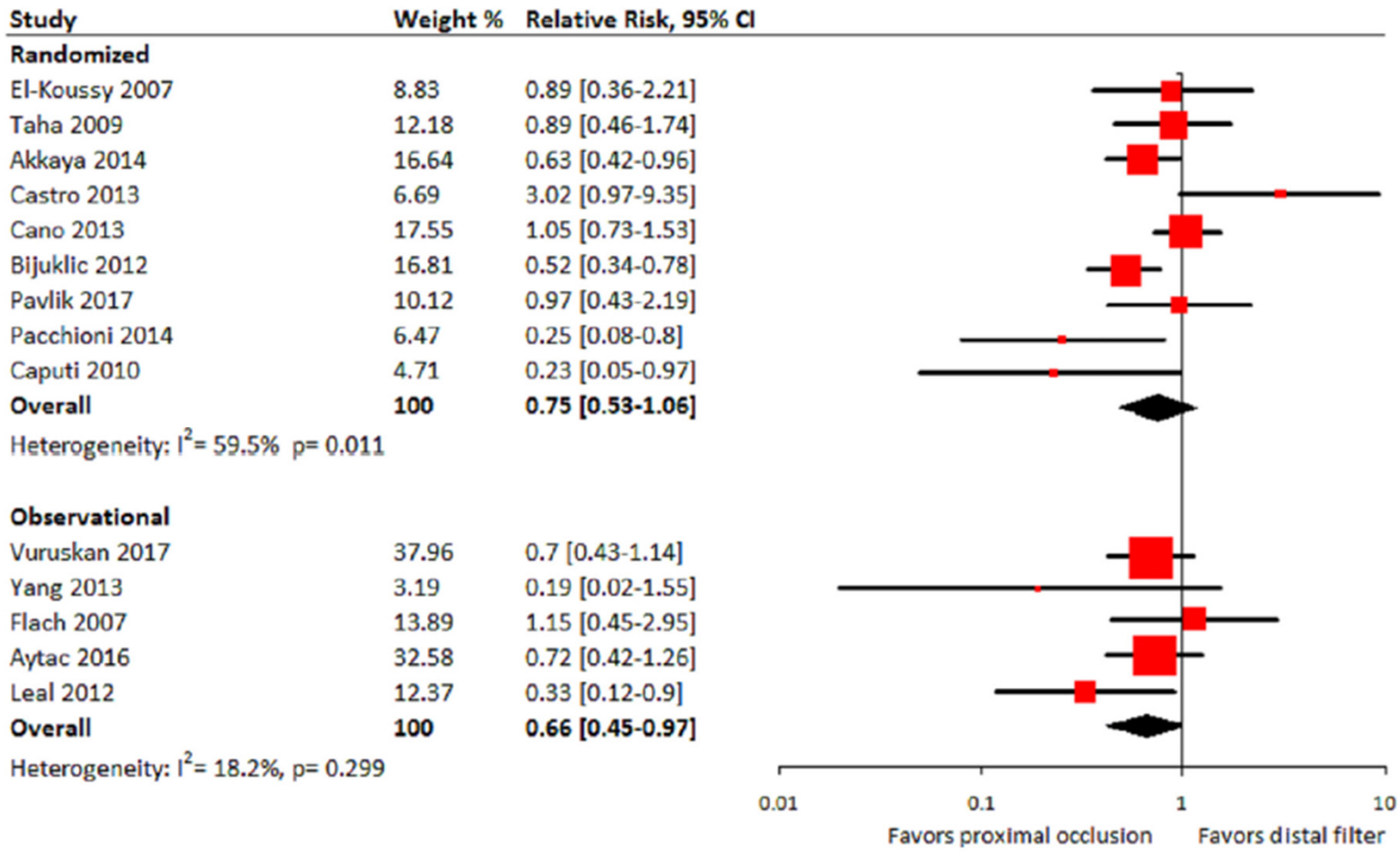
Study ID	ES	95% CI	N
Bijuklic K. et al. 2012	-1.05	-1.58 , -0.52	62
Cano N.M. et al. 2013	-0.54	-1.06 , -0.03	60
Castro-Afonso LH. et al. 2013	0.64	0.00 , 1.28	40
El-Koussy M. et al. 2007	-0.61	-1.22 , -0.00	44
Flach Z.H. et al. 2007	0.37	-0.38 , 1.11	33
Leal I. et al. 2012	-0.60	-1.10 , -0.10	64
Montorsi P. et al. 2011	-0.52	-1.21 , 0.17	35
Taha M.M. et al. 2009	-1.25	-2.42 , -0.08	19
Overall (random-effects model)	-0.43	-0.84 , -0.02	357



