CGuard™ MicroNET–covered embolic prevention system routine use in carotid revascularisation for stroke prevention: Accumulating clinical evidence

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Disclosure

Speaker name: Piotr Musialek

I have the following potential conflicts of interest to report:

✓ Consulting

☐ Employment in industry

☐ Stockholder of a healthcare company

☐ Owner of a healthcare company

☐ Other(s)

☐ I do not have any potential conflict of interest
‘Dual-Layer’ Carotid Stents

From Rationale and Designs ...

RoadSaver  Gore Carotid Stent  CGuard EPS
’Dual-Layer’ Carotid Stents

From Rationale and Designs ...

RoadSaver  Gore Carotid Stent  CGuard EPS

...to ≥1-Year Clinical Evidence
The Problem of Conventional Carotid Stents
The Problem of Conventional Carotid Stents

Human carotid artery treated using a conventional stent; OCT

Image courtesy Joan Rigla, MD PhD; Perceptual Imaging Lab, Univerity of Barcelona
Post-procedural Embolization with conventional carotid stents

DW-MRI post CAS

Mean total lesion area

Schofer J et al, JACC Cardiovasc interv 2008
Timing of neuro-embolic events after CAS

40-80% stroke timing with CAS in CAPTURE and CREST

D. McCormick TCT 2012, modified
Timing of neuro-embolic events after CAS

- **Embolic Events %**
  - 3
  - 2
  - 1

- **Neurological events**
  - **Procedural**
    - Plaque
    - EPD
    - Stent
  - **Post-procedural**
    - Plaque
    - Stent

- **40-80%**

* post-procedural strokes with CAS in CAPTURE and CREST

D. McCormick  TCT 2012, modified
• CEA excludes the plaque
• CEA excludes the plaque

• In CAS, the **stent should exclude the plaque too**
Anti-Embolic Carotid Stent

Plaque protrusion may lead to early and late distal embolization

K. Mathias 2013

J. Schofer, P. Musialek et al. TCT 2014
Conventional Carotid Stent

Human Carotid OCT Image Courtesy Dr Juan Rigla, MD PhD
Perceptual Imaging Lab, University of Barcelona

P Musialek @ LINC 2017
Anti-Embolic Carotid Stent

Plaque protrusion may lead to early and late distal embolization
Pore Size

CGUARD™

ROADSAVER=CASPER

GORE
Closed cell stent

Open cell stent

*150–180µm
<table>
<thead>
<tr>
<th>Name</th>
<th>RoadSaver <em>aka</em> Casper</th>
<th>Gore® Carotid Stent</th>
<th>CGuard™ Embolic Prevention Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent frame</td>
<td>closed-cell Nitinol</td>
<td>open-cell Nitinol</td>
<td>open-cell Nitinol</td>
</tr>
<tr>
<td>Mesh position in relation to frame</td>
<td>inside</td>
<td>outside</td>
<td>outside</td>
</tr>
<tr>
<td>Mesh material</td>
<td>Nitinol</td>
<td>PTFE</td>
<td>PET</td>
</tr>
<tr>
<td>Mesh structure</td>
<td>braided</td>
<td>inter-woven</td>
<td>single-fiber knitted</td>
</tr>
<tr>
<td>Pore size</td>
<td>375 μm</td>
<td>500 μm</td>
<td>150 - 180 μm</td>
</tr>
</tbody>
</table>
Gore Mesh-Covered Carotid Stent
Preclinical Studies

- Canine artery model
- Biologically acceptable tissue response
  - All sidebranches and devices patent through 56 days
  - Full device endothelialization at 30 days
  - Comparatively less medial compression
RoadSaver

Histology and REM after 6 months

Proximal

Mid

Distal

Data by Terumo / used with permission
CGuard EPS 90 days / pig

InspireMD data / by permission
CGuard EPS 30 & 90 days/pig

**Mean ± SD Standard Histomorphology Parameters (2 of 2)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 30</th>
<th>Day 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS (n=3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CGuard (n=9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neointimal Maturation (0-3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation (0-3)</td>
<td>0.43 ± 0.23</td>
<td>0.41 ± 0.22</td>
</tr>
<tr>
<td>Neointimal Fibrin (0-3)</td>
<td>1.13 ± 0.23</td>
<td>0.82 ± 0.37</td>
</tr>
<tr>
<td>Adventitial Fibrosis (0-3)</td>
<td>0.00 ± 0.00</td>
<td>0.02 ± 0.07</td>
</tr>
<tr>
<td>Neointimal Maturation (0-3)</td>
<td>3.00 ± 0.00</td>
<td>3.00 ± 0.00</td>
</tr>
<tr>
<td>Endothelialization (0-4)</td>
<td>3.67 ± 0.42</td>
<td>3.62 ± 0.35</td>
</tr>
</tbody>
</table>

