CGuard™ MicroNet-Covered Embolic Prevention Stent System
A Game Changer in Carotid Revascularization

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ICI meeting 2015
December 13-15, 2015
Tel-Aviv, Israel
Disclosures

ABs / Research Support / Consulting / Speaker Bureau
Abbott, Balton, InspireMD, Medtronic, Penumbra

NB. The PARADIGM study has been Investigator-Initiated and Investigator-Executed (no industry support)
CGuard™ embolic prevention stent
A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent

The CGuard CARENET Trial
(Carotid Embolic Protection Using MicroNet)

Joachim Schofer, MD,* Piotr Musialek, MD, DPm,† Klaudija Bijuklic, MD,* Ralf Kolvenbach, MD,‡ Mariusz Trystula, MD,‡ Zbigniew Siudak, MD,§ Horst Sievert, MD ¶

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 ± 0.08 cm³. The 30-day diffusion-weighted magnetic resonance imaging showed complete resolution of all but 1 periprocedural lesion and only 1 new minor (0.116 cm³) lesion in relation to the 48-h scan.
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Mandatory DW-MRI

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PARADIGM & PARADIGM-EXTEND STUDIES

December 13-15, 2015 Tel-Aviv, Israel

P. Musialek @ ICI 2015
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PARADIGM & PARADIGM-EXTEND


Mandatory DW-MRI

CARENRT 03-007; PJ (Krakow)

Prior to CAS 24 h after 30 d after CAS

Rec.Symptomatic LICA

Note self-tapering

Musialek P @ ICI 2015
A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent

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PARADIGM & PARADIGM-EXTEND

CAROTID PARADIGM REVASCULARIZATION

ROUTINE CLINICAL PRACTICE 2015+

P. Musialek @ ICI 2015
CAS (and CEA) are—and will remain—emboli-generating procedures.

**Figure 1.** Microembolic profile during unprotected CAS. The mean MES counts during various phases of the procedure are displayed.
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Figure 1. Microembolic profile during unprotected CAS. The mean MES counts during various phases of the procedure are displayed.
Post-procedural Embolization with conventional carotid stents

DW-MRI post CAS

Mean total lesion area

Schofer J et al, JACC Cardiovasc interv 2008
Does Free Cell Area Influence the Outcome in Carotid Artery Stenting?

M. Bosiers,1† G. de Donato,2 K. Deloose,1 J. Verbist,3 P. Peeters,3 F. Castriota,4 A. Cremonesi4 and C. Setacci4

Overview of event rates related to the different stents

<table>
<thead>
<tr>
<th></th>
<th>Total population</th>
<th>Symptomatic population</th>
<th>Asymptomatic population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>All events</td>
<td>Post-procedural events</td>
</tr>
<tr>
<td>Stent name</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>X-act</td>
<td>1.9%</td>
<td>1.9%</td>
<td></td>
</tr>
<tr>
<td>Nexstent</td>
<td>3.3%</td>
<td>3.3%</td>
<td></td>
</tr>
<tr>
<td>Wallstent</td>
<td>2.3%</td>
<td>1.2%</td>
<td></td>
</tr>
<tr>
<td>Precise</td>
<td>4.1%</td>
<td>3.1%</td>
<td></td>
</tr>
<tr>
<td>Protégé</td>
<td>3.0%</td>
<td>3.0%</td>
<td></td>
</tr>
<tr>
<td>Acculink</td>
<td>4.2%</td>
<td>3.7%</td>
<td></td>
</tr>
<tr>
<td>Exponent</td>
<td>11.8%</td>
<td>5.9%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3179</td>
<td>2.83%</td>
<td>1.9%</td>
</tr>
</tbody>
</table>

2/3 CAS neuro events are POST-procedural

Eur J Vasc Endovasc Surg Vol 33, February 2007
**FREE CELL AREA** drives CAS neurologic adverse events (and majority occur *post-procedure*)

<table>
<thead>
<tr>
<th>Free cell area</th>
<th>Total population</th>
<th></th>
<th>Symptomatic population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All events</td>
<td>Post-procedural events</td>
<td>All events</td>
</tr>
<tr>
<td>&lt;2.5 vs [2.5, 5]</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>&lt;2.5 vs [5, 7.5]</td>
<td>0.054</td>
<td>0.072</td>
<td>0.048</td>
</tr>
<tr>
<td>&lt;2.5 vs &gt;7.5</td>
<td>0.27</td>
<td>0.006</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

