ROADSTER 2

• **CONDITION:** Carotid artery disease

• **PI:** Jessica Titus, MD

• **CONTACT INFO:** Jo Anne Goldman | JoAnne.Goldman@allina.com | 612-863-3793

• **DESCRIPTION:** The study is intended to evaluate real world usage of the ENROUTE transcarotid stent when used with the ENROUTE transcarotid neuroprotection system by physicians of varying experience with the transcarotid technique.

• **CRITERIA LIST/ QUALIFICATIONS:** Patient must meet one of the following criteria regarding neurological symptom status and degree of stenosis:
  - Symptomatic: Stenosis must be ≥ 50% as determined by an angiogram and the patient has a history of stroke (minor or non-disabling), TIA and/or amaurosis fugax within 180 days of the procedure ipsilateral to the carotid artery to be stented, OR
  - Asymptomatic: Stenosis must be ≥ 80% as determined by angiogram without any neurological symptoms within the prior 180 days.
  - Patient has a discrete lesion located in the internal carotid artery (ICA) with or without involvement of the contiguous common carotid artery (CCA). Patient must have a life expectancy ≥ 3 years at the time of the index procedure without contingencies related to other medical, surgical or endovascular intervention.

• **SPONSOR:** Silk Road Medical
Cutting Out the Middle Man: Transcervical Approach to Carotid Artery Stenting.

Jessica M Titus, MD  
Vascular and Endovascular Surgery  
Minneapolis Heart Institute  
Abbott Northwestern Hospital  
Minneapolis, MN

History of Carotid Surgery
Rationale for “Minimally Invasive Approaches”

• Shortened operative times
• Smaller Incisions
• Decreased length of stay
• No need for general anesthesia

Carotid Endarterectomy Today

• Average Operative Times
  – CEA: ~120 min
  – Transfemoral Stenting: 69 min

• Average Length of Stay
  – CEA: 1 day
  – Transfemoral Stenting: 1 day
Carotid endarterectomy in awake patients: safety, tolerability and results

Abstract

Objective: To analyze the results of 125 carotid endarterectomies under loco-regional anesthesia, with selective use of shunt and bovine pericardium patch.

Methods: One hundred and seventeen patients with stenosis ≥ 70% in the internal carotid artery on dopplex scan – arteriography or magnetic resonance angiography underwent 125 carotid endarterectomies. Intraoperative pharmacological cerebral protection included intravenous administration of alfenanil and dexametason. Clopidogrel, aspirin and statins were used in all cases. Seventy-seven patients were males (65.8%). Mean age was 70.8 years, ranging from 48 to 88 years. Surgery was performed to treat symptomatic stenosis in 69 arteries (55.2%) and asymptomatic stenosis in 56 arteries (44.8%).

Results: A carotid shunt was used in 3 cases (2.4%) due to signs and symptoms of cerebral ischemia after carotid artery clamping during the operation, and all 3 patients had a good outcome. Bovine pericardium patch was used in 71 arteries ≤ 6 mm in diameter (56.8%). Postoperative mortality was 0.8%: one patient died from a myocardial infarction. Two patients (1.6%) had minor ipsilateral strokes with good recovery, and 2 patients (1.6%) had non-fatal myocardial infarctions with good recovery. The mean follow-up period was 32 months. In the late postoperative period, there was restenosis in only three arteries (2.4%).

Conclusion: Carotid artery endarterectomy can be safely performed in the awake patient, with low morbidity and mortality rates.


WHY DO YOU NEED ANYTHING BUT CEA???
High Risk Patients

The Infancy of Carotid Stenting

- 1977: Angioplasty first reported
- 1994: Stent placement for spontaneous dissection in 2 patients
- First two trials
  - 1993-95: 110 patients
    - 10.9% stroke/TIA rate
  - 1998: 17 patients
    - Stopped because of 70% neuro event rate in the stenting arm
### Carotid Stenting Trials

**Stroke within 30 days**

<table>
<thead>
<tr>
<th>Trial</th>
<th>CEA</th>
<th>CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPPHIRE 2004</td>
<td>3.0%</td>
<td>3.6%</td>
</tr>
<tr>
<td>N=167 CEA, 167 CAB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVA-3S 2006</td>
<td>3.4%</td>
<td>8.1%</td>
</tr>
<tr>
<td>N=282 CEA, 285 CAB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPACE 2006</td>
<td>6.2%</td>
<td>7.5%</td>
</tr>
<tr>
<td>N=594 CEA, 599 CAB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICSS 2009</td>
<td>4.0%</td>
<td>7.8%</td>
</tr>
<tr>
<td>N=887 CEA, 883 CAB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meta-Analysis, Meier 2010</td>
<td>4.7%</td>
<td>7.2%</td>
</tr>
<tr>
<td>N=2235 CEA, 2232 CAB</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Carotid Stenting Trials

