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The **CARENET** all-comer trial using the **CGuard™** micronet-covered **carotid embolic prevention stent**

6 month data

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Jagiellonian University Dept. of Cardiac & Vascular Diseases
John Paul II Hospital, Krakow, Poland

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Disclosures

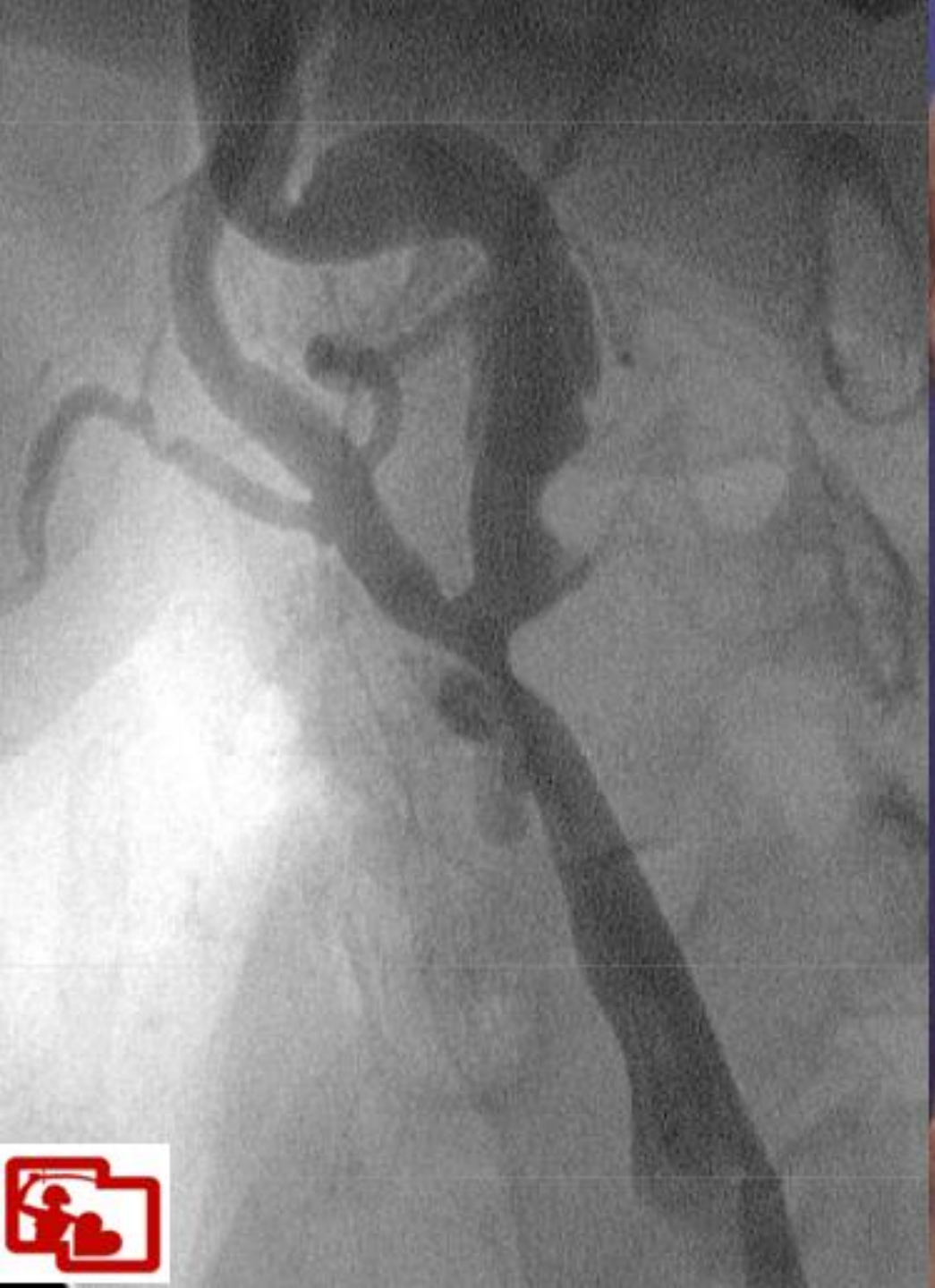
Research / Consulting / Speaker Beureau

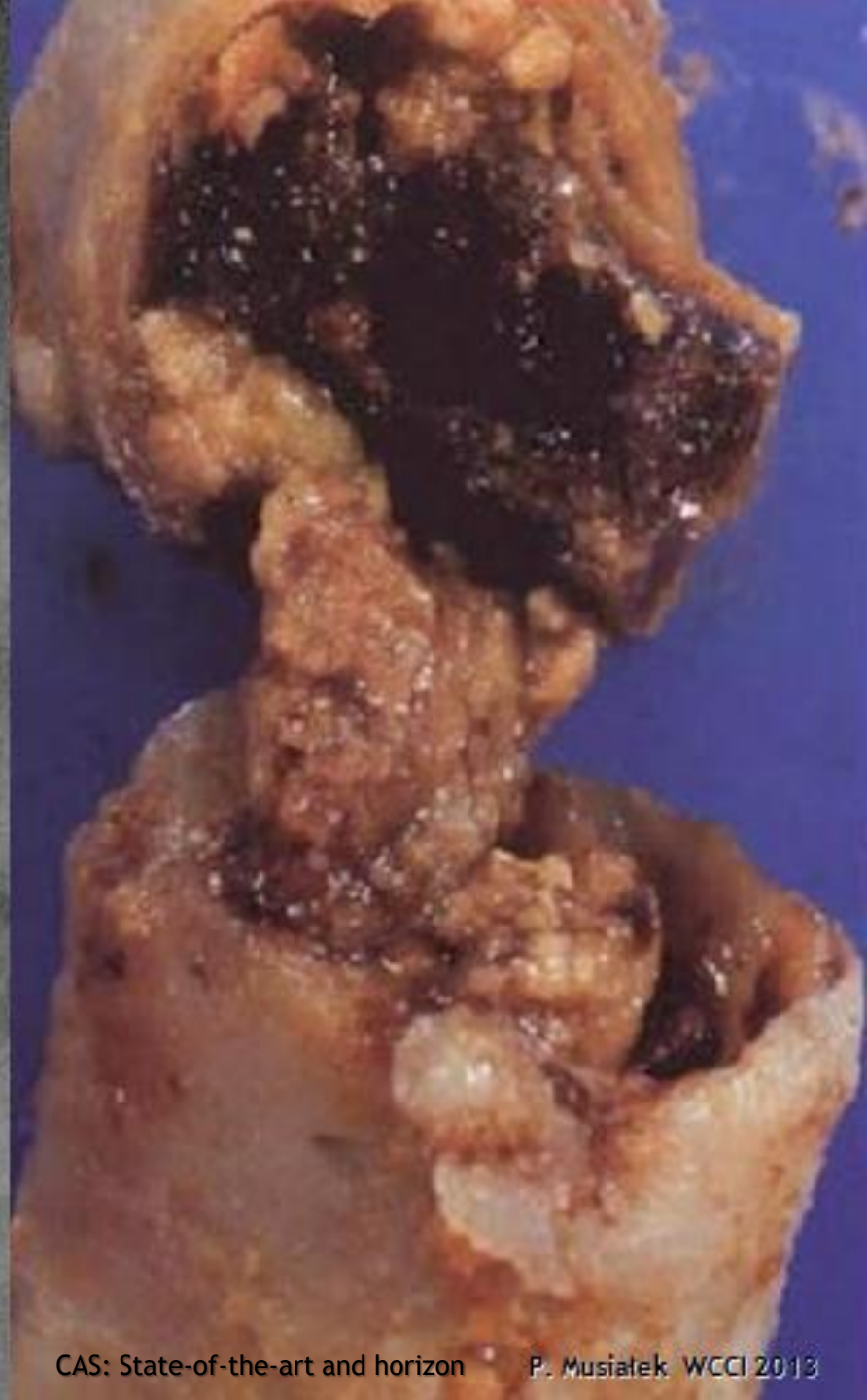
Abbott

Cardio3 Biosciences

InspireMD

Medtronic





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

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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

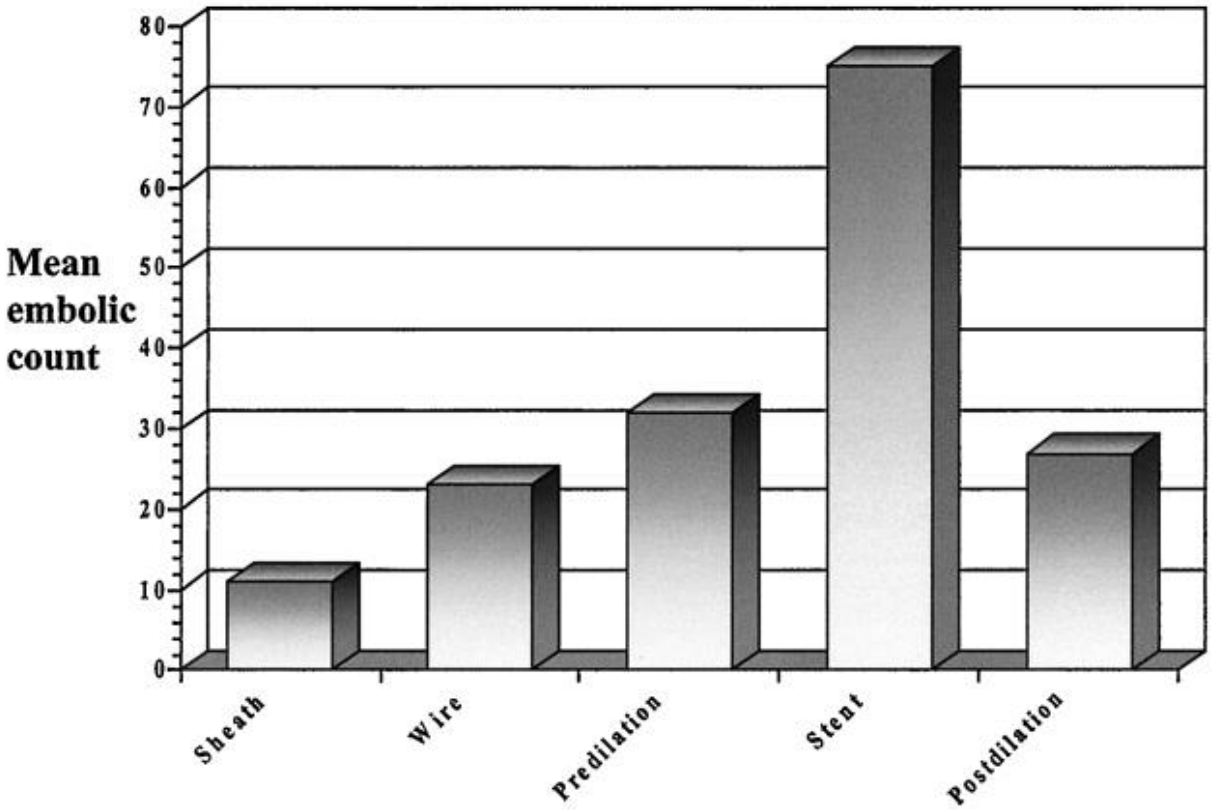

Figure 1. Microembolic profile during unprotected CAS. The mean MES counts during various phases of the procedure are displayed.

