The role of transcervical Protection in symptomatic patients versus CEA
Conflict of Interest: None
Previous Treatment Options for Carotid Revascularization

Gold Standard: Carotid Endarterectomy

Low stroke risk\(^1\), but...
Invasive; risk of surgical complications
  - Risk of cranial nerve injury\(^2\)
  - Return to OR for wound complications

Less Invasive Alternative: Transfemoral, Filter Protected CAS

Patient friendly, long-term durability\(^1\), \textbf{but}...
Excess procedural stroke risk\(^1\)
  - Procedure itself can create thrombo-embolic event

CREST: 2.1% unresolved at 6 months\(^2\) (80% motor)

\(^1\) CREST Trial: N Engl J Med 2010;363:11-23
\(^2\) Circulation. 2012;125:2256-2264
CAS vs CEA: CREST Periprocedural Data

- Carotid endarterectomy (CEA) associate with more MI
- Carotid-artery stenting (CAS) associate with more minor stroke

Brott et al. NEJM, 2010;363
<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>N</th>
<th>Sx</th>
<th>Death</th>
<th>Major CVA</th>
<th>Minor CVA</th>
<th>AMI</th>
<th>CNI</th>
<th>Access Site Comp</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPACE</td>
<td>2006</td>
<td>1200</td>
<td>SYMP</td>
<td>0.67vs0.86%</td>
<td>4vs2.9%</td>
<td>3.5vs3.25%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>EVA-3S</td>
<td>2006</td>
<td>527</td>
<td>SYMP</td>
<td>0.8vs1.2% P=0.68</td>
<td>2.7vs0.4</td>
<td>6.1vs2.3%</td>
<td>0.4vs0.8% P=0.62</td>
<td>1.1vs7.7</td>
<td>3.1vs1.2</td>
</tr>
<tr>
<td>ICSS (Interim)</td>
<td>2010</td>
<td>1713</td>
<td>SYMP</td>
<td>1.4vs0.5% P=0.072</td>
<td>1.6%vs1.7%</td>
<td>4.3%vs1.2%</td>
<td>0.3vs0.6%</td>
<td>0.1vs5.5%</td>
<td>0.9vs3.4%</td>
</tr>
<tr>
<td>CREST</td>
<td>2010</td>
<td>2505</td>
<td>SYMP &amp; ASYMP</td>
<td>0.7vs0.3 P=0.18</td>
<td>0.9vs0.6 P=0.52</td>
<td>3.2vs1.7 P=0.01</td>
<td>1.1vs2.3 P=0.03</td>
<td>0.3vs4.7% HR=0.07</td>
<td>1.1vs3.5% P=0.001</td>
</tr>
<tr>
<td>ACT-1</td>
<td>2016</td>
<td>1453</td>
<td>ASYMP</td>
<td>0.1vs0.3 P=0.43</td>
<td>0.5vs0.3 P=1.0</td>
<td>2.4vs1.1 P=0.20</td>
<td>0.5vs0.9% P=0.41</td>
<td>0.1vs1.1% P=0.02</td>
<td>0.3vs1.1% P=0.07</td>
</tr>
</tbody>
</table>

*Minor Stroke is More Common After CAS: Factor ≈2:1*
ACT1: CEA-CAS Clinical Outcomes
No differences in Long Term Follow-up

Rosenfield et al. NEJM, DOI: 10.1056/NEJMoa1515706
CAS vs CEA: CREST 10y Data

CEA and CAS are SIMILAR at Long Term FU

Long-Term Results of Stenting versus Endarterectomy for Carotid-Artery Stenosis
Thomas G. Brott, M.D., George Howard, Dr.P.H., Gary S. Roubin, M.D., Ph.D., James F. Meschia, M.D., Ariane Mackey, M.D., William Brooks, M.D., Wesley S. Moore, M.D., Michael D. Hill, M.D., Vito A. Mantese, M.D., Wayne M. Clark, M.D., Carlos H. Timaran, M.D., Donald Heck, M.D., Pierre P. Leimgruber, M.D., Alice J. Sheffet, Ph.D., Virginia J. Howard, Ph.D., Seemant Chaturvedi, M.D., Brajesh K. Lal, M.D., Jenifer H. Voeks, Ph.D., and Robert W. Hobson, II, M.D., for the CREST-2 Investigators†
March 17, 2016 DOI: 10.1056/NEJMoa1505215
CREST Trial – Late Strokes after CAS

40% of Stroke occurred after 24 hours!