Eur J Vasc Endovasc Surg Vol 33, February 2007
Conventional Carotid Stent

Plaque protrusion may lead to early and late distal embolization

K. Mathias 2013
Conventional Carotid Stent

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

P. Musialek @ ICI 2015
ANY data on the incidence of PLAQUE PROLAPSE in conventional carotid stents?
Post-procedural **PLAQUE PROLAPSE** through **conventional stent struts**

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

30.7%

81 y.o. Female, Symptomatic

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

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

*Eur Heart J.* 2014;35(Abstr Suppl):178
Post-procedural **PLAQUE PROLAPSE** through conventional stent struts

<table>
<thead>
<tr>
<th></th>
<th>Closed cell (n = 17)</th>
<th>Open cell (n = 13)</th>
<th>Hybrid cell (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque prolapse</td>
<td>17.6%, (3)</td>
<td>61.5%, (8)</td>
<td>30%, (3)</td>
</tr>
</tbody>
</table>


b At least 10 appreciable tissue prolapses between the stent struts per patient.
Conventional Carotid Stent

Plaque protrusion may lead to early and late distal embolization.

Debris Arterial Wall

Stent Struts

K. Mathias 2013
Anti-Embolic Carotid Stent

Plaque protrusion may lead to early and late distal embolization
CGuard™ embolic prevention system
# CGuard™—Carotid Embolic Prevention System

## System specifications

<table>
<thead>
<tr>
<th>Feature</th>
<th>Specification</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>

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NB. CGuard™ EPS is not yet available in the US

CE Mark – March 2014

Specific, carotid-dedicated design
CARENET – Study Design

Prospective, multi-center, all-comer

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

Sites:
- Joachim Schofer (PI), Hamburg University Cardiovascular Center
- Piotr Musialek (Co-PI), Jagiellonian University Medical College
- Ralf Kolvenbach, Augusta Hospital
- Horst Sievert, Cardiovascular Center Frankfurt

Endpoints:
- Acute /30-day Cerebral Embolization by DWI (incidence, volume)
- 30 day MACCE (death, stroke, MI)

J. Schofer, P. Musialek et al. JACC Intv 2015;8:1229-34
Evaluation of PET Mesh Covered Stent in Patients with Carotid Artery Disease

The CARENET-Trial
(CARotid Embolic protection using microNET)

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

30 d data

Joachim Schofer, MD, PhD, Hamburg University Cardiovascular Center, Hamburg, Germany
Piotr Musialek, MD, PhD, Jagiellonian University Medical College at John Paul II Hospital, Krakow, Poland,
Ralf Kolvenbach, MD, PhD, Augusta Hospital, Dusseldorf, Germany,
Horst Sievert, MD, PhD, Cardiovascular Center Frankfurt, Frankfurt, Germany
A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent
The CGuard CARENET Trial
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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.
DW-MRI:
the *unforgiving* testimony
of what you’ve done
to the TARGET ORGAN...
The Power of DW-MRI...

48h after LICA-CAS

M. Urbanczyk, P. Banys, Dept. Radiology, JP2 Hospital, Krakow, Poland
# CARENET DW-MRI analysis

### DW-MRI analysis @ 48 h

<table>
<thead>
<tr>
<th></th>
<th>CARENET (n=27)</th>
</tr>
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<tbody>
<tr>
<td><strong>Incidence of new ipsilateral lesions</strong></td>
<td>37.0%</td>
</tr>
<tr>
<td><strong>Average lesion volume (cm³)</strong></td>
<td>0.039 ± 0.08</td>
</tr>
<tr>
<td><strong>Maximum lesion volume (cm³)</strong></td>
<td>0.445</td>
</tr>
</tbody>
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---

*External Core Lab analysis (US)*


† bilateral lesions

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

---

see patient fluxogram
# CARENET DW-MRI analysis

<table>
<thead>
<tr>
<th>DW-MRI analysis @ 48 hours</th>
<th>CARENET (n=27)</th>
<th>PROFI (all) (n=62)</th>
<th>ICSS† (n=56)</th>
</tr>
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<tbody>
<tr>
<td>Incidence of new ipsilateral lesions</td>
<td>37.0%</td>
<td>66.2%</td>
<td>68.0%</td>
</tr>
<tr>
<td>Average lesion volume (cm³)</td>
<td>0.039 ± 0.08</td>
<td>0.375</td>
<td>-</td>
</tr>
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<td>Maximum lesion volume (cm³)</td>
<td>0.445</td>
<td></td>
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≈50% reduction in new ipsilateral lesion incidence

see patient fluxogram

*External Core Lab analysis (US)
† bilateral lesions

J. Schofer, P. Musialek et al. *JACC Intv* 2015;8:1229-34
## CARENET DW-MRI analysis*  

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<td>66.2%</td>
<td>68.0%</td>
</tr>
<tr>
<td>Average lesion volume (cm³)</td>
<td>0.039</td>
<td>0.375</td>
<td>-</td>
</tr>
<tr>
<td>Maximum lesion volume (cm³)</td>
<td>0.415</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

