EuroPCR 2015
19th-22nd May, 2015 - Paris

Prospective evaluation of All-comer peRcutaneous cArotiD revascularization In symptomatic and increased-risk asymptomatic carotid artery stenosis using CGuard™ Micronet-covered embolic prevention stent system: The PARADIGM Study

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Potential conflicts of interest

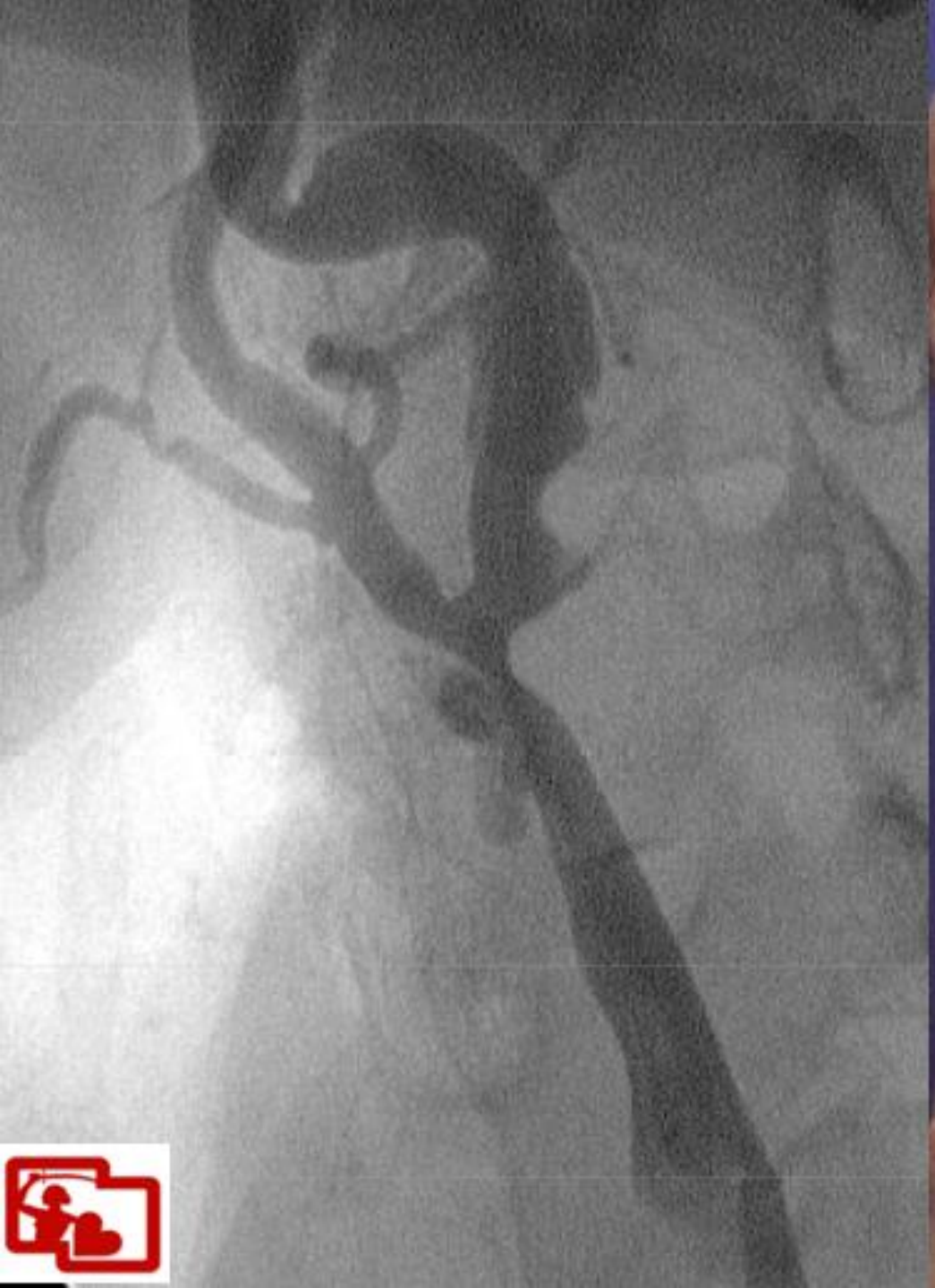
Speaker's name: Piotr Musialek

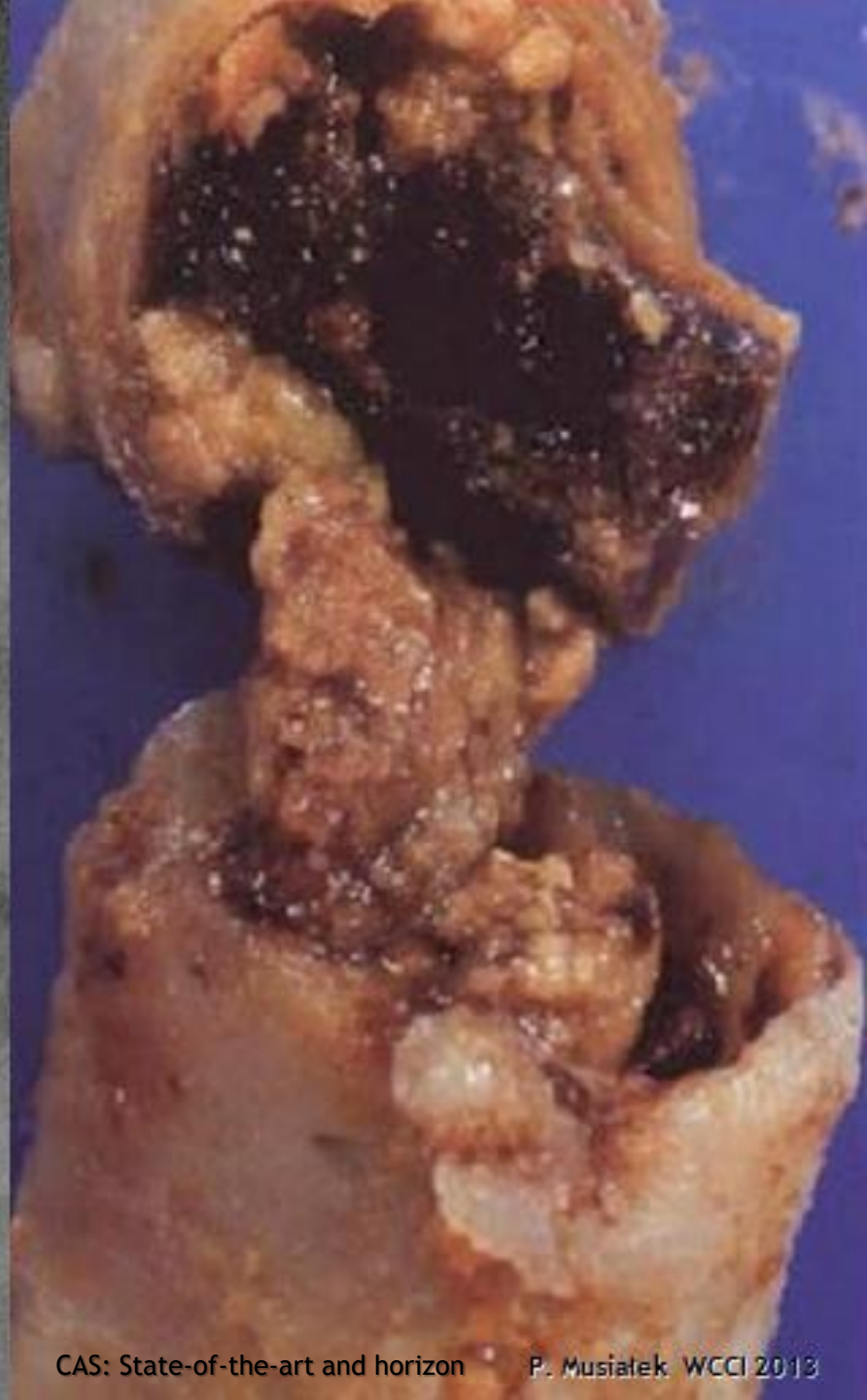
☑ **I have the following potential conflicts of interest to report:**

Consulting / Research Support / Speaker Bureau

ABBOTT VASCULAR
Balton Ltd
InspireMD
MEDTRONIC

NB. Research in this presentation is **not** industry-funded





CAS (and CEA) are –and will remain– emboli-generating procedures

Effect of the Distal-Balloon Protection System on Microembolization During Carotid Stenting

Nadim Al-Mubarak, MD; Gary S. Roubin, MD, PhD; Jiri J. Vitek, MD, PhD; Sriram S. Iyer, MD; Gishel New, MD; Martin B. Leon, MD

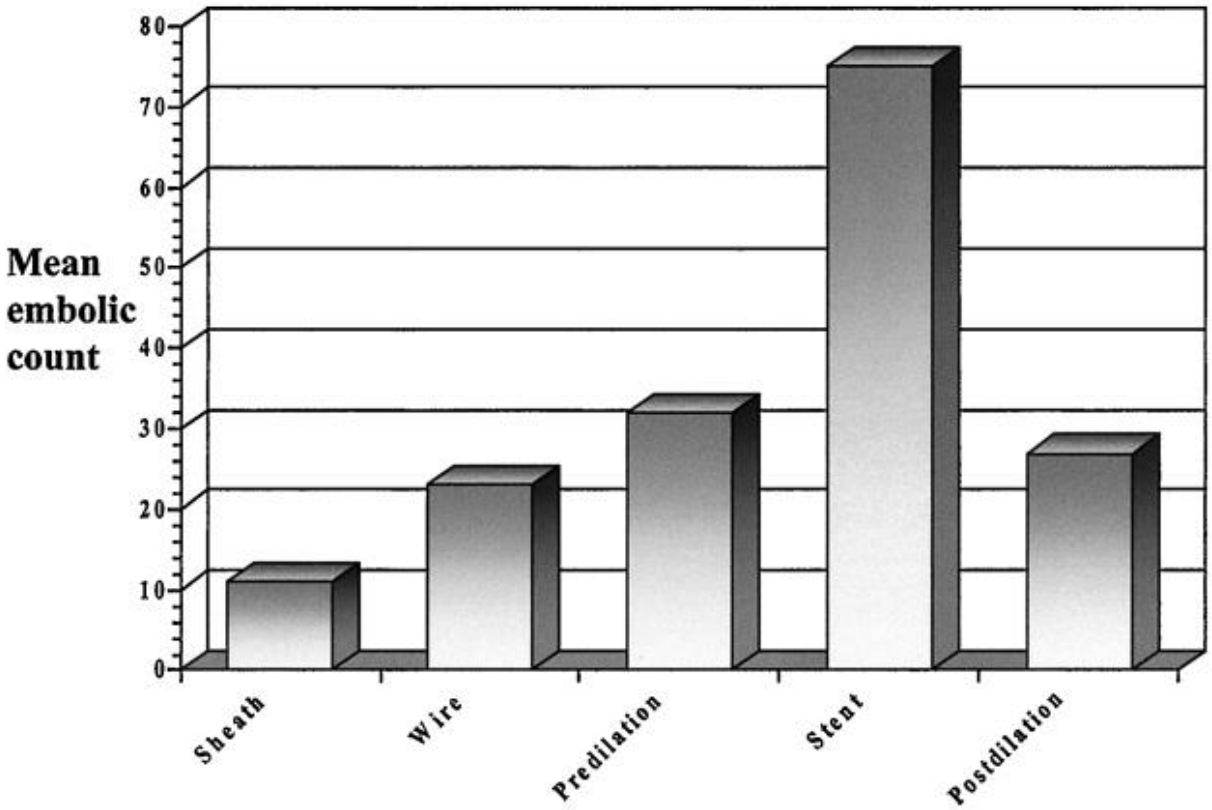


Figure 1. Microembolic profile during unprotected CAS. The mean MES counts during various phases of the procedure are displayed.