**MI within 30 days**

<table>
<thead>
<tr>
<th>Trial</th>
<th>CEA</th>
<th>CAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPPHIRE 2004</td>
<td>7.2%</td>
<td>3.0%</td>
</tr>
<tr>
<td>N=187 CEA, 187 CAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVA-3S 2006</td>
<td>0.8%</td>
<td>0.4%</td>
</tr>
<tr>
<td>N=282 CEA, 285 CAB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meta-Analysis, Meier 2010</td>
<td>2.5%</td>
<td>0.9%</td>
</tr>
<tr>
<td>N=692 CEA, 693 CAB</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Carotid Stenting Trials

Death within 30 days

<table>
<thead>
<tr>
<th>Trial</th>
<th>CEA (%)</th>
<th>CAS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPPHIRE 2004</td>
<td>2.4%</td>
<td>1.2%</td>
</tr>
<tr>
<td>N=187 CEA, 187 CAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVA-3S 2006</td>
<td>1.1%</td>
<td>0.8%</td>
</tr>
<tr>
<td>N=262 CEA, 265 CAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPACE 2006</td>
<td>0.9%</td>
<td>0.7%</td>
</tr>
<tr>
<td>N=584 CEA, 599 CAS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meta-Analysis, Meler 2010</td>
<td>1.2%</td>
<td>1.1%</td>
</tr>
<tr>
<td>N=1391 CEA, 1399 CAS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST)

- **Largest randomized controlled trial**
  - 108 US centers, 9 Canadian centers

- 2502 patients followed over median 2.5 years in symptomatic and asymptomatic patients

- Examined 4-year rates of primary end point between CAS and CEA
  - Stroke
  - MI
  - Death
Study Design

- Operators (477 surgeons, 224 interventionists) required certification
  - Minimum 12 procedures per year
  - Complications and death were
    - <3% among asymptomatic
    - <5% among symptomatic

Primary Endpoints

- Composite: any stroke, MI or Death in peri-procedural period
- Ipsilateral stroke up to 4 years
## Results Summary

<table>
<thead>
<tr>
<th>Event</th>
<th>CAS</th>
<th>CEA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.7%</td>
<td>0.3%</td>
<td>0.18</td>
</tr>
<tr>
<td>Stroke</td>
<td>4.1%</td>
<td>2.3%</td>
<td>0.01</td>
</tr>
<tr>
<td>MI</td>
<td>1.1%</td>
<td>2.3%</td>
<td>0.03</td>
</tr>
<tr>
<td>Death/Stroke/MI</td>
<td>5.2%</td>
<td>4.5%</td>
<td>0.38</td>
</tr>
</tbody>
</table>

### 4-yr Study Period

<table>
<thead>
<tr>
<th>Event</th>
<th>CAS</th>
<th>CEA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>11.3%</td>
<td>12.6%</td>
<td>0.45</td>
</tr>
<tr>
<td>Stroke</td>
<td>10.2%</td>
<td>7.9%</td>
<td>0.03</td>
</tr>
<tr>
<td>Death/Stroke/MI</td>
<td>7.2%</td>
<td>6.8%</td>
<td>0.51</td>
</tr>
</tbody>
</table>

---

**Peri-procedural Period**

---

**Summary**

Background: The International Carotid Stenting Study (ICSS) of stenting and endarterectomy for symptomatic carotid stenosis found a higher incidence of stroke within 30 days of stenting compared with endarterectomy. We aimed to compare the rate of ischemic brain injury denoted on MRI between the two groups.

**Methods**

Patients with recently symptomatic carotid artery stenosis enrolled in ICSS were randomly assigned in a 1:1 ratio to carotid artery stenting or endarterectomy. Of 50 patients in ICSS, seven took part in the MRI substudy. The protocol specified that MRI was done 3-7 days before treatment, 1-3 days after treatment (postprocedural scan) and 12-15 days after treatment. Scans were analyzed in two independent centers who were masked to treatment. The primary endpoint was the presence of at least one new ischemic brain lesion on diffusion-weighted imaging (DWI) on the post-procedural scan. Analysis was post-hoc. This is a substudy of a registered trial, NCT01377470.