>10-fold reduction in cerebral lesion volume

*External Core Lab analysis (US)*


† bilateral lesions

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

See patient fluxogram
Filter-protected CAS procedures

**CARENET vs PROFI**: DW-MRI analysis

---

### DW-MRI analysis @ 48 hours

<table>
<thead>
<tr>
<th></th>
<th>n=27</th>
<th>n=31</th>
</tr>
</thead>
<tbody>
<tr>
<td>new ipsilateral lesions (%)</td>
<td>34.6</td>
<td>87.1</td>
</tr>
</tbody>
</table>

* p < 0.005

*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

VOLUME

new ipsilateral lesions (mL)

CGuard

Conventional Carotid stent (hybrid)

p < 0.005

0.59

0.04

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 (cm(^3))</td>
<td>0.08 ± 0.00</td>
</tr>
<tr>
<td>Permanent lesions at 30 days</td>
<td>1</td>
</tr>
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*External Core Lab analysis (US)*

J. Schofer, P. Musialek et al. JACC Intv 2015;8:1229-34
Anti-Embolic Carotid Stent

Plaque protrusion may lead to early and late distal embolization

K. Mathias 2013
Anti-Embolic Carotid Stent

CGuard Embolic-Prevention Stent  OCT Image  (human, iv vivo)
  Courtesy Dr Juan Rigla, MD PhD
  Perceptual Imaging Lab, University of Barcelona

P. Musialek @ ICI 2015
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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)
Prospective evaluation of All-comer percutaneous carotid revascularization in symptomatic and increased risk asymptomatic carotid artery stenosis using 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)
Methods: The CAS Procedure

- **EPD** use mandatory; EPD selection according to the ‘Tailored CAS’ algorithm*

- **Liberal postdilatation** accepted in order to maximize potential for ‘endovascular full reconstruction’ (minimizing residual stenosis)

  NB. 1. DWI evidence of effective MicroNet prevention against cerebral embolization (CARENET/PROFI)
  2. Residual stenosis after CAS as independent predictor of in-stent restenosis

Cosottini M et al. *Stroke Res* 2010
Musialek P et al. *J Endovasc Ther* 2010
Wasser K et al. *J Neurol* 2012

PARADIGM

Endpoints:

- feasibility of endovascular Tx in unselected referrals using the study device in otherwise routine practice

- device success (able to deliver + implant + <30% DS)

- procedure success (device success w/o clinical compl.)
  (external neurologist, external non-invasive cardiologist)

- clinical efficacy: MACNE (death/stroke/MI )

- in-stent velocities (Duplex)

- 24-48h
- 30 days
- 12 months
- up to 5y

• **ASYMPTOMATIC** patients treated interventionally only if at **stroke risk**

• established lesion-level increased-risk criteria used:
  
  – thrombus-containing
  – tight, near-occlusive
  – documented progressive
  – irregular and/or ulcerated
  – contralateral ICA occlusion/stroke
  – asymptomatic ipsilateral brain infarct

Methods (cont’d)

PARADIGM: investigator – independent

- external study data verification
- external angiographic analysis
- external statistical analysis

97 carotid stenosis patient referrals*
(external >> internal)

Neuro-Vascular Team
- Neurologist
- Interventional Angiologist
- Vascular Surgeon
- Cardiologist

for carotid revascularization
73 patients

NOT for carotid revascularization
24 patients

n=19: lesion increased risk and/or severity criteria not met
n=2: ICA totally occluded on verification
n=2: ICA functionally occluded + h/o prior ipsil. large infarct with hemorrhagic transformation
n=1: severe haemodynamic instability (ICA stenosis asymt.)
Study Flow Chart (2)

73 Patients for carotid revascularization

(92%) → CAS in n=67 Patients (bilateral in 3) (LICA-CEA and RICA-CAS) hybrid management

