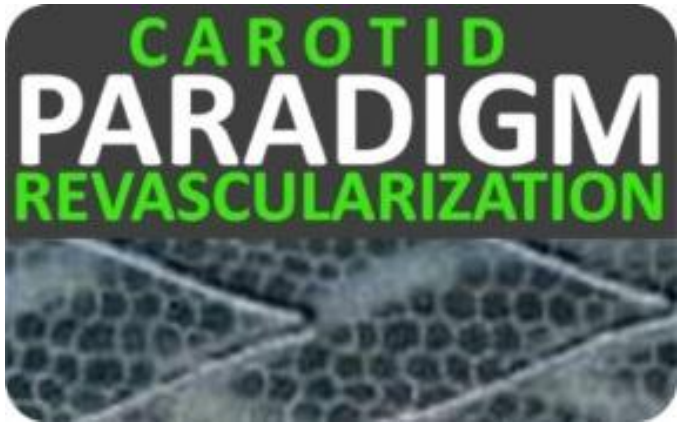

Accumulating long-term evidence for microNET-covered stent safety, efficacy and durability in primary and secondary stroke prevention:

5-year data from the PARADIGM-Extend prospective academic trial

P. Musialek, A. Mazurek, M. Trystuła, A. Borratynska, T. Tomaszewski, A. Lesniak-Sobelga, M. Brozda, U. Gancarczyk, A. Klecha, ST. Kowalczyk, E. Sobieraj, N. Dluzniewska, M. Urbanczyk, P. Banys, J. Miszczuk, P. Judzialo, G. Stankiewicz, T. Drazkiewicz, P. Podolec

Jagiellonian University Dept. of Cardiac & Vascular Diseases
John Paul II Hospital, Kraków, Poland
& Collaborating Vascular Centres

Supported K/ZDS/007819 (Jagiellonian University Medical College)

Disclosure

Speaker name: Piotr Musialek

I have the following potential conflicts of interest to report:

- [x] Consulting
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest

PARADIGM-EXTEND is an Investigator-initiated, academic, non-commercial study

EuroIntervention 2016;12-online publish-ahead-of-print May 2016

CLINICAL RESEARCH

euro PCR 2016 LATE BREAKING TRIALS

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

PARADIGM-Extend = **P**rospective evaluation of **A**ll-comer pe**R**cutaneous c**A**roti**D** revascularization in symptomatic and **I**ncreased-stroke-risk asymptomatic carotid artery stenosis using C**G**uard™ **M**icronet-covered embolic prevention stent system – clinical trial multi-centre extension

EuroIntervention 2016;12-online publish-ahead-of-print May 2016

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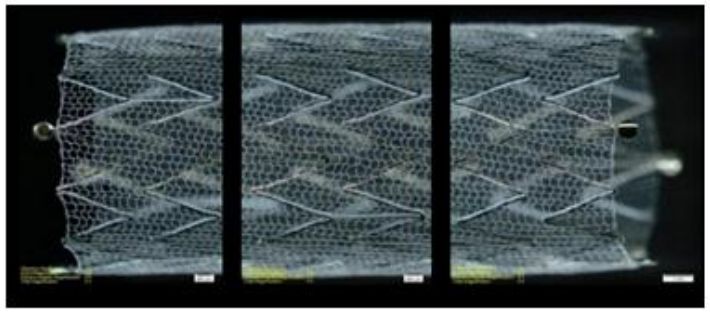
CGuard™– Carotid Embolic Prevention System

System specifications	
Stent type	Nitinol – self expanding
Micronet aperture size	150-180 µm
Guidewire	0.014”
Sizes - Diameter - Length	 6-10mm 20-60mm