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

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

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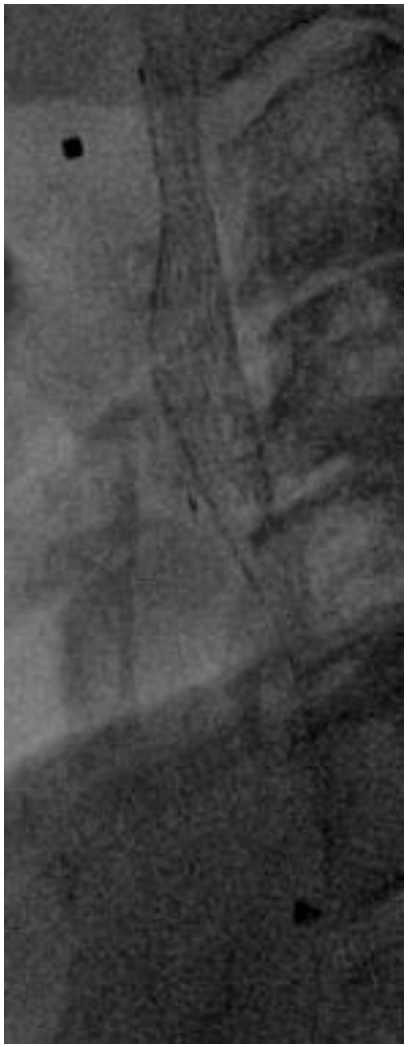
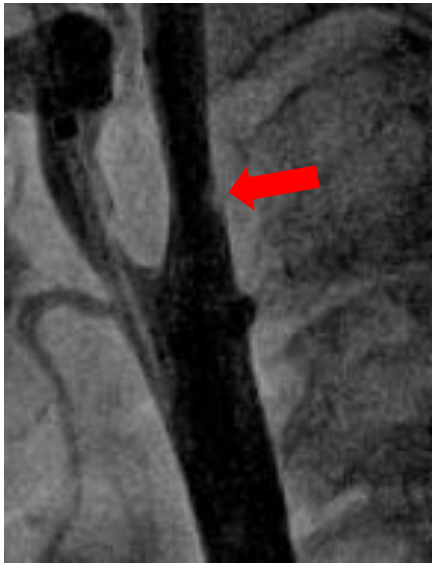
Free cell area	Total population		Symptomatic population	
	All events	Post-procedural events	All events	Post-procedural events
<2.5 vs [2.5, 5]	1.00	1.00	1.00	1.00
<2.5 vs [5, 7.5]	0.054	0.072	0.048	0.024
<2.5 vs >7.5	0.27	0.006	0.0006	$2.8\ 10^{-6}$

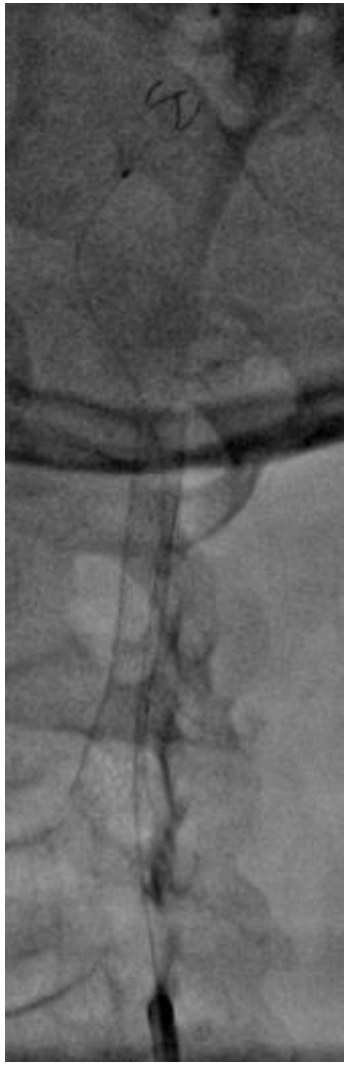
Eur J Vasc Endovasc Surg Vol 33, February 2007

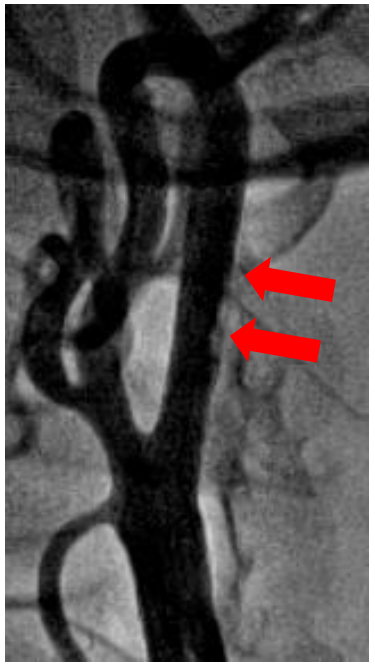
conventional best-in-class
Hybrid stent
('open-close-open')





conventional
best-in-class
Closed-cell stent



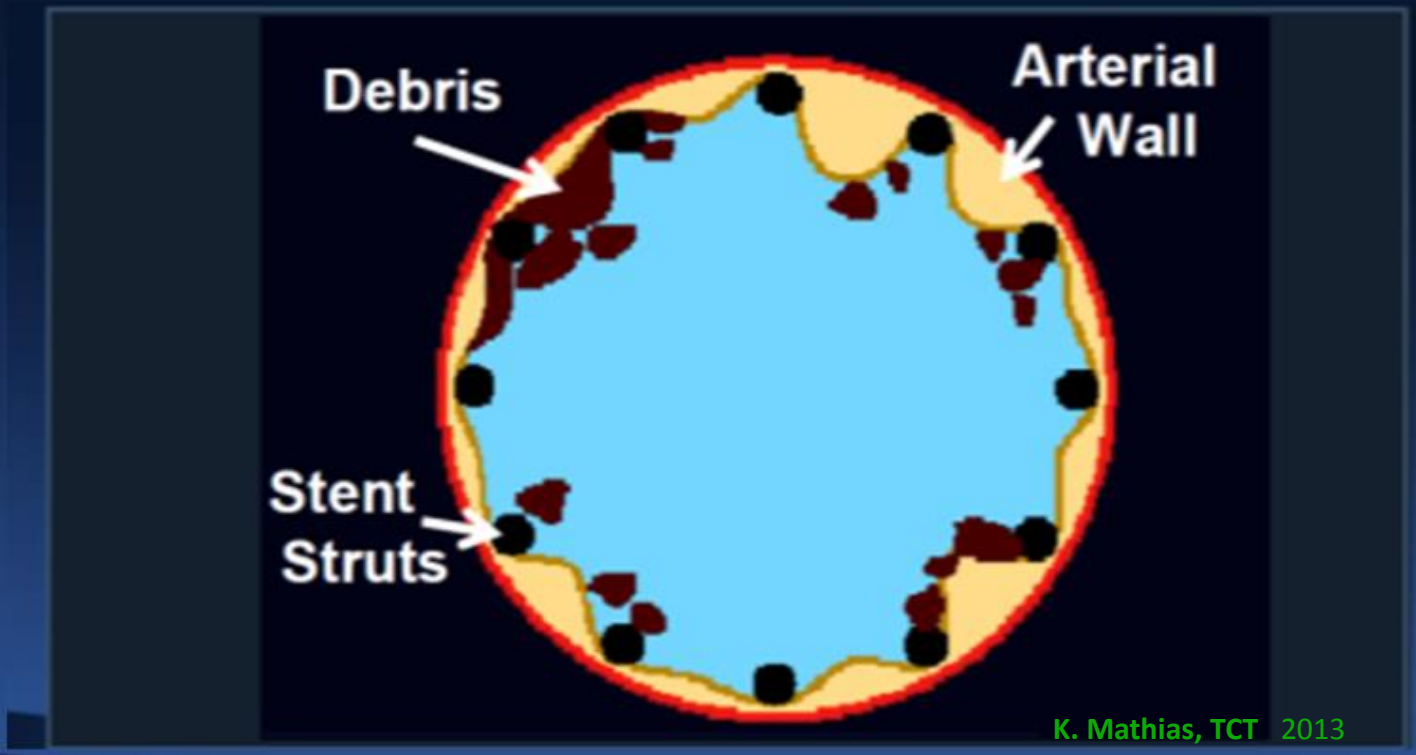


P Musialek, LINC 2015

Rationale of Technology

Conventional Carotid Stent

Plaque protrusion may lead to early and late distal embolization



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ANY data

on incidence of

PLAQUE PROLAPSE

in

conventional carotid stents?

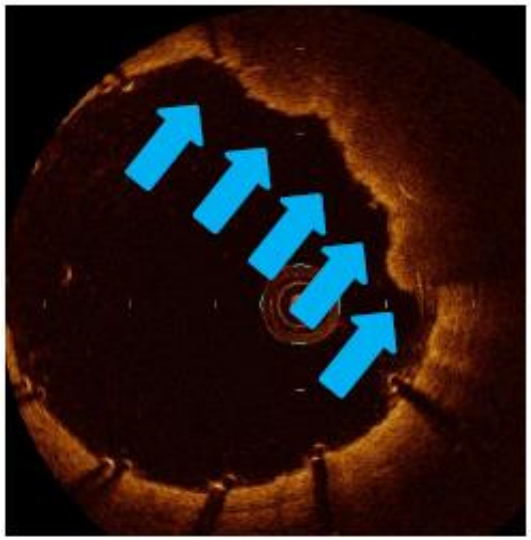
Post-procedural **PLAQUE PROLAPSE** through **conventional stent** struts

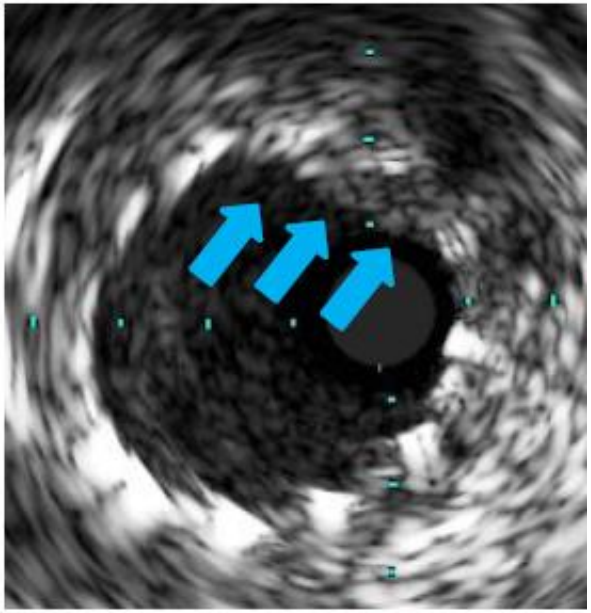
Suzuki M et al.
ESC 2014
Presentation
www.escardio.org