Circulation. 2001;104:1999-2002

Does Free Cell Area Influence the Outcome in Carotid Artery Stenting?

M. Bosiers,[1*] G. de Donato,[2] K. Deloose,[1] J. Verbist,[3] P. Peeters,[3]
F. Castriota,[4] A. Cremonesi[4] and C. Setacci[4]

Overview of event rates related to the different stents

n = 3179 consecutive CAS patients

	Total population			Symptomatic population			Asymptomatic population		
	Patients	All events	Post-procedural events	Patients	All events	Post-procedural events	Patients	All events	Post-procedural events
Stent name									
X-act		1.9%	1.9%		2.2%	2.2%		1.7%	1.7%
Nexstent		3.3%	3.3%		0.0%	0.0%		4.2%	4.2%
Wallstent		2.3%	1.2%		2.3%	1.2%		2.3%	1.2%
Precise		4.1%	3.1%		6.3%	4.9%		2.0%	1.3%
Protégé		3.0%	3.0%		6.7%	6.7%		1.4%	1.4%
Acculink		4.2%	3.7%		7.7%	7.1%		1.7%	1.2%
Exponent		11.8%	5.9%		9.1%	9.1%		13.0%	4.3%
Total	3179	2.83%	1.9%		3.6%	2.73%	1862	2.25%	1.3%

2/3

CAS neuro events (stroke, TIA) are POST-procedural

Eur J Vasc Endovasc Surg Vol 33, February 2007

FREE CELL AREA drives CAS neurologic adverse events (and majority are those during stent healing !)

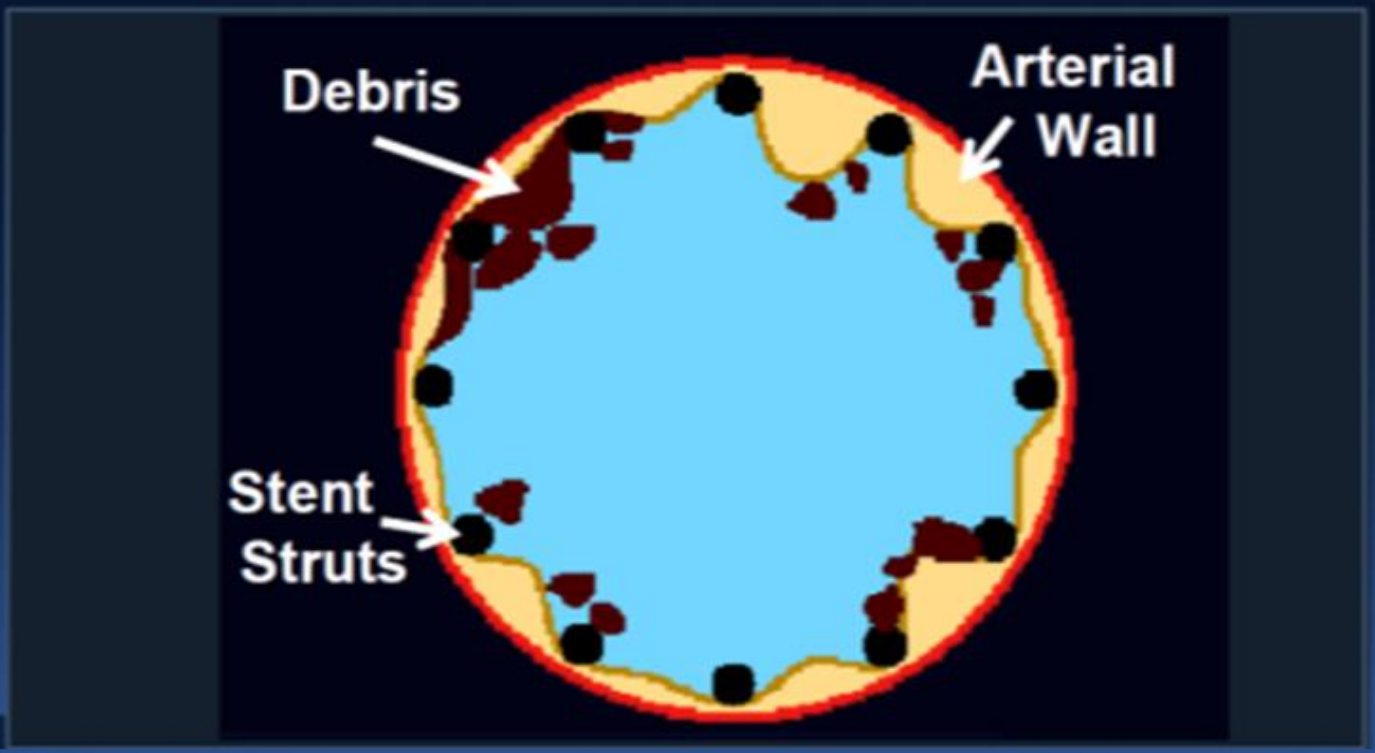
Free cell area	Total population		Symptomatic population	
	All events	Post-procedural events	All events	Post-procedural events
<2.5 *vs* [2.5, 5]	1.00	1.00	1.00	1.00
<2.5 *vs* [5, 7.5]	0.054	0.072	0.048	0.024
<2.5 *vs* >7.5	0.27	0.006	0.0006	$2.8\ 10^{-6}$

Eur J Vasc Endovasc Surg Vol 33, February 2007

CAS using conventional carotid stents in high-risk lesions

Conventional Carotid Stent

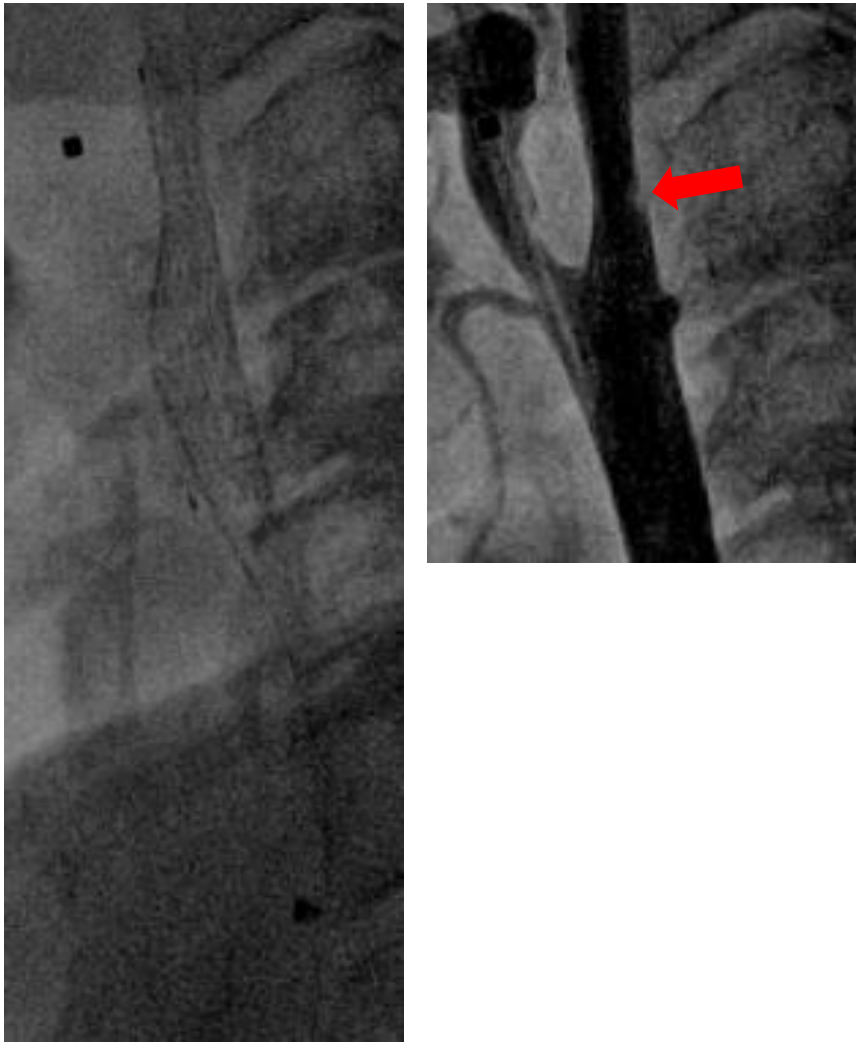
Plaque protrusion may lead to early and late distal embolization