CE Mark – March 2014

carotid-dedicated design

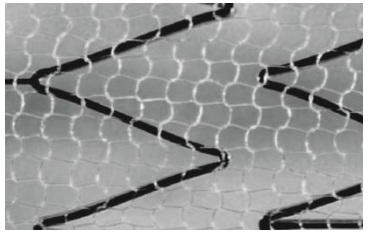


Nitinol frame open-cell area ≈ 21 mm^2

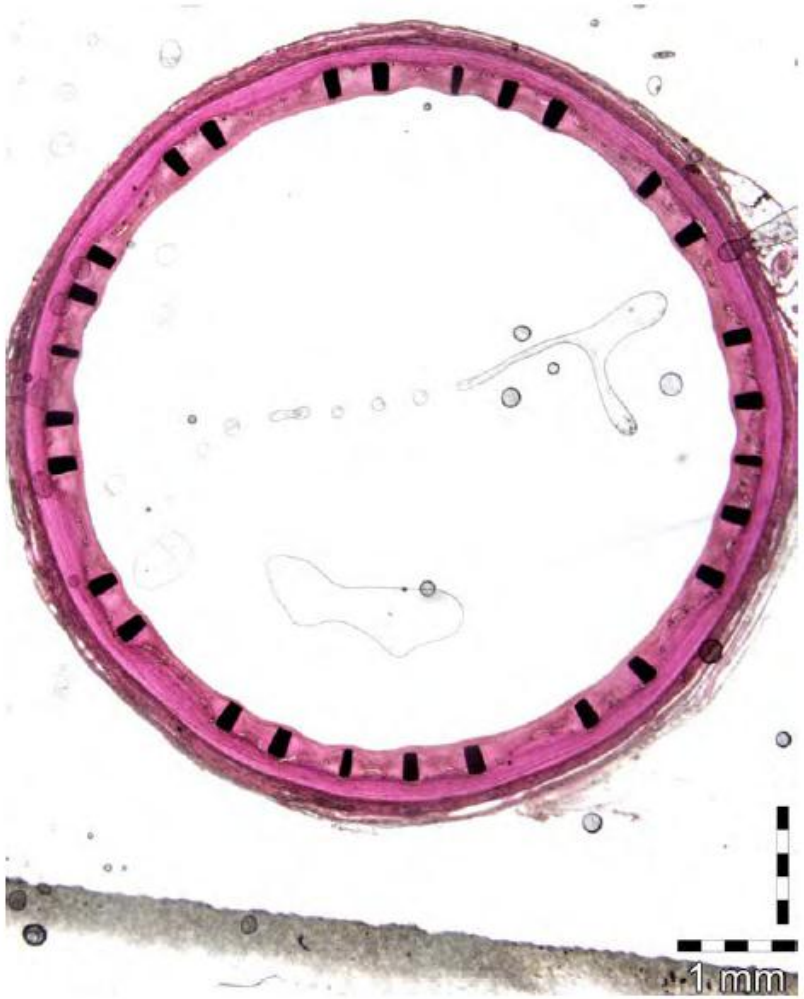
MicroNet closed-cell area ≈ 0.3mm^2

LARGEST √

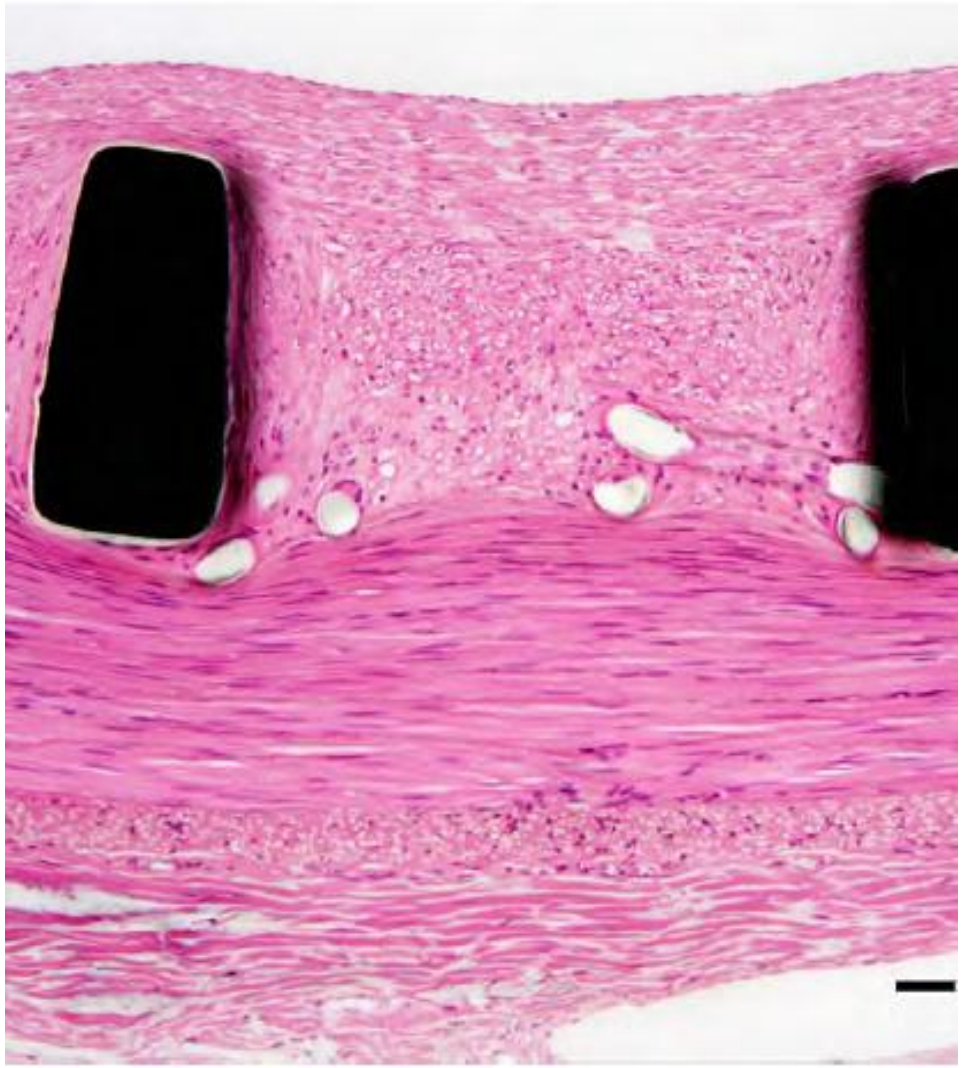
SMALEST √



CGuard EPS 90 days/pig



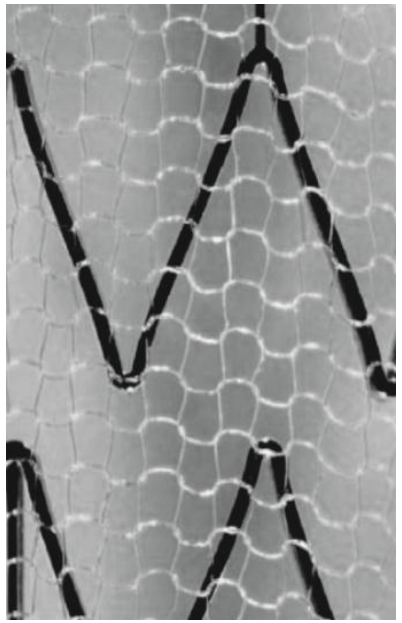
12-105 LCCA-S 3 13-1689-3 1.25x H&E.tif

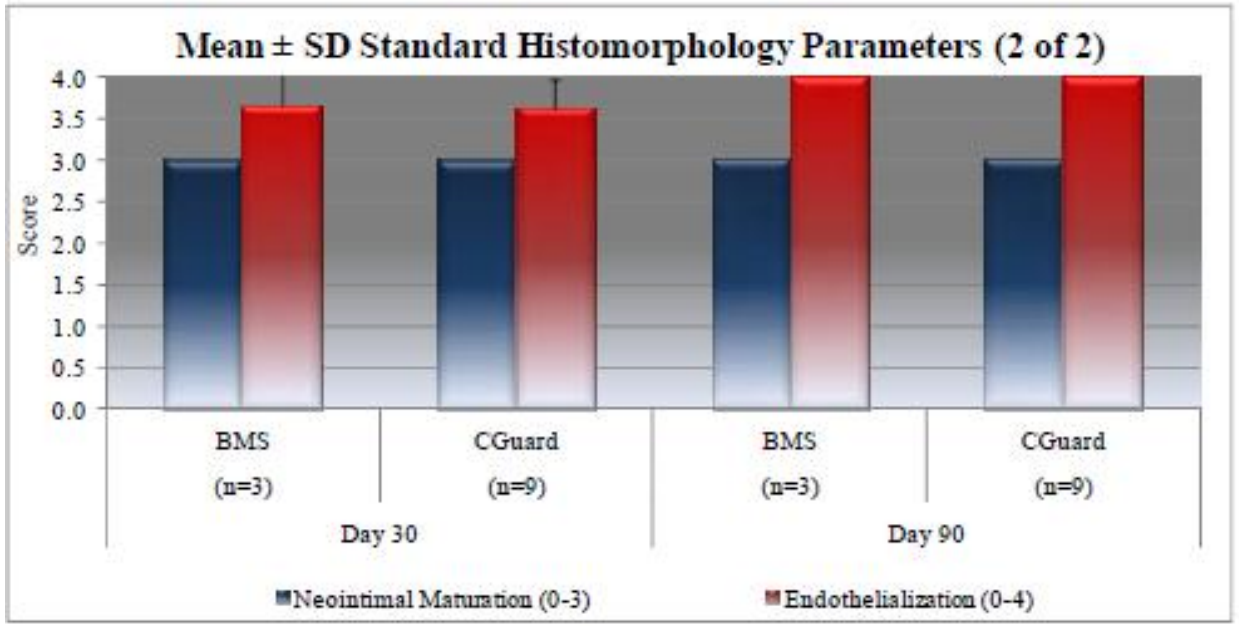


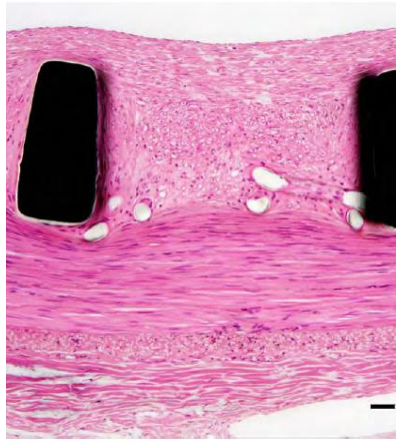
CA-S 3 13-1689-3 10x H&E.tif

InspireMD data / by permission

CGuard EPS 30 & 90 days / pig



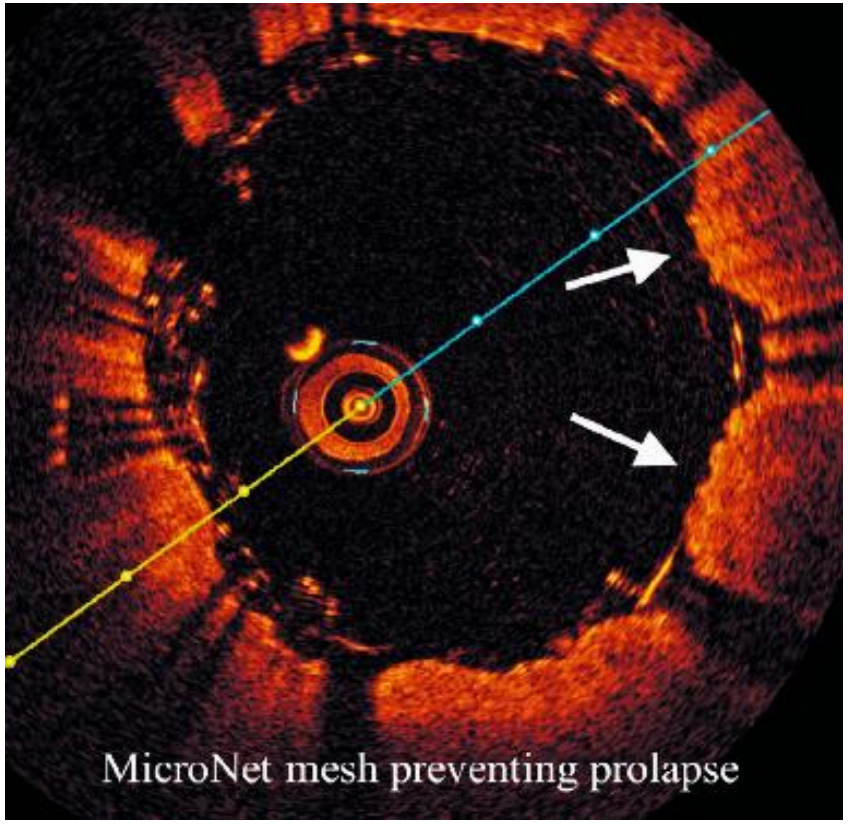




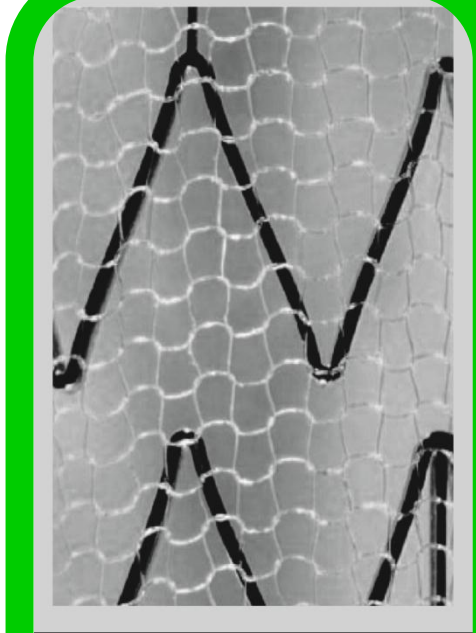
CA-S 3 13-1689-3 10x H&E.tif

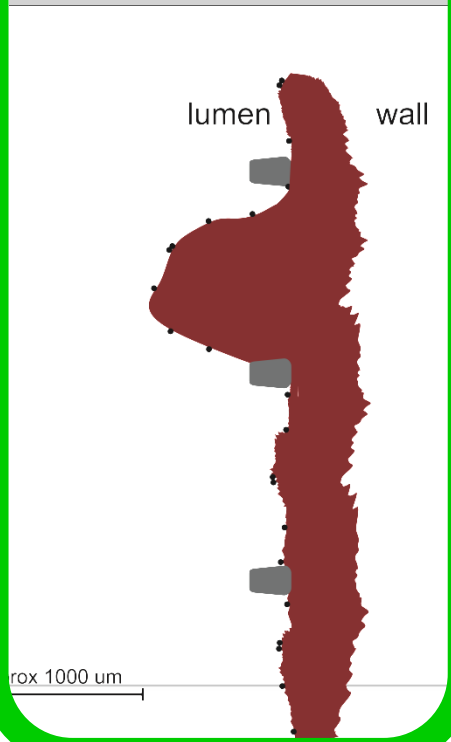
Mean ± SD and Median Standard Histomorphology Parameters								
Parameter	Day 30				Day 90			
	BMS (n=3)		CGuard (n=9)		BMS (n=3)		CGuard (n=9)	
Injury (0-3)	0.00 ± 0.01	0.00	0.00 ± 0.01	0.00	0.01 ± 0.02	0.00	0.00 ± 0.01	0.00
Inflammation (0-3)	0.43 ± 0.23	0.51	0.41 ± 0.22	0.36	0.17 ± 0.16	0.11	0.09 ± 0.08	0.07
Neointimal Fibrin (0-3)	1.13 ± 0.23	1.00	0.82 ± 0.37	1.00	0.00 ± 0.00	0.00	0.00 ± 0.00	0.00
Adventitial Fibrosis (0-3)	0.00 ± 0.00	0.00	0.02 ± 0.07	0.00	0.00 ± 0.00	0.00	0.00 ± 0.00	0.00
Neointimal Maturation (0-3)	3.00 ± 0.00	3.00	3.00 ± 0.00	3.00	3.00 ± 0.00	3.00	3.00 ± 0.00	3.00
Endothelialization (0-4)	3.67 ± 0.42	3.80	3.62 ± 0.35	3.80	4.00 ± 0.00	4.00	4.00 ± 0.00	4.00

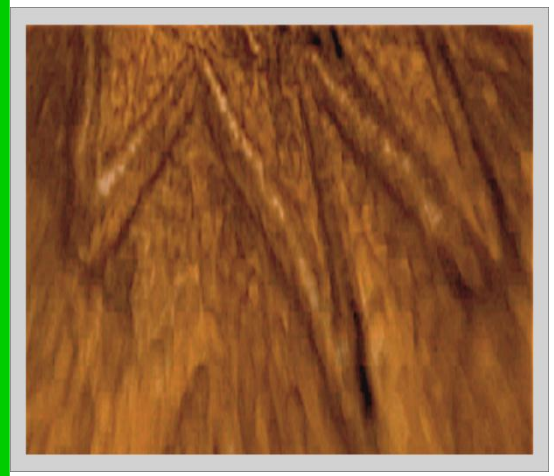
BMS = non mesh-covered CGuard nitynol frame; InspireMD data / used with permission



