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Clinical, MRI, and histopathological data support double filtration during CAS using the Paladin IEP System

Horst Sievert,

Ilona Hofmann, Laura Vaskelyte, Sameer Gafoor, Stefan Bertog, Predrag Matić, Markus Reinartz,
Bojan Jovanovic, Kolja Sievert, Iris Grunwald, Nalan Schnelle

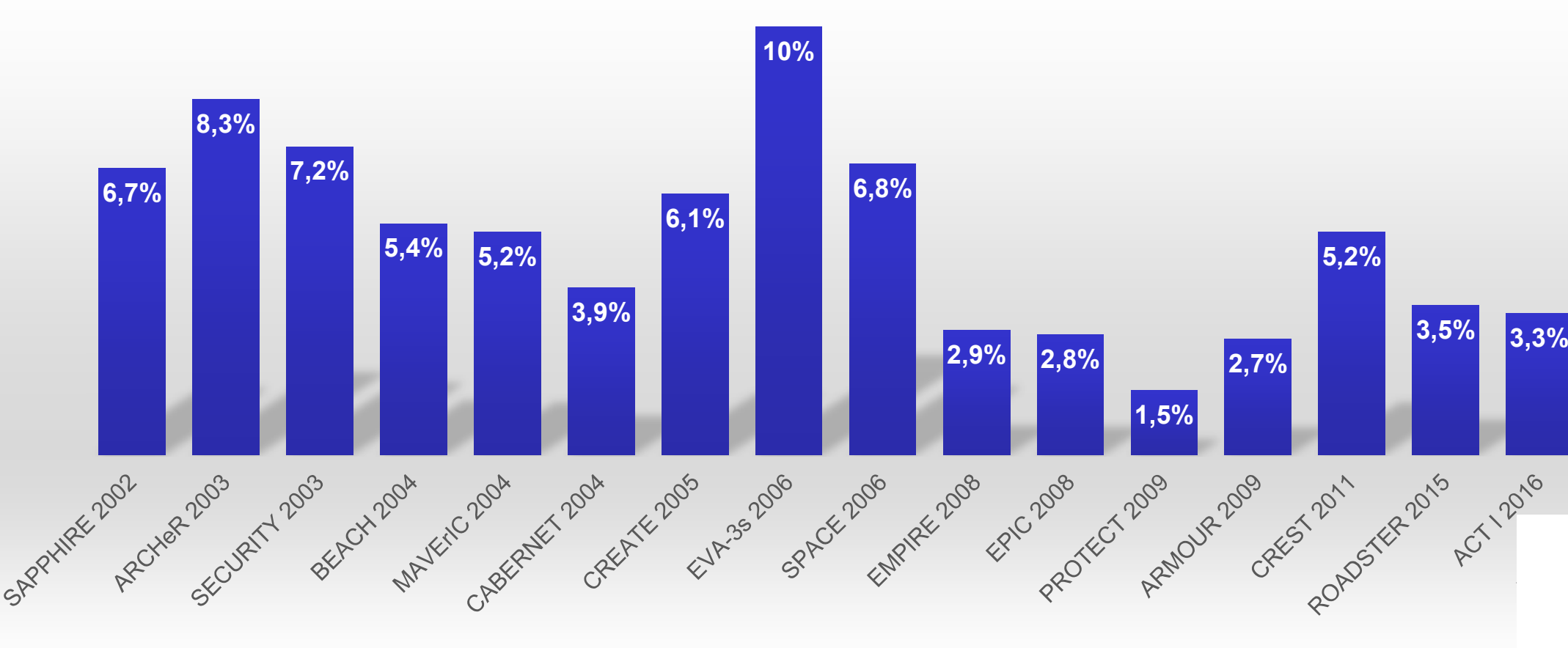
CardioVascular Center Frankfurt - CVC,
Frankfurt, Germany