J. Schofer, P. Musialek et al. TCT 2014

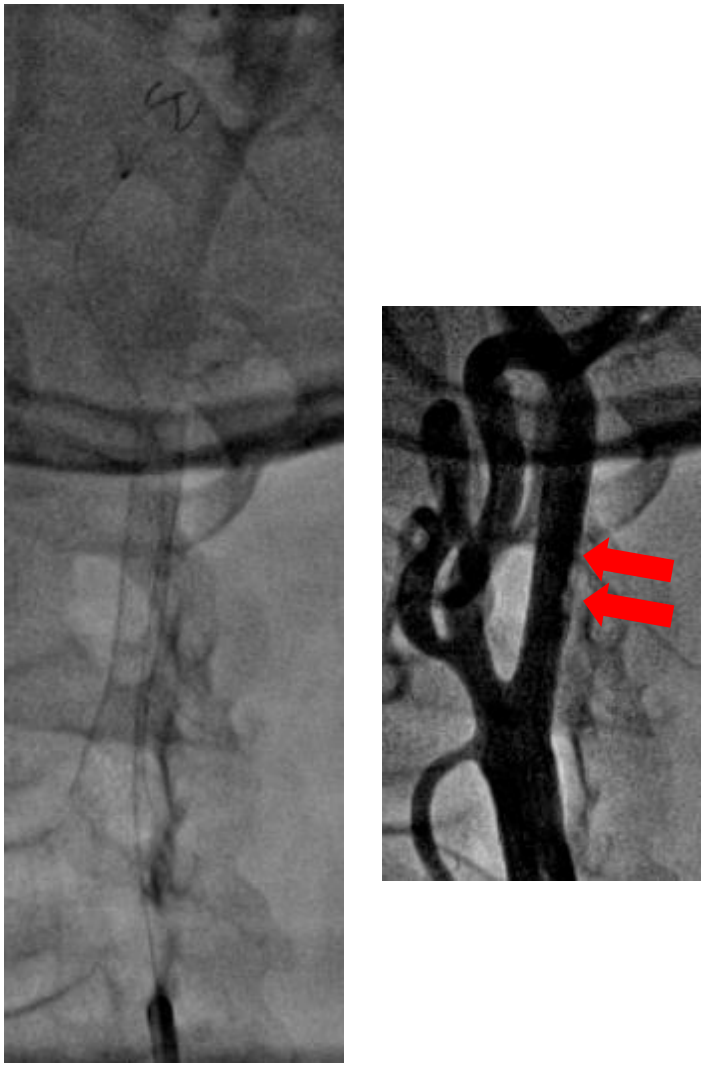
current best-in-class

Hybrid stent



current best-in-class

Closed-cell stent



Post-procedural Embolization with conventional carotid stents

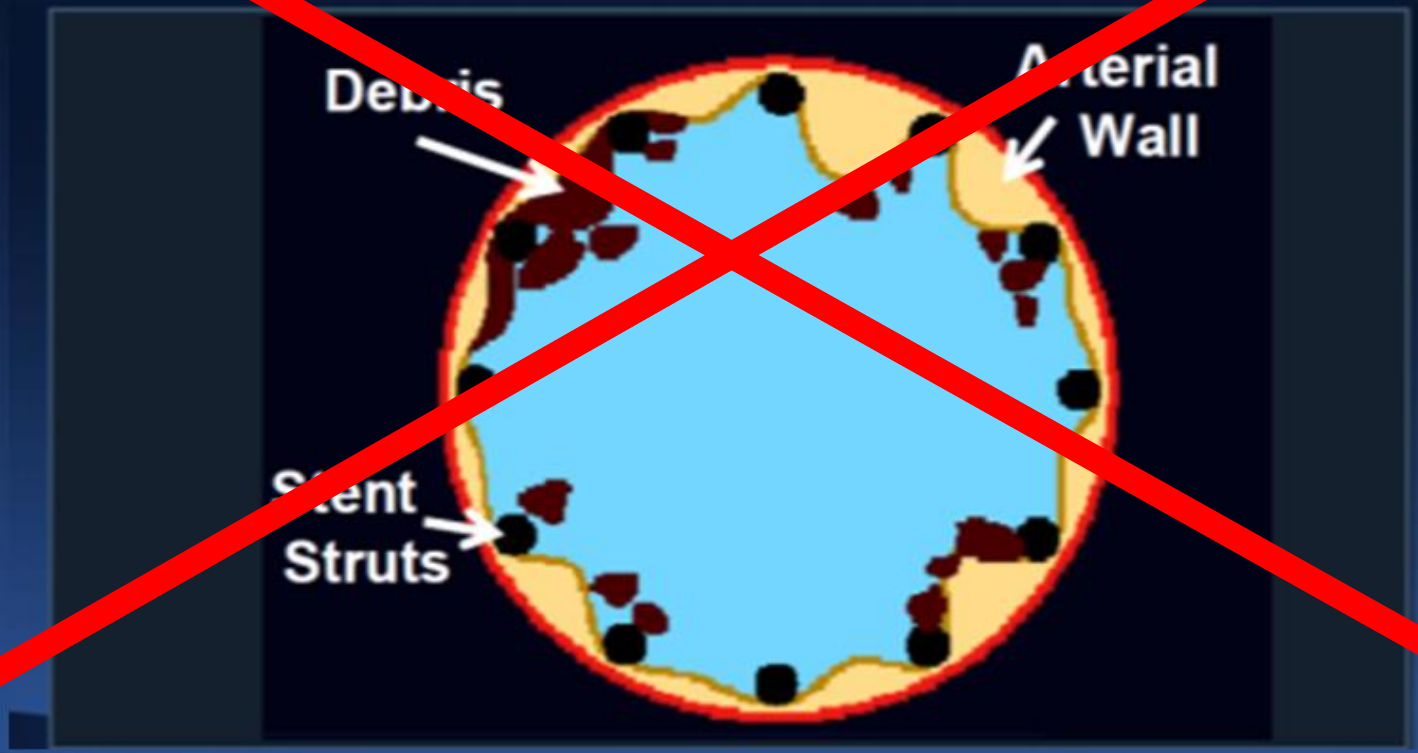
DW-MRI post CAS

Schofer J et al, JACC Cardiovasc interv 2008

CAS using conventional carotid stents in high-risk lesions

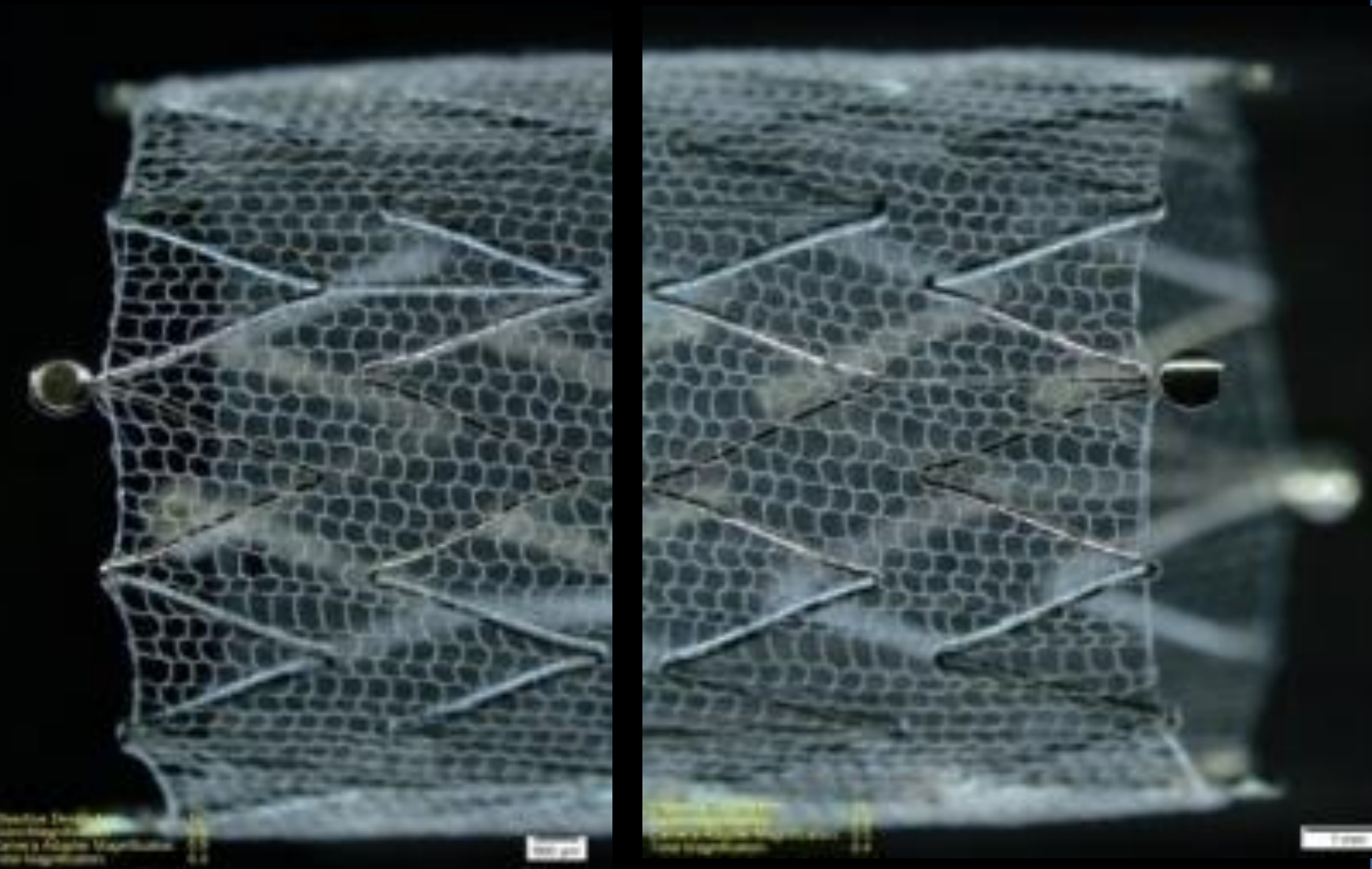
Conventional Carotid Stent

Plaque protrusion may lead to early and late distal embolization



J. Schofer, P. Musialek et al. TCT 2014

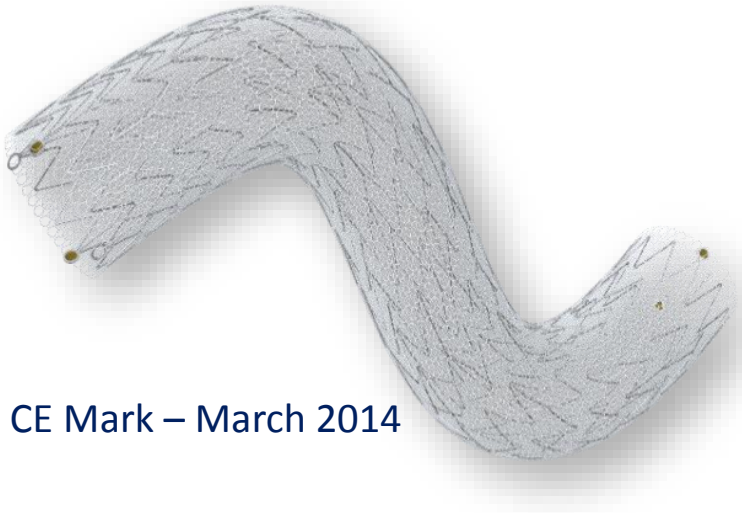
CGuard ™ embolic prevention system



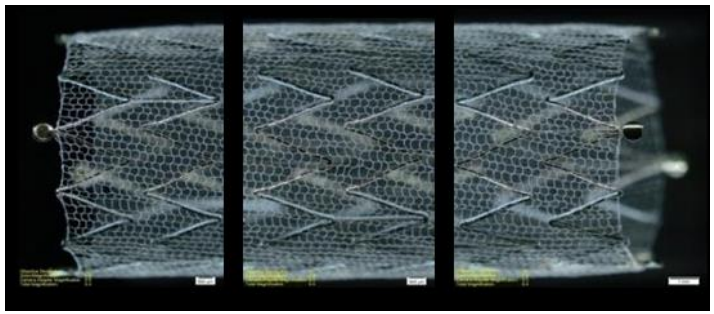
P Musialek @ ePCR 2015

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 PARADIGM REVASCULARIZATION

Objective

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

PARADIGM

Methods:

- academic cardio-vascular centre
- investigator-initiated study
- not industry-funded
- all-comer patient inclusion (six month referral sample)
- all referrals tracked
- routine consultation and management pathways
- qualitative and quantitative lesion & stent evaluation
- ***investigator-independent*** **neurological and angiographic evaluation, and external study data verification**

Methods: The CAS Procedure

- **EPD** use mandatory; EPD selection according to the **'Tailored CAS' algorithm***

- **Liberal postdilatation** accepted in order to maximize potential for '**endovascular full reconstruction**' (minimizing residual stenosis)

