2018 MID-ATLANTIC CONFERENCE

8th ANNUAL CURRENT CONCEPTS IN

VASCULAR THERAPIES

2018

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Clinical Chief

SMG Vascular Surgery

28 April 2018

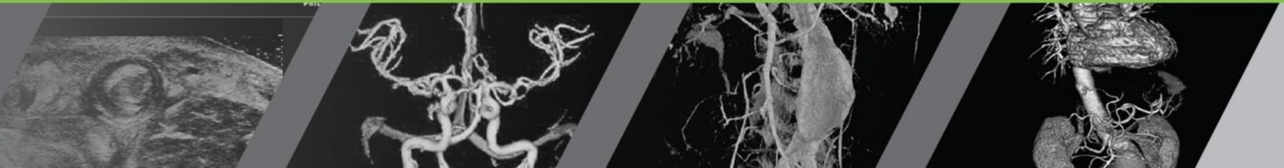
Carotid Stenosis
Is TCAR the answer ????

Relevant disclosure

- Consultant and Proctor for Silk Road Medical

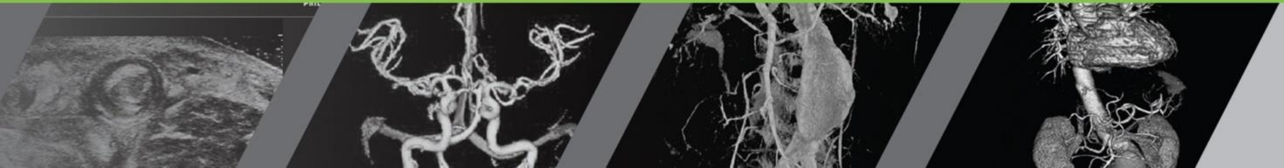
History

- Hippocrates, 400 BC, uses the term ‘apoplexy’
  - – Lesions of the carotid artery could cause contralateral hemiplegia
- Rufus of Ephesus, 100 AD
  - – Carotid derived from the Greek word meaning ‘to stun, stupefy, or fall into deep sleep’



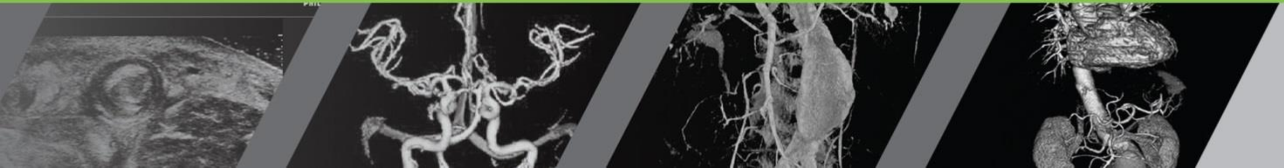
History

- Pare, 1552, carotid ligation for trauma
- Thomas Willis, 1664, ‘Cerebri Anatome’
- Sir Astley Cooper, 1809, carotid ligation for aneurysm
- Gluck, 1898, replaces CCA with vein graft in experimental animals



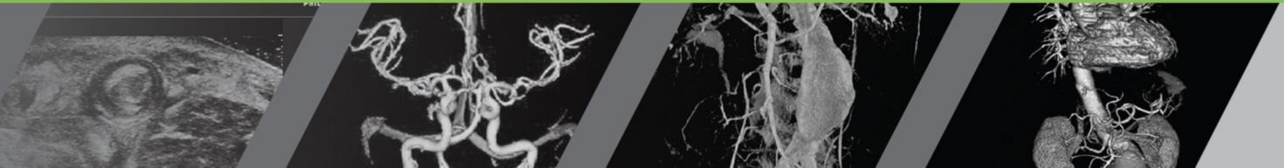
History

- Von Parczewski, 1916, resected CCA aneurysm and did end to end anastomosis
- Von Haberer, 1918, Lexer and Denck, 1918
  - Traumatic CCA aneurysms treated similarly
- Harry Sloan, 1920, surgical oncologist resects and reconstructs CCA during radical neck



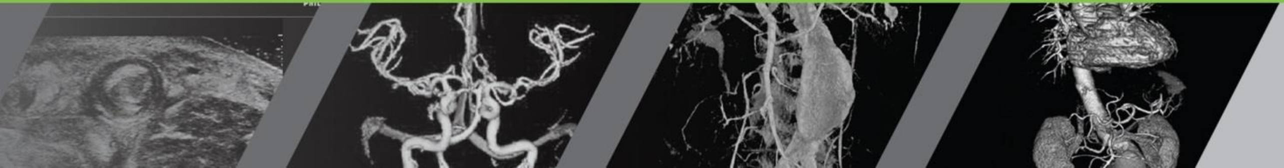
History

- Moniz, 1927, presents the first report on cerebral angiography
- It gradually became clear that the symptoms of carotid disease may be caused not only by complete occlusion but also in a rather sizable group of patients by stenosis of the vessel at one or several points



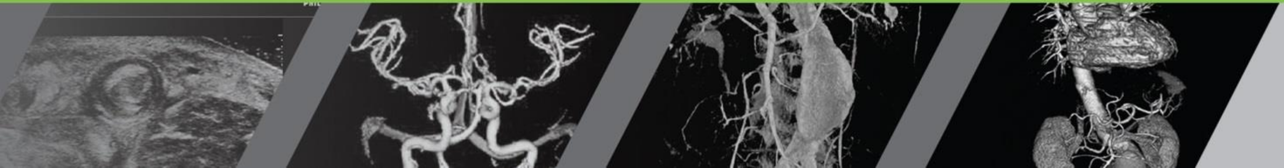
History

- Carl Fisher, 1951, calls attention to the bifurcation atheroma as a frequent cause of contralateral neurologic symptoms.
- went so far as to predict that ‘vascular surgery will find a way to bypass the occluded portion of the artery during the period of ominous fleeting symptoms’



Carotid reconstruction

- DeBakey, 8/7/53, first successful CEA (53 yr old man with tia – no angiogram done)
- Eastcott, Pickering, & Rob, 5/19/54, resection of the bifurcation and end to end anastomosis of the CCA and ICA
- Cooley, et al, first report successful CEA 3/4/56 – also the first reported shunt use



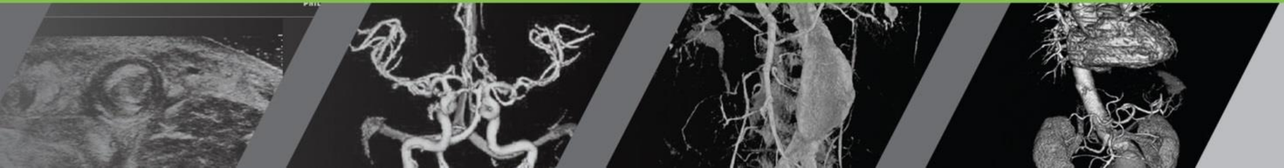
CEA boom

- Rates of CEA rise dramatically through the 1980’s.
- Studies suggest complication rates high
  - Rand corp study suggests 30% inappropriate

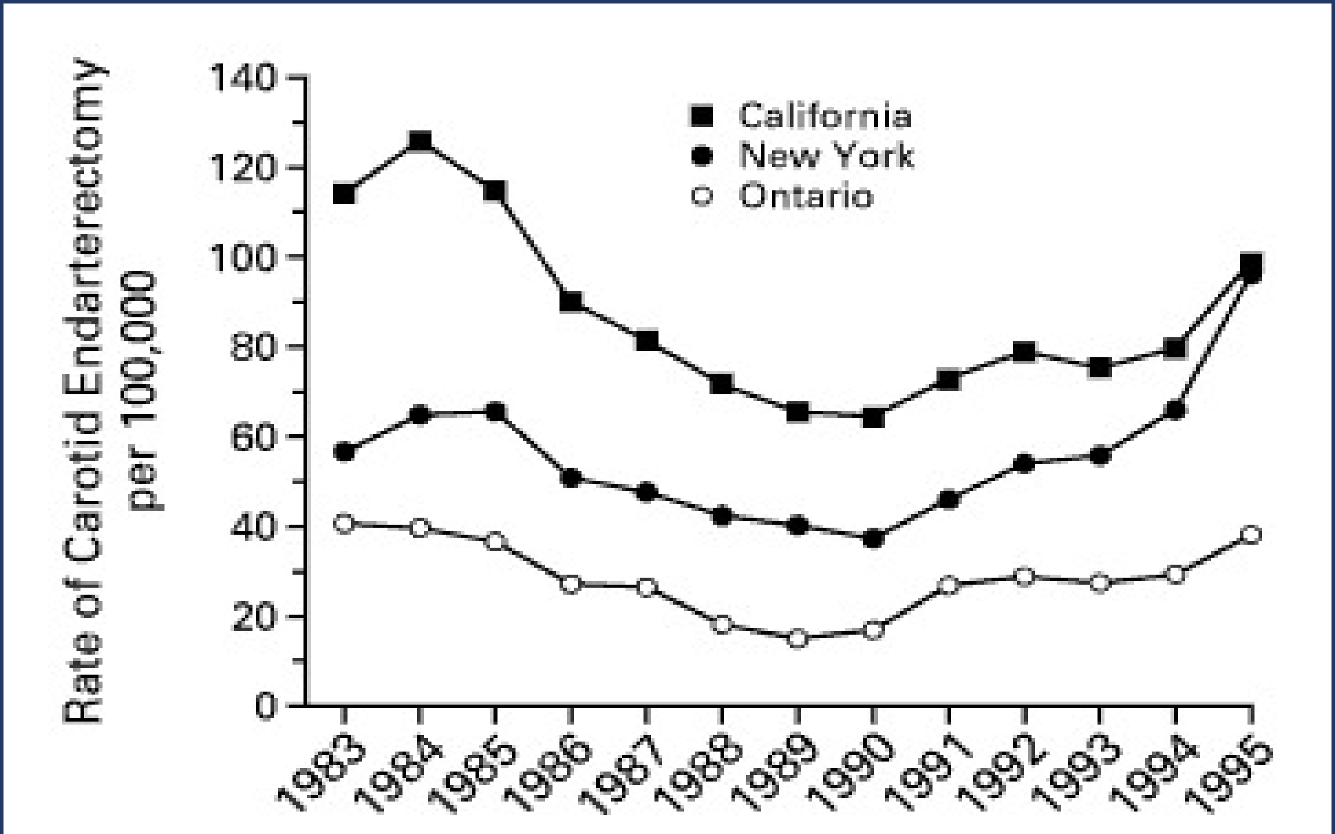
CEA Boom

- North American Symptomatic Carotid Endarterectomy Trial, NASCET, 1991
- Asymptomatic Carotid Atherosclerosis Study, ACAS, 1995
- European Carotid Surgery Trial, ECST, 1996