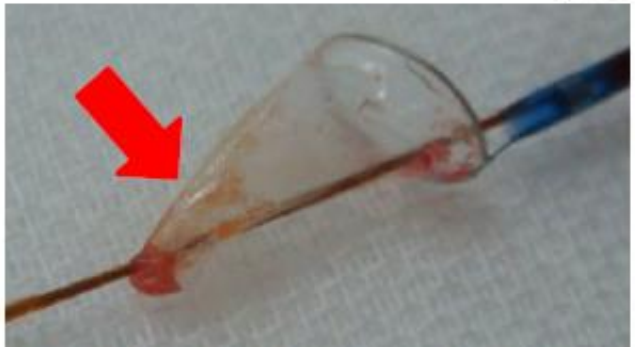
30.7%

1/3 stents = **Precise**
2/3 stents = **Carotid Wallstent**

81 y.o. Female, Symptomatic







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Images: Dr M. Suzuki
ESC 2014
www.escardio.org

Eur Heart J. 2014;35(Abstr Suppl):178

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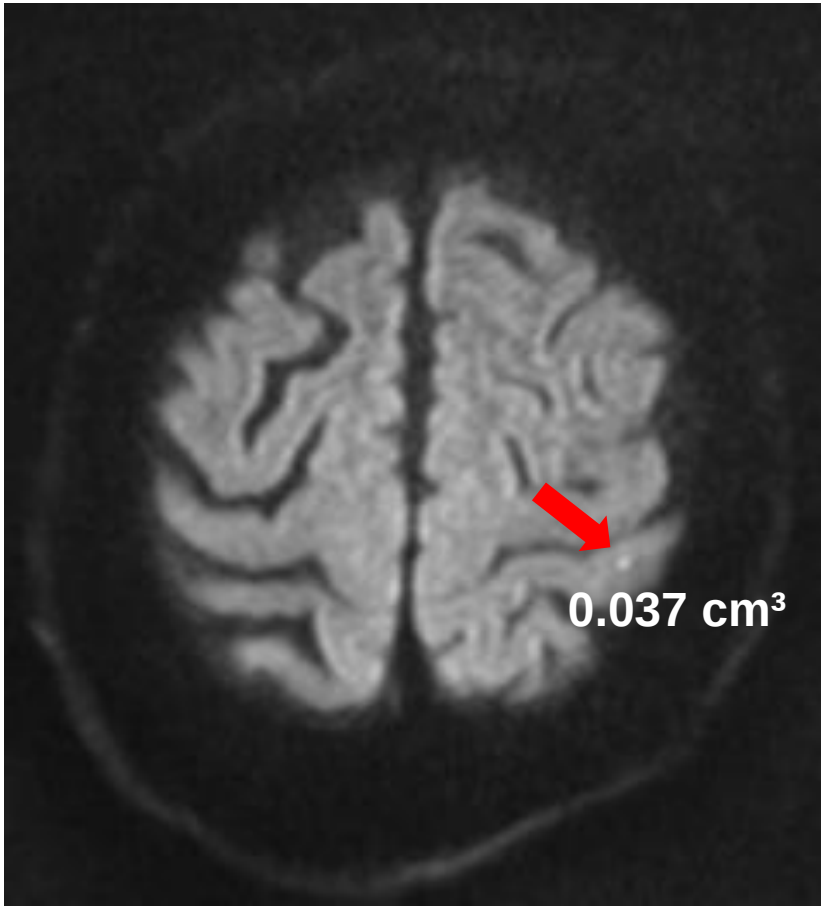
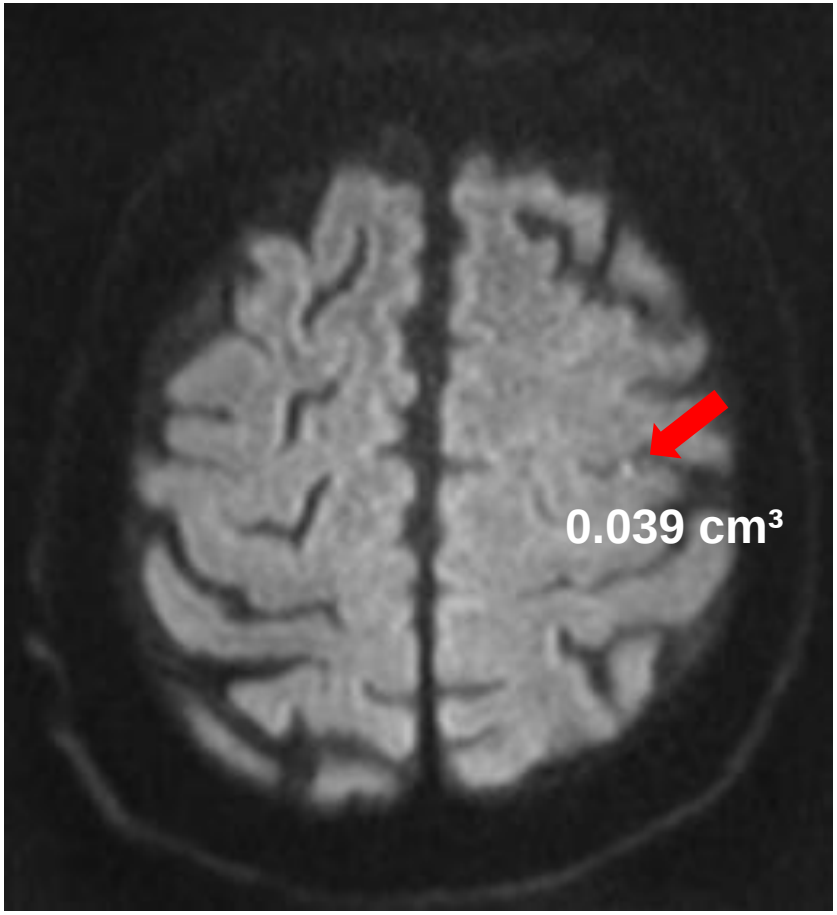
DW-MRI:

the unforgiving testimony of what you've done to the TARGET ORGAN...

The Power of DW-MRI...





48h after LICA-CAS

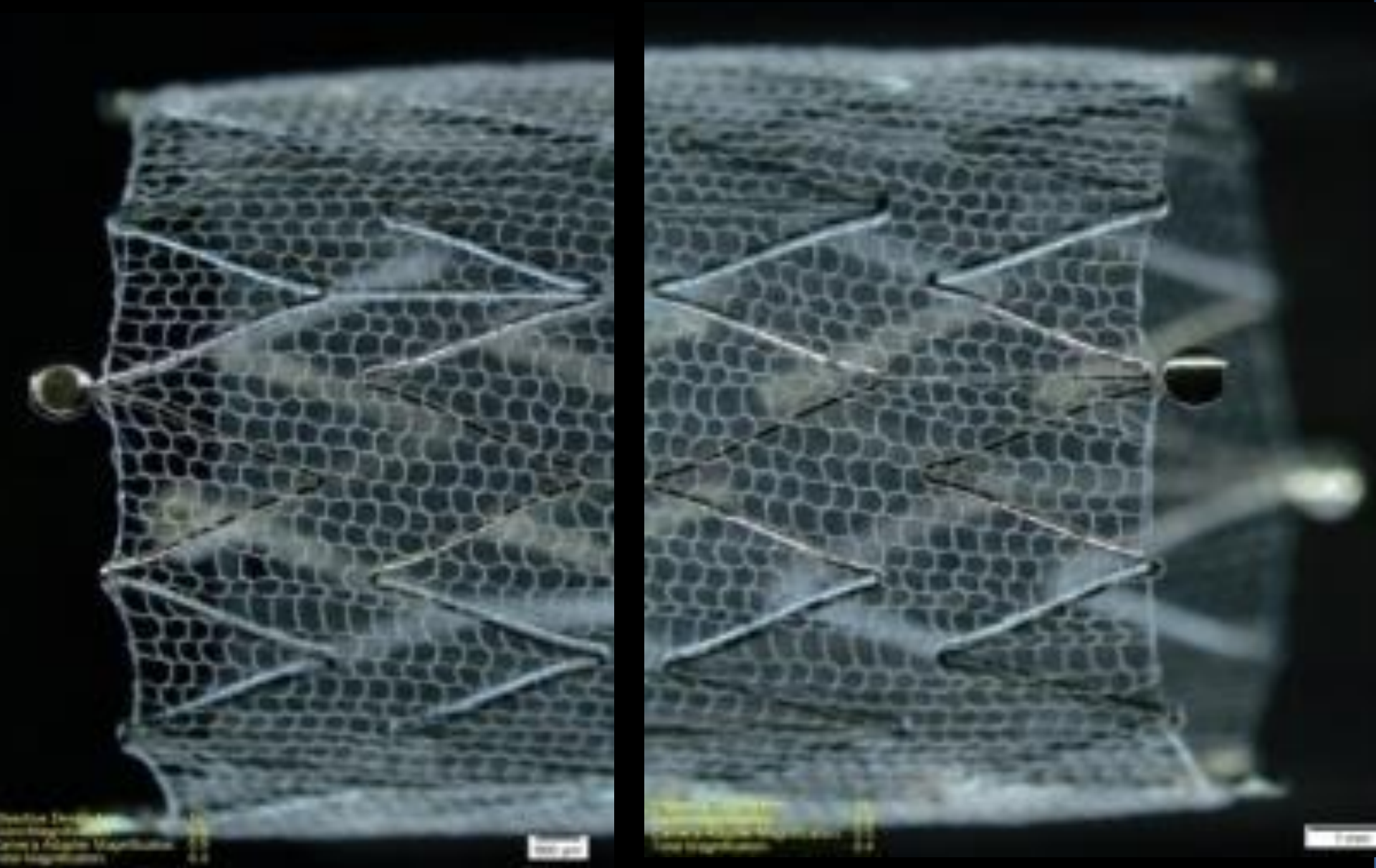
M. Urbanczyk, P. Banys, Dept. Radiology, JP2 Hospital, Krakow, Poland