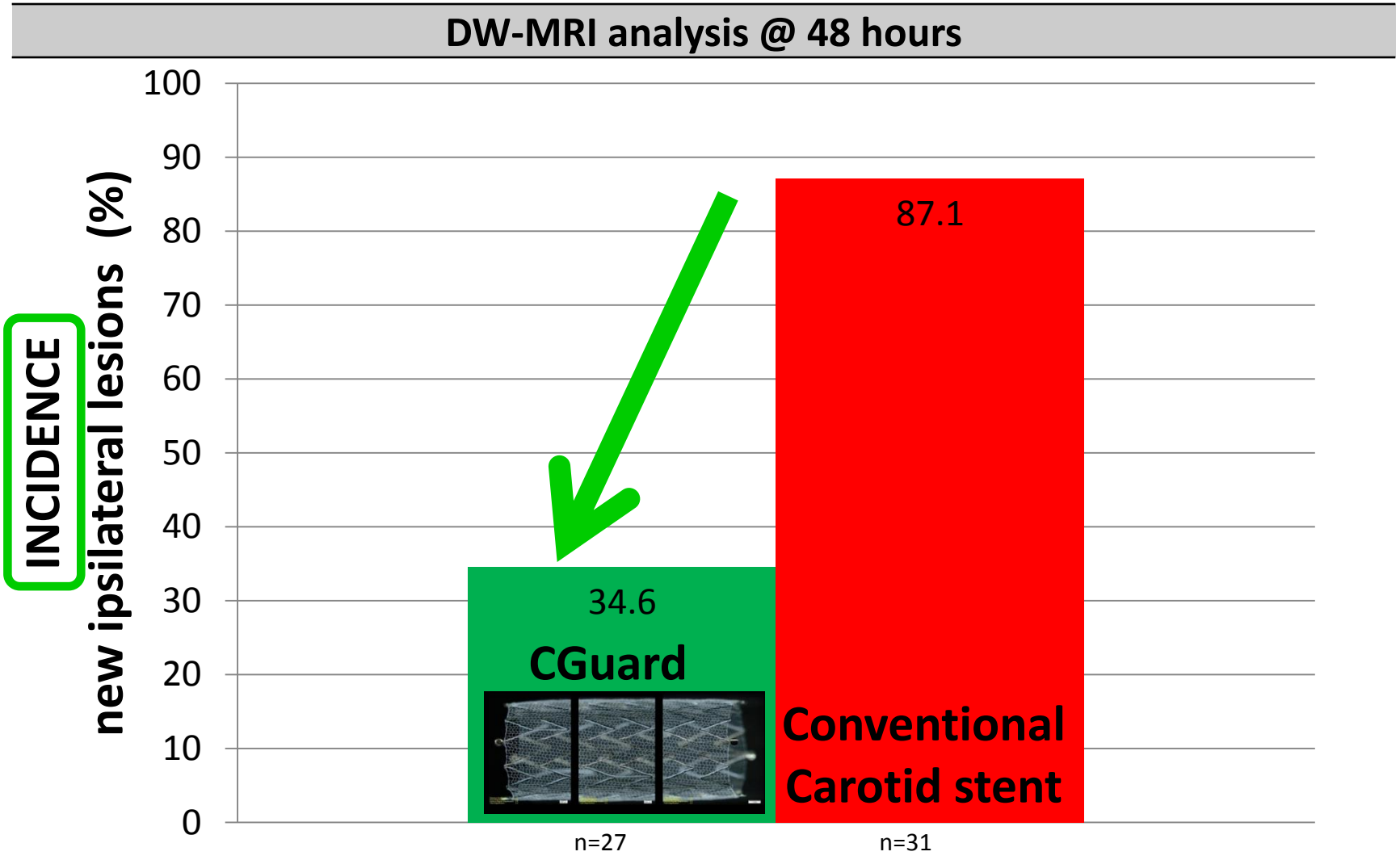
NB. 1. DWI evidence of effective MicroNet prevention against cerebral embolization (CARENET/PROFI)
2. Residual stenosis after CAS as independent predictor of in-stent restenosis

Van Laanen J et al. *J Cardiovasc Surg* 2008
Cosottini M et al. *Stroke Res* 2010
Musialek P et al. *J Endovasc Ther* 2010
Wasser K et al. *J Neurol* 2012

* Pieniazek P, Musialek P et al. *J Endovasc Ther* 2008;15:249-62.
Cremonesi A et al. *EuroInervention* 2009;5:589-98.
Pieniazek P, Musialek P et al. *J Endovasc Ther* 2009;16:744-51.

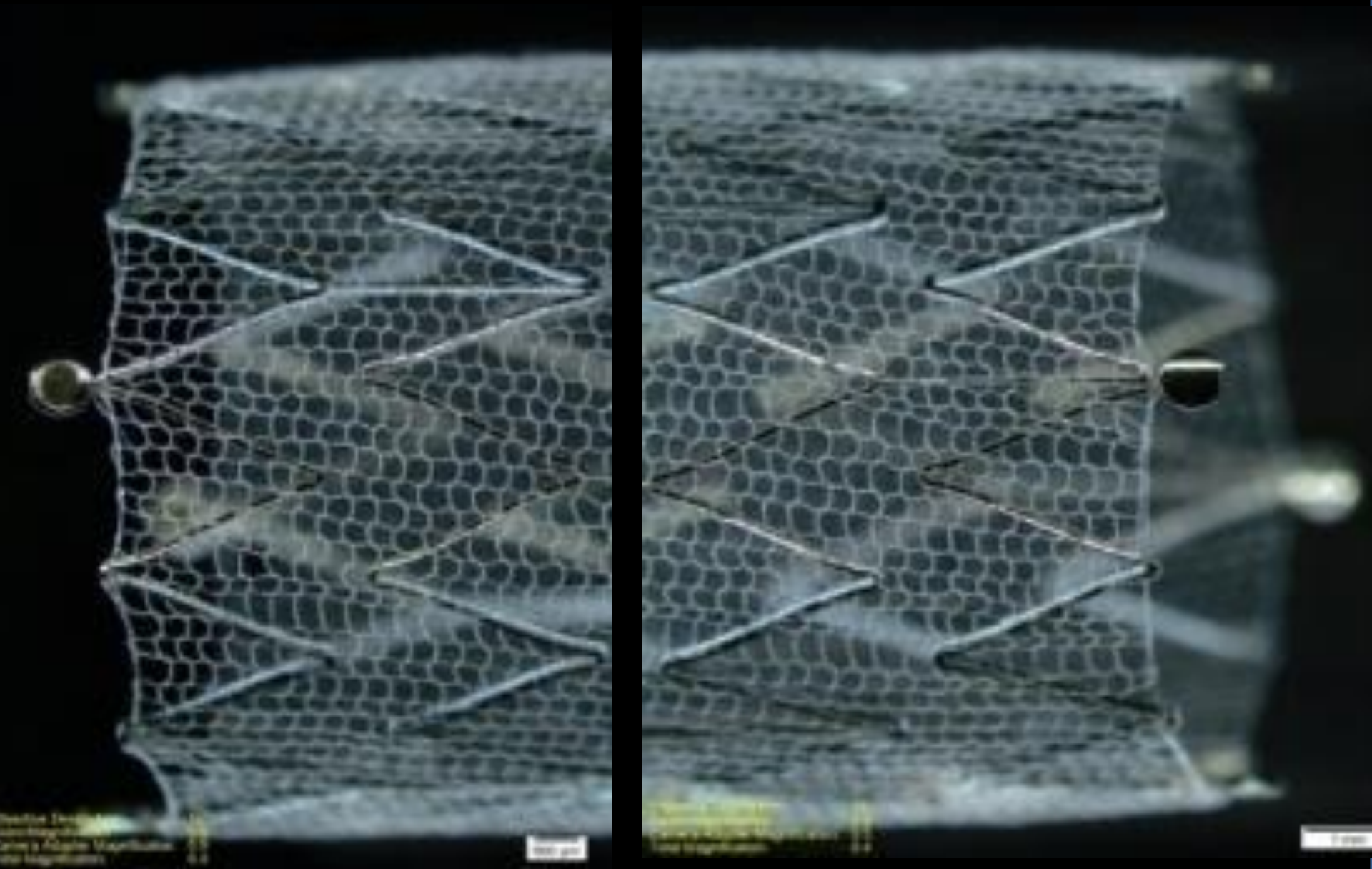
Filter-protected CAS procedures

CARENET vs PROFI: DW-MRI analysis



J. Schofer, P. Musialek et al. ***JACC** Intv* 2015 (in press)
K. Bijuklic et al. *JACC*, 2012;59:1383-9.

CGuard ™ embolic prevention system



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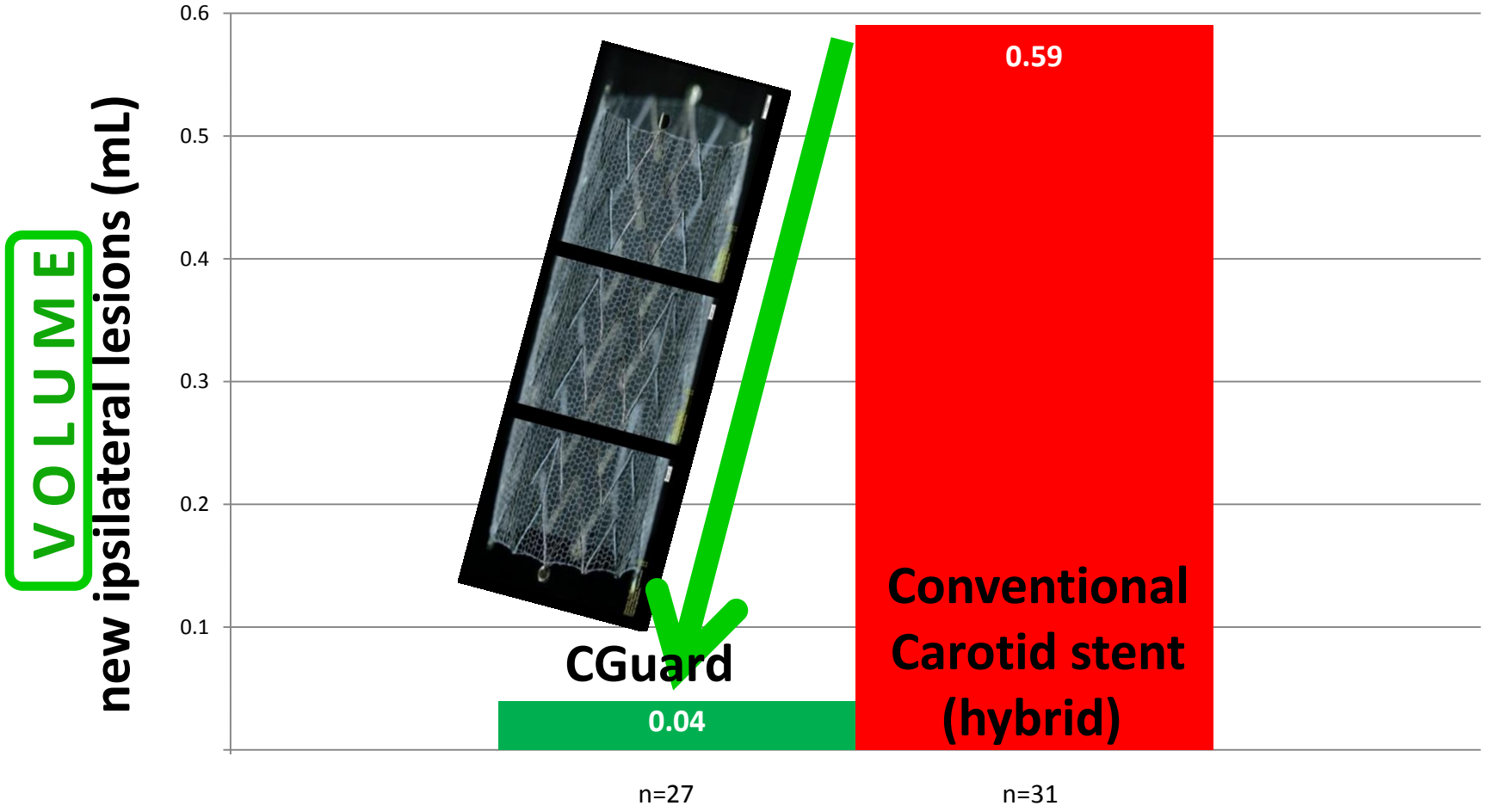
Filter-protected CAS procedures