JACC: CARDIOVASCULAR INTERVENTIONS VOL. 7, NO. 10, 2014

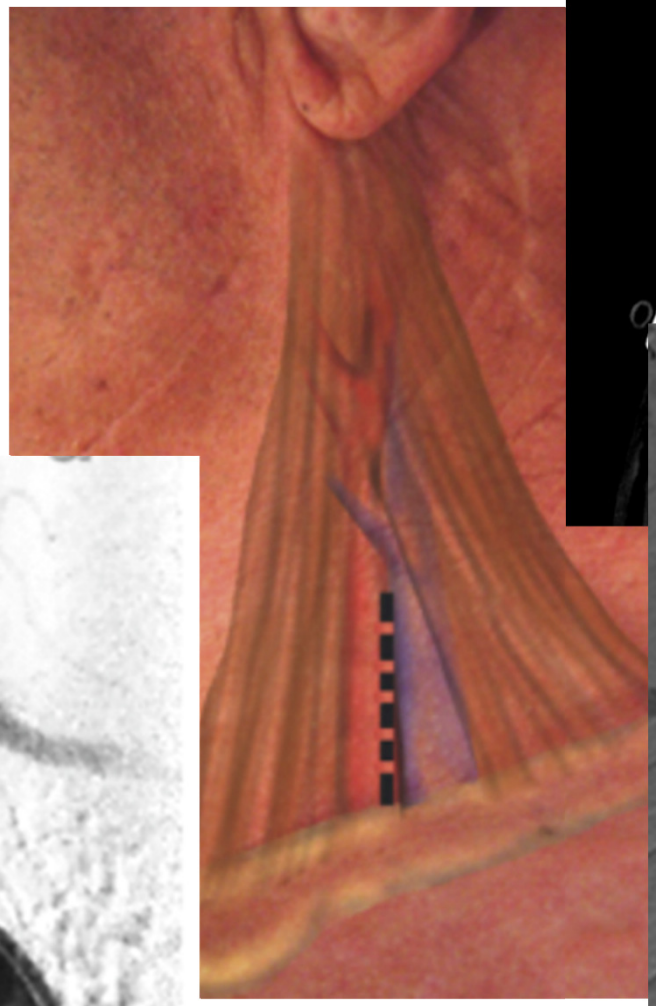
Proximal versus distal embolic protection meta-analysis