**Findings**

33% patients (30/3) in the stenting group and 39% in the endarterectomy group had MRI before and after treatment. At 29.7% of 216 patients in the stenting group and 16% (77) of 477 patients in the endarterectomy group had at least one new DWI lesion detected on postprocedural scans (more than 3 days after treatment; adjusted rate ratio 0.94, 95% CI 0.75-1.13; p=0.50). At 12-15 days, there were more new ischemic brain lesion recovery sequences in 28 (33%) of 82 patients in the stenting group and in 43% of 73 in the endarterectomy group (adjusted OR 1.19, 95% CI 1.02-1.38; p=0.01). In patients treated at a centre with a policy of using cerebral protection devices, 37 (7% of 51) in the stenting group and 51 (20%) of 254 in the endarterectomy group had at least one new DWI lesion on post-procedural scans (adjusted OR 12.20, 95% CI 4.58-32.32; p=0.03). When those treated at a centre with a policy of unassisted stenting, 37 (77%) of 97 patients in the stenting group and 9 (9%) of 108 in the endarterectomy group had new lesions on DWI (adjusted OR 2.70, 1.16-6.24; interaction p=0.03).

**Interpretation**

About three times more patients in the stenting group than in the endarterectomy group had new ischemic lesions on DWI post-procedural scans. The difference in clinical stroke risk in ICSS is therefore unlikely to have been caused by ascertainment bias. Protection devices did not seem to be effective in preventing symptoms ischemic during stenting. DWI might serve as a surrogate outcome measure in future trials of carotid interventions.
CAPTURE REGISTRY DATA
Analysis of Strokes Resulting from Carotid Artery Stenting in the Post Approval Setting

• “Real World” study of Acculink/Accunet
  — Oct 2004-2006
  — 144 sites
  — 353 proceduralists

• Multicenter prospective postmarket registry

• 3500 patients, neurologically audited

• Analysis of stroke timing, severity, locations and type
**CAPTURE STROKE DATA**

- 170 strokes in 168 patients
  - Overall 4.8% rate
- Ischemic 88%
- Increased risk in octogenarians and symptomatic patients
  - 36% and 26% of all strokes respectively
- Ipsilateral 82%
  - Almost one in 5 strokes were contralateral or posterior circulation

**Different Strokes…**

- Protection Devices
Protection Devices

Different Strokes…

• Protection Devices
• Arch Atheromatous Disease
• Tortuous Carotids/Arches
Inception of TCAR

- Eliminate the Arch
- Eliminate Tortuosity Factors
- Facilitate flow reversal set up
TCAR Procedure

Direct Carotid Access — Eliminates Arch Navigation

Silk Road Procedure
### Roadster 1
141 patients at 14 sites

#### ROADSTER Study Demographics and Technical Results

<table>
<thead>
<tr>
<th>High Surgical Risk</th>
<th>ROADSTER Survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>72.9 ±9(40, 90)</td>
</tr>
<tr>
<td>Age ≥75</td>
<td>47%</td>
</tr>
<tr>
<td>Age ≥80</td>
<td>28%</td>
</tr>
<tr>
<td>Female</td>
<td>35%</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>26%</td>
</tr>
<tr>
<td>Local Anesthesia</td>
<td>53%</td>
</tr>
<tr>
<td>Reverse Flow Time (median)</td>
<td>10 mins</td>
</tr>
<tr>
<td>Acute Device Success</td>
<td>99%</td>
</tr>
<tr>
<td>Technical Success</td>
<td>99%</td>
</tr>
<tr>
<td>Procedural Success</td>
<td>96%</td>
</tr>
</tbody>
</table>

#### ROADSTER Study Clinical Results

<table>
<thead>
<tr>
<th>High Surgical Risk</th>
<th>ROADSTER</th>
</tr>
</thead>
<tbody>
<tr>
<td>S/D/MI</td>
<td>5</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>0</td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>2</td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
</tr>
<tr>
<td>MI</td>
<td>1</td>
</tr>
<tr>
<td>Stroke &amp; Death</td>
<td>4</td>
</tr>
<tr>
<td>Cranial Nerve Injury</td>
<td>1</td>
</tr>
<tr>
<td>CNI Unresolved 6 months</td>
<td>0</td>
</tr>
</tbody>
</table>
Safety and feasibility of a novel transcervical access neuroprotection system for carotid artery stenting in the PROOF Study

Lazaro Pintor, MD, Marc Ribó, MD, Christopher Loh, MD, Barton Lane, MD, Tracy Roberts, MT (ASCP), Tony M. Chou, MD, and Ralf R. Kolzenbich, MD, PhD.

