

»Double protection with the new generation of Paladin - Neuroform«

Sasko Kedev

Skopje, Macedonia

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

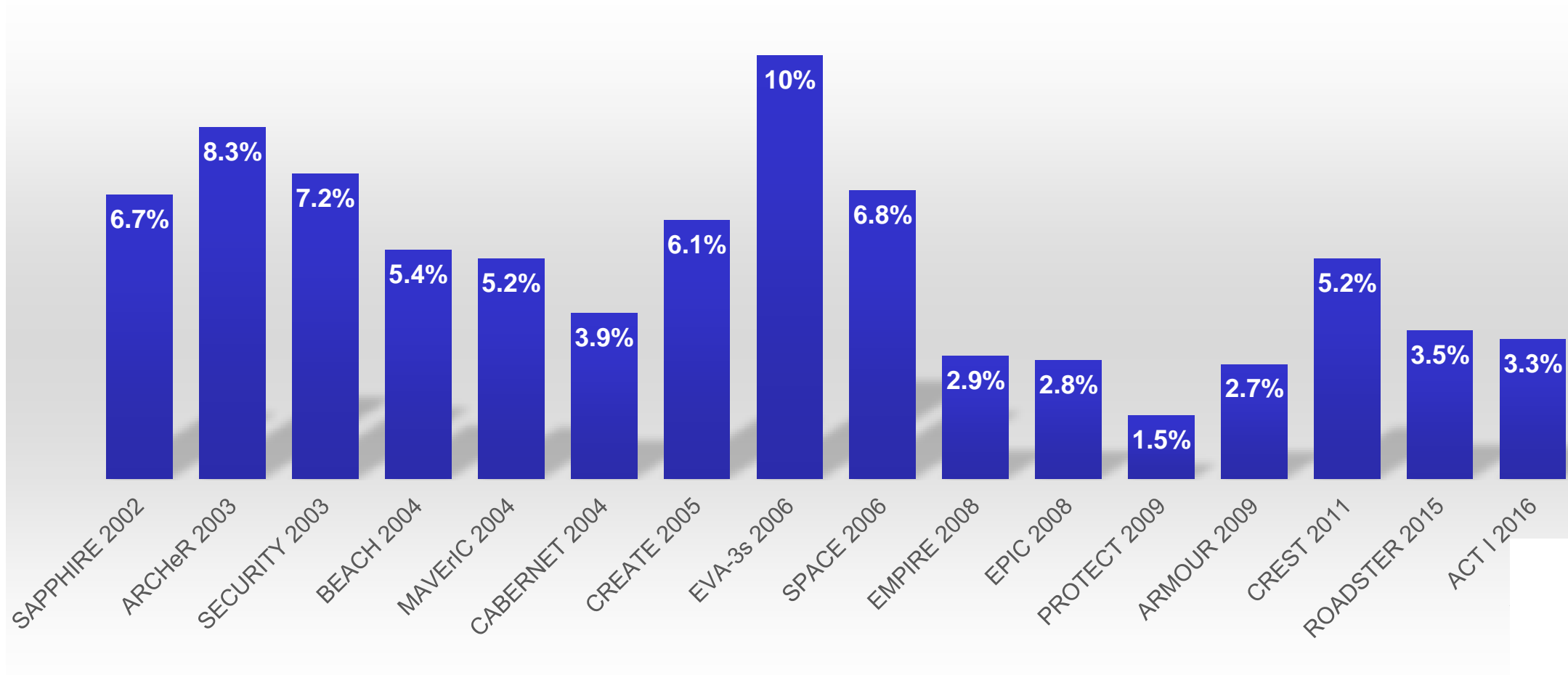
- Consulting Fees/Honoraria

COMPANY

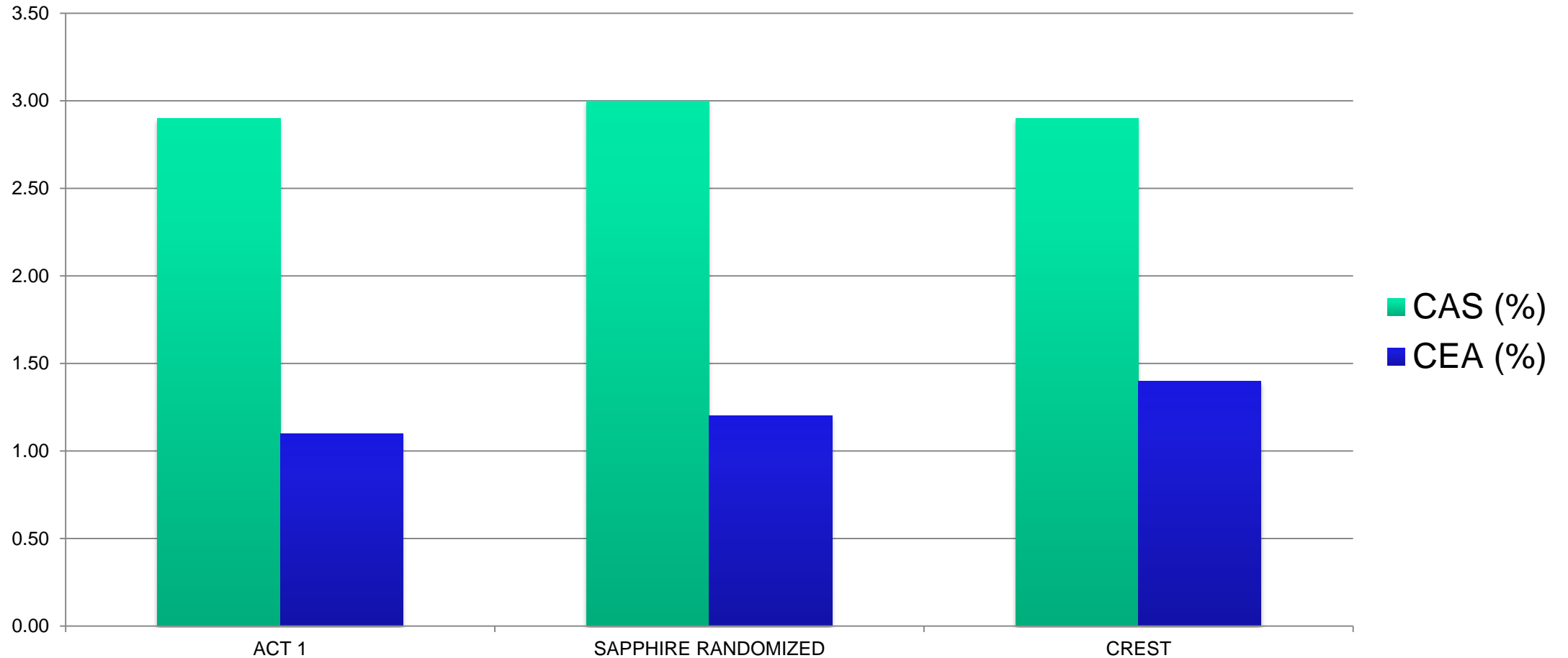
- Medtronic
- Boston Scientific
- Terumo
- Contego

Results of carotid stenting continue to improve

30-Day MAE defined as death, stroke or MI



But, minor stroke during CAS remains an unsolved issue



When do strokes occur during carotid artery stenting?