(1%) → CAS + CEA in n=1 Patient

(7%) → CEA in n=5 Patients

71 ICAs treated endovascularly in 68 patients

n = 1 eGRF 14 => no contrast
n = 1 extreme access tortuosity
n = 1 severe aortic valve disease + calcific LICA (AVR + CEA)
2 floating thrombus in CCA
n = 1 ICA diameter <2.0 mm + contralateral occlusion

<table>
<thead>
<tr>
<th>Clinical characteristics of study patients (n=68)</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/of 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>
PARADIGM: Results (1)

- Percutaneous treatment 100% using the intended MicroNet-covered embolic prevention stent system CGuard (ie, no other stents used during the study period)

- Device success 100%
- Procedure success 100%
- Transient Dopamine infusion 19% (n=14)
- Debris in EPD 18% (n=13)
- Access site complications 0% (n=0)
- Vascular plug closure 45% (n=32)
## PARADIGM: Results (2)

### Index lesion qualitative characteristics (n=71 lesions)

<table>
<thead>
<tr>
<th></th>
<th>All (n=71)</th>
<th>Symptomatic (n=37)</th>
<th>Asymptomatic (n=34)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>thrombus, % (n)</td>
<td>15% (11)</td>
<td>24% (9)</td>
<td>6% (2)</td>
<td>0.025</td>
</tr>
<tr>
<td>near occl./string, % (n)</td>
<td>21% (15)</td>
<td>30% (11)</td>
<td>12% (4)</td>
<td>0.084</td>
</tr>
<tr>
<td>progresive*, % (n)</td>
<td>27% (19)</td>
<td>11% (4)</td>
<td>44% (15)</td>
<td>0.003</td>
</tr>
<tr>
<td>ulcerated, % (n)</td>
<td>41% (29)</td>
<td>46% (17)</td>
<td>35% (12)</td>
<td>0.470</td>
</tr>
<tr>
<td>irregular, % (n)</td>
<td>72% (51)</td>
<td>65% (24)</td>
<td>79% (27)</td>
<td>0.197</td>
</tr>
<tr>
<td>contralateral occl., % (n)</td>
<td>17% (12)</td>
<td>22% (8)</td>
<td>35% (12)</td>
<td>0.291</td>
</tr>
<tr>
<td>highly calcific, % (n)</td>
<td>23% (16)</td>
<td>14% (5)</td>
<td>35% (12)</td>
<td>0.050</td>
</tr>
<tr>
<td>asymptomatic ipsilat. brain embolization/infarct</td>
<td>N/A</td>
<td>N/A</td>
<td>32% (11)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

*verified on imaging

### CoreLab-Quantified
- ICA reference diameter: $4.99 \pm 0.36\text{mm}$ (from 4.27 to 6.02mm)
- Lesion length: $19.9 \pm 5.8\text{mm}$ (from 8.19 to 30.25mm)
## PARADIGM: Results (3)

### Index lesion quantitative characteristics (n=71 lesions)

<table>
<thead>
<tr>
<th></th>
<th>All (n=71 lesions)</th>
<th>Symptomatic n=37</th>
<th>Asymptomatic n=34</th>
<th>p</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>3.8 ± 1.3</td>
<td>3.7 ± 1.1</td>
<td>3.8 ± 1.5</td>
<td>0.862</td>
</tr>
<tr>
<td>EDV, m/s</td>
<td>1.3 ± 0.7</td>
<td>1.4 ± 0.6</td>
<td>1.3 ± 0.8</td>
<td>0.687</td>
</tr>
<tr>
<td>Diameter stenosis % (QA)</td>
<td>82 ± 9</td>
<td>79 ± 9</td>
<td>84 ± 9</td>
<td>0.021</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>0.092</td>
</tr>
<tr>
<td>Proximal*</td>
<td>35% (25)</td>
<td>44% (16)</td>
<td>26% (9)</td>
<td></td>
</tr>
<tr>
<td>Distal**</td>
<td>65% (46)</td>
<td>56% (21)</td>
<td>74% (25)</td>
<td></td>
</tr>
<tr>
<td>post-dilat balloon# peak pressure, mmHg</td>
<td>18.4 ± 3.4</td>
<td>17.5 ± 3.6</td>
<td>19.2 ± 2.9</td>
<td>0.037</td>
</tr>
<tr>
<td><strong>After CAS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent length (QA)§</td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Nominal 30 mm (min-max)</td>
<td>29.66 ± 0.30</td>
<td>29.66 ± 0.28</td>
<td>29.65 ± 0.32</td>
<td></td>
</tr>
<tr>
<td>(28.73-30.07)</td>
<td>(29.02-30.07)</td>
<td>(28.73-30.02)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nominal 40 mm (min-max)</td>
<td>39.73 ± 0.34</td>
<td>39.69 ± 0.41</td>
<td>39.77 ± 0.28</td>
<td></td>
</tr>
<tr>
<td>(38.88-40.22)</td>
<td>(38.88-40.22)</td>
<td>(39.14-40.04)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residual diam. stenosis</td>
<td>7 ± 4%</td>
<td>5 ± 4%</td>
<td>7 ± 5%</td>
<td>0.257</td>
</tr>
<tr>
<td>in-stent PSV, m/s</td>
<td>0.70 ± 0.28</td>
<td>0.66 ± 0.29</td>
<td>0.74 ± 0.27</td>
<td>0.266</td>
</tr>
<tr>
<td>in-stent EDV, m/s</td>
<td>0.17 ± 0.07</td>
<td>0.17 ± 0.07</td>
<td>0.18 ± 0.07</td>
<td>0.457</td>
</tr>
</tbody>
</table>