Disclosures: Barcelona, Spain; and Los Angeles, Palo Alto, San Francisco, Calif.

Background: Randomized controlled trials have shown that periprocedural rates of stroke and death are higher with carotid artery stenting (CAS) than with carotid endarterectomy (CEA). Diffusion weighted magnetic resonance imaging (DW-MRI) has shown higher rates of clinically silent new ischemic brain lesions when CAS is performed as compared with CEA. The Silk Road Medical Embolic PROtection System (SRS) Study is a single-arm feasibility study using the MEDTRONIC Neuroprotection System (Silk Road Medical Inc, Sunnyvale, Calif), a novel transcervical access and cerebral embolic protection system. This system enables safe implantation under controlled blood flow reversal of the carotid artery, also known as Flow Arrested Stent Transcervical Carotid Artery Stenting (FAST-CAS).

Methods: Between March 2009 and February 2010, a total of 44 subjects were enrolled in the study. The primary composite endpoint was major stroke, myocardial infarction, or death within 30 days. Forty-three patients (97.7%) completed the study through the 30-day endpoint. One patient was lost to follow-up. In a subgroup of consecutive subjects, DW-MRI examinations were performed preprocedure and within 24 to 48 hours after the stent implantation. Blinded independent neuroradiologists reviewed all DW-MRI studies and confirmed the absence or presence of new ischemic brain lesions.

Results: All enrolled patients were successfully treated, and no major adverse events were seen through the follow-up period. Thirty-one subjects had DW-MRI examinations. Of these, two patients (6.5%) had evidence of new ischemic brain lesions but no clinical sequelae. Transition tolerance to reverse flow was reported in 9 of 11 cases, but in all cases, a stent was successfully placed, and the tolerance was managed by minimizing the duration of reverse flow during the procedure.

Conclusion: In this first-in-man experience, FAST-CAS using the MEDTRONIC Neuroprotection System was shown to be a safe and feasible method for carotid revascularization. DW-MRI findings suggest controlled reverse flow provides cerebral embolic protection similar to that seen with CEA. (J Vasc Surg 2013;68(1):23-31)

**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>PROOF¹</td>
<td>Silk Road</td>
<td>Transcarotid Access w/ Flow Reversal</td>
<td>56</td>
<td>18%</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 (Embosshield)</td>
<td>31</td>
<td>87%</td>
</tr>
</tbody>
</table>
ROADSTER 2

- Evaluate real world usage of the ENROUTE Transcarotid Stent
  - Used with the ENROUTE Transcarotid Neuroprotection System
  - Includes physicians of varying experience with the transcarotid technique

- Started enrolling Sept 2015

- Estimated end March 2018

ROADSTER 2

Study Population

- Patients with atherosclerotic extracranial internal carotid stenosis (ICA) with or without involvement of the contiguous common artery
  - Symptomatic: greater than or equal to 50% stenosis
  - Asymptomatic: greater than or equal to 80% stenosis
ROADSTER 2
Study Endpoints

- **Primary**
  - Rate of procedural success through 30 days without MAE following stent implant

- **Secondary**
  - Acute device success
  - Technical Success
  - Rate of cranial nerve injury
  - Rate of cardiac death
  - Rate of neurological death
  - Rate of hierarchical stroke, death, and MI by symptom status
  - Acute device success by
    - Physician experience
    - Physician training level
    - Enrollment Quartile

ROADSTER 2
Inclusion Criteria

- **Target vessel must meet all requirements for ENROUTE Transcarotid Neuroprotection System and ENROUTE Stent System**
  - 4-9mm vessel in treatment area
  - Common carotid artery diameter at least 5mm
  - At least 5cm to carotid bifurcation from clavicle
  - Vessel access area in common carotid free of disease

- **Patient must have a life expectancy ≥ 3 years at the time of the index procedure without contingencies related to other medical, surgical or endovascular intervention.**

- **SURGICAL HIGH RISK**
  - Anatomic
    - Contralateral carotid artery occlusion
    - Tandem stenosis >70%
    - High cervical carotid artery stenosis
    - Restenosis after carotid endarterectomy
    - Bilateral carotid artery stenosis requiring treatment within 30 days after index treatment
    - Hostile Necks which the investigator deems safe for transcarotid access including but not limited to:
      - Prior neck irradiation
      - Radical neck dissection
      - Cervical spine immobility
ROADSTER 2
Inclusion Criteria