- A significant number of strokes occurs during post-dilation
- During this phase the stent is pushed up against the plaque at high pressure, resulting in a massive release of macro and micro-embolic particles
- Studies with **proximal** protection using standard carotid stents show a very low risk of procedural and late stroke¹
- This indicates that the majority of the risk of stroke is due to inadequate embolic protection during the index CAS procedure when performed with distal filtration

¹ Hornung M, Bertog SC, Franke J, Id D, Grunwald I, Sievert H. Evaluation of proximal protection devices during carotid artery stenting as the first choice for embolic protection. EuroIntervention. 2015 Mar;10(11):1362-7

The Problem:

- Significant portion of the risk of stroke during CAS occurs due to micro-embolic debris reaching the brain during post-dilation
- Increasing the degree of protection during this phase would be clinically beneficial
- A novel balloon catheter with an integrated filter could help capture micro-emboli and thereby reduce the risk of stroke

The Solution:

Integrated Embolic Protection (IEP)TM

- Integrated Filter:
- 40 Micron pores
 - Baseline closed
 - Sheathless



Angioplasty
Balloon

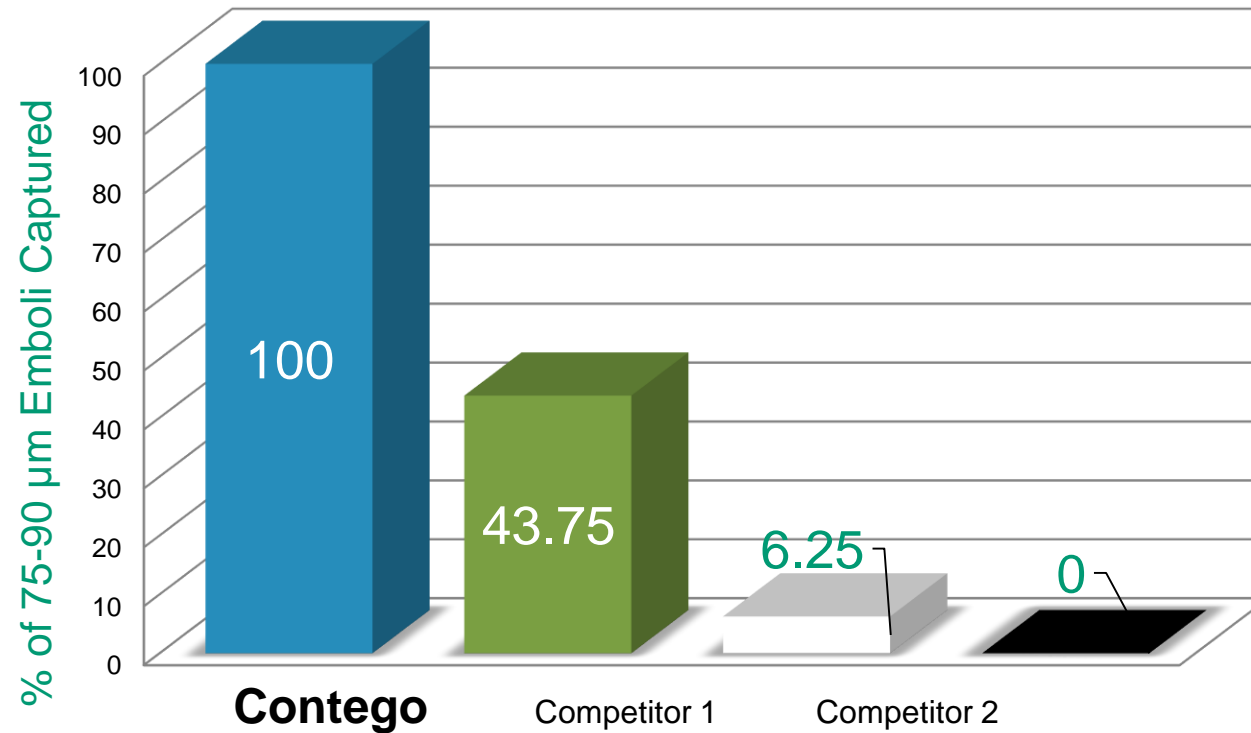
Catheter

- ✓ The first device that combines an embolic protection filter and balloon
- ✓ 40 micron pore size allows micro-embolic capture
- ✓ Filter size can be adjusted to suit each patient's unique anatomy