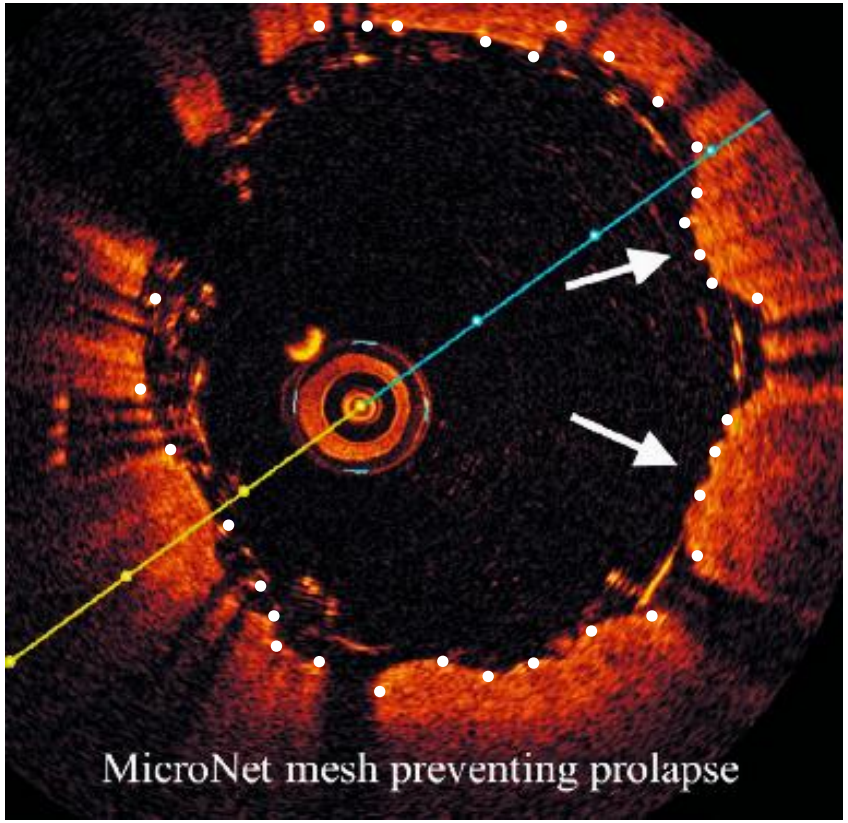
Tomyuki Umemoto et al.
EuroIntervention 2017







Musialek & Stabile
EuroIntervention 2017



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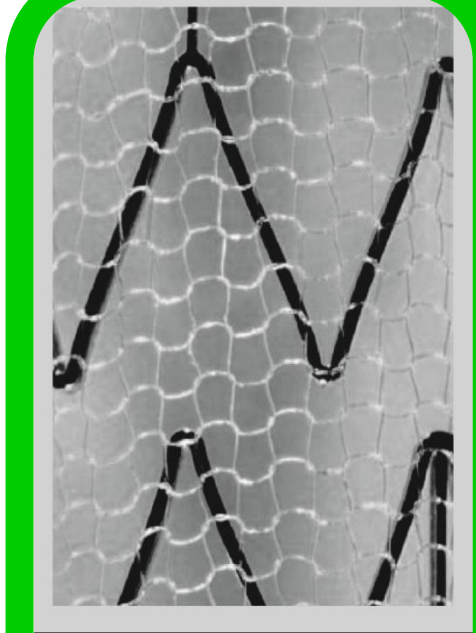
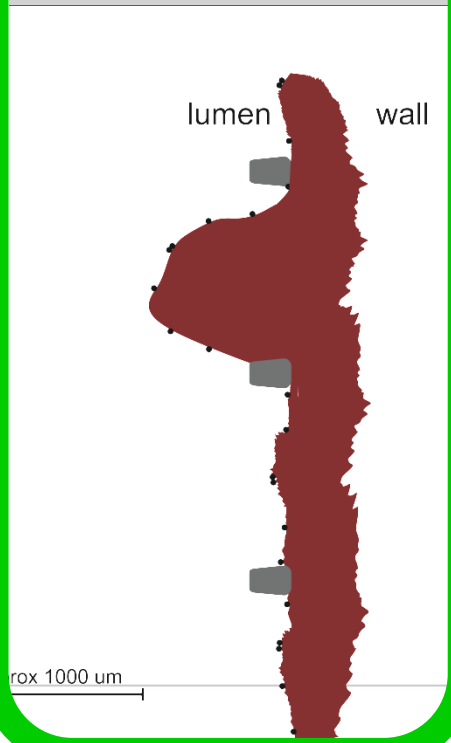
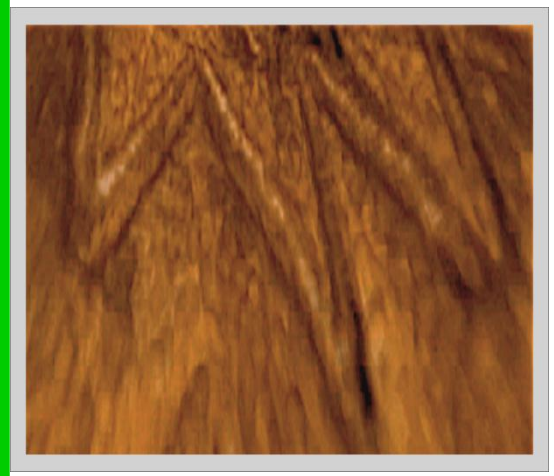
EuroIntervention 2017







Musialek & Stabile
EuroIntervention 2017

Objective

- to evaluate feasibility and outcome of routine **anti-embolic stent system** use in unselected, consecutive patients referred for carotid revascularization ('all-comer' study)

Prospective evaluation of **A**ll-comer pe**R**cutaneous c**A**roti**D** revascularization in sympto-matic and **I**ncreased-risk asymptomatic carotid artery stenosis using the C**G**uard™ **M**icronet-covered embolic prevention stent system

The PARADIGM Study

euro PCR 2016 LATE BREAKING TRIALS

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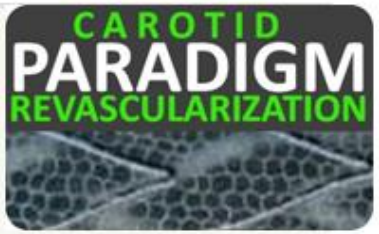
PARADIGM study: referrals flow chart

139 carotid stenosis patient referrals



Neuro Vascular Team

- Neurologist
- Interventional angiologist
- Vascular surgeon
- Cardiologist

for carotid revascularisation 108 patients

NOT for carotid revascularisation 31 patients

n=24: increased stroke risk and/or lesion severity criteria not met
n=2: ICA totally occluded on verification
n=2: ICA functional occluded + h/o prior ipsilateral large cerebral infarct with haemorrhagic transformation
n=1: major post-stroke disability, ICA functionally occluded
n=1: severe circulatory failure (ICA stenosis asympt.)
n=1: malignancy with limited life expectancy (ICA stenosis asympt.)

P. Musialek, A. Mazurek et al. *EuroIntervention* 2016;12:e658-70

PARADIGM

Methods (cont'd):

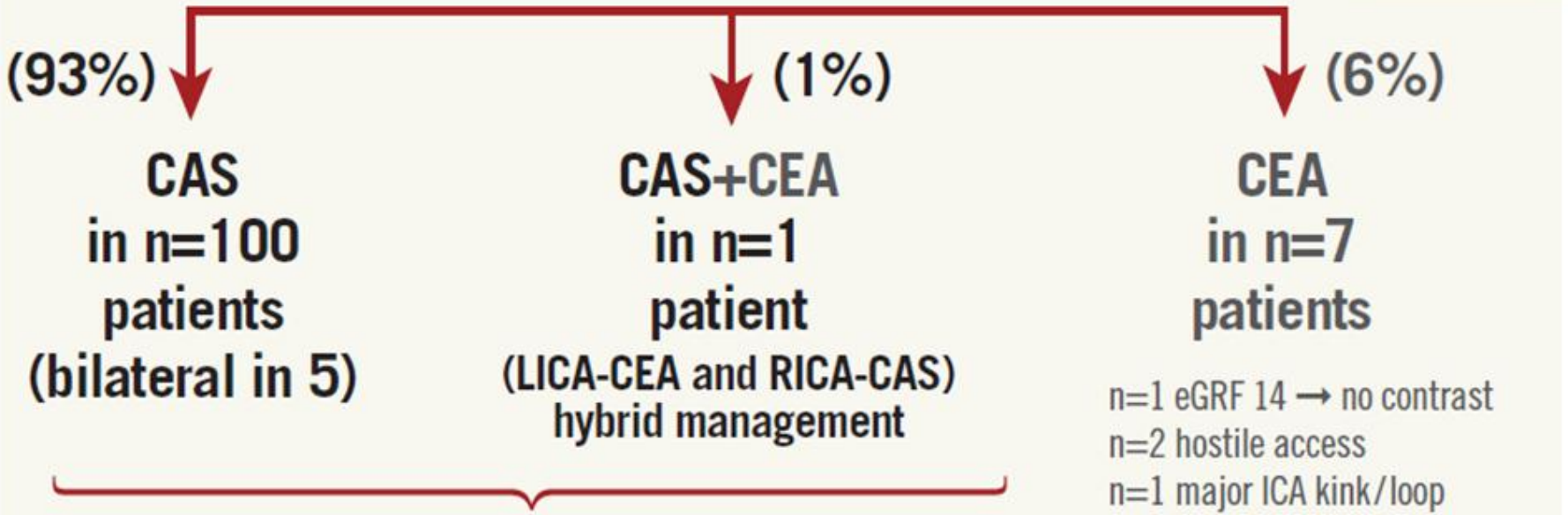
- **ASYMPTOMATIC patients treated interventionally only if at ↗ stroke risk**
- **established lesion-level increased-risk crieria used:**
  - **thrombus-containing**
  - **documented progressive**
  - **irregular and/or ulcerated**
  - **contralateral ICA occlusion/stroke**
  - **asymptomatic ipsilateral brain infarct**

euro PCR 2016 LATE BREAKING TRIALS

AbuRahma A et al. *Ann Surg.* 2003;238:551-562.
Ballotta E et al. *J Vasc Surg* 2007;45:516-522.
Kakkos SK et al. (ACSRS) *J Vasc Surg.* 2009;49:902-909.
Lovett JK et al. *Circulation* 2004;110:2190-97
Nicolaides AN et al. *J Vasc Surg* 2010;52:1486-96.
Taussky P et al. *Neurosurg Focus* 2011;31:6-17.

