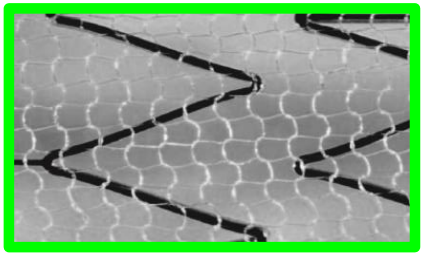

WIST

ICCA STROKE 2019

CAROTID PARADIGM REVASCULARIZATION

# CGuard™ Embolic Prevention Stent System

## Accumulating Clinical Evidence


**Piotr Musiałek**

**ESC Research Committee** & **Congress Programme Committee**

***Polish Cardiac Society Board Representative - Stroke and Vascular Interventions***

Jagiellonian University Dept. of Cardiac & Vascular Diseases

John Paul II Hospital, Kraków, Poland

ICCA STROKE 2019

WIST

# DISCLOSURE STATEMENT OF FINANCIAL INTEREST

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below

| AFFILIATION/FINANCIAL RELATIONSHIP | COMPANY |
|---|---|
| Grant/Research Support | Abbott |
| Consulting Fees/Honoraria | Abbott, InspireMD, Medtronic |
| Major Stock Shareholder/Equity | **No** |
| Royalty Income | **No** |
| Ownership/Founder | **No** |
| Intellectual Property Rights | **No** |
| Other Financial Benefit | **No** |

# AHA Statistical Update

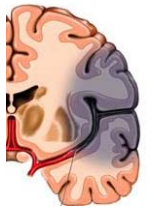

**Table 14-2. Modifiable Stroke Risk Factors**

| Factor | Prevalence, % | PAR, %* | RR |
|---|---|---|---|
| Cigarette smoking | | | |
| Overall | 19.8 | 12–14† | 1.9 |
| Men | 22.3 | | |
| Women | 17.4 | | |
| Hypertension | | ‡ | 8 |
| Ages 20–34 y | | | |
| Men | 13.4 | 99 | |
| Women | 6.2 | 98 | |
| Ages 35–44 y | | | |
| Men | 23.2 | 99 | |
| Women | 16.5 | 106 | |
| Ages 45–54 y | | | |
| Men | 36.2 | 100 | |
| Women | 35.9 | 103 | |
| Ages 55–64 y | | | |
| Men | 53.7 | 100 | |
| Women | 55.8 | 102 | |
| Ages 65–74 y | | | |
| Men | 64.7 | 100 | |
| Women | 69.6 | 101 | |
| Ages ≥75 y | | | |
| Men | 64.1 | 100 | |
| Women | 76.4 | 101 | |
| Diabetes mellitus | 7.3 | 5–27 | 1.8–6.0 |
| High total cholesterol | Data calculated for highest quintile (20%) vs lowest quintile | 9.1 (5.7–13.8) | 1.5 (95% CI, 1.3–1.8) |
| | Continuous risk for ischemic stroke | … | 1.25 per 1-mmol/L (38.7 mg/dL) increase |
| AF (nonvalvular) | | | |
| 50–59 | 0.5 | 1.5 | 4.0 |
| 60–69 | 1.8 | 2.8 | 2.6 |
| 70–79 | 4.8 | 9.9 | 3.3 |
| 80–89 | 8.8 | 23.5 | 4.5 |
| Asymptomatic carotid stenosis | 2–8 | 2–7§ | 2.0 |

European Heart Journal (2015) 36, 281–287
doi:10.1093/eurheartj/ehu307

CLINICAL RESEARCH
*Atrial fibrillation*

# Risk of ischaemic stroke according to pattern of atrial fibrillation: analysis of 6563 aspirin-treated patients in ACTIVE-A and AVERROES

**Thomas Vanassche[1]*, Mandy N. Lauw[1], John W. Eikelboom[1], Jeff S. Healey[1], Robert G. Hart[1], Marco Alings[2], Alvaro Avezum[3], Rafael Díaz[4], Stefan H. Hohnloser[5], Basil S. Lewis[6], Olga Shestakovska[1], Jia Wang[1], and Stuart J. Connolly[1]**

[1]Population Health Research Institute, McMaster University and Hamilton Health Sciences, 237 Barton St. E., Hamilton, ON, Canada L8L 2X2; [2]Amphia Ziekenhuis, Breda, The Netherlands; [3]Instituto Dante Pazzanese de Cardiologia, São Paulo, Brazil; [4]Estudios Clínicos Latinoamérica, Rosario, Argentina; [5]Department of Cardiology, Johann-Wolfgang-Goethe-Universität, Frankfurt, Germany; and [6]Cardiovascular Clinical Research Institute, Lady Davis Carmel Medical Center and the Ruth and Bruce Rappaport School of Medicine, Technion-IIT, Haifa, Israel

*Received 21 April 2014; revised 20 June 2014; accepted 16 July 2014; online publish-ahead-of-print 3 September 2014*

**Aims** The pattern of atrial fibrillation (AF) occurrence—paroxysmal, persistent, or permanent—is associated with progressive stages of atrial dysfunction and structural changes and may therefore be associated with progressively higher stroke risk. However, previous studies have not consistently shown AF pattern to predict stroke but have been hampered by methodological shortcomings of low power, variable event ascertainment, and variable anticoagulant use.

**Methods and results** We analysed the rates of stroke and systemic embolism in 6563 aspirin-treated patients with AF from the ACTIVE-A/AVERROES databases. There was thorough searching for events and adjudication. Multivariable analyses were performed with the adjustment for known risk factors for stroke. Mean age of patients with paroxysmal, persistent, and permanent AF was 69.0 ± 9.9, 68.6 ± 10.2, and 71.9 ± 9.8 years ($P < 0.001$). The $CHA_2DS_2$-VASc score was similar in patients with paroxysmal and persistent AF (3.1 ± 1.4), but was higher in patients with permanent AF (3.6 ± 1.5, $P < 0.001$). Yearly ischaemic stroke rates were 2.1, 3.0, and 4.2% for paroxysmal, persistent, and permanent AF, respectively, with adjusted hazard ratio of 1.83 ($P < 0.001$) for permanent vs. paroxysmal and 1.44 ($P = 0.02$) for persistent vs. paroxysmal. Multivariable analysis identified age ≥ 75 year, sex, history of stroke or TIA, and AF pattern as independent predictors of stroke, with AF pattern being the second strongest predictor after prior stroke or TIA.

**Conclusion** In a large population of non-anticoagulated AF patients, pattern of AF was a strong independent predictor of stroke risk and may be helpful to assess the risk/benefit for anticoagulant therapy, especially in lower risk patients.

**Keywords** Atrial fibrillation • Paroxysmal • Permanent • Stroke

# How asymptomatic is "asymptomatic" carotid stenosis?

## Resolving fundamental confusion(s)—and confusions yet to be resolved

Piotr Musiałek[1], Iris Q. Grunwald[2,3]

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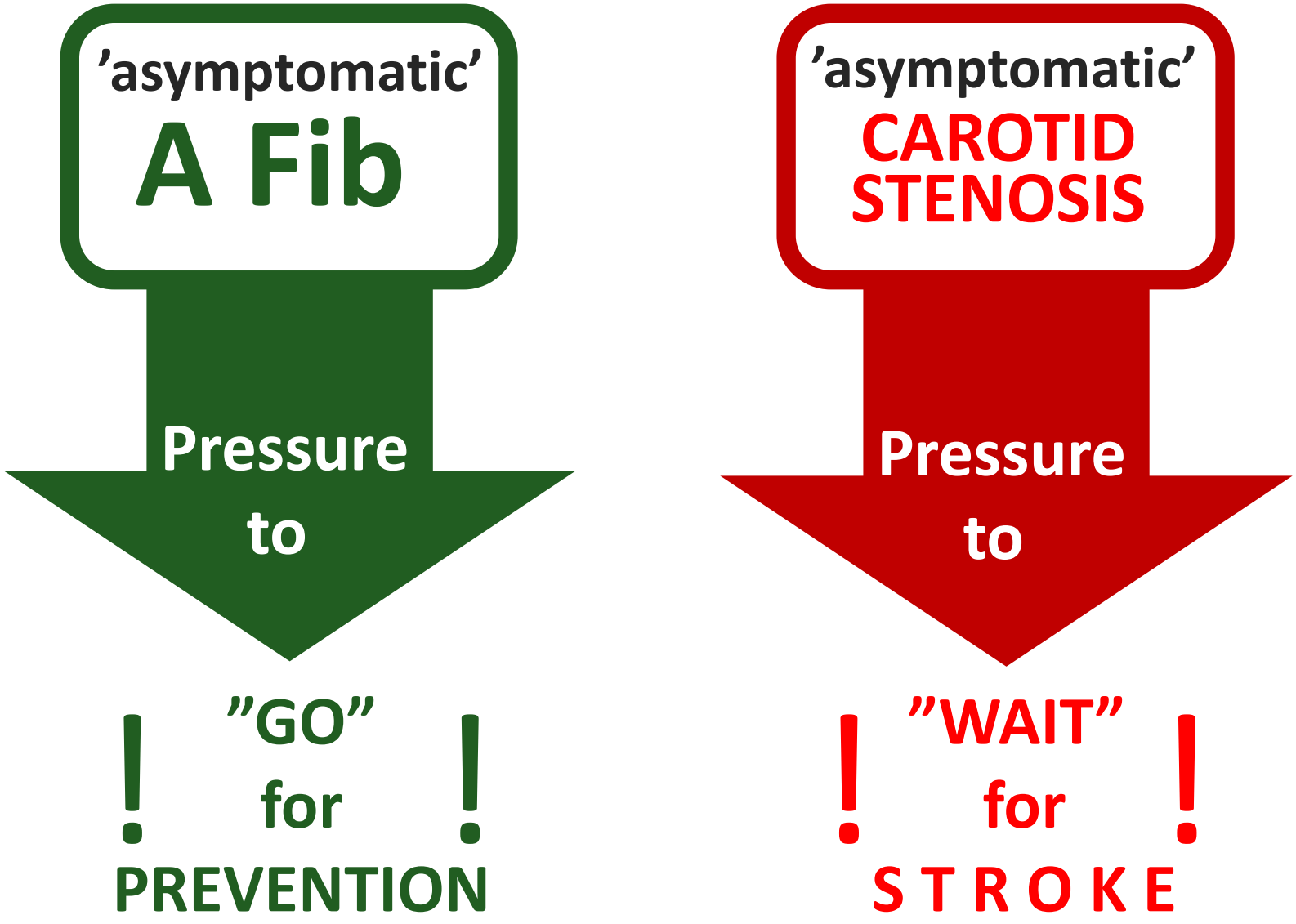
2 Neuroscience and Vascular Simulation, Anglia Ruskin University, Chelmsford, United Kingdom
3 Southend University Hospital NHS Foundation Trust, Westcliff-on-Sea, United Kingdom

2 recent independent studies demonstrated an annual stroke rate of 2.4%[7] or 2.9%[8] in vascular clinic patients with asymptomatic CS on optimized medical therapy (OMT). As the risk is cumulative, the annual risk level of about 2.5% to 3.0% indicates—for instance for a 50-year-old man with an asymptomatic CS on contemporary OMT—a statistical stroke risk of about 25% to 30% by the age of 60 and 50% to 60% by the age of 70 (the actual risk can be still higher when additional risk factors, such as diabetes, are present).[2] As 85% of strokes occur without a warning sign, and of those who survive stroke (about 40% at 5 years) about half are disabled,[2] many families and physicians find it difficult to ignore such a risk.[4] This is particularly relevant because contemporary CS revascularization studies continue to enroll patients with CS strokes despite OMT; this provdes circumstantial evidence that OMT, at least in some patients, does not sufficiently protect against stroke.[4]


'asymptomatic'
A Fib
Pressure
to
"GO"
for
!
!
PREVENTION


'asymptomatic'
CAROTID
STENOSIS
Pressure
to
! "WAIT" !
for
S T R O K E

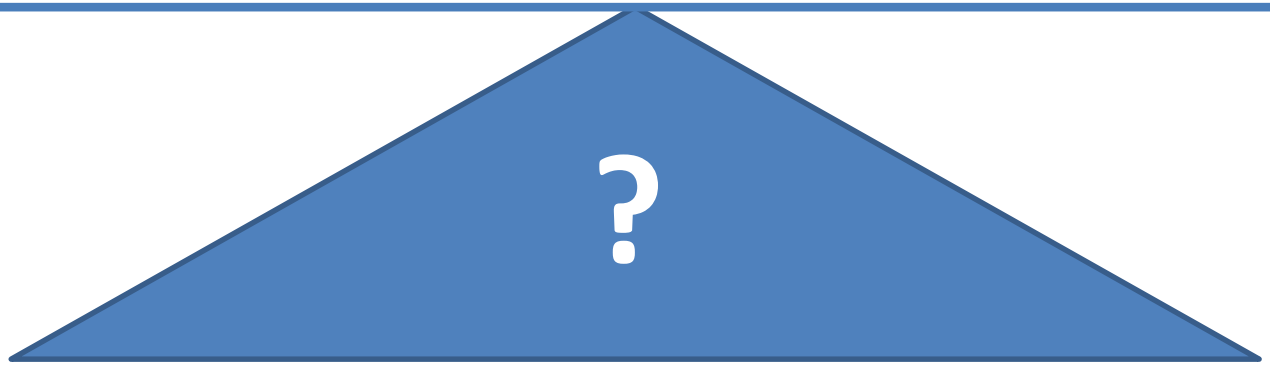
# logic ???


'asymptomatic'
A Fib
Pressure to
! "GO" for !
PREVENTION
'asymptomatic'
CAROTID STENOSIS
Pressure to
! "WAIT" for !
S T R O K E

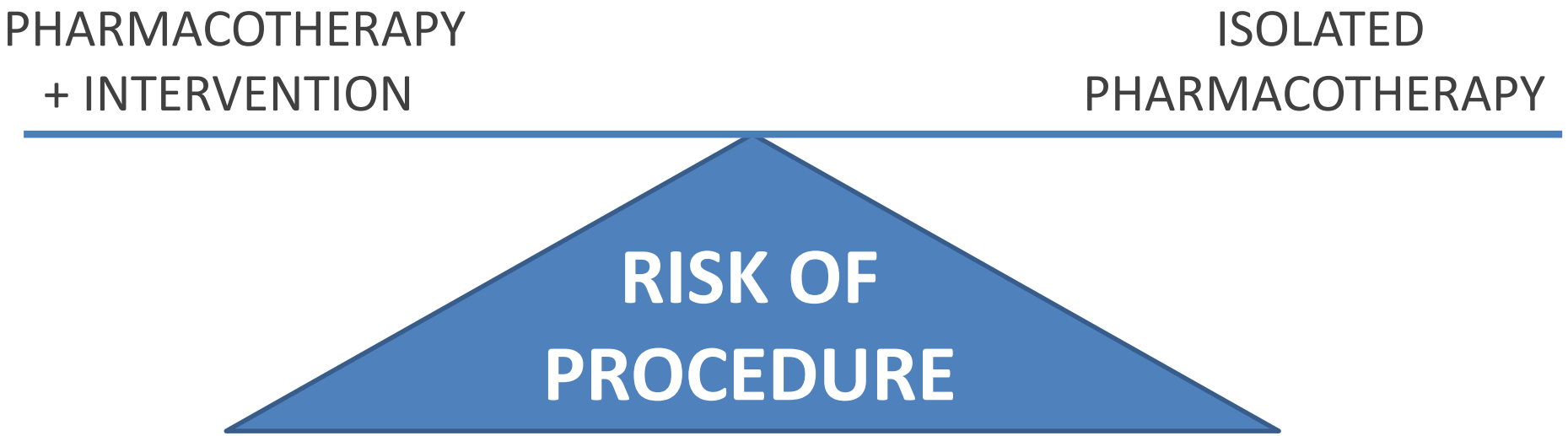
# Carotid Stenosis
# Decision-making

PHARMACOTHERAPY
+ INTERVENTION

ISOLATED
PHARMACOTHERAPY

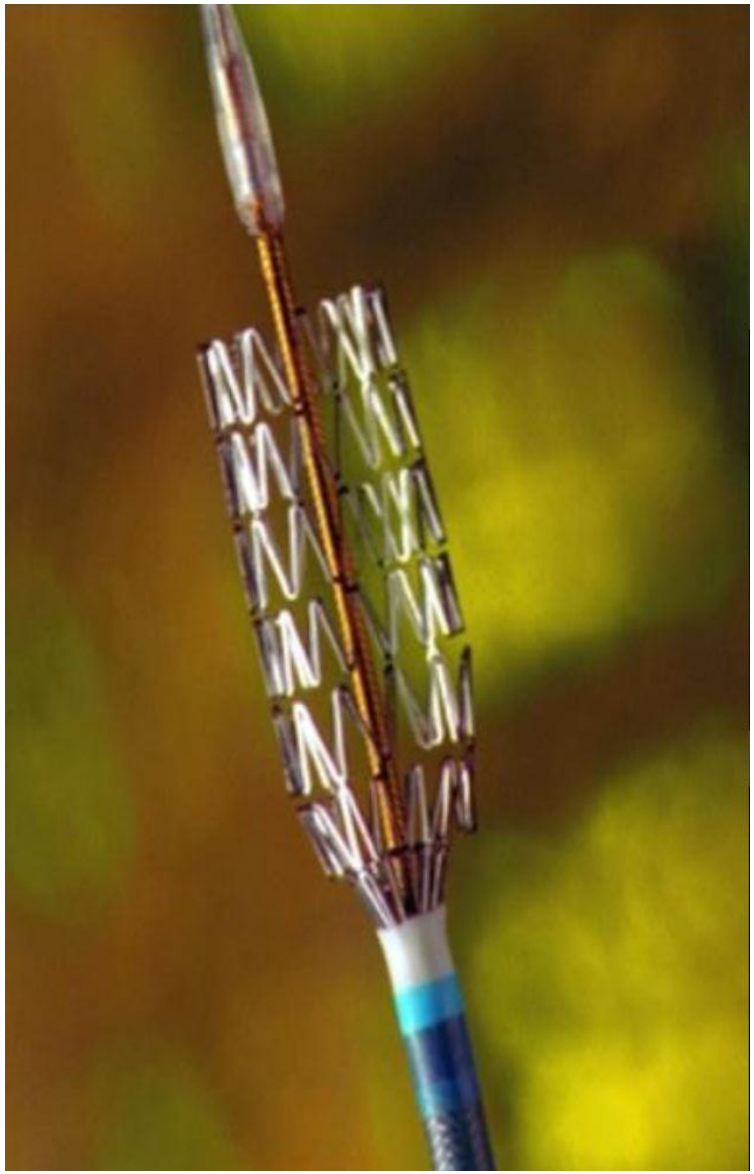


# Carotid Stenosis
# Decision-making



# Conventional Carotid Stents

# Do Have A Problem



Human carotid artery treated using a conventional stent; OCT

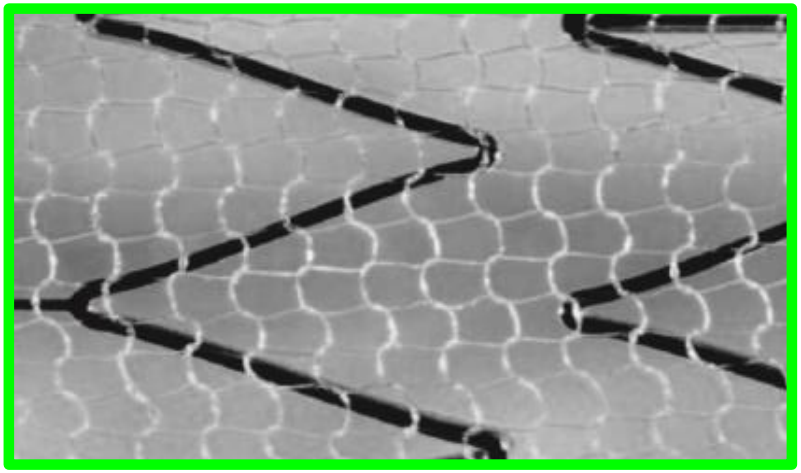
Image courtesy Joan Rigla, MD PhD; Perceptual Imaging Lab, Univerity of Barcelona

# Conventional Carotid Stents

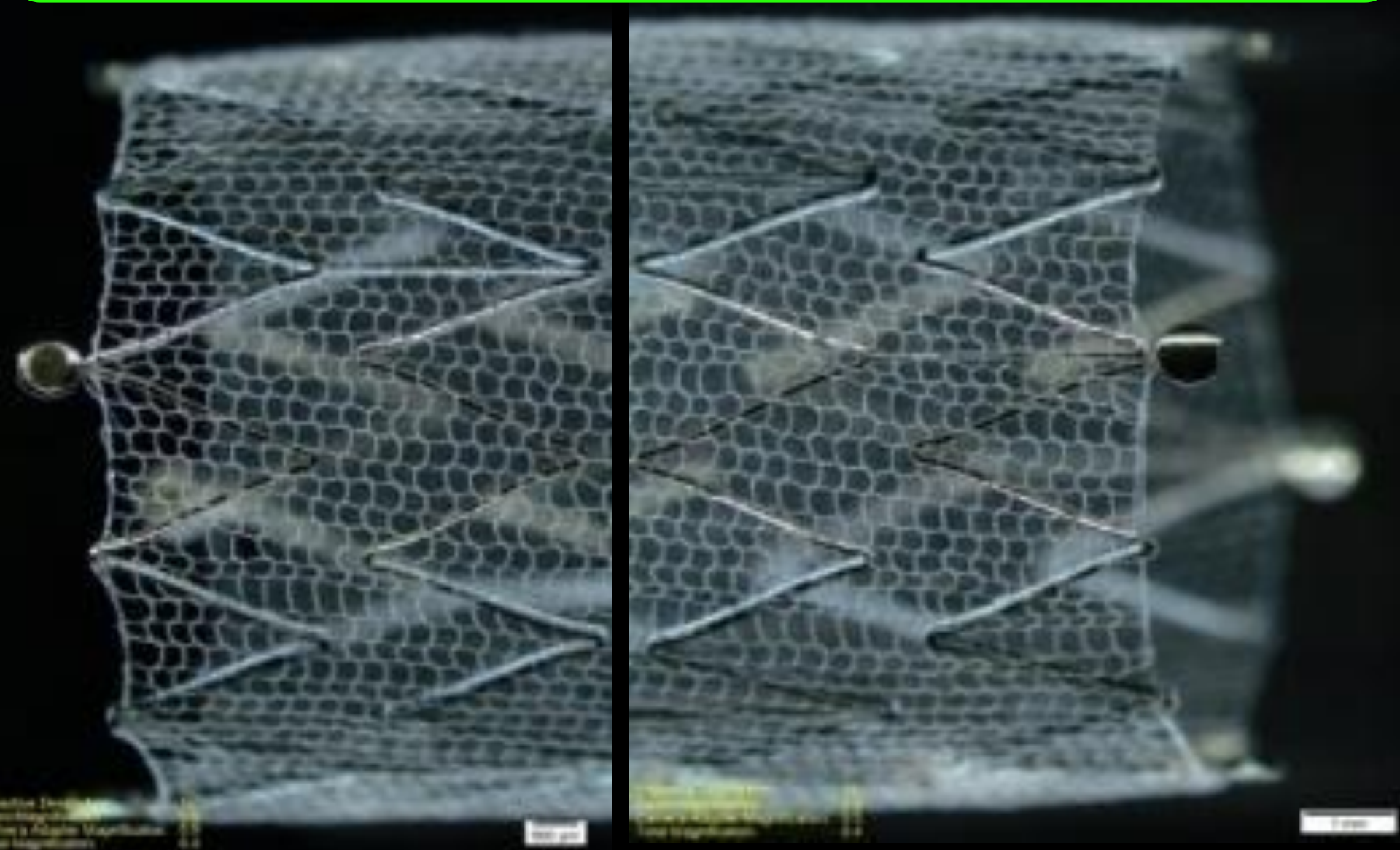
# Do Have A Problem

- CEA excludes the plaque
- In CAS, the stent should exclude the plaque too

- CEA excludes the plaque
- In CAS, the stent should exclude the plaque too



# CGuard™ embolic prevention system

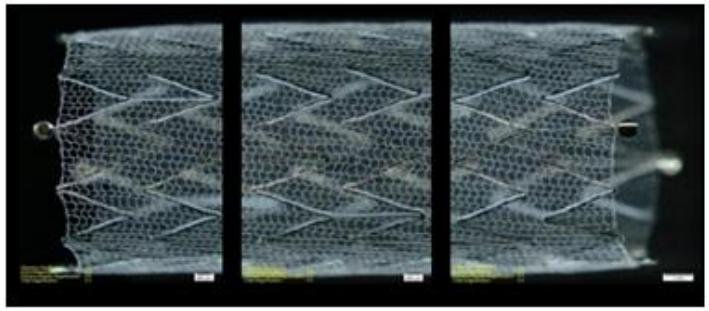


# CGuard™– Carotid Embolic Prevention System

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

CE Mark – March 2014

carotid-dedicated design

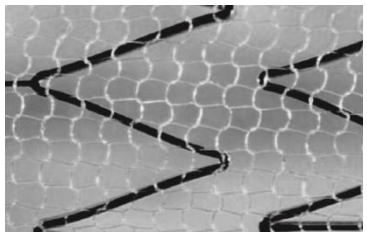


Nitinol frame open-cell area ≈ 21 $mm^2$

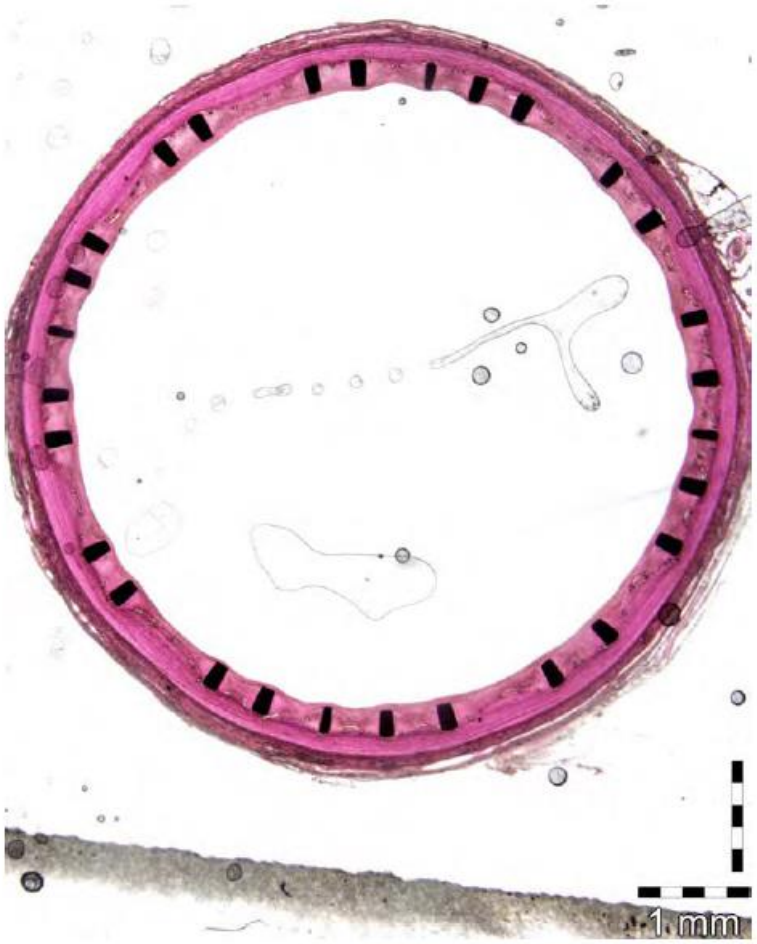
MicroNet closed-cell area ≈ 0.3$mm^2$

LARGEST √

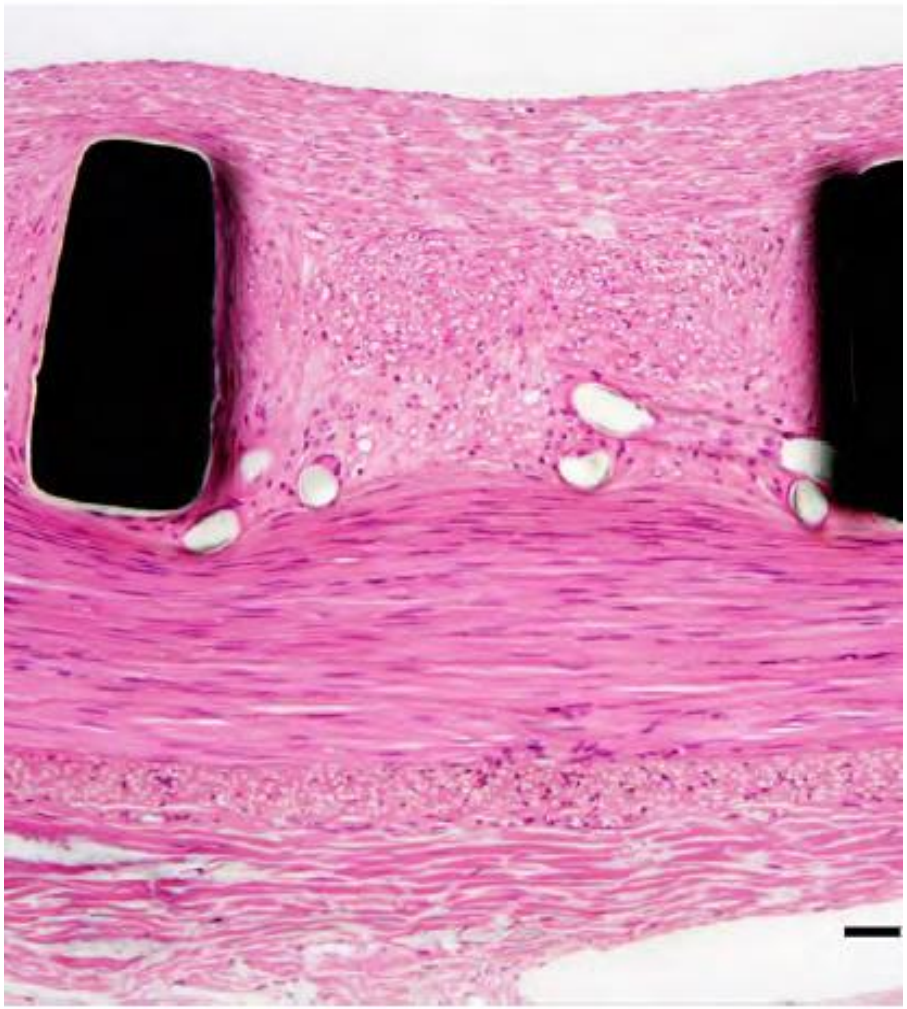
SMALEST √



# CGuard EPS 90 days/pig



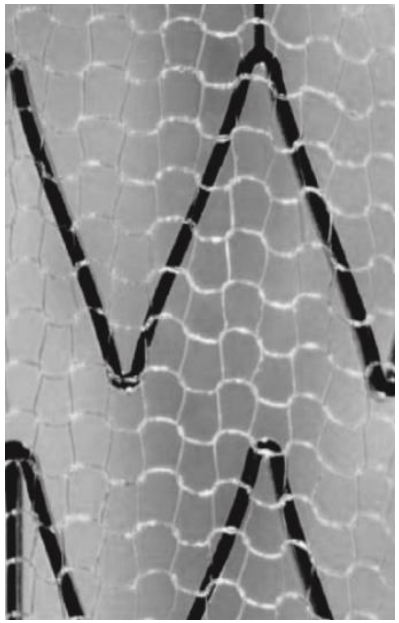

12-105 LCCA-S 3 13-1689-3 1.25x H&E.tif

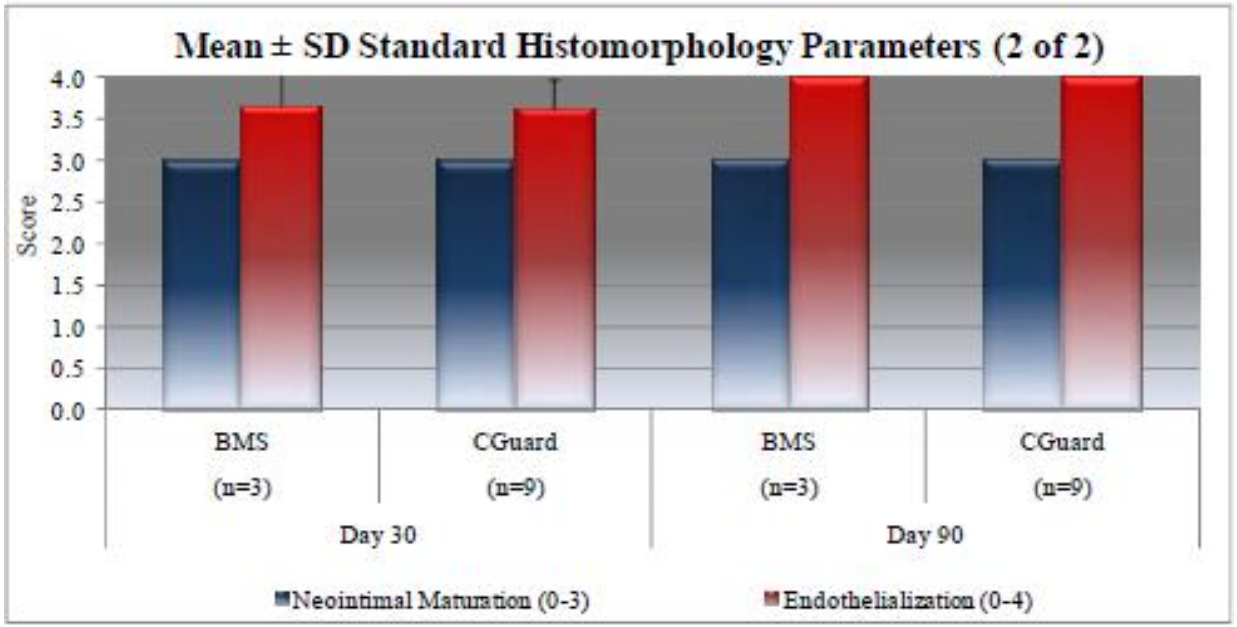


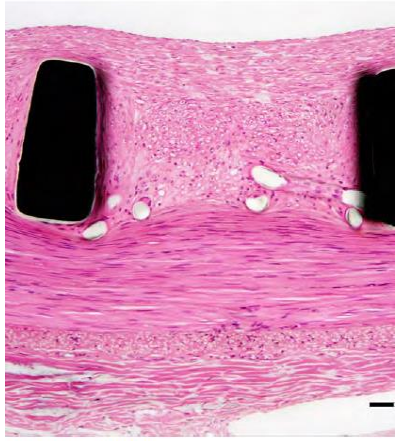
CA-S 3 13-1689-3 10x H&E.tif

**InspireMD data / by permission**

# CGuard EPS 30 & 90 days / pig





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

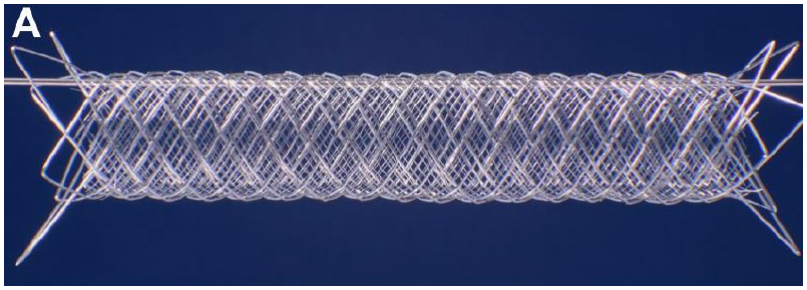
| Mean ± SD and Median Standard Histomorphology Parameters | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Parameter | Day 30 | | | | Day 90 | | | |
| | BMS (n=3) | | CGuard (n=9) | | BMS (n=3) | | CGuard (n=9) | |
| Injury (0-3) | 0.00 ± 0.01 | 0.00 | 0.00 ± 0.01 | 0.00 | 0.01 ± 0.02 | 0.00 | 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 |