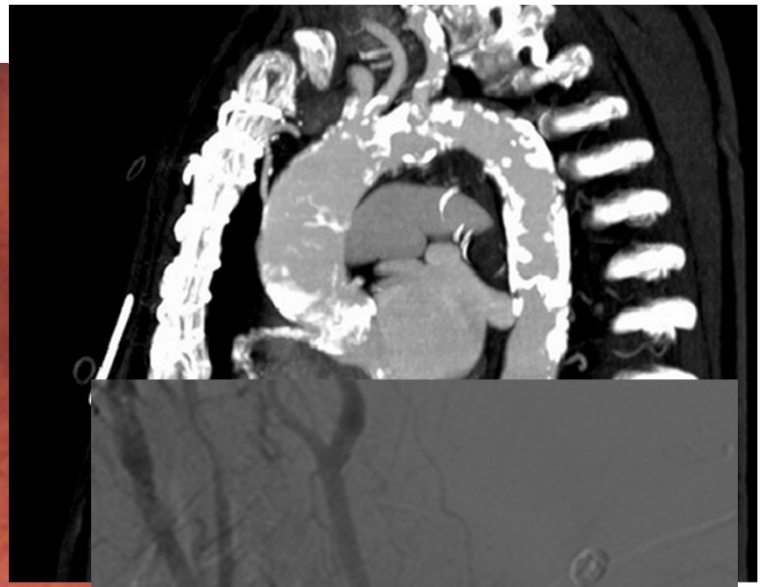
New DW-MRI brain lesions after CAS

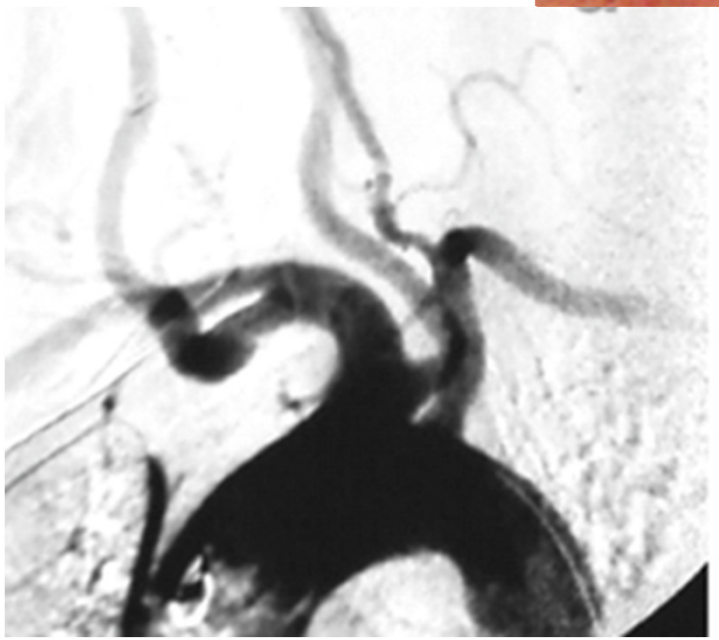


Texakalidis et al. CRM 2017

Direct carotid access: Why?

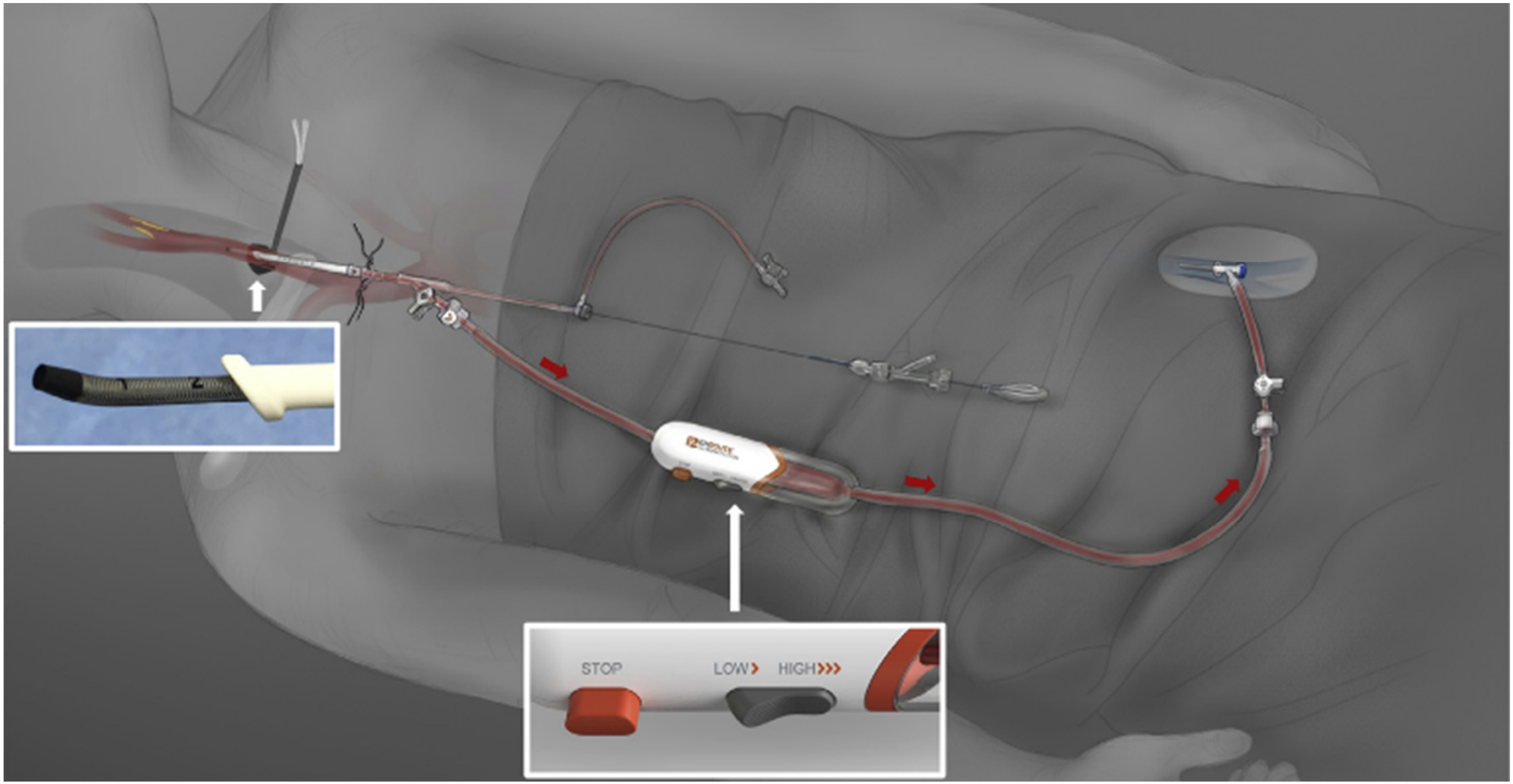






Malas wet al. J Vasc Surg 2017;65:916-20

Direct carotid access: How?