Disclosures

Physician name	Company	Relationship
Horst Sievert	4tech Cardio, Abbott, Ablative Solutions, Ancora Heart, Bavaria Medizin Technologie GmbH, Bioventrix, Boston Scientific, Carag, Cardiac Dimensions, Celonova, Cibiem, CGuard, Comed B.V., Contego, CVRx, Edwards, Endologix, Hemoteq, InspireMD, Lifetech, Maquet Getinge Group, Medtronic, Mitralign, Nuomao Medtech, Occlutech, pfm Medical, Recor, Renal Guard, Rox Medical, Terumo, Vascular Dynamics, Vivasure Medical, Venus, Veryan	Consulting fees, Travel expenses, Study honoraria

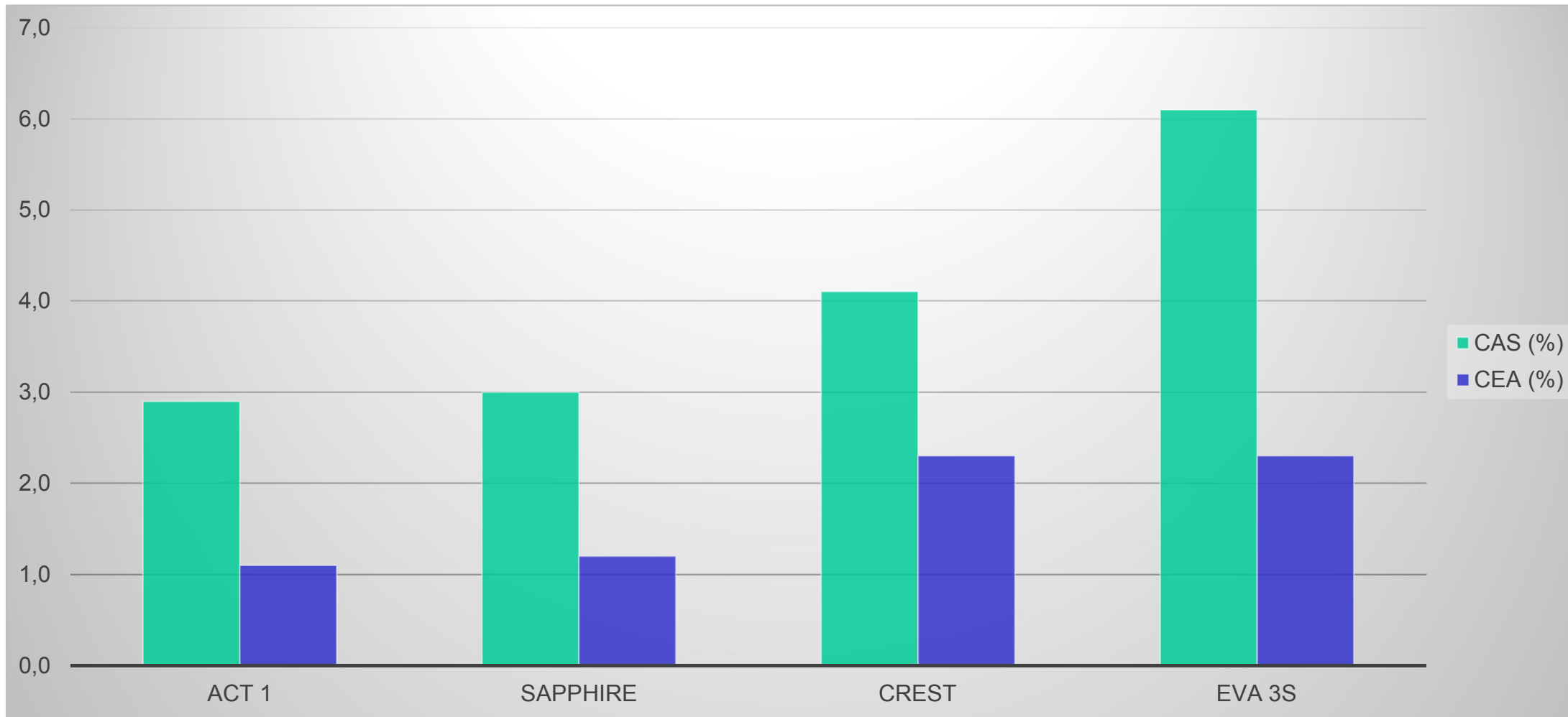
Results of carotid stenting continue to improve