PARADIGM study: revascularisation flow chart

108 patients for carotid revascularisation



106 ICAs
treated endovascularly
in 101 patients
using exclusively the MicroNet-covered embolic prevention stent system

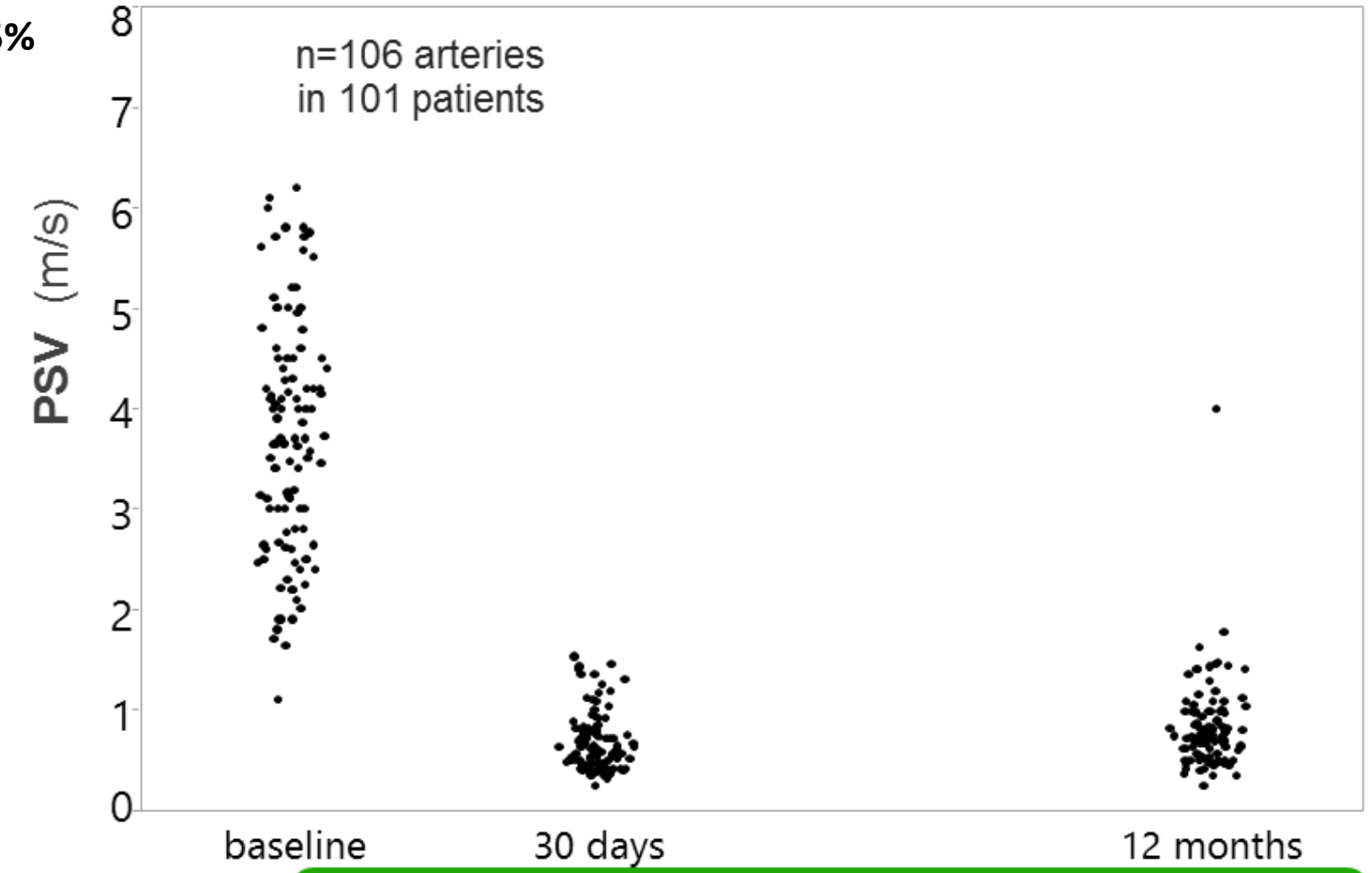
P. Musialek, A. Mazurek et al. *EuroIntervention* 2016;12:e658-70

CGuard™ EPS Carotid **PARADIGM** Study
12mo Duplex Ultrasound Data

CAROTID PARADIGM REVASCULARIZATION

12month data

Symptomatic – 54.5%



ECA* patency

ECA

100/106 ECAs were patent prior to CAS

baseline	30 days	12 months
97.0% 3 ECAs occluded at CAS	**97.0%** 97/100 ECAs patent	**96.9%** 93/96 ECAs patent

PARADIGM – Extend

continues as an ALL-Comer Multi-Centre Study

No exclusion criteria

other than absence of carotid stenosis that requires revascularization by NVT recommendation

428 patients
(48-87 years, 62.1% symptomatic)
465 lesions

PARADIGM study: revascularisation flow chart

108 patients for carotid revascularisation

(93%) → **CAS** in n=100 patients (bilateral in 5)

(1%) → **CAS+CEA** in n=1 patient (LICA-CEA and RICA-CAS) hybrid management

(6%) → **CEA** in n=7 patients

- n=1 eGRF 14 → no contrast
- n=2 hostile access
- n=1 major ICA kink/loop
- n=1 severe aortic valve disease +calcific LICA (AVR+CEA)
- n=1 floating thrombus in CCA
- n=1 ICA diameter <2.0 mm +contralateral ICA occlusion

106 ICAs treated endovascularly in 101 patients
using exclusively the MicroNet-covered embolic prevention stent system

P. Musialek, A. Mazurek et al. *EuroIntervention* 2016;12:e658-70

PARADIGM – Extend

continues as an ALL-Comer Multi-Centre Study

- 100% MicroNet-covered embolic prevention stent system use (ie, not a single other stent type has been used throughout study duration).
- Proximal/distal intra-procedural neuroprotection use was 38.3%/61.7%.
- Large balloon/high-pressure stent optimization was routinely performed, leading to a single-digit (6.9%) mean post-procedural residual angiographic stenosis.
- Adequate heparinization, with ACT control (≥250 s)
- Independent neurologist and duplex evaluation are performed before and after (48h and 30 days, then yearly) carotid revascularization.

Results

Peri-procedural safety:

- peri-procedural death or major ischemic stroke (IS) rate was 0%.
- One event was adjudicated as minor IS (0.23%) – extension of prior infarct scar in a patient with prolonged hypotension
- one as myocardial infarction (MI) (type2; 0.23%) - two-vessel non-revascularizable CTO.

30-day follow-up:

- total death/ stroke rate at 30 days - 0.7%, and total death/stroke/MI rate at 30 days was 0.93%
- one IS haemorrhagic transformation leading to death (0.23 %)
- one bleeding-related death (0.23%)
- no major IS by 30 days (0.0%)

Duplex ultrasound (DUS) in-stent/ lesion velocites [m/s]

	PSV ± SD	EDV ± SD
Baseline	3.72 ± 1.25	0.63 ± 0.69
Post-procedural	0.67 ± 0.28	0.18 ± 0.08
12 - mo	0.78 ± 0.40	0.21 ± 0.10
24 - mo	0.75 ± 0.36	0.19 ± 0.09
36 - mo	0.75 ± 0.35	0.21 ± 0.09
48 - mo	0.72 ± 0.27	0.20 ± 0.07
60 - mo	0.79 ± 0.58	0.21 ± 0.11

PARADIGM – Extend

	12 mo	24 mo	36 mo	48 mo	60 mo
	n = 326	n= 211	n= 129	n=75	n=21
Ipsilateral stroke	0	0	0	0	1 (device unrelated)
Any stroke	0	2 (1-cerebellum)	1 (brain stem)	1 (contralateral)	1
Stroke related death	0	0	0	0	1
MI or other non - cerebral VA	1	3	2	2	0
Restenosis	1 (after RTh)	1	0	0	0
Any death	13 (CHF – 4, Ca–3, PE–1, urosepsis – 1, MI-2, COPD-1, surg-1)	10 (CHF – 3, Ca -2, MI - 2, intracranial bleed -1, surg-2)	6 (Ca – 2, CHF -2, MI – 1, pneumonia/ sepsis - 1)	6 (CHF -2, MI – 2, Ca - 2)	1 (stroke)

PARADIGM – Extend

	12 mo	24 mo	36 mo	48 mo	60 mo
Ipsilateral stroke	0	0	0	0	1 (device unrelated)
Any stroke	0	2 (1-cerebellum)	1 (brain stem)	1 (contralateral)	1
Stroke related death	0	0	0	0	1
MI or other non - cerebral VA	1	3	2	2	0
Restenosis	1	1	0	0	0
Any death	13 (CHF – 4, Ca–3, PE–1, urosepsis – 1, MI-2, COPD-1, surg-1)	10 (CHF – 3, Ca -2, MI - 2, intracranial bleed -1, surg-2)	6 (Ca – 2, CHF -2, MI – 1, pneumonia/ sepsis - 1)	6 (CHF -2, MI – 2, Ca - 2)	1 (stroke)

By 60 months

Normal healing

No Stent Thrombosis

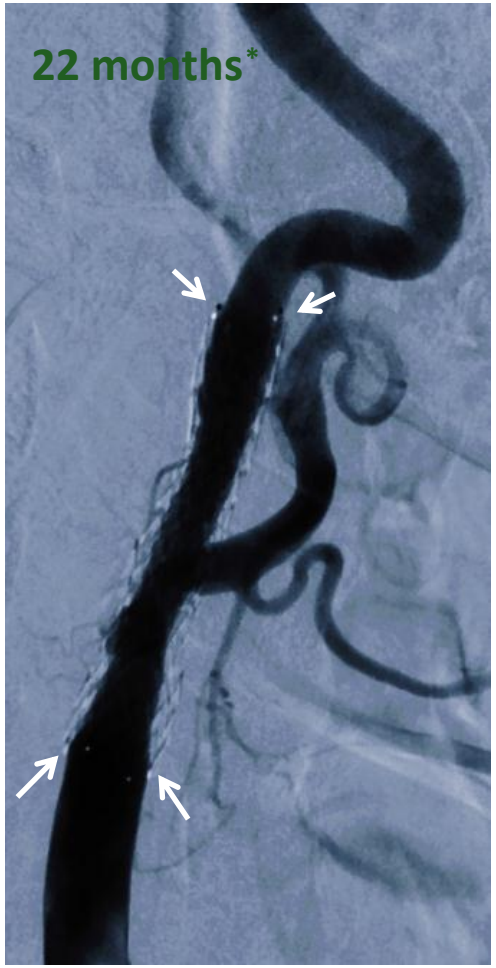
No abnormal ISR signal

(Per-vessel ISR 0.92% - 4/436; DEB-PTA)