Post-procedural Embolization with conventional carotid stents

DW-MRI post CAS

Schofer J et al, JACC Cardiovasc interv 2008

CGuard ™ embolic prevention stent



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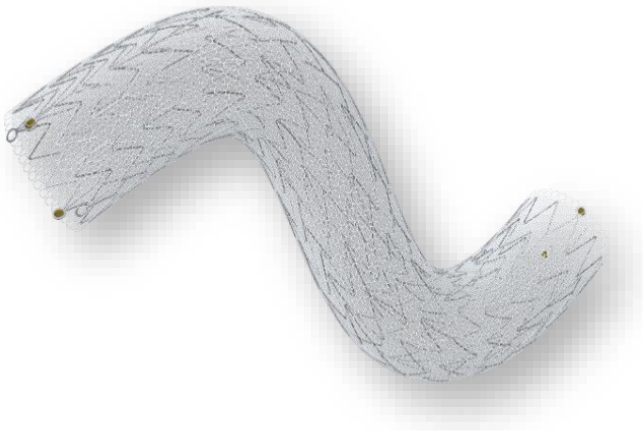
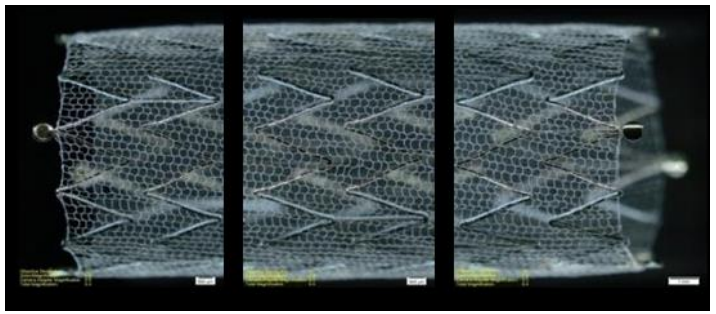
CGuard™– Carotid Embolic Prevention System

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





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Evaluation of PET Mesh Covered Stent in Patients with Carotid Artery Disease

The CARENET-Trial

(CARotid Embolic protection using microNET)

Joachim Schofer (PI)
Piotr Musialek (Co-PI)
On behalf of the CARENET Investigators

Joachim Schofer, MD,PhD, Hamburg University CardiovascularCenter, Hamburg Germany
Piotr Musialek, MD, PhD, Jagiellonian University Medical College at John Paul II Hospital, Krakow, Poland,
Ralf Kolvenbach, MD, PhD, Augusta Hospital, Dusseldorf, Germany,
Horst Sievert, MD, PhD, Cardiovascular Center Frankfurt, Frankfurt, Germany

tct2014 In Partnership with the ACC
Columbia University Medical Center
NewYork-Presbyterian

CARENET – Study Design

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Study Design:

Prospective, multi-center, single arm, all-comer

Objectives:

To evaluate the periprocedural safety and efficacy of the CGuard stent in the treatment of carotid lesions in thirty consecutive patients with symptomatic and asymptomatic carotid artery stenosis, suitable for CAS

Sites:

- *Joachim Schofer,* Hamburg University Cardiovascular Center
- *Piotr Musialek,* Jagiellonian University Medical College
- *Ralf Kolvenbach,* Augusta Hospital
- *Horst Sievert,* Cardiovascular Center Frankfurt

Primary Endpoint:

30 day MACCE (death, stroke, MI)

CARENET – Baseline Characteristics

Baseline characteristics	
	CARENET (n=30)
Age (years)	71.6 ±7.6
Male	63.4%
Symptomatic	33.3 (10)
BMI	26.4 ±3.9
Hypertension	83.3% (25)
Hyperlipidemia	90% (27)
Diabetes mellitus	23.3% (7)
Cigarette smoking, current	13.4% (4)
Prior myocardial infarction	26.7% (8)

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J. Schofer, P. Musialek et al. 2015
(manuscript at review)

CARENET – Procedure Results

Target vessel - Left ICA - Right ICA	 33.3% (10) 66.6% (20)
Protection used -Distal filter protection -Proximal balloon protection	 96.6% (29) 3.4% (1)
Pre dilatation	70.9% (22)
Post dilatation	77.4% (24)
Post dilatation Pressure (ATM)	13.6 ±4.5
Stent deployed	100% (30)
Procedure success	100% (30)
Stent diameter (Mean)	8.23mm ± 0.8
Stent length (Mean)	34.8 mm ± 5.0
Second stent used	3.33% (1)

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J. Schofer, P. Musialek et al. 2015
(manuscript at review)

CARENET – Procedure Results

Angiographic assessment, CARENET (n=30)		
	Baseline	**Final**
Lesion location in left/right ICA	33/67%	-
Lesion length [mm]	16.94±4.7	-
MLD [mm]	1.25±0.34	4.82±0.60
% Diameter stenosis	79.9±5.0	16.9±6.5
TIMI III flow in the ECA	100%	100%

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J. Schofer, P. Musialek et al. 2015
(manuscript at review)

CARENET Clinical Events

	30 days (n=30)	6 months (n=28*)
MACCE (MI, stroke, death)	(0) 0.0%	(1) 3.6%
MI	(0) 0.0%	(0) 0.0%
stroke	(0) 0.0%	(0) 0.0%
death	(0) 0.0%	(1) 3.6%

Comparative data from other CAS trials

	30 days** (14 trials)	6 months† (3 trials)
MACCE (MI, stroke, death)	5.72%	8.09%

* See patient fluxogram

** Trials included in analysis: ARCHeR pooled, ARMOUR, BEACH, CABERNET, CREATE, EMPIRE, EPIC, MAVErIC 1+2, MAVErIC International, PRIAMUS, SAPPHIRE, SECURITY, PROFI, ICSS

† Values extrapolated from event curves

J. Schofer, P. Musialek et al. 2015
(manuscript at review)

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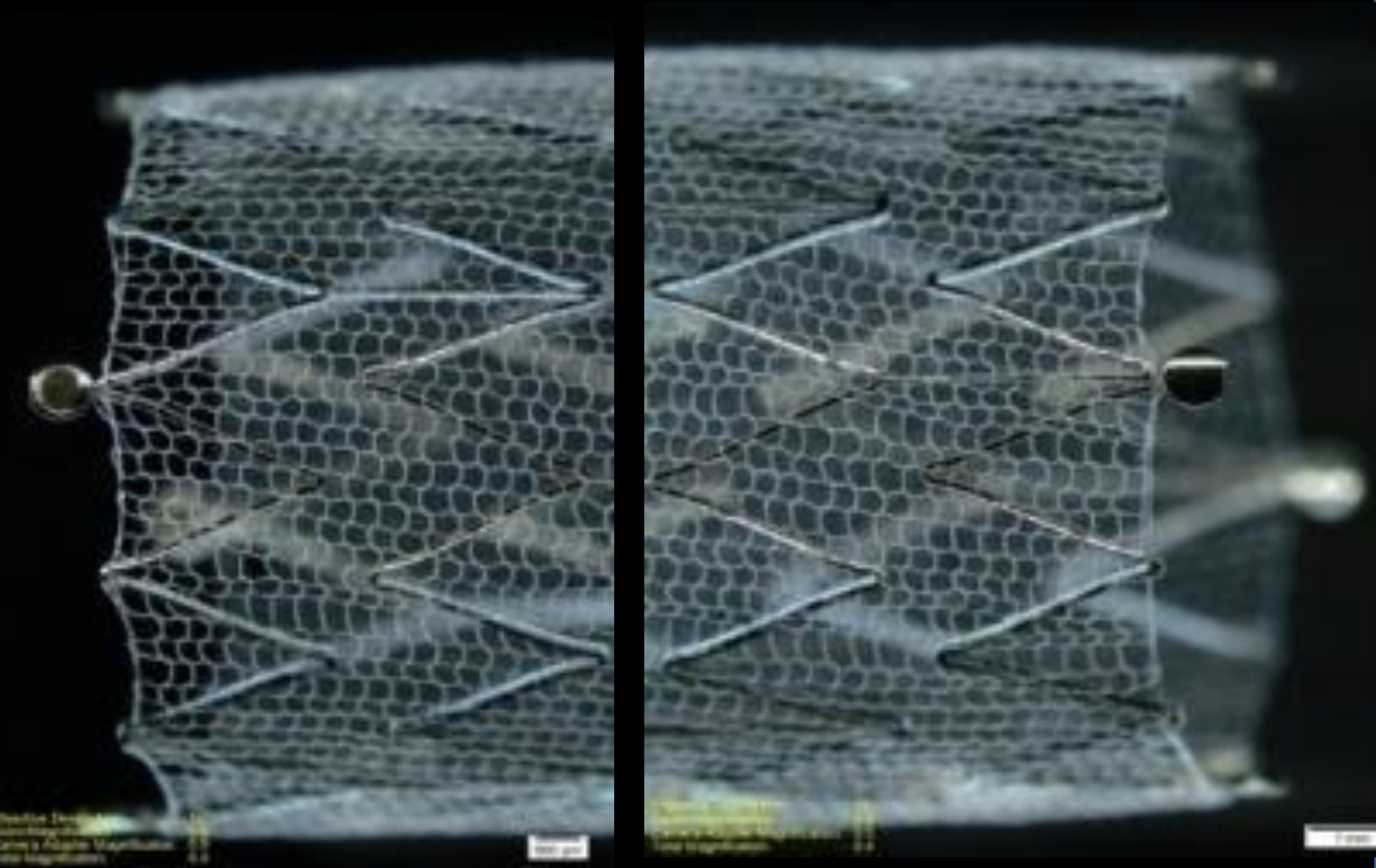
DW-MRI:

the unforgiving testimony of what you've done to the TARGET ORGAN...

CGuard ™ embolic prevention stent



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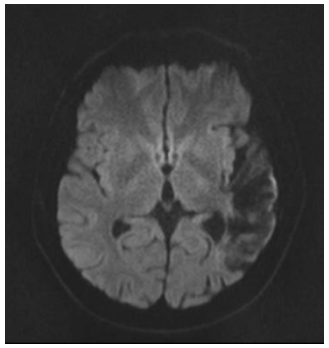
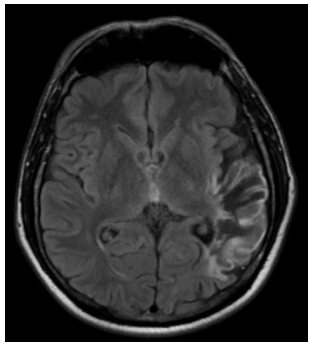
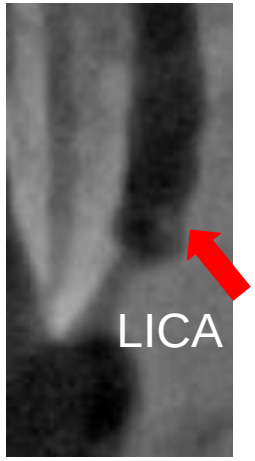
DWI



Flair



CARENET
PJ, **03-007**
(Krakow)



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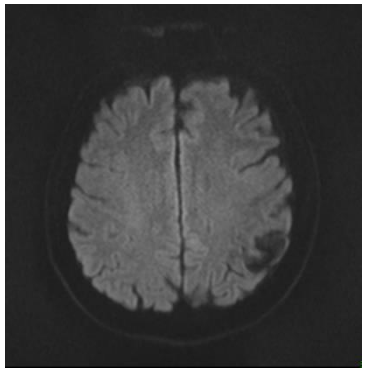
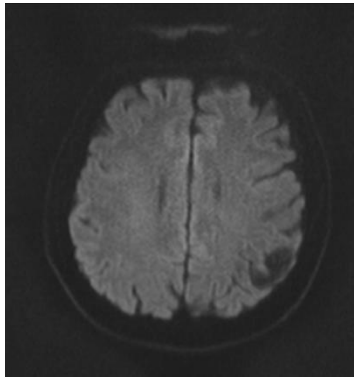
Baseline
Prior to CAS