Malas wet al. J Vasc Surg 2017;65:916-20

Direct carotid access

Malas wet al. J Vasc Surg 2017;65:916-20

ROADSTER

Variables	*Mean ± SD (min, max) or No. (%) (N = 141)*
Age, years	72.9 ± 9 (40, 90)
≥75	66 (47)
≥80	39 (27.7)
Sex	
Male	91 (65)
Female	50 (35)
Medical history	
Diabetes	52 (36.9)
Hyperlipidemia	109 (77.3)
Hypertension	122 (86.5)
Coronary artery disease	59 (41.8)
Peripheral vascular disease	41 (29.1)
Current smoker	32 (22.7)
Symptom status	
Symptomatic	36 (25.5)
Asymptomatic	105 (74.5)

SD, Standard deviation.

J Vasc Surg 2015;62:1227-35.)

ROADSTER

Inclusion criteria	*No. (%) (N = 141)*
Anatomic	
Contralateral carotid occlusion	11 (7.8)
Tandem stenosis >70%	1 (0.7)
High cervical carotid artery stenosis	42 (29.8)
Restenosis after CEA	29 (20.6)
Hostile neck	22 (15.6)
Bilateral carotid artery stenosis requiring treatment	6 (4.3)
Physiologic	
Age >75 years	66 (46.8)
>2 vessel CAD and history of angina	15 (10.6)
History of angina	2 (1.4)
CCF NYHA functional class III/IV	1 (0.7)
LVEF <30%	2 (1.4)
MI >72 hours and <6 weeks before the procedure	1 (0.7)
Severe COPD	6 (4.3)
Permanent contralateral CNI	0
Chronic renal insufficiency	1 (0.7)

J Vasc Surg 2015;62:1227-35.)

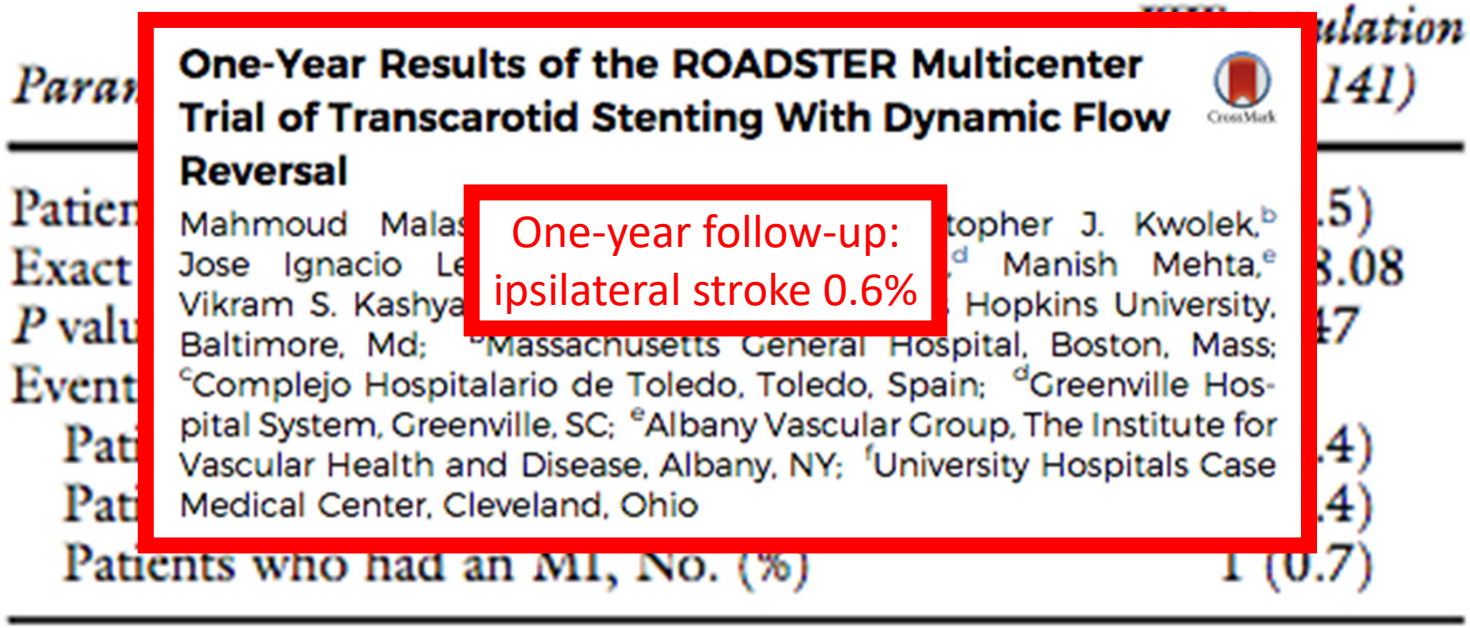
ROADSTER

Variables	*No. (%) or mean ± SD (min, max) (N = 141)*
Anesthetic modality	
Local anesthesia	74 (53)
General anesthesia	67 (47)
Flow reversal time, minutes	
Time on high-flow	12.9 ± 8.6
Tolerance	
To flow reversal	141 (100)
To high-flow	140 (99)
Procedure time: CCA cutdown to skin closure, minutes	73.6 ± 30.77 (68.2, 78.2)
Acute device success	140 (99)
Technical success	140 (99)
Procedural success	135 (96)

J Vasc Surg 2015;62:1227-35.)