CARENET vs PROFI: DW-MRI analysis

DW-MRI analysis @ 48 hours



J. Schofer, P. Musialek et al. ***JACC** Intv* 2015 (in press)
K. Bijuklic et al. *JACC*, 2012;59:1383-9.

PARADIGM

Endpoints:

- **feasibility of endovascular Tx in unselected referrals using the study device in otherwise routine practice**

- **device success** (able to deliver + implant + <30% DS)

- **procedure success** (device success w/o clinical compl.)
  (external neurologist, external non-invasive cardiologist)

- **clinical efficacy: MACNE** (death/stroke/MI)
- **in-stent velocities** (Duplex)

- 24-48h
- 30 days
- 12 months
- up to 5y

euro PCR 2015

PARADIGM

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

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.

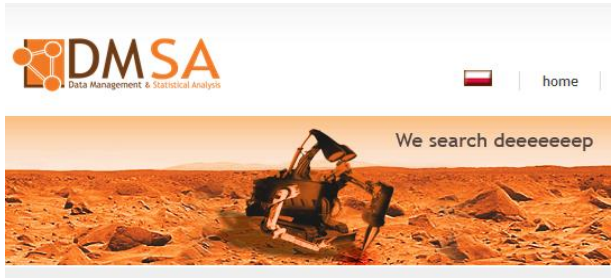
Methods (cont'd)

PARADIGM: investigator – independent

- external study data verification

- external angiographic analysis

- external statistical analysis



Study Flow Chart (1)

97 carotid stenosis patient **referrals***

(external >> internal)

*Dept. of Cardiac & Vascular Dieases, John Paul II Hospital, Krakow, Poland; 10.2014–03.2015

Study Flow Chart (1)

97 carotid stenosis patient **referrals***

(external >> internal)

Neuro-Vascular Team

- **Neurologist**
- **Interventional Angiologist**
- **Vascular Surgeon**
- **Cardiologist**

Gupta K et al. A multispecialty consensus-based approach to carotid revascularization. *J Invasive Cardiol*. 2014;26:123-7.
Tomai F et al. Carotid artery revascularization selected by consensus of a cardiovascular team. *EuroIntervention* 2014;9:1294-300.
Kole MK et al. A multidisciplinary carotid revascularization board. *Surg Neurol Int.* 2012;3:117.

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Study Flow Chart (1)

97 carotid stenosis patient **referrals***

(external >> internal)

Neuro-Vascular Team

- Neurologist
- Interventional Angiologist
- Vascular Surgeon
- Cardiologist

for carotid revascularization
73 patients

NOT for carotid revascularization
24 patients

n=19: lesion increased risk and/or severity criteria not met
n=2: ICA totally occluded on verification
n=2: ICA functionally occlded + h/o prior ipsil. large infarct with hemorrhagic transformation
n=1: severe haemodynamic instability (ICA stenosis a sympt.)

Gupta K et al. A multispecialty consensus-based approach to carotid revascularization. *J Invasive Cardiol*. 2014;26:123-7.
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***Dept. of Cardiac & Vascular Dieases, John Paul II Hospital, Krakow, Poland; 10.2014–03.2015**

Study Flow Chart (2)

73 Patients for carotid revascularization

(92%) → **CAS in n=67 Patients (bilateral in 3)**

(1%) → **CAS + CEA in n=1 Patient**

(LICA-CEA and RICA-CAS) hybrid management

(7%) → **CEA in n=5 Patients**

- n=1 eGRF 14 => no contrast
- n=1 extreme access tortuousity
- n=1 severe aortic valve disease + calcific LICA (AVR + CEA)
- n=1 floating thrombus in CCA
- n=1 ICA diameter <2.0 mm + contralat. occlusion

Study Flow Chart (2)

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- n=1 floating thrombus in CCA
- n=1 ICA diameter <2.0 mm + contralat. occlusion

71 ICAs treated endovascularly in 68 patients

Clinical characteristics of study patients (n=68)

age, mean±SD (min–max)	69 ±7 (55–83)
male, % (n)	66% (45)
symptomatic, % (n) symptomatic ≤ 14 days, % (n) acutely symptomatic (emergent CAS) , % (n)	53% (36) 28% (19) 9% (6)
index lesion (CAS) , % (n) RICA LICA RICA+LICA	 52% (35) 44% (30) 4% (3)
CAD, % (n)	65% (44)
h/of MI, % (n)	27% (18)
CABG or PCI in the past, % (n)	38% (26)
PCI as bridge to CAS, % (n)	16% (11)
AFib (h/o or chronic), % (n)	6% (4)
diabetes, % (n)	35% (24)
h/o neck or chest radiotherapy, % (n)	4% (3)

PARADIGM: Results (1)

- **Percutaneous treatment 100% using the intended MicroNet-covered embolic prevention stent system CGuard** (ie, no other stents used during the study period)

Device success	**100%**
Procedure success	**100%**
Transient Dopamine infusion	**19%** (n=14)
Debris in EPD	**18%** (n=13)
Access site complications	**0%** (n=0)
Vascular plug closure	**45%** (n=32)

PARADIGM: Results (2)

Index lesion qualitative characteristics (n=71 lesions)

	All (n=71)	Symptomatic (n=37)	Asymptomatic (n=34)	p
thrombus, % (n)	15% (11)	24% (9)	6% (2)	0.025
near occl./string, % (n)	21% (15)	30% (11)	12% (4)	0.084
proggressive*, % (n)	27% (19)	11% (4)	44% (15)	0.003
ulcerated, % (n)	41% (29)	46% (17)	35% (12)	0.470
irregular, % (n)	72% (51)	65% (24)	79% (27)	0.197
contralateral occl. , % (n)	17% (12)	22% (8)	35% (12)	0.291
highly calcific, % (n)	23% (16)	14% (5)	35% (12)	0.050
asymptomatic ipsilat. brain embolization/infarct	N/A	N/A	32% (11)	N/A

* veriified imaging

Quantified

- **ICA reference diameter** **4.99 ± 0.36mm** (from 4.27 to 6.02mm)
- **Lesion length** **19.9 ± 5.8mm** (from 8.19 to 30.25mm)

PARADIGM: Results (3)

Index lesion quantitative characteristics (n=71 lesions)

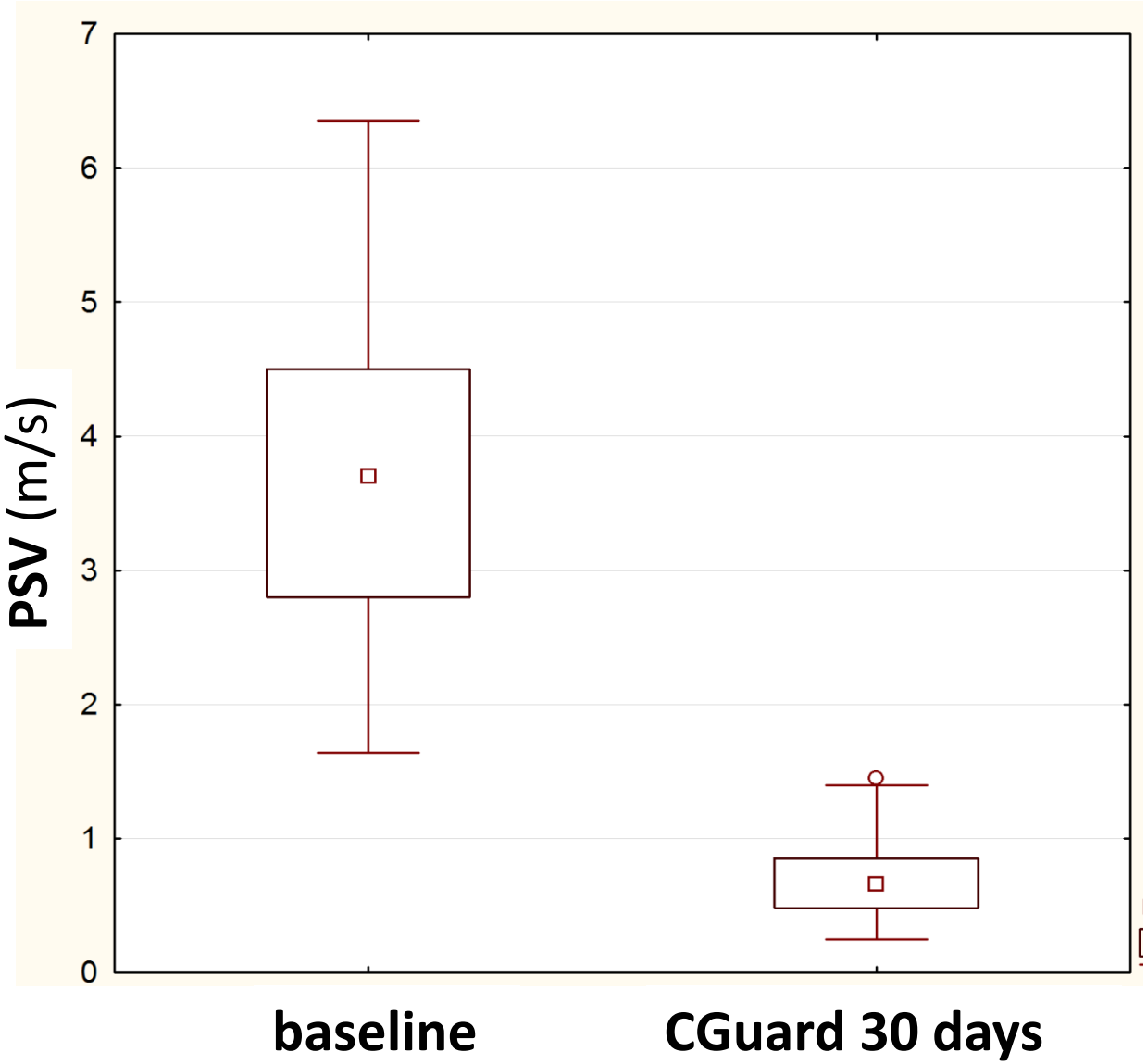
	All (n=71 lesions)	**Symptomatic** n=37	**Asymptomatic** n=34	p
Before CAS				
PSV, m/s	3.8 ± 1.3	3.7 ± 1.1	3.8 ± 1.5	0.862
EDV, m/s	1.3 ± 0.7	1.4 ± 0.6	1.3 ± 0.8	0.687
Diameter stenosis % (QA)	82 ± 9	79 ± 9	84 ± 9	0.021
CAS				
EPD type				0.092
Proximal*	35% (25)	44% (16)	26% (9)	
Distal**	65% (46)	56% (21)	74% (25)	
post-dilat balloon# peak pressure, mmHg	18.4 ± 3.4	17.5 ± 3.6	19.2 ± 2.9	0.037
After CAS				
Stent length (QA)§				NA
Nominal 30 mm	29.66 ± 0.30	29.66 ± 0.28	29.65 ± 0.32	
(min-max)	(28.73-30.07)	(29.02-30.07)	(28.73-30.02)	
Nominal 40 mm	39.73 ± 0.34	39.69 ± 0.41	39.77 ± 0.28	
(min-max)	(38.88-40.22)	(38.88-40.22)	(39.14-40.04)	
Residual diam. stenosis	7 ± 4%	5 ± 4%	7 ± 5%	0.257
in-stent PSV, m/s	0.70 ± 0.28	0.66 ± 0.29	0.74 ± 0.27	0.266
in-stent EDV, m/s	0.17 ± 0.07	0.17 ± 0.07	0.18 ± 0.07	0.457