* Emboshield (n=7); FilterWire (n=14); Spider (n=25)
** Gore FlowReversal (n=4) or flow reversal with MoMa (n=21)
(NB. mean flow reversal time was 6min 48s, from 5min 18s to 11min 2s)
# ø 4.5mm (n=5); ø 5.0mm (n=36); ø 5.5mm (n=29); ø 6.0mm (n=1)
§ 30mm in 51 lesions; 40mm in 18 lesions (2 other lesions required two stents each)
PARADIGM: Results (4)

- Death/stroke/MI @ 48h  0%
- Death/stroke/MI @ 30d  0%
Evolving L Haemisph stroke

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

NO new brain lesions

M. Urbanczyk, P. Banys, Dept. Radiology, JP2 Hospital, Krakow, Poland
R Haemisph minor stroke 4 d before, now recurrent TIAs

Note self-tapering
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
L Haemisph minor stroke 5 d before
L Haemisph minor stroke 5 d before

Case # 068 (Krakow)

NO new brain lesions

NO new brain lesions

M. Urbanczyk, P. Banys, Dept. Radiology, JP2 Hospital, Krakow, Poland
L Haemisph minor stroke 5 d before

Case # 068 (Krakow)

NO new brain lesions

NO new brain lesions

M. Urbanczyk, P. Banys, Dept. Radiology, JP2 Hospital, Krakow, Poland
L Haemisph minor stroke 5 d before

Case # 67
(Krakow)

M. Urbanczyk, P. Banys, Dept. Radiology, JP2 Hospital, Krakow, Poland
RICA 6.2/1.5 m/s

Highly-calcific I

Predilatation 3.0x20mm followed by NC 4.5x15/20atm
CGuard™ 9.0x30mm, postdilated ø5.5x20mm/16atm

A. Mazurek, P. Musialek ePCR2015
Highly-calcific II

NO brain lesions with CAS

Predilatation 2.0x20 followed by NC 4.0x15, CGuard™ 8.0x40mm, postdilated ø 5.0mm/16 atm

A. Mazurek, P. Musialek  ePCR2015
Highly-calcific III

Predilatation 2.5x15mm followed by 4.0x15, CGuard™ 9.0x30mm, postdilated ø5.0mmx20/24atm

A. Mazurek, P. Musialek   ePCR2015
CGuard 5 months follow-up
RCCA & RICA

LICA CGuard
5 months follow-up
Patient #101 in 'PARADIGM-EXTEND' (a.k.a. 'PARADIGM 101')
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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30d data

ZERO

Stroke/MI/death

12mo data

ICI meeting 2015

December 13-15, 2015
Tel-Aviv, Israel
A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent
The CGuard CARENET Trial
(Carotid Embolic Protection Using MicroNet)

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- 2 asymptomatic self-withdrawals @ 30 days
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- 2 asymptomatic self-withdrawals @ 30 days
- 100% follow up of the remaining patients

30d data
ZERO Stroke/MI/death

12mo data
A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent

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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

30d data

12mo data
A Prospective, Multicenter Study of a Novel Mesh-Covered Carotid Stent
The CGuard CARENET Trial
(Carotid Embolic Protection Using MicroNet)

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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*

Peak Systolic Velocity (cm/sec)

ECA patency

<table>
<thead>
<tr>
<th>Time</th>
<th>30 d</th>
<th>6 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECA patency</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

* Setacci et. Al., Grading Carotid Intrastent Restenosis of 814 CAS patients Stroke 2008  
P. Musialek @ ICI 2015
CARENET in-stent Peak Systolic Velocities