**Mean ± SD and Median Standard Histomorphology Parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Day 30</th>
<th>Day 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS (n=3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CGuard (n=9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injury (0-3)</td>
<td>0.00 ± 0.01</td>
<td>0.01 ± 0.02</td>
</tr>
<tr>
<td>Neointimal Maturation (0-3)</td>
<td>3.00 ± 0.00</td>
<td>3.00 ± 0.00</td>
</tr>
<tr>
<td>Endothelialization (0-4)</td>
<td>3.80 ± 0.40</td>
<td>3.80 ± 0.35</td>
</tr>
</tbody>
</table>

BMS = non mesh-covered CGuard nitrinol frame; InspireMD data / used with permission
Strut diameter to Mesh diameter

RoadSaver aka Casper

Gore® Carotid Stent

CGuard™ Embolic Prevention Stent

P. Musialek @ LINC 2017
# CGuard™– Carotid Embolic Prevention System

## System specifications

<table>
<thead>
<tr>
<th>Specification</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent type</td>
<td>Nitinol – self expanding</td>
</tr>
<tr>
<td>Micronet aperture size</td>
<td>150-180 μm</td>
</tr>
<tr>
<td>Guidewire</td>
<td>0.014”</td>
</tr>
<tr>
<td>Sizes</td>
<td></td>
</tr>
<tr>
<td>- Diameter</td>
<td>6-10mm</td>
</tr>
<tr>
<td>- Length</td>
<td>20-60mm</td>
</tr>
</tbody>
</table>

*CE Mark – March 2014*
### CGuard™—Carotid Embolic Prevention System

#### System specifications

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<tr>
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<td>20-60mm</td>
</tr>
</tbody>
</table>

- **CE Mark** – March 2014
- **Nitinol frame open-cell area** ≈ 21 mm²
- **MicroNet closed-cell area** ≈ 0.3 mm²
- **LARGEST**
- **SMALLEST**
CGuard™ Embolic Prevention Stent System

6F guiding sheath compatibility

Images by InspireMD, used with permission
Mesh-Covered Stents for Carotid Intervention

mechanical Properties
RoadSaver / Casper

CGuard EPS

C. Wissgott and colleagues. *J Endovasc Ther.* 2016 Oct 12 [epub ahead of print]
CGuard™ EPS

Thrombotic material trapped between the stent MicroNET and the vessel wall

Image Courtesy Dr Joan Rigla, MD PhD
Perceptual Imaging Lab, University of Barcelona

P. Musialek @ LINC 2017
clinical Evidence
cguard™ = the only mesh-covered stent with 12 month data from clinical studies
Mesh-Covered Stents for Carotid Intervention

clinical Evidence

CGuard™ = the only mesh-covered stent with 12 month data from clinical studies
CGuard™ embolic prevention system
A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent
The CGuard CARENET Trial (Carotid Embolic Protection Using MicroNet)

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
The Power of DW-MRI...

48h after LICA-CAS

M. Urbanczyk, P. Banys, Dept. Radiology, JP2 Hospital, Krakow, Poland
Filter-protected CAS procedures

CARENET vs PROFI: DW-MRI analysis

DW-MRI analysis @ 48 hours

p < 0.005

INCIDENCE

new ipsilateral lesions (%)

CGuard

Conventional Carotid stent

n=27

n=31

34.6

87.1

* 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**

**DW-MRI analysis @ 48 hours**

<table>
<thead>
<tr>
<th>VOLUME</th>
<th>new ipsilateral lesions (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGuard</td>
<td>0.04</td>
</tr>
<tr>
<td>Conventional Carotid stent (hybrid)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

- p < 0.005
- n=27
- n=31

*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)
# CARENET DW-MRI analysis

All but one peri-procedural ipsilateral lesions

**RESOLVED**

<table>
<thead>
<tr>
<th>DW-MRI analysis @ 30 days*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of new ipsilateral lesions</td>
<td>1</td>
</tr>
<tr>
<td>Average lesion volume (cm³)</td>
<td>0.08 ± 0.00</td>
</tr>
<tr>
<td>Permanent lesions at 30 days</td>
<td>1</td>
</tr>
</tbody>
</table>