ROADSTER

One death at day 15 from MI after pneumonia and diabetic ketoacidosis, one death from respiratory complications in an elderly woman with prior respiratory co-morbidities



One-Year Results of the ROADSTER Multicenter Trial of Transcarotid Stenting With Dynamic Flow Reversal

One-year follow-up: ipsilateral stroke 0.6%

Mahmoud Malas … topher J. Kwolek,[b] Jose Ignacio Le … [d] Manish Mehta,[e] Vikram S. Kashya … Hopkins University, Baltimore, Md; [b]Massachusetts General Hospital, Boston, Mass; [c]Complejo Hospitalario de Toledo, Toledo, Spain; [d]Greenville Hospital System, Greenville, SC; [e]Albany Vascular Group, The Institute for Vascular Health and Disease, Albany, NY; [f]University Hospitals Case Medical Center, Cleveland, Ohio

One minor stroke during procedure, one evening of the procedure, second within 48 hours

J Vasc Surg 2015;62:1227-35.)

Malas et al. Journal of Vascular Surgery 2018; January, Volume 67, issue 1

ROADSTER-2

- Open label
- Single arm
- Postapproval
- Planned enrollment: 600 (up to 100 sites)
- Primary endpoint: procedural success

ROADSTER-2

- Interim analysis presented at LINC 2017

Parameter	n=270
Age ≥80	**21.9%**
Female	**31.9%**
Symptomatic	**28.3%**
Physiologic Risk Factors only	**32.5%** ←
Anatomic Risk Factors only	**44.3%** ←
- Hostile Neck - Restenosis post CEA - Contralateral Occlusion	**17.0%** **20.3%** **12.9%**
Physiologic & Anatomic Risk Factors	**23.2%** ←

Schneider at LINC 2017

ROADSTER-2

Parameter	ROADSTER 1 N=219	ROADSTER 2 n=270
ROADSTER 1 Investigators	N/A	26%
New Operators	N/A	74%
Enrollment by New Operators	N/A	58%
Skin-to-Skin Time (median)	70 mins	70 mins
Reverse Flow/Clamp Time (median)	9 mins	10 mins
Tolerance to High Flow	98.6%	99.3%
Tolerance to Low Flow	100%	100%
Acute Technical Success	99.5%	98.9 %
Fluoro Time (median)	N/R	5 mins
Contrast Usage (median)	62 cc	40 cc

Schneider at LINC 2017

ROADSTER-2

Acute	n=252	
Acute Device Success	249	98.8%
Technical Success	249	98.8%
30 Days	**n=227**	
Procedural Success	222	97.8%

Primary endpoint analysis

Schneider at LINC 2017

ROADSTER-2

	ROADSTER 1 n=203		ROADSTER 2 n=227		ROADSTER 2 n=252	
	Patients with 30-day F/U		*Patients with 30-day F/U*		*All Patients*	
Stroke/Death/MI	6	3.0%	2	0.9%	2	0.8%
Stroke	1	0.5%	2	0.9%	2	0.8%
Death	2	1.0%	0	0.0%	0	0.0%
MI	3	1.5%	0	0.0%	0	0.0%
Stroke/Death	**3**	**1.5%**	**2**	**0.9%**	**2**	**0.8%**
CNI (permanent)	0	0.0%	0	0.0%	0	0.0%

Schneider at LINC 2017

PROOF

- N=75
- 16% symptomatic
- 40% with contralateral stenosis
- 5 patients with transient intolerance to flow reversal
- Mean flow reversal time 19.1 min
- 17.9% of patients had DW-MRI defects
- No death/major stroke at 30 days
- One minor stroke

Alpaslam et al. Journal of Endovascular Therapy 2017, Vol. 24(2) 265–270

PROOF

Table 2. Outcomes of the 75 Procedures.[a]

Acute device success	68 (90.6)
Procedural success	68 (90.6)
Establishment of reverse flow circuit	71 (94.6)
Tolerance to reverse flow (n=71)	71 (100)
Average time of reverse flow, min	19.1±8.2
Average time on high flow, min	12.2±5.6
Residual stenosis, %	12.4±14.4