70% in-stent stenosis threshold

Peak Systolic Velocity (cm/sec)

ECA patency 30 d 6 mo 12 mo

100% 100% 100%

* Setacci et. Al.. Grading Carotid Intrastent Restenosis of 814 CAS patients Stroke 2008

P. Musialek @ VEITH 2015
CARENENET in-stent Peak Systolic Velocities

70% in-stent stenosis threshold*

- NO in-stent restenosis concern

Peak Systolic Velocity (cm/sec)

ECA patency

<table>
<thead>
<tr>
<th></th>
<th>30 d</th>
<th>6 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

* Setacci et. Al. Grading Carotid Intrastent Restenosis of 814 CAS patients *Stroke* 2008  
P. Musialek @ ICI 2015
CARENET in-stent Peak Systolic Velocities

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

* Setacci et. Al. Grading Carotid Intrastent Restenosis of 814 CAS patients Stroke 2008

ECA patency

- 30 d: 100%
- 6 mo: 100%
- 12 mo: 100%
CAS (and CEA) are—and will remain—emboli-generating procedures amenable to elimination with MicroNet.
Endovascular Solution for All-Comers

Endovascular Reconstruction of the Carotid Bifurcation

Note self-tapering
CGuard embolic prevention stent system

- Full respect of the carotid bifurcation anatomy
  -> ‘endovascular anatomic reconstruction’

- Optimal performance across all lesion subsets (including high calcium/thrombus/string)

‘The most OPEN of open-cell stent designs’
and
‘The most CLOSED of the closed-cell designs’
This concept has been desired.
This concept has been desired.

And it works.
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 Stenting
This concept has been desired.
And it works.

This is the future of Carotid Artery Stenting revascularization?
Improved technology for CAS — better EPDs (flow reversal and proximal occlusion) and better stents (membrane-covered, ultra-closed cell, and biodegradable). Several issues may improve CAS outcomes, such as the introduction of new and better stents. An ex vivo study showed that use of a polyurethane membrane-covered stent resulted in lower cerebral embolization rates.
Improved technology for CAS — better EPDs (flow reversal and proximal occlusion) and better stents (membrane-covered, ultra-closed cell, and biodegradable). Several issues may improve CAS outcomes, such as the introduction of new and better stents. An ex vivo study showed that use of a polyurethane membrane-covered stent resulted in lower cerebral embolization rates.69
Back-up slides
CREST

Freedom from Primary End Point (%)