24h after CAS

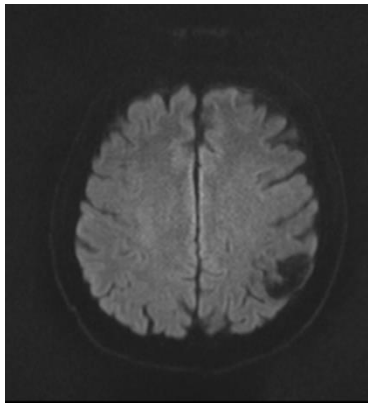
30 days after CAS

DWI



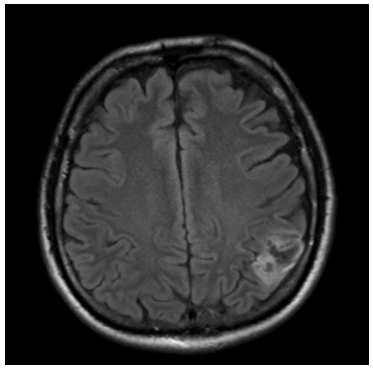


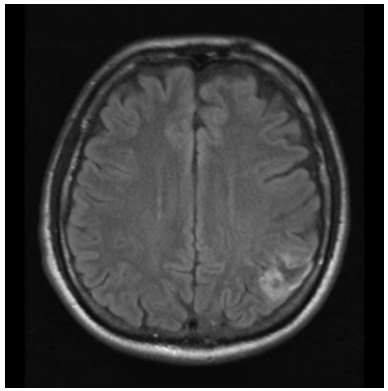
No new CAS-related lesions

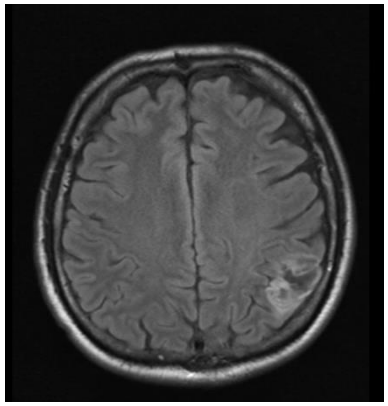


No new lesions between 24h and 30d

Flair







External, blinded CoreLab MRI image analysis and quantification (USA)

CARENET DW-MRI analysis *

DW-MRI analysis @ 48 hours			
	CARENET (n=27)	**PROFI (all)** (n=62)	**ICSS†** (n=56)
Incidence of new ipsilateral lesions	**37.0%**	**66.2%**	68.0%
Average lesion volume (cm^3)	0.039 ± 0.08	0.375	-
Maximum lesion volume (cm^3)	0.445		

≈50% reduction

in new ipsilateral lesion **incidence**

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***External Core Lab analysis (US)**

Bijuklic et al. *JACC*, 2012; Bonati et. al, *Lancet Neurol* 2010
† bilateral lesions

J. Schofer, P. Musialek et al. 2015
(manuscript at review)

CARENET DW-MRI analysis *

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Incidence of new ipsilateral lesions	37.0%	66.2%	68.0%
Average lesion volume (cm^3)	**0.039**	**0.375**	-
Maximum lesion volume (cm^3)	0.415		

>10-fold reduction

in cerebral lesion **volume**

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***External Core Lab analysis (US)**

Bijuklic et al. *JACC*, 2012; Bonati et. al, *Lancet Neurol* 2010
† bilateral lesions

J. Schofer, P. Musialek et al. 2015
(manuscript at review)

CARENET – DW-MRI analysis

DW-MRI analysis @ 48 hours			
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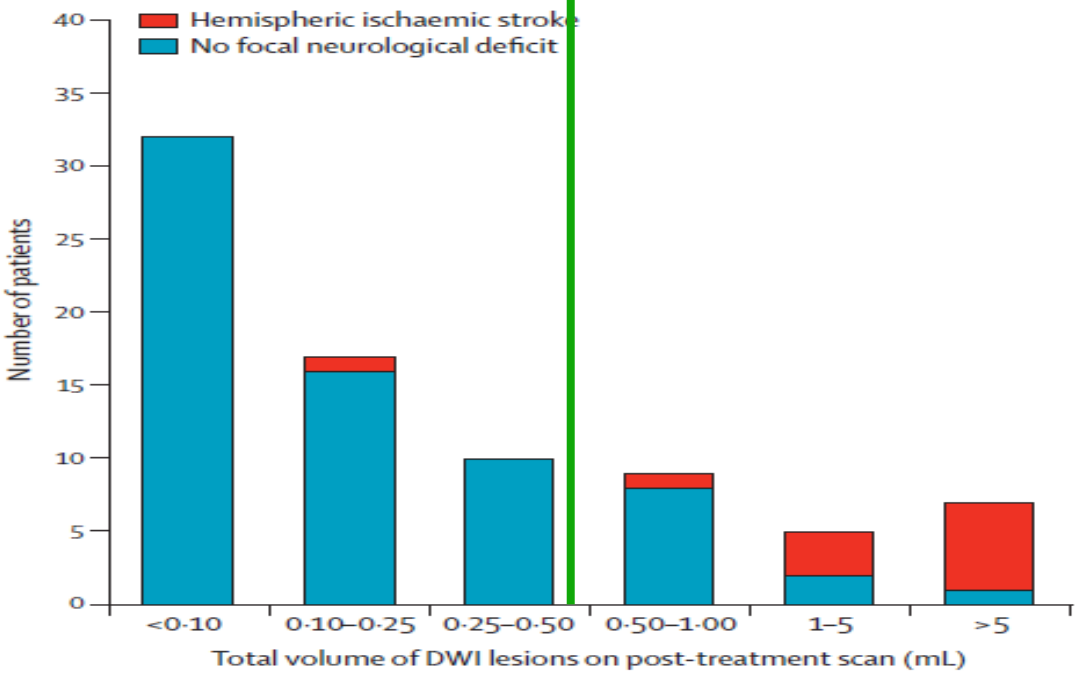
ICSS



Bijuklic et al. *JACC*, 2012; Bonati et. al, *Lancet Neurol* 2010

† bilateral lesions

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CARENET: DW-MRI analysis

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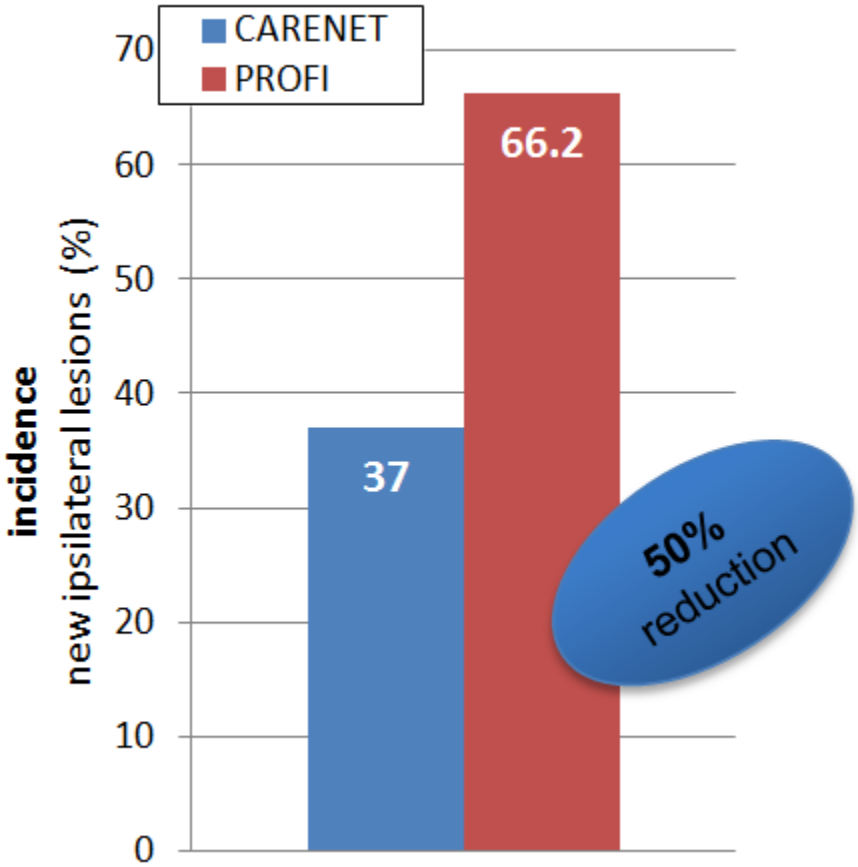
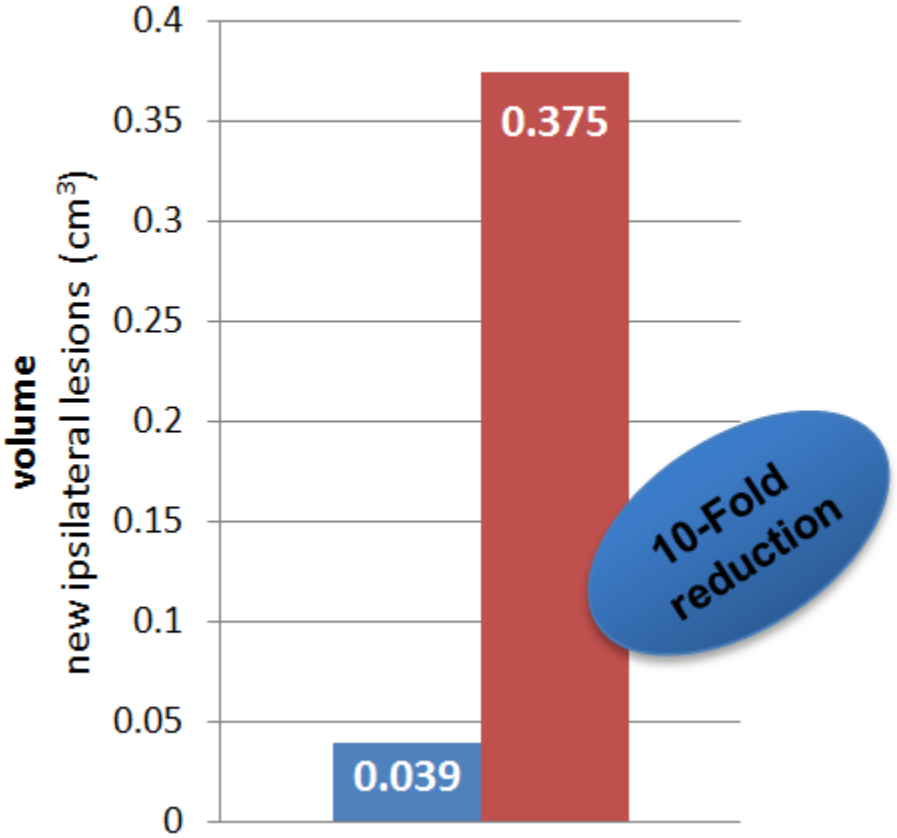
DW-MRI analysis @ 48 hours*