*External Core Lab analysis (US)

J. Schofer, P. Musialek et al. *JACC Intv* 2015;8:1229-34
A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent

The CGuard CARENET Trial
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RESULTS The primary combined endpoint was the procedure success of the CGuard system and the number and volume of new lesions on the ipsilateral side assessed by diffusion-weighted magnetic resonance imaging at 48 h post-procedure and at 30 days. The secondary endpoint was 30-day major adverse cardiac or cerebrovascular events (death, stroke, or myocardial infarction). Protection devices were used in all procedures. Procedure success was 100%, with 0% procedural complications. The 30-day major adverse cardiac or cerebrovascular events rate was 0%. New ipsilateral ischemic lesions at 48 h occurred in 37.0% of patients and the average lesion volume was $0.039 \pm 0.08 \text{ cm}^3$. The 30-day diffusion-weighted magnetic resonance imaging showed complete resolution of all but 1 periprocedural lesion and only 1 new minor ($0.116 \text{ cm}^3$) lesion in relation to the 48-h scan.

CONCLUSIONS The use of the CGuard system in patients undergoing carotid artery stenting is feasible. In addition, the benefit of using CGuard may extend throughout the stent healing period. (J Am Coll Cardiol Intv 2015;8:1229-34)
CARENET DW-MRI demonstrated CGuard™ EPD MicroNet

Embolic Prevention Efficacy

CGuard EPS Image Courtesy Dr Joan Rigla, MD PhD Perceptual Imaging Lab, University of Barcelona

The TORINO Vascular Radiology DW-MRI Study

## Incidence, Number, Site and Volume of New Ischemic Brain Lesions at 24 Hours DWI-MR

<table>
<thead>
<tr>
<th></th>
<th>Roadsaver Stent</th>
<th>CGuard Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence of New Ischemic Lesions @ 24 H</strong></td>
<td>37.5%</td>
<td>36.5%</td>
</tr>
<tr>
<td><strong>Number of New Lesions on DWI Over All Patients</strong></td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 pts. had 4 ipsilateral lesions accompanied by 6 controlateral ischemic lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 pts. had a total of 10 stand-alone ipsilateral lesions</td>
<td>None of the patients showed bilateral lesions</td>
<td></td>
</tr>
<tr>
<td>None of the patients showed stand-alone controlateral lesions</td>
<td>3 pts. had a total of 5 stand-alone ipsilateral lesions</td>
<td></td>
</tr>
<tr>
<td>All lesions were asymptomatic</td>
<td>1 pt. had 1 stand-alone controlateral lesion</td>
<td></td>
</tr>
<tr>
<td><strong>Median Pool Volume of Ipsilateral Lesions</strong></td>
<td>0.076 cm³</td>
<td>0.04 cm³</td>
</tr>
<tr>
<td></td>
<td>IQR = 0.064 - 0.138 cm³</td>
<td>IQR = 0.025 - 0.05 cm³</td>
</tr>
<tr>
<td></td>
<td>TR = 0.027 - 0.289 cm³</td>
<td>TR = 0.011 - 0.68 cm³</td>
</tr>
</tbody>
</table>

MA Ruffino & C Rabia – LINC 2016
Intra-procedural cerebral embolization is minimized.

Post-procedural cerebral embolization is eliminated.

A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent

The CGuard CARENET Trial
(Carotid Embolic Protection Using MicroNet)

Joachim Schofer, MD,* Piotr Musiałek, MD, DPhil,† Klaudija Bijuklic, MD,* Ralf Kolvenbach, MD,‡ Mariusz Trystula, MD,† Zbigniew Siudak, MD,†§ Horst Sievert, MD||
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- 2 asymptomatic self-withdrawals @ 30 days
- 100% follow up of the remaining patients

ZERO Stroke Deaths @ 12mo
ZERO Strokes
Per-Protocol independent neurological assessment

- 1 pulmonary embolism death @ 5 mo
- 1 respiratory failure death @ 8 mo
- 1 malignant tumor death @ 9 mo
• NO device-related adverse events
• NO procedure-related events

CARENET Multicenter Trial  12 mo data
CARENET in-stent Peak Systolic Velocities

70% in-stent stenosis threshold

ECA patency

30 d

6 mo

12 mo

100%

100%

100%

* Setacci et. Al., Grading Carotid Intrastent Restenosis of 814 CAS patients Stroke 2008
Prospective evaluation of All-comer percutaneous carotid revascularization in symptomatic and Increased-risk asymptomatic carotid artery stenosis using the CGuard™ Micronet-covered embolic prevention stent system

The PARADIGM Study
Objective

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

Study questions:

(1) feasibility of routine use of CGuard MN-EPS in an all-comer carotid stenosis requiring revasc.