- ALL SUPPORTED CEA over medical therapy

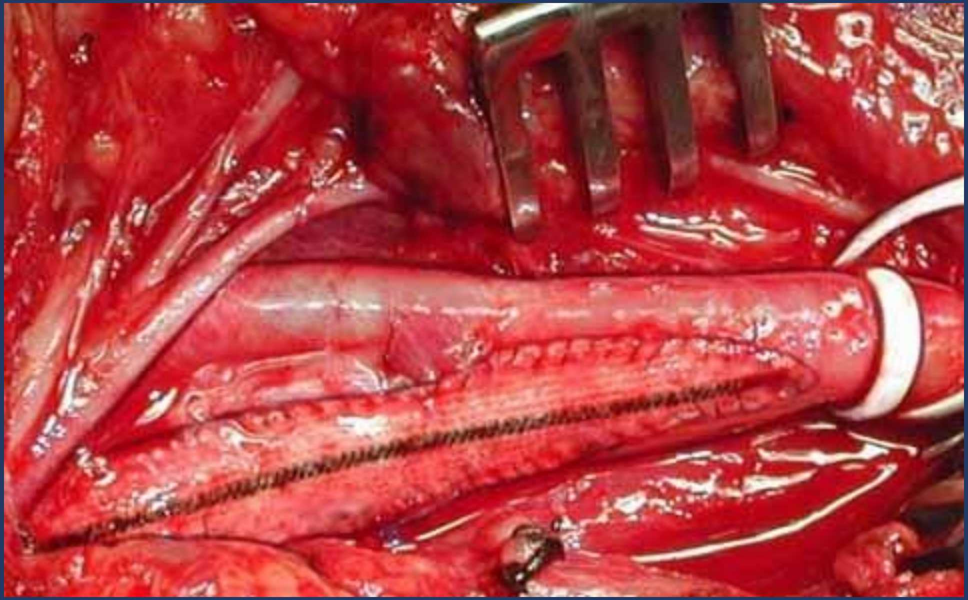


CEA rates



Rate of Carotid Endarterectomy per 100,000
140
120
100
80
60
40
20
0
California
New York
Ontario
1983
1984
1985
1986
1987
1988
1989
1990
1991
1992
1993
1994
1995

CEA

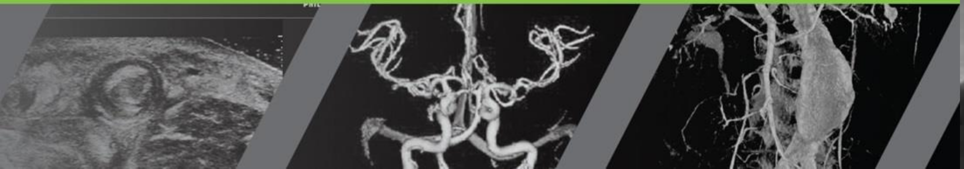


The interventional express

- 1929 Forssmann does first cardiac catheterization does his own cutdown and inserts catheter into antecubital vein, threads it into right atrium.

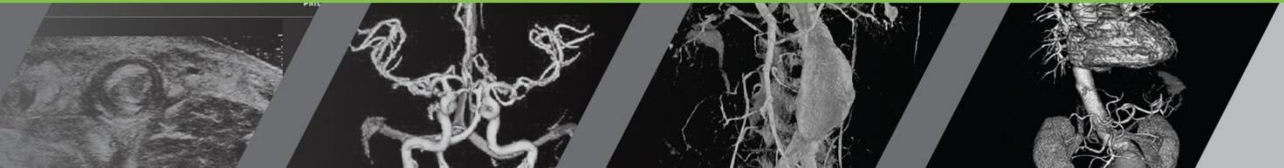
- 1956 shares Nobel Prize with Cournand and Richards.
- 1958 Sones does first coronary angiogram.
- 1964 Dotter introduces concept of transluminal angioplasty.

- 1974 Gruentzig performs first peripheral balloon angioplasty.



Carotid Angioplasty

- DeBakey, 1967, open angioplasty with gradual dilatation for FMD
- Mathias, 1977, first PTA
- Marks, et al, 1994, Stanford – Palmaz stents in the ICA after failed medical Rx for dissection
- Dietrich et al, 1993-1995, 117 arteries treated with primary pta / stenting - 11% cva / tia



Stenting Arrives

- 2000 Jun;50(2):160-7.
- **Global experience in cervical carotid artery stent placement.**
- Wholey MH[1], Wholey M, Mathias K, Roubin GS, Diethrich EB, Henry M, Bailey S, Bergeron P, Dorros G, Eles G, Gaines P, Gomez CR, Gray B, Guimaraens J, Higashida R, Ho DS, Katzen B, Kambara A, Kumar V, Laborde JC, Leon M, Lim M, Londero H, Mesa J, Musacchio A, Myla S, Ramee S, Rodriquez A, Rosenfield K, Sakai N, Shawl F, Sievert H, Teitelbaum G, Theron JG, Vaclav P, Vozzi C, Yadav JS, Yoshimura SI.

- The total number of endovascular carotid stent procedures that have been performed worldwide to date included 5,210 procedures involving 4,757 patients. There was a technical success of 98.4% with 5,129 carotid arteries treated. Complications that occurred during the carotid stent placement or within a 30-day period following placement were recorded. Overall, there were 134 transient ischemic attacks (TIAs) for a rate of 2.82%. Based on the total patient population, there were 129 minor strokes with a rate of occurrence of 2.72%. The total number of major strokes was 71 for a rate of 1.49%. There were 41 deaths within a 30-day postprocedure period resulting in a mortality rate of 0.86%. The combined minor and major strokes and procedure-related death rate was 5.07%.

CAS
Trials

- SAPPHIRE
- ARCHeR
- BEACH
- CABERNET
- CREST
- MAVErIC
- SECURITY
- CARESS
- CAPTURE
- PASCAL
- TACIT
- CAVATAS
- VIVA

- MOMA ROADSTER
- SPACE CANOPY
- EVA-3S SCAFFOLD
- CREATE ROADSTER 2
- CASES PROOF
- EXACT CONFIDENCE
- ACT-1
- EMPIRE
- EPIC EU
- SAPPHIRE WW
- SONOMA
- CHOICES
- PROTECT

CAS

Selective Lt Carotid Angio

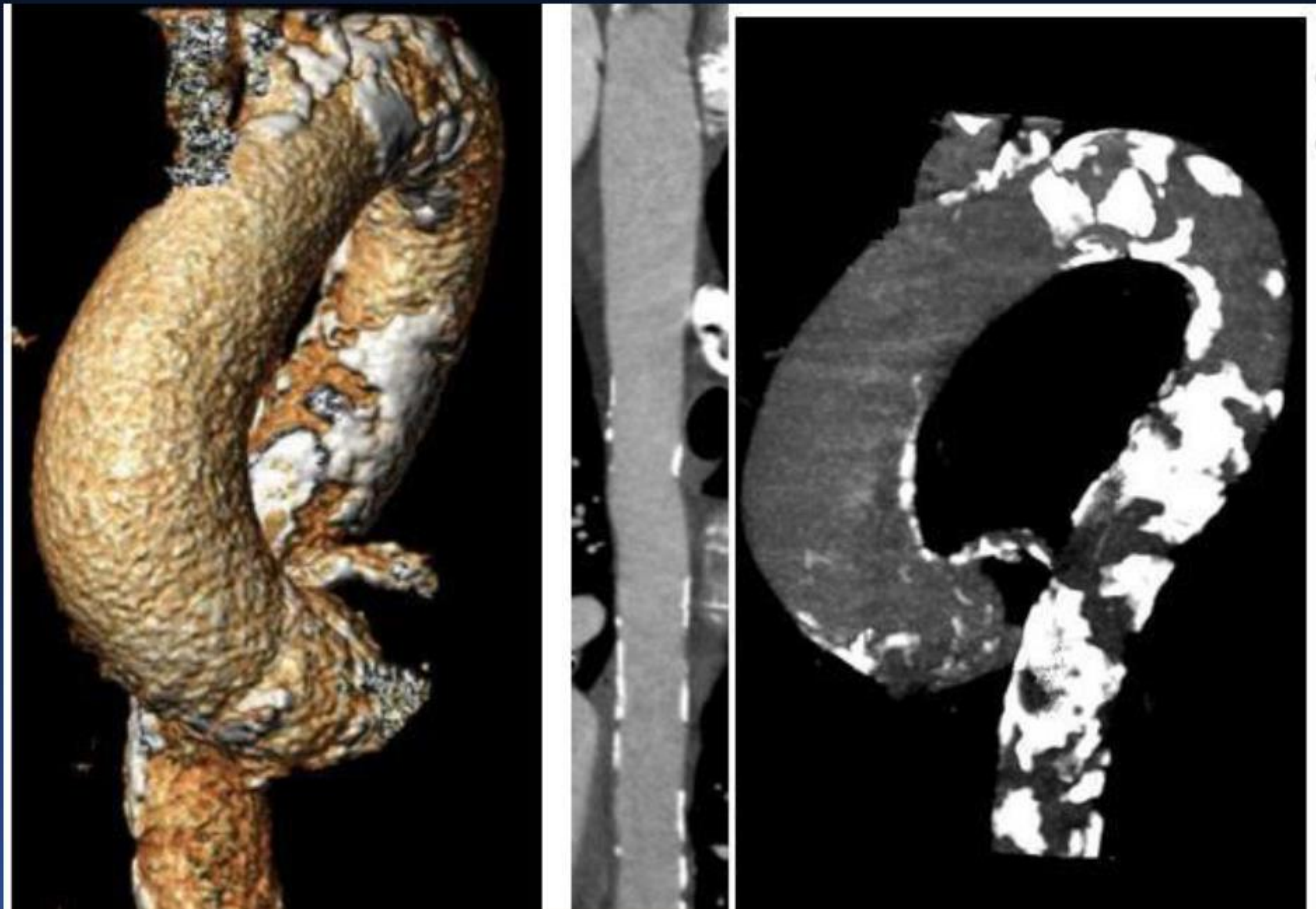
Long Lt ICA ulcerated lesion (>80% stenosis)