* see patient fluxogram

Bijuklic et al. *JACC*, 2012;59

CARENET vs. PROFI

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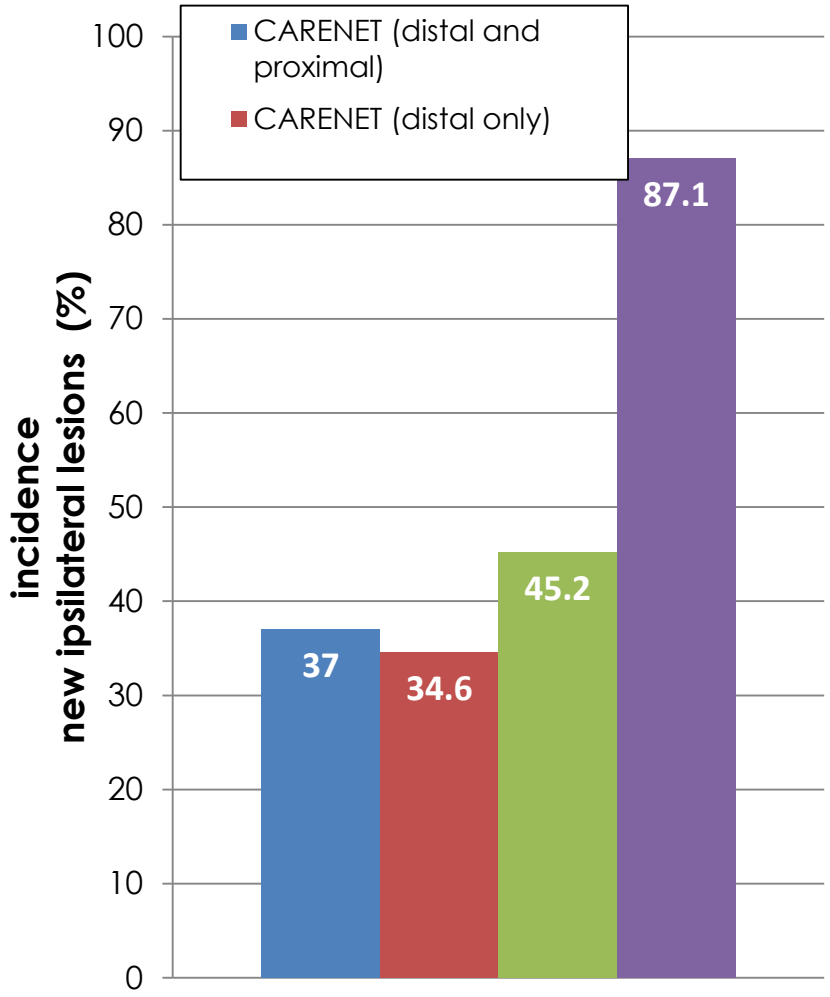
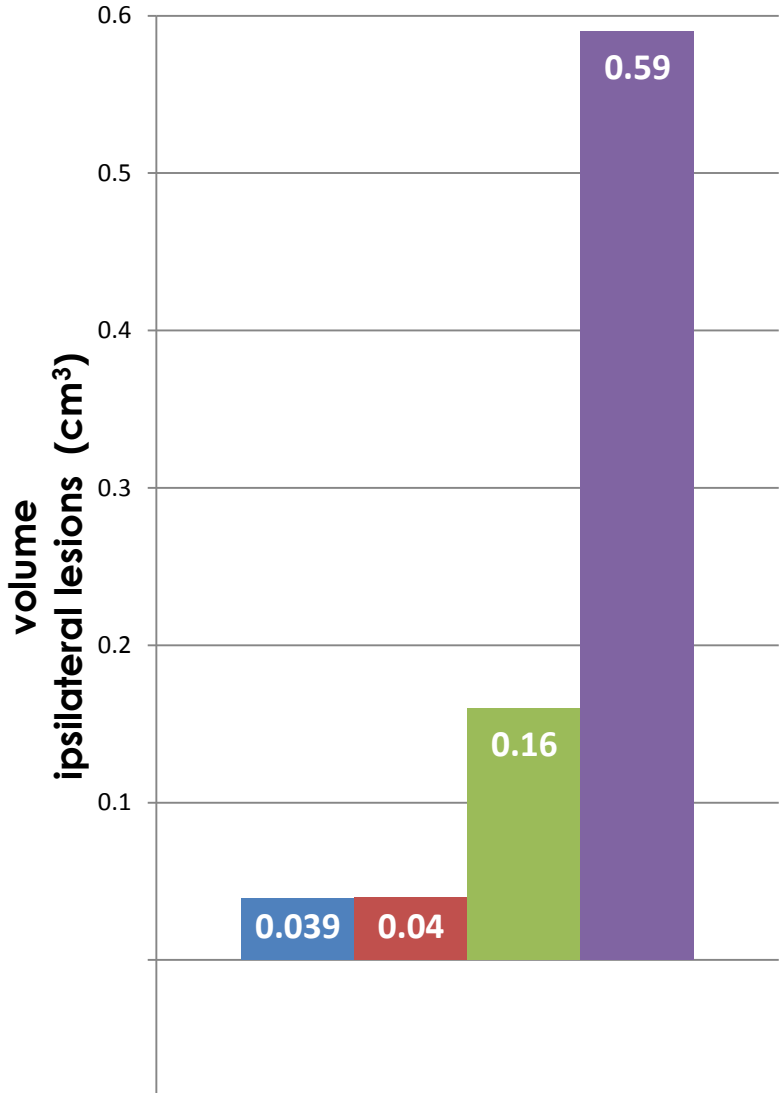
DW-MRI analysis @ 48 hours*





* See patient fluxogram

Bijuklic et al. *JACC*, 2012;59

CARENET: **30-day** DW-MRI analysis*

All but one peri-procedural ipsilateral lesions

RESOLVED

DW-MRI analysis @ 30 days*	
Incidence of new ipsilateral lesions	1
Average lesion volume (cm^3)	0.08 ± 0.00
Permanent lesions at 30 days	1

***External Core Lab analysis (US)**

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* see patient fluxogram

J. Schofer, P. Musialek et al. 2015
(manuscript at review)

CGuard: Long-term Stent Evaluation

- **Routine Duplex Doppler ultrasound**
  at discharge, 30 days, 6 and 12 months and then yearly
- **(Intravascular ultrasound)**
- **(CT angiography)**

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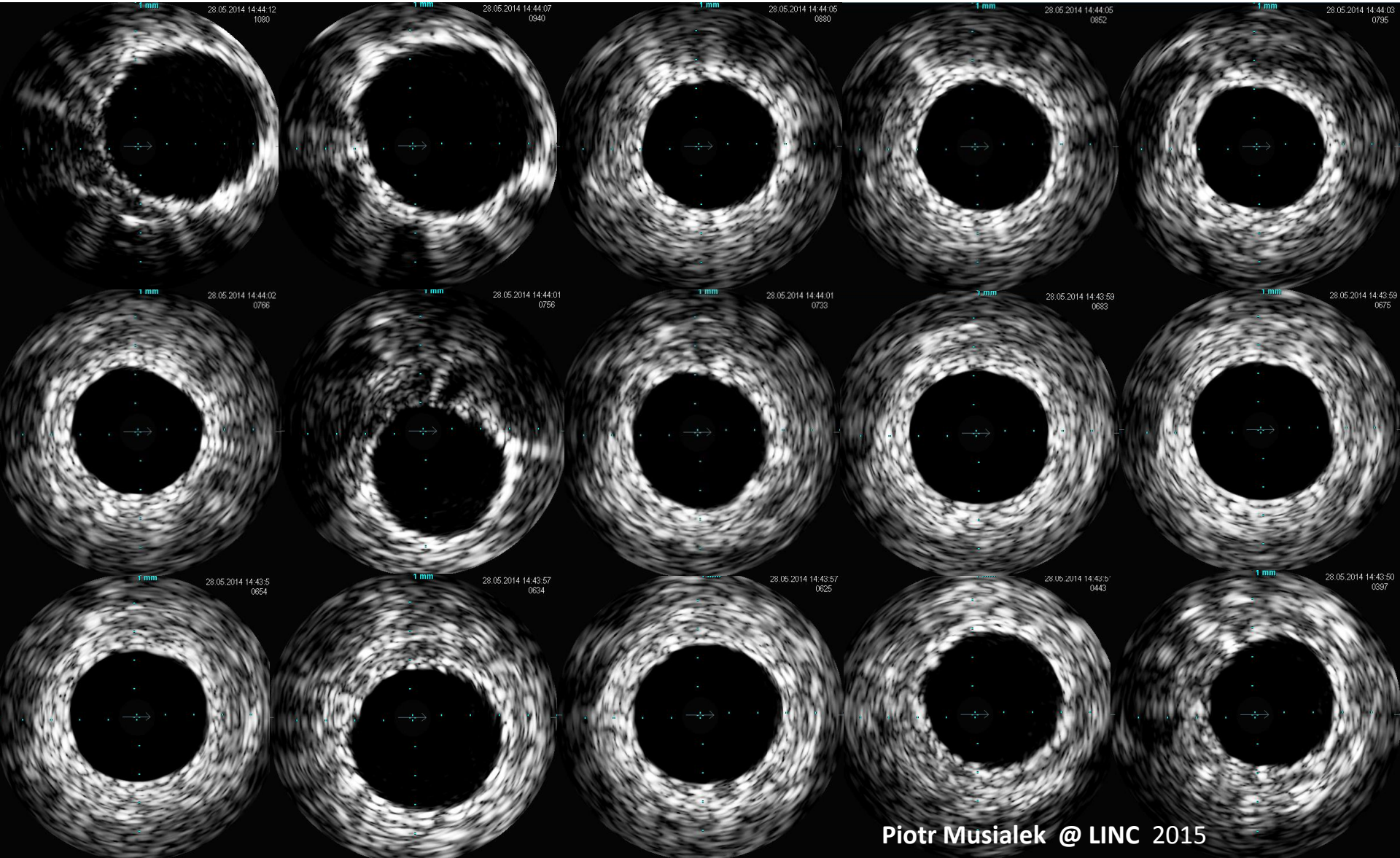
J. Schofer, P. Musialek et al. 2015
(manuscript at review)

Initial series of IVUS CGuard™ studies suggests...