(2) CGuard EPS device/procedure acute success rate

(3) safety clinical efficacy @30-days and @12 months

(4) proportion of all-comer carotid stenosis patients that can be treated through the endovascular route

(5) feasibility of MN-EPS post-dilatation optimization (full endo reconstruction; "CEA-like" effect of CAS)
PARADIGM

Methods:

- academic cardio-vascular centre
- investigator-initiated study
- not industry-funded
- all-comer inclusion (target = 101 consecutive patients)
- no exclusion criteria, all referrals tracked
- routine consultation and management pathways
- qualitative and quantitative lesion & stent evaluation
- investigator-independent neurological and angiographic evaluation, and external study data verification

PARADIGM

Methods (cont’d):

- **ASYMPTOMATIC** patients treated interventionally only if at [stroke risk]
- established lesion-level increased-risk criteria used:
  - thrombus-containing
  - documented progressive
  - irregular and/or ulcerated
  - contralateral ICA occlusion/stroke
  - asymptomatic ipsilateral brain infarct

PARADIGM

PARADIGM: investigator – independent

- external source data verification
- external angiographic analysis
- external statistical analysis

(PARADIGM design and 30-day outcome data)

TCT 2016 Featured Research – 12 month data
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 Musialek¹*, MD, DPhil; Adam Mazurek¹, MD; Mariusz Trystula², MD, PhD; Anna Borratynska³, MD, PhD; Agata Lesniak-Sobelga¹, MD, PhD; Malgorzata Urbanczyk⁴, MD; R. Pawel Banys⁴, MSc; Andrzej Brzychczy², MD, PhD; Wojciech Zajdel⁵, MD, PhD; Lukasz Partyka⁶, MD, PhD; Krzysztof Zmudka⁵, MD, PhD; Piotr Podolec¹, 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
The PARADIGM study

100 consecutive CAS pts / 12mo*

* determined by typical yearly volume
PARADIGM study: referrals flow chart
139 carotid stenosis patient referrals

- Neurologist
- Interventional angiologist
- Vascular surgeon
- Cardiologist

Neuro Vascular Team

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.)

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

Increased-Stroke-Risk
"Asymptomatic" lesion
Symptomatic lesion
(+ contralat. occlusion)
<table>
<thead>
<tr>
<th>Clinical characteristics of the study patients (n=101).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD (min-max)</td>
</tr>
<tr>
<td>Male, % (n)</td>
</tr>
<tr>
<td>Symptomatic, % (n)</td>
</tr>
<tr>
<td>Symptomatic ≤14 days, % (n)</td>
</tr>
<tr>
<td>Acutely symptomatic (emergent CAS), % (n)</td>
</tr>
<tr>
<td>Index lesion (CAS), % (n)</td>
</tr>
<tr>
<td>RICA</td>
</tr>
<tr>
<td>LICA</td>
</tr>
<tr>
<td>RICA+LICA</td>
</tr>
<tr>
<td>CAD, % (n)</td>
</tr>
<tr>
<td>h/o MI, % (n)</td>
</tr>
<tr>
<td>CABG or PCI in the past, % (n)</td>
</tr>
<tr>
<td>PCI as bridge to CAS, % (n)</td>
</tr>
<tr>
<td>AFib (h/o or chronic), % (n)</td>
</tr>
<tr>
<td>Diabetes, % (n)</td>
</tr>
<tr>
<td>h/o neck or chest radiotherapy, % (n)</td>
</tr>
</tbody>
</table>

* proportion of symptomatic patients; ** simultaneous (one-stage)
PCI+CAS in 4 patients; h/o: history of

* EuroIntervention 2016;12:e658-70
Table 2. Quantitative lesion characteristics (n=106), NPD type, CGuard MN-EPS in situ characteristics.