CAS

Completion Angiogram

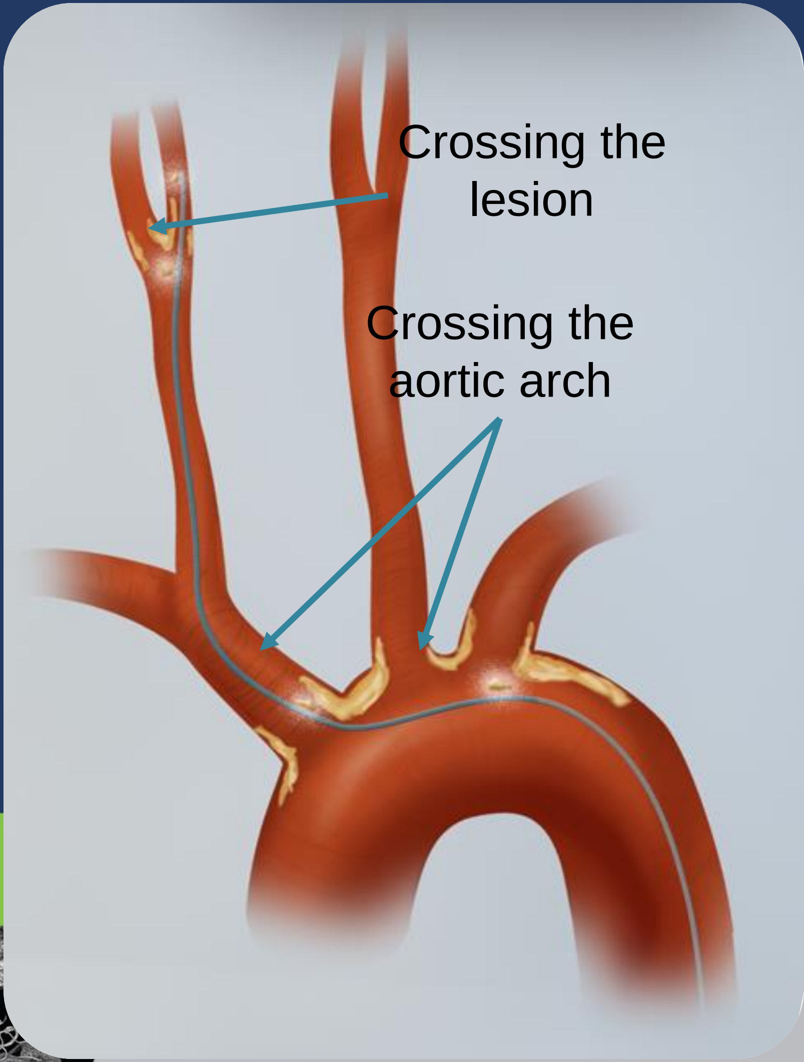
Free flow into the ICA

Why embolic protection?



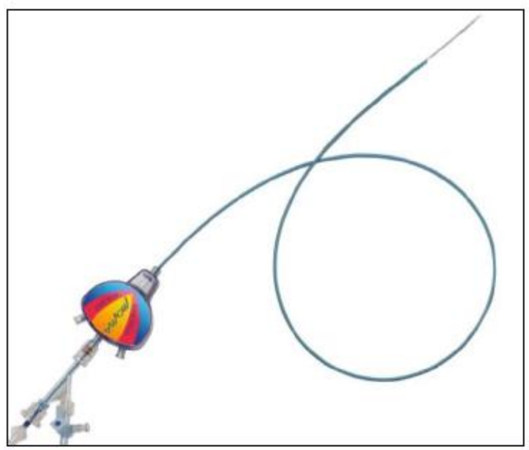
Causes of Peri-procedural Stroke

- Traditional CAS requires several steps that create embolic risk
  - Advancing a catheter from the femoral artery
  - Navigating the lesion before a protection device is in place