30-Day MAE defined as death, stroke or MI



References available for individual study results
Prospective multi-center studies with >100 patients

But, minor stroke during carotid stenting
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

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



- ✓ 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



Paladin System



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**

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

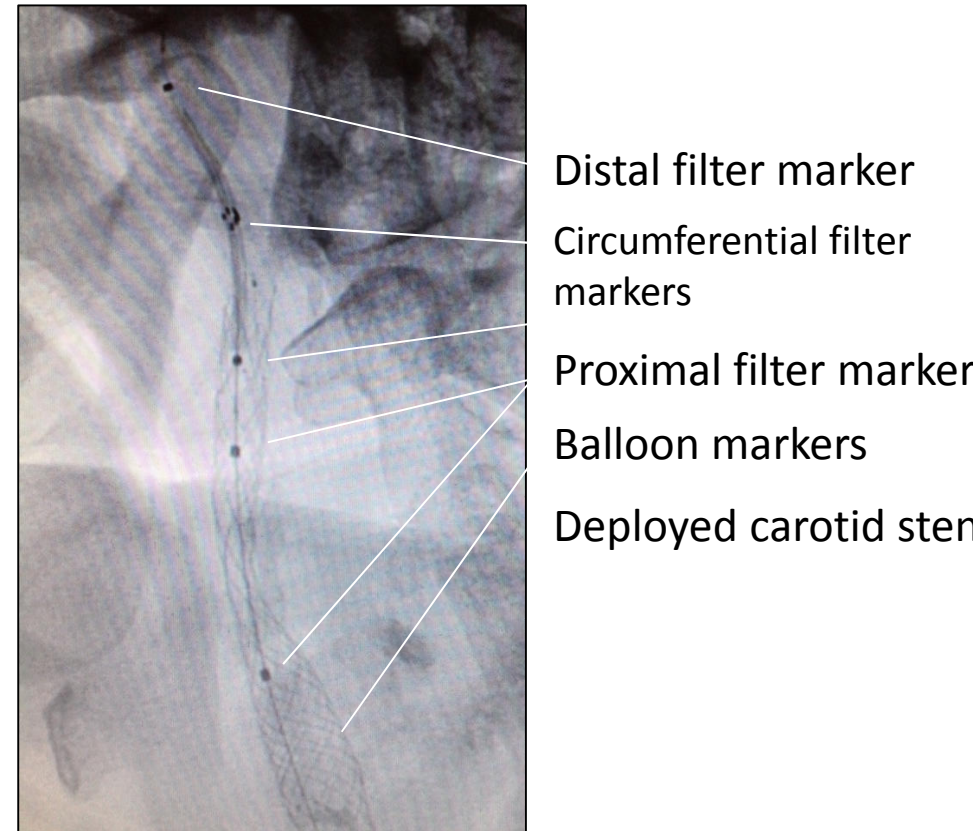
- Symptomatic patients with carotid stenosis $\geq 50\%$ by angiography
 - history of ipsilateral TIA, stroke or amaurosis fugax within the past 6 months
- Asymptomatic patients with carotid stenosis $\geq 70\%$ by angiography