<table>
<thead>
<tr>
<th></th>
<th>All (n=106 lesions)</th>
<th>Symptomatic n=55</th>
<th>Asymptomatic n=51</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Before CAS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSV, m/s</td>
<td>3.7±1.2</td>
<td>3.7±1.1</td>
<td>3.7±1.2</td>
<td>0.964</td>
</tr>
<tr>
<td>EDV, m/s</td>
<td>1.2±0.5</td>
<td>1.1±0.5</td>
<td>1.2±0.5</td>
<td>0.268</td>
</tr>
<tr>
<td>Diameter stenosis % (QA)</td>
<td>83±9</td>
<td>80±9</td>
<td>86±9</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>CAS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPD type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>46% (49)</td>
<td>56% (31)</td>
<td>35% (18)</td>
<td>0.030</td>
</tr>
<tr>
<td>Distal</td>
<td>54% (57)</td>
<td>44% (24)</td>
<td>65% (33)</td>
<td></td>
</tr>
</tbody>
</table>

ICA reference diameter: 4.99 ± 0.36mm (from 4.27 to 6.02 mm)

Lesion length: 19.9 ± 5.8mm (from 8.19 to 30.25 mm)

* Emboshield (n=11); FilterWire (n=15); Spider (n=31)

Gore FlowReversal (n=6) or flow reversal with MoMa (n=43); (mean flow reversal time was 6min 35s, from 3min 51s to 11min 2s)

Direct (primary) stenting in 9 (8.5%); predilatation in 97 (91.5%) lesions

Postdil. balloon: ø 4.5mm (n=9); ø 5.0mm (n=55); ø 5.5mm (n=37); ø 6.0mm (n=57)

* EuroIntervention 2016;12:e658-70
Stroke-in-Evolution
Emergent CAS
Table 2. (cont’d) CGuard MN-EPS in situ characteristics.

<table>
<thead>
<tr>
<th></th>
<th>All (n=106 lesions)</th>
<th>Symptomatic (n=55)</th>
<th>Asymptomatic (n=51)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>After CAS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent length (QA, CoreLab)$^$</td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Nominal 30 mm</td>
<td>29.82±0.68</td>
<td>29.83±0.76</td>
<td>29.80±0.59</td>
<td></td>
</tr>
<tr>
<td>Nominal 40 mm</td>
<td>39.89±0.59</td>
<td>39.80±0.70</td>
<td>39.97±0.51</td>
<td></td>
</tr>
<tr>
<td>(min-max)</td>
<td>(38.88-41.43)</td>
<td>(38.88-41.43)</td>
<td>(39.14-41.01)</td>
<td></td>
</tr>
<tr>
<td>Residual diameter stenosis</td>
<td>6.7±5%</td>
<td>6.1±5%</td>
<td>7.8±5%</td>
<td>0.262</td>
</tr>
<tr>
<td>In-stent PSV, m/s</td>
<td>0.68±0.29</td>
<td>0.64±0.26</td>
<td>0.72±0.31</td>
<td>0.121</td>
</tr>
<tr>
<td>In-stent EDV, m/s</td>
<td>0.18±0.08</td>
<td>0.16±0.07</td>
<td>0.19±0.08</td>
<td>0.087</td>
</tr>
</tbody>
</table>

$^\$In three cases two overlapping stents were used to cover the whole lesion length; these are not included in the in situ stent length evaluation. N/A: not applicable

⇒ 'CAE-like' effect of CAS

*EuroIntervention 2016;12:e658-70*
Evolving L Haemisph stroke

Case # 063 (Krakow)
Case # 063
(Krakow)

NO new brain lesions

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

P. Musialek @ LINC 2017
R Haemisph minor stroke 4 d before, now recurrent TIAs

Note self-tapering

Case # 067 (Krakow)
R Haemisph minor stroke 4 d before, now recurrent TIAs

Case # 067 (Krakow)

NO new brain lesions

NO new brain lesions

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

CEA-like effect of CAS
**PARADIGM:**

**Independent Neurologist Evaluation**

<table>
<thead>
<tr>
<th>Patient number</th>
<th>≤24 hrs prior to CAS</th>
<th>48 hours after CAS</th>
<th>30 days after CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>#5</td>
<td>6</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>#6</td>
<td>5</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>#7</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>#9</td>
<td>6</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>#13</td>
<td>6</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>#15</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>#18</td>
<td>9</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>#20</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>#22</td>
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<td>1</td>
<td>2</td>
</tr>
<tr>
<td>#23</td>
<td>4</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>#25</td>
<td>6</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>#26</td>
<td>4</td>
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<td>4</td>
</tr>
<tr>
<td>#28</td>
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<td>2</td>
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</tr>
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<td>3</td>
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<tr>
<td>#41</td>
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<td>3</td>
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</tr>
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<td>9</td>
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<tr>
<td>#48</td>
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</tr>
<tr>
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<td>#86</td>
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<td>2</td>
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</tr>
<tr>
<td>#94</td>
<td>1</td>
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</tr>
<tr>
<td>#98</td>
<td>3</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>#99</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>#100</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>#101</td>
<td>7</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