* **Emboshield** (n=7); **FilterWire** (n=14); **Spider** (n=25)
** **Gore FlowReversal** (n=4) or flow reversal with **MoMa** (n=21);
(NB. mean flow reversal time was 6min 48s, from 5min 18s to 11min 2s)
ø 4.5mm (n=5); ø 5.0mm (n=36); ø 5.5mm (n=29); ø 6.0mm (n=1);
§ 30mm in 51 lesions; 40mm in 18 lesions (2 other lesions required two stents each)

PARADIGM: Results (4)

- **Death/stroke/MI @ 48h** **0%**
- **Death/stroke/MI @ 30d** **0%**

PARADIGM: Results (5)



PARADIGM: Results (4)

- **Death/stroke/MI @ 48h** **0%**
- **Death/stroke/MI @ 30d** **0%**

PARADIGM: Conclusions

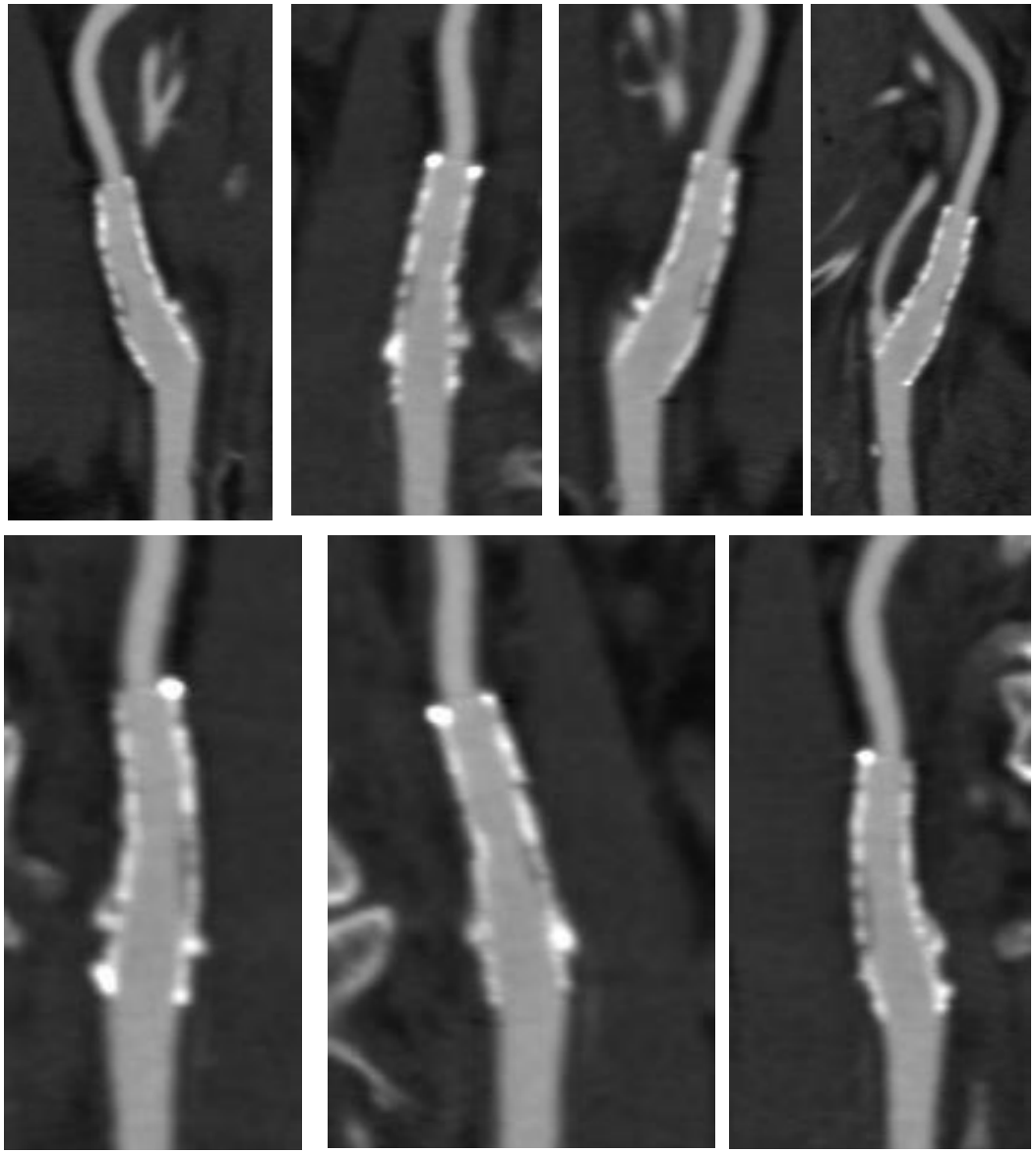
- >90% all-comer carotid artery stenosis patients, including >50% symptomatic presentations, can be treated endovascularly using the MicroNet-covered embolic prevention stent system CGuard

- endovascular revascularization with routine use of the MicroNet--covered embolic prevention stent system CGuard in an unselected patient polulation is extremely safe

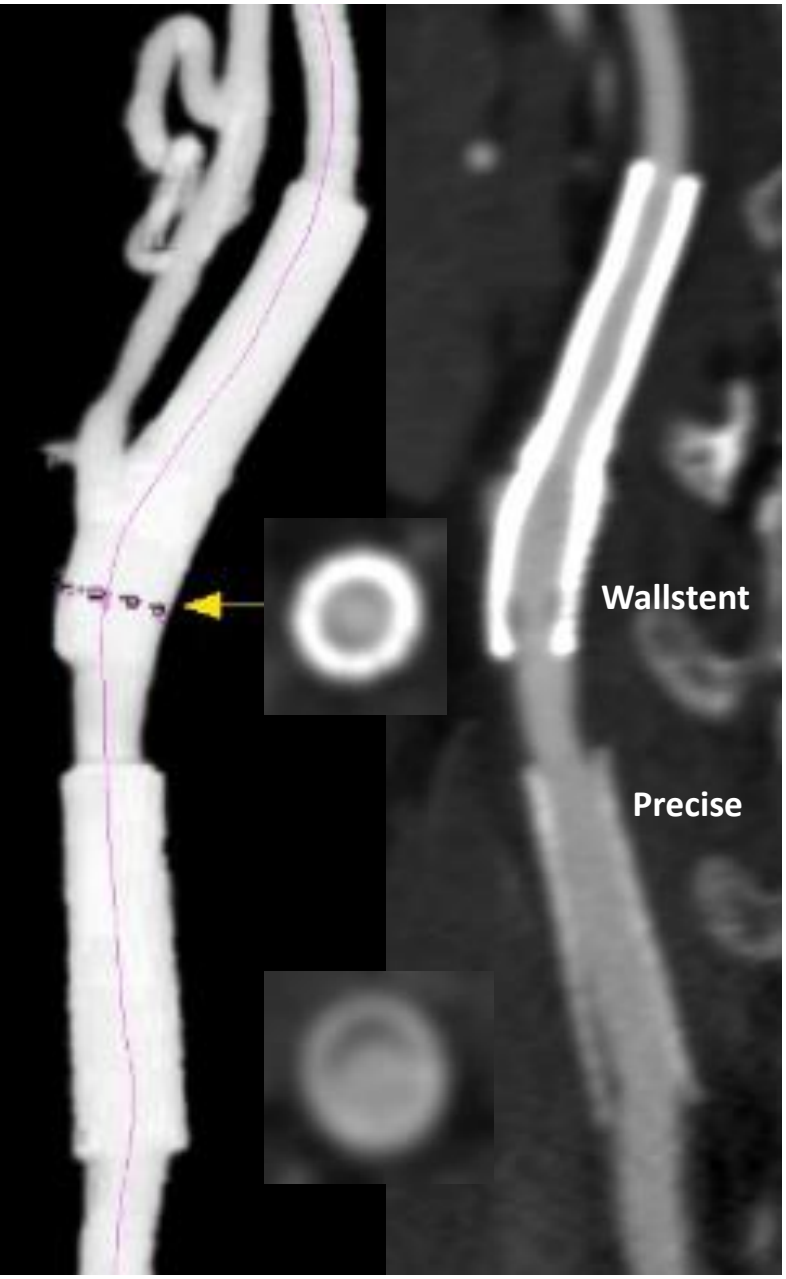
- use of the MicroNet-covered embolic prevention stent system enables '**endovascular reconstruction**' of the diseased carotid artery across a wide lesion spectrum (from extremely tight and thrombotic to highly calcific) in absence of periprocedual clinical complications

- procedural safety of the MicroNet-covered embolic prevention system extends throughtout the stent healing period