Paladin System Features

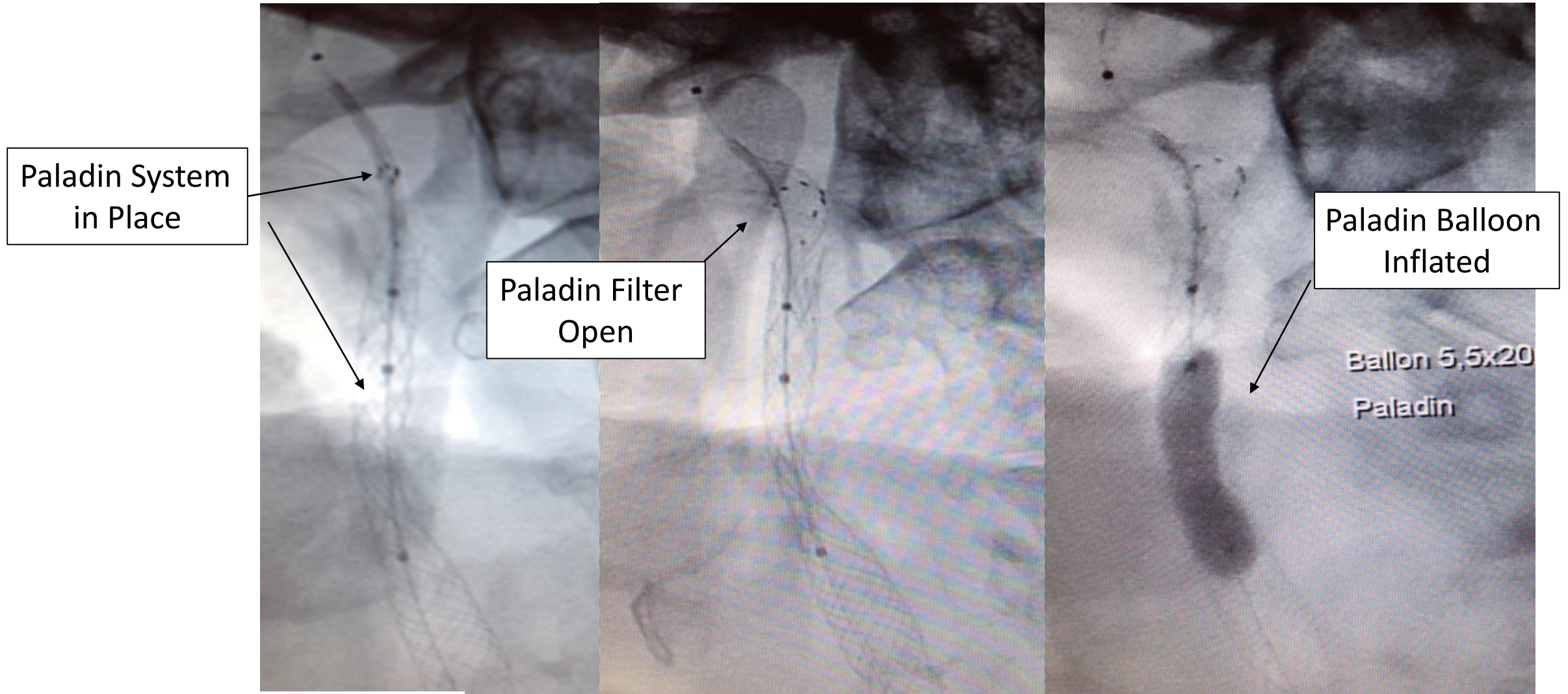
Delivery System	5F Rapid Exchange
Guidewire compatibility	0.014"
Balloon Sizes	Diameter: 5.0 mm – 5.5 mm Length: 20 mm – 30 mm
Filter membrane pore size	40 microns
Catheter length	140 cm

The Contego Filter has the Highest Capture Efficiency of 4 Embolic Filters Tested



Contego filter captured 100% of 75-90 µm embolic particles

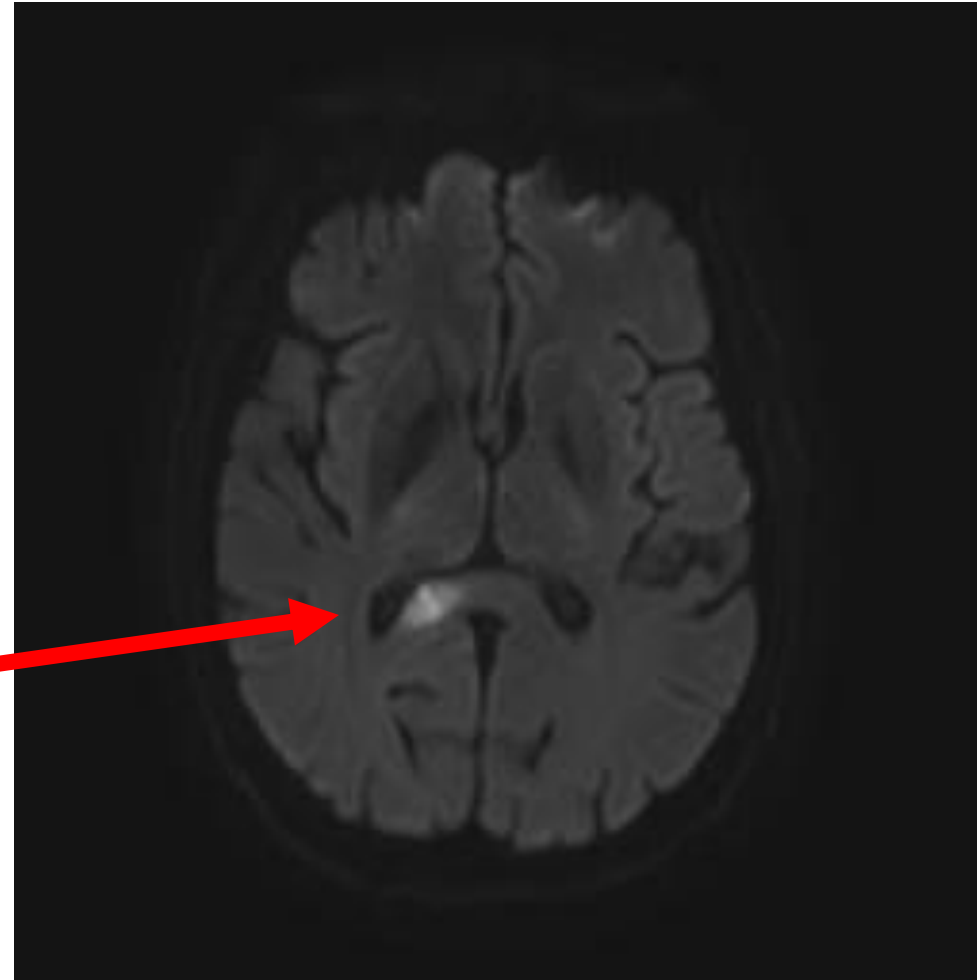
Paladin System



Case Study: Same Patient Undergoing Bilateral Carotid Stenting

Right Carotid Stent
Procedure Done
Without Contego
Technology:

2 cm Stroke on MRI at 48
hours post-procedure



Left Carotid Stent
Procedure Done
With Contego
Technology:

No Stroke on MRI at 48
hours post-procedure

The PALADIN Study

- Objective: To evaluate the procedural safety and technical success of the Paladin System in subjects with carotid artery stenosis
- Co-Principle Investigators: **Profs. Horst Sievert and Thomas Zeller**