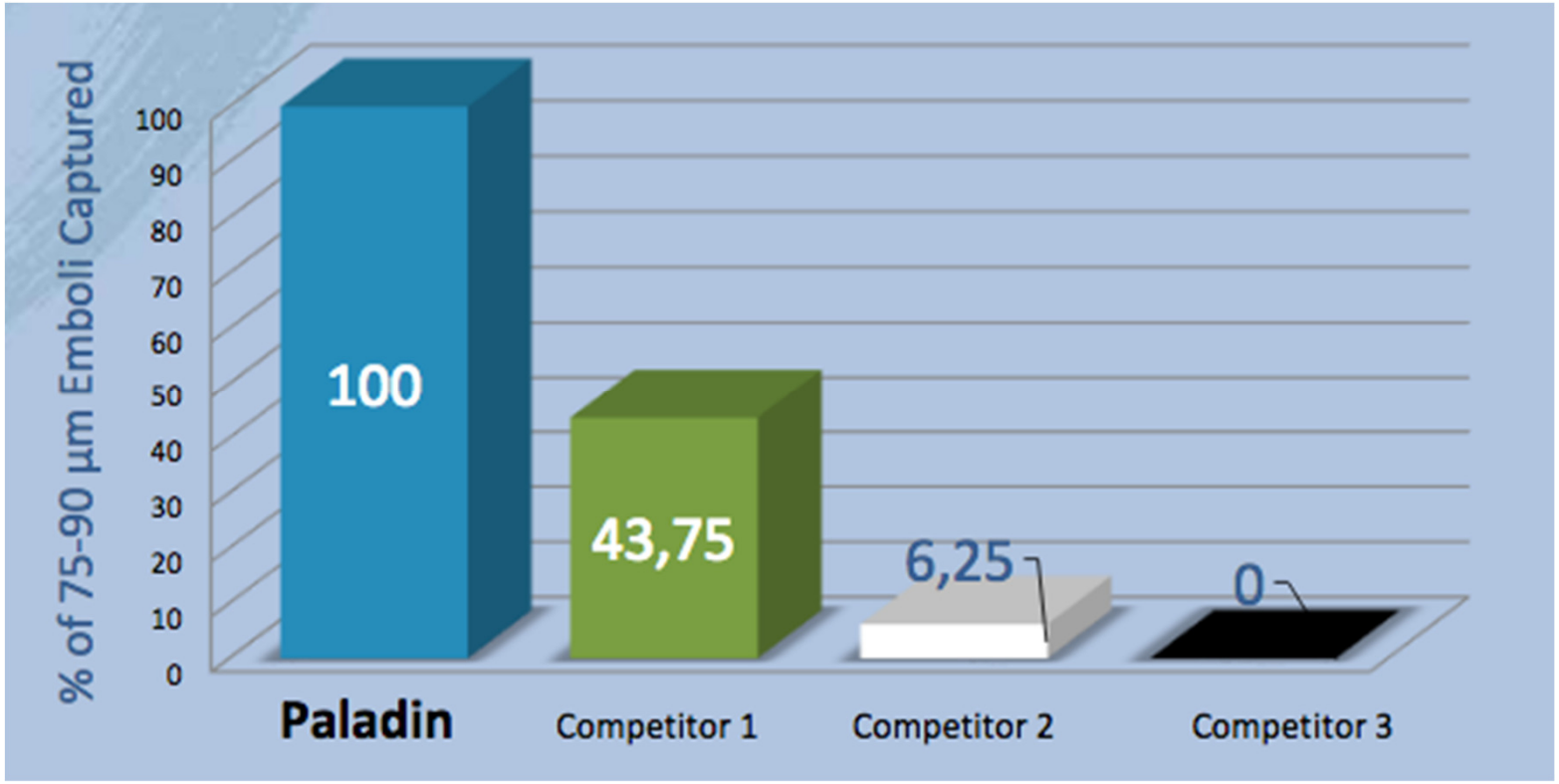
Alpaslam et al. Journal of Endovascular Therapy 2017, Vol. 24(2) 265–270

Integrated embolic protection (Paladin balloon, Contego Medical)

- Balloon with incorporated filer using ultra-small pores

40 micron filter

Integrated embolic protection (Paladin balloon, Contego Medical)



Ravish Sachar LINC 2018

Integrated embolic protection (Paladin balloon, Contego Medical)

Cognitive Impairment Due to Embolization

Importance of Micro-Embolization

Journal of the Neurological Sciences
Volume 328, Issue 1-2, 15 May 2013, Pages 58-63

Diffusion-weighted lesions after carotid artery stenting are associated with cognitive impairment

Maggio, P.a, Altamura, C.a, Landi, D.a, Migliore, S.a, Lupoi, D.b, Moffa, F.c, Quintiliani, L.a, Vollaro, S.a, Palazzo, P.a, Altavilla, R.a, Pasqualetti, P.de, Errante,

CONCLUSIONS:

Our study showed that peri-procedural brain microembolic load impacts negatively on cognitive functions, independently from the influence of patients-related variables. © 2013 Elsevier B.V.