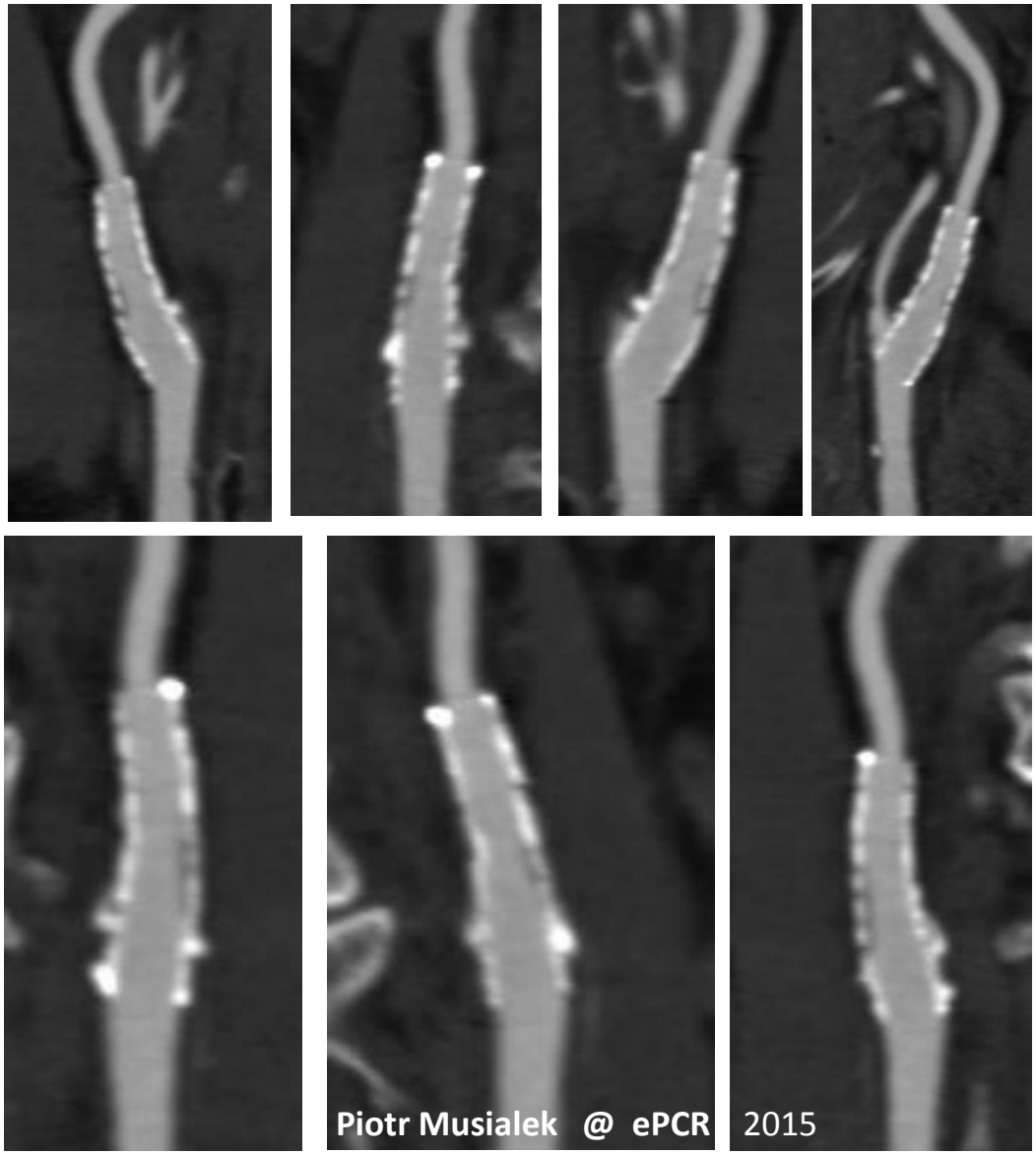
CGuard 5 month follow-up



RCCA & RICA



LICA CGuard
@ 5 months



CGuard: Endovascular Solution For All-comers

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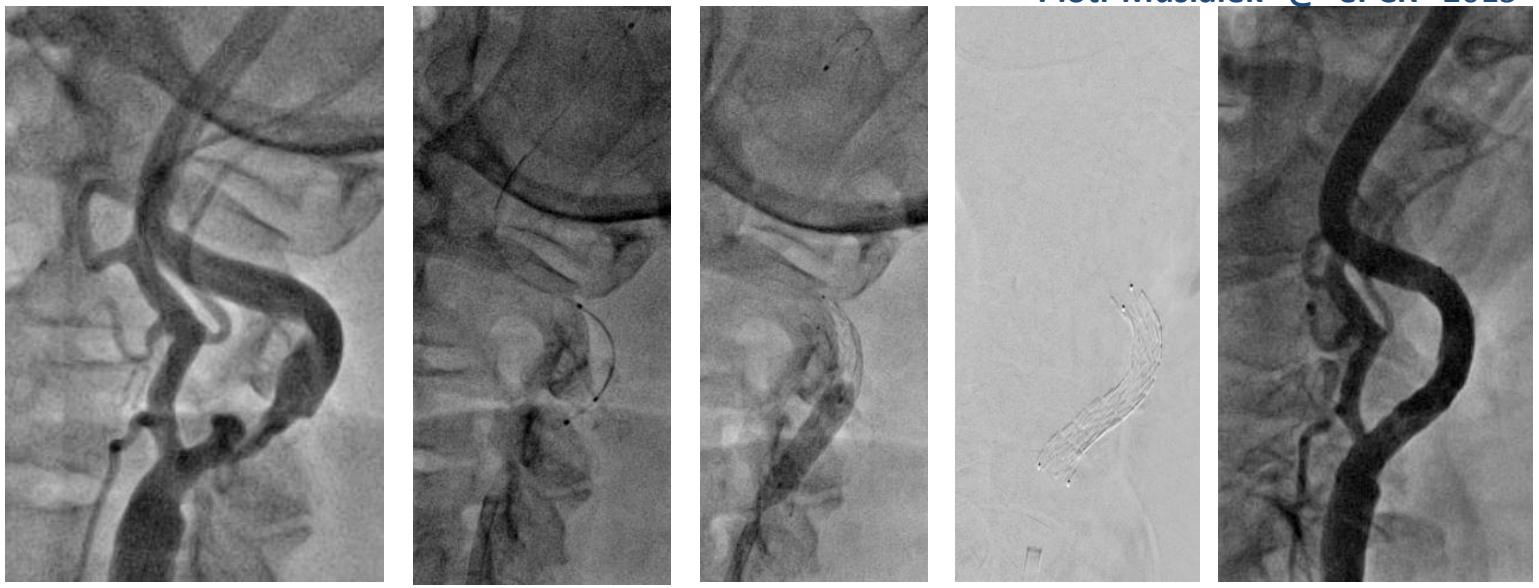
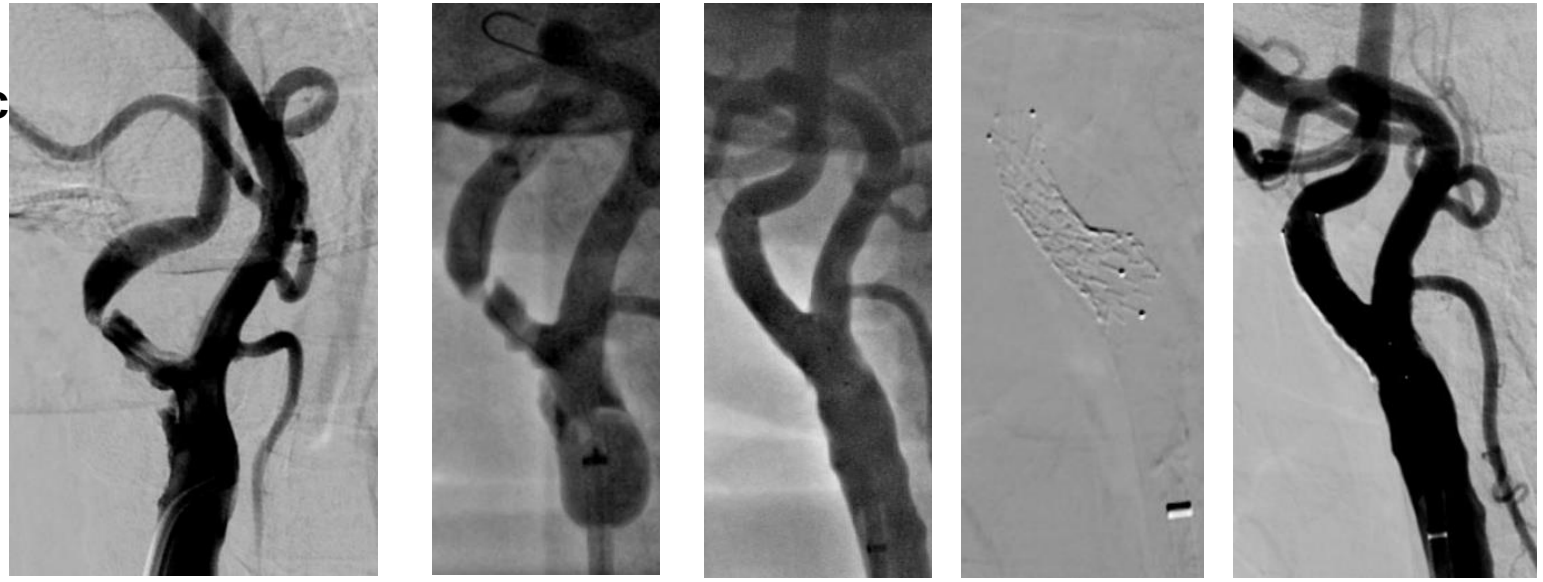
61 yo symptomatic LICA



72 yo asymptomatic RICA



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Endovascular Reconstruction of the Carotid Bifurcation

CAS (and CEA) are –and will remain– emboli-generating procedures

Effect of the Distal-Balloon Protection System on Microembolization During Carotid Stenting

Nadim Al-Mubarak, MD; Gary S. Roubin, MD, PhD; Jiri J. Vitek, MD, PhD; Sriram S. Iyer, MD; Gishel New, MD; Martin B. Leon, MD