- Excellent stent expansion and apposition √
- ZERO tissue protrusion though mesh-and-struts √



Piotr Musialek @ LINC 2015

5 months follow-up

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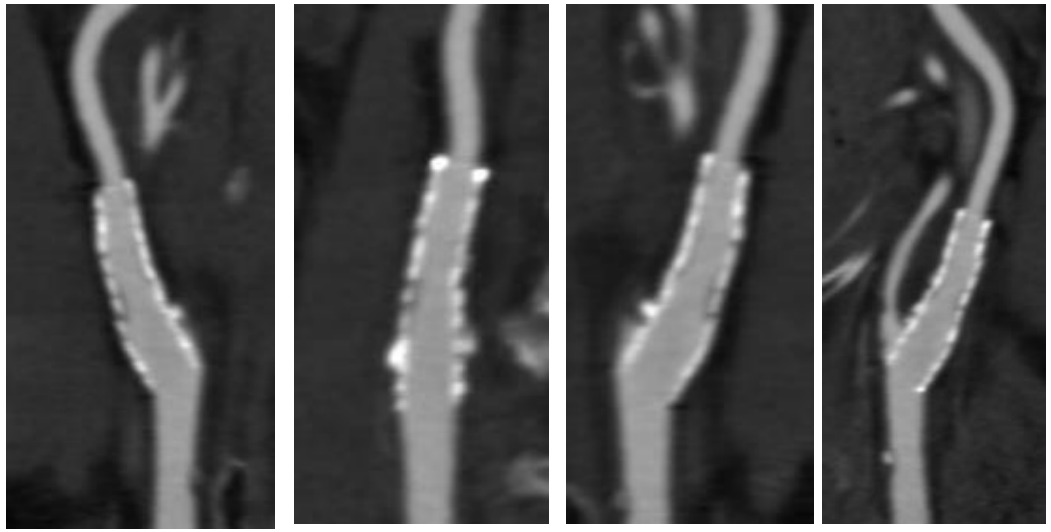
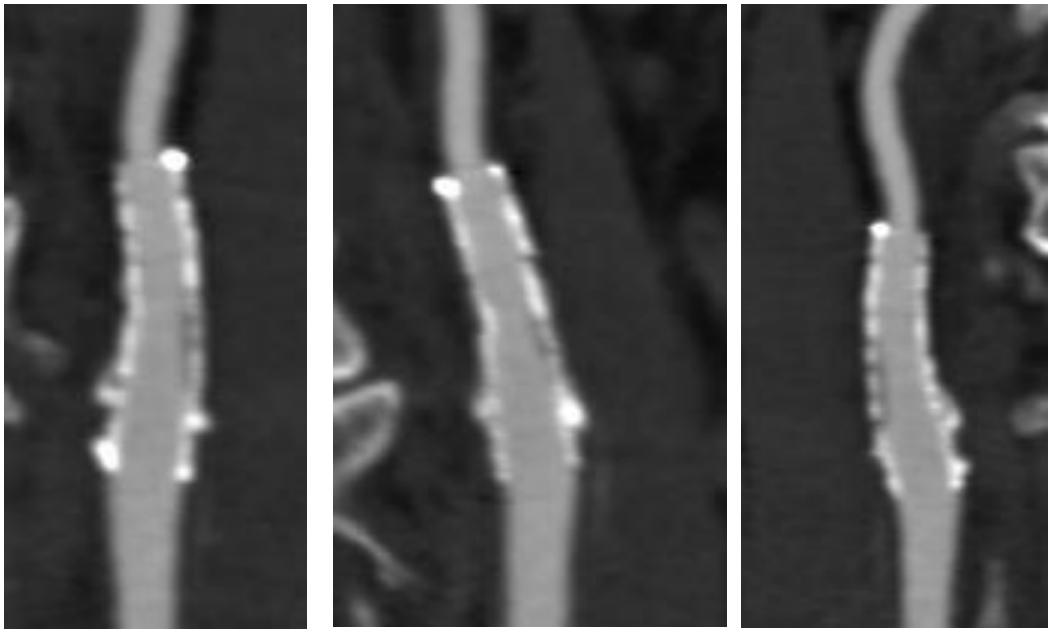
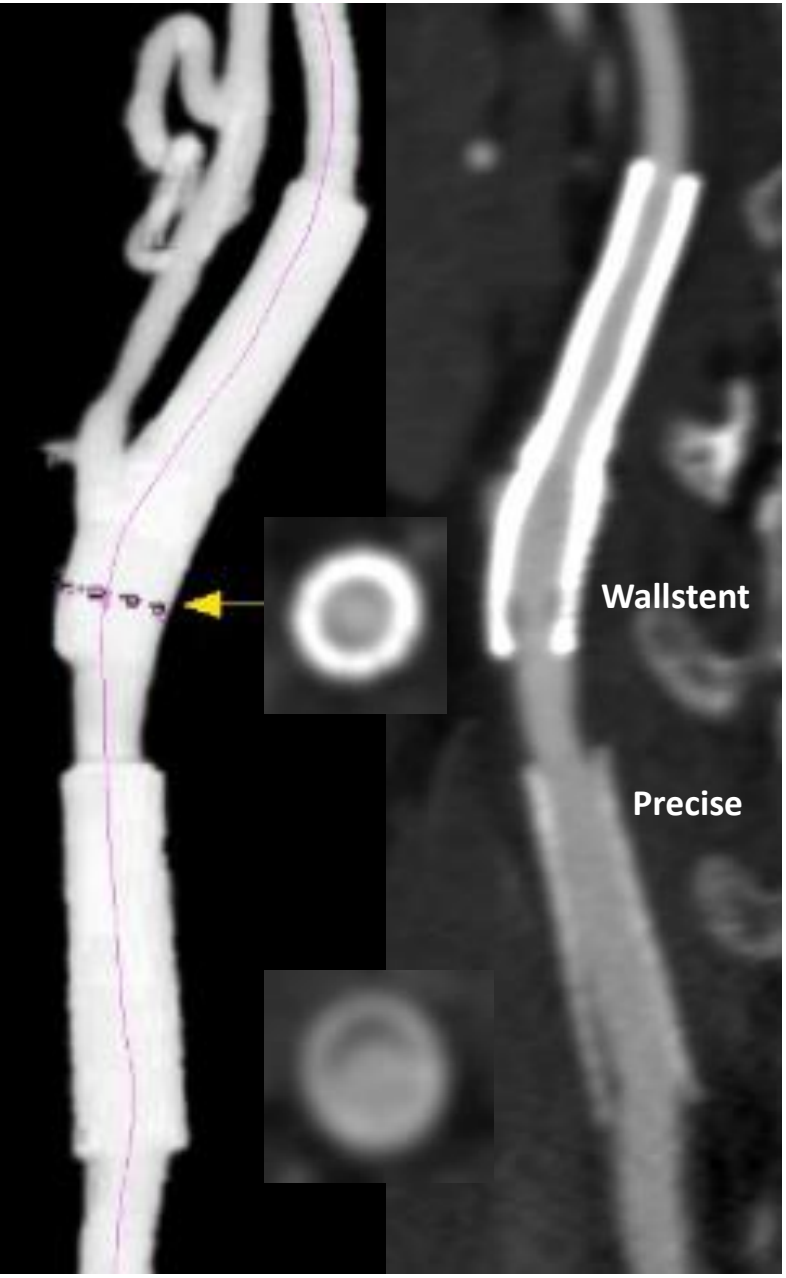