ICSS DWI sub study

- 73% of CAS patients with distal filter protection developed new ischemic infarcts by DWI-MRI
- 17% of Carotid Endarterectomy

*Distal filters produce > 4X higher incidence of cerebral embolization vs. CEA*
We need better protection against LATE emboli

- CREST timing of Stroke after CAS

<table>
<thead>
<tr>
<th>0-24 hours</th>
<th>1-30d</th>
<th>% of strokes that occurred after 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 events</td>
<td>19 events</td>
<td>40%</td>
</tr>
</tbody>
</table>
Conventional Carotid Stent

Plaque protrusion may lead to early and late distal embolization

Debris Arterial Wall
Stent Struts

K. Mathias 2013
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, 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 97.0% of patients and the average lesion volume was 0.033 ± 0.06 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.

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

## Clinical Events

<table>
<thead>
<tr>
<th></th>
<th>30 days (n=30)</th>
<th>6 months (n=28*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACCE (MI, stroke, death)</td>
<td>(0) 0.0%</td>
<td>(1) 3.6%</td>
</tr>
<tr>
<td>MI</td>
<td>(0) 0.0%</td>
<td>(0) 0.0%</td>
</tr>
<tr>
<td>Stroke</td>
<td>(0) 0.0%</td>
<td>(0) 0.0%</td>
</tr>
<tr>
<td>Death</td>
<td>(0) 0.0%</td>
<td>(1) 3.6%</td>
</tr>
</tbody>
</table>

Comparative data from other CAS trials include higher 30 day and 6 month MACCE rates:

<table>
<thead>
<tr>
<th></th>
<th>30 days** (14 trials, 5255 patients)</th>
<th>6 months† (3 trials, 1053 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACCE (MI, stroke, death)</td>
<td>5.72%</td>
<td>8.09%</td>
</tr>
</tbody>
</table>

* 2 patients exited the study  
** Trials included in analysis: ARChER pooled, ARMOUR, BEACH, CABERNET, CREATE, EMPIRE, EPIC, MAVERIC 1+2, MAVERIC International, PRIAMUS, SAPPHIRE, SECURITY, PROFI, ICSS  
† Values extrapolated from event curves
## 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(\dagger) (n=56)</th>
</tr>
</thead>
<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 (cm(^3))</td>
<td>0.039</td>
<td>0.375</td>
<td>-</td>
</tr>
<tr>
<td>Maximum lesion volume (cm(^3))</td>
<td>0.415</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

> 10-fold reduction in cerebral lesion volume

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*External Core Lab analysis (US)*

Bijuklic et al. JACC, 2012; Bonati et. al, Lancet Neurol 2010

\(\dagger\) bilateral lesions

J. Schofer, P. Musialek et al. JACC Intv 2015;8:1229-34
Increased number of stent occlusions?

Does Type of Mesh covered stent matter?
Volume of subclinical embolic infarct correlates to long-term cognitive changes after carotid revascularization

Wei Zhou, MD,1,2,3 Brittanie D. Baughman, MS,4 Sallie Soman, MD,1 Max Wintermark, MD,3 Laura C. Lazzeroni, PhD,5 Elizabeth Hitchner, MS,5 Jyoti Bhat, MS,5 and Allyson Rosen, PhD,1,5 Palo Alto and Stanford, Calif. and Cambridge, Mass

ABSTRACT

Objective: Carotid intervention is safe and effective in stroke prevention in appropriately selected patients. Despite minimal neurologic complications, procedure-related subclinical microemboli are common and their cognitive effects are largely unknown. In this prospective longitudinal study, we sought to determine long-term cognitive effects of embolic infarcts.

Methods: The study recruited 19 patients including 46% symptomatic patients who underwent carotid revascularization. Neuropsychological testing was administered preoperatively and at 1 month, 6 months, and 12 months postoperatively. Rey Auditory Verbal Learning Test (RAVLT) was the primary cognitive measure with parallel forms to avoid practice effect. All patients also received 3T brain magnetic resonance imaging with a diffusion-weighted imaging (DWI) sequence preoperatively and within 48 hours postoperatively to identify procedure-related new embolic lesions. Each DWI lesion was manually traced and input into a neuroimaging program to define volume. Embolic infarct volumes were correlated with cognitive measures. Regression models were used to identify relationships between infarct volumes and cognitive measures.

Results: A total of 587 DWI lesions were identified on 3T magnetic resonance imaging in 81.7% of carotid artery stenting (CAS) and 36.4% of carotid endarterectomy patients with a total volume of 29,327 mm³. Among them, 54 DWI lesions were found in carotid endarterectomy patients and 533 in the CAS patients. Four patients had transient postoperative neurologic symptoms and one had a stroke. CAS was an independent predictor of embolic infarction (odds ratio, 6.6 [2.2-20.4]; P < .01) and infarct volume (P = .004). Diabetes and contralateral carotid severe stenosis or occlusion had a trend of positive association with infarct volume, whereas systolic blood pressure >140 mm Hg had a negative association (P = .1, .09 and 1, respectively). There was a trend of improved RAVLT scores overall after carotid revascularization. Significantly higher infarct volumes were observed among those with RAVLT decline. Within the CAS cohort, infarct volume was negatively correlated with short- and long-term RAVLT changes (P < .05).