5 Sites in Germany:

- Universitätsklinikum Leipzig, Leipzig, **Prof. Dierk Scheinert**
- Cardiovasculäres Centrum, Frankfurt, **Prof. Horst Sievert**
- Mathey Schofer Clinic, Cardiovascular Center Hamburg, **Prof. Joachim Schofer**
- Universitäts Herzzentrum-Bad Krozingen, Freiberg, **Prof. Thomas Zeller**
- Sankt Gertrauden-Krankenhaus, Berlin, **Dr. Ralf Langhoff**

PALADIN Study

Study Population

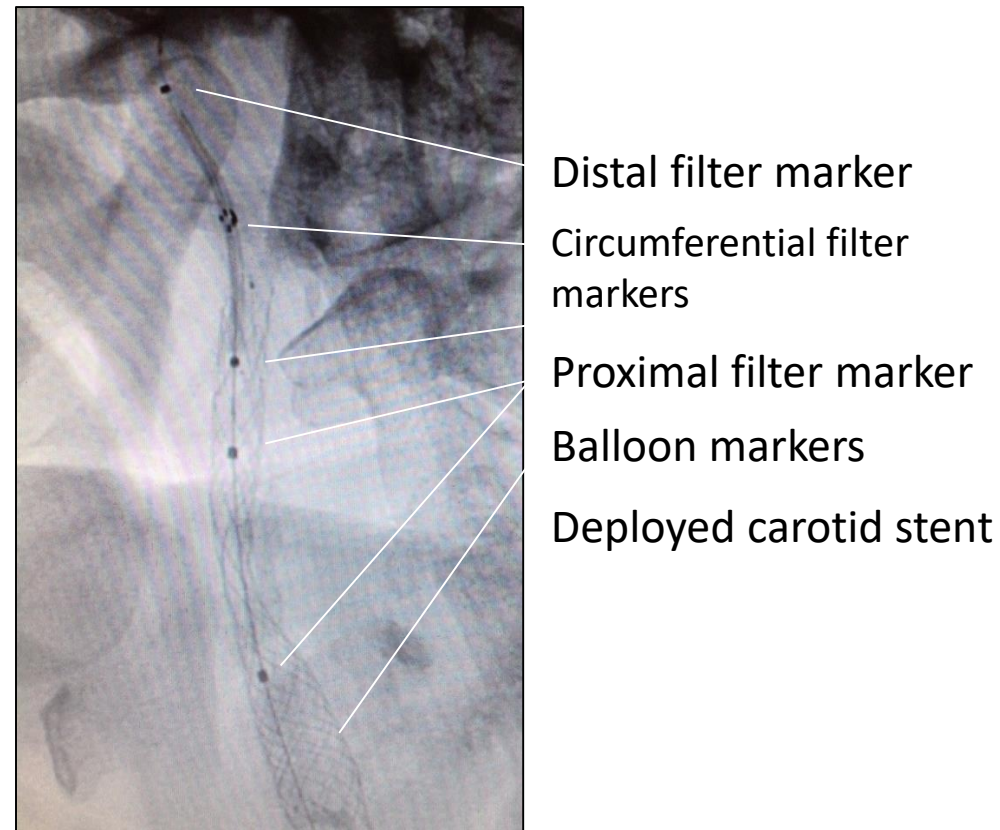
- Symptomatic patients with carotid stenosis $\geq 50\%$ by angiography
 - history of ipsilateral TIA, stroke or amaurosis fugax within the past 6 months
- Asymptomatic patients with carotid stenosis $\geq 70\%$ by angiography

Primary Endpoints

- Acute technical success
- 30 day (neurological death and stroke)

Carotid Stenting Procedure

- Pre-Dilation at discretion of the operator
- Carotid stenting performed with commercially available carotid stents
- Distal filter used in all cases
- Paladin System used for post-dilation in all patients



Detail of the Paladin System shown following post-dilation of a self-expanding stent. The filter is collapsed and the balloon deflated. *Images courtesy of Dr. R. Langhoff, Sankt-Gertrauden-Krankenhaus, Berlin, Germany*

Baseline Patients Characteristics

Demographics (n=106)	%	
Age	70 ± 8.3	
Male sex	74.5	(79)
Symptomatic	19.8	(21)
Current smoker	34.0	(36)
Previous myocardial infarction	11.3	(12)
History of CABG	9.4	(10)
Hyperlipidemia	83.3	(83)
Hypertension	82.1	(87)
History of neck radiation	5.7	(6)
History of peripheral vascular disease	36.8	(39)
History of CEA	15.1	(16)
Diabetes	36.3	(37)

Stents Used

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

Procedural Results

n=106

Characteristic	N	%
Procedure success	106/106	100
Target vessel		
Left ICA	46/106	43.1
Right ICA	50/106	56.9
Distal Embolic Protection	99/106	93.4
Proximal Embolic Protection	7/106	6.6
Pre-dilation performed	45/106	42.5
Post-dilation performed with the Paladin System	106/106	100