- **CLINICAL HIGH RISK**
  - ≥ 75 years of age
  - ≥ 2-vessel coronary artery disease and history of angina of any severity
  - History of Canadian Cardiovascular Society angina class 3 or 4 or unstable angina
  - Congestive heart failure (CHF) - New York Heart Association (NYHA) Functional Class III or IV
  - Known severe left ventricular dysfunction LVEF <30%.
  - Myocardial infarction > 72 hours and < 6 weeks prior to procedure.
  - Severe pulmonary disease (COPD) with either:
    - FEV1 <50% predicted or chronic oxygen therapy or
    - resting (PO2 of < 60 mmHg (room air)
  - Permanent contralateral cranial nerve injury
  - Chronic renal insufficiency (serum creatinine > 2.5 mg/dL).

- **Anatomy that renders transfemoral CAS hazardous can be included in study**
  - Type II, III, or Bovine arch
  - Arch atheroma or calcification
  - Atheroma of the great vessel origins
  - Tortuous distal ICA
  - Tortuous or occluded iliofemoral segments
  - Occluded aortic segments

ROADSTER 2
Exclusion Criteria

- **Patient has an alternative source of cerebral embolus, including but not limited to:**
  - Chronic atrial fibrillation.
  - Paroxysmal afib within past 6 months of history requiring chronic anticoagulation.

- **Known cardiac sources of emboli**
  - Left ventricular aneurysm
  - Intracardiac filling defect
  - Cardiomyopathy
  - Aortic or mitral prosthetic heart valve
  - Calcific aortic stenosis
  - Mitral stenosis
  - Mitral valve regurgitation
  - Atrial septal defect or septal aneurysm
  - Left atrial myxoma

- **Recently (<60 days) implanted heart valve (either surgically or endovascularly), which is a known source of embolus as confirmed on echocardiogram.**

- **Abnormal intracranial angiographic findings:**
  - Patellar intracranial or extracranial arterial stenosis greater in severity than the lesion to be treated
  - Cerebral aneurysm > 5 mm
  - AVM of the cerebral vasculature
ROADSTER 2

- 40 sites, 600 patients
  - Halfway through enrollment!

VQI Registry

- Started in Nov 2016
- TCAR surveillance project including “real world” patients to compare to CEA
- Allows treatment for those patients who are not trial candidates
  - Afib
  - Statin intolerance
  - Symptomatics with life expectancy <3 years
Case 1

- 72yo female with recurrent TIAs
  - Blood pressure related
  - Dense hemiparesis right side

- History of left radical neck followed by high dose radiation for parotid cancer in 1990s
  - Carotid visible from skin
Follow-up

• Discharged uneventfully POD 1
  – No further neurologic events
  – Temporary vocal weakness
    • Resolved by one month

• Last followup visit: 14 months postop
  – Carotid remains widely patent

Case 2

• 68yo male presented with angina
  – Severe 2 vessel disease
  – CABG recommended

• Incidental finding right ICA occlusion and left 90% stenosis
  – 2009 supraglottic laryngeal resection and tracheostomy for cancer
  – Left subclavian occlusion
Follow-up

• No neurologic events

• Returned 3 months postop
  – Left subclavian stent
  – 3 vessel CABG following day

• Last follow-up at 4 months out
  – Duplex with widely patent carotid
On the Radar: Common Carotid Dissection
Recognition
Troubleshooting and Completion

Hindsight...
Abbott Experience

- **20 performed**
  - 11 study
  - 9 VQI

- **100% technical success**
  - 100% procedural success

- **Anesthesia**
  - 80% general
  - 20% local

- **Operative Times**
  - Ave 77.7 min
  - Range 52-103 min

TCAR – Flow Reversal Times

- **Abbott NW**
  - **12.14** Min. Average
    - High 33, Low 5

- **ROADSTER Study**
  - **12.9** Min. Average
    - High 63, Low 4

- **All TCAR 10 Min.**
**TCAR – contrast used in cc/ml**

- **Abbott NW**
  - 23.73 cc/ml
    - High 50, Low 8

- **All TCAR**
  - 35 cc/ml

**TCAR – Fluoro time in minutes**

- **Abbott Northwestern**
  - 7.16 Avg. Minutes
    - High 18.9, Low 2.3

- **All TCAR**
  - 4.9 Avg. Minutes
Abbott Outcomes

• No deaths
• No strokes
• No MIs
• No major adverse events

SPECIAL THANKS TO JOANNE GOLDMAN!!!
QUESTIONS???