CGuard: Long-Term Angiography

78 yo man, symptomatic LICA

Optimal endovascular reconstruction



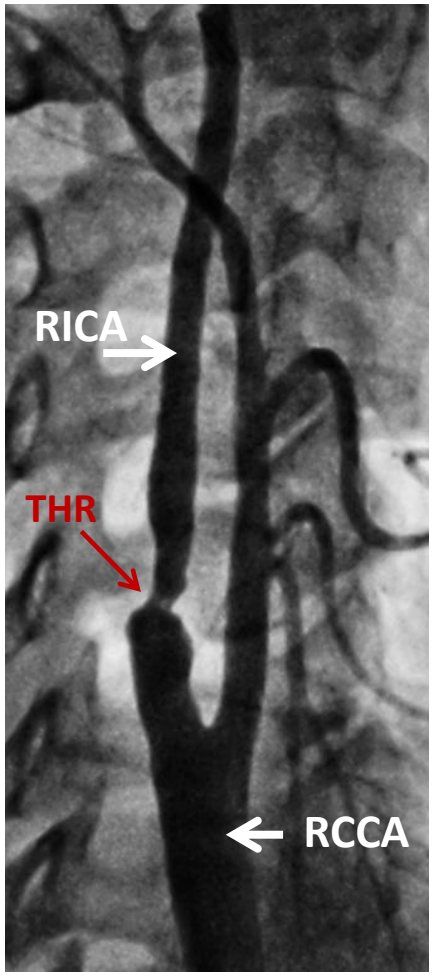
CGuard 9.0x40mm
Post-dil 5.0/24atm

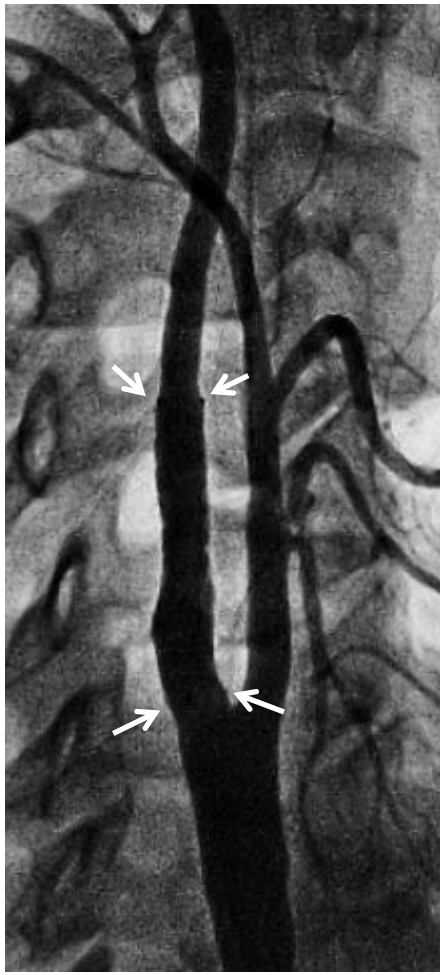
NORMAL healing

*Aortic stenosis progression to severe AS

CGuard: Long-Term Angiography

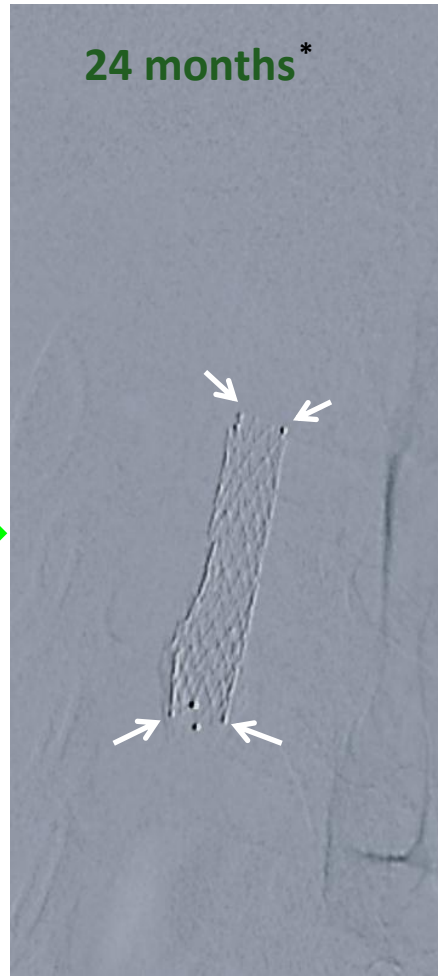
46 yo man, asymptomatic RICA
(progressive *plus* increased-stroke-risk morphology)