J Vasc Surg. 2016 Dec 23. pii: S0741-5214(16)31513-0. doi: 10.1016/j.jvs.2016.09.057.

Volume of subclinical embolic infarct correlates to long-term cognitive changes after carotid revascularization.

Zhou W, Baughman BD, Soman S, Wintermark M, Lazzeroni LC, Hitchner E, Bhat J, Rosen A

.

CONCLUSIONS:
Cognitive assessment of procedure-related subclinical microemboli is challenging. Volumes of embolic infarct correlate with long-term cognitive changes, suggesting that microembolization should be considered a surrogate measure for carotid disease management.
Published by Elsevier Inc.

PALADIN study

- PI Thomas Zeller, Horst Sievert
- N=106

Stent Implanted	% (n = 106)	
Roadsaver	43.4	(46)
Xact	31.1	(33)
Cristallo Ideale	17.0	(18)
Wallstent	4.7	(5)
Adapt	2.8	(3)
Precise	0.9	(1)

Ravish Sachar LINC 2018

PALADIN

- 30-day results

	Discharge (n=106)	30 Days (n=105*)
MAE (death, stroke, MI)	0.0 % (0)	0.95 % (1)*
All Death	0.0 % (0)	0.0 % (0)
Stroke	0.0 % (0)	0.95% (1)
Myocardial Infarction	0.0 % (0)	0.0 % (0)

Ravish Sachar LINC 2018

PALADIN

- Substudy
  - N=30, DW MRI
  - New ischemic lesions 37%
  - Ipsilateral 27%
  - Average number of new lesions per patient 0.5