Year of Follow-up

No. at Risk

CAS

CEA

0 1 2 3 4

30 d

1262 1100 787 460 162

1240 1099 770 430 145

December 13-15, 2015
Tel-Aviv, Israel
<table>
<thead>
<tr>
<th>Event</th>
<th>CAS (N = 1262)</th>
<th>CEA (N = 1240)</th>
<th>Absolute Treatment Effect of CAS vs. CEA (95% CI)</th>
<th>Hazard Ratio for CAS vs. CEA (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>9 (0.7±0.2)</td>
<td>4 (0.3±0.2)</td>
<td>0.4 (−0.2 to 1.0)</td>
<td>2.25 (0.69 to 7.30)†</td>
<td>0.18†</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>52 (4.1±0.6)</td>
<td>29 (2.3±0.4)</td>
<td>1.8 (0.4 to 3.2)</td>
<td>1.79 (1.14 to 2.82)</td>
<td>0.01</td>
</tr>
<tr>
<td>Major ipsilateral</td>
<td>11 (0.9±0.3)</td>
<td>4 (0.3±0.2)</td>
<td>0.5 (−0.1 to 1.2)</td>
<td>2.67 (0.85 to 8.40)</td>
<td>0.09</td>
</tr>
<tr>
<td>Major nonipsilateral</td>
<td>0</td>
<td>4 (0.3±0.2)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Minor ipsilateral</td>
<td>37 (2.9±0.5)</td>
<td>17 (1.4±0.3)</td>
<td>1.6 (0.4 to 2.7)</td>
<td>2.16 (1.22 to 3.83)</td>
<td>0.009</td>
</tr>
<tr>
<td>Minor nonipsilateral</td>
<td>4 (0.3±0.2)</td>
<td>4 (0.3±0.2)</td>
<td>0.0 (−0.4 to 0.4)</td>
<td>1.02 (0.25 to 4.07)</td>
<td>0.98†</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>14 (1.1±0.3)</td>
<td>28 (2.3±0.4)</td>
<td>−1.1 (−2.2 to −0.1)</td>
<td>0.50 (0.26 to 0.94)</td>
<td>0.03</td>
</tr>
<tr>
<td>Any periprocedural stroke or postprocedural ipsilateral stroke</td>
<td>52 (4.1±0.6)</td>
<td>29 (2.3±0.4)</td>
<td>1.8 (0.4 to 3.2)</td>
<td>1.79 (1.14 to 2.82)</td>
<td>0.01</td>
</tr>
<tr>
<td>Major stroke</td>
<td>11 (0.9±0.3)</td>
<td>8 (0.6±0.2)</td>
<td>0.2 (−0.5 to 0.9)</td>
<td>1.35 (0.54 to 3.36)</td>
<td>0.52</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>41 (3.2±0.5)</td>
<td>21 (1.7±0.4)</td>
<td>1.6 (0.3 to 2.8)</td>
<td>1.95 (1.15 to 3.30)</td>
<td>0.01</td>
</tr>
<tr>
<td>Any periprocedural stroke or death or postprocedural ipsilateral stroke</td>
<td>55 (4.4±0.6)</td>
<td>29 (2.3±0.4)</td>
<td>2.0 (0.6 to 3.4)</td>
<td>1.90 (1.21 to 2.98)</td>
<td>0.005</td>
</tr>
<tr>
<td>Primary end point (any periprocedural stroke, myocardial infarction, or death or postprocedural ipsilateral stroke)</td>
<td>66 (5.2±0.6)</td>
<td>56 (4.5±0.6)</td>
<td>0.7 (−1.0 to 2.4)</td>
<td>1.18 (0.82 to 1.68)</td>
<td>0.38</td>
</tr>
<tr>
<td>Event</td>
<td>CAS (N = 1262)</td>
<td>CEA (N = 1240)</td>
<td>Periprocedural Period</td>
<td>Hazard Ratio for CAS vs. CEA (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>---------------</td>
<td>---------------</td>
<td>-----------------------</td>
<td>---------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td></td>
<td>no. of patients (% ±SE)</td>
<td>percentage points</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 (0.7±0.2)</td>
<td>4 (0.3±0.2)</td>
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<td>0.18†</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
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<td>0.09</td>
</tr>
<tr>
<td>Major nonipsilateral</td>
<td>0</td>
<td>4 (0.3±0.2)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
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<td>0.009</td>
</tr>
<tr>
<td>Minor nonipsilateral</td>
<td>4 (0.3±0.2)</td>
<td>4 (0.3±0.2)</td>
<td>0.0 (−0.4 to 0.4)</td>
<td>1.02 (0.25 to 4.07)</td>
<td>0.98†</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>14 (1.1±0.3)</td>
<td>28 (2.3±0.4)</td>
<td>−1.1 (−2.2 to −0.1)</td>
<td>0.50 (0.26 to 0.94)</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Any periprocedural stroke or postprocedural ipsilateral stroke</strong></td>
<td>52 (4.1±0.6)</td>
<td>29 (2.3±0.4)</td>
<td>1.8 (0.4 to 3.2)</td>
<td>1.79 (1.14 to 2.82)</td>
<td>0.01</td>
</tr>
<tr>
<td>Major stroke</td>
<td>11 (0.9±0.3)</td>
<td>8 (0.6±0.2)</td>
<td>0.2 (−0.5 to 0.9)</td>
<td>1.35 (0.54 to 3.36)</td>
<td>0.52</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>41 (3.2±0.5)</td>
<td>21 (1.7±0.4)</td>
<td>1.6 (0.3 to 2.8)</td>
<td>1.95 (1.15 to 3.30)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Any periprocedural stroke or death or postprocedural ipsilateral stroke</strong></td>
<td>55 (4.4±0.6)</td>
<td>29 (2.3±0.4)</td>
<td>2.0 (0.6 to 3.4)</td>
<td>1.90 (1.21 to 2.98)</td>
<td>0.005</td>
</tr>
<tr>
<td>Primary end point (any periprocedural stroke, myocardial infarction, or death or postprocedural ipsilateral stroke)</td>
<td>66 (5.2±0.6)</td>
<td>56 (4.5±0.6)</td>
<td>0.7 (−1.0 to 2.4)</td>
<td>1.18 (0.82 to 1.68)</td>
<td>0.38</td>
</tr>
</tbody>
</table>
What would **CREST** show today with