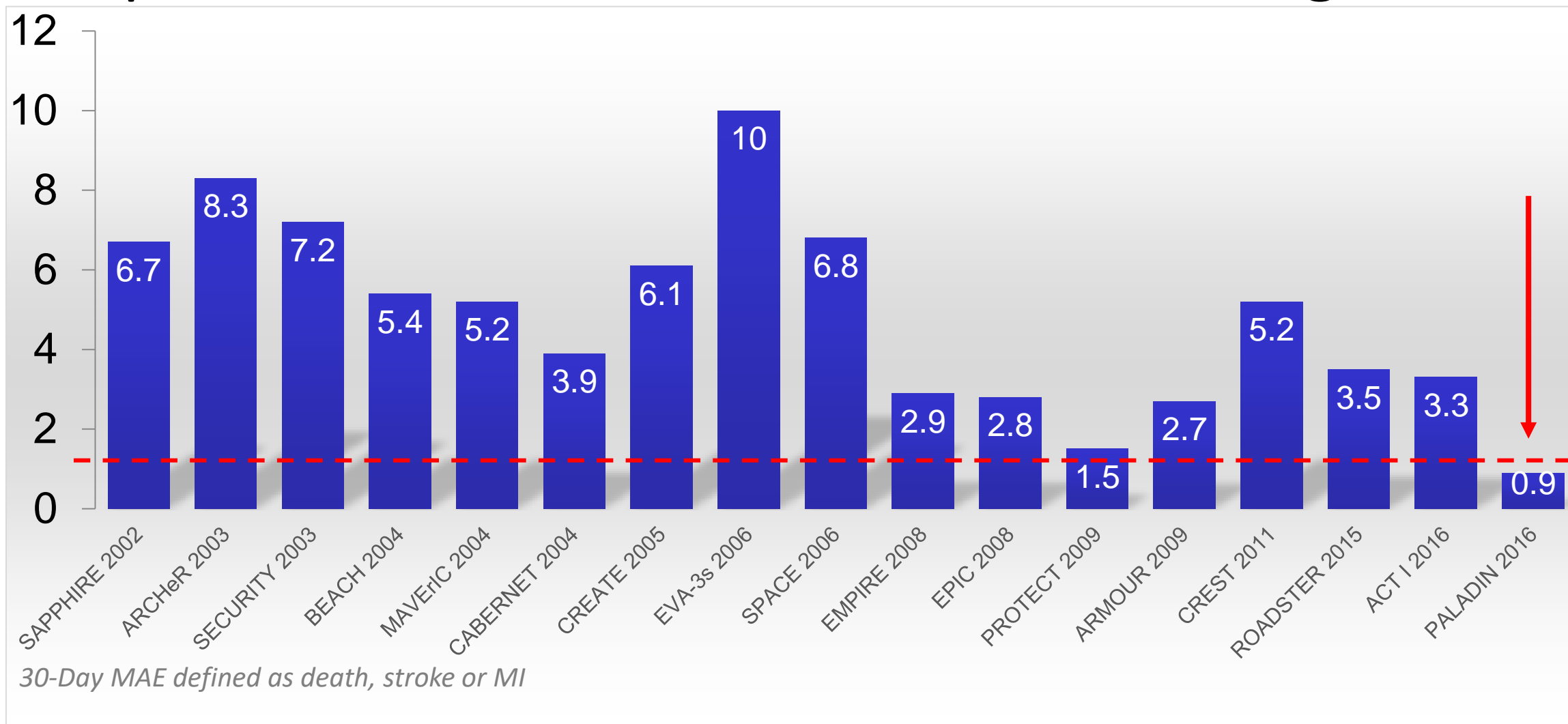
Clinical Outcome

PALADIN Registry	
Post-Procedural and 30-Day Outcomes	% (N/105 ¹)
Stroke, Death and MI	0.95 (1)
Death	0
Stroke	0.95 (1)
Myocardial Infarction	0
Stroke and Death	0.95 (1)

- 106 patients
- Technical success 99%
- No Deaths, strokes, MI or other Major Adverse Events (MAE) through discharge
- **1 stroke at day 12 due to stent thrombosis of a mesh-covered stent**

¹ Of the 106 subjects enrolled, one (1) subject withdrew consent following discharge, and 105 were eligible for follow up at 30 days.
This patient had no neurological events

Using PALADIN, clinical outcome was superior compared to almost all other carotid stenting studies



30-Day MAE defined as death, stroke or MI

Prospective multi-center studies with >100 patients

DW-MRI Results

Subgroup of 39 patients

Pre and post carotid stenting MRI performed in 33/39 patients

Procedural characteristics	N (%)
De novo lesions	39 (100)
Distal filter-based embolic protection device	39 (100)
Pre-dilation performed	5 (12.8)
Stent deployed	
Xact (Abbott Vascular)	34 (87.2)
Protégé (Covidien)	3 (7.7)
Cristallo Ideale (Medtronic)	2 (5.1)
Peri-procedural neurological events	0 (0)

Demographics, co-morbidities	
Age (year)	70 ± 9 years
Male sex	61.5 %
Symptomatic	17.9 %
Hypertension	94.9
Current smoker	7.7

DW-MRI Results from a Single Center

DW-MRI performed in 33 patients (84%)

# of subjects with new ischemic lesions	7
% of subjects with new ischemic lesions	21.2%
Total number of new ischemic lesions	8*
Mean Lesion Volume – Only patients with new lesions	0.024 cm ³
Mean Lesion Volume – All Patients	0.005 cm ³

* 2 lesions were one patient, and a single lesion was observed in the remaining 6 patients.

DW-MRI Results from a Single Center

8 new ischemic lesions in 7 subjects treated with Xact stent

Patient Number	Lesion Number	Stent Used	Individual lesion volume (cm ³)
1	1	Xact	0.029
2	2	Xact	0.022
3	3, 4	Xact	0.01 and 0.027*
4	5	Xact	0.018
5	6	Xact	0.017
6	7	Xact	0.024
7	8	Xact	0.011

* 2 lesions were one patient, and a single lesion was observed in the remaining 7 patients.

Data courtesy Joachim Schofer MD et al.

Using PALADIN, DW-MRI showed less and smaller lesions compared to other technologies

(Subgroup of 33 patients)

Comparative DW-MRI Results	Paladin (n=33)	PROFI ¹ Proximal group (n=31)	PROFI ¹ Filter group (n=31)	ICSS ² Filter group (n=37)	CARENET ³ CGuard (n=26)
Incidence of New Lesions	21.2%	45%	87%	73%	48%
Mean number of lesions per pt.	0.24	1.0 +/- 1.4	3.6 +/- 3.2		
Mean Lesion Volume (cm ³)	0.005	0.16	0.59	NA	0.05

Data courtesy Joachim Schofer MD et al.