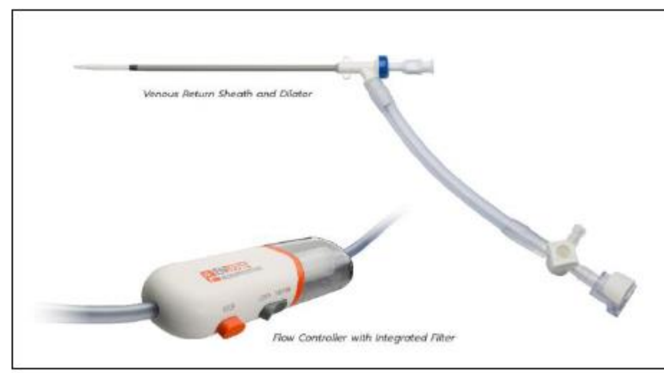


Progression of EPD Technology in CAS

Distal Protection

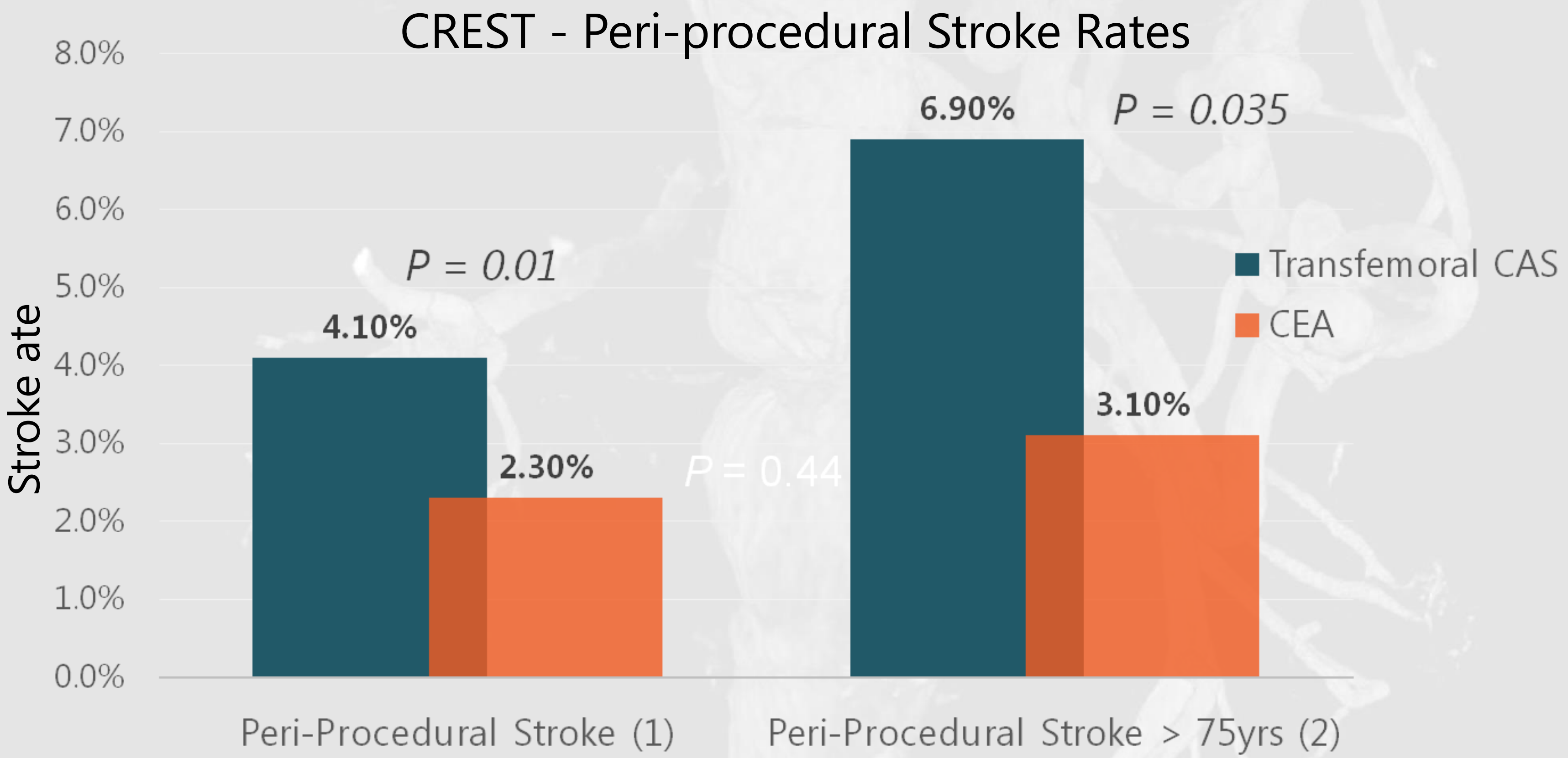


Proximal Protection



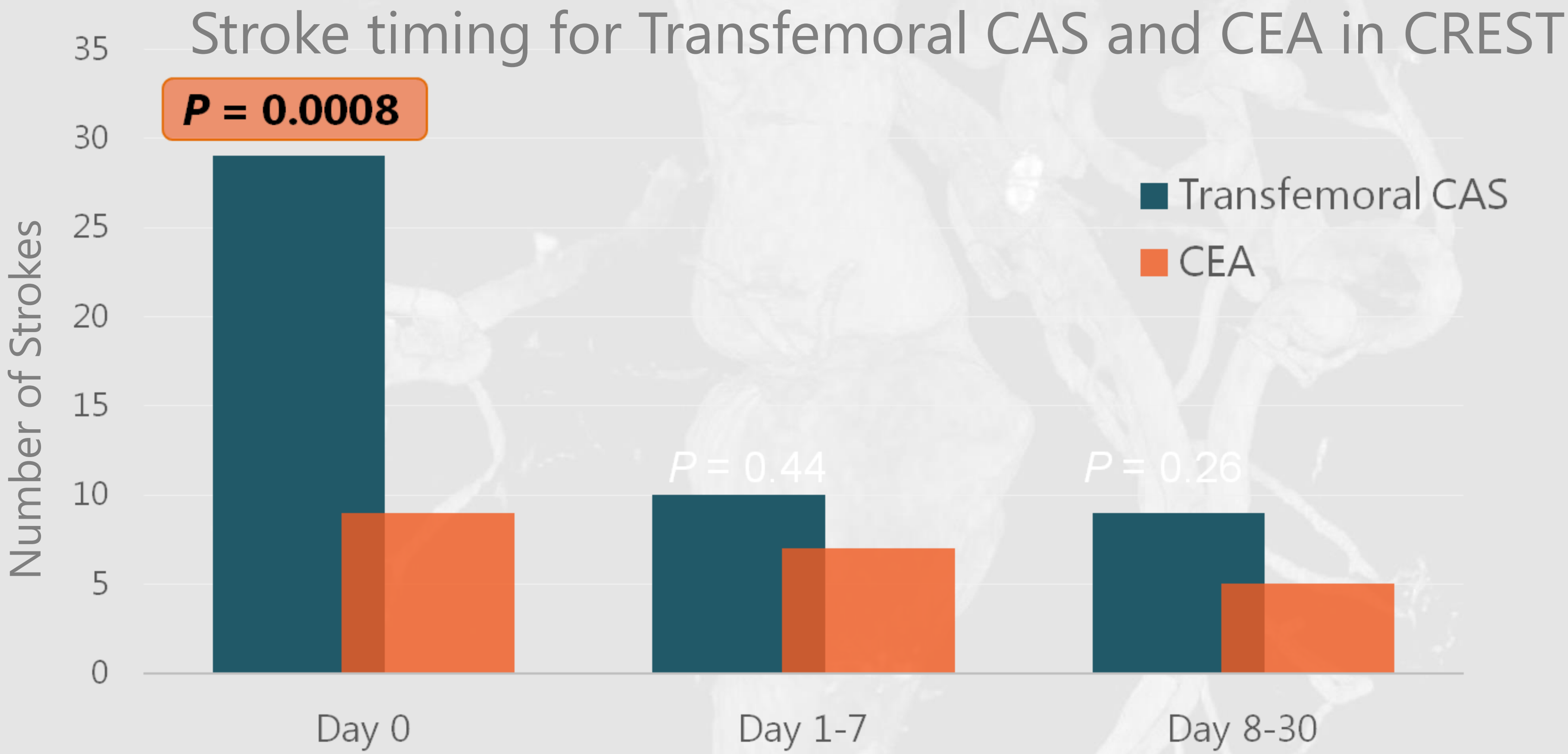
Transcervical Access with Flow Reversal

2x Peri-Procedural Stroke rate for Transfemoral CAS



1. N Engl J Med 2010;363:11-23.
2. Stroke 2011;42:00-00.

Day 0 Stroke is the Culprit

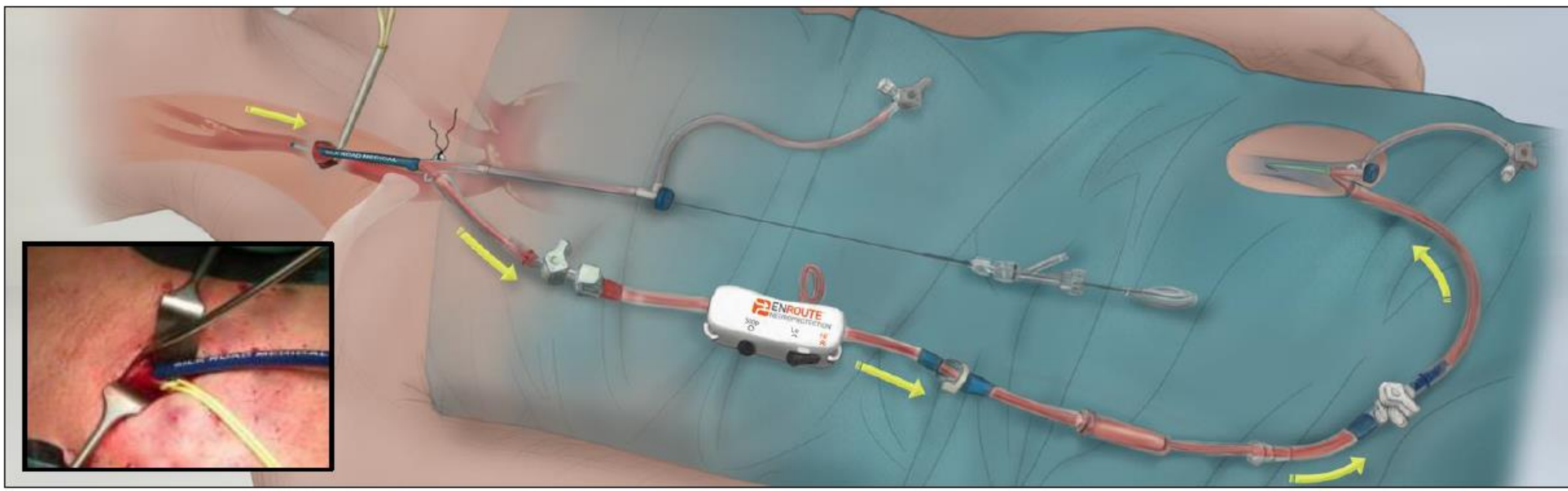


[1]Circulation, Nov. 29, 2012. P-value calculated post hoc by independent statistician.

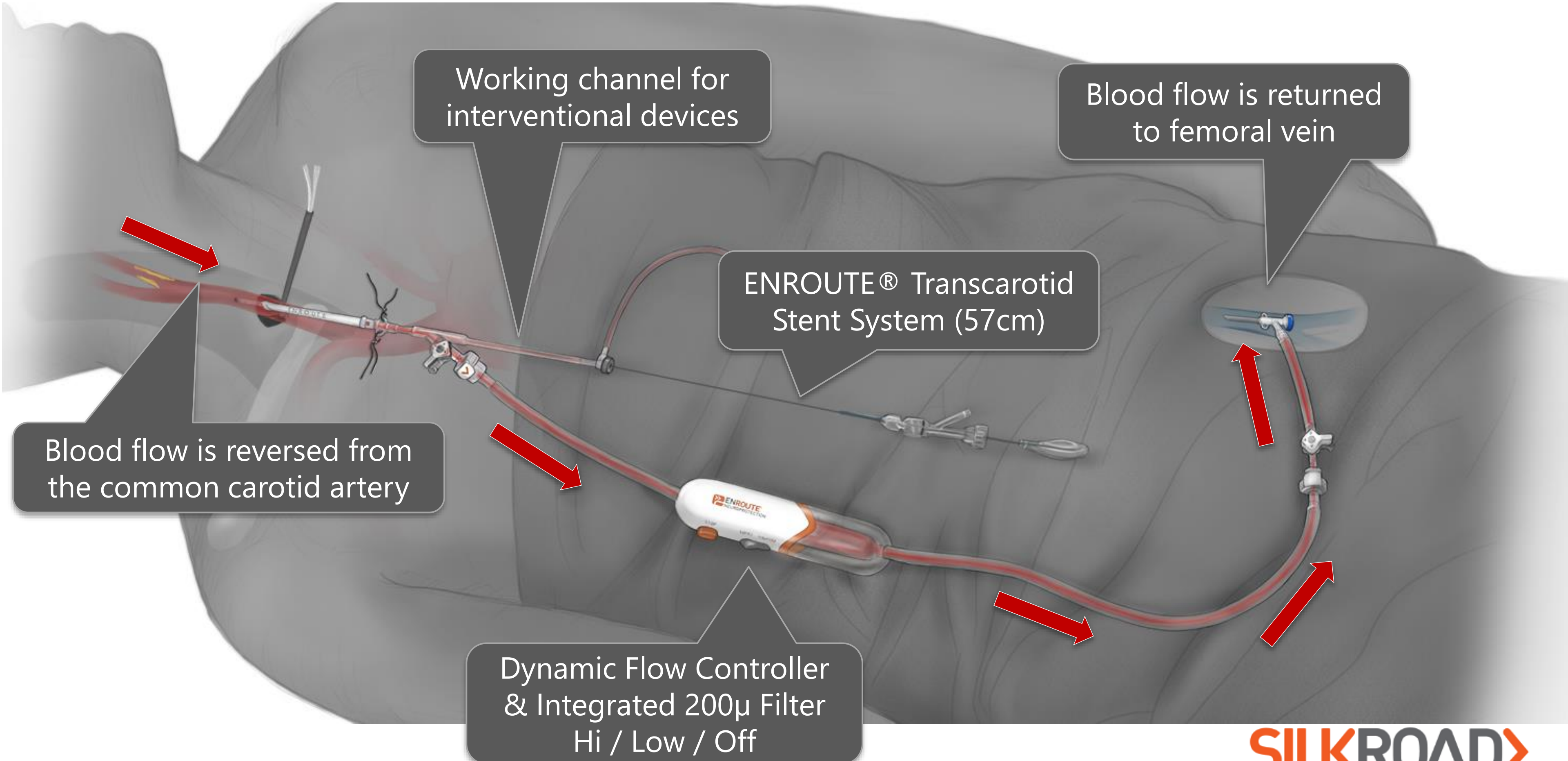
Transcervical Carotid Artery Revascularization

TCAR

- 1-2cm Incision
- Local anesthesia
- Flow reversal circuit: carotid artery to femoral vein



TCAR: TRANSCAROTID ARTERY REVASCULARIZATION



SILKROAD

Transcervical Carotid Artery Revascularization

TCAR

Advantages of TCAR Procedure:

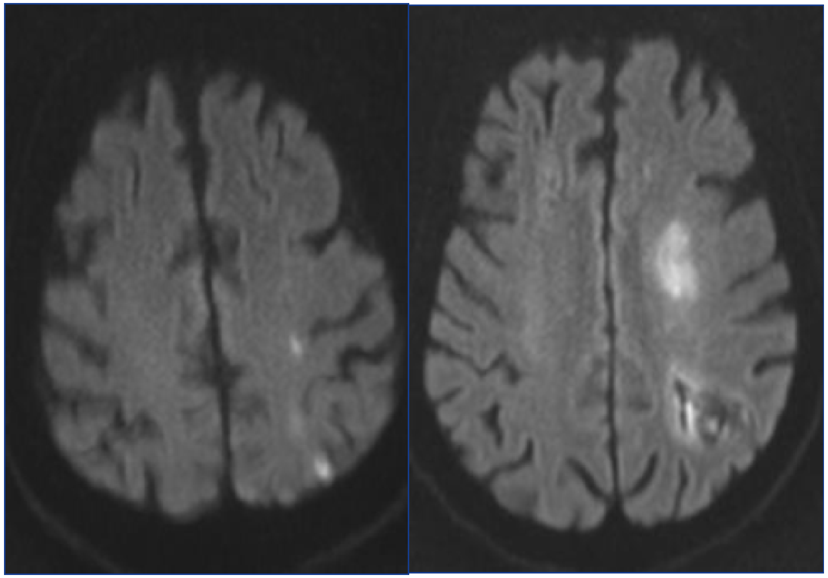
- Establish embolic protection before lesion crossing (proximal protection)
- Flow reversal ("surgical" back-bleeding)
- Avoiding the aortic arch

Transcervical Carotid Artery Revascularization

TCAR

Advantages of TCAR Procedure:

- Avoiding the aortic arch



DW-MRI Lesions with CAS/CEA

- Common after carotid intervention
- Incidence / location varies approach
- Bilateral w/ transfemoral CAS
- Evidence of correlation to neurocognitive decline [1]

[1] Akkaya E, et al. Int J Cardiol. 2014;176(2):478-83.