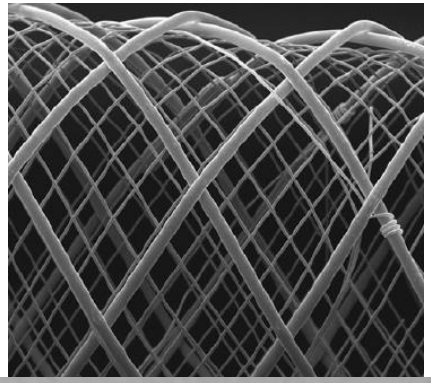
**BMS = non mesh-covered CGuard nitynol frame; InspireMD data / used with permission**

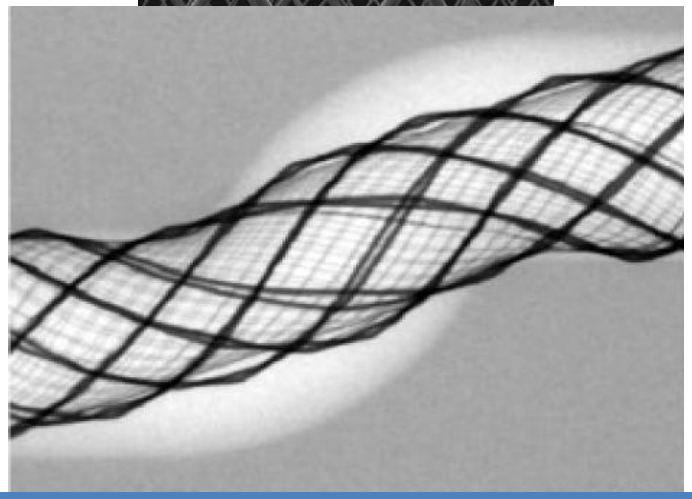
## mechanical

# Properties

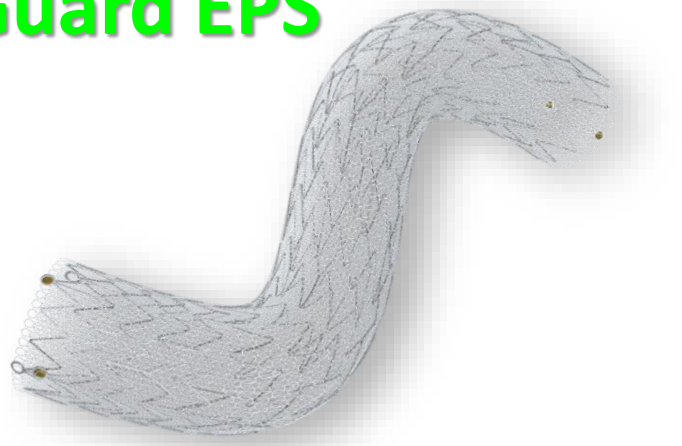
# RoadSaver / Casper

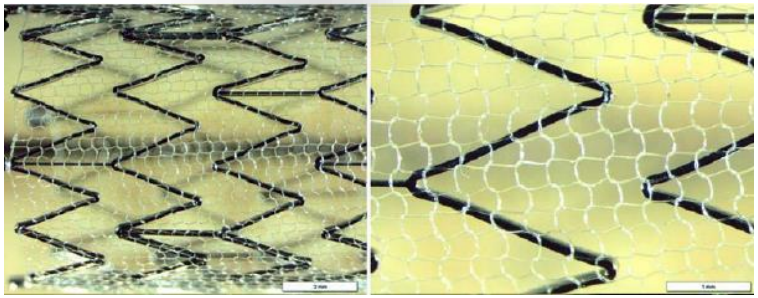


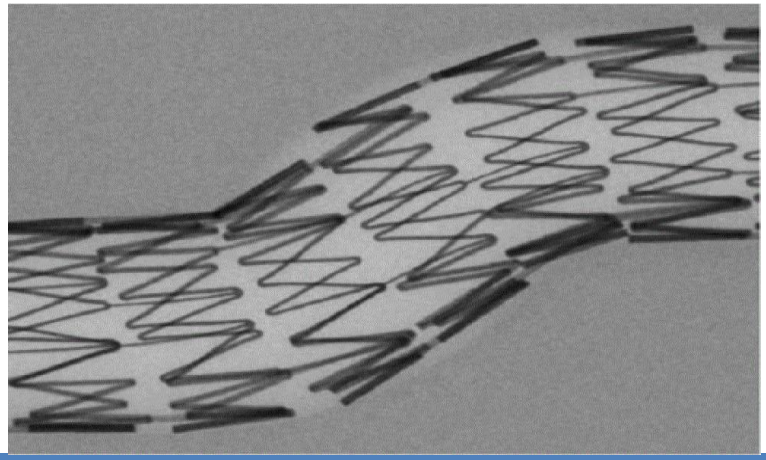





# CGuard EPS



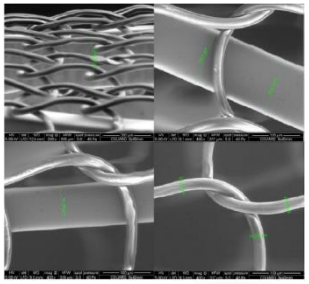




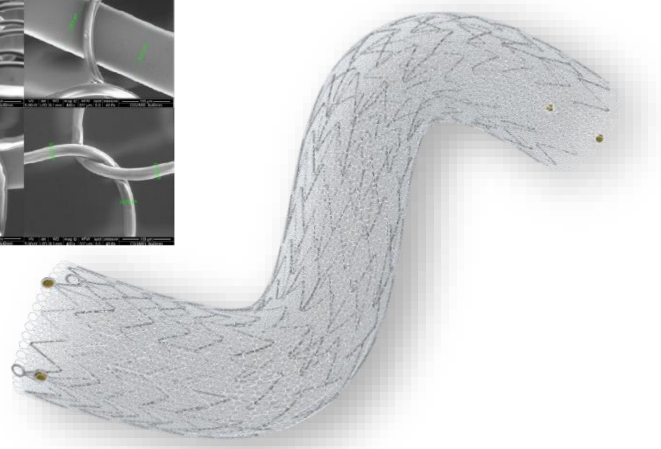
C. Wissgott and colleagues. *J Endovasc Ther.* 2015;22:634-39
C. Wissgott and colleagues. *J Endovasc Ther.* 2017;24:130-7

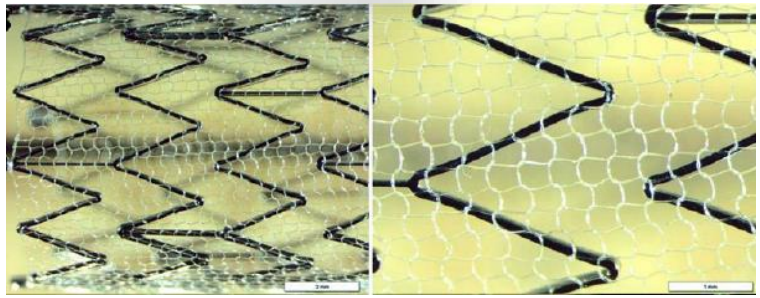
# CGuard EPS

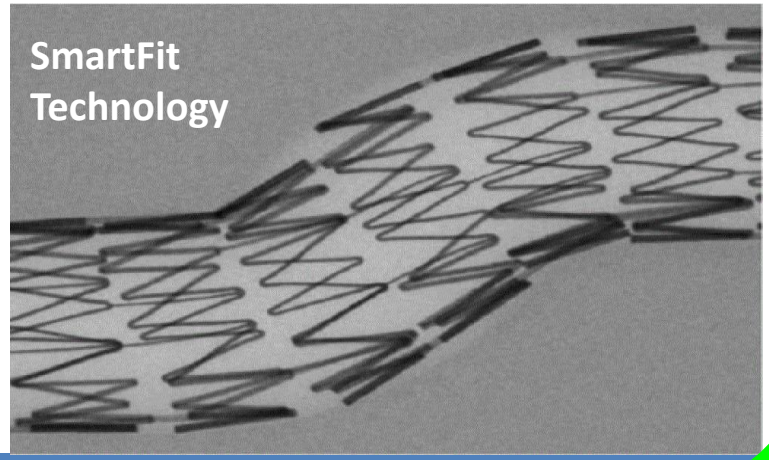
- Radial Force as the PRECISE stent
- NO foreshortening/elongation
- Widely open-cell structure of the stent frame results in a FULL APPOSITION

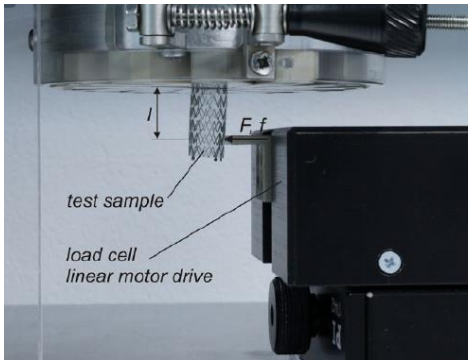


SEM

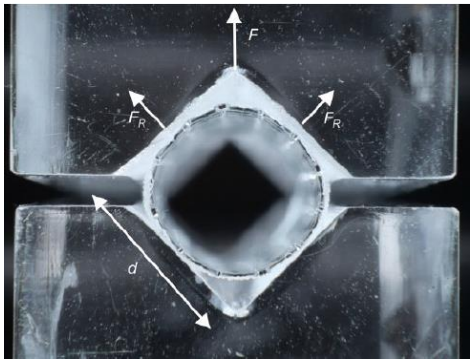






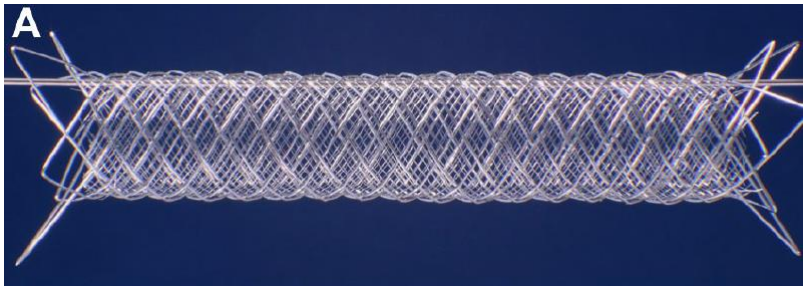

Bending Stifness

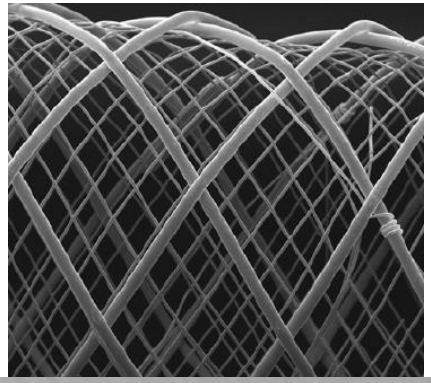


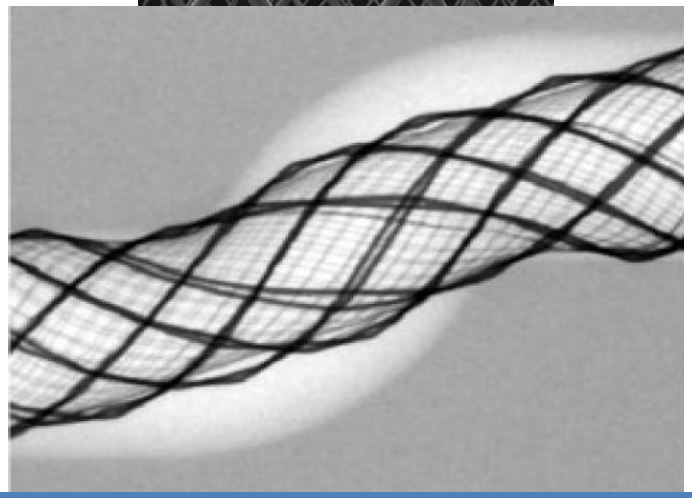

Radial Force

C. Wissgott and colleagues. *J Endovasc Ther.* 2015;22:634-39
C. Wissgott and colleagues. *J Endovasc Ther.* 2017;24:130-7

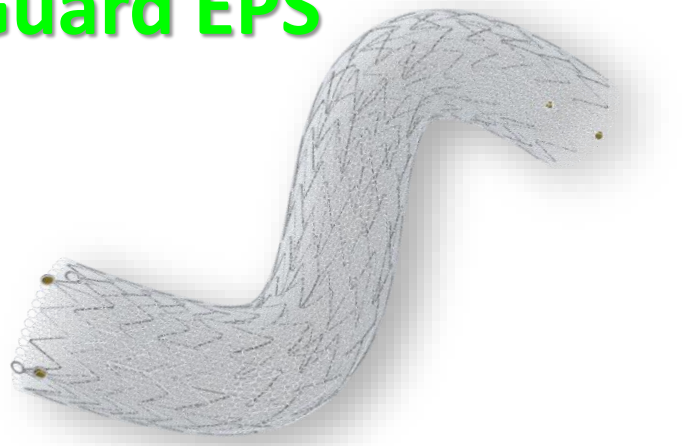
# RoadSaver / Casper

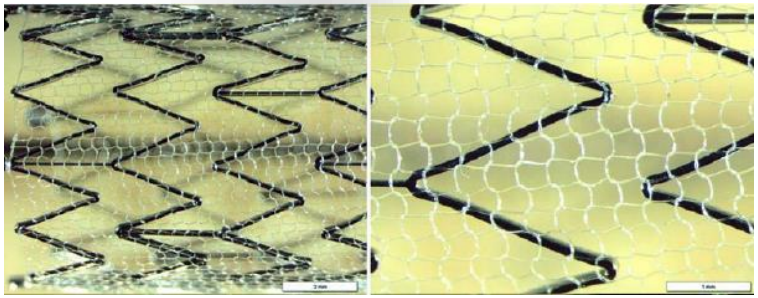


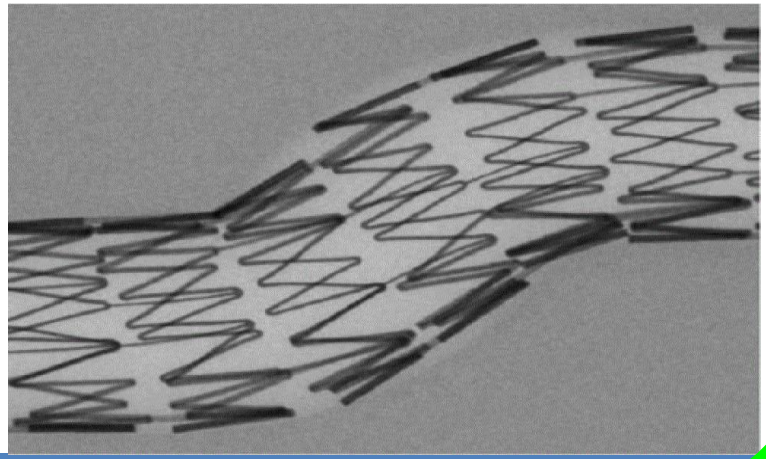





# CGuard EPS







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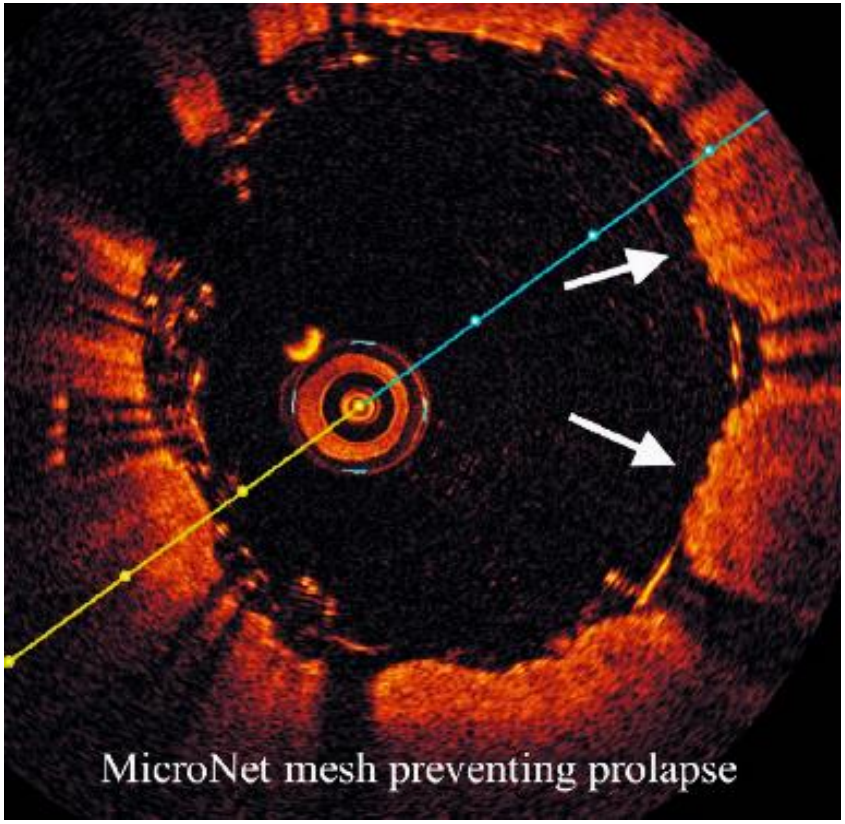


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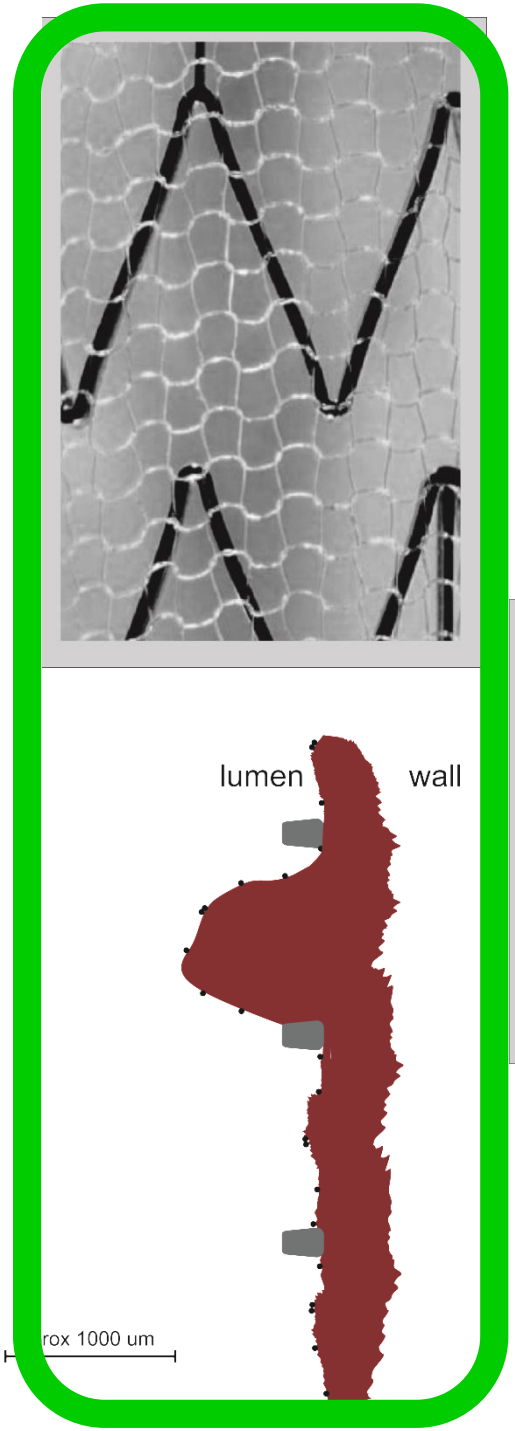
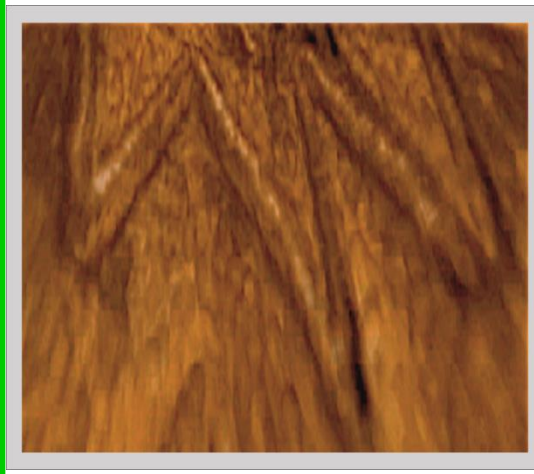
*EuroIntervention* 2017



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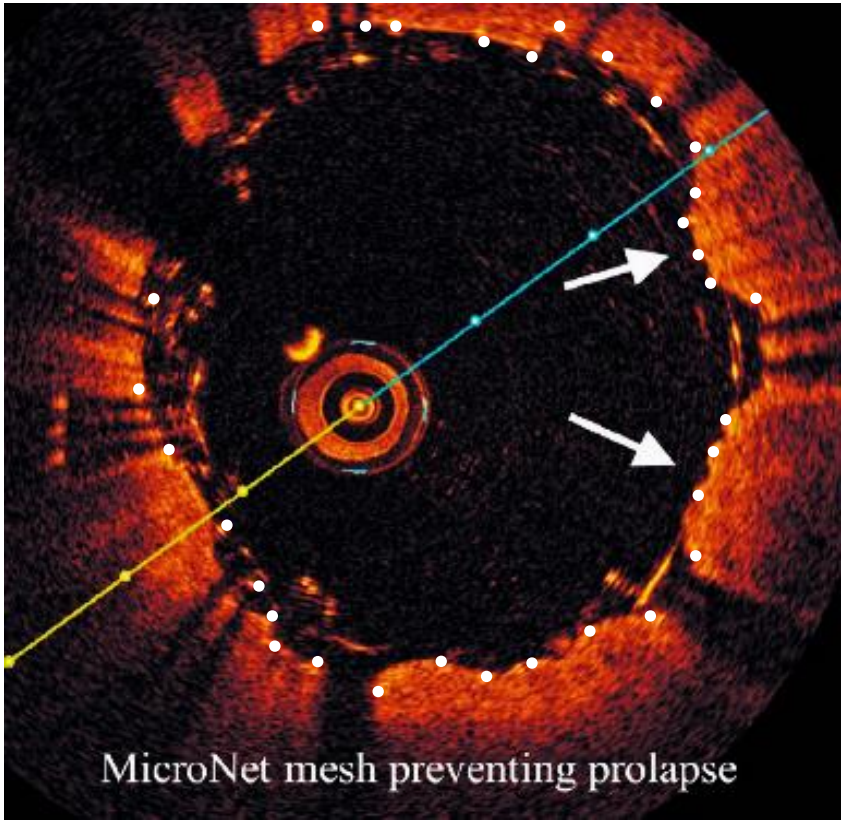
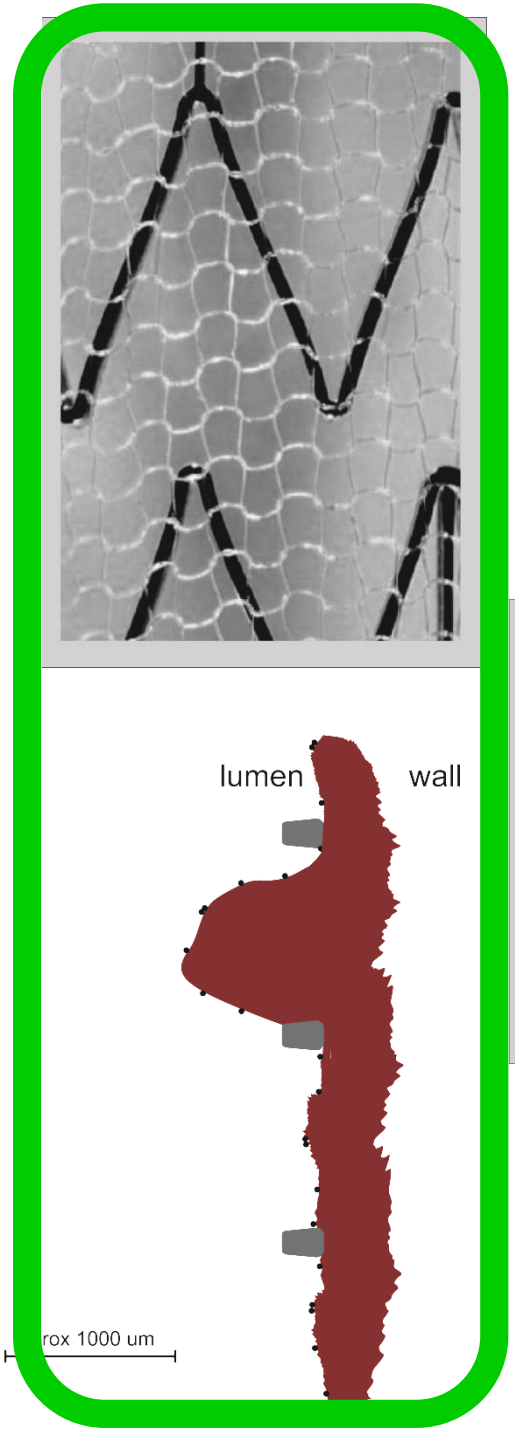
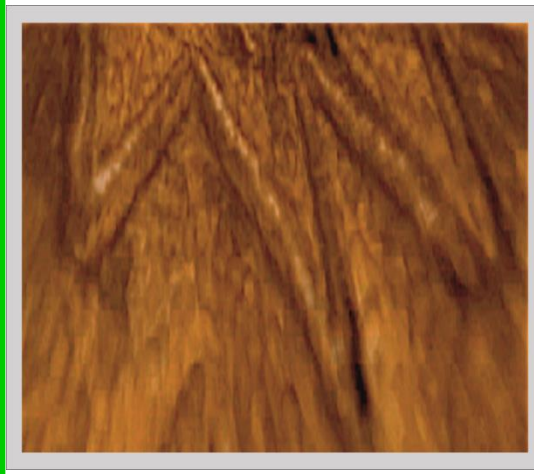



Tomyuki Umemoto et al.
*EuroIntervention* 2017



Musialek & Stabile
*EuroIntervention* 2017

JACC: CARDIOVASCULAR INTERVENTIONS
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# A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent

## The CGuard CARENET Trial (Carotid Embolic Protection Using MicroNet)

**CGuard™**

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

**Per-Protocol DW-MRI cerebral imaging at B/L, 24-48h after CAS, and at 30 days**

**ABSTRACT**

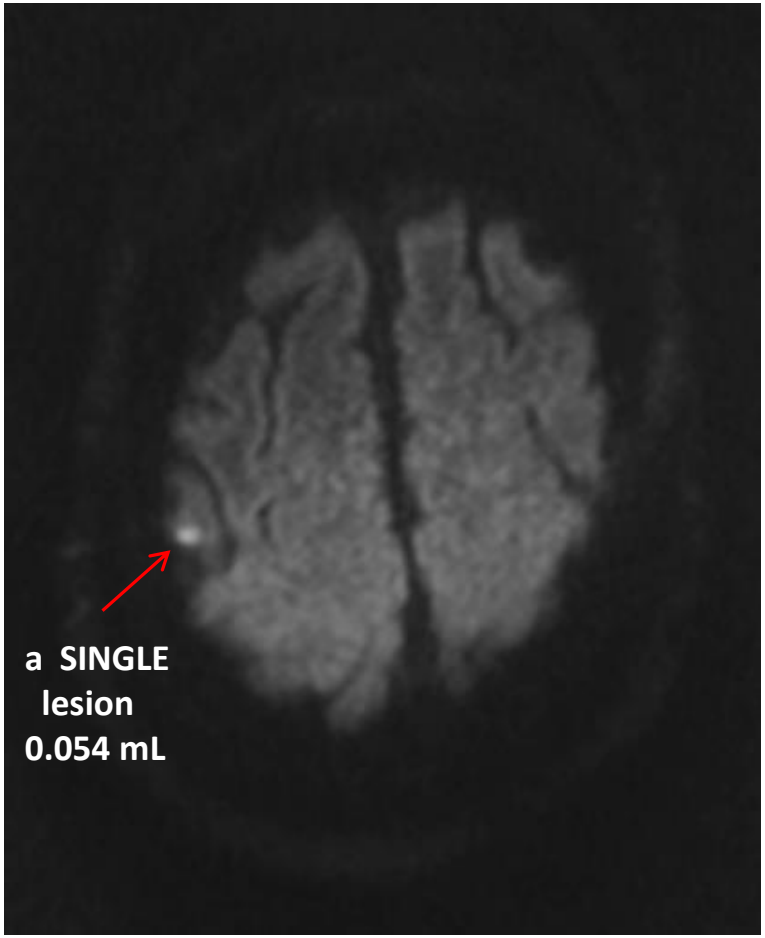
**OBJECTIVES** This study sought to evaluate the feasibility of the CGuard Carotid Embolic Protective Stent system—a novel thin strut nitinol stent combined with a polyethylene terephthalate mesh covering designed to prevent embolic events from the target lesion in the treatment of carotid artery lesions in consecutive patients suitable for carotid artery stenting.

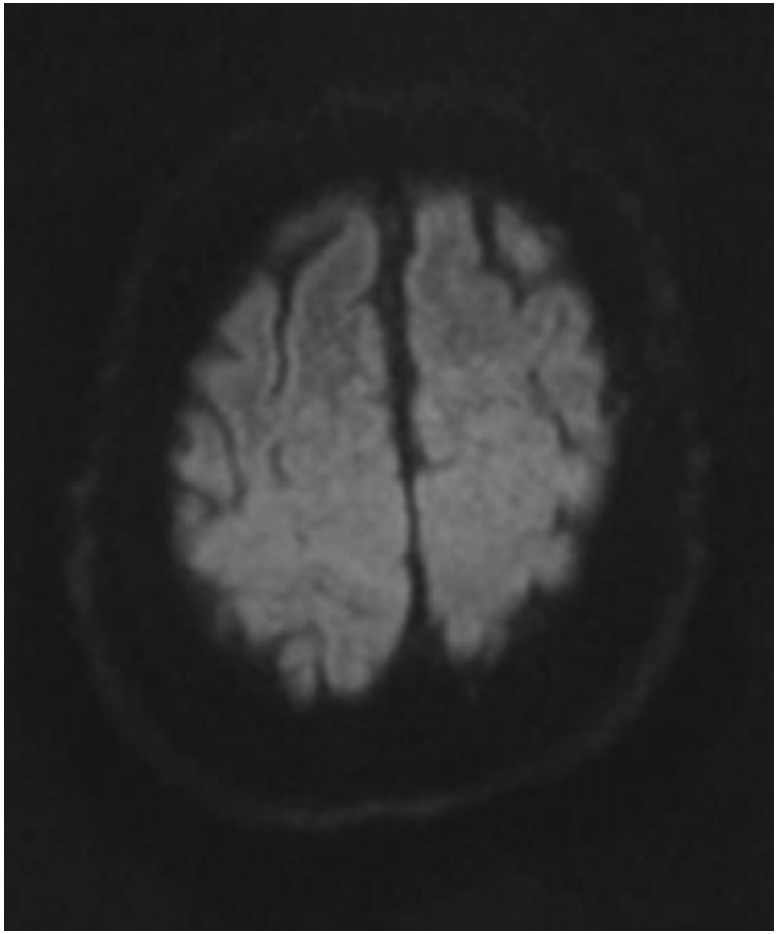
**BACKGROUND** The risk of cerebral embolization persists throughout the carotid artery stenting procedure and remains during the stent healing period.

**METHODS** A total of 30 consecutive patients (age 71.6 ± 7.6 years, 63% male) meeting the conventional carotid artery stenting inclusion criteria were enrolled in 4 centers in Germany and Poland.