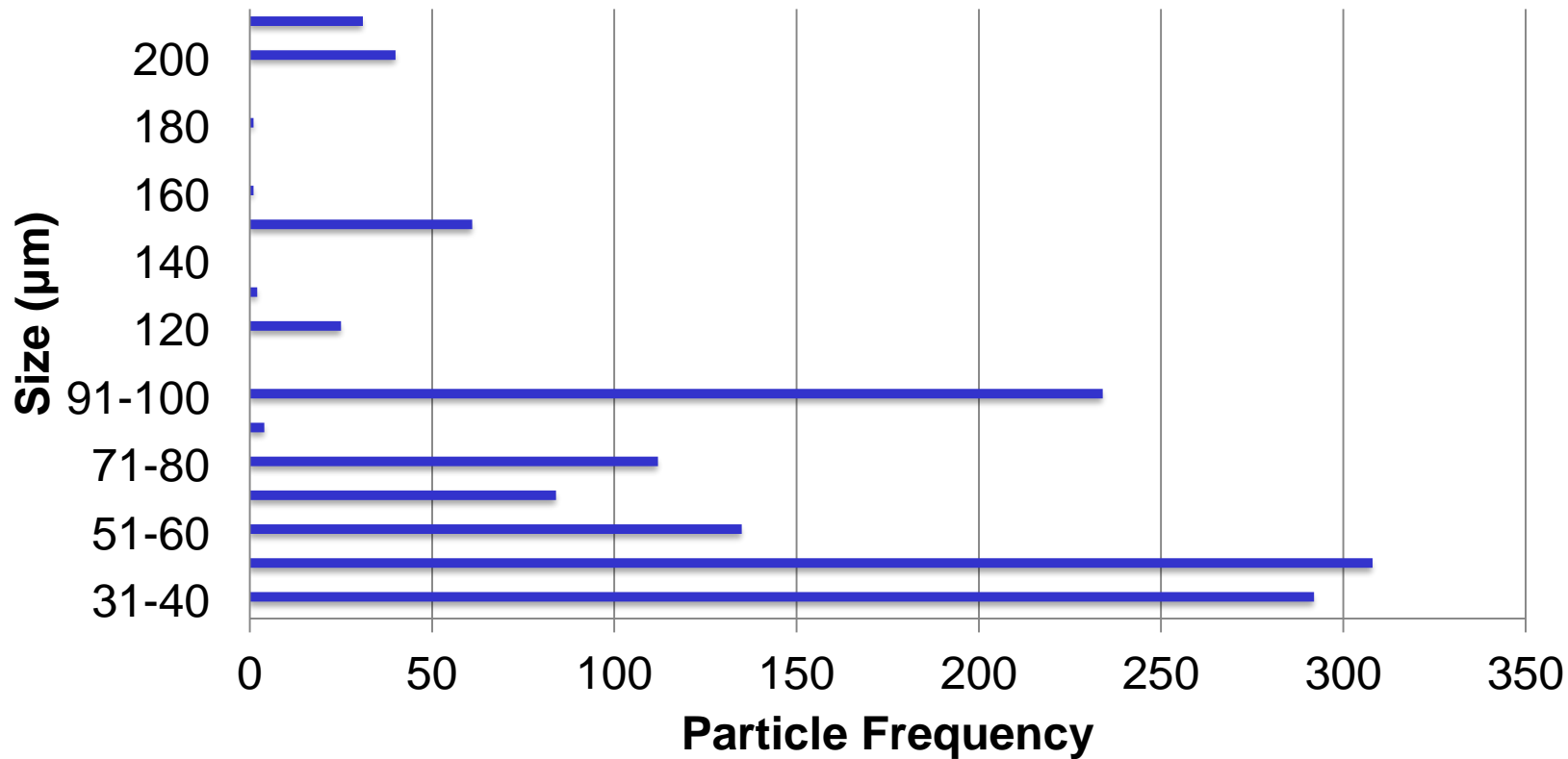
¹ Bijuklic K, Wandler A, Hazizi F, Schofer J. The PROFi Study. JACC 2012 Apr 10;59(15):1383-9.

² Bonati LH, et al, ISCC-MRI Study group. New ischaemic brain lesions on MRI after stenting or CEA for symptomatic carotid stenosis: a substudy of ICSS. Lancet Neurol. 2010 Apr;9(4):353-62.

³ Schofer J, Musialek P, Bijuklic K, Kolvenbach R, Trystula M, Siudak Z, Sievert H. The CGuard CARENET Trial. JACC Cardiovas Interv. 2015 Aug 17;8(9):1299-34.

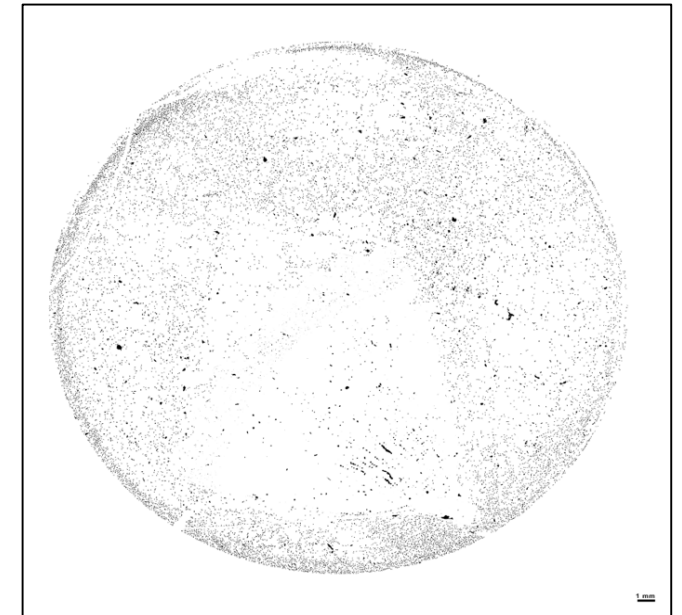
Filter Histological Analysis: Particle Size