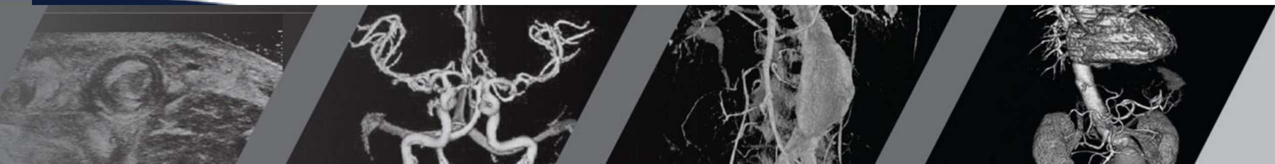
Transcervical Carotid Artery Revascularization

TCAR

Advantages of TCAR Procedure:

- Avoiding the aortic arch

Study	Access	EPD	Embolic Protection	Patients	% w/ New DWI Lesions
ICSS[2]	CEA	Clamp, backbleed	Clamp, backbleed	107	17%
ICSS[2]	Femoral	Distal	Distal filter (various)	51	73%
PROFI[1]	Femoral	Distal	Distal filter (Emboshield)	31	87%
PROFI[1]	Femoral	Transfemoral CAS	Proximal occlusion (MoMA)	31	45%
PROOF[3]	Transcervical	Flow Reversal	Transcarotid Access, w/ Flow Reversal	56	19%



Transcervical Carotid Artery Revascularization

TCAR

ROADSTER Trial

- Prospective, single arm multicenter trial
- ENROUTE Transcarotid NPS during CAS procedures
- Pivotol trial enrolled 141 patients at 18 sites*
- Symptomatic (>50%) and Asymptomatic (>70%)
- High surgical risk patients only
- 30 day stroke, death, stroke/death, MI

* 220 included in continued access, equivalent all stroke rate at 30 days.

Transcervical Carotid Artery Revascularization

TCAR

ROADSTER Trial 12-month Outcomes

High Surgical Risk	Pivotal Group, ITT (n=141)		Pivotal Group, PP (n=136)	
S/D/MI*	5	3.5%	4	2.9%
Major Stroke	0	0%	0	0%
Minor Stroke	2	1.4%	1	0.7%
Death	2	1.4%	2	1.5%
MI	1	0.7%	1	0.7%
Stroke & Death	4	2.8%	3	2.2%
Cranial Nerve Injury (CNI)	1	0.7%	1	0.7%
CNI Unresolved at 6 Mos	0	0%	0	0%

ROADSTER 1 IDE
OUTCOMES COMPARE FAVORABLY

TCAR 30-Day Outcomes on Par with CEA

	ROADSTER 1* High Surgical Risk			CREST** Standard Surgical Risk
	Pivotal (n=141)	Con't Access (n=78)	All (n=219)	CEA Arm (n=1251)
S/D/MI	3.5%	3.8%	3.7%	4.5%
Stroke	1.4%	1.3%	1.4%	2.3%
Death	1.4%	0.0%	0.9%	0.3%
MI	0.7%	2.6%	1.4%	2.3%
Stroke & Death	2.8%	1.3%	2.3%	2.6%
Cranial Nerve Injury (CNI)	0.7%	1.3%	0.9%	4.8%
Unresolved at 6 Mos	0.0%	0.0%	0.0%	2.0%

*Kwolek, LaMuraglia, Cambria. SVS Vascular Annual Meeting 2016
**Brott, et al. N Engl J Med 2010;363:11

SILKROAD

ROADSTER 1 STUDY OUTCOMES

TCAR ***not*** contraindicated in "at risk" sub-groups

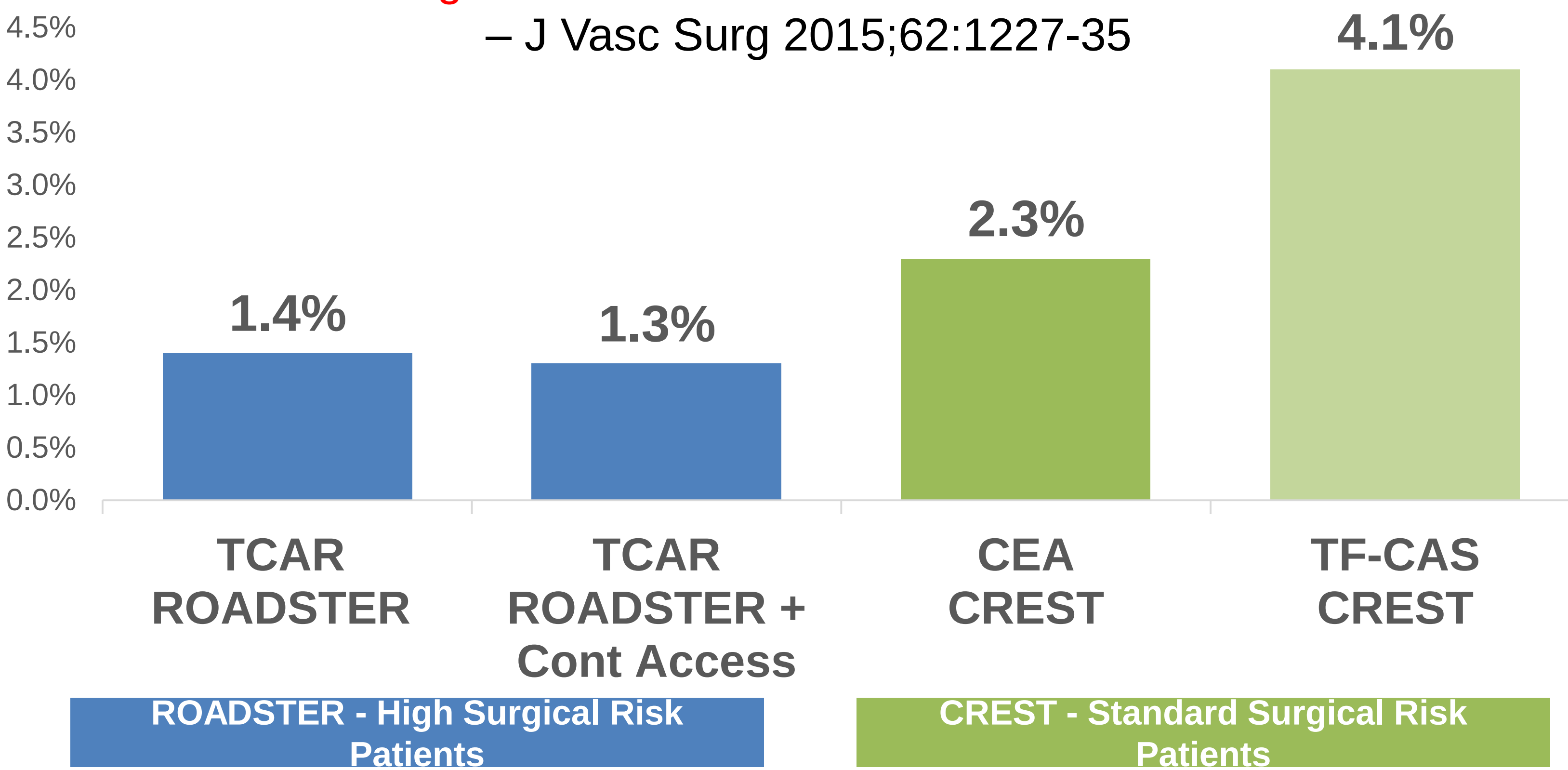
High Surgical Risk	Age ≥ 75 (n=91)	Symptomatic (n=43)	Female (n=83)
S/D/MI	6.6%	2.3%	2.4%
Major Stroke	0.0%	0.0%	0.0%
Minor Stroke	1.1%	0.0%	0.0%
Death	2.2%	2.3%	1.2%
MI	3.3%	0.0%	1.2%
Stroke & All Death	3.3%	2.3%	1.2%
Stroke & Cardiovascular or Neurological Death	1.1%	0.0%	0.0%

SILKROAD

ROADSTER 1:
30 Day Stroke Outcomes vs Standard Risk in CREST

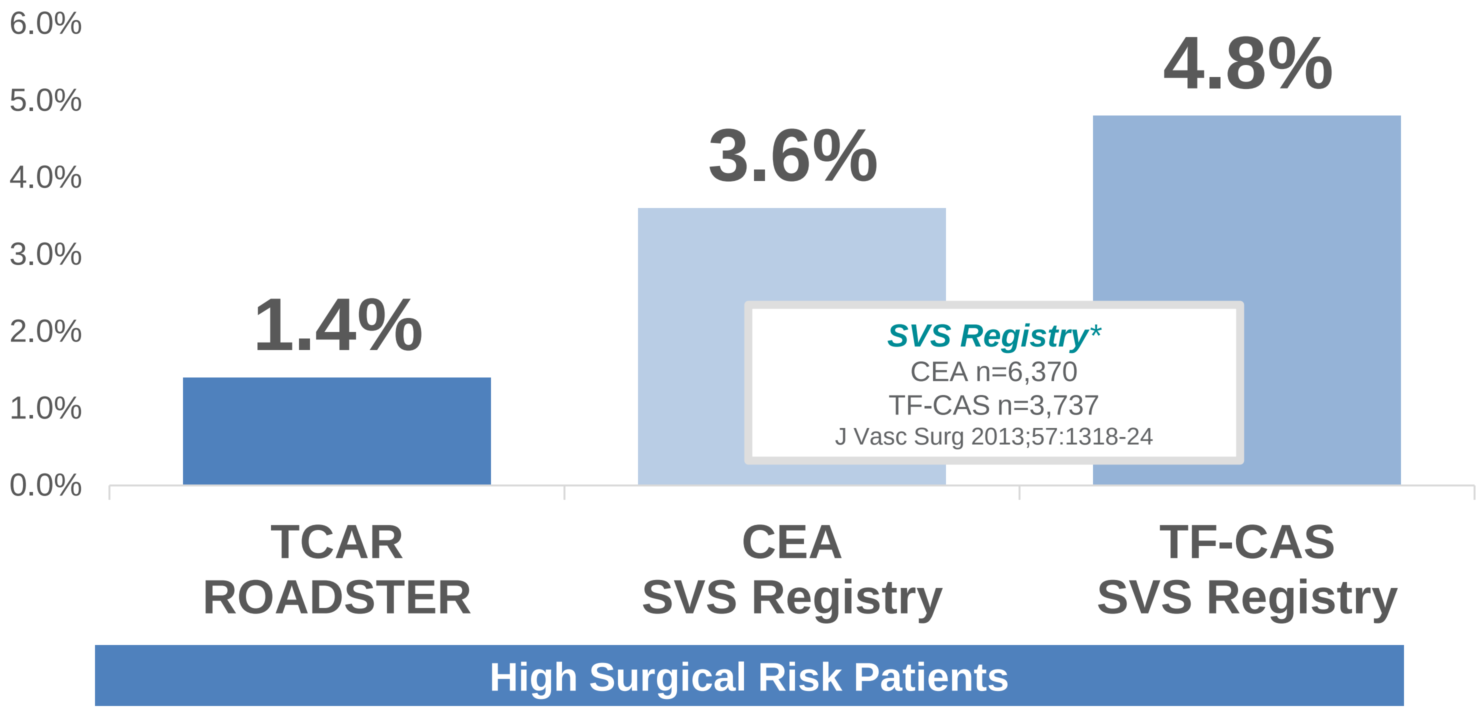
“The overall stroke rate of 1.4% is the lowest reported to date for any prospective, multi-center trial of carotid stenting.”