P Musialek @ ICCA Stroke 2019

# The Power of DW-MRI…



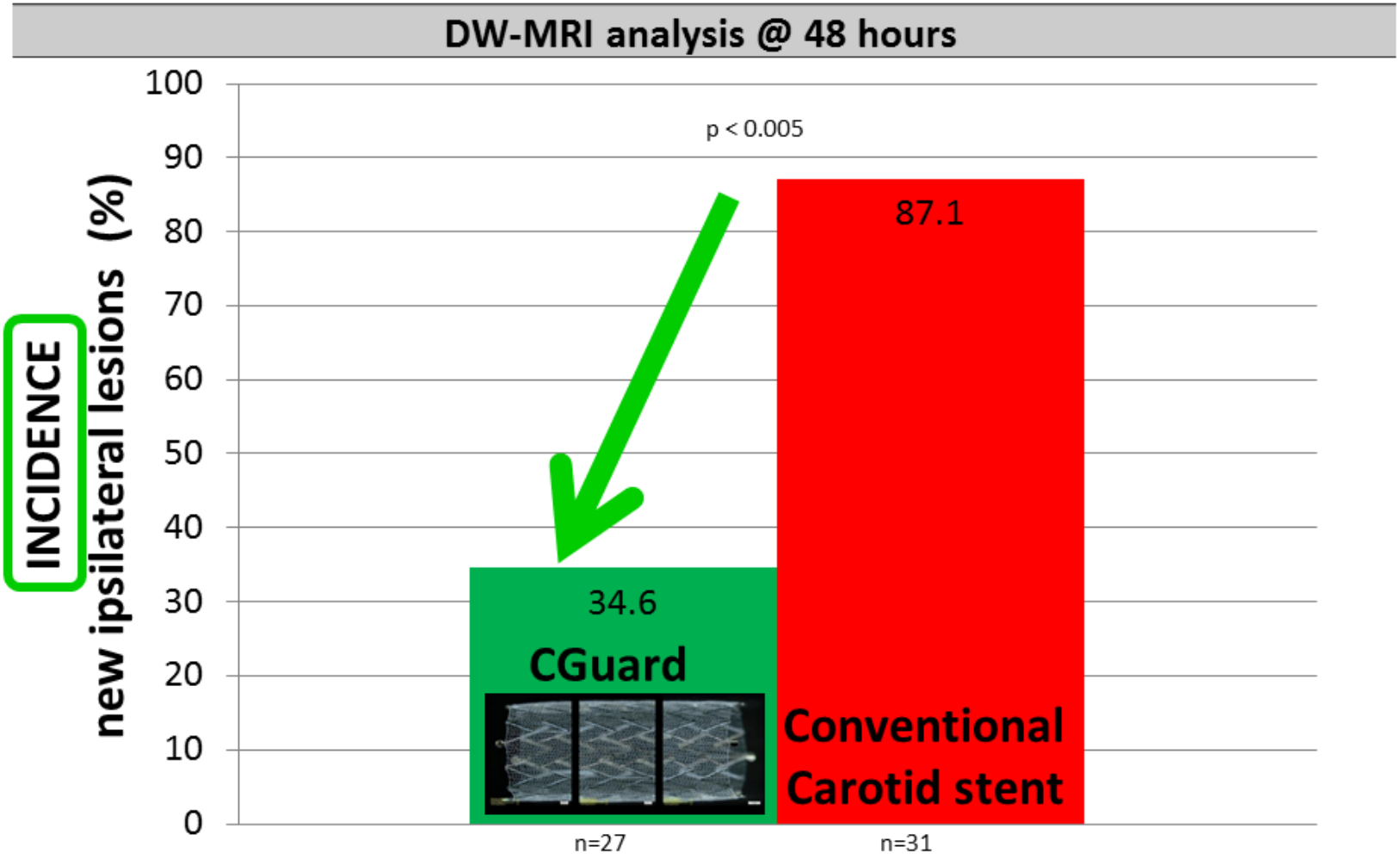
**24h after RICA-CAS**

**Complete Resolution on 30d follow-up**

**M. Urbanczyk, RP. Banys – Dept. Radiology JP2 Hospital, Krakow**

# Filter-protected CAS procedures

# CARENET vs PROFI: DW-MRI analysis

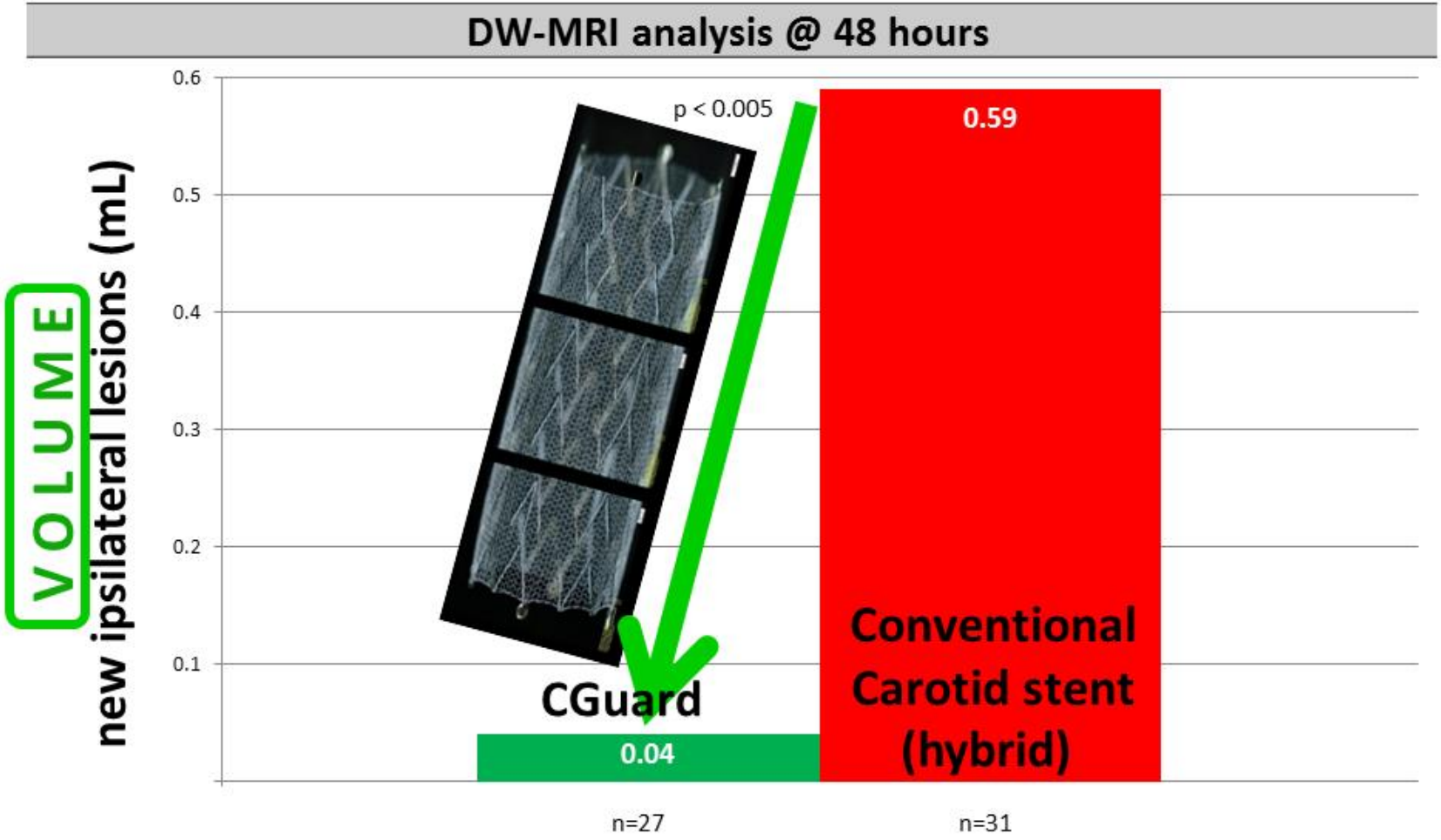



* see patient fluxogram
Bijuklic et al. *JACC*, 2012;59

J. Schofer, P. Musialek et al. ***JACC** Intv* 2015;8:1229-34
Bijuklic et al. (manuscript in preparation)

# Filter-protected CAS procedures

# CARENET vs PROFI: DW-MRI analysis

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Bijuklic et al. *JACC*, 2012;59

J. Schofer, P. Musialek et al. ***JACC** Intv* 2015;8:1229-34
Bijuklic et al. (manuscript in preparation)

# CARENET 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)**

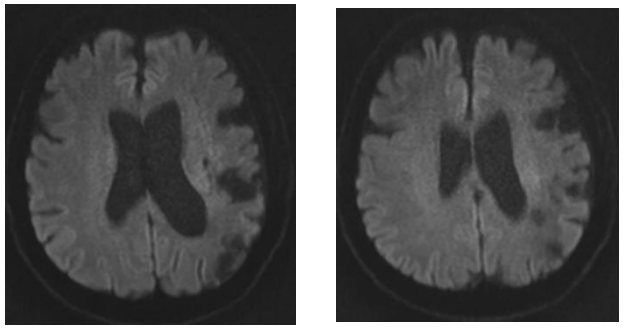
J. Schofer, P. Musialek et al. ***JACC** Intv* 2015;8:1229-34

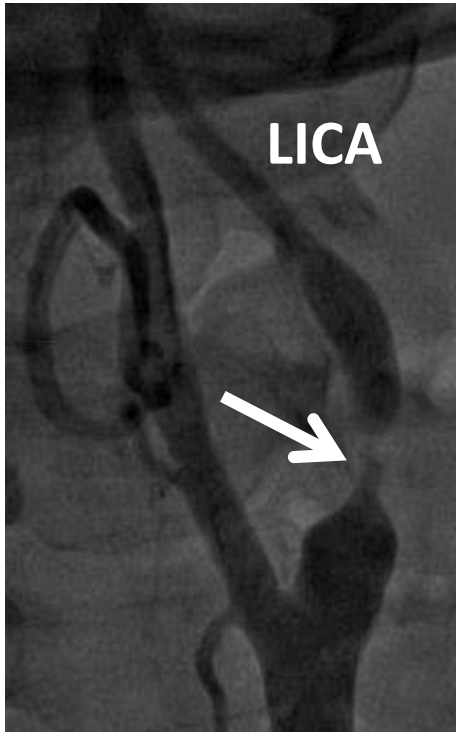
## => near-elimination of post-procedural embolism!

T.W., man 69 yo

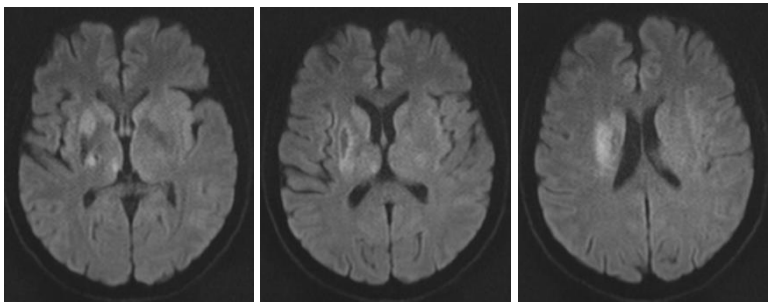
critical LICA stenosis

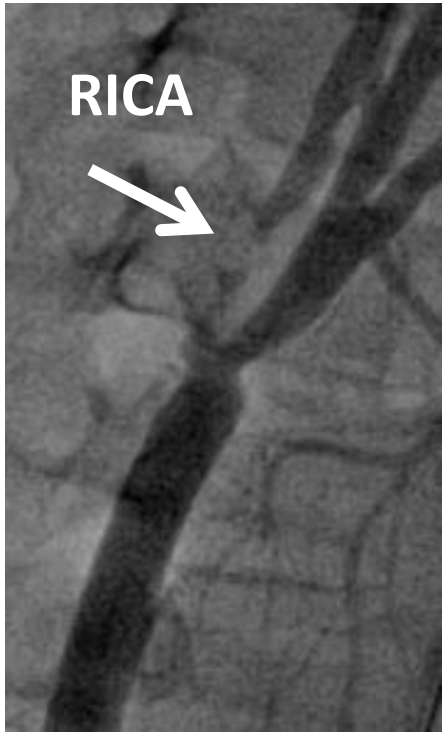
L haemisph stroke 5mo






E.W., woman, 58 y,
TWO recent ( 20d and 5d )
R haemispheric
minor strokes despite OMT !





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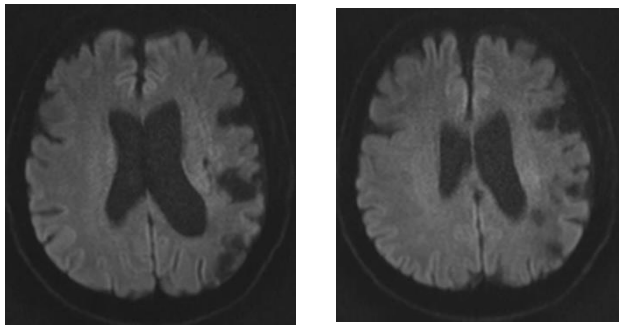

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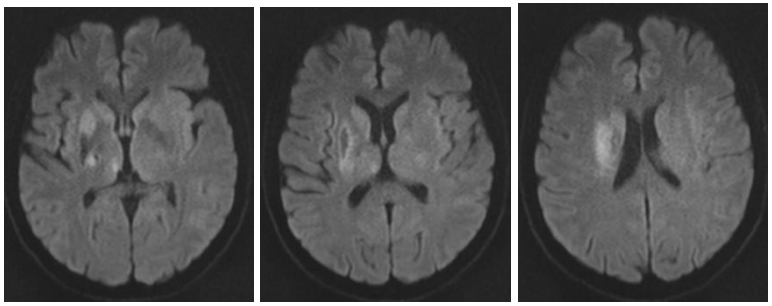
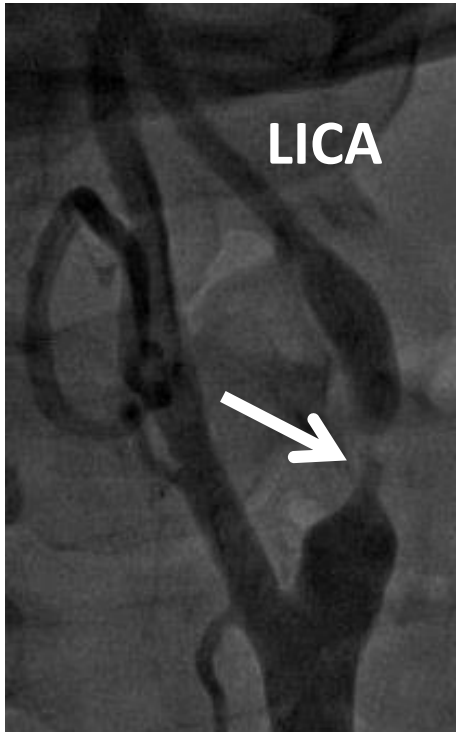
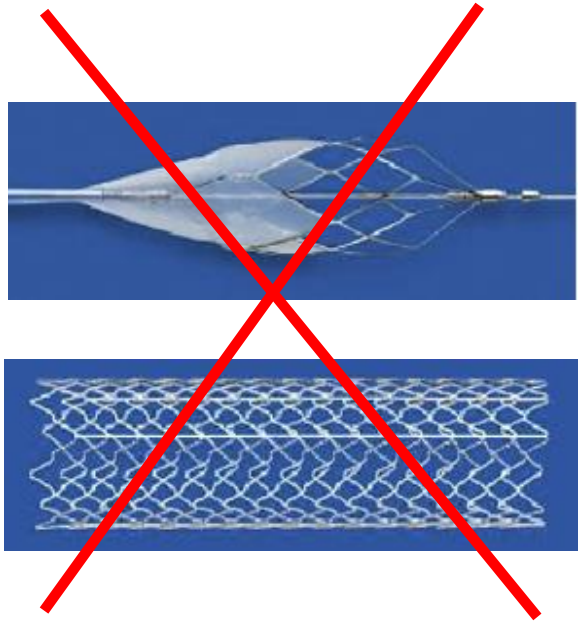
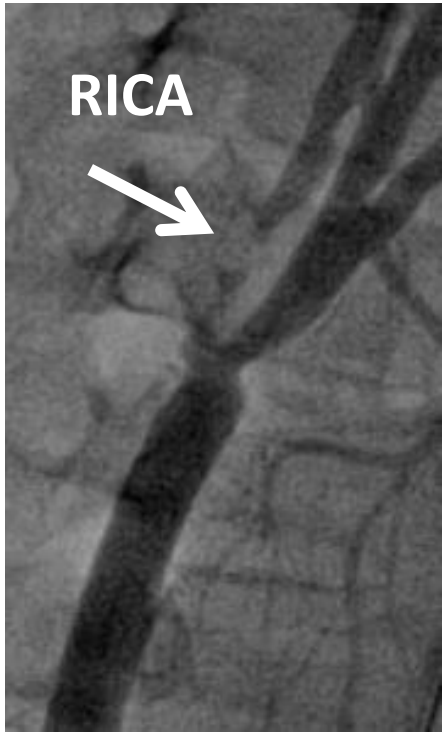
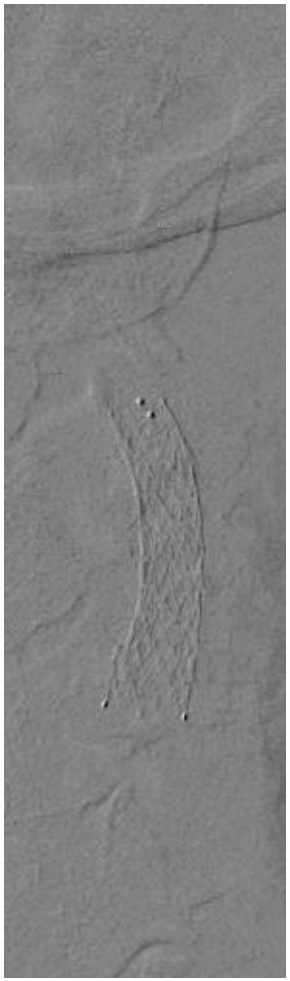


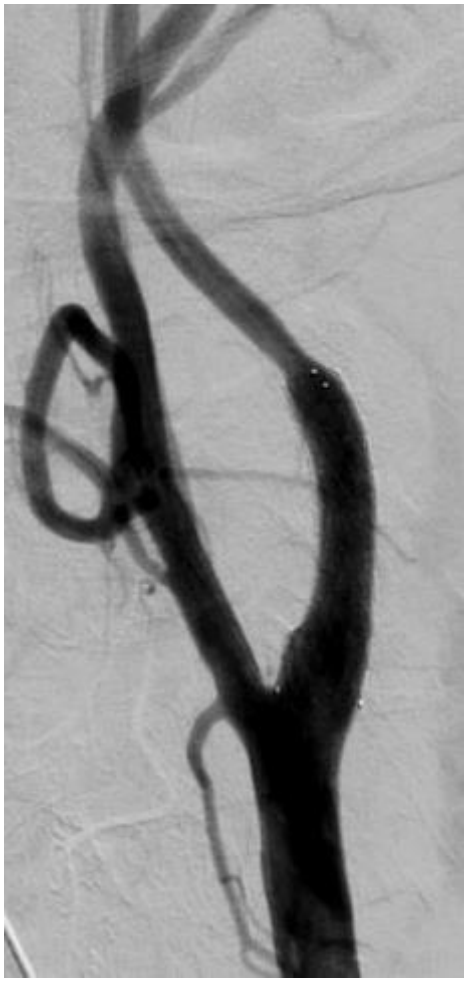


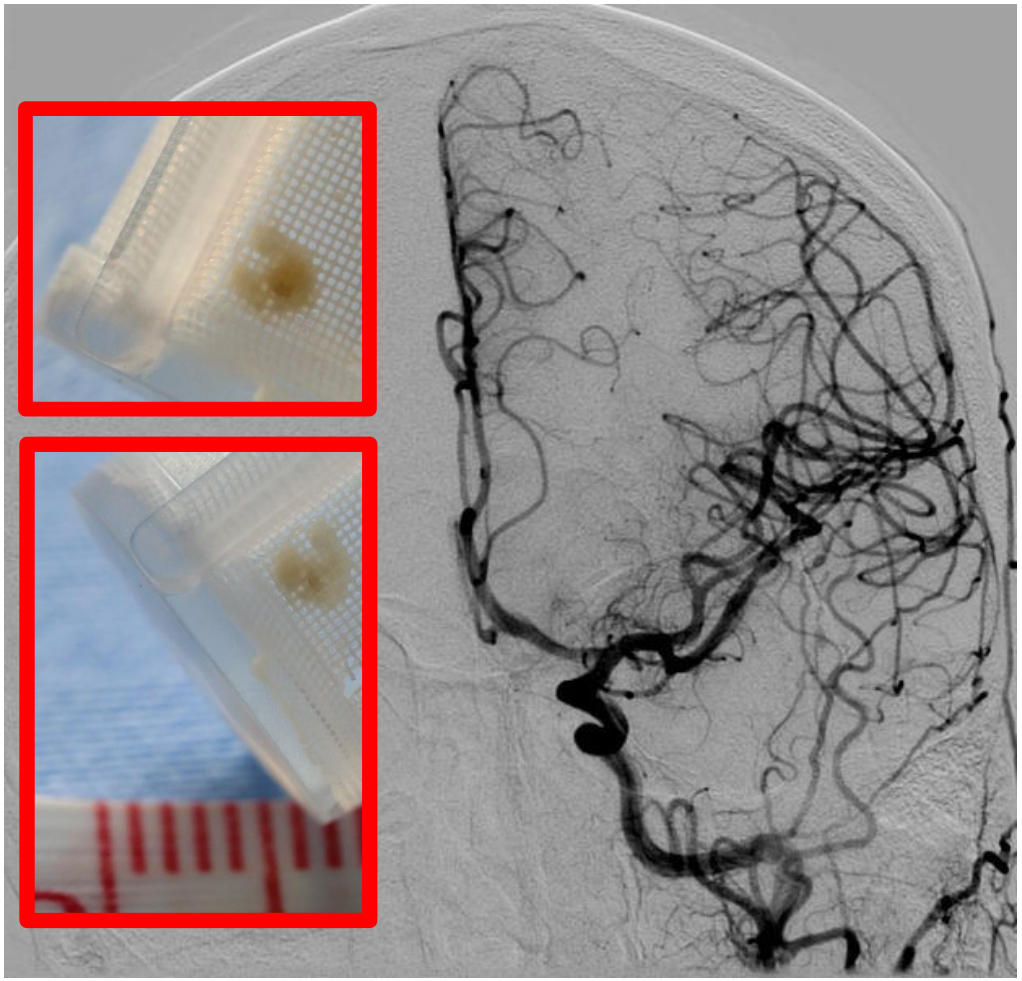





# TW, man 69 yo
# critical LICA stenosis, post-stroke





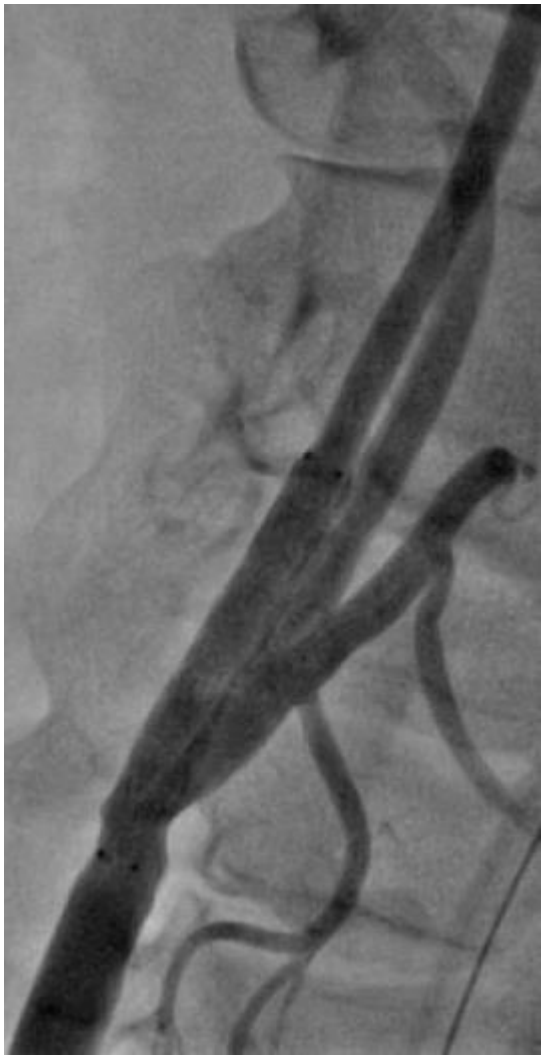


**CGuard** **7.0x30mm** **full endovascular reconstruction**

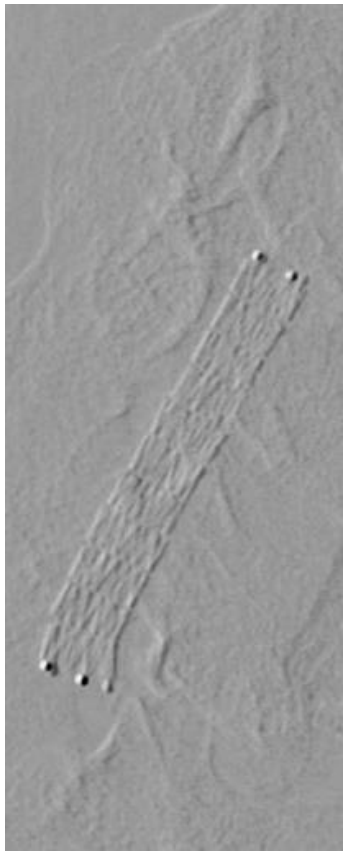
**direct carotid access CAS under**
**En Route (SilkRoad Medical) Flow Reversal**

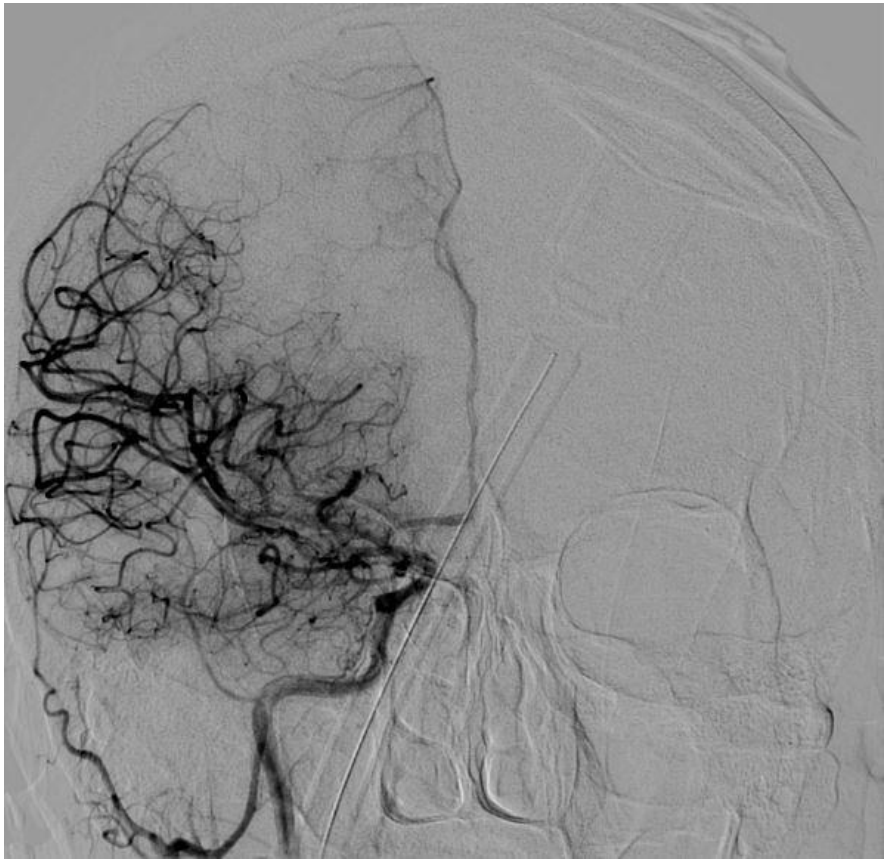
WE, woman, 58 y, **R** haemispheric minor stroke x 2

**TCAR** plus **CGuard**



## Final Result





**CGuard 7.0x30 mm** **full endovascular reconstruction**

**plus NO new lesions on DW-MRI !**

P Musialek @ ICCA Stroke 2019

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



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

*1. Jagiellonian University Department of Cardiac & Vascular Diseases, John Paul II Hospital, Krakow, Poland; 2. Department of Vascular Surgery, John Paul II Hospital, Krakow, Poland; 3. Neurology Outpatient Department, John Paul II Hospital, Krakow, Poland; 4. Department of Radiology, John Paul II Hospital, Krakow, Poland; 5. Jagiellonian University Department of Interventional Cardiology, John Paul II Hospital, Krakow, Poland; 6. KCRI, Krakow, Poland*

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)



P. Musialek, A. Mazurek et al. *EuroIntervention* 2016;12:e658-70 (PARADIGM design and 30-day outcome data)

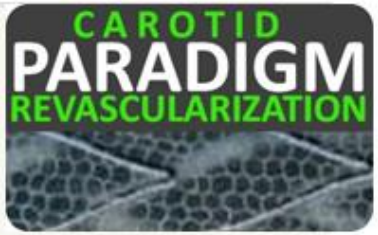
**P**rospective evaluation of **A**ll-comer pe**R**cutaneous c**A**roti**D** revascularization in sympto-matic and **I**ncreased-risk asymptomatic carotid artery stenosis using the C**G**uard™ **M**icronet-covered embolic prevention stent system

# The PARADIGM Study


euro PCR
2016 LATE BREAKING TRIALS

# 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 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


## 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.

P. Musialek, A. Mazurek et al. EuroIntervention 2016;12:e658-70
(PARADIGM design and 30-day outcome data)

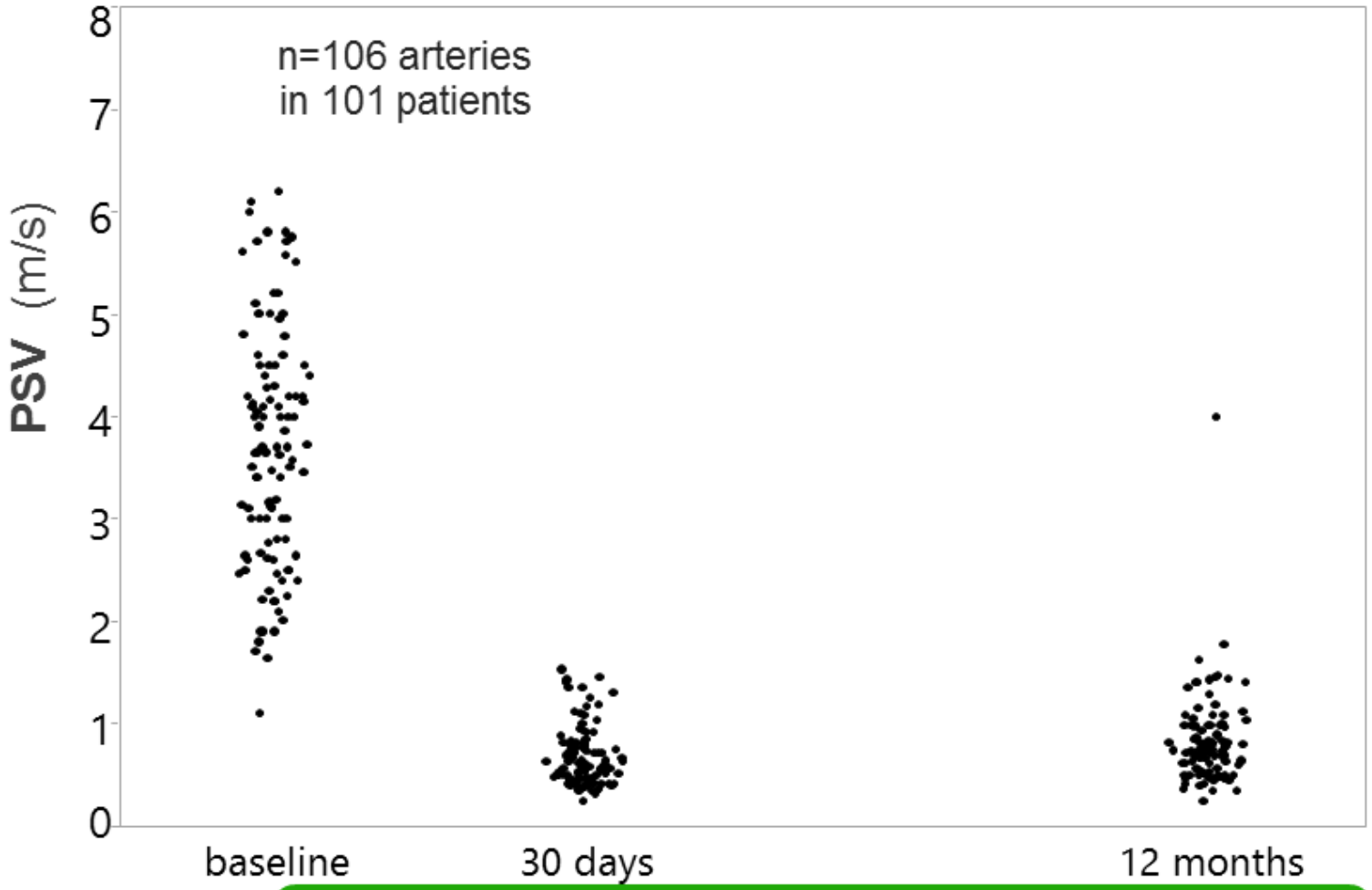
# CGuard™ EPS Carotid **PARADIGM** Study

## 12mo Duplex Ultrasound Data

CAROTID PARADIGM REVASCULARIZATION

12month data

**ECA* patency**



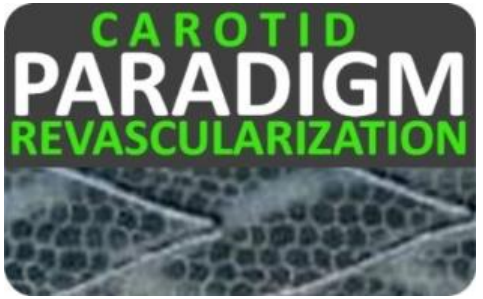

**ECA**

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

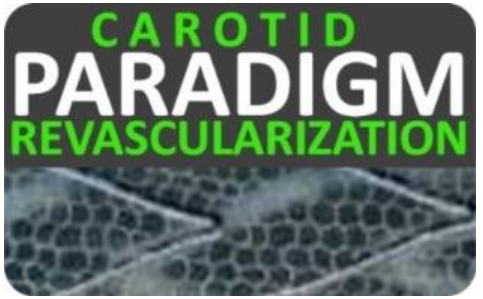
## continues as an ALL-Comer Study




- 251 patients / 263 arteries
  *NeuroVascular Team decision-making on revascularization*
- Age 51-87 years, 57.1% symptomatic
- Crossed the trial first follow-up window (30d)
- 100% CGuardEPS use, Proximal/distal EPD ≈ 50% : 50%
- Angiographic diameter stenosis was reduced from 83±9% to only 6.7±5% (p<0.001, 'CEA-like' effect of CAS)

# PARADIGM – Extend

251 patients / 263 arteries




- *Peri-procedural outcome*

  **0 death/major stroke** – **0%**
  **1 minor stroke – 0.4%**
  **1 MI** (type2) **– 0.4%**

- *By 30 days*

  **1 haemorrhagic transformation** of prior ischaemic cerebral infarct, leading to **death – 0.4%**

# PARADIGM – Extend

| *1-12 mo* | *12-24 mo* | *24-36 mo* |
|---|---|---|
| n=251 | n=185 | n=93 |

# PARADIGM – Extend

| | *1-12 mo* | *12-24 mo* | *24-36 mo* |
|---|---|---|---|
| | n=251 | n=185 | n=93 |
| **ipsilateral stroke** | **0** | **0** | **0** |

# PARADIGM – Extend

| | *1-12 mo* | *12-24 mo* | *24-36 mo* |
|---|---|---|---|
| | n=251 | n=185 | n=93 |
| **ipsilateral stroke** | **0** | **0** | **0** |
| **any stroke** | **0** | **1** (cerebellal) | **1** (brain stem) |

# PARADIGM – Extend

| | *1-12 mo* | *12-24 mo* | *24-36 mo* |
|---|---|---|---|
| | n=251 | n=185 | n=93 |
| **ipsilateral stroke** | **0** | **0** | **0** |
| **any stroke** | **0** | **1** (cerebellal) | **1** (brain stem) |
| **stroke-related death** | **0** | **0** | **0** |

# PARADIGM – Extend

| | *1-12 mo* | *12-24 mo* | *24-36 mo* |
|---|---|---|---|
| | n=251 | n=185 | n=93 |
| **ipsilateral stroke** | **0** | **0** | **0** |
| **any stroke** | **0** | **1** (cerebellal) | **1** (brain stem) |
| **stroke-related death** | **0** | **0** | **0** |
| **MI or other non-cerebral VA** | **0** | **3** | **2** |


# PARADIGM – Extend

| | *1-12 mo* | *12-24 mo* | *24-36 mo* |
|---|---|---|---|
| | n=251 | n=185 | n=93 |
| **ipsilateral stroke** | **0** | **0** | **0** |
| **any stroke** | **0** | **1** (cerebellal) | **1** (brain stem) |
| **stroke-related death** | **0** | **0** | **0** |
| **MI or other non-cerebral VA** | **0** | **3** | **2** |
| **any death** | **6** (CHF-2, Ca-2, PE-1, urosepsis -1) | **5** (CHF-2, Ca-2, MI-1) | **2** (Ca-1, MI-1) |