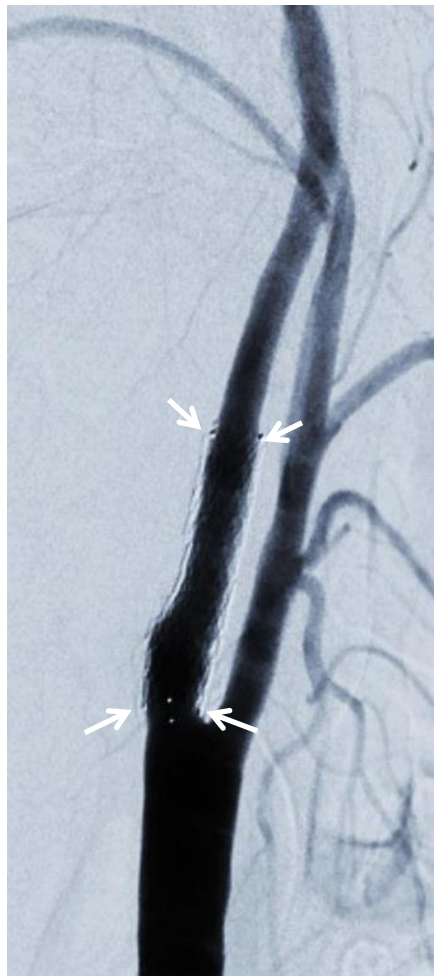




CGuard 8.0x30mm
Post-dil 5.0/20atm

Optimal endovascular reconstruction





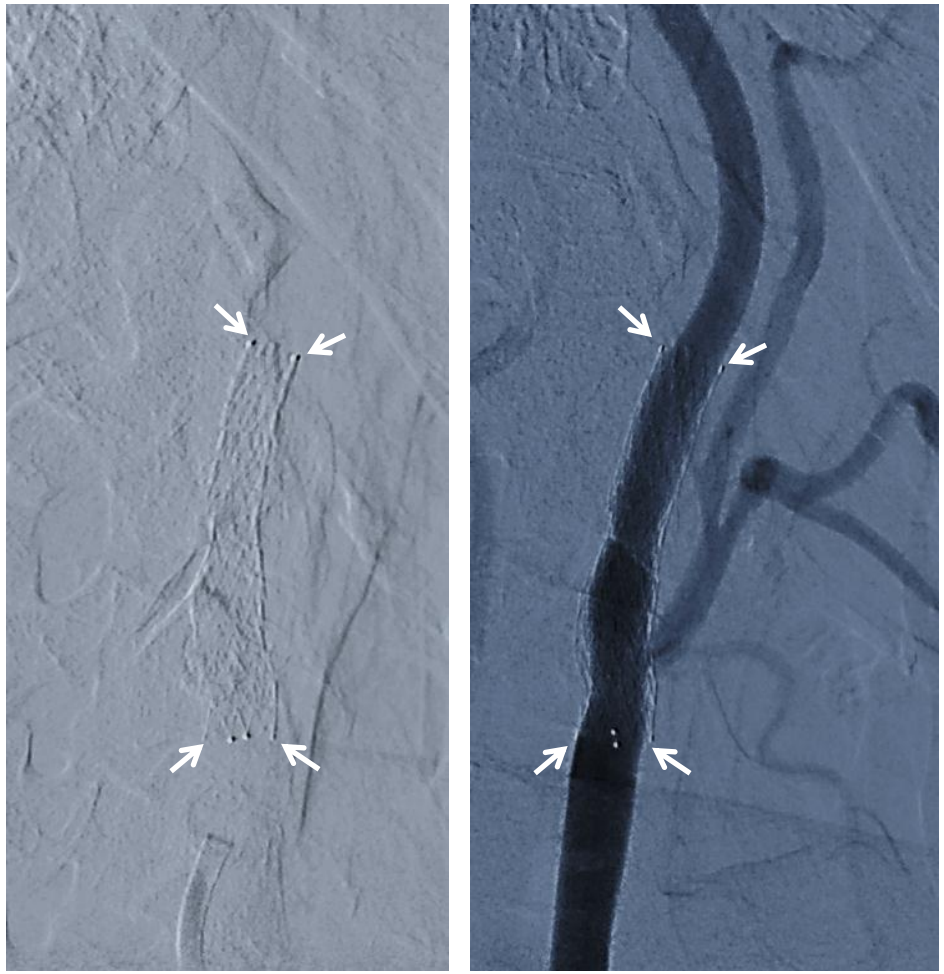
NORMAL healing

*PAD symptomatic progression

CGuard: Long-Term Angiography

54 yo woman, symptomatic RICA **26 months** *

Optimal endovascular reconstruction

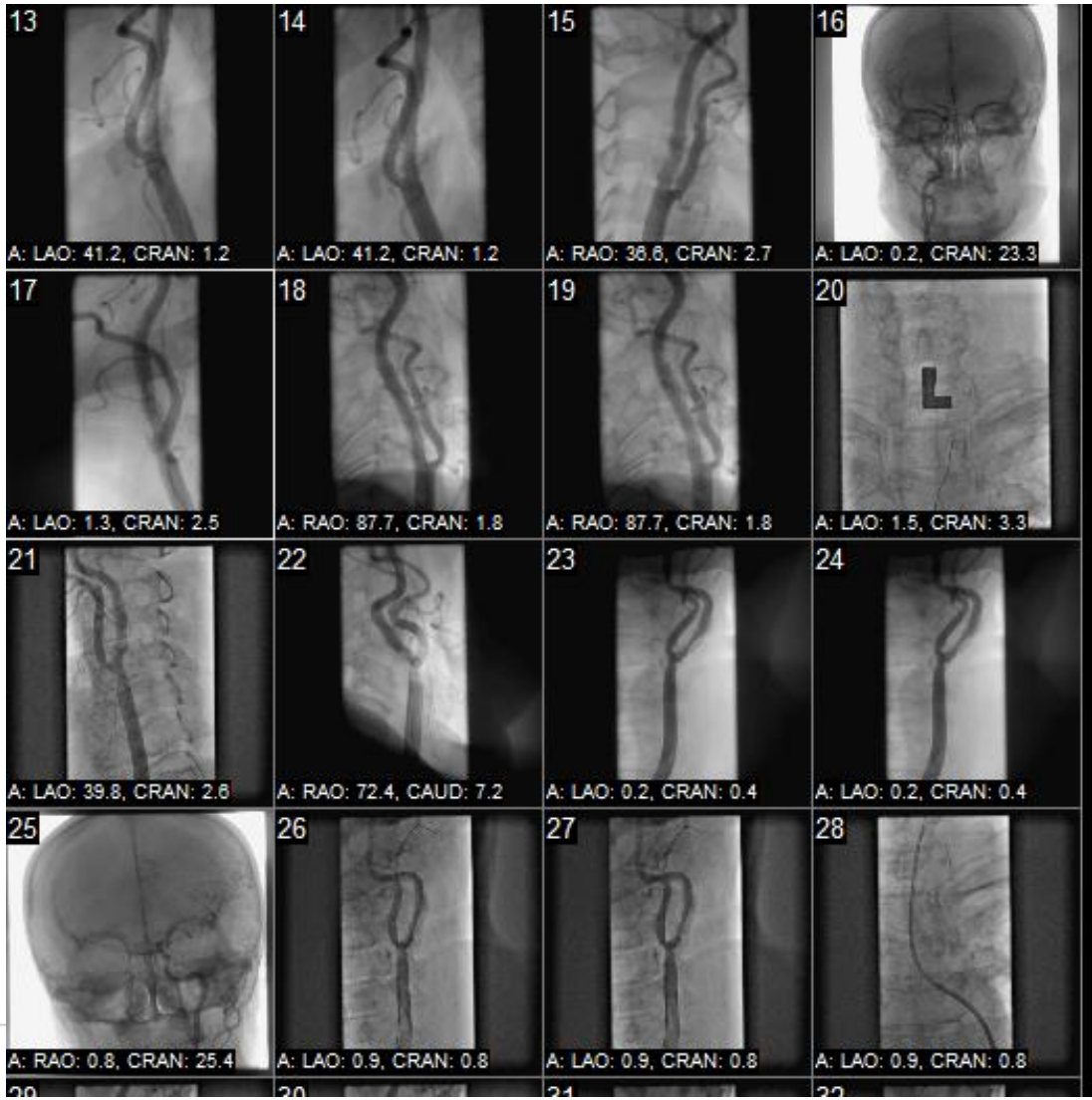


NORMAL healing

*CAD symptomatic progression

PARADIGM – Extend

continues as an ALL-Comer Multi-Centre Study



PARADIGM – Extend

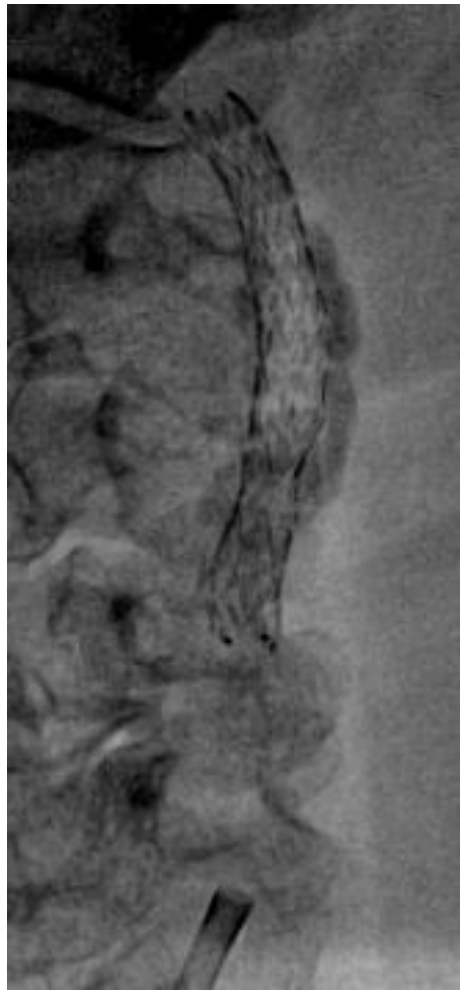
continues as an ALL-Comer Multi-Centre Study

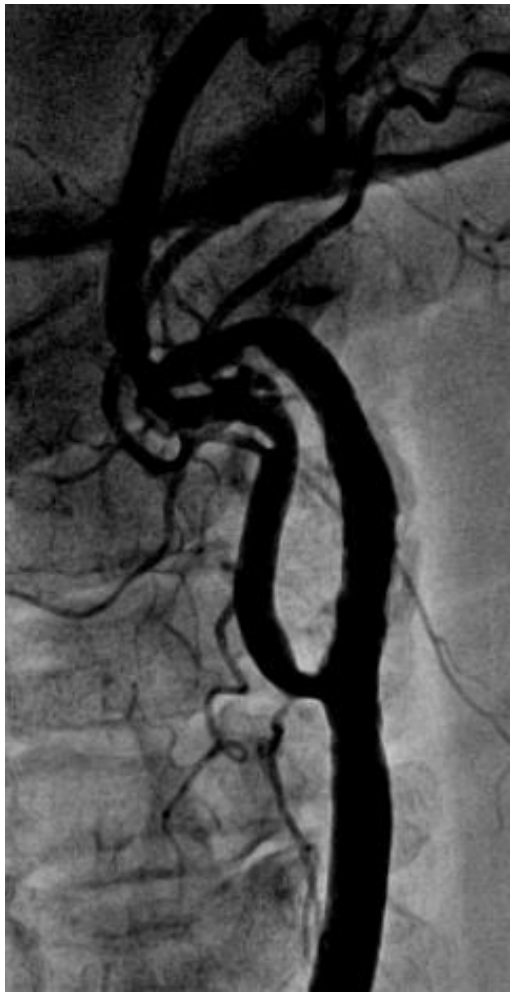
RICA 31mo

LICA progression

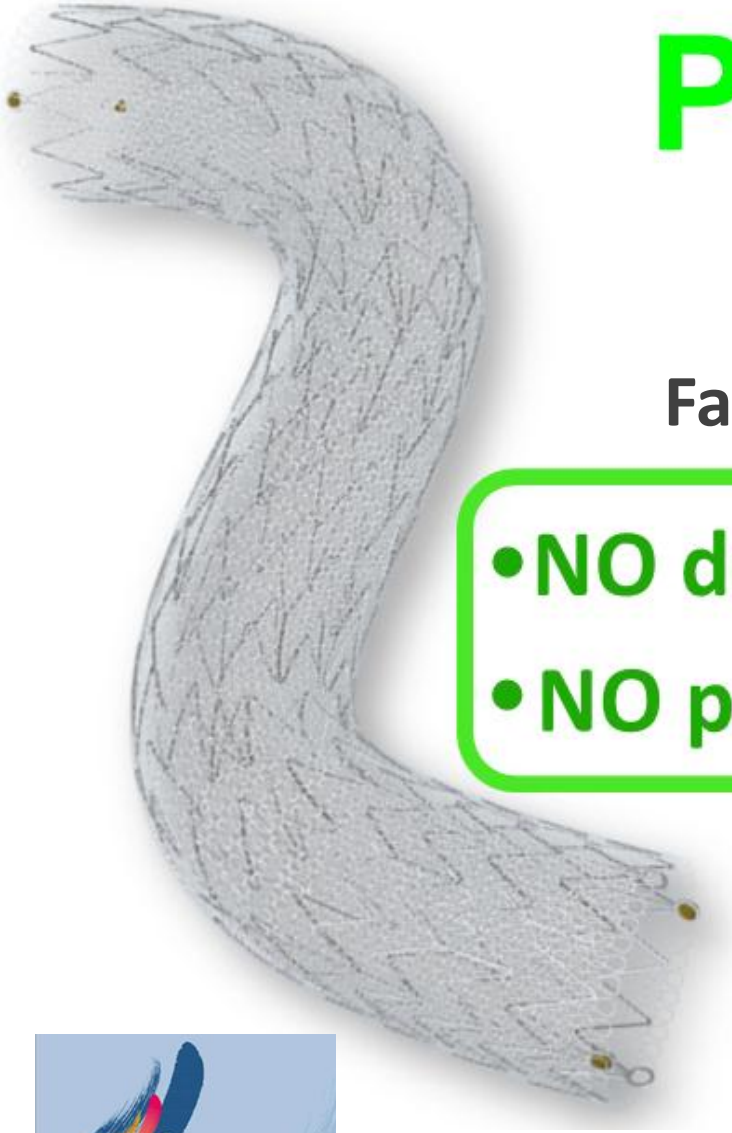
PARADIGM – Extend

continues as an ALL-Comer Multi-Centre Study





CGUARD™
Carotid Embolic Prevention System



PARADIGM–EXTEND

@ 60 months

Favourable Cerebral Outcome

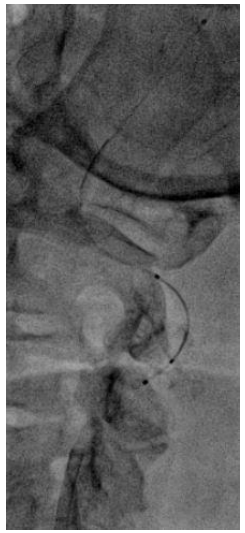
- **NO device-related adverse events**
- **NO procedure-related events**