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

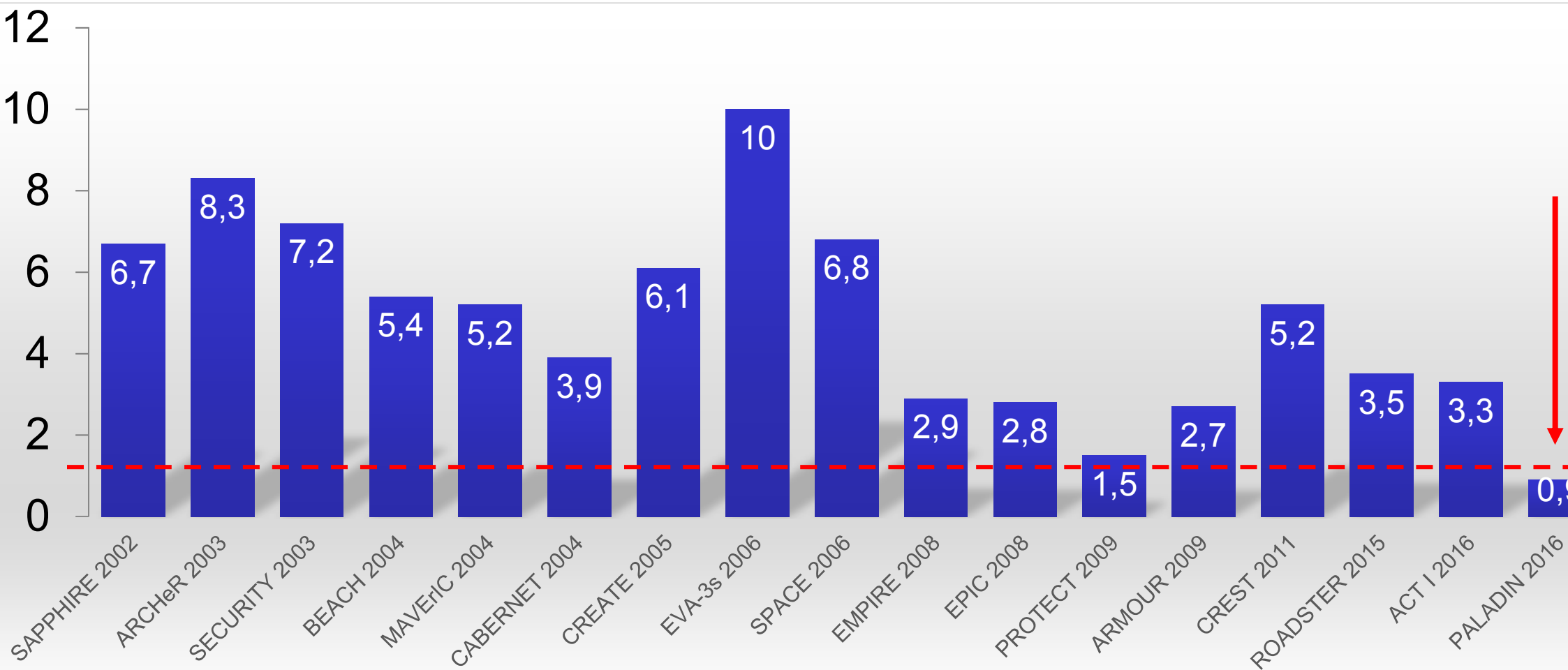
PALADIN Registry

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

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 CGuard (n=26)
Prevalence 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

courtesy Joachim Schofer MD et al.