Subgroup of 23 patients. Paladin and primary EPD filter



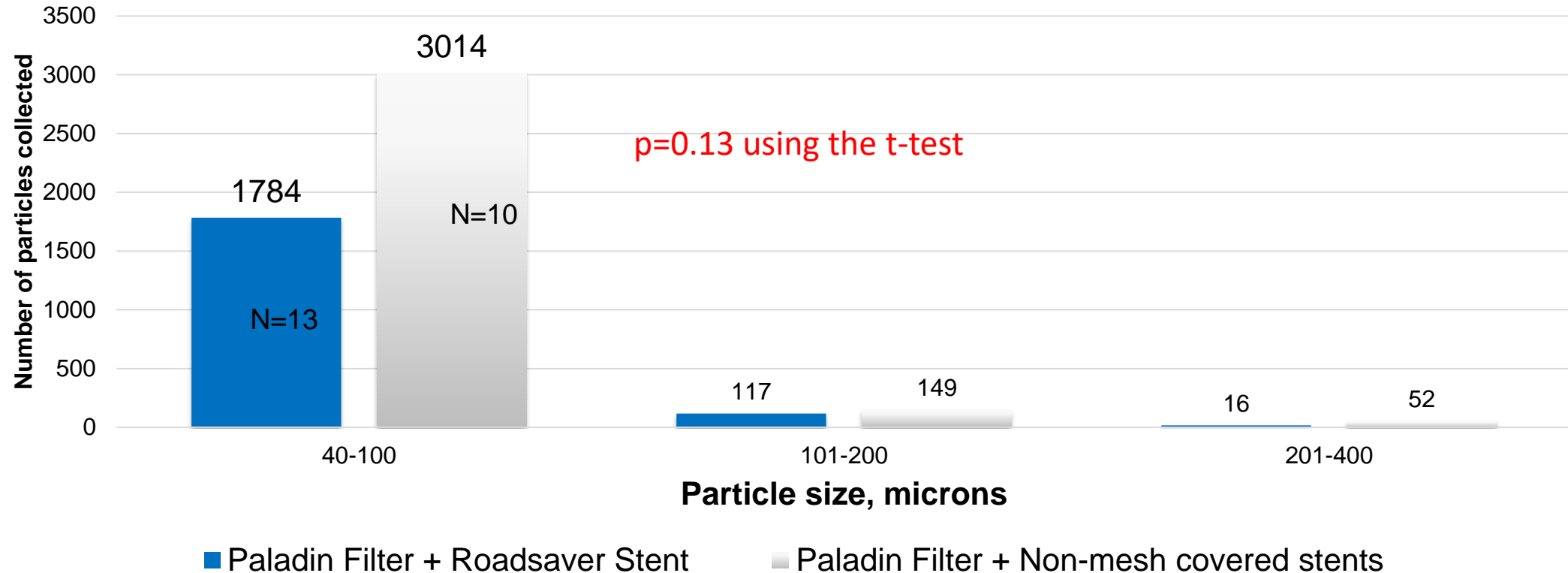
>90% of particles captured were less than 100 microns in size

*Asymptomatic patient, Wallstent
5.0 x 20 mm Paladin System
used for post dilation*



*Scan of particles collected in **Paladin** filter*

The use of PALADIN resulted in an additional benefit even when mesh-covered stents were used



Large number of micro-emboli captured in both mesh-covered and non-mesh covered carotid stents

Paladin Filter Analysis in patients Receiving Mesh Covered Stents

Roadsaver Stent n=25	
Symptomatic	25 (100%)
Sheath 5F	4(16%)
Sheath 6F	21(84%)
30 day MAE rate	0%
Mean # of particles/filter	3352
Mean # particles/filter 40-100µm	2499
Mean # particles/filter 100-200µm	267
Mean # particles/filter 200-400µm	48

RRA CAS of LICA in symptomatic patient

- Triple protection

K.P.