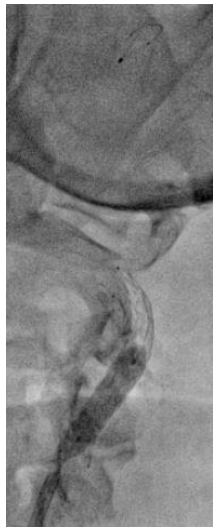
s u s t a i n e d
stroke prevention

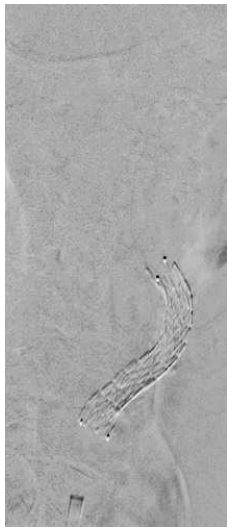
CAROTID PARADIGM REVASCULARIZATION

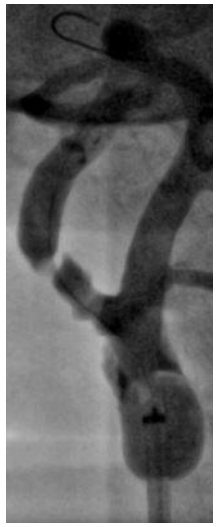
LINC 2020

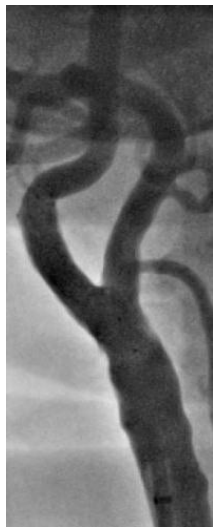
Endovascular Solution for All-Comers







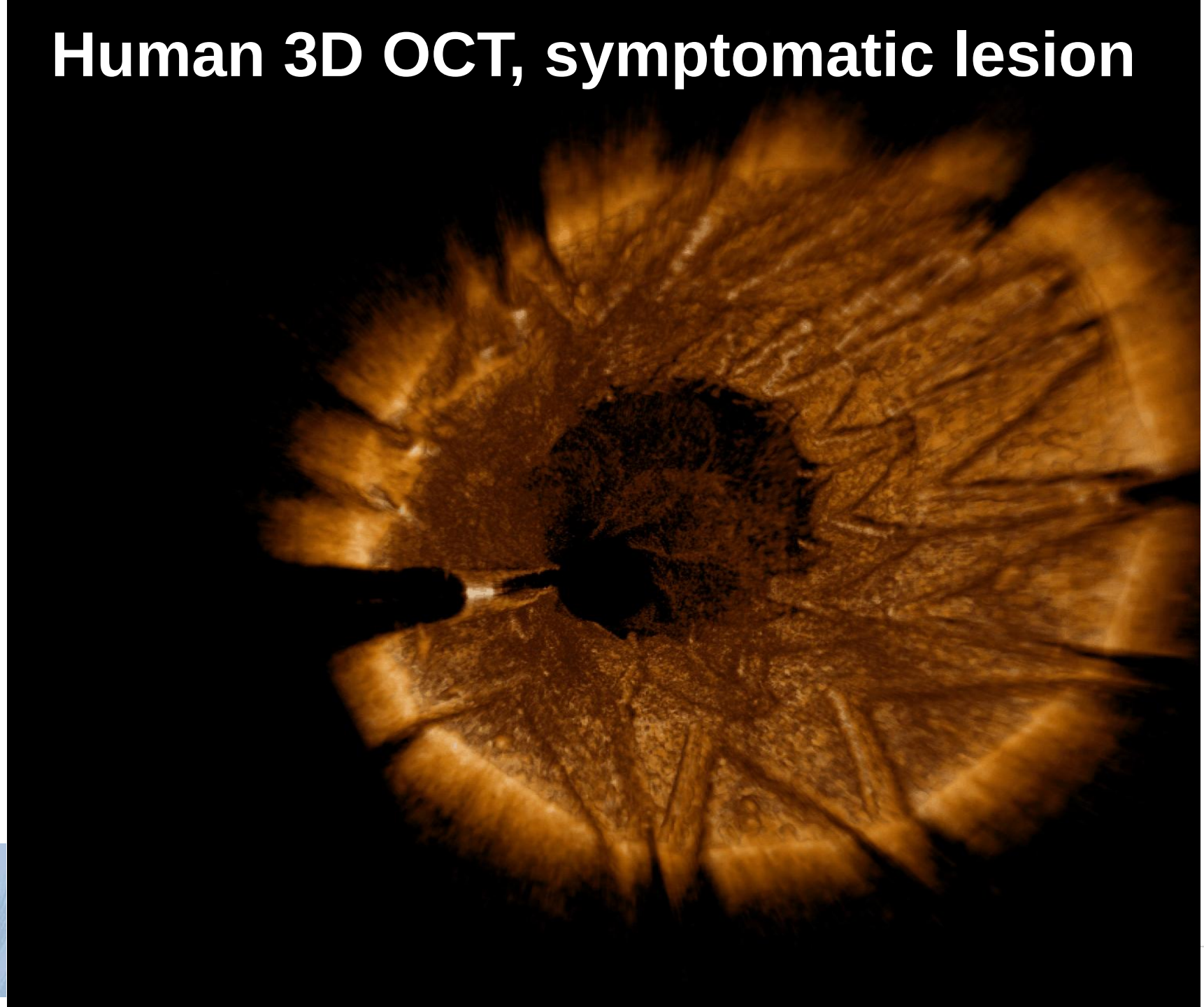


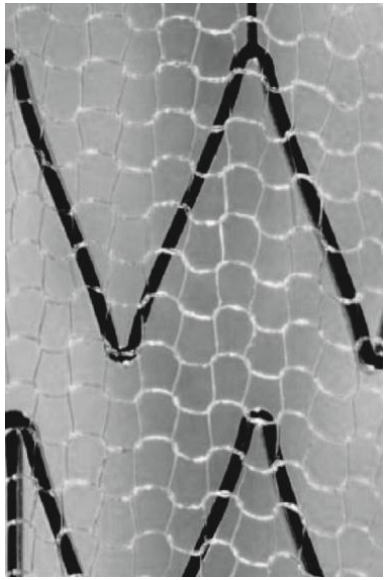


Endovascular Reconstruction of the Carotid Bifurcation

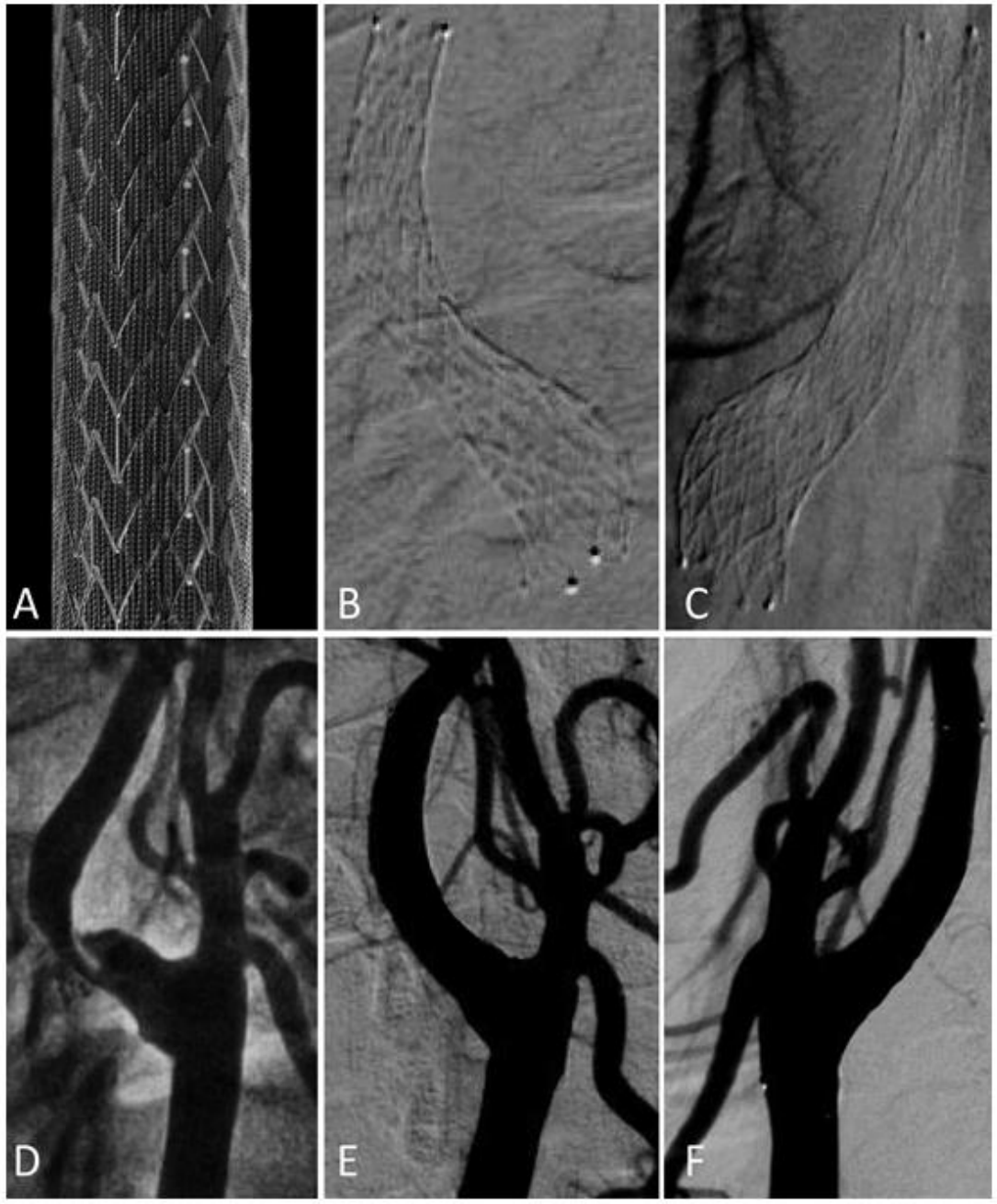
Prevention of embolism, High radial force, Conformability

Human 3D OCT, symptomatic lesion





PARADIGM

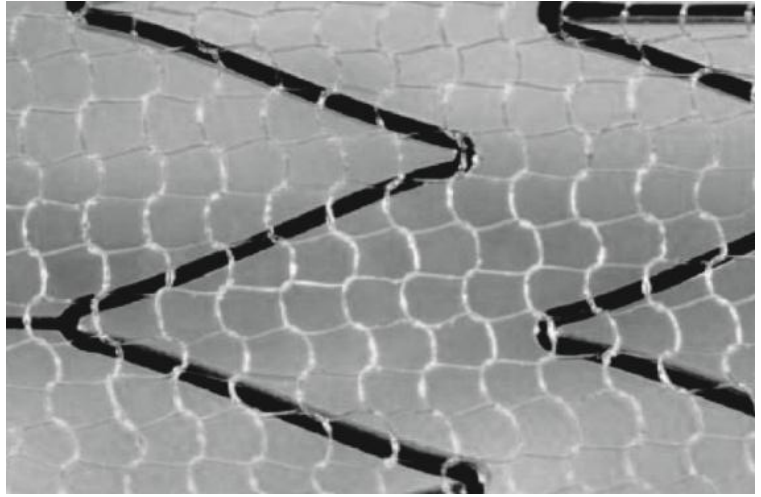


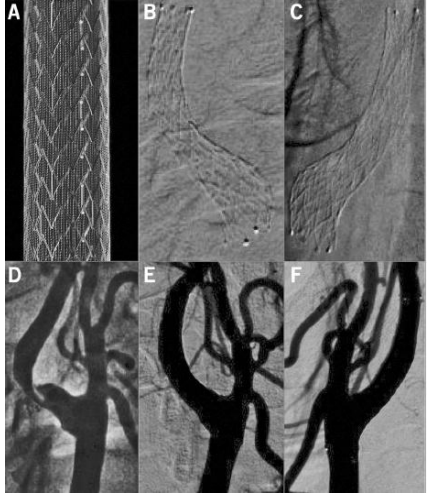
CAROTID PARADIGM REVASCULARIZATION

systematic

CEA-like effect of CAS

LINC 2020





This concept has been desired.

And it works.

This is the future

of Carotid Artery Stenting

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Double-Layer Carotid Stents: From the Clinical Need, through a Stent-in-Stent Strategy, to Effective Plaque Isolation… the Journey Toward Safe Carotid Revascularization Using the Endovascular Route