---

**Freedom from Primary End Point (%)**

- **Year of Follow-up**
  - 30 d

**No. at Risk**

<table>
<thead>
<tr>
<th></th>
<th>CAS</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1262</td>
<td>1240</td>
</tr>
<tr>
<td>1.5</td>
<td>1100</td>
<td>1099</td>
</tr>
<tr>
<td>2</td>
<td>787</td>
<td>770</td>
</tr>
<tr>
<td>3</td>
<td>460</td>
<td>430</td>
</tr>
<tr>
<td>4</td>
<td>162</td>
<td>145</td>
</tr>
</tbody>
</table>
What would CREST show today with instead of?
Feeding today’s CGuard – CAS data to CREST would indicate CAS superiority.
Mesh-Covered Stents for Carotid Intervention: Rationale, Device Designs, Imaging, and Data to Date

Piotr Musialek, MD DPhil

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

* 165μm
* 375μm

1050μm
Closed cell stent

1900μm
Open cell stent

* Average in lesion at expanded state

CGUARD™
ROADSAVER=CASPER
GORE

P. Musialek @ TCT 2015
<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>

PTFE = Polytetrafluoroethylene
PET = poliethylentereaphtalat
Data
histology / animal
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

PA Schneider VERVE 2014, animal data WL Gore / by permission
CGuard EPS 90 days / pig
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>Injury (0-3)</td>
<td>BMS (n=3)</td>
<td>CGuard (n=9)</td>
</tr>
<tr>
<td>Inflammation (0-3)</td>
<td>0.43 ± 0.23</td>
<td>0.51</td>
</tr>
<tr>
<td>Neointimal Fibrin (0-3)</td>
<td>1.13 ± 0.23</td>
<td>1.00</td>
</tr>
<tr>
<td>Adventitial Fibrosis (0-3)</td>
<td>0.00 ± 0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Neointimal Maturation (0-3)</td>
<td>3.00 ± 0.00</td>
<td>3.00</td>
</tr>
<tr>
<td>Endothelialization (0-4)</td>
<td>3.67 ± 0.42</td>
<td>3.80</td>
</tr>
</tbody>
</table>

BMS = non mesh-covered CGuard nitinol frame; InspireMD data / used with permission
<table>
<thead>
<tr>
<th>Name</th>
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<th>Gore® Carotid Stent</th>
<th>CGuard™ Embolic Prevention Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-sheathable?</td>
<td>yes*</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Crossing profile</td>
<td>5F</td>
<td>5F (smaller diam) 6F (larger diam)</td>
<td>6F</td>
</tr>
<tr>
<td>Foreshortening / Elongation</td>
<td>yes</td>
<td>unknown**</td>
<td>no #</td>
</tr>
<tr>
<td>Stent placement accuracy</td>
<td>–</td>
<td>N/D</td>
<td>++ #</td>
</tr>
<tr>
<td>Ability to eliminate residual stenosis</td>
<td>N/D</td>
<td>N/D</td>
<td>yes #</td>
</tr>
<tr>
<td>Externally-analysed systematic DW MRI study data</td>
<td>unknown</td>
<td>unknown</td>
<td>yes ##</td>
</tr>
</tbody>
</table>

*up to 50% released length  
**probably not substantial  
## CARENET JACC Intv 2015;8:1229  
N/D = not determined
Remaining Unknowns (1)

- Is there a product/design-specific "gradient" in the embolic prevention efficacy?
Remaining Unknowns (1)

- Is there a **product/design-specific "gradient"** in the embolic prevention efficacy?
Remaining Unknowns (1)

- Is there a product/design-specific "gradient" in the embolic prevention efficacy?
Remaining Unknowns (2)

- **Large-scale** (multi-center, multi-hundred patient), controlled clinical endpoint data?

- Long-term treatment durability / ’no restenosis’ proof. **NB. so far – no worrying signal**

- Role in **open** (CEA) **vs. endo** (CAS) balance

- Role in **primary** stroke prevention
Clinical evidence in October 2015...

- 1 peer-reviewed, published clinical study
  - multicenter, single-arm
  - DWI controlled (24-48h, 30d, external analysis)
    \[ CARENET, JACC Intv 2015;8:1229-1234 \]

- several moderately-sized investigator-initiated single arm studies with clinical endpoints
  - 1 with full 30-day data now available in all-comers
    \[ PARADIGM, JACC 2015;66(suppl):B33 \]

- > 300pts single-arm clinical-endpoint study due to report in 2017

- mesh-covered carotid stents have individual, specific characteristics but no comparative studies...
  (and such may never be conducted)
NEW PARADIGM AHEAD