– J Vasc Surg 2015;62:1227-35



CREST Trial: N Engl J Med 2010;363:11-23

TCAR in High Surgical Risk Patients 30 Day Stroke Outcomes vs Real World Data

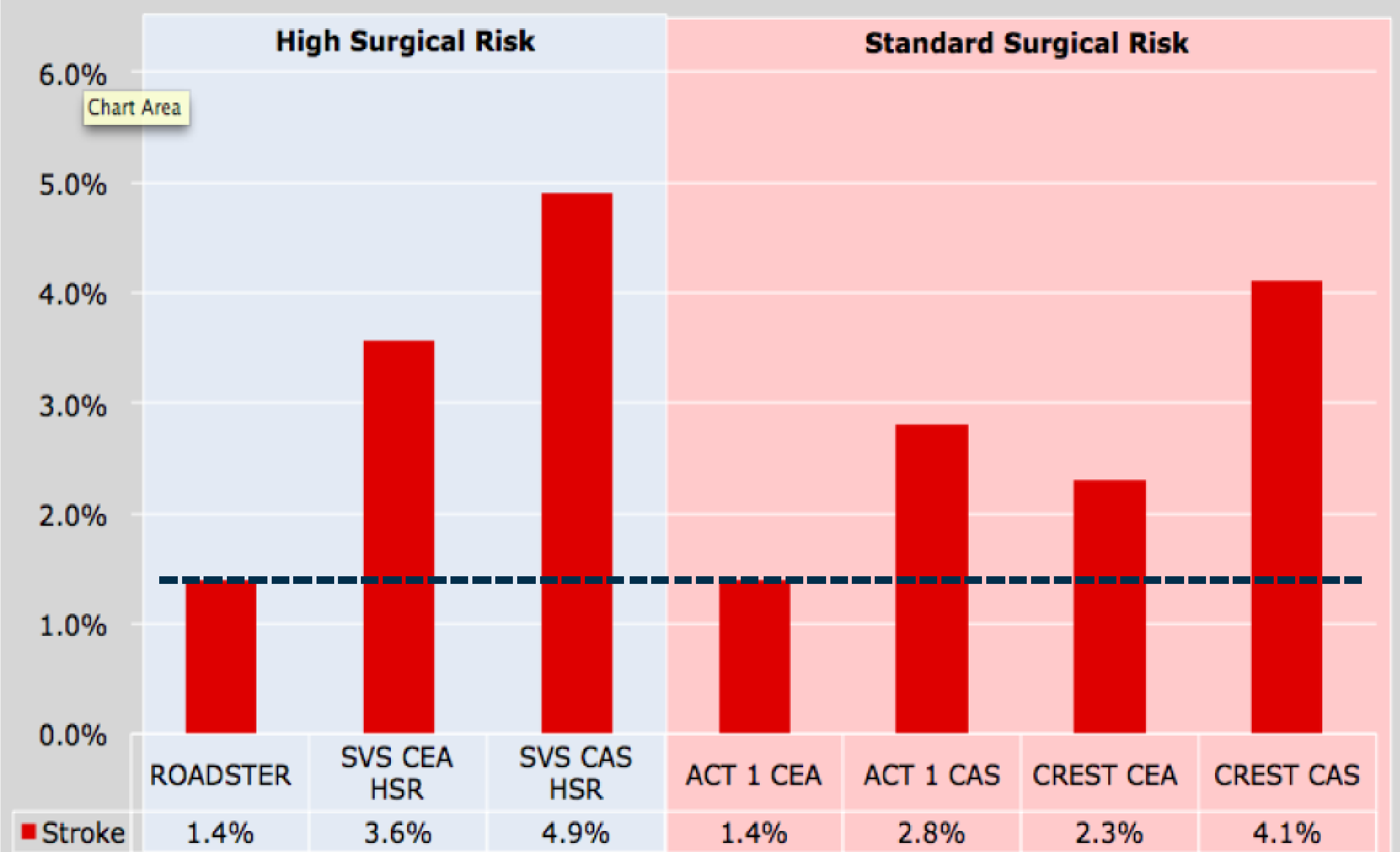


* The impact of Centers for Medicare and Medicaid Services high-risk criteria on outcome after carotid endarterectomy and carotid artery stenting in the SVS Vascular Registry - Marc L. Schermerhorn, MD et al.

Transcervical Carotid Artery Revascularization

Outcomes of Contemporary CAS & CEA Trials

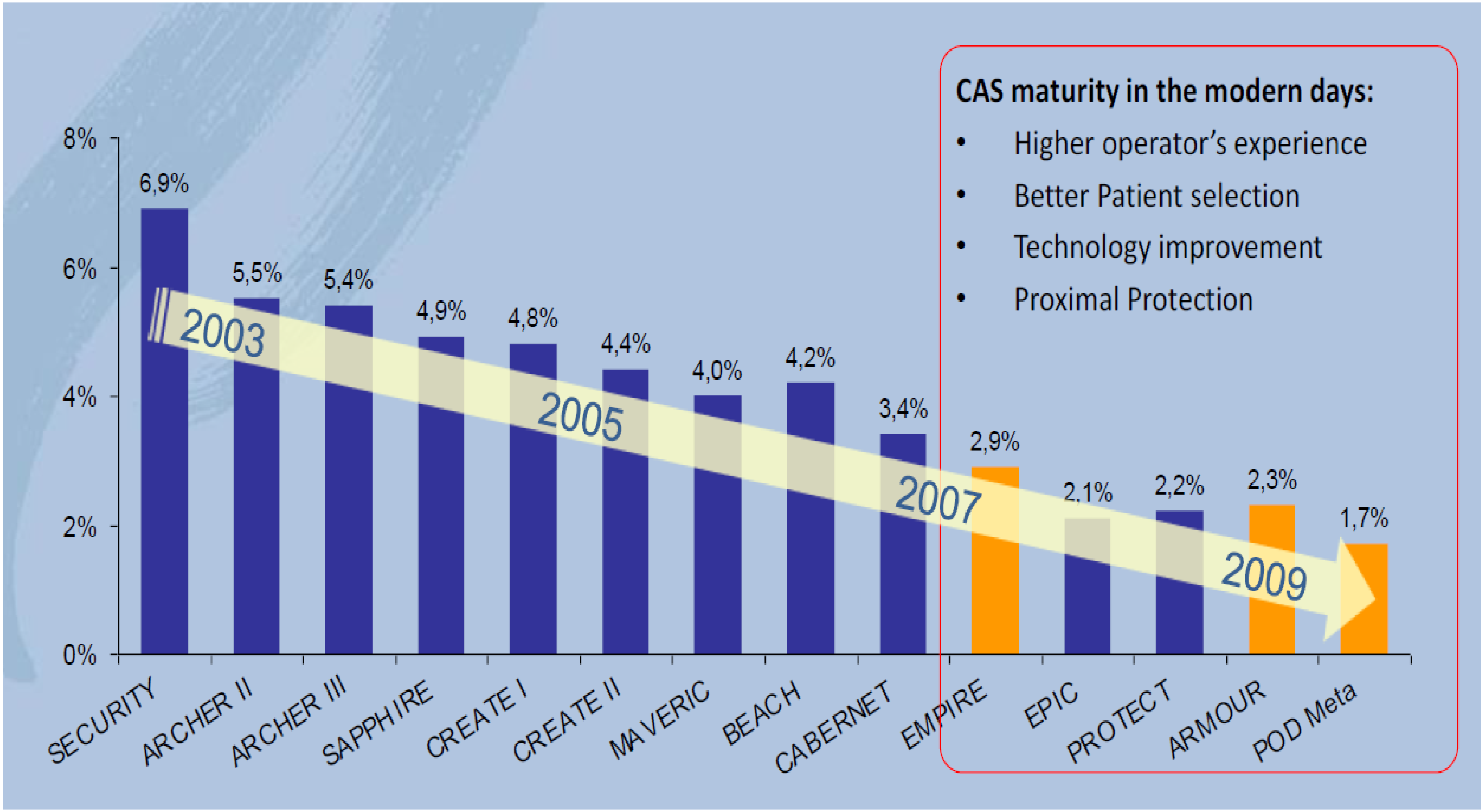
TCAR



The New Bar?

Table 2: Periprocedural Stroke Rates in Contemporaneous Publications of TCAR, CEA and Transfemoral CAS

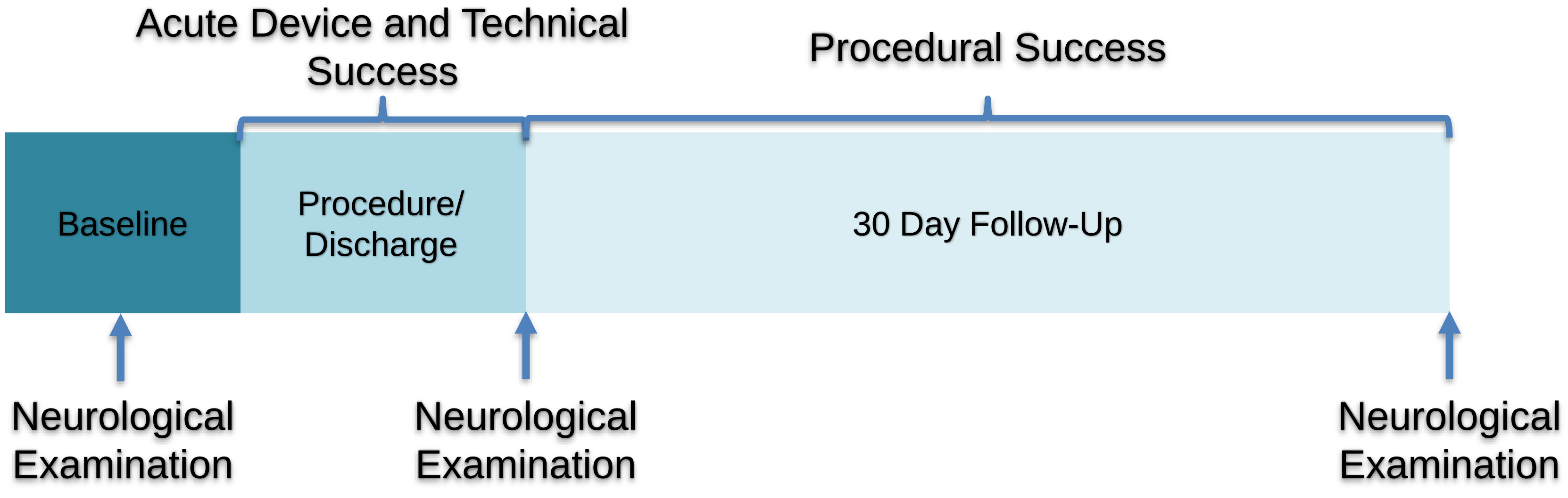
Should All Patients Be Treated with TCAR?