Journal of Endovascular Therapy
2019, Vol. 26(4) 572–577

DOI: 10.1177/1526602819861546
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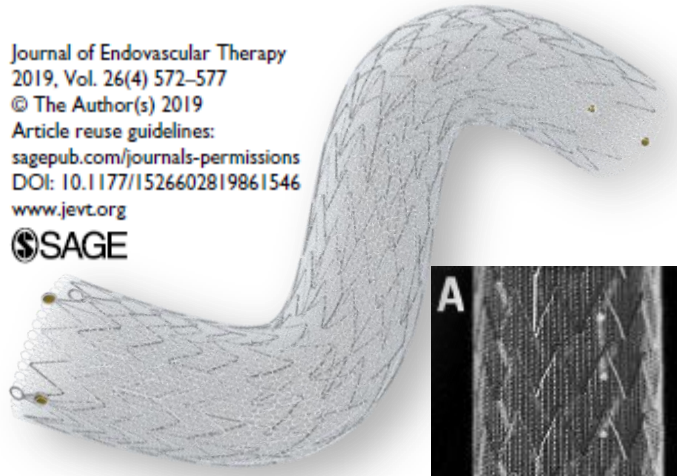
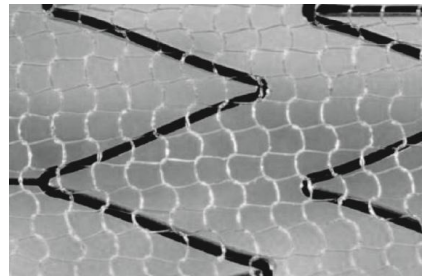
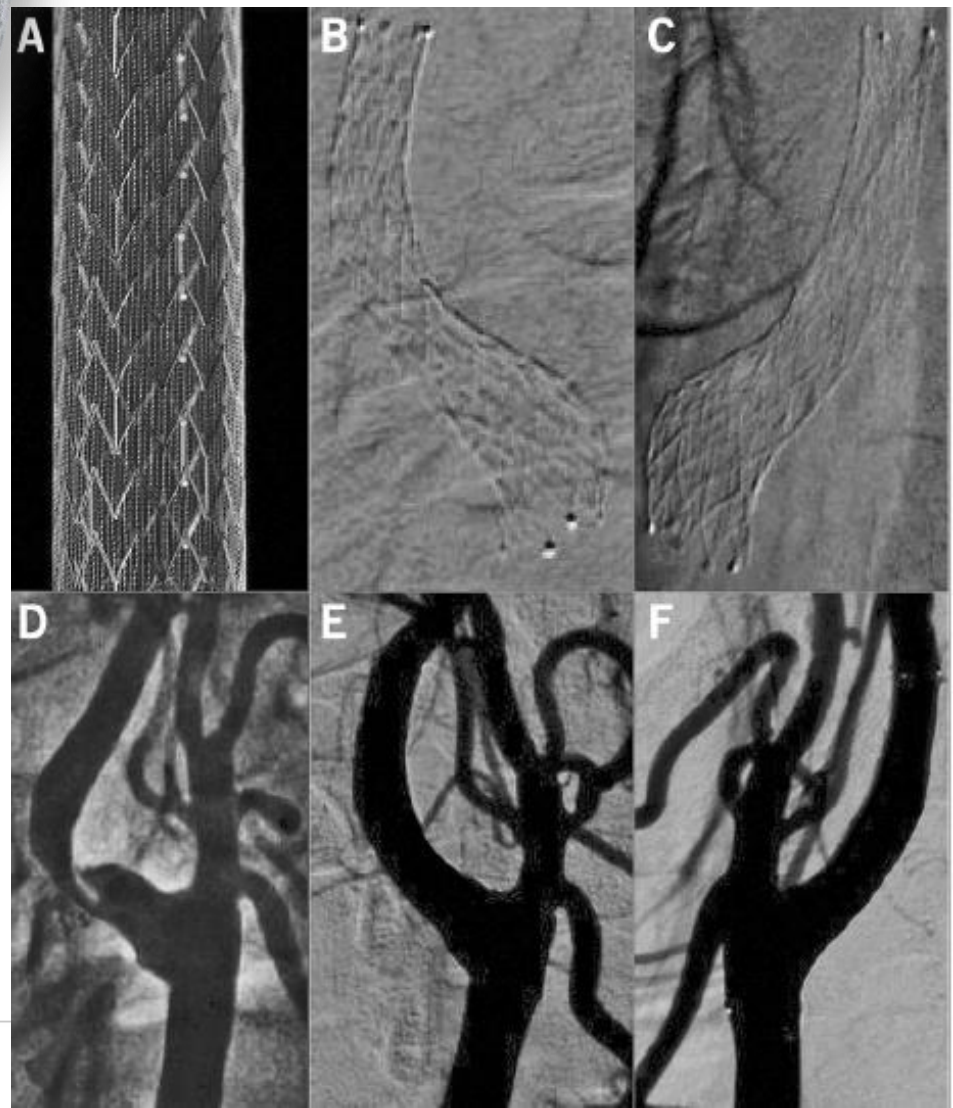


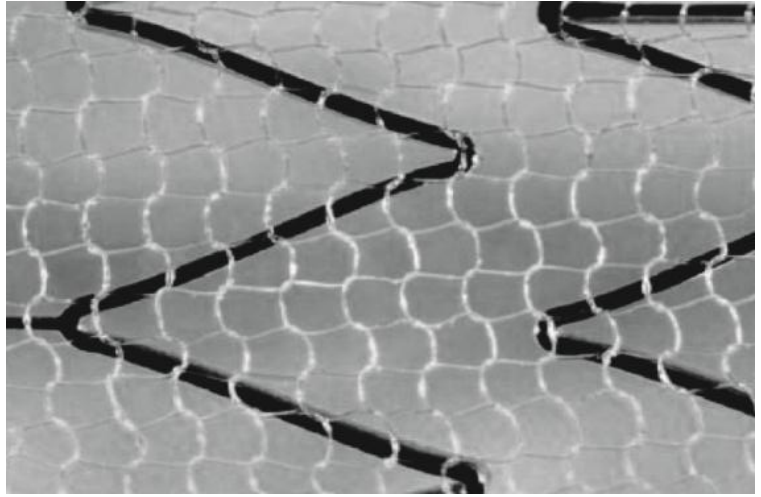


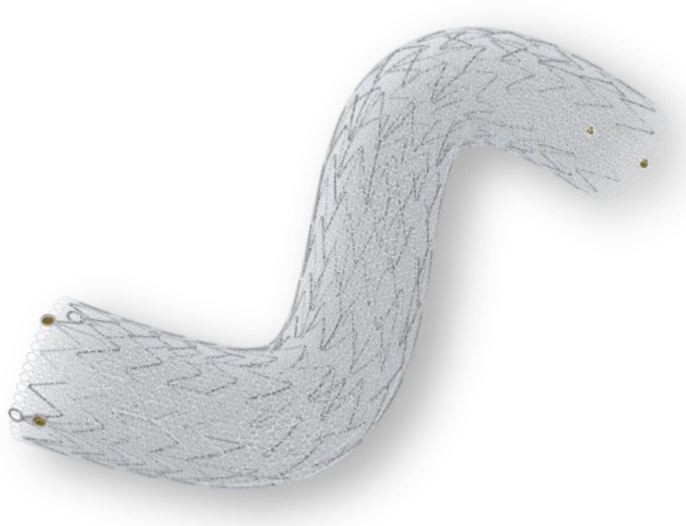
Piotr Musiałek, MD, DPhil[1] and Gary S. Roubin, MD, PhD[2]

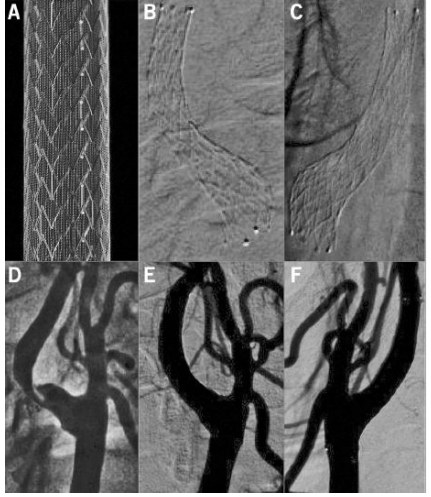
Keywords
carotid artery stenosis, carotid artery stenting, carotid endarterectomy, closed-cell stent, MicroNET, open-cell stent, plaque protrusion, stent-graft, restenosis, double-layer stent, unstable plaque

Both surgical and endovascular routes of carotid revascularization are associated with the risk of symptomatic and asymptomatic cerebral embolism.[1-3] Optimized pharmacotherapy, the mainstay of atherosclerosis management, can reduce or delay but not abolish the risk of stroke from atherosclerotic carotid artery stenosis.[4-7] Interventional elimination or sequestration of the thromboembolic carotid plaque[8-10] remains an important consideration in a significant proportion of patients if carotid stenosis–related strokes are to be prevented rather than experienced. This is the focus and the stent free-cell area also affect the risk of embolism after stent placement. Thus, while optimized neuroprotection during CAS may minimize intraprocedural cerebral embolism,[18-20,23,24] the problem of early or delayed postprocedural embolism remains.[3,25-27] With optimal patient selection technique and antiplatelet therapy, post-stent embolic phenomena are largely related to intrastent plaque prolapse, balloon trauma, and subsequent embolization. This may occur after the period of intraprocedural cerebral protection using flow reversal techniques and/or filters.









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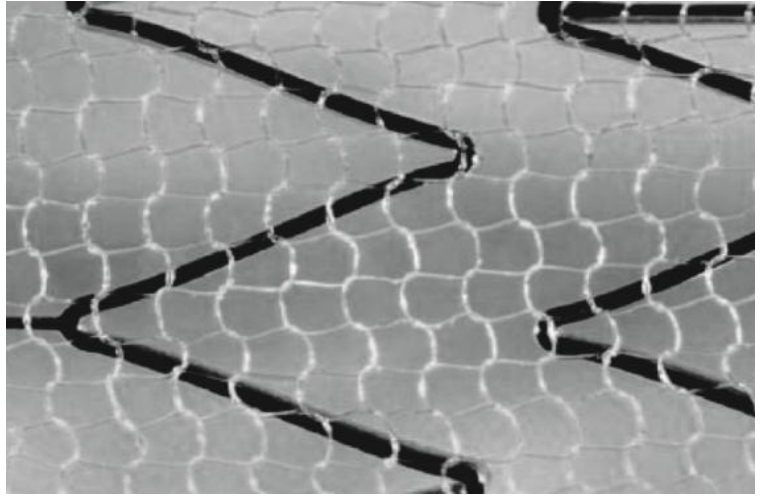
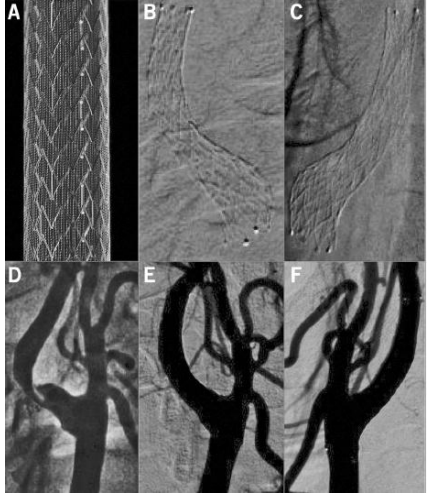
of Carotid Artery ~~Stenting~~





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And it works.

This is the future

of Carotid Artery S[illegible]g

revascularization !

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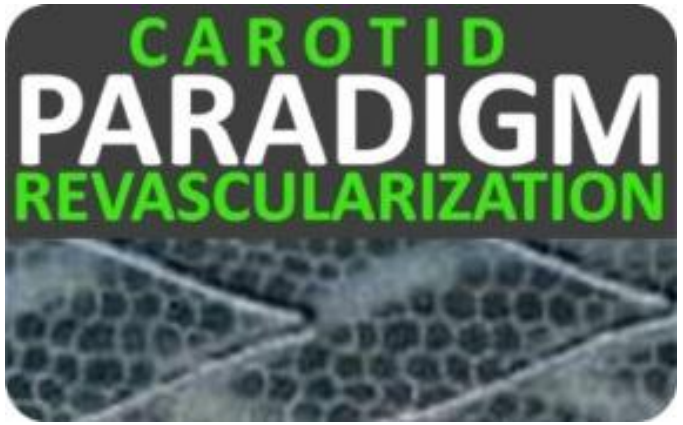

Accumulating long-term evidence for microNET-covered stent safety, efficacy and durability in primary and secondary stroke prevention:

5-year data from the PARADIGM-Extend prospective academic trial

P. Musialek, A. Mazurek, M. Trystuła, A. Borratynska, T. Tomaszewski, A. Lesniak-Sobelga, M. Brozda, U. Gancarczyk, A. Klecha, ST. Kowalczyk, E. Sobieraj, N. Dluzniewska, M. Urbanczyk, P. Banys, J. Miszczuk, P. Judzialo, G. Stankiewicz, T. Drazkiewicz, P. Podolec

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John Paul II Hospital, Kraków, Poland
& Collaborating Vascular Centres

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