# PARADIGM – Extend

| | *1-12 mo* | *12-24 mo* | *24-36 mo* |
|---|---|---|---|
| | n=251 | n=185 | n=93 |
| **ipsilateral stroke** | **0** | **0** | **0** |
| **any stroke** | **0** | **1** (cerebellal) | **1** (brain stem) |
| **stroke-related death** | **0** | **0** | **0** |
| **MI or other non-cerebral VA** | **0** | **3** | **2** |
| **any death** | **6** (CHF-2, Ca-2, PE-1, urosepsis -1) | **5** (CHF-2, Ca-2, MI-1) | **2** (Ca-1, MI-1) |
| **in-stent velocities** | PSV **0.82**±0.48 m/s<br>EDV **0.22**±0.13 m/s | PSV **0.73**±0.31 m/s<br>EDV **0.19**±0.09 m/s | PSV **0.75**±0.27 m/s<br>EDV **0.18**±0.06 m/s |

P Musialek @ ICCA Stroke 2019

# PARADIGM – Extend

## By 36 months

- Normal healing
- No ISR signal

| | 1-12 mo | 12-24 mo | 24-36 mo |
|---|---|---|---|
| | n=251 | n=185 | n=93 |
| ipsilateral stroke | 0 | 0 | 0 |
| any stroke | 0 | 1 (cerebellal) | 1 (brain stem) |
| stroke-related death | 0 | 0 | 0 |
| MI or other non-cerebral VA | 0 | 3 | 2 |
| any death | 6 (CHF-2, Ca-2, PE-1, urosepsis -1) | 5 (CHF-2, Ca-2, MI-1) | 2 (Ca-1, MI-1) |
| in-stent velocities | PSV **0.82**±0.48 m/s<br>EDV **0.22**±0.13 m/s | PSV **0.73**±0.31 m/s<br>EDV **0.19**±0.09 m/s | PSV **0.75**±0.27 m/s<br>EDV **0.18**±0.06 m/s |

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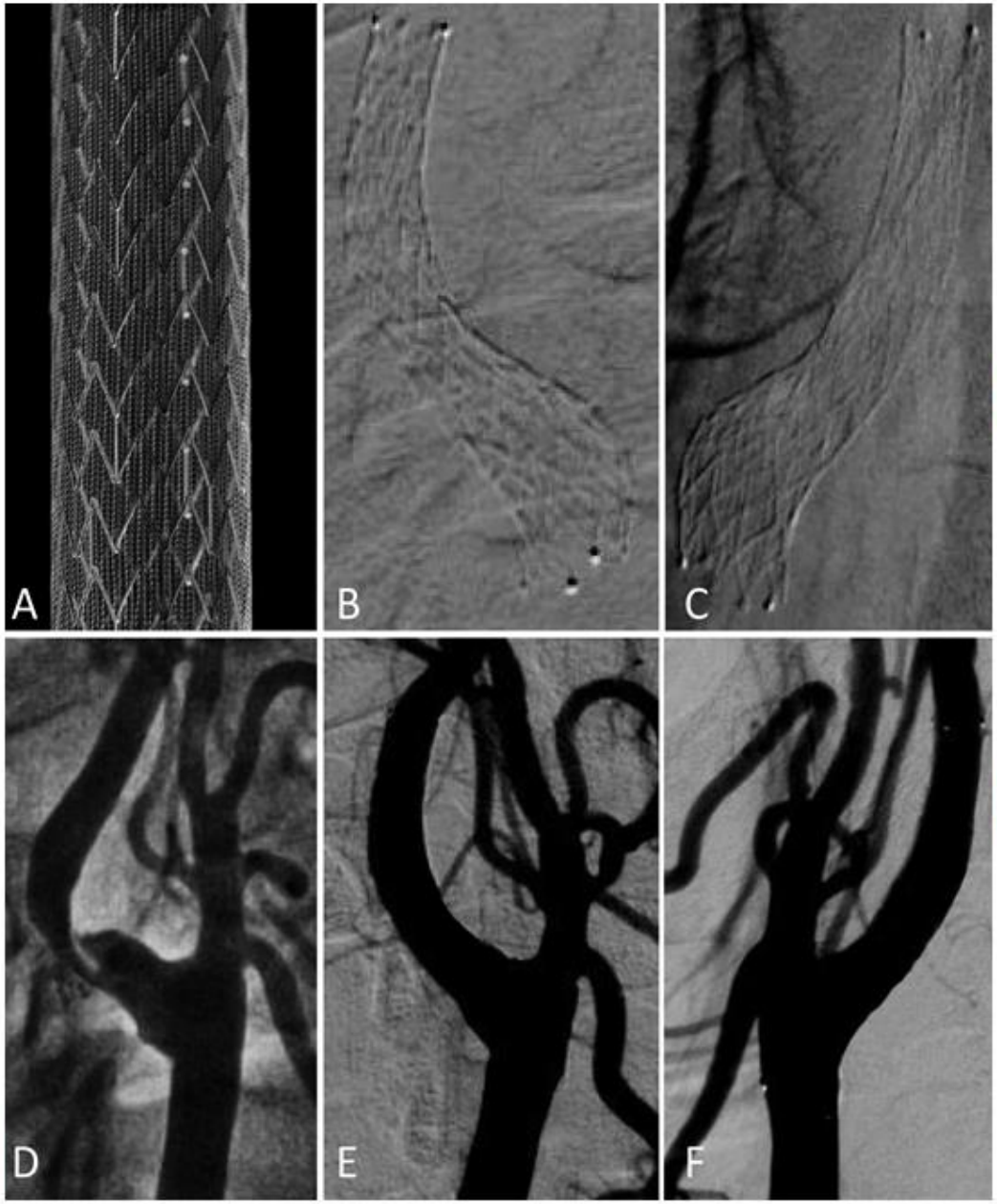
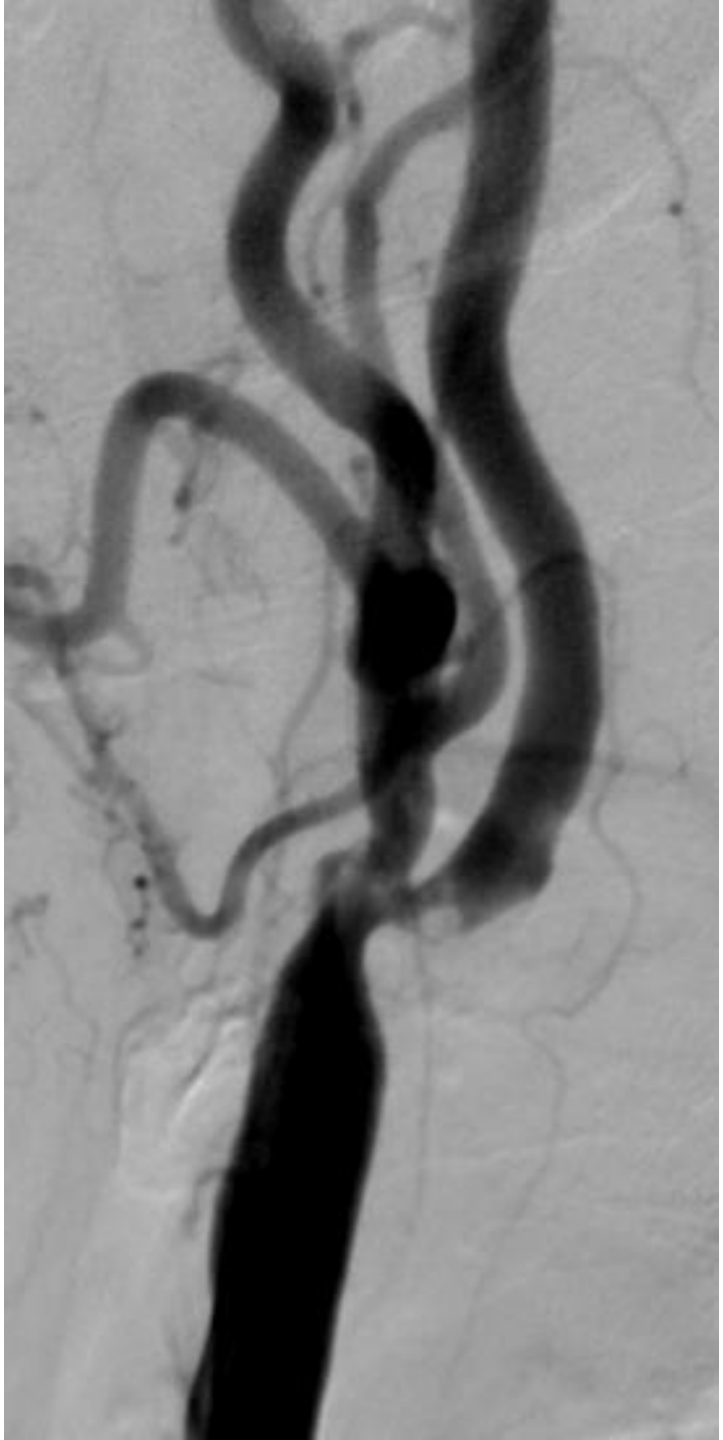



CAROTID PARADIGM REVASCULARIZATION

systematic

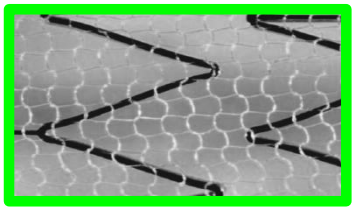
# CEA-like effect of CAS

*EuroIntervention* 2016;12:e658-70




# The Outcome Difference

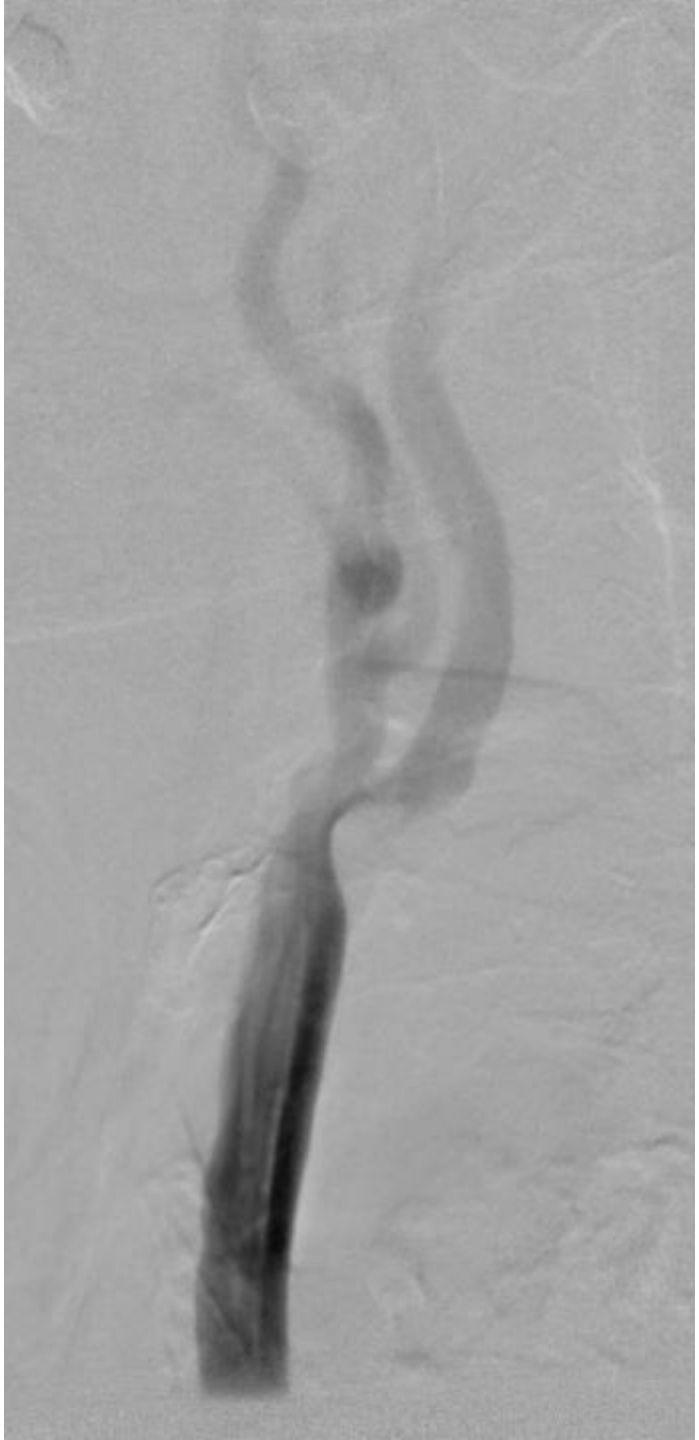
## Between the MicroNet-Covered Stent

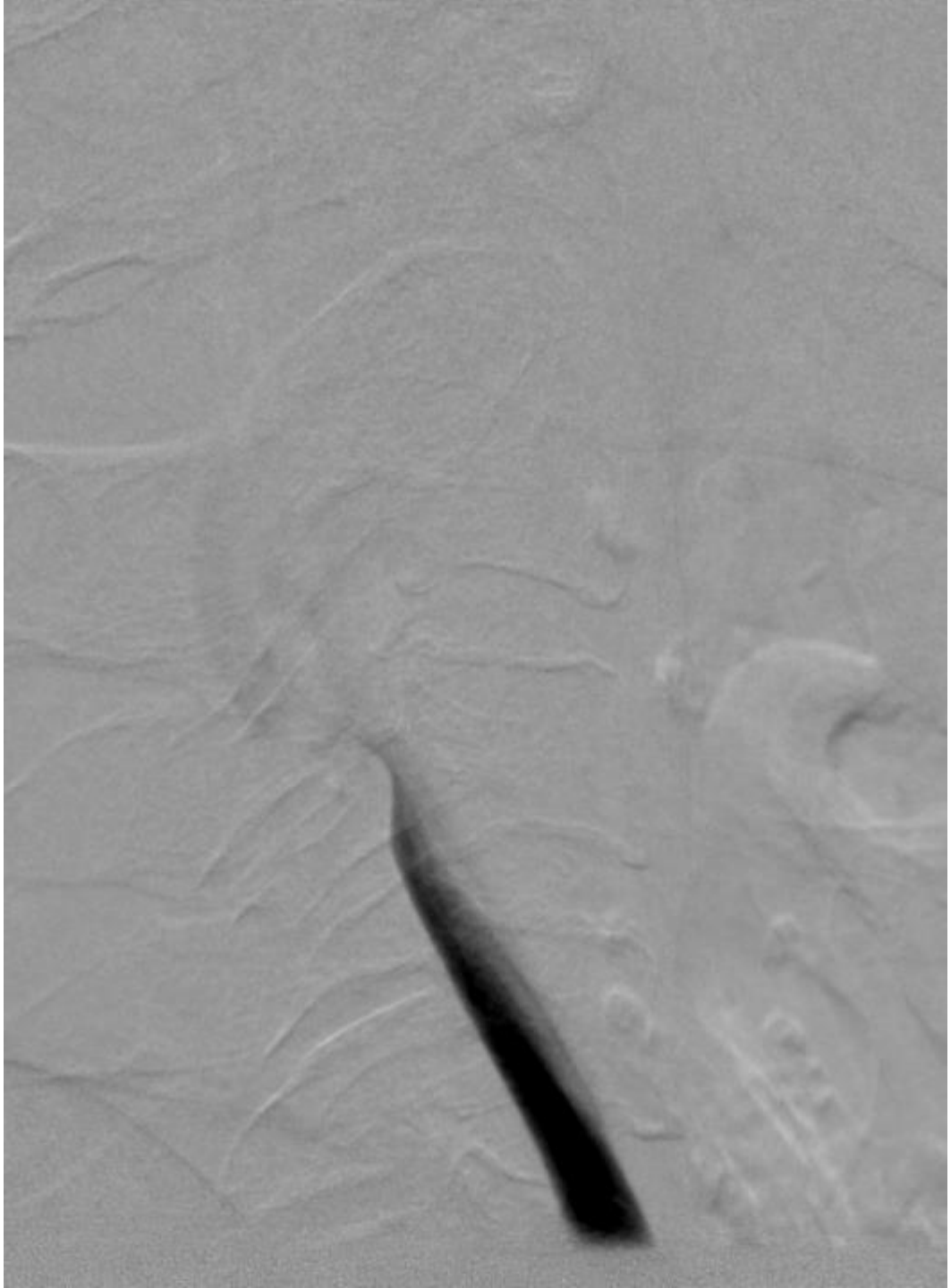


## vs.

## Conventional Carotid Stent(s)

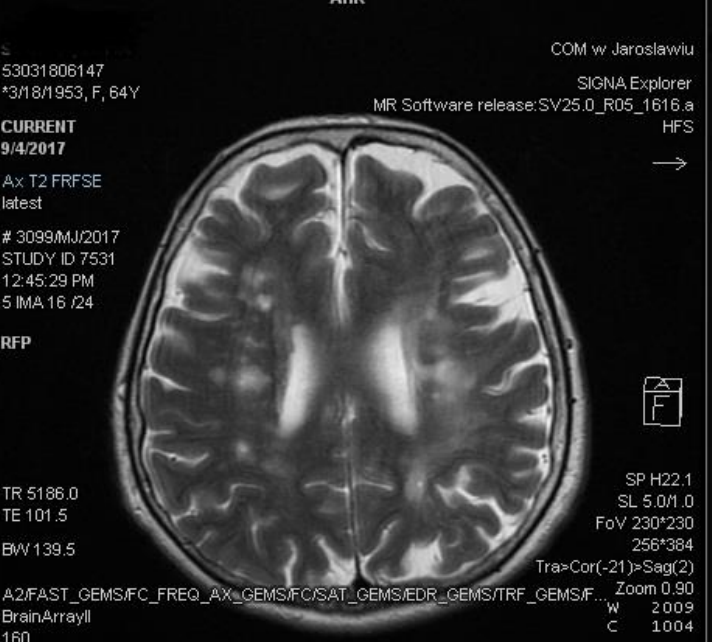
# driven by HIGH-RISK Plaques and Patients



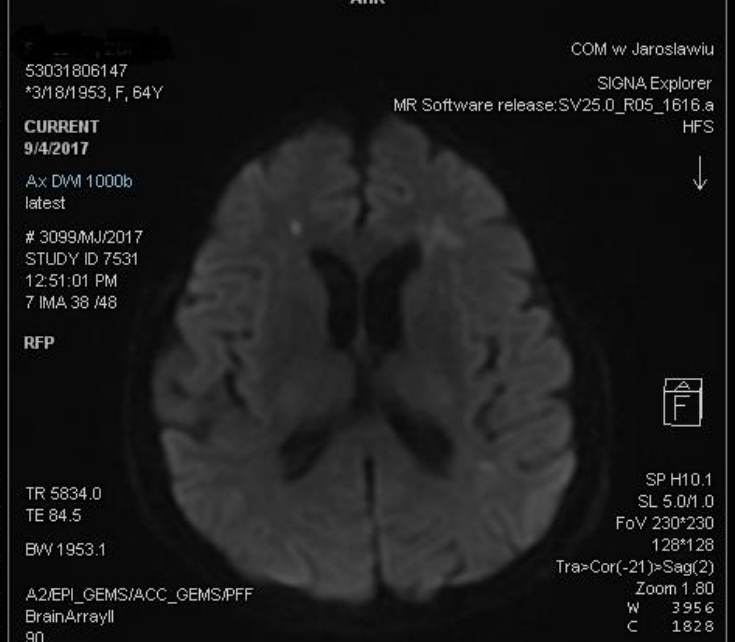


( LICA chronic occlusion )

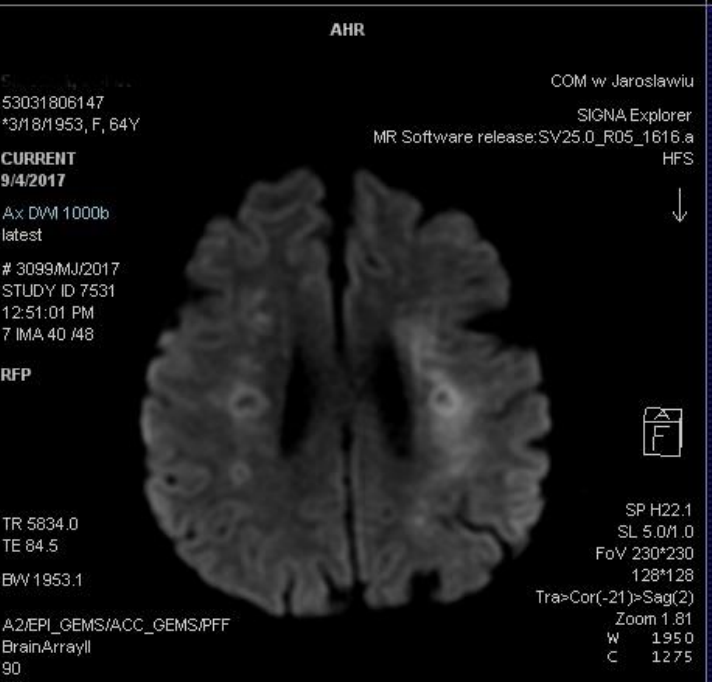
# B/L MRI scan



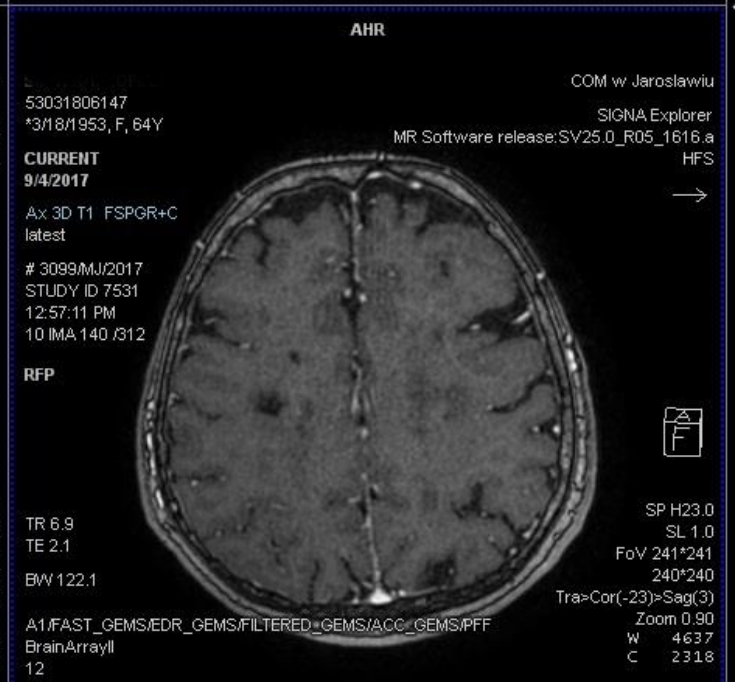

chronic ischemic lesions in both hemispheres




**new** DWI lesion in **R** hemisphere



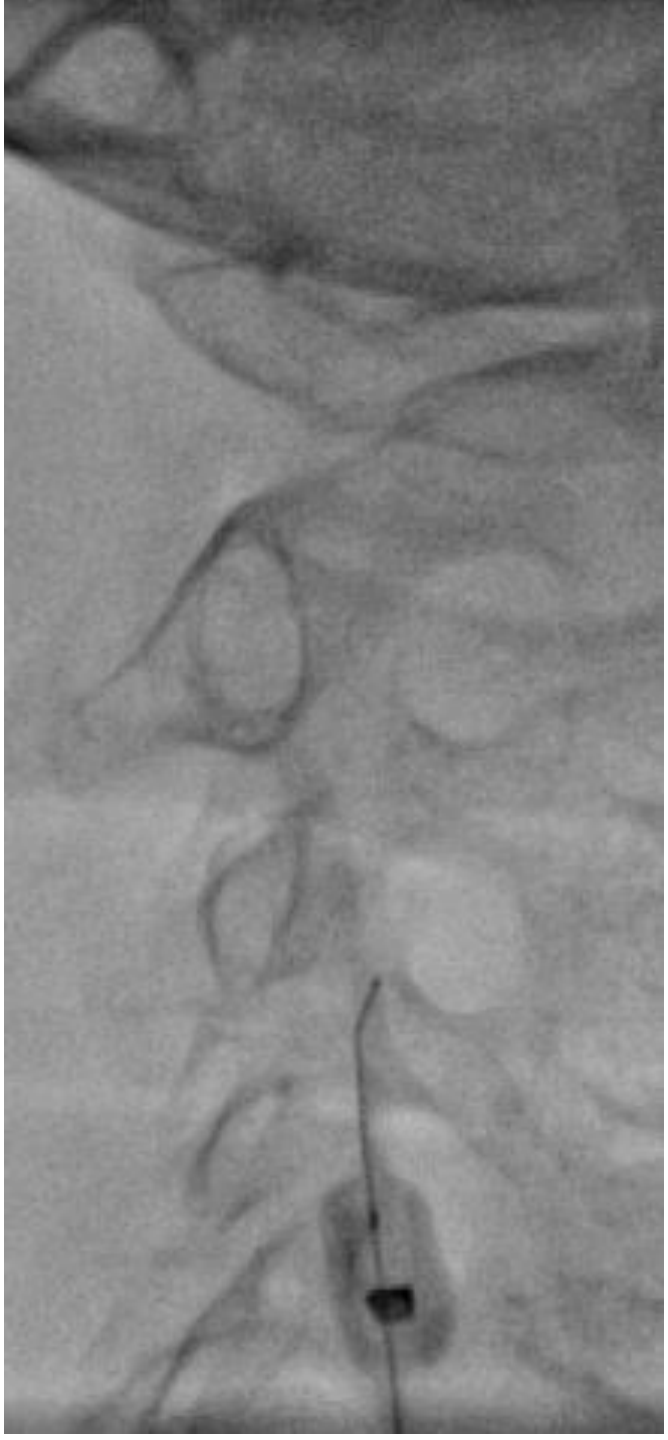

" fresh" ischemia surrounding old lesions

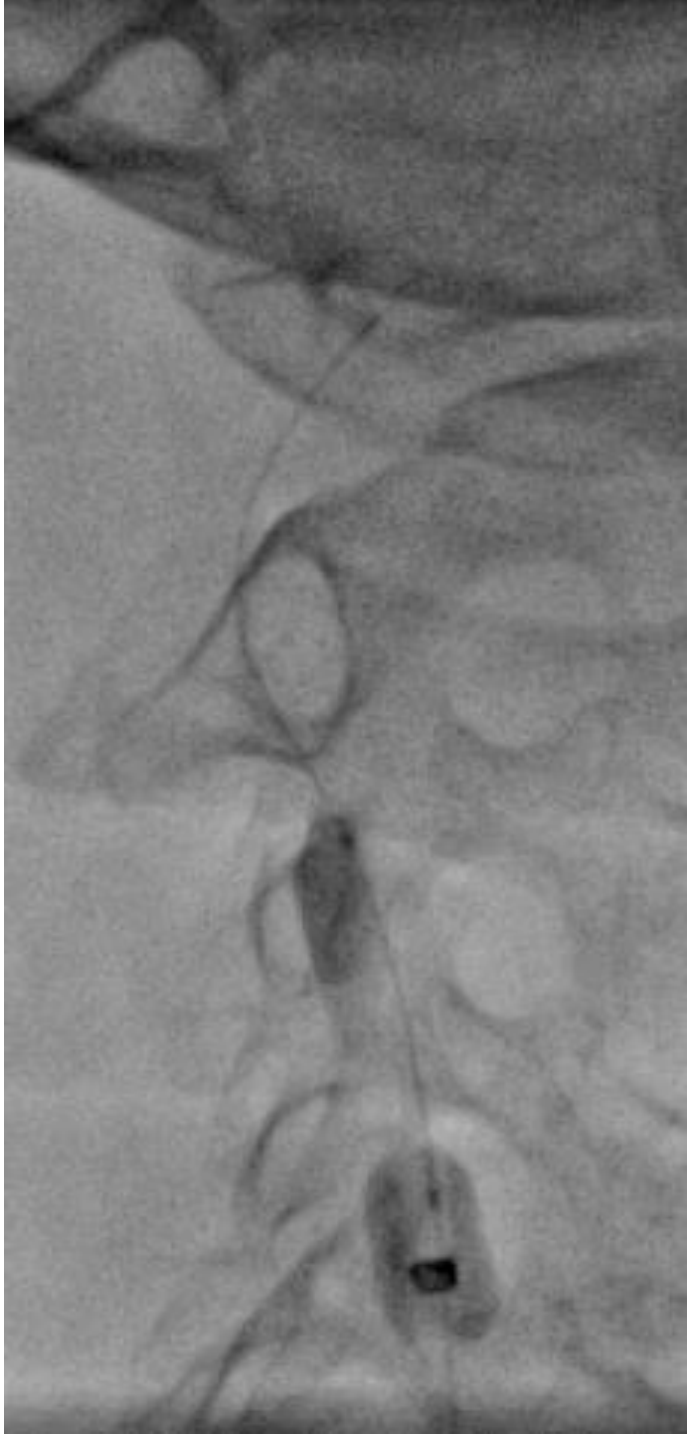


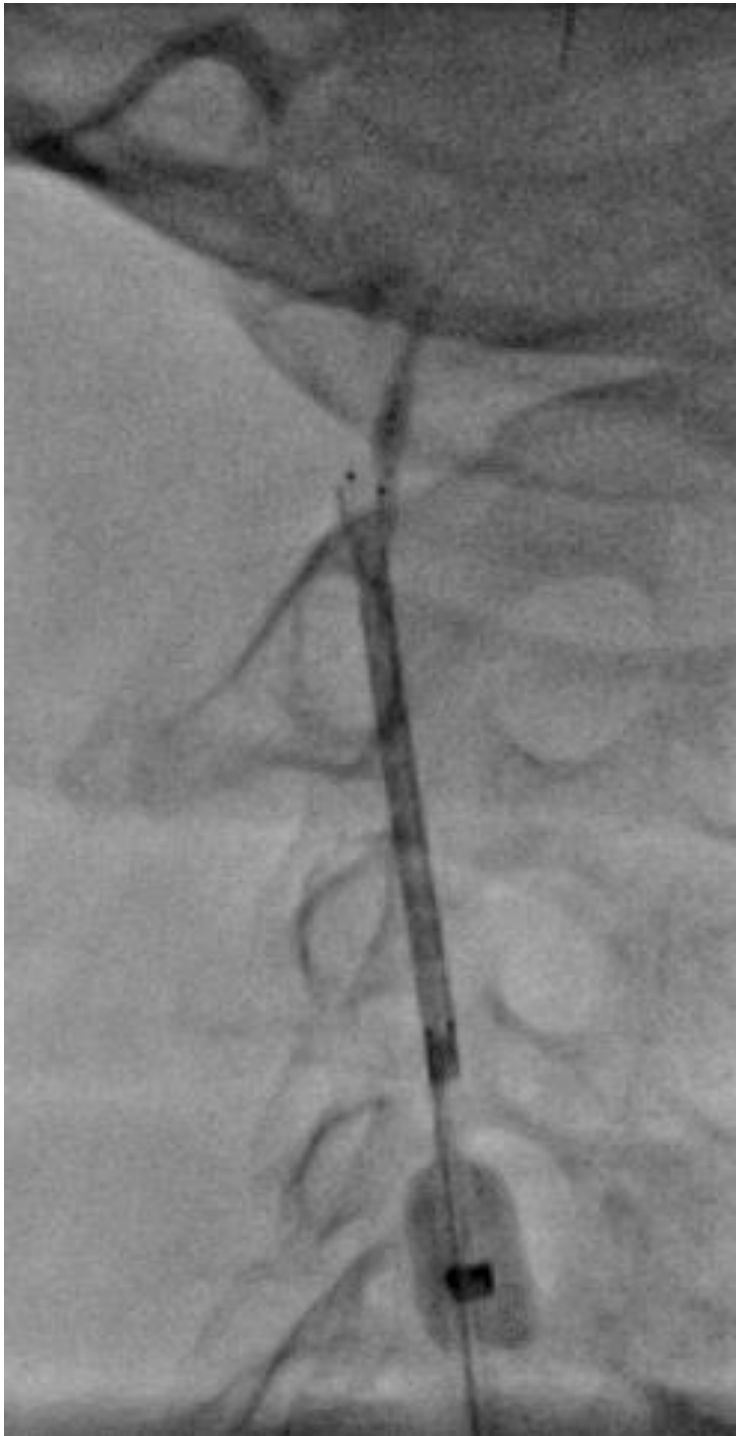

chronic ischemic lesion in R hemisphere

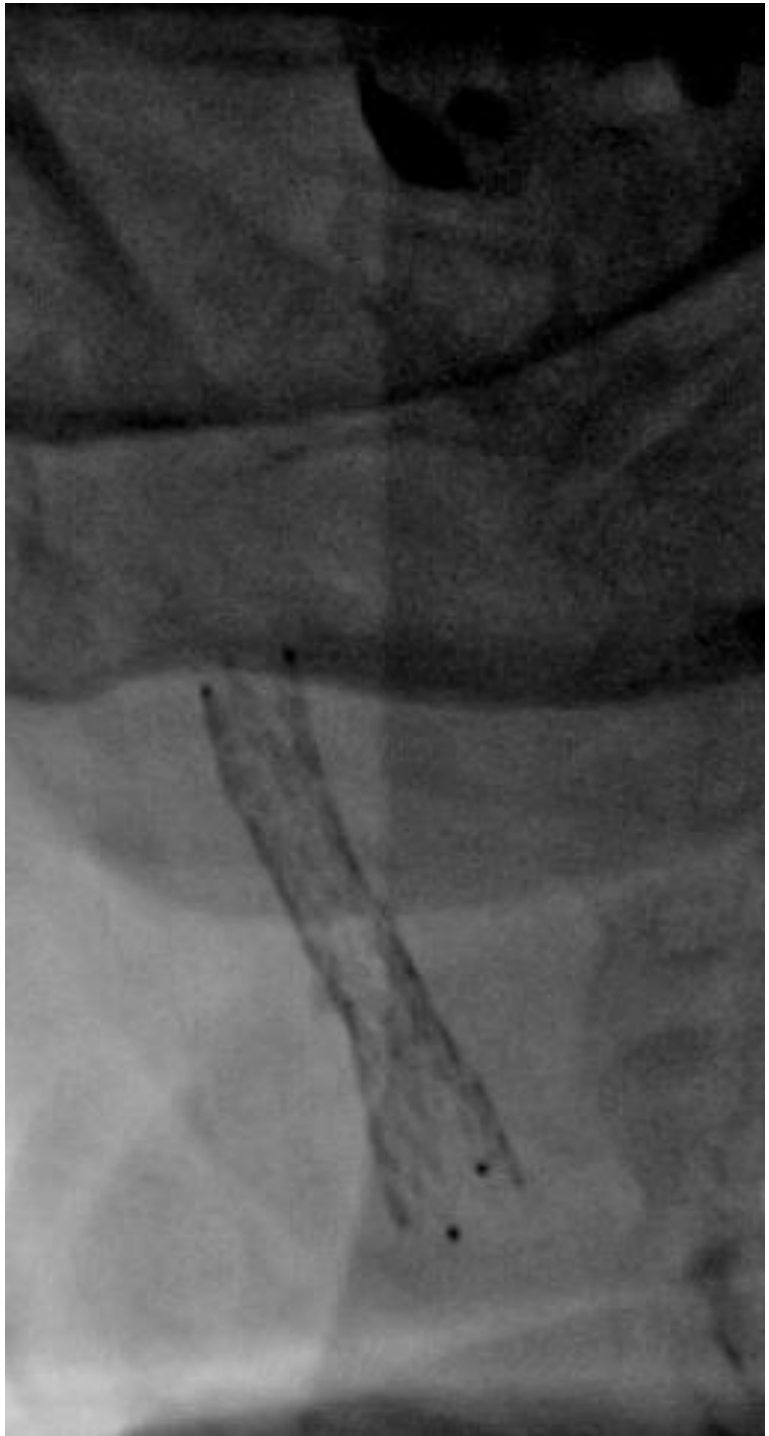
**RICA high-grade highly-thromboltic stenosis**