*Improvement, deterioration (none)*

One patient, with symptomatic RICA stenosis (minor right-hemispheric stroke 2 months prior to CAS), had hypotonia and transient, fluctuating cognitive dysfunction at 24-48h after CAS. The patient had additional neurologic evaluation on discharge (day 7) that showed no change in NIH-SS [=3] and no change in modified Rankin scale [=1] against 48h (and baseline) evaluation. CT scan on day 2 showed no new cerebral lesions but day 6 CT indicated an extension of the prior lesion in the right hemisphere.

The event, in absence of right haemispheric symptoms and in absence of any clinical sequelae, was CEC–adjudicated as ‘minor stroke in relation to CAS’.
CGuard 5 months follow-up
Novel PARADIGM in Carotid Revascularization:

Clinical & Duplex US Outcome Data @ 12 months

CGuard™

12mo data

TCT 2016
12mo Clinical Outcome Data

- 106 index arteries / 101 study subjects
- no patient withdrawals by 12 months
- 100% clinical
  - neurological
  - Duplex US

ZERO Stroke Deaths
ZERO Strokes 30d–12mo
Per-Protocol independent neurological evaluation

- 1 cardiac death @ 11mo (man 68y, heart failure death)
- 3 non-cardiac deaths @ 3mo, 5mo, 11mo
  - urosepsis (woman 73y)
  - pulmonary embolism (woman 67y)
  - microcellular pulmonary cancer (man 71y)
• 0% stroke
• 0% TIA
• 0% MI

between 30 days and 12 months

in n=101 stroke-risk patients
(55% symptomatic)
PARADIGM

12 months

- NO device-related adverse events
- NO procedure-related events
CGuard™ EPS Carotid PARADIGM Study
12mo Duplex Ultrasound Data

n=106 arteries in 101 patients

PSV (m/s)

baseline 30 days 12 months
CGuard™ EPS Carotid PARADIGM Study
12mo Duplex Ultrasound Data

n=106 arteries in 101 patients

PSV (m/s)

baseline 30 days 12 months

1 asymptomatic ISR (treated with PTA+DEB)

NB. CEA ‘arm’
- 1 critical restenosis → CGuard CAS
- 1 silent occlusion
CGuard™ EPS Carotid PARADIGM Study
12mo Duplex Ultrasound Data

n=106 arteries in 101 patients

ECA* patency

100/106 ECAs were patent prior to CAS
3 ECAs occluded at CAS
97/100 ECAs patent
96.9% ECAs patent

* per stented ICAs/patent (patient alive)
CGuard™ EPS Carotid PARADIGM Study 12mo Duplex Ultrasound Data

- NO in-stent restenosis issue
- NO CGuard ECA patency concern

n=106 arteries in 101 patients
CGuard CARENET & PARADIGM data:

**Strengths**

- Prospective
- All-comer, consecutive
- No exclusions / no CAS 'outside’ the study
- DW-MRI consecutive, per protocol (CARENGET) B/L, 24-48h post CAS, and @30d

- 12mo follow up completed => Tx durability!
In conclusion,

**CGuard EPS**

- 2 clinical studies with completed **12mo** follow-up
  - 1 mono-centric;
  - 1 muli-centric, multi-specialty, international (vascular surgery, cardiology, angiology),
  - 1 with routine DW-MRI at baseline, 24-48h, and 30d
In conclusion,

CGuard EPS
In conclusion,

**CGuard EPS**

- DW-MRI evidence – in consecutive, unselected patients – of embolic prevention efficacy that extends throughout the stent healing period (CARENET)
In conclusion, CGuard EPS

- DW-MRI evidence – in consecutive, unselected patients – of embolic prevention efficacy that extends throughout the stent healing period (CARENET)

- 12-month clinical evidence of safety and primary + secondary stroke prevention efficacy (CARENET, PARADIGM)
This concept has been desired.
And it works.