Conclusions: Cognitive assessment of procedure-related subclinical microemboli is challenging. Volumes of embolic infarct correlate with long-term cognitive changes, suggesting that microembolization should be considered a surrogate measure for carotid disease management. (J Vasc Surg 2017;65:886-94.)
Cognitive Changes

The larger the Micro Emboli on DWMRI

The more severe cognitive decline
How to get optimal protection without late emboli and plaque protrusion?

Transcervical proximal flow reversal (TCAR)

Mesh covered Stent?
TCAR a Hybrid procedure
A Less Invasive Surgically Inspired Solution

Direct Carotid Access
CCA Clamp & Loop Control

Back-bleeding to Clear Debris

Direct Carotid Access (avoid arch)
CCA Clamp & Loop Control

Back-bleeding to Clear Debris

CEA

TCAR
Transcervical proximal Flow Reversal
## ROADSTER 2: Clinical Outcomes

### Patients Treated Per Protocol

<table>
<thead>
<tr>
<th></th>
<th>ROADSTER 1 (n=203)</th>
<th>ROADSTER 2 (n=227)</th>
<th>ROADSTER 2 (n=252)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with 30-day F/U</td>
<td>Patients with 30-day F/U</td>
<td>All Patients</td>
</tr>
<tr>
<td>Stroke/Death/MI</td>
<td>6 (3.0%)</td>
<td>2 (0.9%)</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (0.5%)</td>
<td>2 (0.9%)</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>Death</td>
<td>2 (1.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>MI</td>
<td>3 (1.5%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td><strong>Stroke/Death</strong></td>
<td><strong>3 (1.5%)</strong></td>
<td><strong>2 (0.9%)</strong></td>
<td><strong>2 (0.8%)</strong></td>
</tr>
<tr>
<td>CNI (permanent)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

**ROADSTER 2 Stroke in Asymptomatic Patients** = 0.5%  
**ROADSTER 2 Stroke in Symptomatic Patients** = 1.3%

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Schneider P. LINC 2017
What is it all about?

Type of Stent?

Proximal protection with flow reversal

With TCAR the type of stent does not matter any more?
THE PROOF IS IN THE FILTER
Macro & Micro emboli in ENROUTE® NPS FILTERS
The PROOF Study
Micro-Emboli Measurement

DW-MRI Studies - Silk Road’s CEA-Like Outcomes

<table>
<thead>
<tr>
<th>Study</th>
<th>Procedure</th>
<th>Embolic Protection</th>
<th>Patients</th>
<th>% w/ New DWI Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICSS²</td>
<td>CEA</td>
<td>Clamp, backbleed</td>
<td>107</td>
<td>17%</td>
</tr>
<tr>
<td>PROOF³</td>
<td>Silk Road</td>
<td>Transcarotid Access, w/ Flow Reversal</td>
<td>56</td>
<td>16.1%</td>
</tr>
<tr>
<td>PROFI¹</td>
<td>Transfemoral CAS</td>
<td>Proximal occlusion (MoMA)</td>
<td>31</td>
<td>45%</td>
</tr>
<tr>
<td>ICSS²</td>
<td>Transfemoral CAS</td>
<td>Distal filter (various)</td>
<td>51</td>
<td>73%</td>
</tr>
<tr>
<td>PROFI¹</td>
<td>Transfemoral CAS</td>
<td>Distal filter (Emboshield)</td>
<td>31</td>
<td>87%</td>
</tr>
</tbody>
</table>

1 J Am Coll Cardiol. 2012 Jan 19. [Epub ahead of print]
Proof Study  \( n = 75 \)

1 transient stroke on the contralateral side
Hypothesis

TCAR the most effective way to prevent intraoperative emboli

But....... Only mesh covered stents prevent late emboli yielding results at least as good as CEA ??
Registry - High Risk Symptomatic Patients
TCAR

Mesh covered Stents
81 years old, Symptomatic

Do we know whether these small emboli will cause cognitive function loss?
The best of 2 Worlds?

Prospective Registry

50 Patients  CEA
DWMRI  before and 24 h post intervention

50 Patients TCAR + C Mesh Covered Stent
DWMRI before and 24 h post

21 Patients enrolled
Conclusion

TCAR can most probably yield results identical to CEA

Mesh covered stents can be a "Game Changer", but the proof is still lacking

Combining the "Best of two Worlds" can theoretically give results superior to CEA
The role of transcervical Protection in symptomatic patients versus CEA