**LICA chronic occlusion**



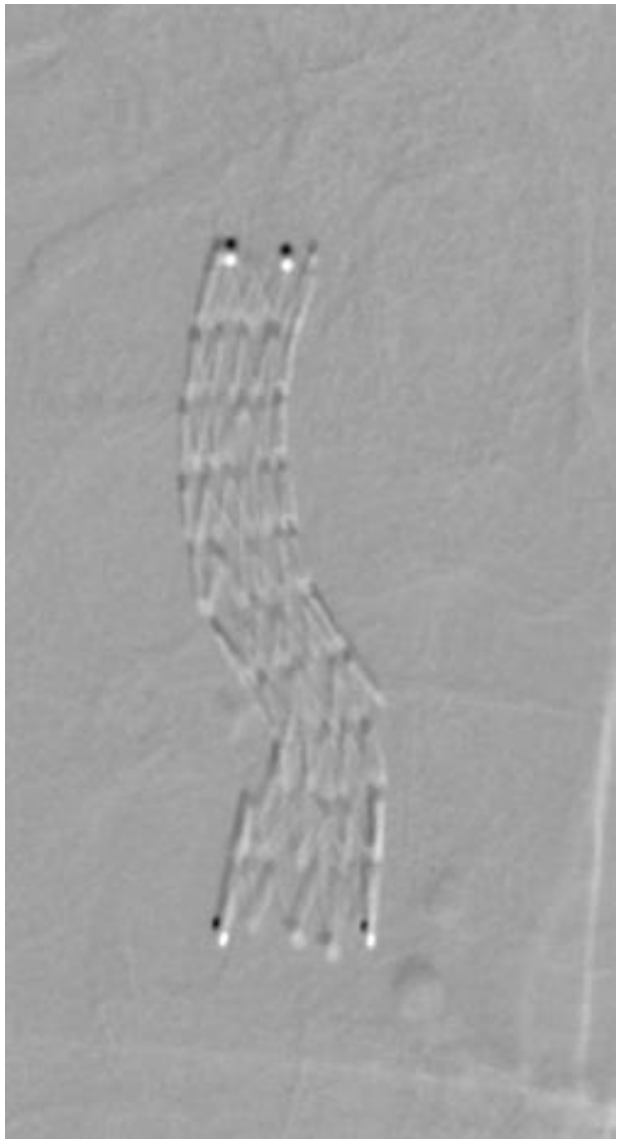


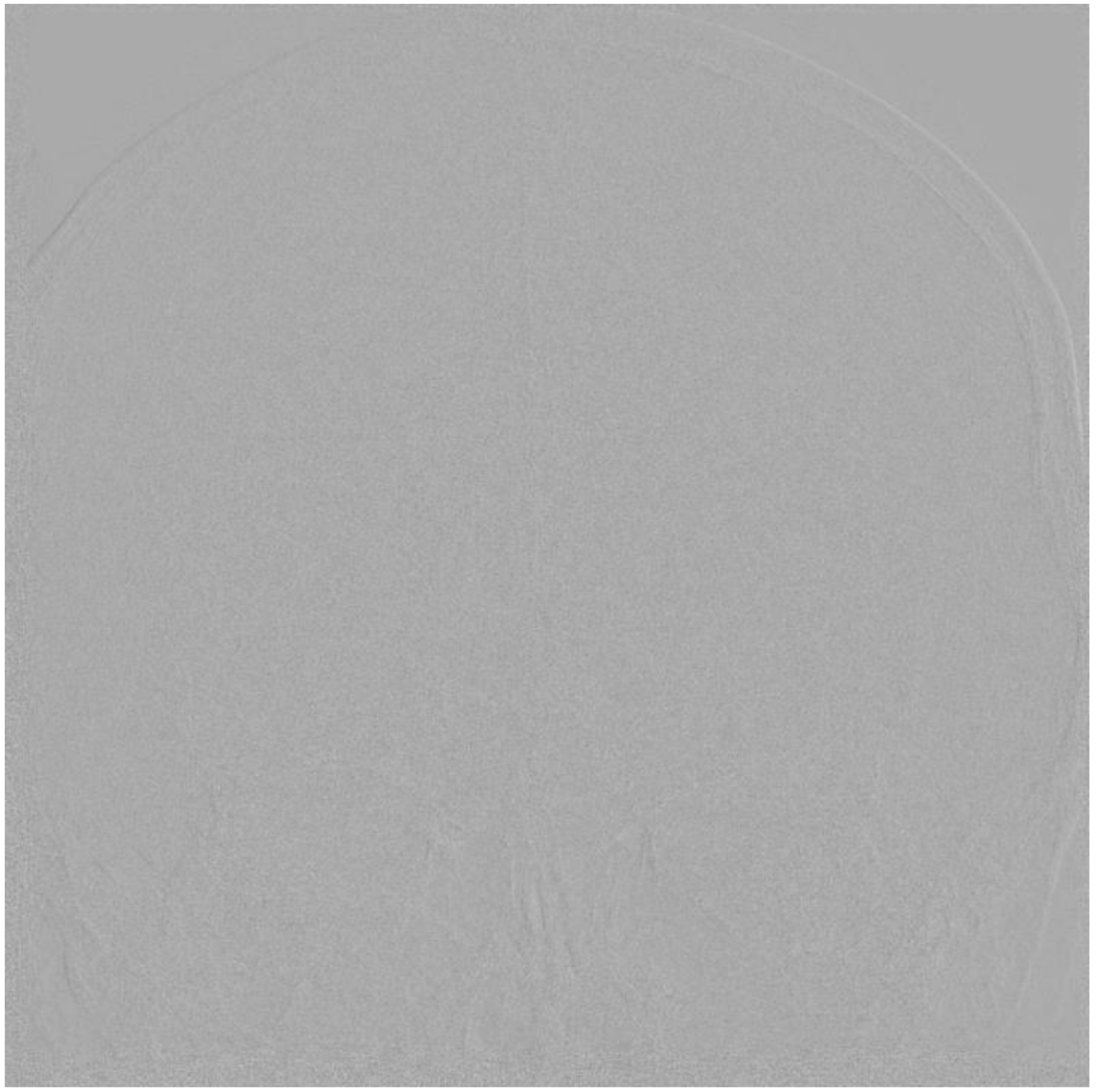




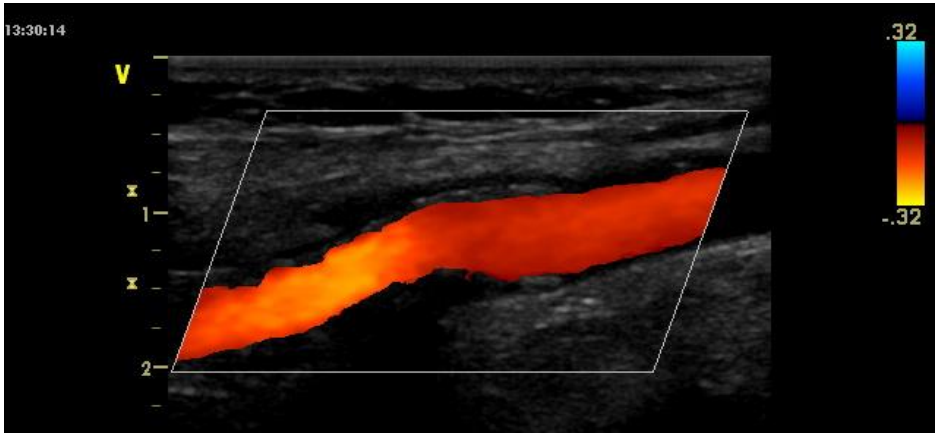
**Flow reversal time 7min 10sec**
**Intolerance in the last 80sec**
**(active aspiration still !! performed)**

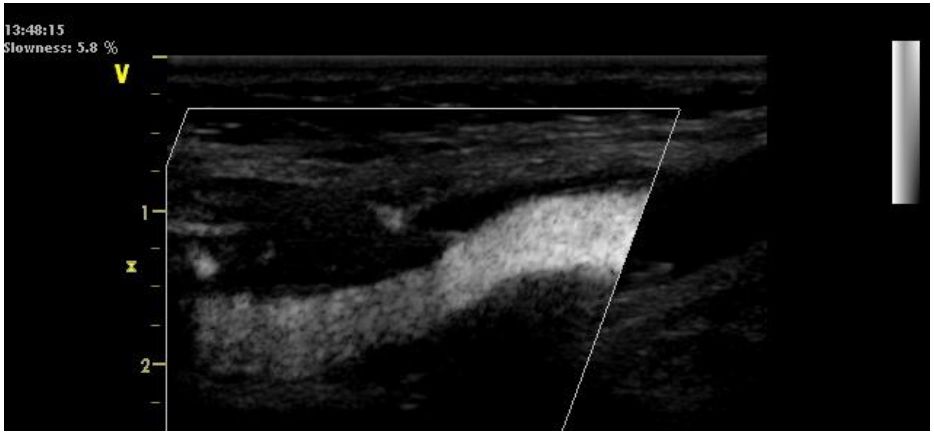
# Final Result



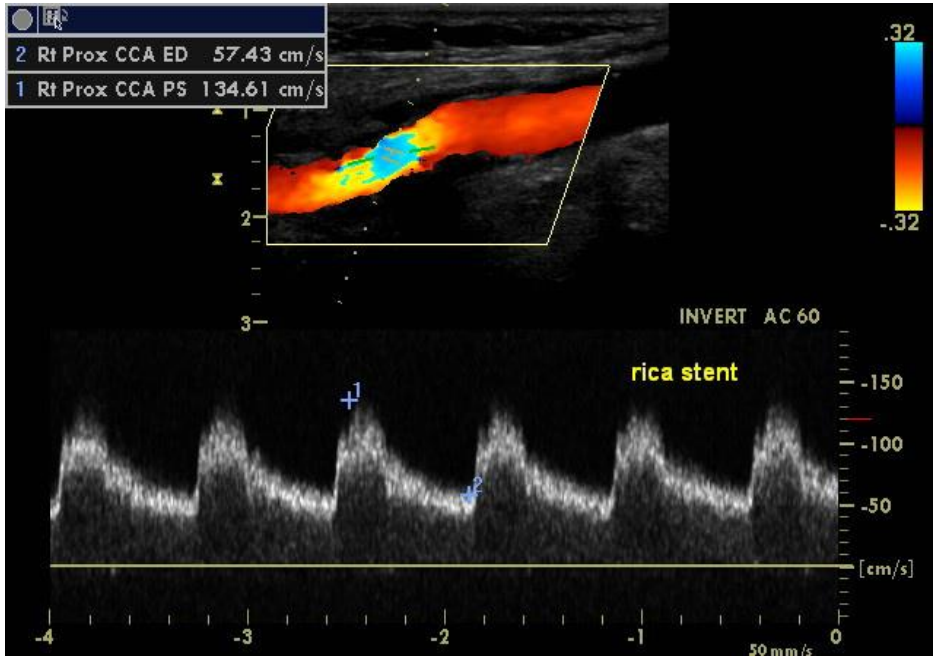


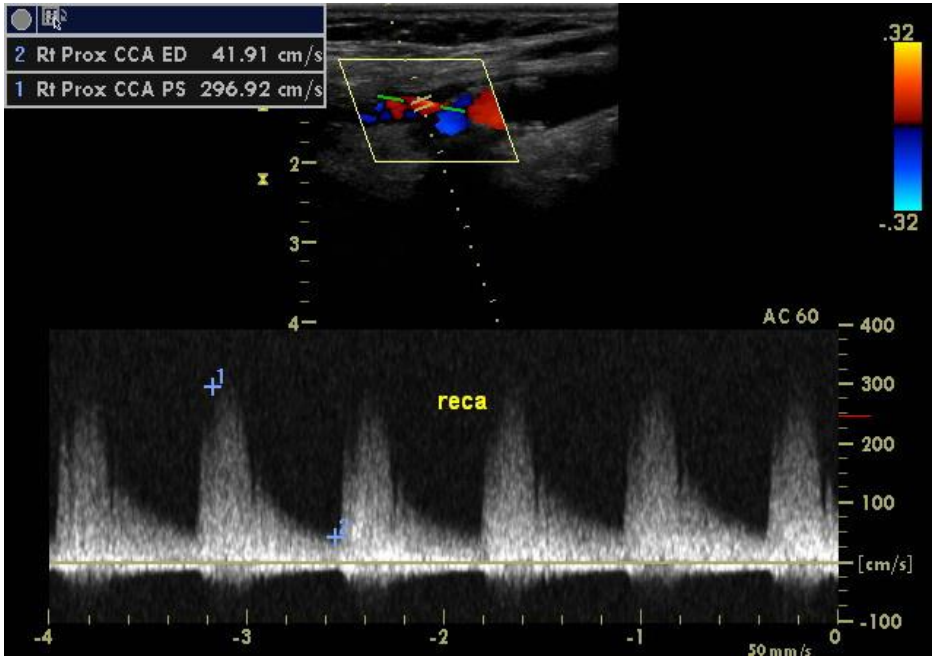
# Patient A/S, discharged home, unremarkable follow-up



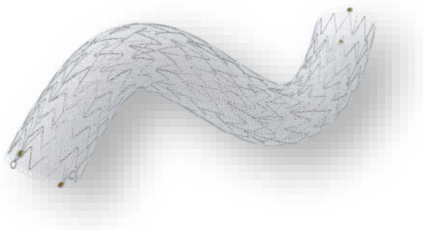

Normal stent image



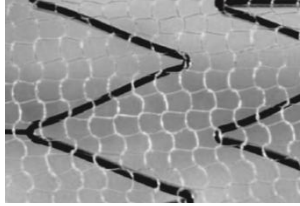




Normal velocities

ECA patent



# CGuard Clinical Studies



- CARENET (MRI) *Multi-specialty*
- PARADIGM *Multi-specialty*
- Hamburg/Heide *INR*
- IRON-Guard *Vascular Surgery*
- TORINO (MRI) *INR*
- Milan (MRI substudy) *Vascular Surgery*
- **PARADIGM-Extend** *Multi-specialty*
- **CEA vs. TCAR-CGurad** *Vascular Surgery*
- **CGuard vs. Acculink RCT** (DW-MRI)

**2018 IRON-Guard II** ( n=500, *Vascular Surgery* )

**2019 CGuard OPTIMAL** ( Sympt, IVUS, *Multi-specialty* )

**2019 CGuard PRO** ( n=500, *Vascular Surgery* )

# CGuard Clinical Studies

- CARENET (MRI) *Multi-specialty*
- PARADIGM *Multi-specialty*
- Hamburg/Heide *INR*
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- **PARADIGM-Extend** *Multi-specialty*
- **CEA vs. TCAR-CGurad** *Vascular Surgery*
- **CGuard vs. Acculink RCT** (DW-MRI)

≈ 1000

2018 **IRON-Guard II** ( n=500, *Vascular Surgery* )

2019 **CGuard OPTIMA** ( Symp, IVUS, *Multi-specialty* )

2019 **CGuard PRO** ( n=500, *Vascular Surgery* )

>1500

# 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]

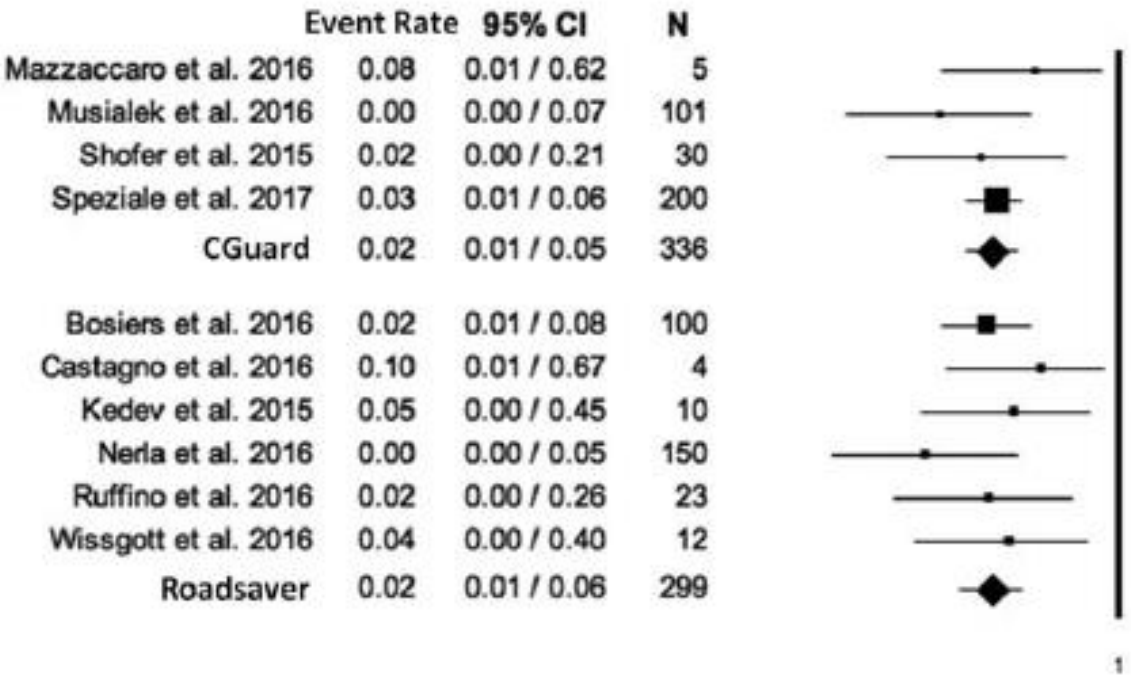



**FIGURE 2** 30-day mortality and stroke rate. Random effects event rate and 95% confidence interval for 30-day mortality and stroke (A) and relative subgroup analysis (B)

# Use of Dual-Layered Stents in Endovascular Treatment of Extracranial Stenosis of the Internal Carotid Artery

## Results of a Patient-Based Meta-Analysis of 4 Clinical Studies

Eugenio Stabile, MD, PhD,[a] Gianmarco de Donato, MD, PhD,[b] Piotr Musialek, MD, PhD,[c] Koen De Loose, MD,[d] Roberto Nerla, MD,[e] Pasqualino Sirignano, MD,[f] Salvatore Chianese, MD,[a] Adam Mazurek, MD,[c] Tullio Tesorio, MD,[g] Marc Bosiers, MD,[d] Carlo Setacci, MD,[b] Francesco Speziale, MD,[f] Antonio Micari, MD,[d] Giovanni Esposito, MD, PhD[a]

**ABSTRACT**

**OBJECTIVES** The aim of this study was to evaluate the clinical efficacy of dual-layered mesh-covered carotid stent systems (DLS) for carotid artery stenting (CAS).

**BACKGROUND** The need to minimize the risk for plaque debris prolapsing between stent struts following CAS has resulted in the development of DLS. Small clinical studies evaluating 2 available devices, Roadsaver and CGuard, have been recently published; none of these studies is sufficiently powered to test the role of common risk factors on the occurrence of stroke at 30 days post-CAS.

**METHODS** A search was performed of multiple electronic databases for studies larger than 100 cases of CAS with DLS. Four single-arm prospective studies were identified, and individual patient data were collected. The primary endpoint was the occurrence of stroke at 30 days; secondary endpoints were technical and procedural success, periprocedural stroke, and in-hospital and 30-day rates of death.

**RESULTS** The Roadsaver and CGuard stents were used in similar proportions, and technical success was achieved in all procedures (100% [n = 556]). There were 6 periprocedural strokes (1.08%; all minor). During 30-day follow-up, there was 1 death (0.17%) from myocardial infarction and 1 additional minor stroke (0.17%). The cumulative 30-day mortality rate was 0.17%, and the incidence of stroke at 30 days was 1.25%. No predictors of stroke at 30 days could be identified.

**TABLE 1** Clinical and Procedural Characteristics of Studied Population

| | CLEAR-ROAD (11) (n = 100) | IRON-GUARD (12) (n = 200) | PARADIGM (9) (n = 106) | Italian Roadsaver Registry (10) (n = 150) | Total (N = 556) |
|---|---|---|---|---|---|
| General characteristics | | | | | |
| Age (yrs) | 73.4 ± 9.5 | 72.6 ± 7.1 | 68.98 ± 7.5 | 74 ± 7.8 | 72 ± 8.02 |
| Octogenarians | 30 (30) | 24.5 (49) | 4.7 (5) | 25.3 (38) | 21.9 (122) |
| Male | 70 (70) | 66 (132) | 69.8 (74) | 75.3 (113) | 70.0 (389) |
| Risk factors | | | | | |
| Smoking history | 67 (67) | 62 (124) | 60.3 (64) | 55.3 (83) | 60.8 (338) |
| Hypertension | 80 (80) | 87 (174) | 92.4 (98) | 80 (120) | 84.9 (472) |
| Hypercholesterolemia | 74 (74) | 74 (148) | 80.1 (85) | 71.3 (107) | 74.5 (414) |
| Diabetes mellitus | 31 (31) | 28 (56) | 42.4 (45) | 27.3 (41) | 31.1 (173) |
| Symptomatic carotid disease | 31 (31) | 1.5 (3) | 46.2 (49) | 8.7 (13) | 17.3 (96) |
| High-risk characteristics | 100 (100) | 46.5 (93) | 52.8 (56) | 25.3 (38) | 51.6 (287) |
| Vascular characteristics | | | | | |
| Target lesion site | | | | | |
| Left | 49 (49) | 35.5 (71) | 48.1 (51) | 46 (69) | 43.2 (240) |
| Right | 51 (51) | 64.5 (129) | 51.9 (55) | 54 (81) | 56.8 (316) |
| % Stenosis | 85.3 ± 8.0 | 78.6 ± 6.7 | 83 ± 9.7 | 81 ± 7.6 | 81.2 ± 8.2 |
| Contralateral disease | | | | | |
| <50% | 0 | 57.5 (115) | 80.2 (85) | 66.7 (100) | 53.9 (300) |
| 50%-70% | 0 | 37 (74) | 0 | 6 (9) | 14.9 (83) |
| 70%-99% | 0 | 5.5 (11) | 4.7 (5) | 27.3 (41) | 10.2 (57) |
| Occlusion | 0 | 0 | 15.1 (16) | 0 | 2.9 (16) |
| Procedural characteristics | | | | | |
| Use of EPD | 58 (58) | 100 (200) | 100 (106) | 100 (150) | 92.4 (514) |
| Proximal protection | 10 (10) | 9 (18) | 46.2 (49) | 41.3 (62) | 25 (139) |
| Distal protection | 48 (48) | 91 (182) | 53.8 (57) | 58.7 (88) | 67.4 (375) |
| Pre-dilatation | 21 (21) | 32 (64) | 91.5 (97) | 7.3 (11) | 34.7 (193) |
| Type of stent | | | | | |
| CGuard | 0 (0) | 100 (200) | 100 (106) | 0 (0) | 55.0 (306) |
| Roadsaver | 100 (100) | 0 (0) | 0 (0) | 100 (150) | 45.0 (250) |
| Post-dilatation | 94 (94) | 86 (172) | 100 (106) | 100 (150) | 93.9 (522) |

**CONCLUSIONS** This meta-analysis suggests that DLS can be safely used for CAS, and their use minimizes the incremental risk related to symptomatic status and other risk factors. (J Am Coll Cardiol Intv 2018;11:2405–11)

# CGuard™ EPS Trials

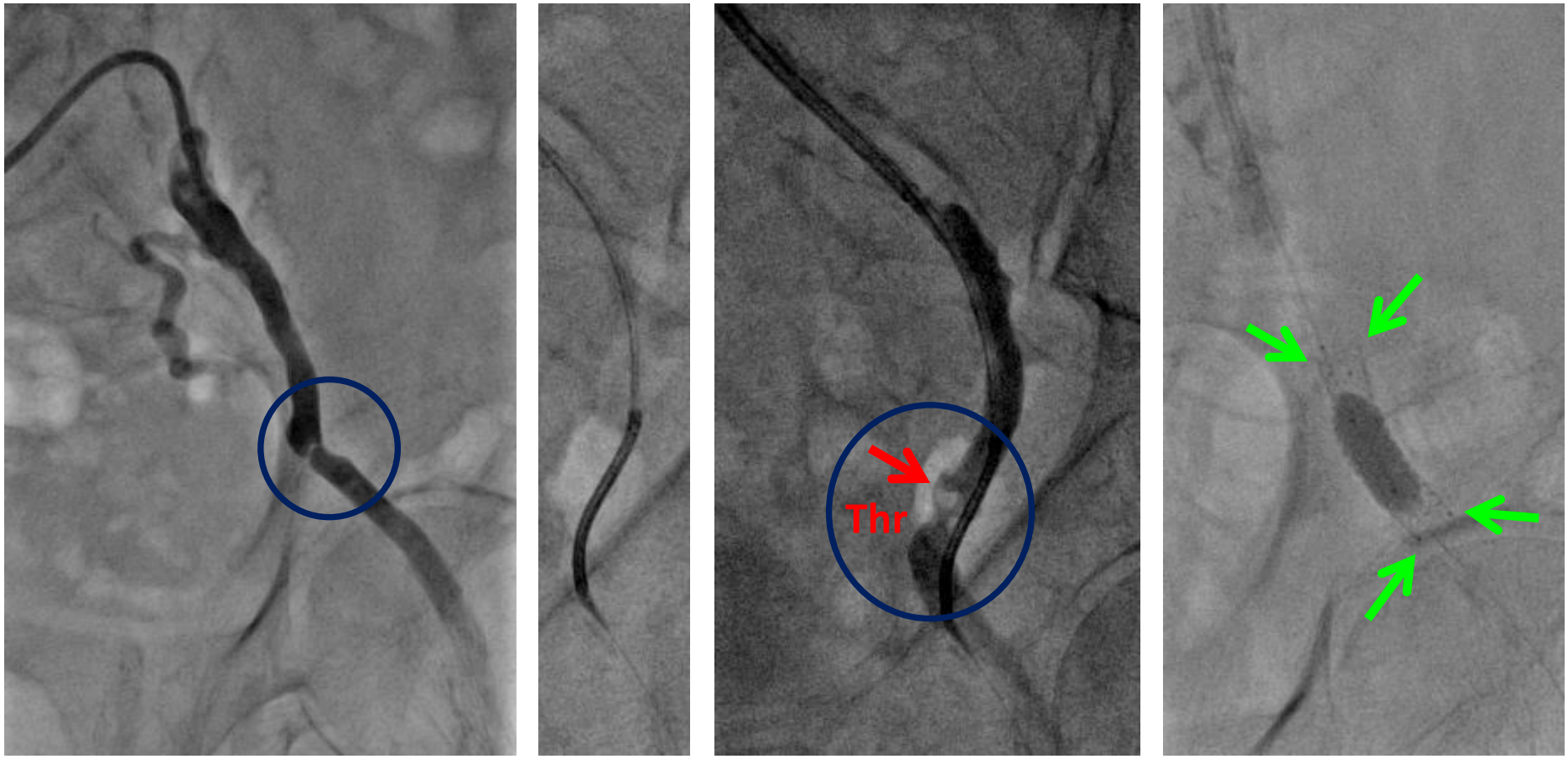
| Study | 2200 pts | | Specialist | Status |
|---|---|---|---|---|
| CARENET | 30 pts | DW-MRI | Multi | Published |
| PARADIGM | 100 pts | All comer | Multi | Published |
| IRON-Guard | 200 pts | Real World | Vasc Surgery | Published |
| TORIN (MRI) | 30 pts | DW-MRI | INR | Published |
| Wissgott | 30 pts | Mechanics | Angiology | Published |
| Casana | 80 pts | Real World | Vasc Surgery | Published |
| Wissgott NG | 20 pts | New Gen | | Finish |
| IRON-Guard 2 | 500 pts | Real World | Vasc Surgery | On-going |
| PARADIGM-Extend | 300 pts | All comer | Multi | On-going |
| CGuard Vasc Surg (Poland) | 500 pts | Real World | Vasc Surgery | On-going |
| CGuard vs. Acculink RCT | 100 pts | (DW-MRI) | Vasc Surgery | On Going |
| CGuard PRO | 500 pts | Real World | Vasc Surgery | |
| CGuard OPTIMAL | 100 pts | with IVUS | EU KOL | |
| TBC: FDA | 300 pts | | Multi | |

## Moving beyond routine CAS…

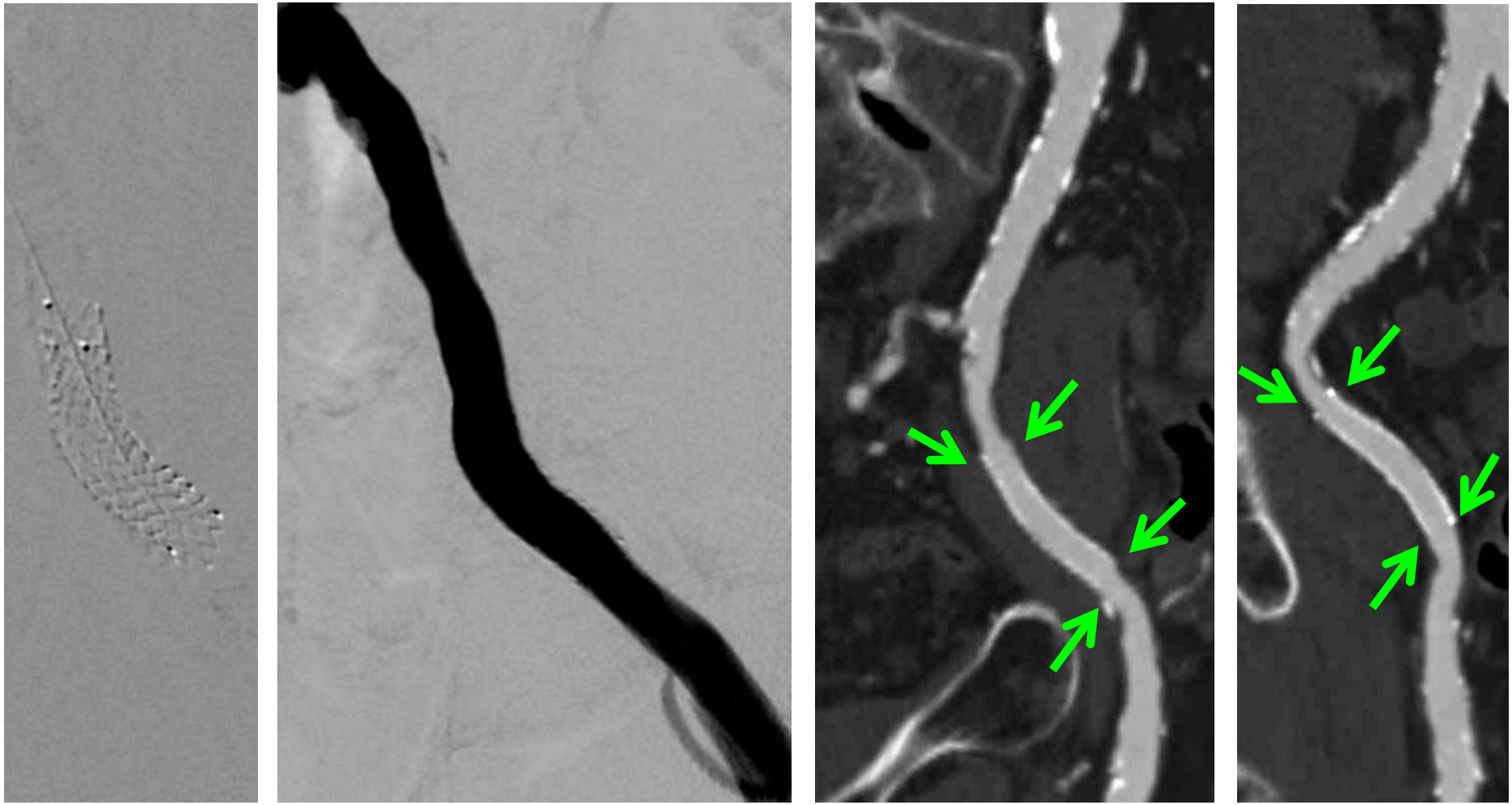
# CGuard™ MicroNet Covered Stent:

# ADDRESSING UNMET NEEDS IN OTHER VASCULAR BEDS

# Thrombus-containing/high-embolic risk lesions in iliacs or subclavians



# Thrombus-containing/high-embolic risk lesions in iliacs or subclavians

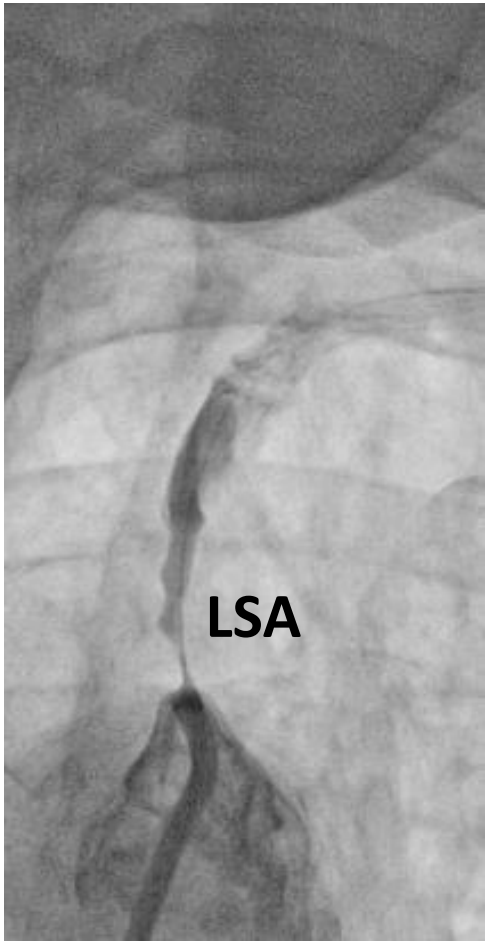


**OPTIMAL procedural result**

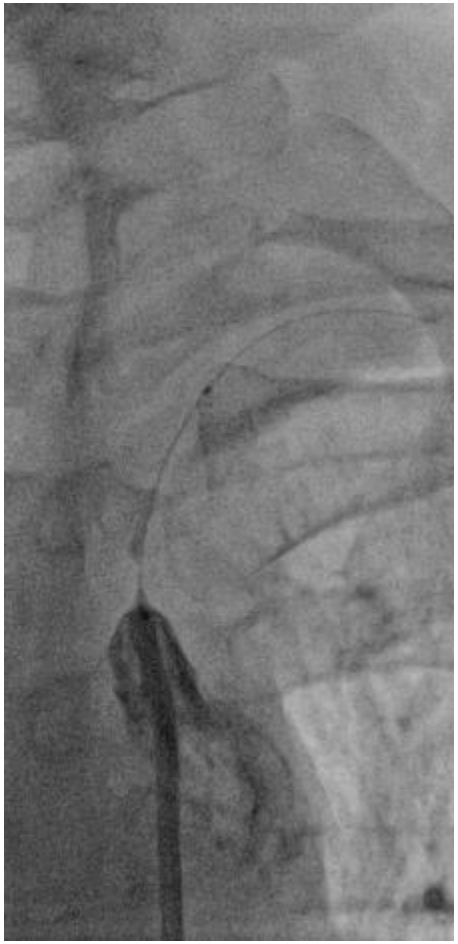
**Normal 6mo follow-up**

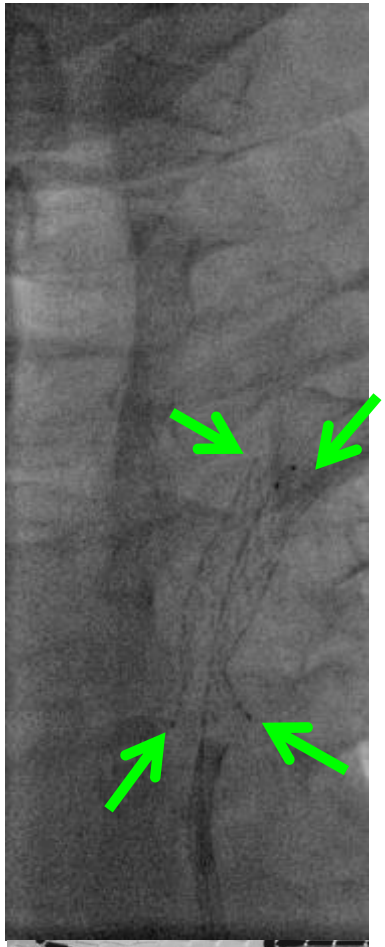
P Musialek @ ICCA Stroke 2019

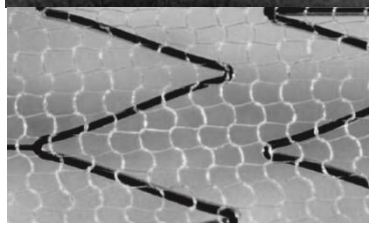
# Thrombus-containing/high-embolic risk lesions in iliacs or subclavians