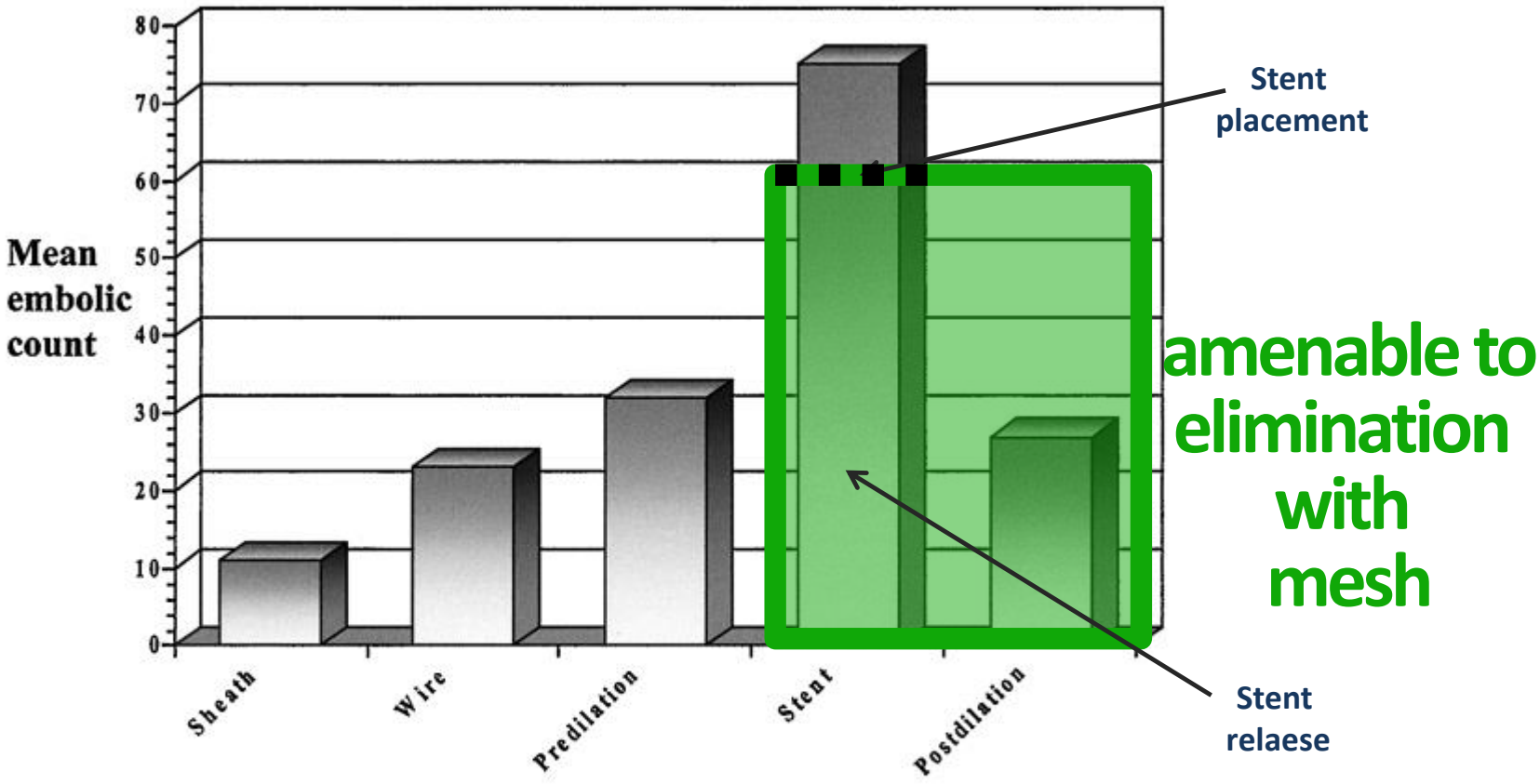


Figure 1. Microembolic profile during unprotected CAS. The mean MES counts during various phases of the procedure are displayed.

Circulation. 2001;104:1999-2002

P Musialek @ ePCR 2015

CGuard embolic prevention stent system

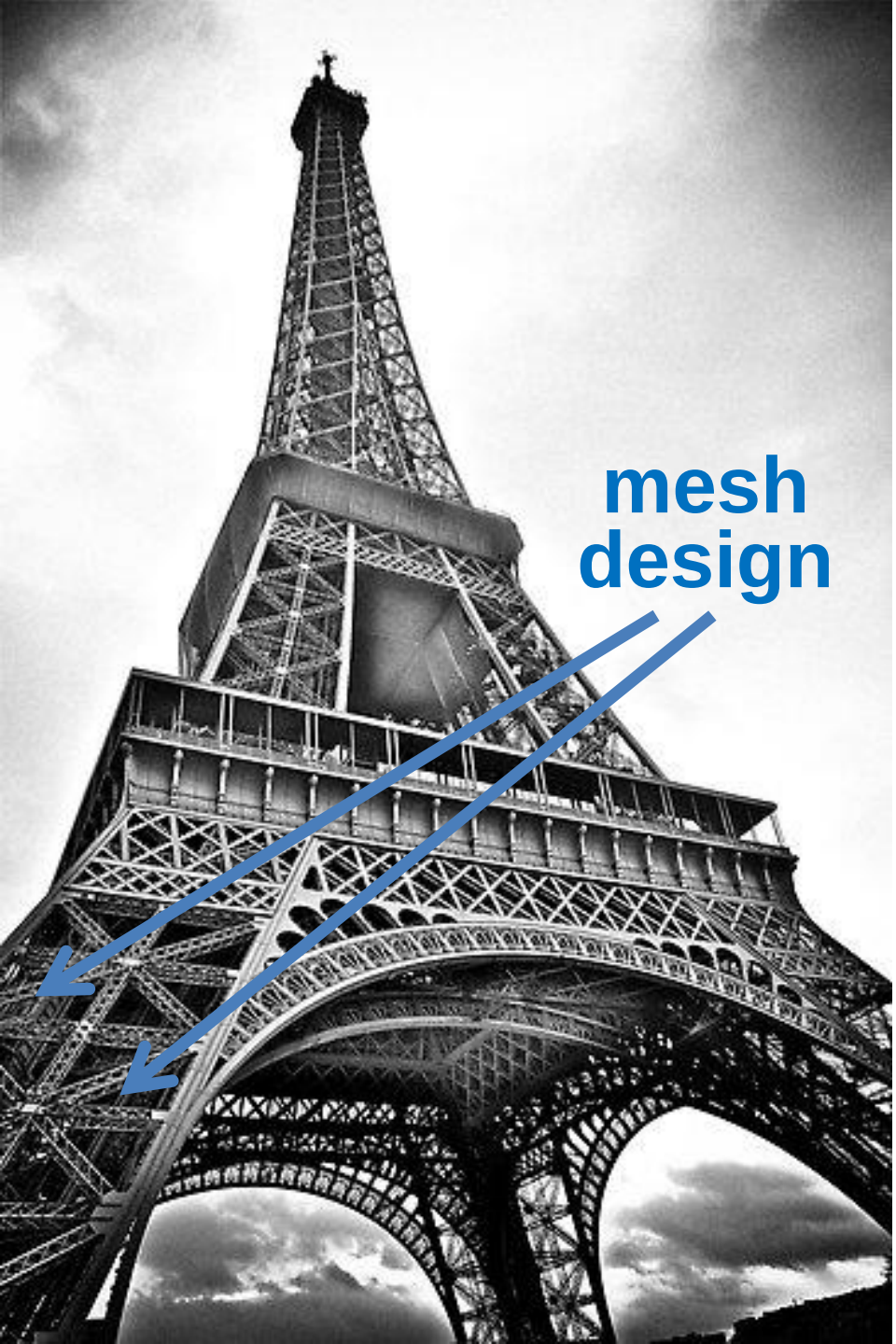
- Compatible with ALL EPD types √
- Deliverable in hard-access anatomies √
- Optimal visibility √
- Reliable, predictable, and extremely precise placement √
- No indication of foreshortening √
- Radial strength sufficient for v. hard lesions √

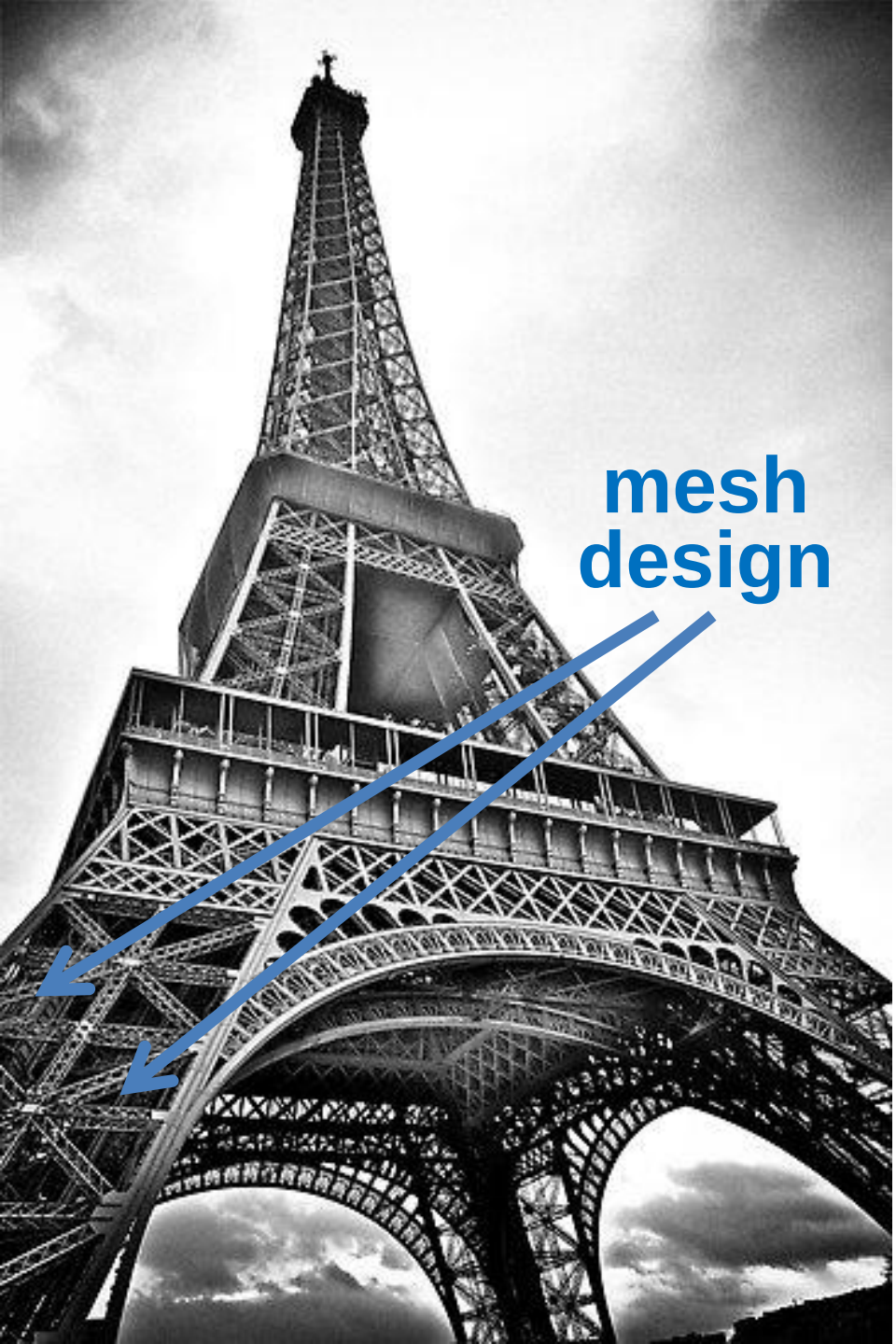
CGuard embolic prevention stent system

- **Full respect of the carotid bifurcation anatomy**
  -> 'endovascular anatomic reconstruction' √

- **Optimal performance across all lesion subsets (including high calcium/thrombus/string)** √

'The most OPEN of open-cell stent designs'
and
'The most CLOSED of the closed-cell designs'


mesh
design



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Novel PARADIGM in carotid revascularization

Prospective evaluation of **A**ll-comer pe**R**cutaneous c**A**roti**D** revascularization **I**n *symptomatic* and *increased-risk asymptomatic* carotid artery stenosis using C**G**uard™ **M**esh-covered embolic prevention stent system

Prospective evaluation of **A**ll-comer pe**R**cutaneous c**A**roti**D** revascularization **I**n symptomatic and increased-risk asymptomatic carotid artery stenosis using C**G**uard™ **M**esh-covered embolic prevention stent system

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NEW
PARADIGM
AHEAD