RCCA & RICA



LICA CGuard
5 months follow-up

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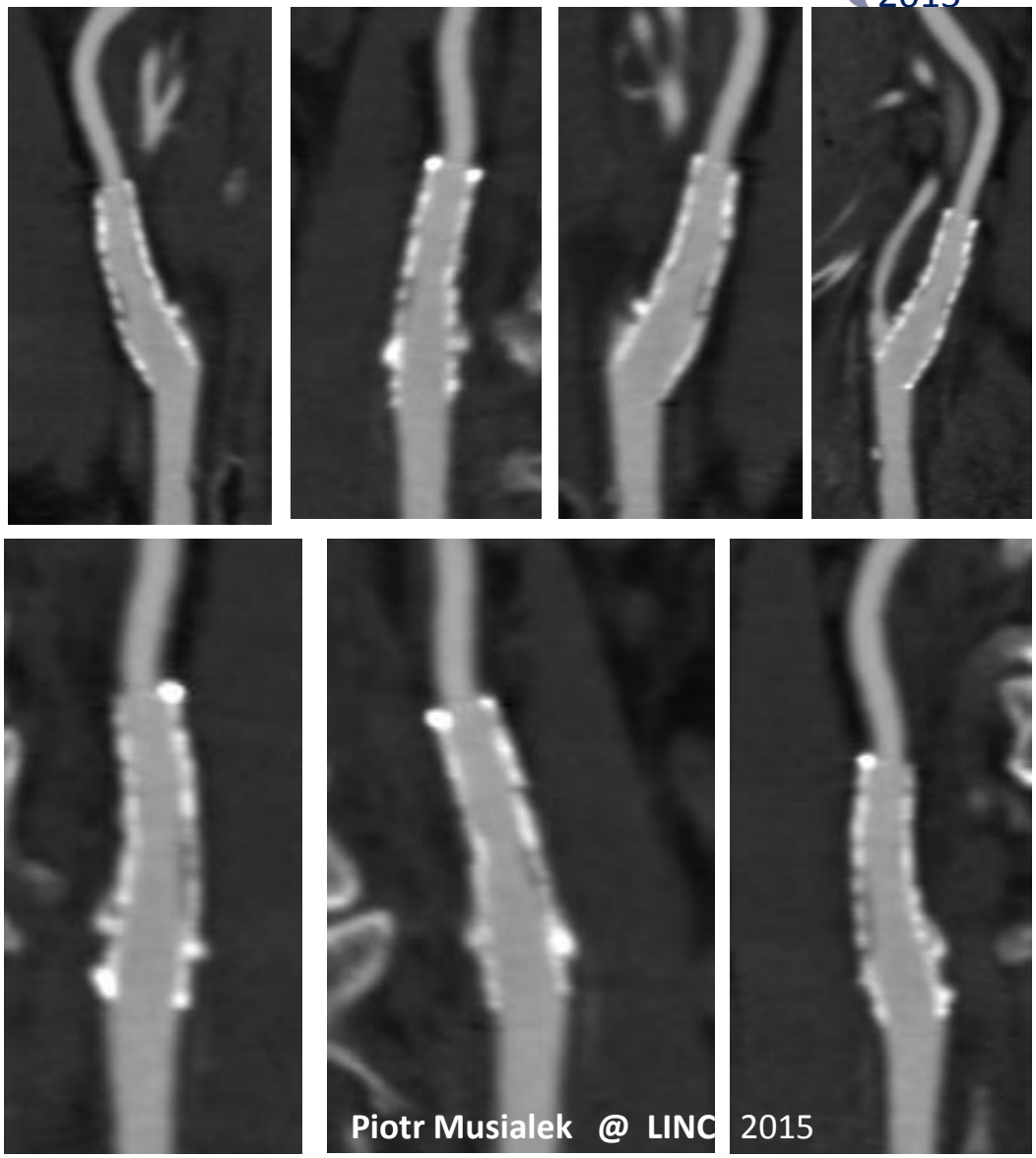
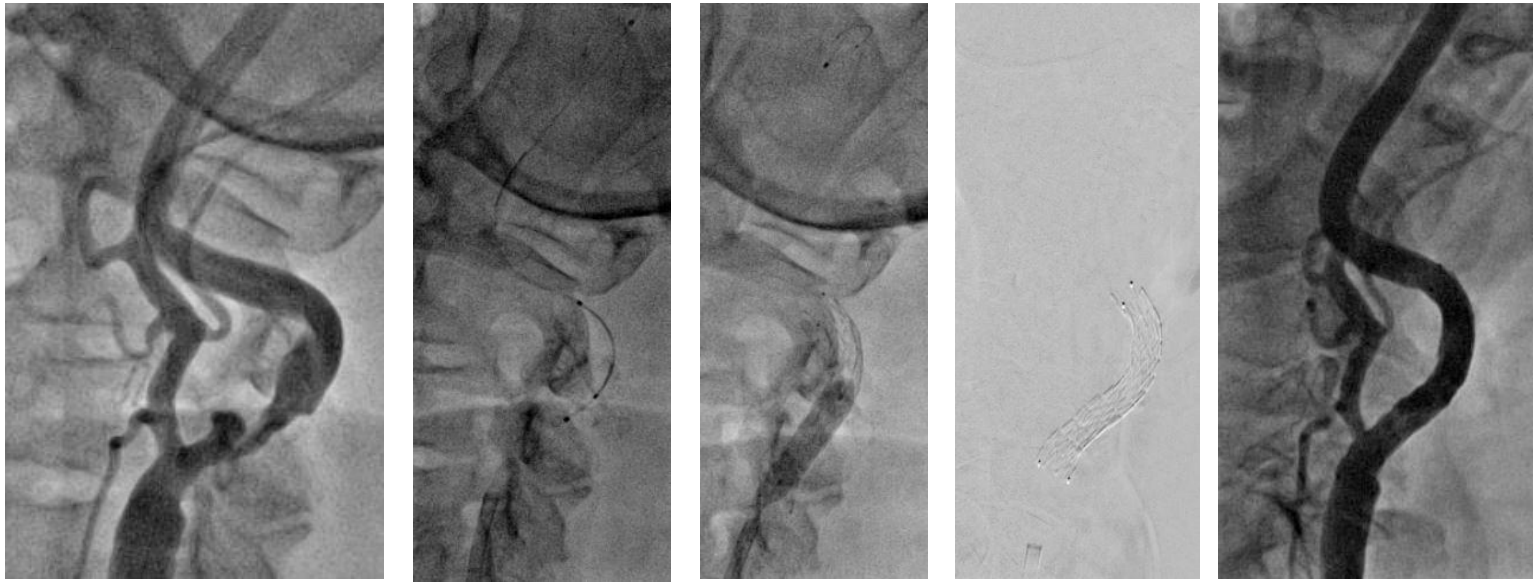
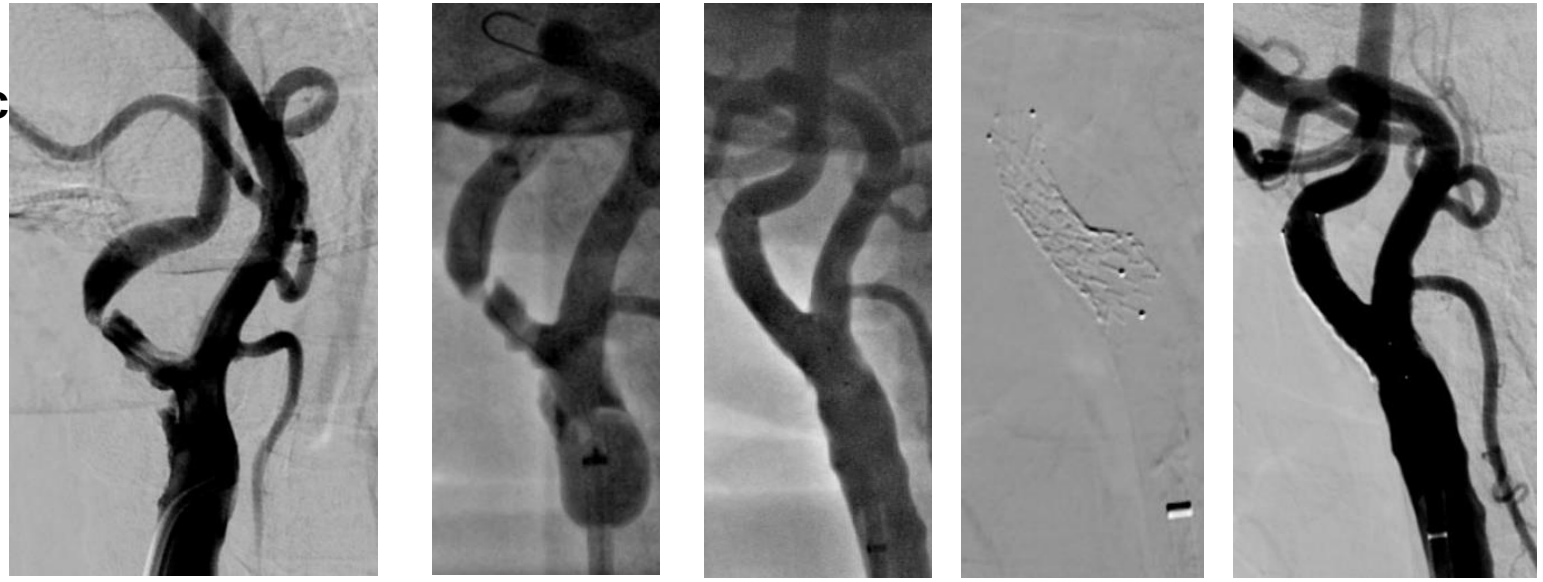


CGuard: Endovascular Solution For All-comers

61 yo symptomatic LICA



72 yo asymptomatic RICA



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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

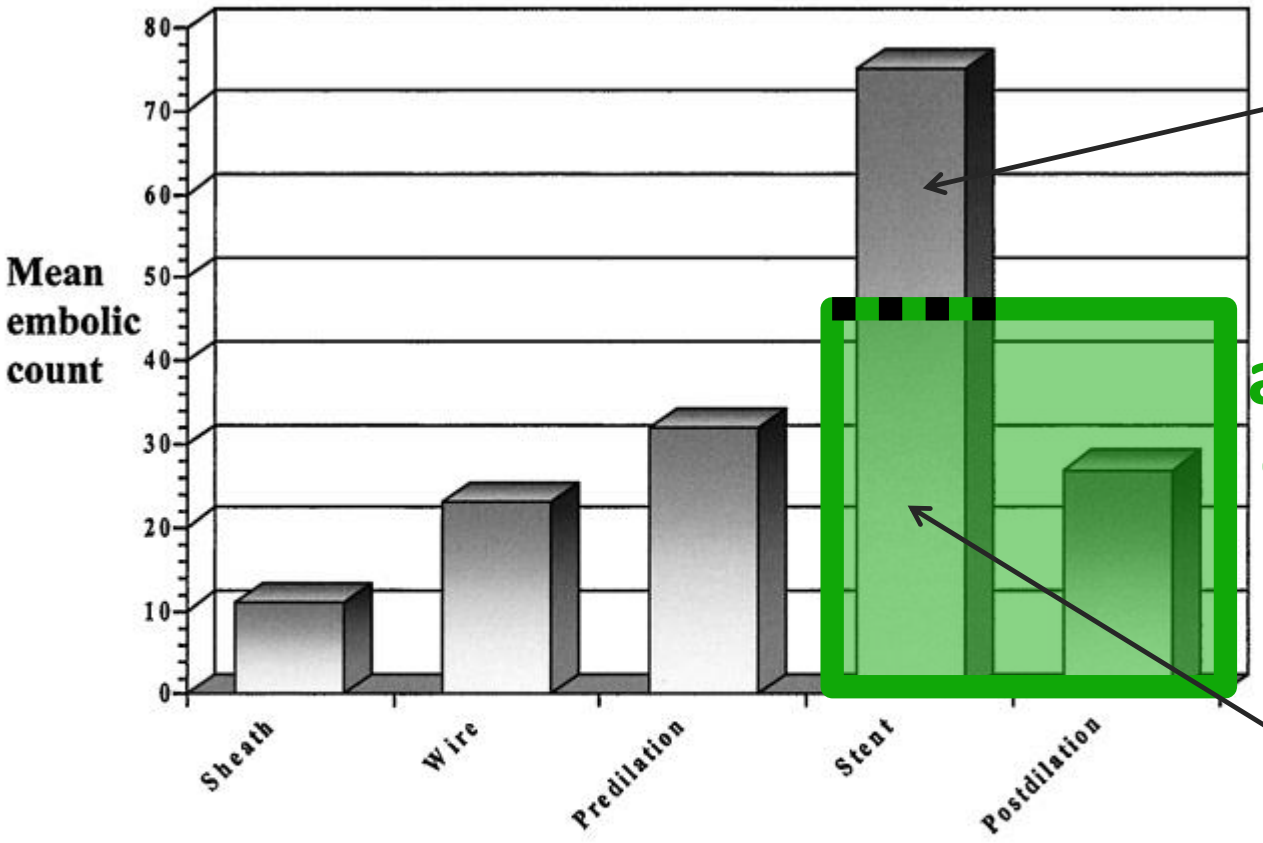

Figure 1. Microembolic profile during unprotected CAS. The mean MES counts during various phases of the procedure are displayed.

Circulation. 2001;104:1999-2002

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JOURNAL OF VASCULAR SURGERY
November 2010

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CAS: 2010 Vision

Kosmas I. Paraskevas, MD,[a] Dimitri P. Mikhailidis, MD, FFPM, FRCPath, FRCP,[b] and Frank J. Veith, MD, FACS,[c,d] *Athens, Greece; London, United Kingdom; Cleveland, Ohio; and New York, NY*

Improved technology for CAS — better EPDs (flow reversal and proximal occlusion) and better stents (membrane-covered, ultra-closed cell, and biodegragable). Several issues may improve CAS outcomes, such as the introduction of new and better stents. An ex vivo study showed that use of a polyurethane membrane-covered stent resulted in lower cerebral embolization rates.[69] Membrane-covered stents also have the potential to reduce the incidence of late embolization, that is, after the removal of the EPD.[70] Furthermore, proximal EPDs (such as the Mo.Ma flow interruption device [Invatec, Roncadelle, Italy][71] or the Parodi flow reversal Anti-Emboli System [W.L. Gore, Flagstaff, AZ])[72] offer the advantage of cerebral protection during most of the procedure.

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CGuard embolic prevention stent system

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- 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)** √

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CARENET Conclusions

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- CARENET Trial demonstrated unprecedented safety of the CGuard stent, with 30-day MACCE rate of 0%.
- The CGuard device success and procedure success rate were 100%.
- Majority of patients treated with CGuard have zero ipsilateral lesions on post-procedural DWI.

CARENET Conclusions

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- 10-fold reduction in average lesion volume when compared to conventional carotid stents.
- All but one peri-procedural lesion had resolved completely by 30 days.
- CARENET data indicates that CGuard may offer **unique clinical benefits** for patients undergoing CAS – with unprecedented safety.