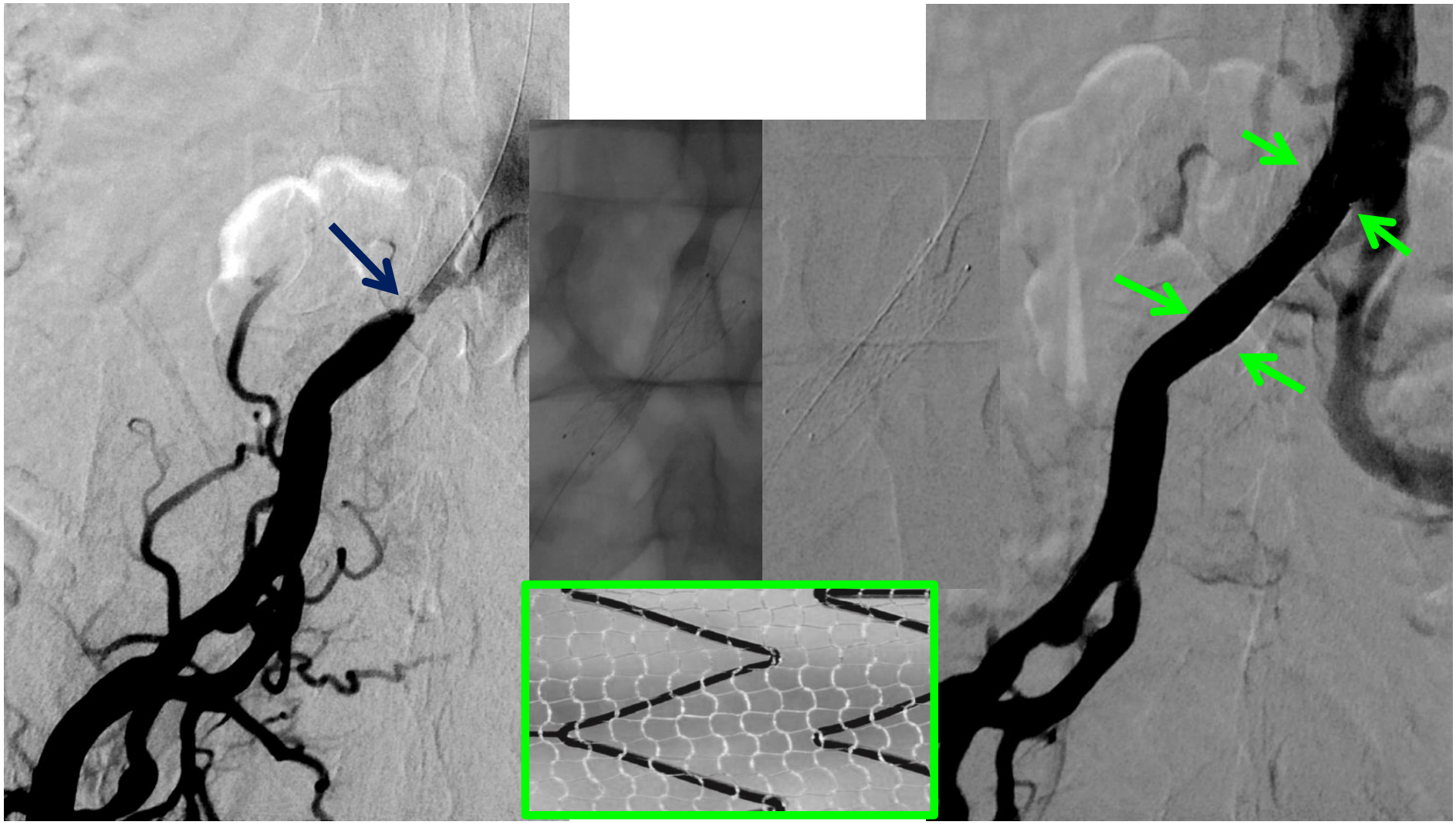


# Thrombus-containing/high-embolic risk lesions in iliacs or subclavians

## Procedural result


## Normal 6mo follow-up

# Thrombus-containing/high-embolic risk lesions in iliacs or subclavians

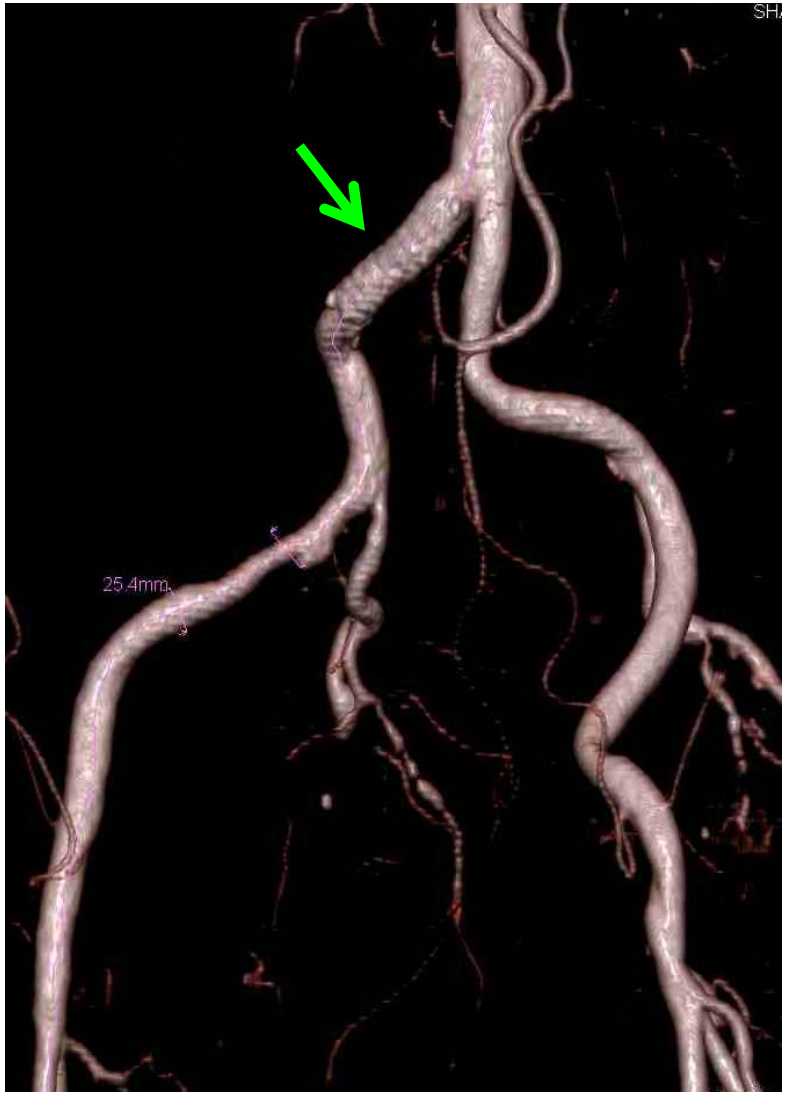


**Procedural result**

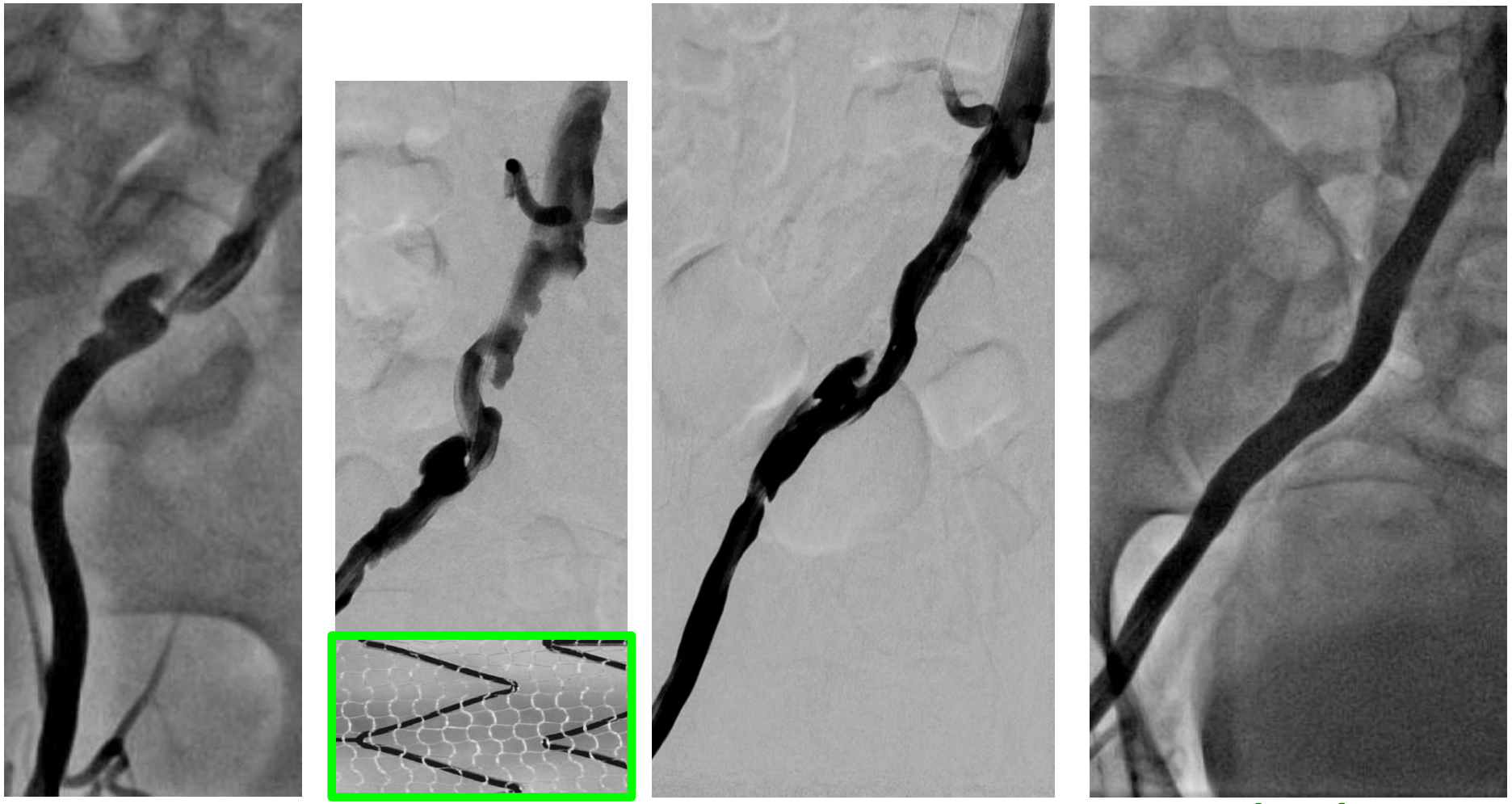
# Thrombus-containing/high-embolic risk lesions in iliacs or subclavians

**CGuard™**

**Normal Result @follow-up**



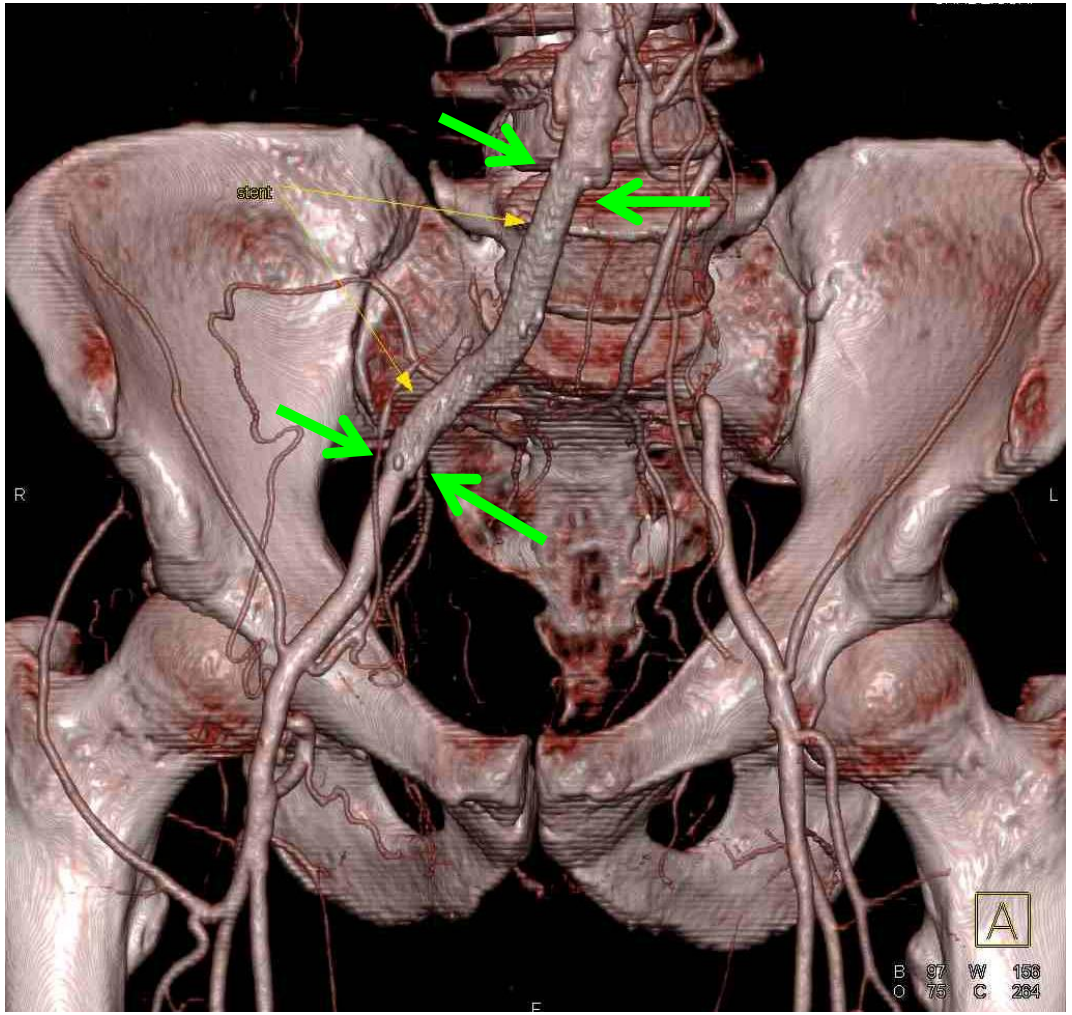
# Thrombus-containing/high-embolic risk lesions in iliacs or subclavians and



**Procedural acute outcome**

# Thrombus-containing/high-embolic risk lesions in iliacs or subclavians

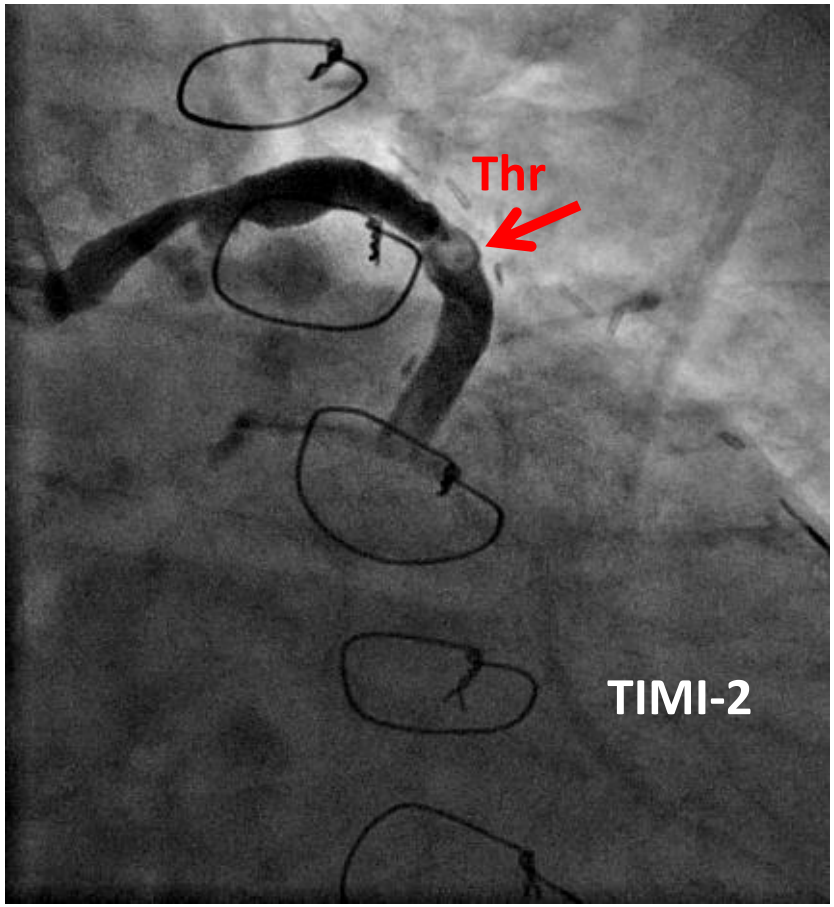
**OPTIMAL 6mo result**

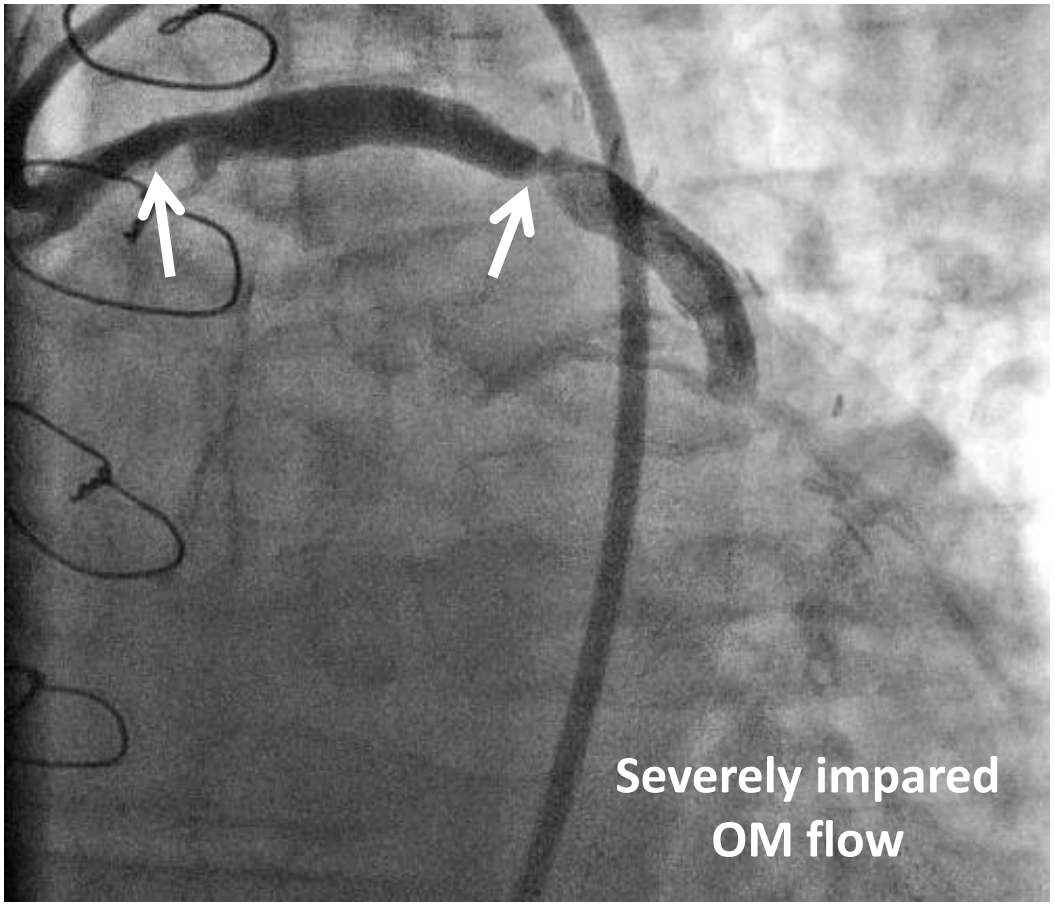



**Pt ready for fem-fem** (NB. several prior attempts to recanalize LCIA had failed)

# Large-diameter SVG disease problem

**AK, 58y, NSTE Acute Myocardial Infarction**

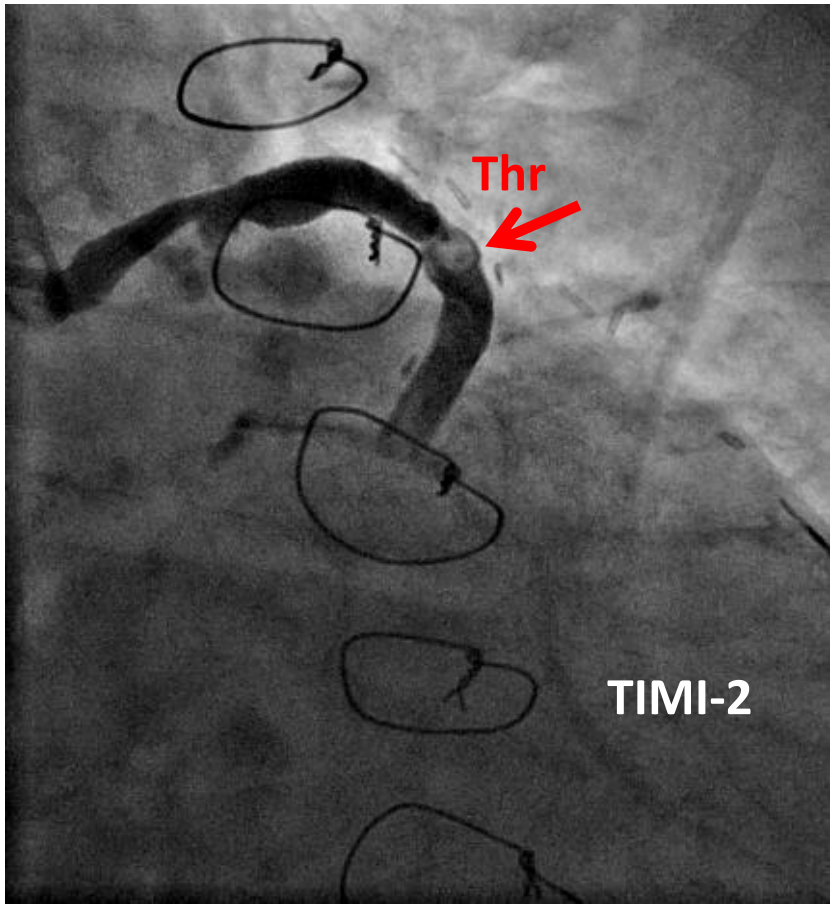


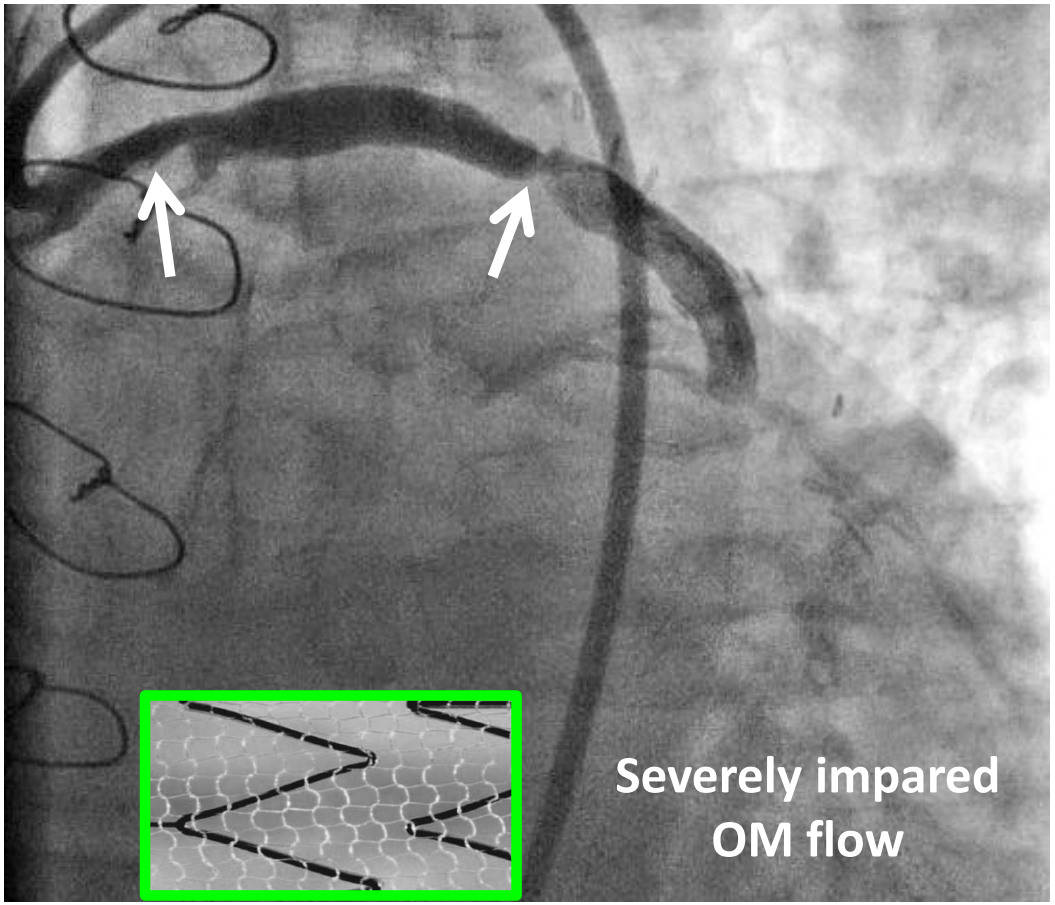




**SVG RD 7.5 mm (!)**

# Large-diameter SVG disease problem

## AK, 58y, NSTE Acute Myocardial Infarction

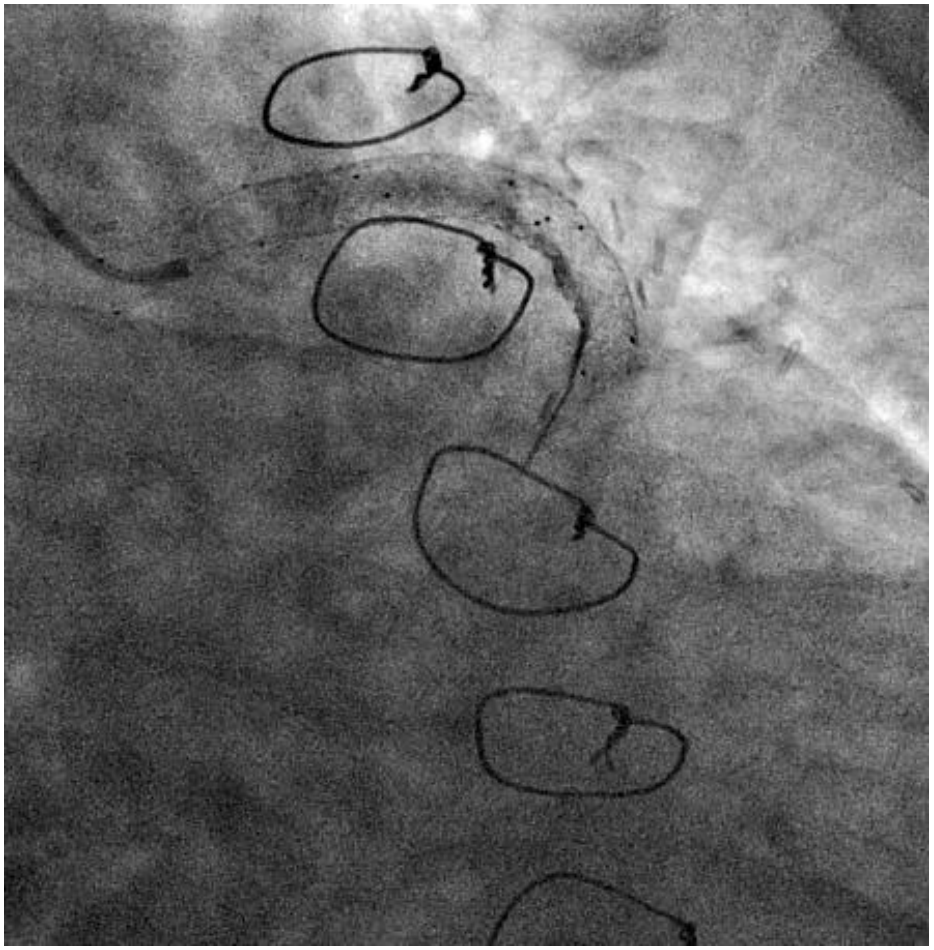


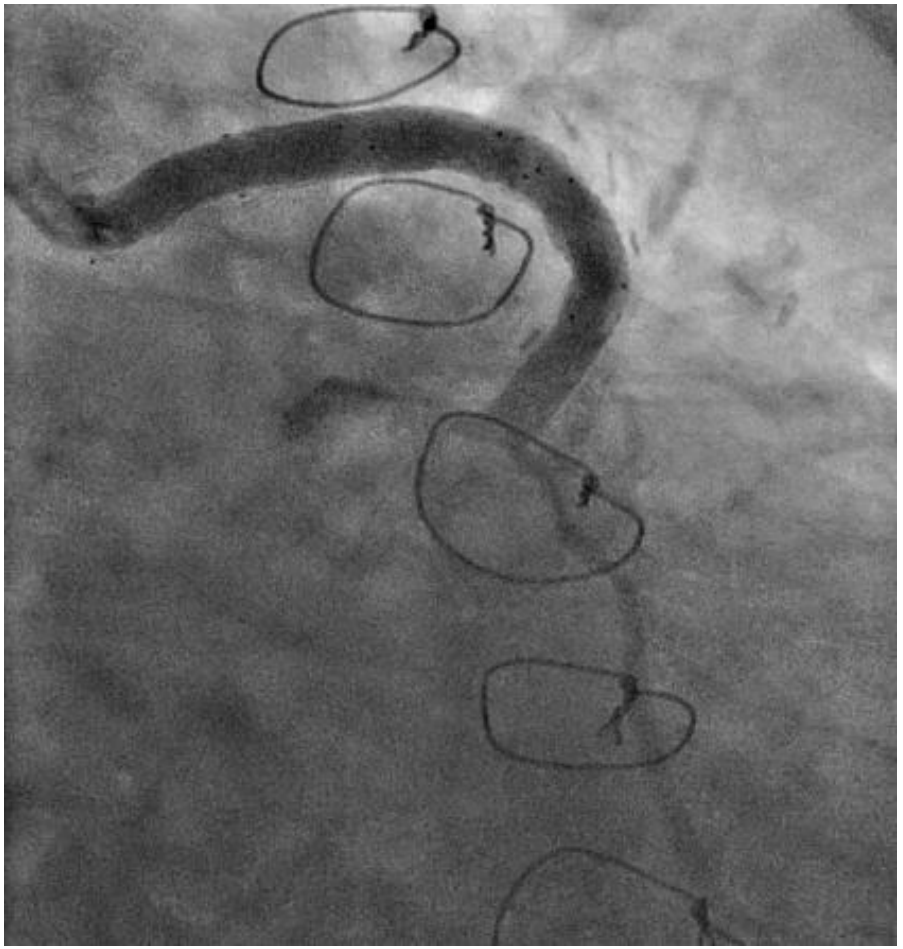




## SVG ref diameter 7.5 mm (!)

# Large-diameter SVG disease / NSTE-acute MI

## post PCI/direct stenting with overlapping MicroNet–covered CGuard™ stents

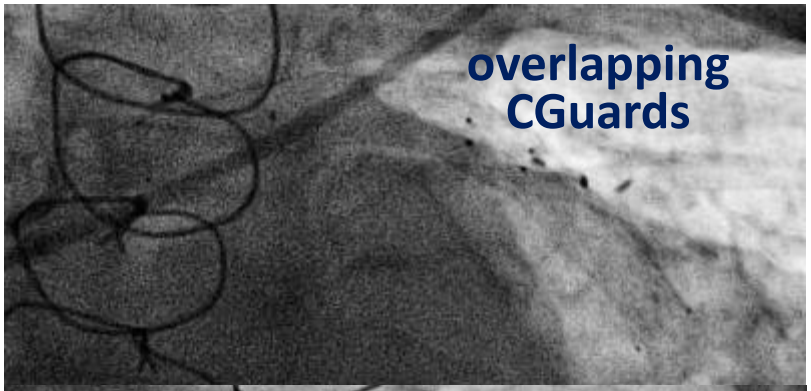


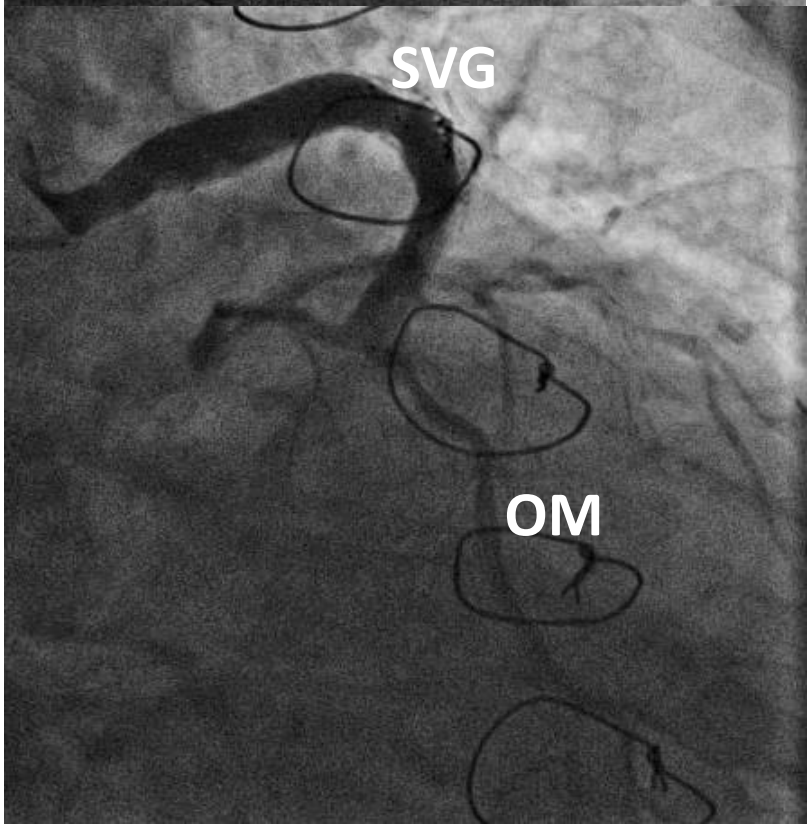


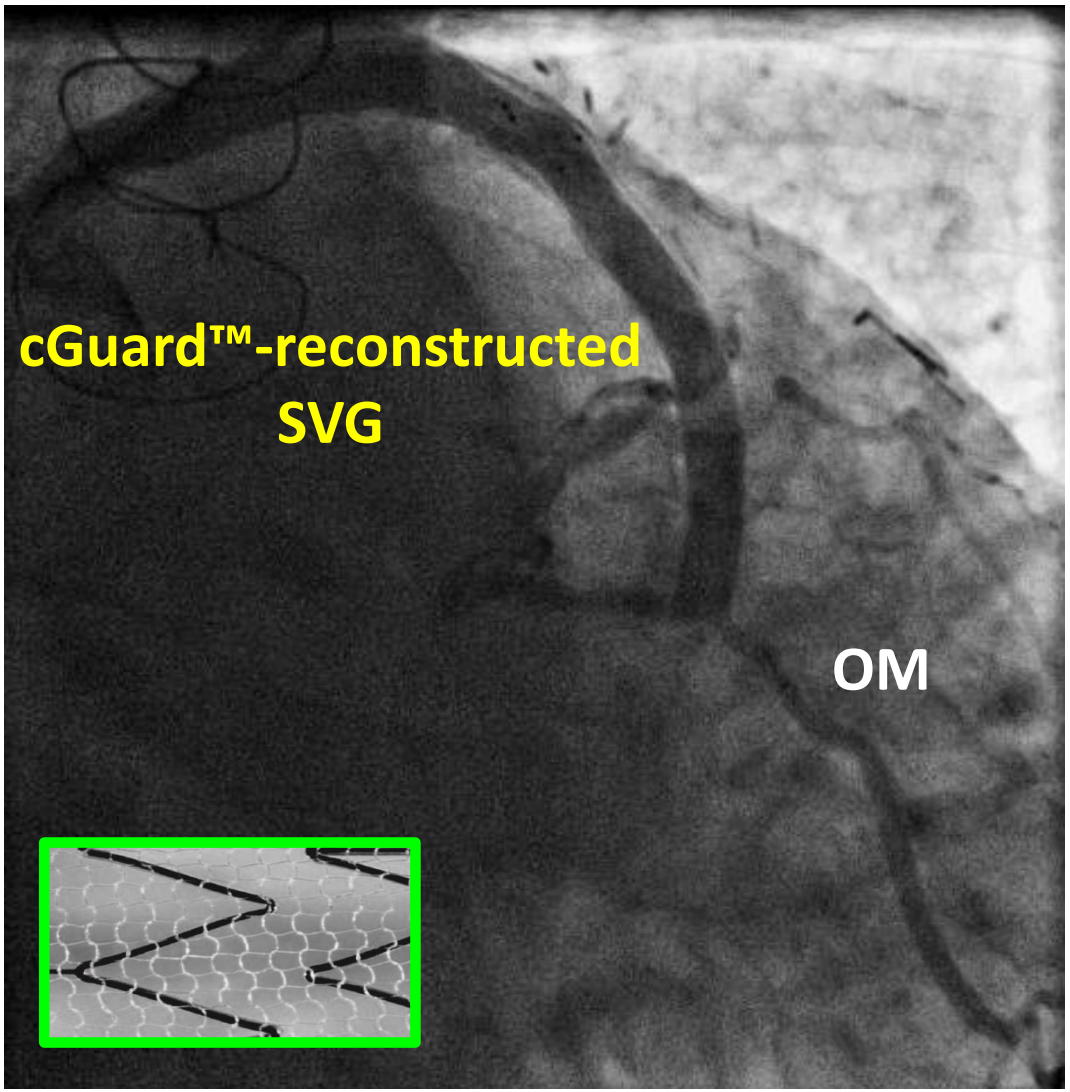
**NB. absence of distal embolizm, normal OM flow, no further troponin rise**