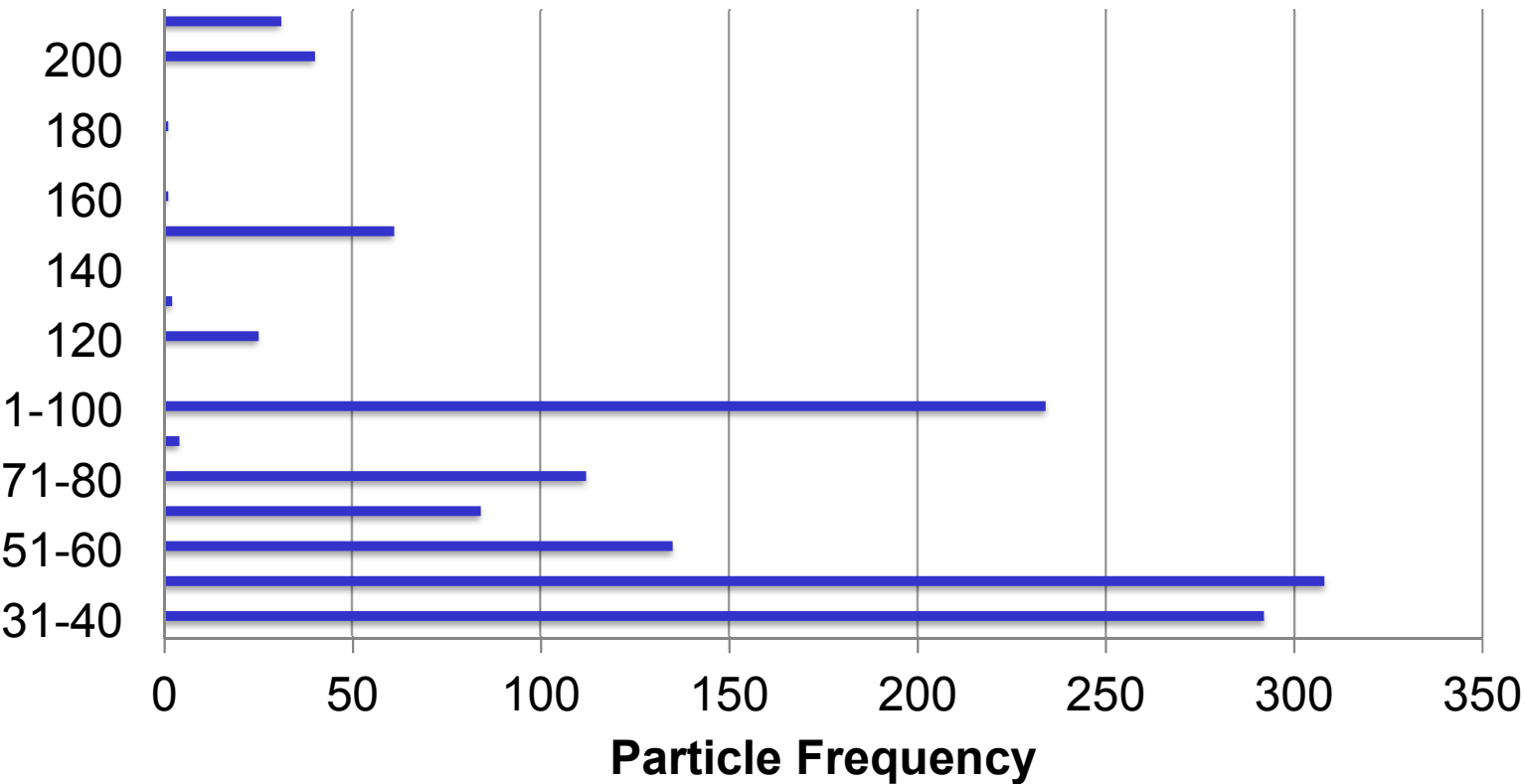
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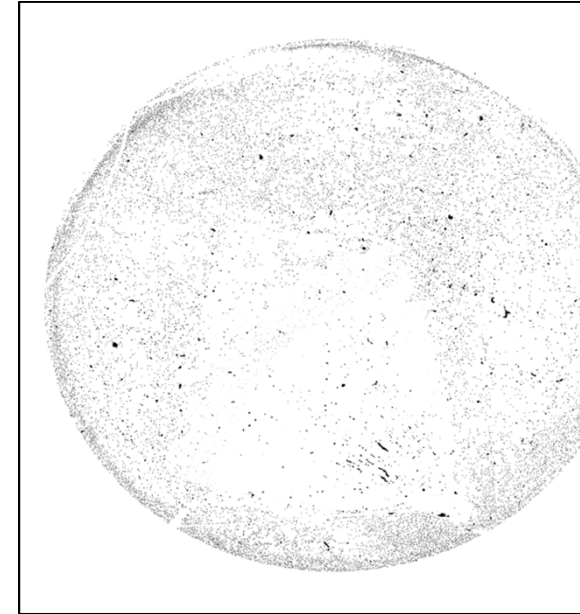
Filter Histological Analysis: Particle Size