This is the future of Carotid Artery Stenting.
Endovascular Solution for All-Comers

Prevention of embolism, Optimal radial force, Conformability

Note self-tapering
Endovascular Solution for All-Comers

Endovascular Reconstruction of the Carotid Bifurcation
Prevention of embolism, Optimal radial force, Conformability
PARADIGM - Extend
TCAR DW-MRI Substudy
PARADIGM - Extend
TCAR DW-MRI Substudy

- Symptomatic – 73%; LICA – 64% (RICA – 36%)
- Contralateral occlusion – 27%
- PSV 2.4 – 4.7 (median 3.4) m/s
- EDV 0.5 – 1.9 (median 1.1) m/s
- Diabetes – 36%
- Known CAD – 54% (h/o PCI or CABG = 67% CAD)
- h/o RadioTx – 9%
- All (100%) subjects – ipsilateral ischemic lesions on baseline MRI
All TCAR & CGuard CAS study patients (ie, clinically “asymptomatic” and clinically symptomatic) had *ipsilateral* cerebral ischemic lesions on MRI prior to CAS.

< examples >

Pt AK
KRK-PARADIGM TCAR + CGuard #3
RICA 78%, irregular lesion

Pt ZC
KRK-PARADIGM TCAR + CGuard #5
(LICA 100%, target RICA 90%)

=> HIGH CEREBRAL RISK cohort!
PARADIGM - Extend
TCAR DW-MRI Substudy

MRI Protocol & Analysis:

- MRI Cerebral Imaging (incl. DW-MRI with ADC)
- 3 time points: ≤24h before CAS
  ≤48h after CAS
  @ 90 ± 10 days after CAS
- slice thickness 5mm
- median slice number per patient/time-point – 19
- 2 independent radiologists, per-agreement evaluation
- Medis QBrain 1.1

100% clinical, neurologic, and MRI follow-up
No death, no stroke, no MI up to 90 days
PARADIGM - Extend
TCAR DW-MRI Substudy

- New lesion incidence: 17%
- Number of lesions*: 1 - 3
- Lesion size*: (range) 0.054 - 0.422 mL

All lesions resolved on 90-day MRI imaging
ZERO new lesions on 90-day MRI imaging

100% clinical, neurologic, and MRI follow-up
No death, no stroke, no MI up to 90 days
TW, man 69 yo (Case #1) 12 Jan 2016

critical LICA stenosis, post-stroke

Surgical Team: M. Trystula, M. Kazubudzki, J. Krzywoń, A. Brzychczy; L. Pinter
Endo: P. Musialek & A. Mazurek

First-in-Poland direct carotid access CAS (TCAR)
Under En Route (SilkRoad Medical) Flow Reversal
TW, man 69 yo
critical LICA stenosis, post-stroke
TW, man 69 yo
critical LICA stenosis, post-stroke

lesion crossing, predil, CGuard stent implantation and postdil
under En Route (SilkRoad Medical) Flow Reversal

P Musialek @ VEITH 2016
TW, man 69 yo

critical LICA stenosis, post-stroke

CGuard 7.0 x 30mm full endovascular reconstruction

First-in-Poland direct carotid access CAS under En Route (SilkRoad Medical) Flow Reversal

P Musialek @ VEITH 2016
TW, man 69 yo

critical LICA stenosis, post-stroke

First-in-Poland direct carotid access CAS under En Route (SilkRoad Medical) Flow Reversal

CGuard 7.0x30mm full endovascular reconstruction
TW, man 69 yo
critical LICA stenosis, post-stroke

Z E R O  new lesions

24h prior to CAS

First-in-Poland direct carotid access CAS under En Route (SilkRoad Medical) Flow Reversal + CGuard™ MicroNet Stent

48h after CAS

Brain Imaging: M. Urbanczyk, RP. Banys, Dept. Radiology, JP2 Hospital, Krakow
TW, man 69 yo  
critical LICA stenosis, post-stroke  
Z E R O new lesions

24h prior to CAS  
48h after CAS

First-in-Poland direct carotid access CAS under En Route (SilkRoad Medical) Flow Reversal + CGuard™ MicroNet Stent

Brain Imaging: M. Urbanczyk, RP. Banys, Dept. Radiology, JP2 Hospital, Krakow
WE, woman, 58 y, R haemispheric (minor) stroke 22 Dec and 30 Dec 2015

TCAR plus CGuard™ (Krakow, 12 January 2016; (Case #2)

RICA
WE, woman, 58 y, R haemispheric minor stroke 22 Dec and 30 Dec 2015
TCAR plus CGuard (Krakow, 12 January 2016)

En Route (SilkRoad Medical) Dynamic Flow Reversal
WE, woman, 58 y, R haemispheric minor stroke 22 Dec and 30 Dec 2015