From Biamino, LINC 2016

ROADSTER 2 Study Design

- Minimum of **600 patients**
- **Per-protocol analysis** (all subjects enrolled without major protocol deviation)
- Life expectancy **≥3 years**
- The primary endpoint is the rate of **procedural success** (includes 30 day S/D/MI and procedural failures)
- **70% new sites**, 30% ROADSTER 1 sites
- **Dedicated TCAR System** = ENROUTE NPS + ENROUTE Stent



ROADSTER 2:
High Surgical Risk Patient Population

Physiologic HSR Inclusion

- Severe cardiac disease; severe COPD;
- chronic renal insufficiency
- Age ≥75

Anatomic HSR Inclusion

- Contralateral occlusion; bilateral or high or tandem stenoses
- Restenosis post CEA
- Permanent contralateral CNI
- Hostile neck
  - Irradiation
  - Radical neck dissection
  - Cervical spine immobility

Exclusion: Common to CAS

- Afib; recent valve or MI; bleeding
- Evolving stroke; neuro disorders
- Occlusion; ostial CCA or intracranial stenosis; string sign; previous stent

Exclusion: Transcarotid

- CCA disease at entry site
- <5cm clavicle to bifurcation

ROADSTER 2: Baseline Characteristics

Parameter	n=486
Age ≥75	41.4%
Female	33.7%
Symptomatic	24.9%
Physiologic Risk Factors only	31.7%
Anatomic Risk Factors only	41.5%
Both Physiologic & Anatomic Risk Factors	26.8%
Top 3 Physiologic Risk Factors	
Age ≥ 75 Years (17.9% as sole criterion)	42.0%
Hx of CAD (≥2 vessel disease)	14.7%
COPD	5.6%
Top 3 Anatomic Risk Factors	
High Cervical Stenosis	25.4%
Restenosis after CEA	20.0%
Hostile Neck	17.0%

ROADSTER 2:
Procedure Information

Parameter	ROADSTER 1 n=219	ROADSTER 2 n=486
ROADSTER 1 Operators	100%	17.9%
New TCAR Operators	76.2%	82.1%
Enrollment by New Operators	65.3%	70.0%
Skin-to-Skin Time (median)	70 mins	69 mins
Reverse Flow/Clamp Time (median)	9 mins	9 mins
Tolerance to High Flow	98.6%	98.6%
Tolerance to Low Flow	100%	100%
Fluoro Time (median)	N/R	4.3 mins
Contrast Usage (median)	62 cc	30 cc

ROADSTER 2:
FDA Endpoints to Date

Patients Treated Per Protocol

Acute	n=438	
Acute Device Success	438	100.0%
Technical Success	438	100.0%
30 Days	n=415	
Procedural Success	409	98.6%

Primary Endpoint Analysis

- **Acute device success** is defined as the ability to insert the device, establish flow reversal, and remove the device
- **Technical success** is defined as acute device success plus the ability to deliver interventional tools
- **Procedural success** is defined as technical success in the absence of hierarchical stroke, death or myocardial infarction

ROADSTER 2:
Clinical Outcomes

Patients Treated Per Protocol

	ROADSTER 1 n=203		ROADSTER 2 n=486	
Stroke/Death/MI	6	3.0%	6	1.4%
Stroke	1	0.5%	3	0.7%
Death	2	1.0%	1*	0.2%
MI	3	1.5%	2	0.5%
Stroke/Death	3	1.5%	4	0.9%
Neurological Death	0	0.0%	0	0.0%
CNI (permanent)	0	0.0%	0	0.0%

*One patient expired ~2 weeks post-procedure due to ruptured AAA.

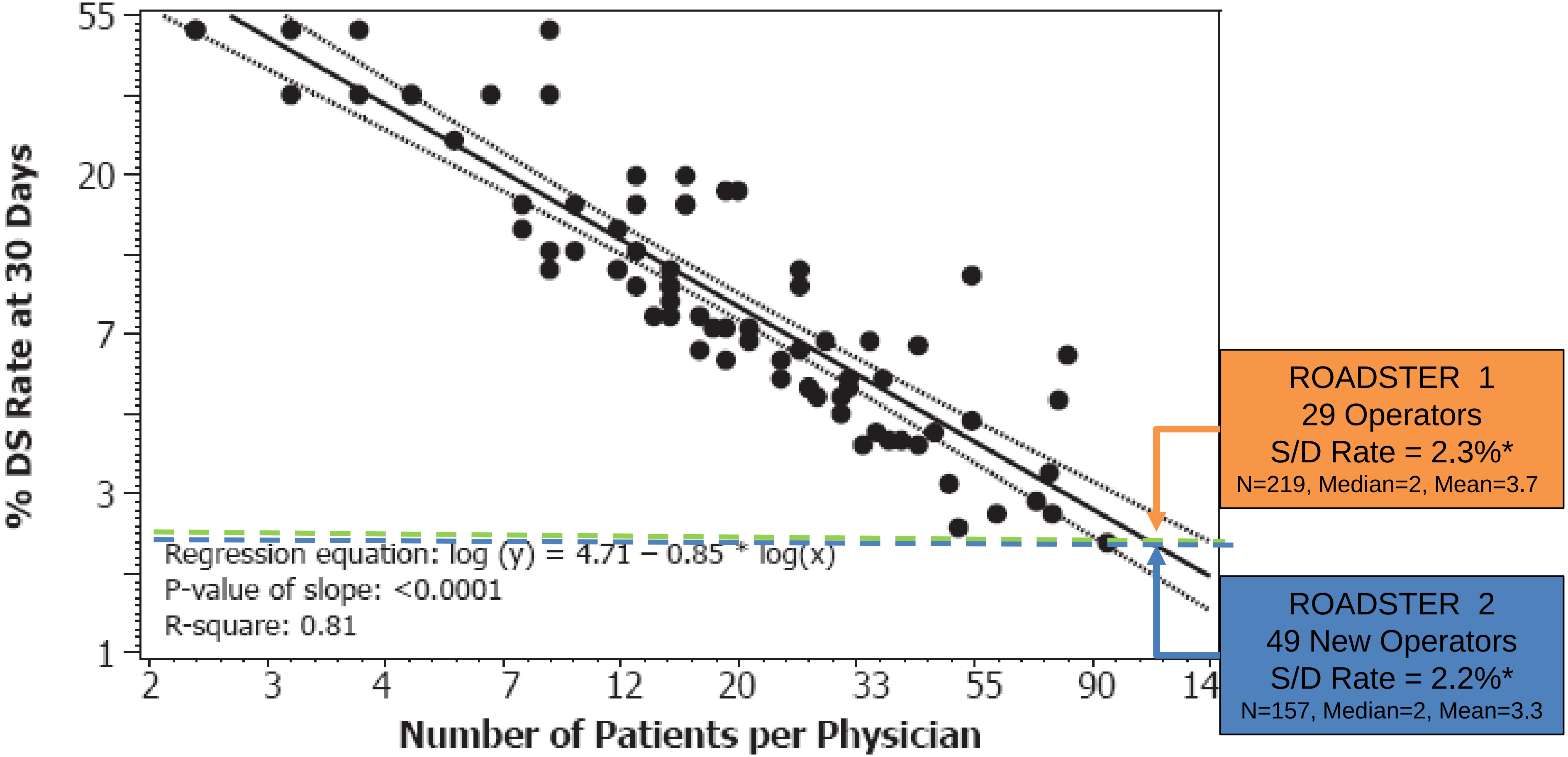
ROADSTER 2 Interim Results

Conclusion

- Clinical outcomes in the ROADSTER 2 post-approval study are comparable to the those of ROADSTER 1 IDE Study.
  - >50% of enrollment in ROADSTER 2 is from operators with no prior TCAR experience
- ROADSTER 2 demonstrates comparable outcomes to CEA in high surgical risk patients.

CEA-like outcomes with shorter learning curve than transfemoral-distal filter CAS

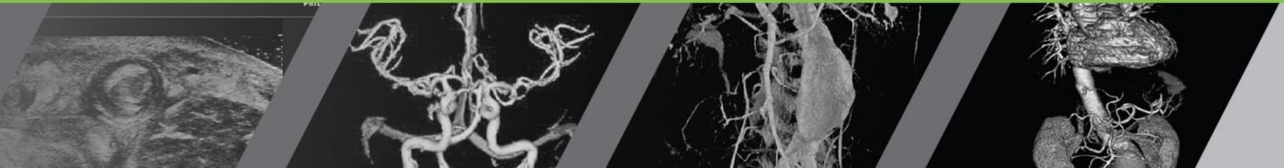
Gray WA et al. CAPTURE 2 Registry. JACC Cardiovasc Interv 2011;4:235-246



*Includes patients with Major Protocol Deviations

TCAR by SVS

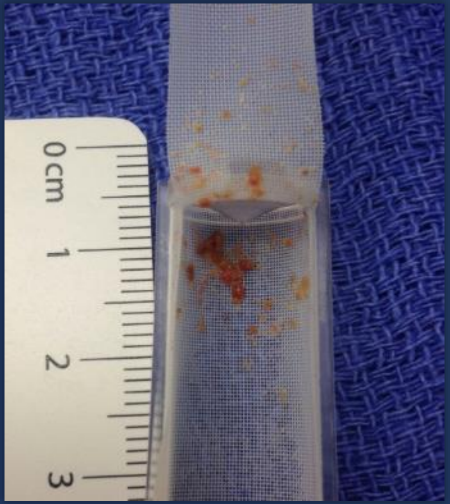
- Roadster 1 — 27
- Roadster 2 — 48
- Commercial — 59
- Total — 134