Subgroup of 23 patients. Paladin and primary EPD filter



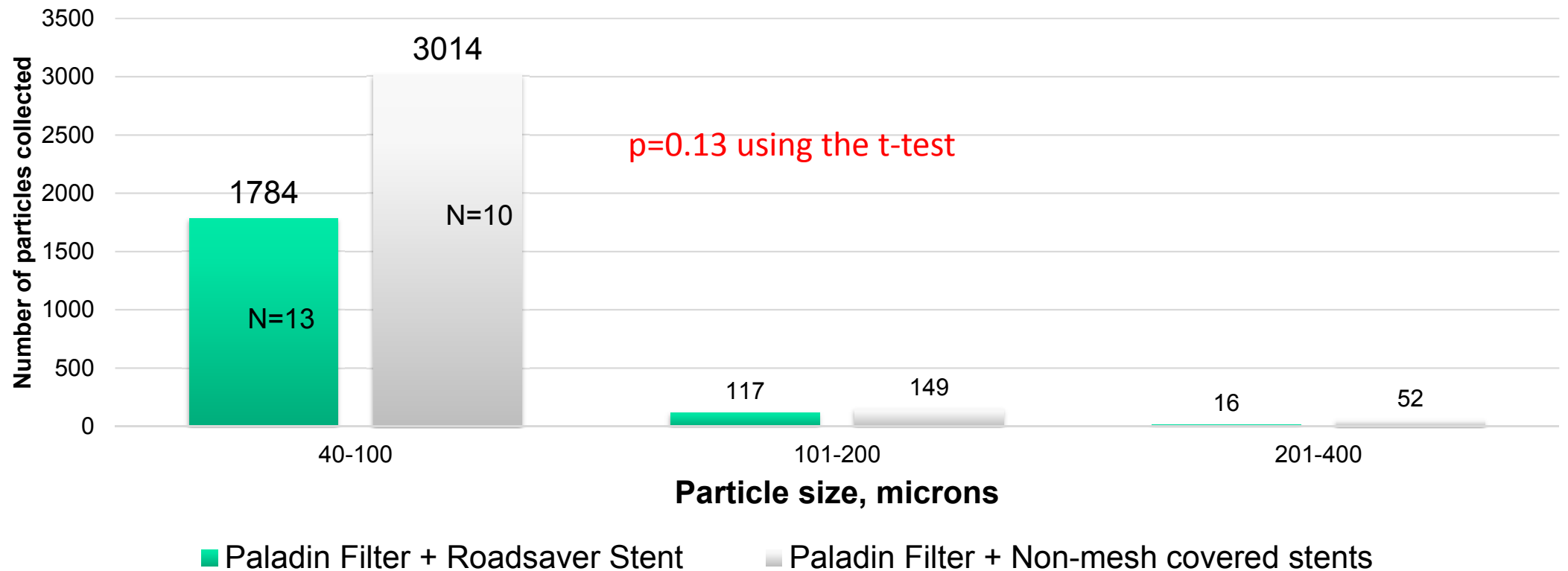
>90% of particles captured were less than 100 microns in size

*Asymptomatic patient, Wallste
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

Conclusions

- Minor stroke remains an unresolved issue during carotid stenting
- The majority of the risk of minor 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 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 problem of minor stroke during carotid stenting independent of the type of stent used*