**TCAR plus CGuard** (Krakow, 12 January 2016)

Lesion crossing, predil, CGuard stent implantation and postdil under En Route (SilkRoad Medical) Flow Reversal

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WE, woman, 58 y, R haemispheric minor stroke 22 Dec and 30 Dec 2015

TCAR plus CGuard (Krakow, 12 January 2016)

Lesion crossing, predil, CGuard stent implantation and postdil under En Route (SilkRoad Medical) Flow Reversal

Debris captured in the A-V shunt filter

Movie of debris captured in this procedure

P Musialek @ VEITH 2016
WE, woman, 58 y, R haemispheric minor stroke 22 Dec and 30 Dec 2015

TCAR plus CGuard  (Krakow, 12 January 2016)

Lesion crossing, predil, CGuard stent implantation and postdil under En Route (SilkRoad Medical) Flow Reversal

P Musialek @ VEITH 2016
WE, woman, 58 y, R haemispheric minor stroke 22 Dec and 30 Dec 2015
TCAR plus CGuard  (Krakow, 12 January 2016)

**Final Result**

CGuard 7.0x30 mm  full endovascular reconstruction
plus NO new lesions on DW-MRI !
TCAR + CGuard For Symptomatic and High-Embolism Risk "Asymptomatic" Carotid Stenosis*

- Uncomplicated procedure
- No neuro complications by discharge and 90 days

- Nearly eliminated peri-procedural embolism (MRI)
  - V. low incidence (!)
  - V. low number (!)
  - V. low volume (!)

- Totally eliminated post-procedural embolism during stent healing and by 90 days (MRI)

*High-risk plaque features plus MRI evidence of ipsilateral ischemic lesions in ALL study subjects
This concept has been desired.
And it works.

This is the future of Carotid Artery Stenting revascularization?
Carotid Artery Revascularization for Stroke Prevention: A New Era

Piotr Musialek, MD, DPhil1, and Silke Hopf-Jensen, MD2

Keywords
atherosclerosis, carotid artery stenosis, carotid artery stent, double-layered stent, embolic prevention stent, MicroNet-covered stent, mesh-covered stent, stroke

Carotid Artery Stenosis

“Significant” atherosclerotic carotid artery disease [usually, though not always rightly4 understood as ≥50% diameter reduction at the carotid bifurcation and/or in the proximal internal carotid artery (ICA)] is present in 2% to 8% of the general population, making it a relatively common pathology.2 Its prevalence is similar to that of nonvalvular atrial fibrillation (AF), and similar to AF, it increases with age.2,3 Carotid stenosis (CS) is notably more prevalent in patients with diabetes, coronary artery disease, and peripheral artery disease.4,5

Atherosclerotic carotid artery disease is associated with stroke risk through plaque rupture or erosion and consequent thrombus formation, and the stroke mechanism is predominately embolic.1,5,11,12,13 This association is even stronger in patients with diabetes.11-13 The recognition that carotid atherosclerotic disease is a source of embolic stroke can be traced back to the early 1960s by John Zabramski (1960)13 and Ivan Stary (1967),14 who made the first histological demonstration of atheromatous fragments appearing in the wall of the carotid vessel. Further evidence that the carotid atheroma is a source of embolic stroke was provided by the early reports of carotid endarterectomy for symptomatic and asymptomatic carotid stenosis.15,16,17,18

The high prevalence of carotid atherosclerotic disease in the general population and the high embolic stroke risk associated with carotid atherosclerotic disease is likely the reason that the role of carotid atherosclerotic disease as a source of embolic stroke has been recognized for over 50 years.6,14,19,20 Despite the long history of recognition of carotid atherosclerotic disease as a source of embolic stroke, the use of carotid endarterectomy for the primary prevention of stroke has been limited.6,21,22,23

CS and Stroke Risk

Recently, a series of influential communications have been addressed to the medical community with the message of a currently “low” (<1.0%10,16 or −0.5%17) yearly incidence of stroke in relation to asymptomatic CS on medical management.19,16,17 This is in contrast to contemporary data from vascular clinics that show a yearly stroke rate of ~2.0% to 2.5% in real-life cohorts including OMT patients.15,18 This apparent difference in stroke risk between the general popu

P Musialek @ LINC 2017
CGuard™ MicroNET–covered embolic prevention system routine use in carotid revascularisation for stroke prevention: Accumulating clinical evidence

Piotr Musialek, MD DPhil FESC
Jagiellonian University Professor of Cardiovascular Medicine

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