## OPTIMAL acute result

# Large-diameter SVG disease treated with CGuards (angio @3mo)



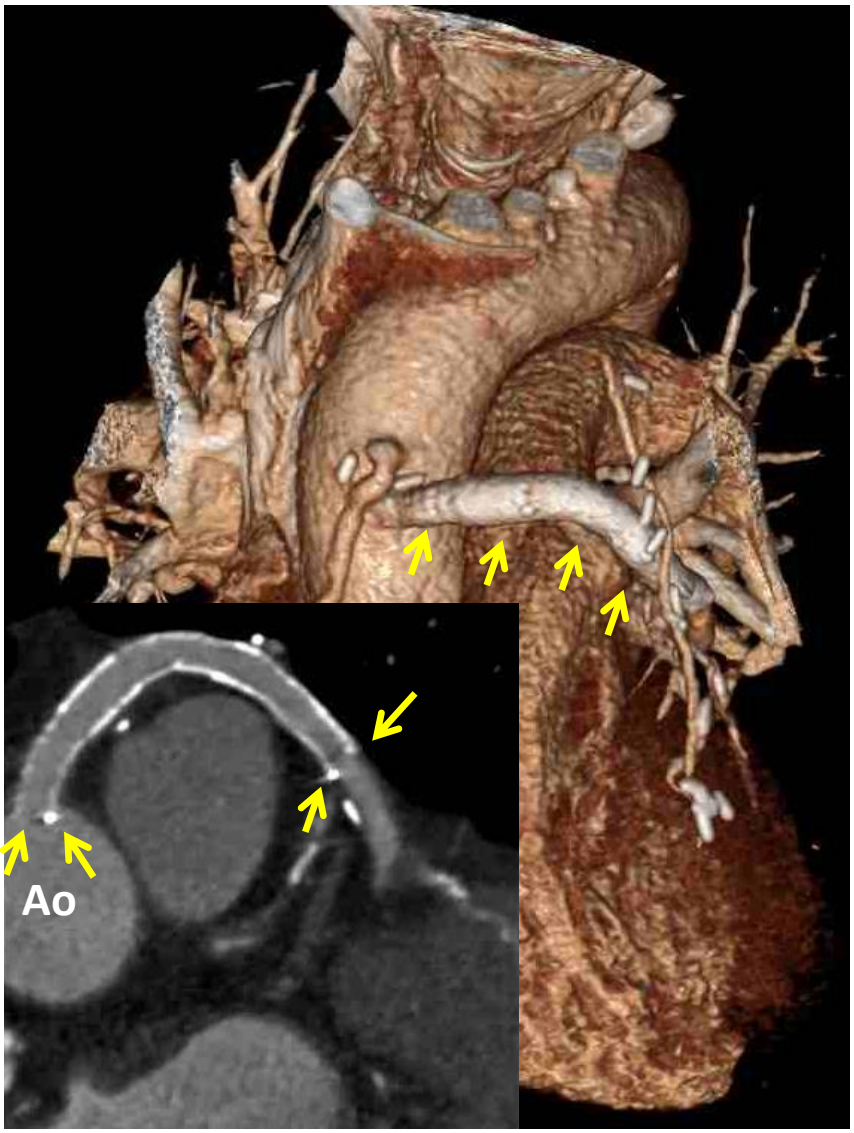



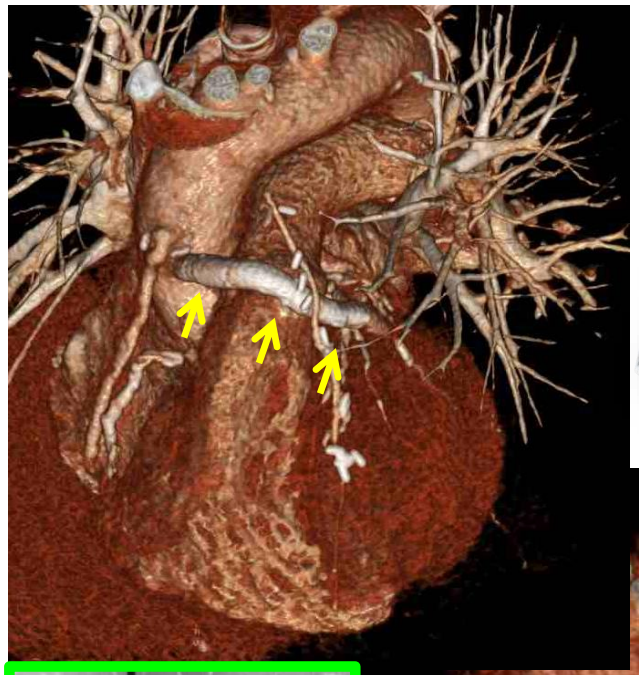



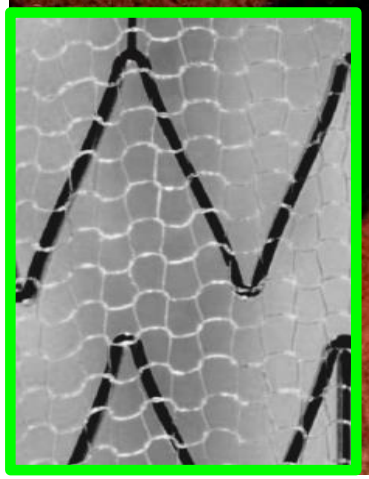

**OPTIMAL result @ 3mo**

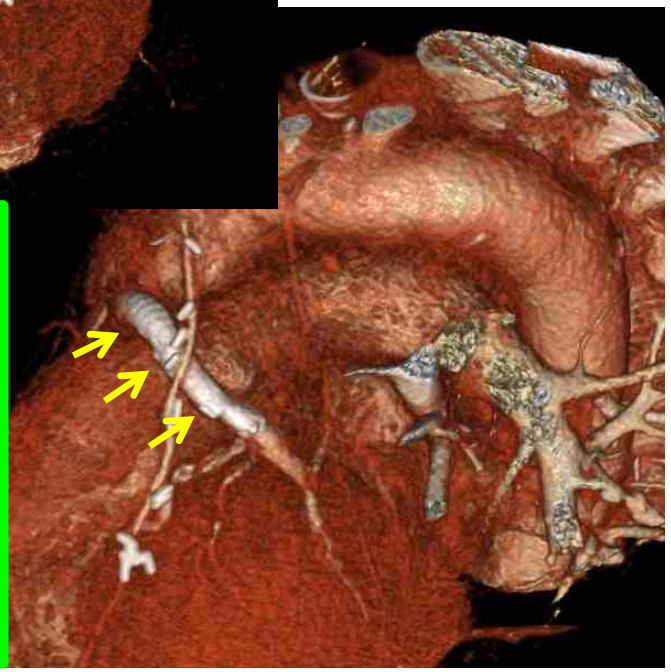
P Musialek @ ICCA Stroke 2019

# Large-diameter SVG disease treated with CGuards (CT-angio @6mo)





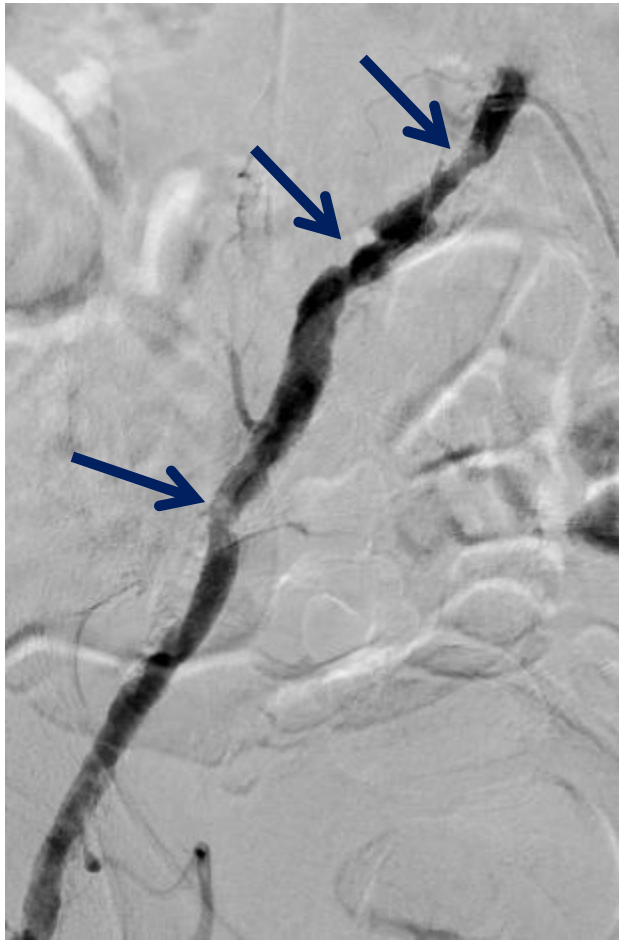
NOTE ostial placement precision feasibility

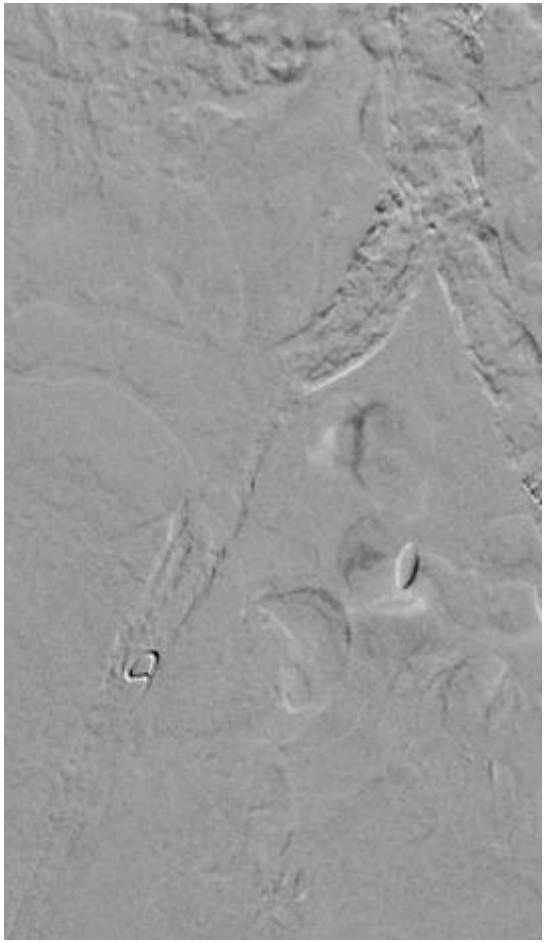
**OPTIMAL result @ 6mo**

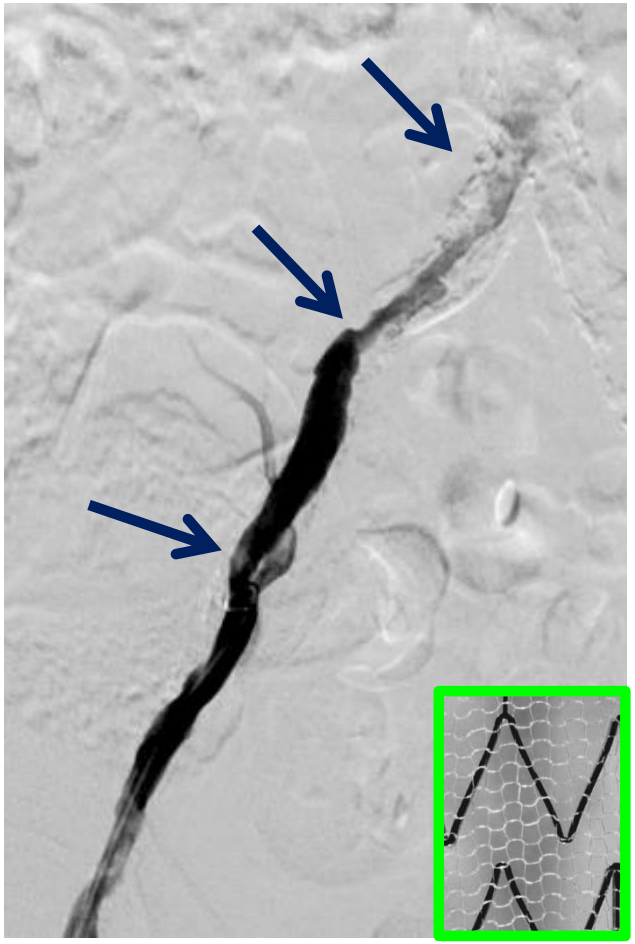
P Musialek @ ICCA Stroke 2019

# (V) Higly calcific disease

## (note: adequate radial force need)

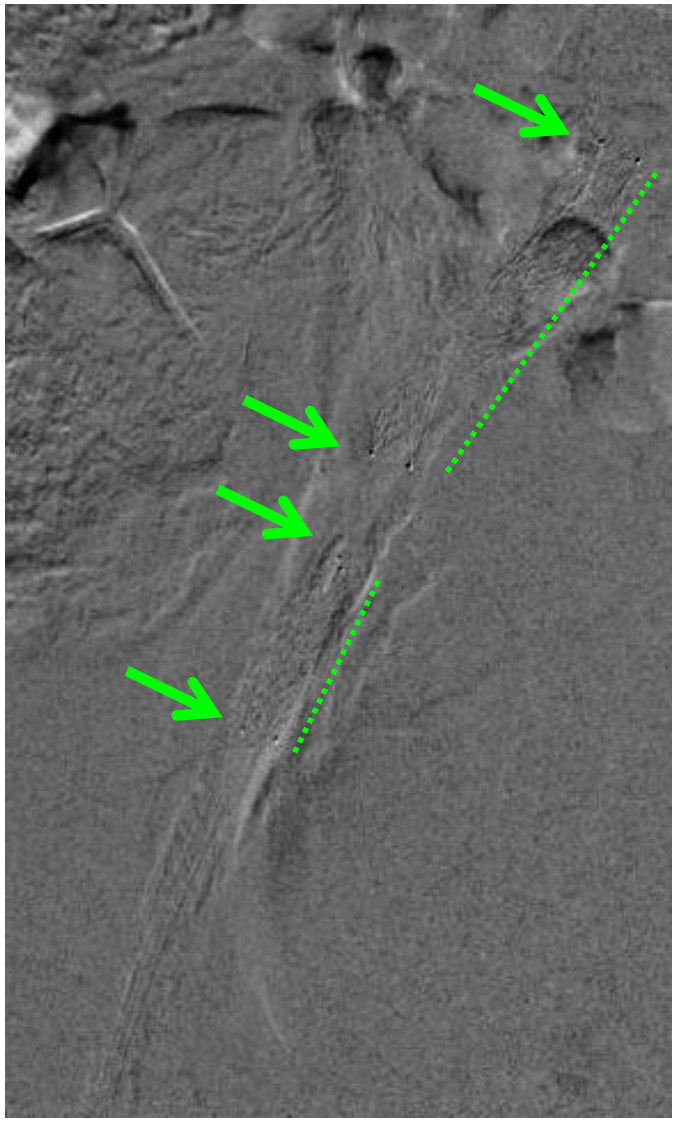






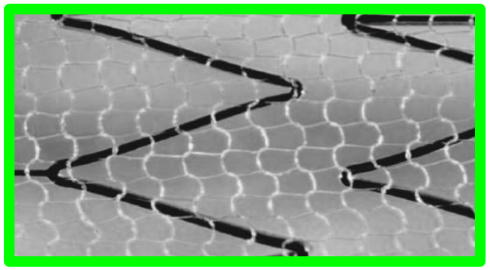
# (V) Higly calcific disease

## (note adequate radial force need)



CGuard™

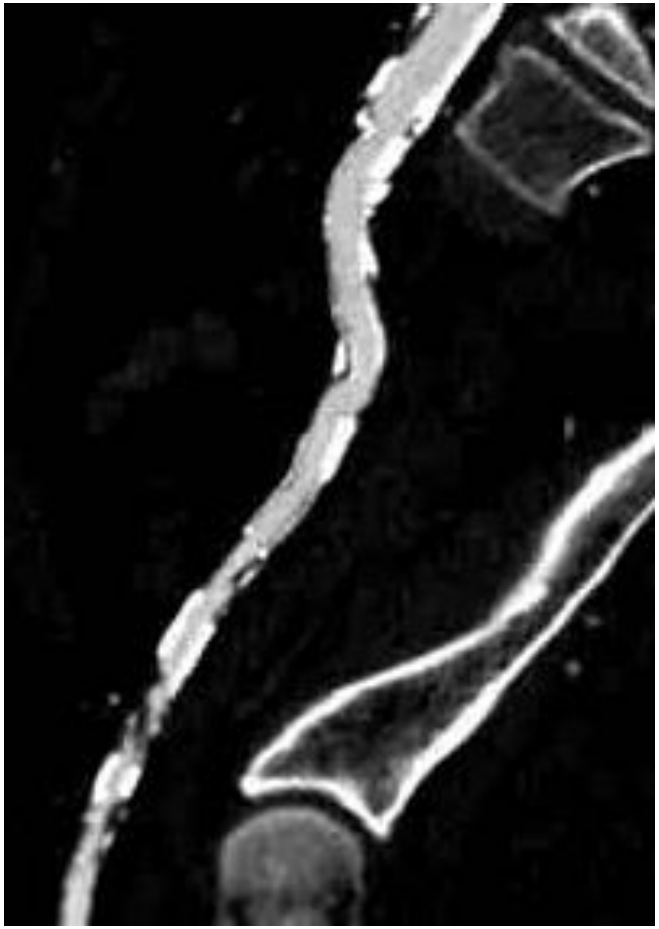
**Acute Procedural Result**

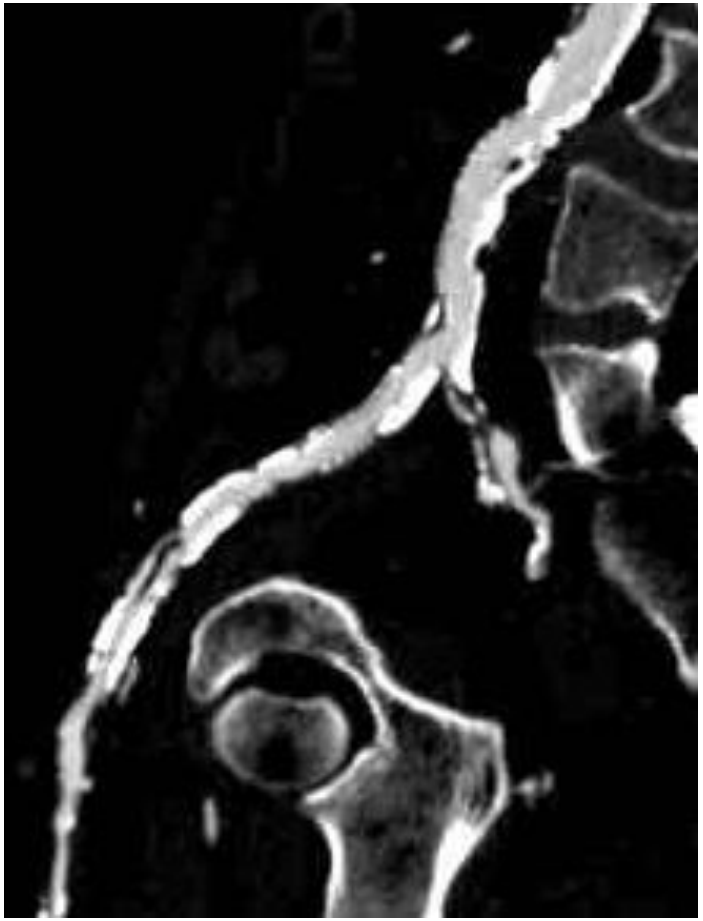


# (V) Higly calcific disease

## (note: adequate radial force provided)

CGuard™



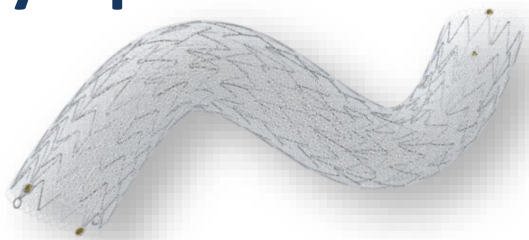


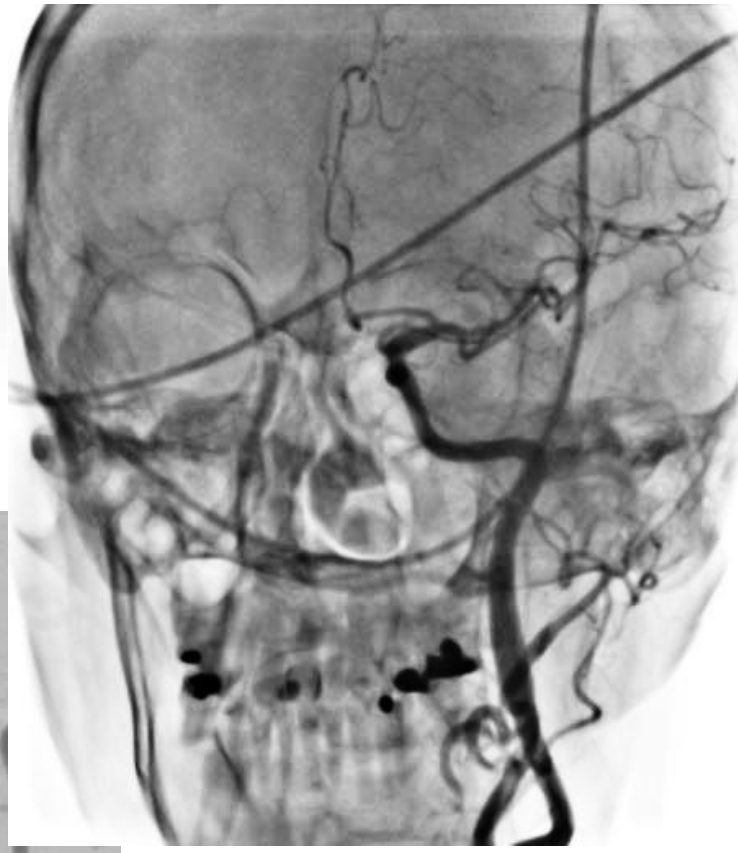
**OPTIMAL result @ 6mo**

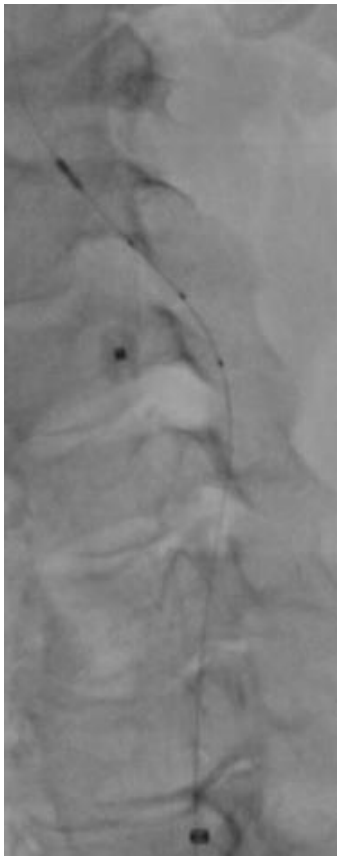
# Non-Healing Dissection

## with recurrent symptoms

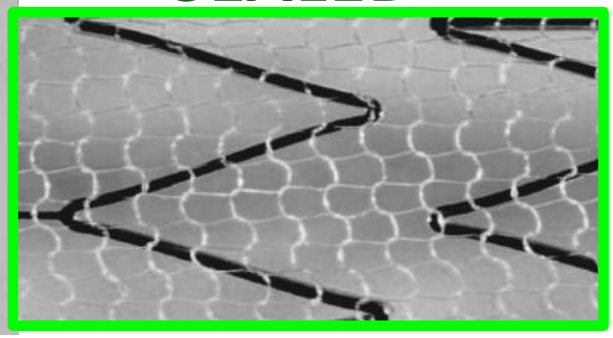
**CGuard™**





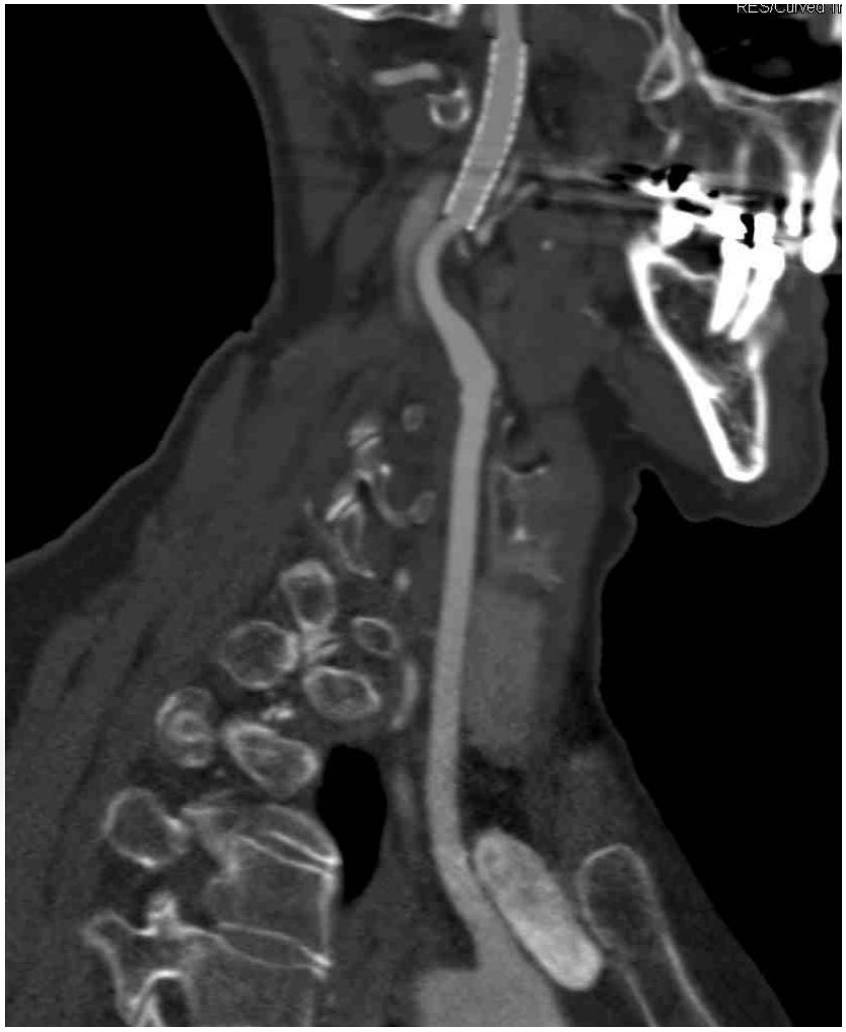
**Immediately SEALED**



**MoMa, IVUS**

# Non-Healing Dissection

## with recurrent symptoms



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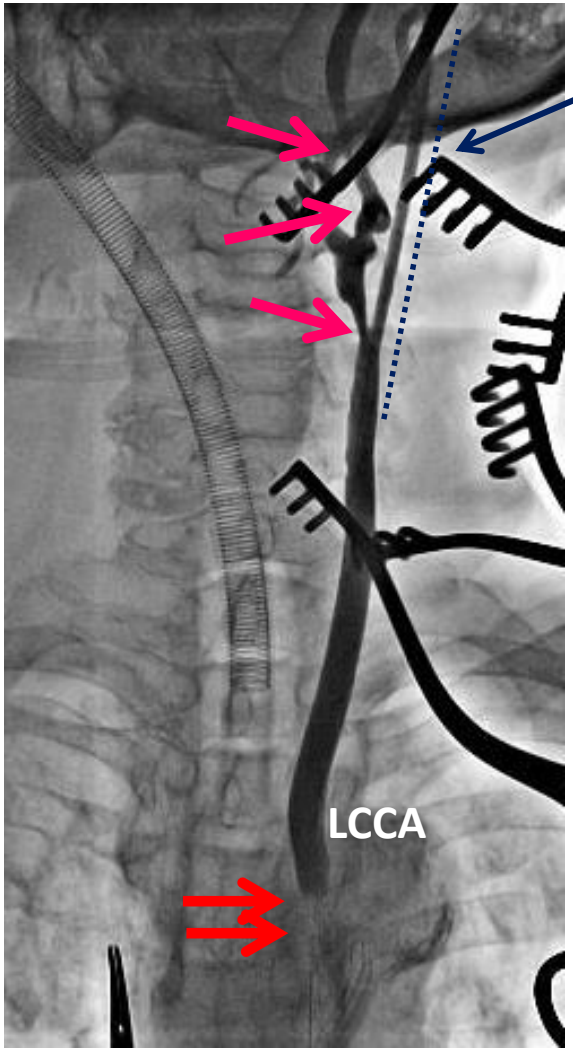
**Normal 12 mo Follow-up Result**

P Musialek @ ICCA Stroke 2019

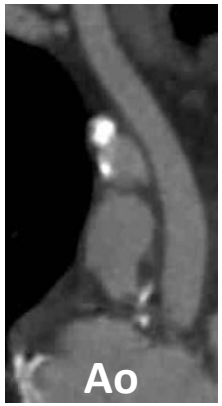
# Ostial CCA lesions

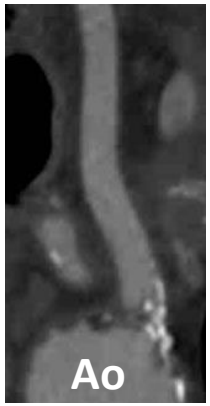
## (note adequate radial force and placement percision need)



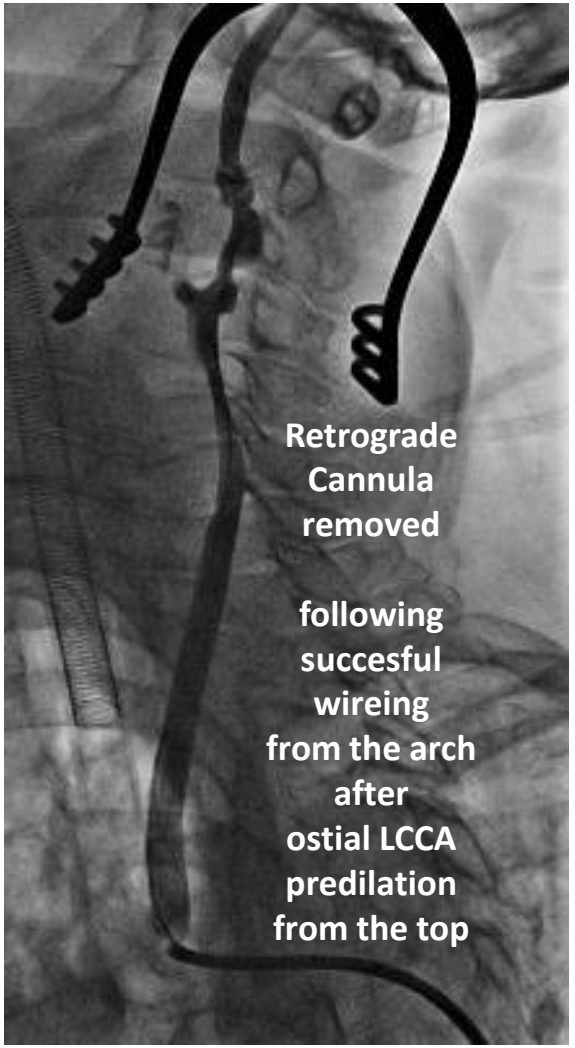

LCCA Retrograde Cannulation from the neck

(to wire and predilate the subtotal ostial LCCA; NB. failed access from the arch)