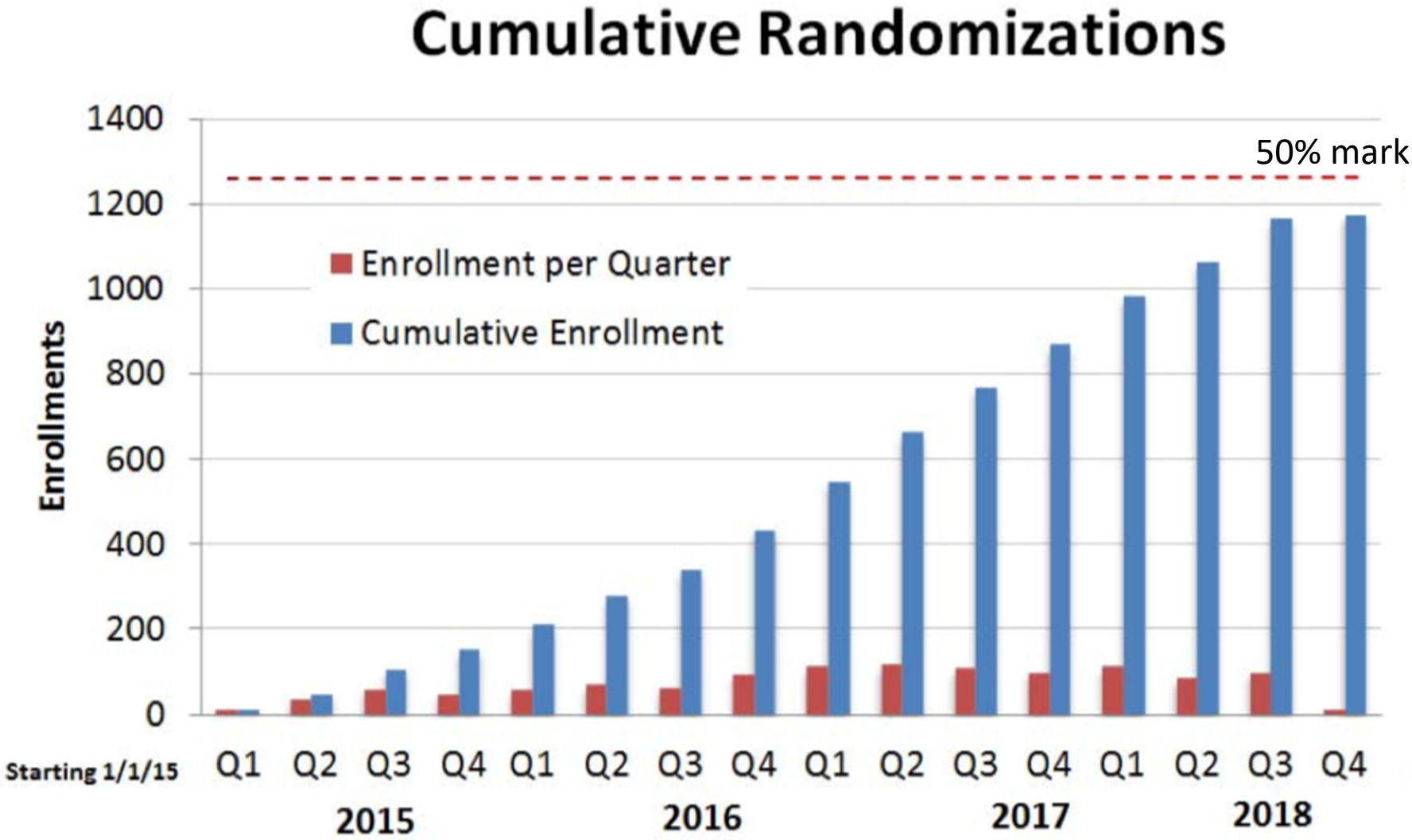
CREST-2

- Ten-year follow-up from the CREST trial and 5-year follow-up from the ACT I study, presented at the 2016 International Stroke Conference, showed that CAS holds up well over the long term against CEA in asymptomatic and symptomatic patients with severe carotid stenosis. Neither of these trials assessed how revascularization compares to medical therapy alone.
- CREST-2, launched in late 2014, aims to answer that question. However, its unusual, two-arm design may preclude direct comparisons between stenting and surgery. The trial is enrolling patients who have ≥ 70% asymptomatic stenosis, with a primary endpoint of any stroke or death within 44 days of randomization or ipsilateral ischemic stroke thereafter up to 4 years.

CREST-2

- seeks to enroll 2480 participants, 40% women and 12% minorities. Patients are eligible to participate if they are ≥35 years, have narrowing (≥70%) of at least 1 of their carotid arteries, no medical history of ipsilateral stroke or TIA within 180 days of randomization in the distribution of the target artery, carotid stenosis that is treatable with CEA or CAS, and lack other serious medical conditions.

- As of December 2016, the registry included 84 approved sites and 164 approved interventionists, with more than 1,300 patients enrolled. By December 2017, there were nearly 2,200 patients. Overall, fewer than half of operators who expressed interest in the registry were allowed to participate.


Cumulative Randomizations
1400
1200
1000
800
600
400
200
0
Enrollments
50% mark
Enrollment per Quarter
Cumulative Enrollment
Starting 1/1/15
Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4 Q1 Q2 Q3 Q4
2015
2016
2017
2018

- The primary outcome in CREST-2 is the proportion of patients who experience the composite end point of any stroke or death within 44 days of randomization or ipsilateral stroke ≤4 years thereafter.

Randomised trials of treatment for carotid stenosis

BMT vs CEA	Asymptomatic	ACAS, ACST
	Symptomatic	NASCET, ECST,
CEA vs CAS	Symptomatic	EVA3S-2008, SPACE-2008
		ICSS-2010
	CEA high risk	SAPPHIRE-2004,
	Any risk	CREST -2010,
	Asymptomatic	ACT-1-2016
BMT vs BMT+CEA vs BMT +CAS		
	Asymptomatic	ACST2, CREST2
	Any risk	ECST 2

ECST 2 & ACST 2

- ECST-2 and ACST-2 both seek to recruit patients with asymptomatic carotid artery stenosis, but the trials are not competing for patients because the questions they ask are different and complementary. ACST-2 is recruiting patients in whom it has been decided that revascularisation of asymptomatic stenosis is definitely required, but the clinicians are uncertain whether stenting or endarterectomy should be used. Patients in ACST-2 are therefore randomised between carotid endarterectomy and stenting. ECST-2 is recruiting patients with asymptomatic or symptomatic carotid stenosis in whom the clinicians are uncertain whether revascularisation is required. Patients in ECST-2 are randomised to immediate revascularisation or initial optimised medical management alone. All the patients in both trials will have appropriate medical management.

ACST 2

ECST 2

30 May 2017: 247 patients randomised at 28 Centres

Conclusion

- CEA will remain the first choice as long as the stroke rate remains higher with CAS
- Newer technology suggests that we can reach a stroke rate similar to CEA (while avoiding the surgical risks [cranial nerve injury/periprocedural MI])
- Need a randomized trial with new technology to prove equivalency of CAS to CEA

- Newer technologies may further improve CAS outcomes but [they] do not replace good CAS technique and judgement