Male

79 y.o

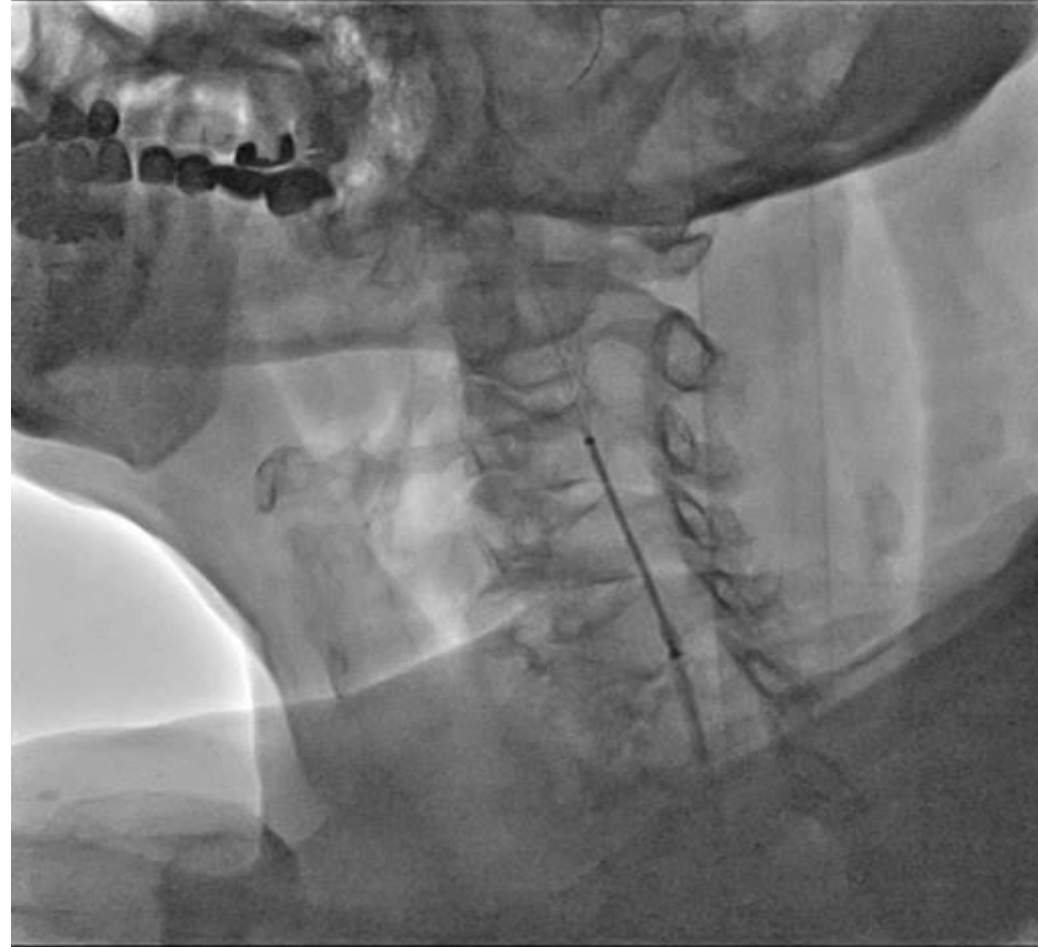
5F Destination: LICA 99%



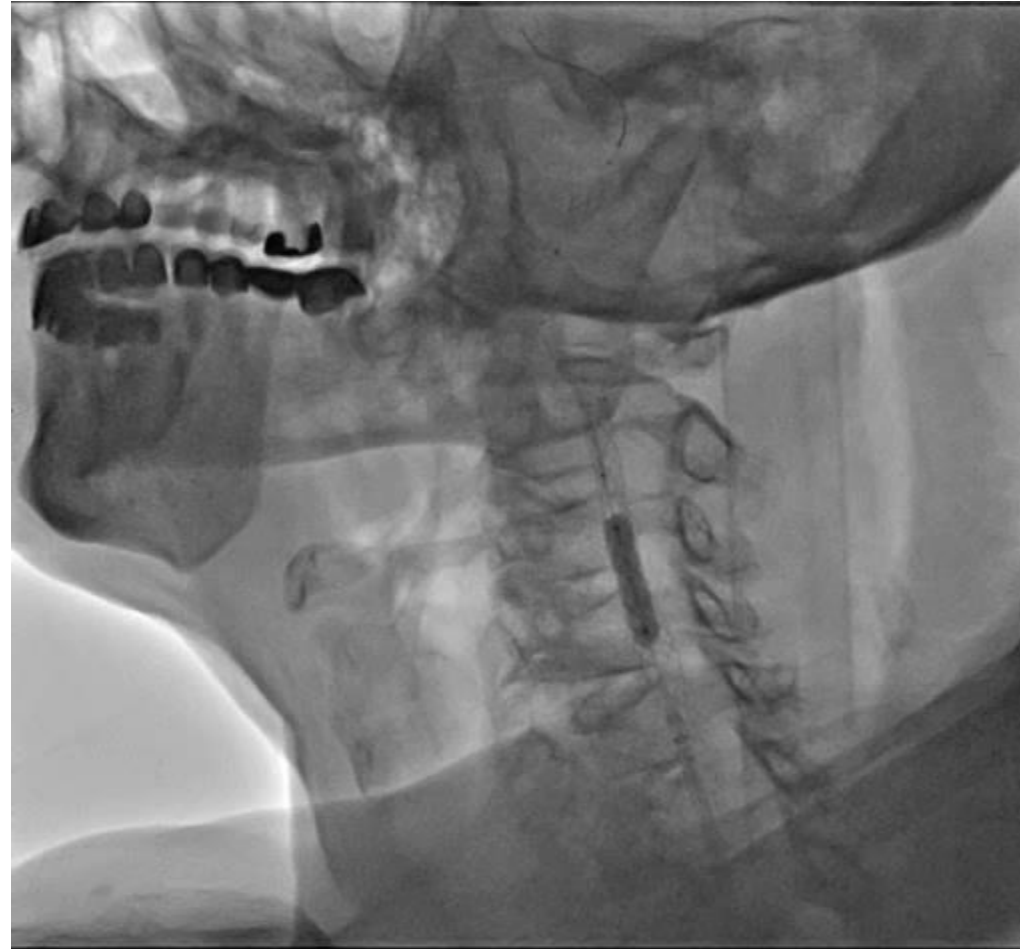
1. NAV 6



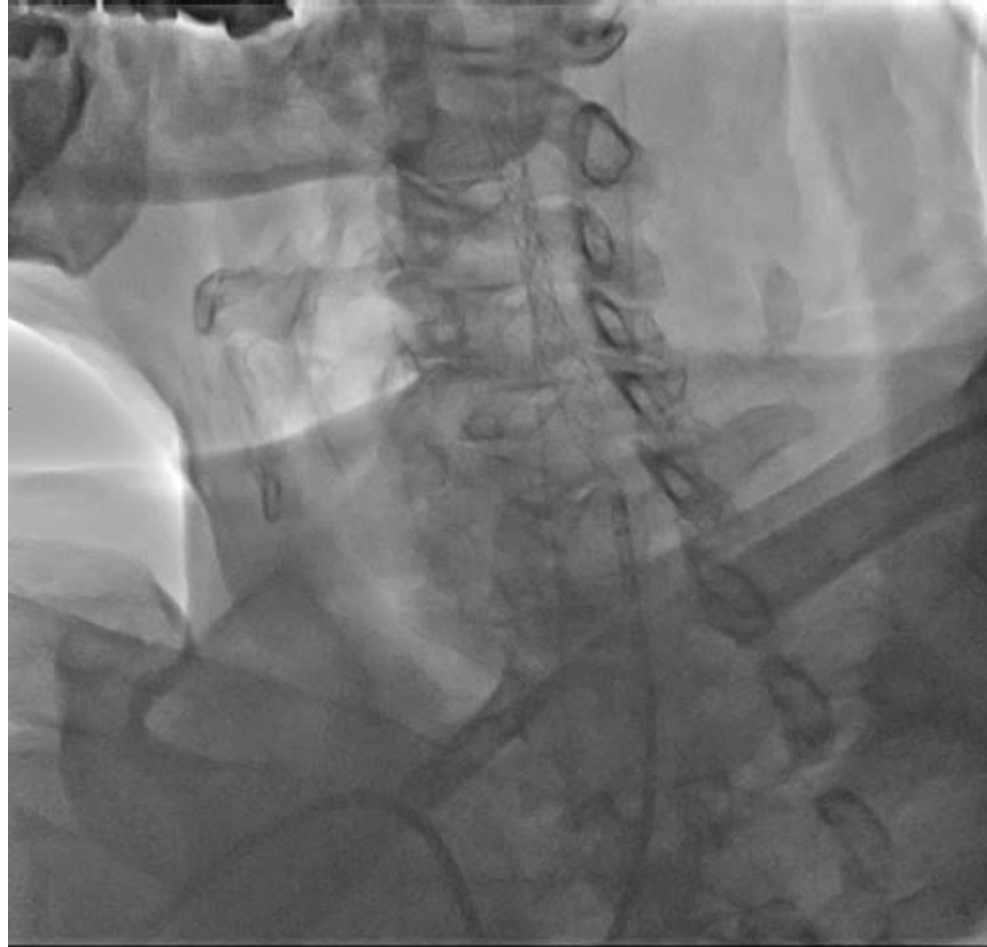
2. Stent: Roadsaver



3. Paladin system



Final result



Conclusions

- The majority of the risk of stroke appears to be due to micro-embolization during carotid stenting which is not caught by a single distal filter or prevented by any currently available stent
- The use of the Paladin System for post-dilation during carotid stenting in this PALADIN study resulted in zero procedural strokes
- The majority of particles caught in the Paladin filter were <100 microns, which are not caught by mesh-covered stents
- MRI results showed very low incidence and volume of new ischemic lesions
- *Use of the Paladin System appears to reduce the risk of stroke during carotid stenting independent of the type of stent used*