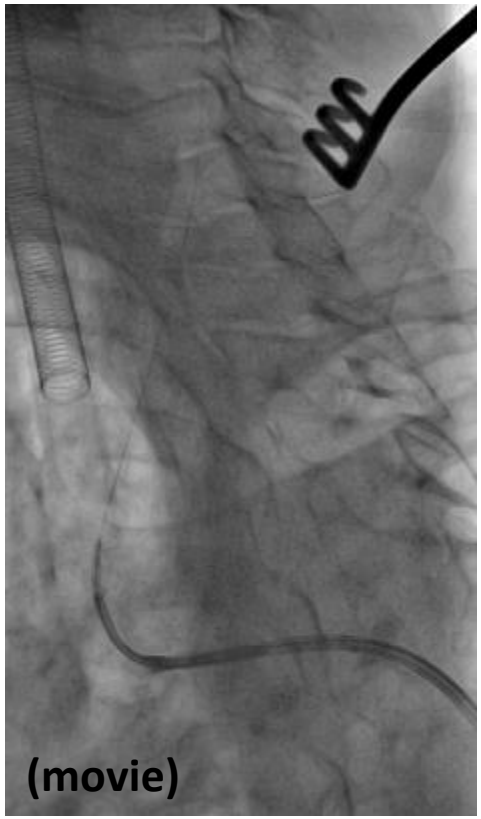




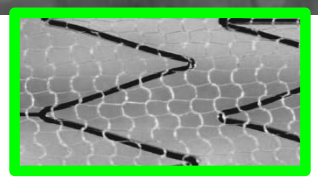

**Lady 68 yo, retinal TIAs followed by <u>retinal stroke</u> while on OMT (mother to cathlab nurse)**

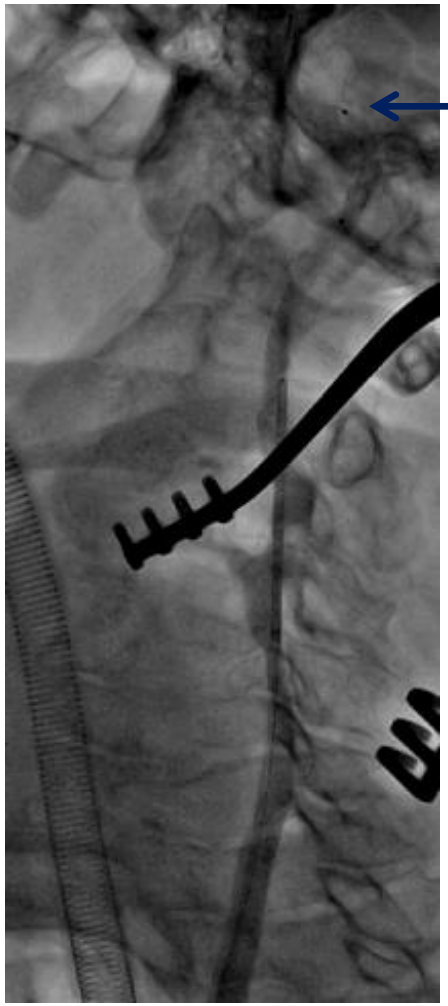
# Ostial CCA lesions

## (note adequate radial force and placement percision)



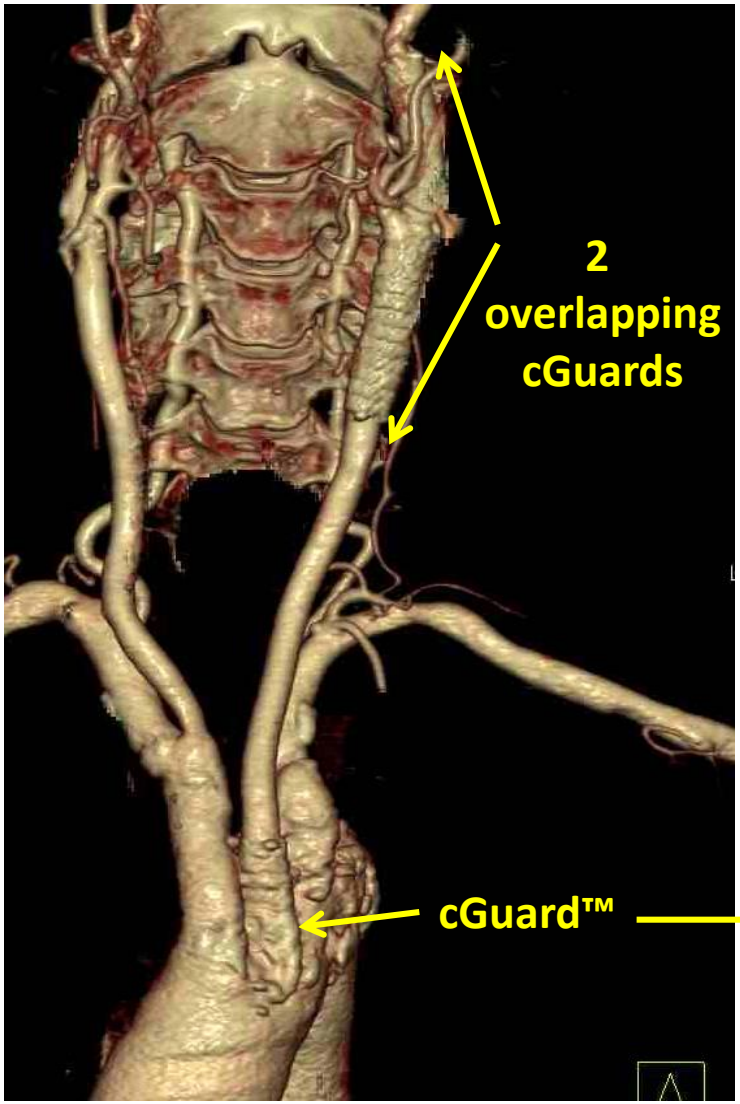


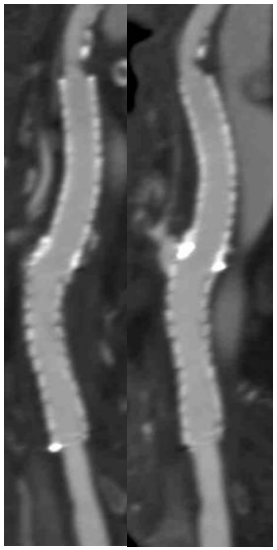




# Ostial CCA lesions

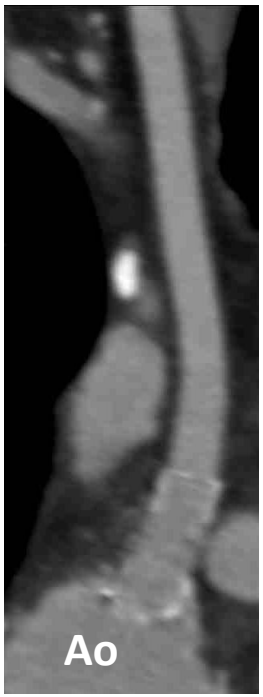
## (note adequate radial force and placement percision)



**OPTIMAL angiographic + clinical + duplex result @ 12mo**

(and LECA patent)


# Acknowledgements

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Piotr Wilkołek
Agnieszka Zwolińska

CGUARD™
Carotid Embolic Prevention System

CAROTID PARADIGM REVASCULARIZATION

36-month data

# PARADIGM

## @ 36 months

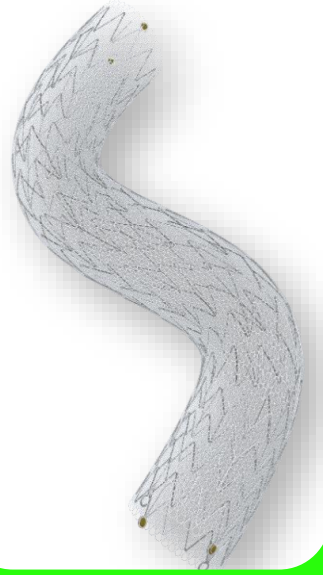
**Favourable Clinical Outcome**

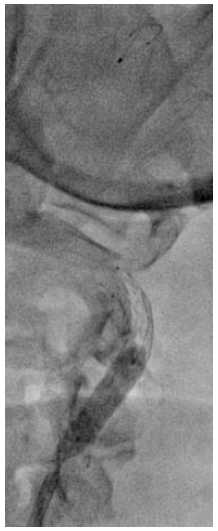
- NO device-related adverse events
- NO procedure-related events

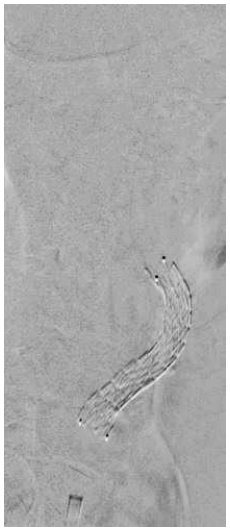
**sustained stroke prevention**

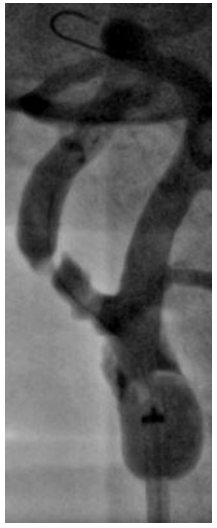
P Musialek @ ICCA Stroke 2019

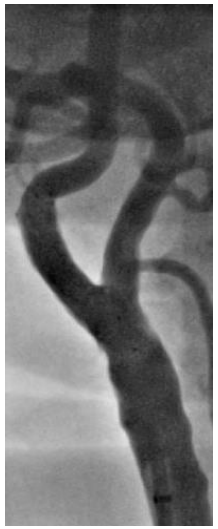
# Endovascular Solution for All-Comers

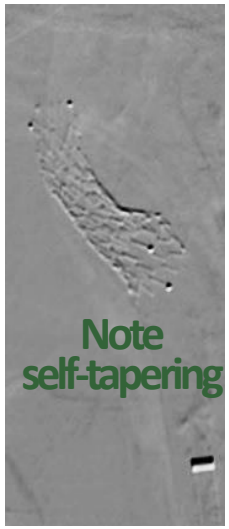








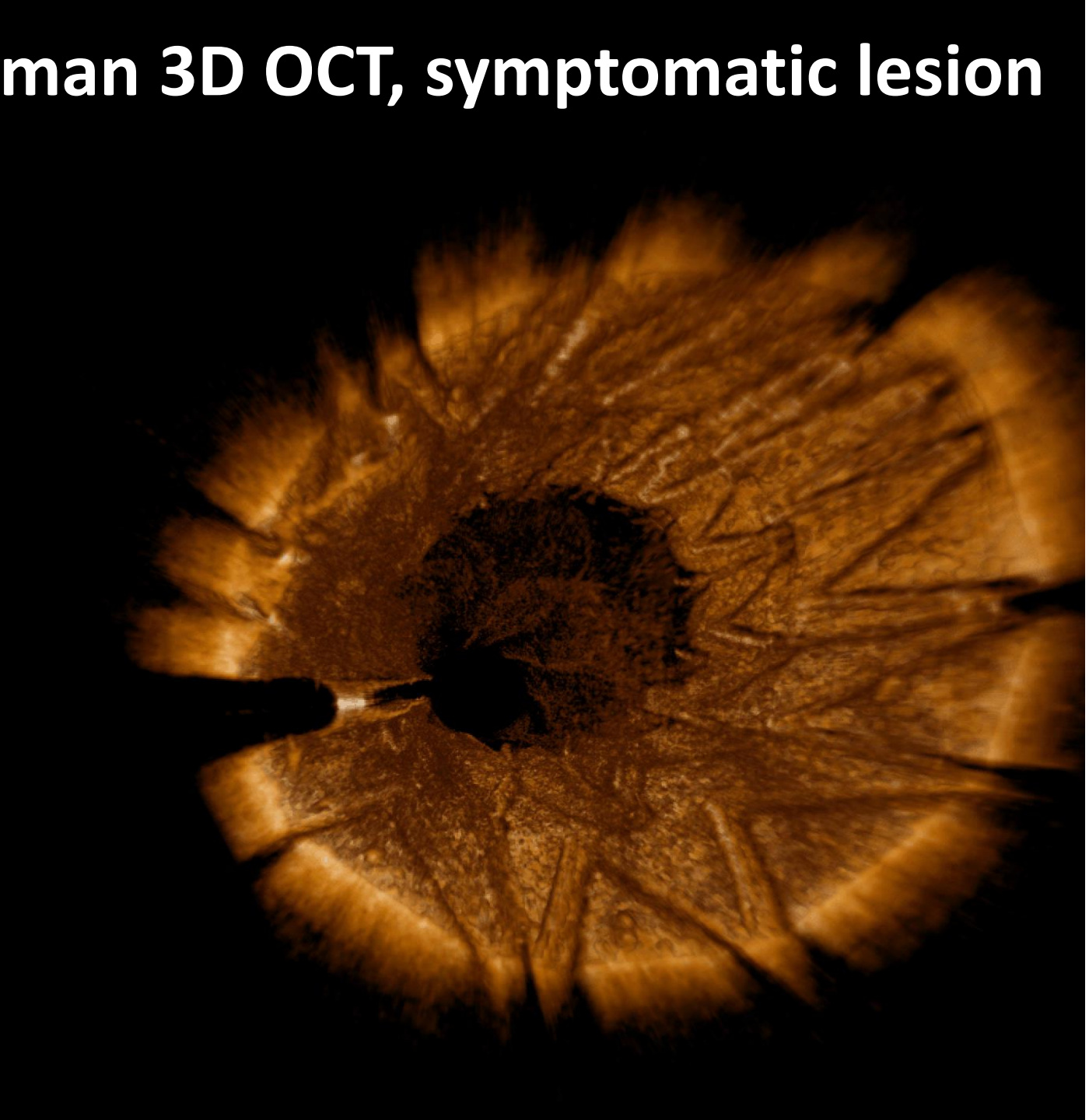




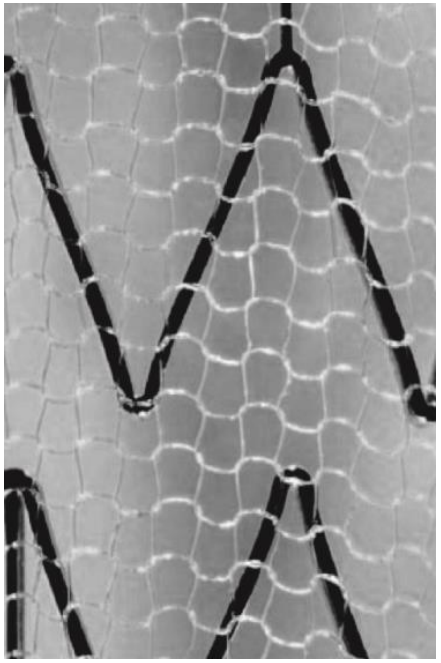

## Endovascular Reconstruction of the Carotid Bifurcation

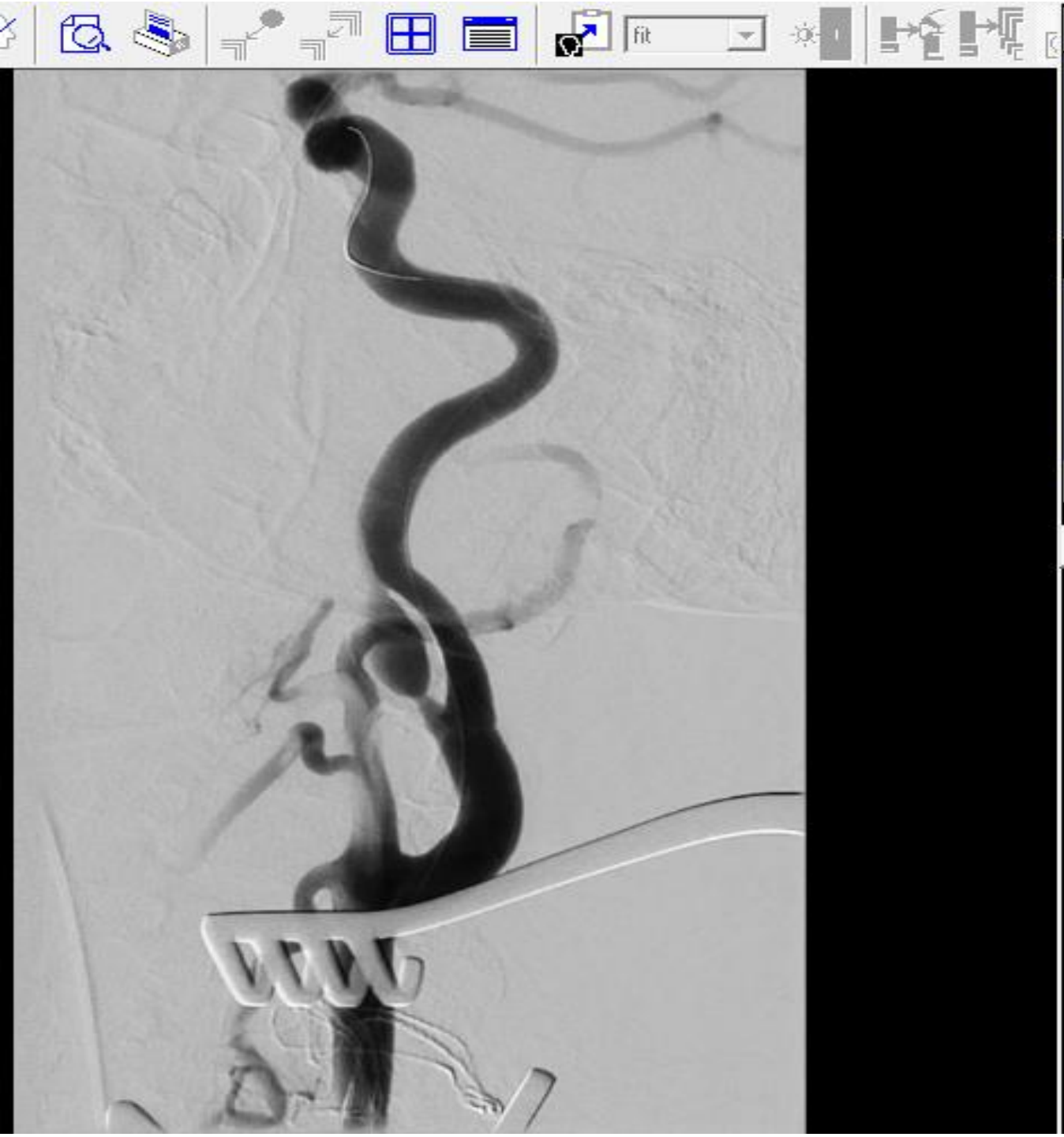
**Prevention of embolism, High radial force, Conformability**

# man 3D OCT, symptomatic lesion



## CGuard™ EPS




fit
Patient/Examination
181374
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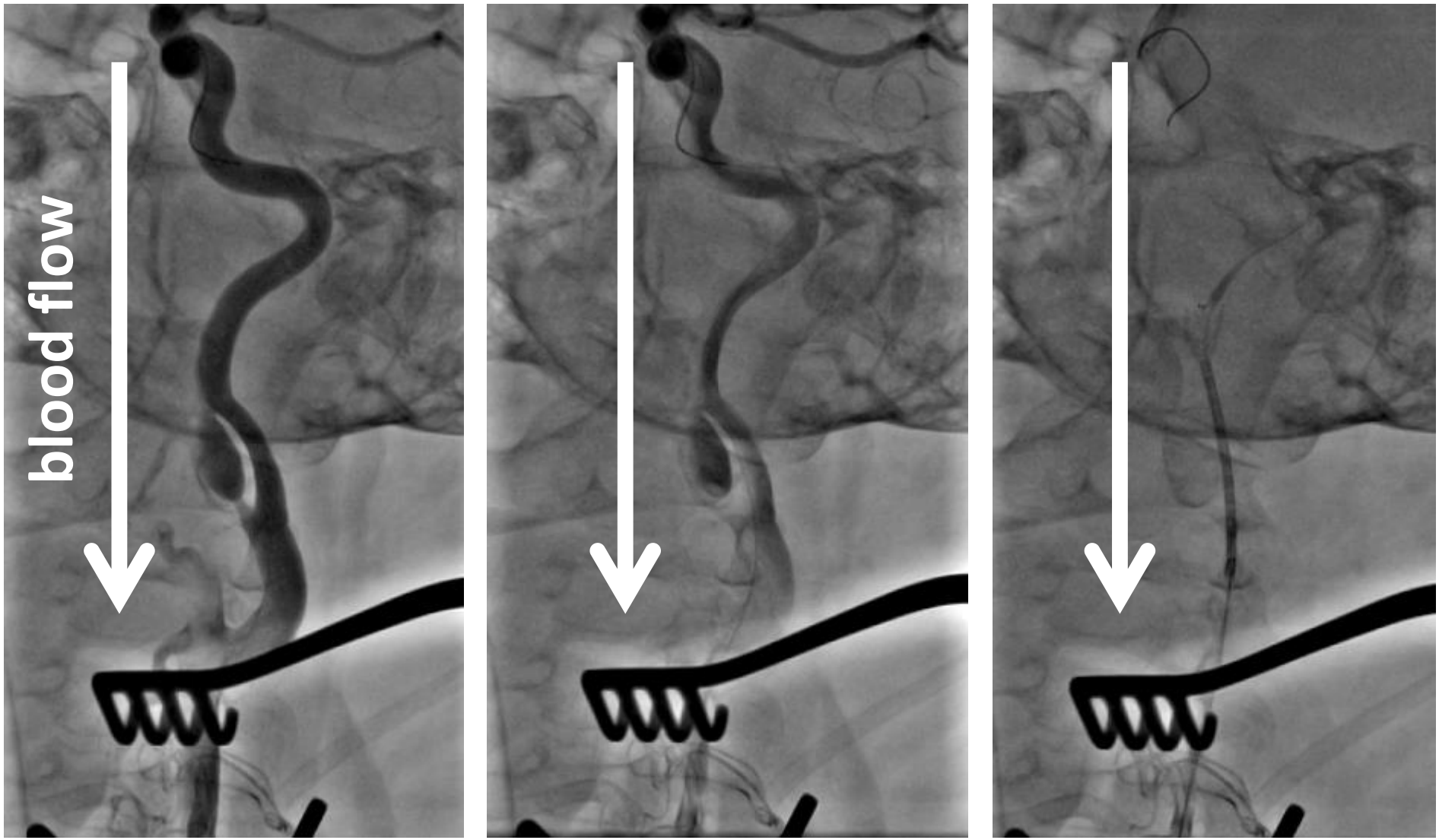
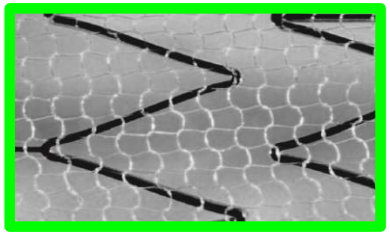
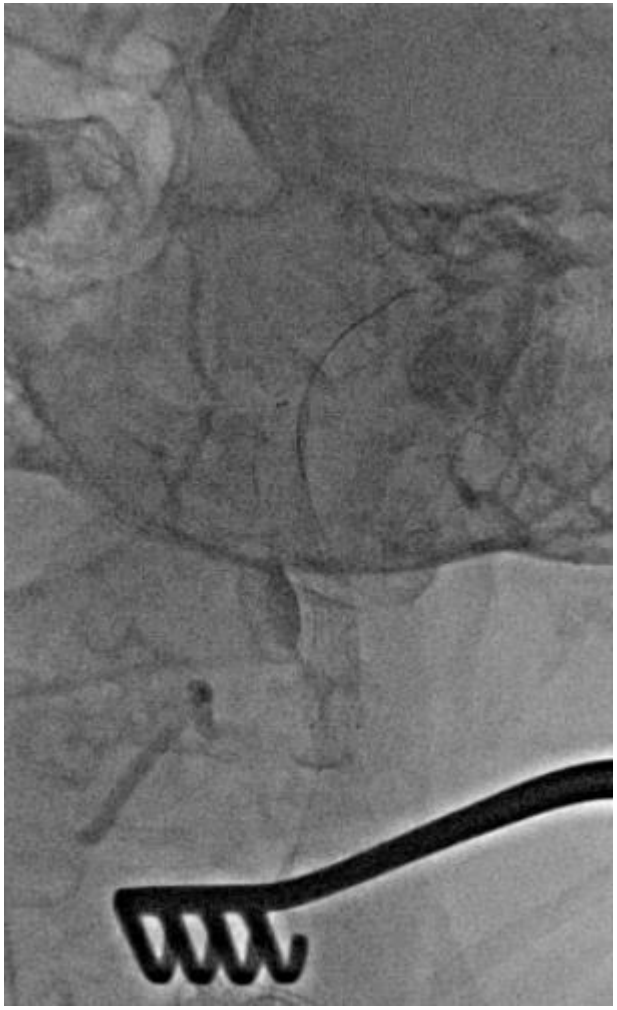
F
329612440S
329612440S
CARD HDR
Scenes
Reports
REF
2019-02-26 10:13:53
A: LAO 33.4 CRAN 1.3 [Plane A]
Scene: 8 of 24
Frame: 1 of 1
CARE Body.4
A
B
Scene
Frame
Plane
-30 -15 0 15 30
Apply To All
Auto
4094
WT
0
WB
P Musialek @ ICCA Stroke 2019
Apply To All
0
SF

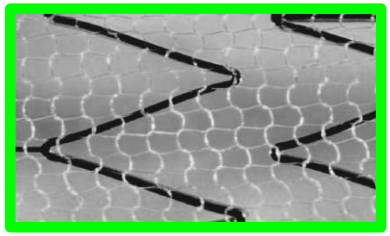



# ICA transient FLOW REVERSAL

(TCAR, EnRoute, SilkRoad)

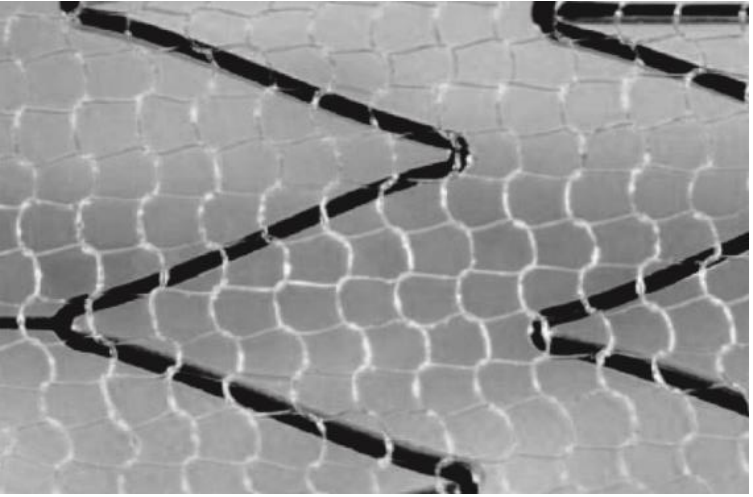


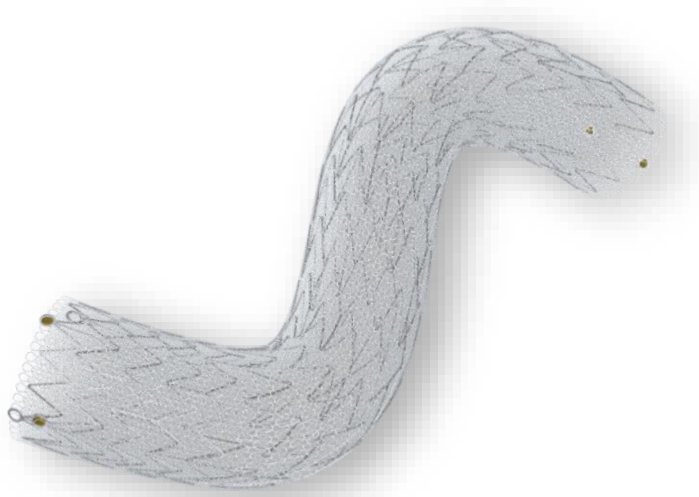


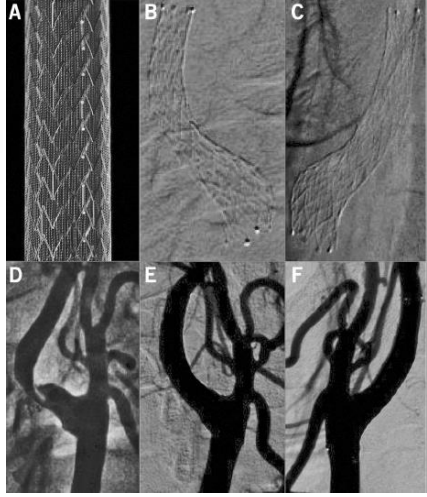


**next day CT angio**:
Aneurysm COMPLETELY excluded,
normal ICA reconstructed

Peri-procedural near-exclusion of the S aneurysm







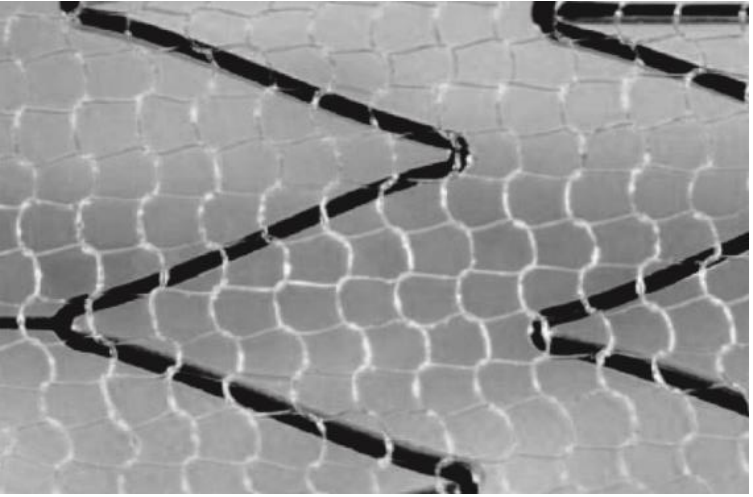

This concept has been desired.

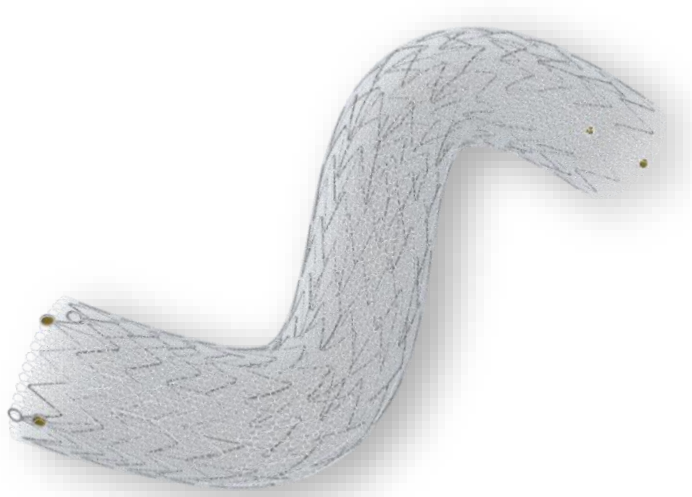
And it works.

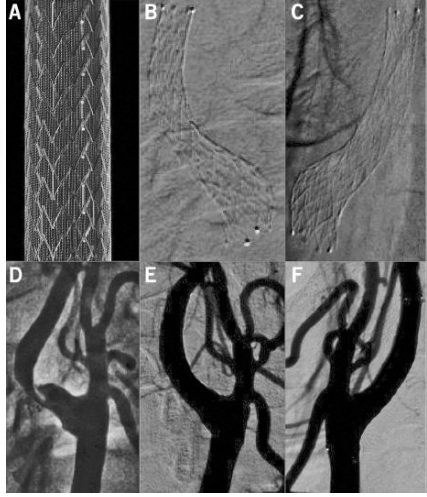
---

# This is the future

## of Carotid Artery ~~Stenting~~








This concept has been desired.

And it works.

---

This is the future

of Carotid Artery S[illegible]g

revascularization !

CGuard™ OCT

# One swallow does not a summer make but many swallows do: accumulating clinical evidence for nearly-eliminated peri-procedural and 30-day complications with mesh-covered stents transforms the carotid revascularisation field

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[2]Departments of Neurosurgery and Radiology, School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, Jacobs Institute, Gates Vascular Institute Kaleida Health, Buffalo, New York, USA

Adv Interv Cardiol 2017; 13, 2 (48): 95–106
DOI: https://doi.org/10.5114/pwki.2017.69012

## Abstract

Atherosclerotic carotid artery stenosis (CS) continues to be a common cause of acute ischaemic stroke. Optimised medical therapy (OMT), the first-line treatment modality in CS, may reduce or delay – but it does not abolish – CS-related strokes. As per current AHA/ASA and ESC/ESVS/ESO guidelines, carotid artery stenting (CAS) is a less-invasive alternative to carotid endarterectomy (CEA) for CS revascularisation in primary and secondary stroke prevention.

Ten-year follow-up from the CREST trial in patients with symptomatic and asymptomatic CS confirmed equipoise of CAS and CEA in the primary endpoint. Nevertheless CAS – using a widely open-cell, first-generation stent and first-generation (distal/filter) neuroprotection – has been criticised for its relative excess of (mostly minor) strokes by 30 days, a significant proportion of which were post-procedural.

Atherosclerotic plaque protrusion through conventional carotid stent struts, confirmed on intravascular imaging, has been implicated as a leading mechanism of the relative excess of strokes with CAS vs. CEA, including delayed strokes with CAS. Different designs of mesh-covered carotid stents have been developed to prevent plaque prolapse. Several multi-centre/multi-specialty clinical studies with CGurad MicroNet-Covered Embolic Prevention Stent System (EPS) and RoadSaver/Casper were recently published and included routine DW-MRI cerebral imaging peri-procedurally and at 30 days (CGuard EPS).

Data from more than 550 patients in mesh-covered carotid stent clinical studies to-date show an overall 30-day complication rate of ~1% with near-elimination of post-procedural events. While more (and long-term) evidence is still anticipated, these results – taken together with optimised intra-procedural neuroprotection in CAS (increased use of proximal systems including trans-carotid dynamic flow reversal) and the positive 12-month mesh-covered stent data reports in 2017 – are transforming the carotid revascularisation field today.

Establishing effective algorithms to identify the asymptomatic subjects at stroke risk despite OMT, and large-scale studies with mesh-covered stents including long-term clinical and duplex ultrasound outcomes, are the next major goals.

**Key words:** carotid artery stenting, mesh, stroke, endarterectomy, neuroprotection.