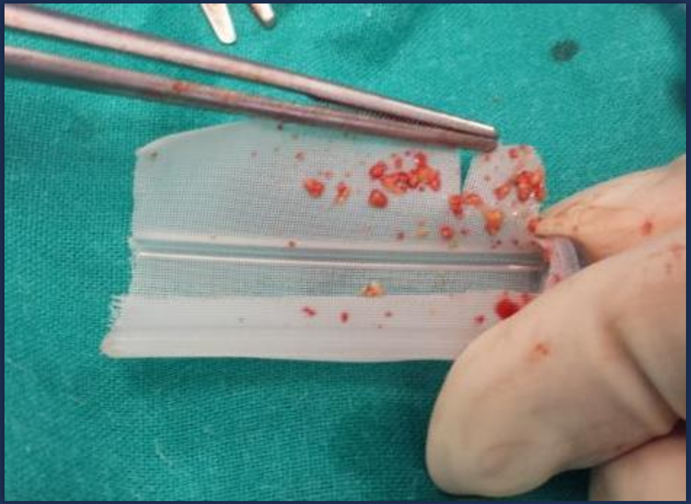


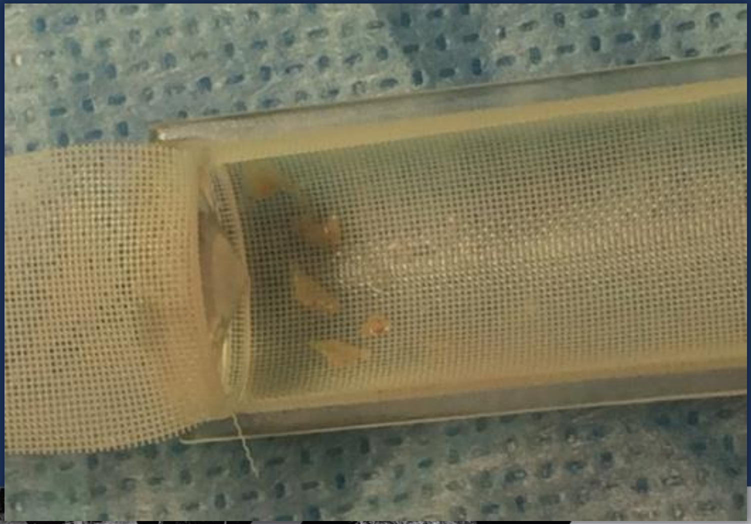
TCAR – Clinically Proven Alternative to CEA and TF-CAS for High Surgical Risk Patients

THE PROOF IS IN THE FILTER

Macro & Micro emboli in ENROUTE™ NPS FILTERS







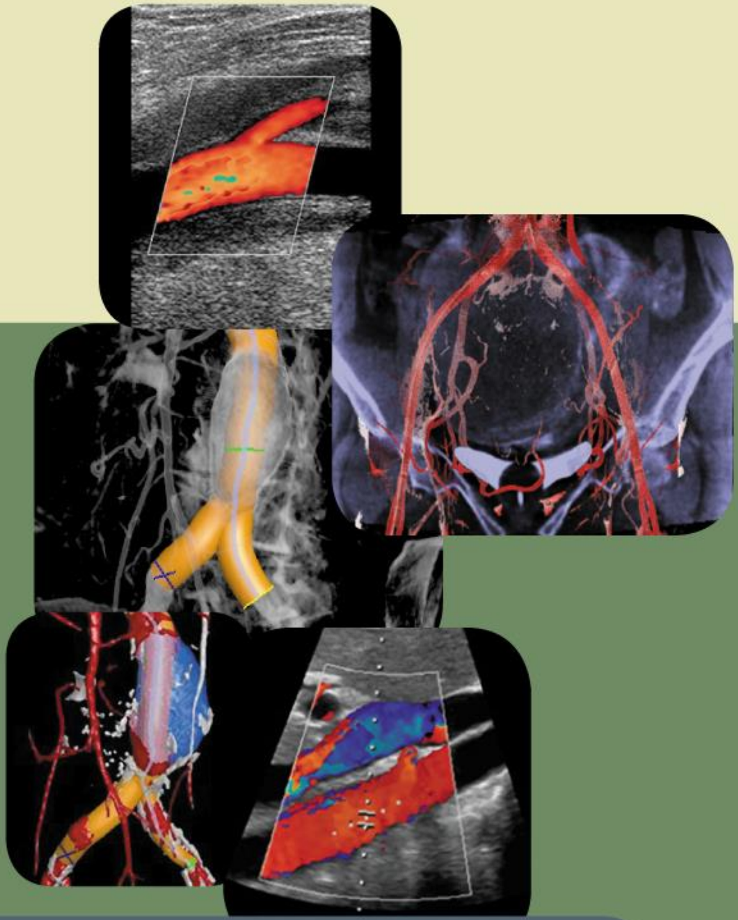
Carotid Artery Stenting

The End of CEA????

Rasesh Shah, MD

1 April 2011

SENTARA®



TCAR

The End of CAS????

Rasesh M. Shah, MD

22 April 2017

SENTARA

2018 MID-ATLANTIC CONFERENCE

8th ANNUAL CURRENT CONCEPTS IN VASCULAR THERAPIES 2018

TCAR

The end of CEA and TF-CAS ???

2018 MID-ATLANTIC CONFERENCE

8th ANNUAL CURRENT CONCEPTS IN VASCULAR THERAPIES 2018

TCAR

The end of CEA and TF- CAS ???

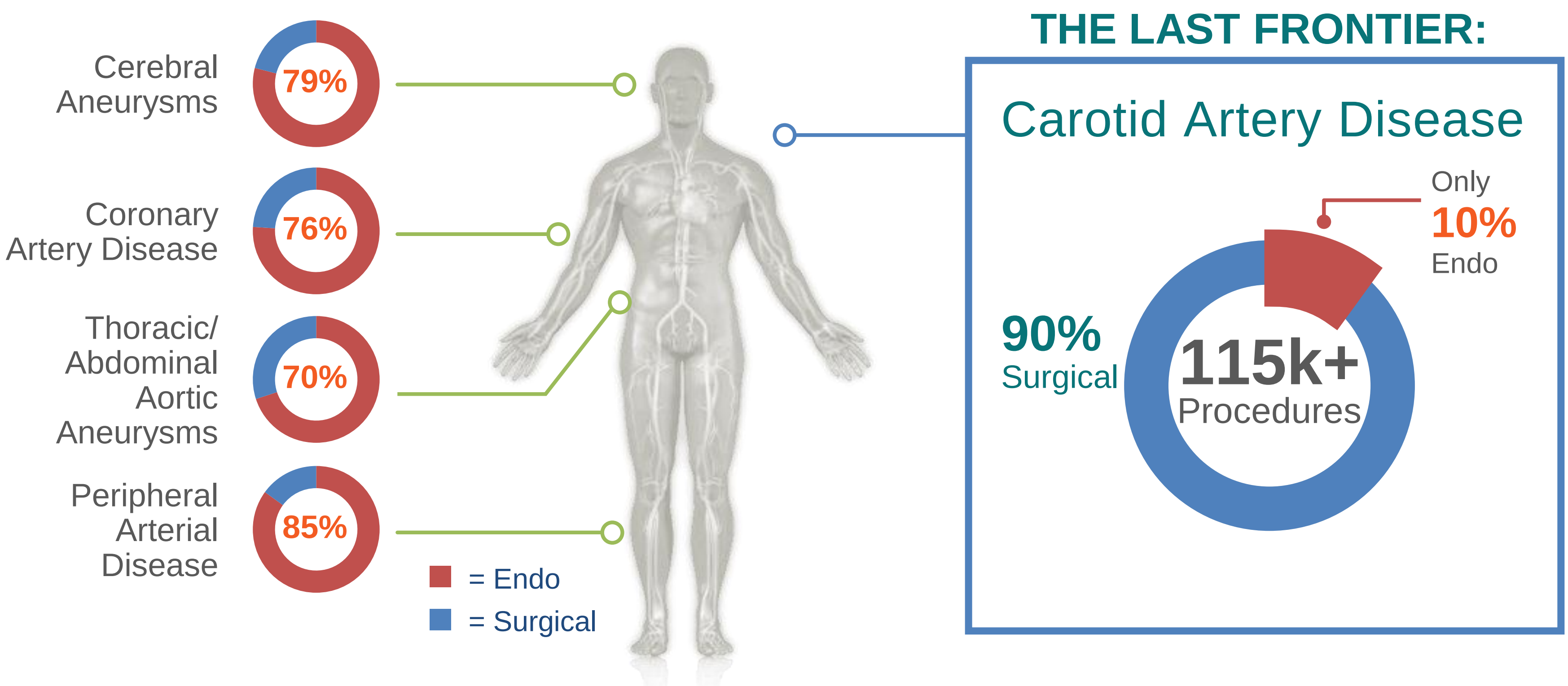
NO, but an increasingly important tool !!!

THANK YOU

tha

The New Normal

Endovascular Procedures



Trans-Femoral Carotid Artery Stenting (TF-CAS)

15 years on Market

10% of procedures

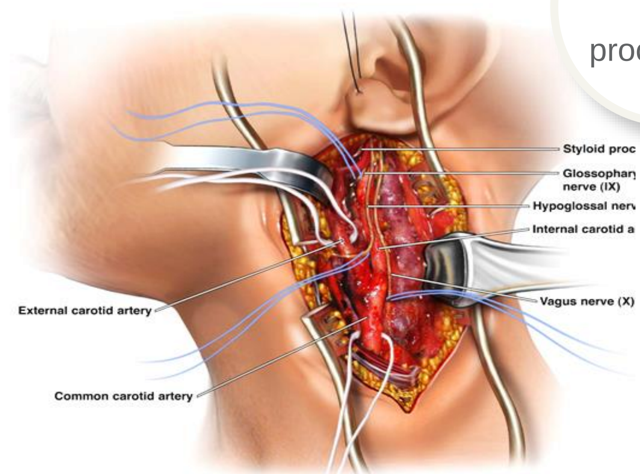
HIGH (2X) peri-procedural stroke risk

CREST 30-day All Stroke[1]: 2.3% CEA vs 4.1% TF CAS

Carotid Endarterectomy (CEA)

65 years: Gold standard

90% of procedures



Low stroke rates & **Higher surgical morbidity**

CREST CNI[2]: 2.1% CNI unresolved at 6 months (80% motor)

CREST MI[1]: 2.3% CEA vs 1.1% TF CAS

[1] CREST Trial: N Engl J Med 2010;363:11-23 [2] Circulation. 2012;125:2256-2264

TCAR – Clinically Proven Alternative to CEA for High Surgical Risk Patients

2.3%
CEA in CREST
Standard Surgical Risk

1.4%
ROADSTER
High Surgical Risk

30 Day All Stroke (ITT)

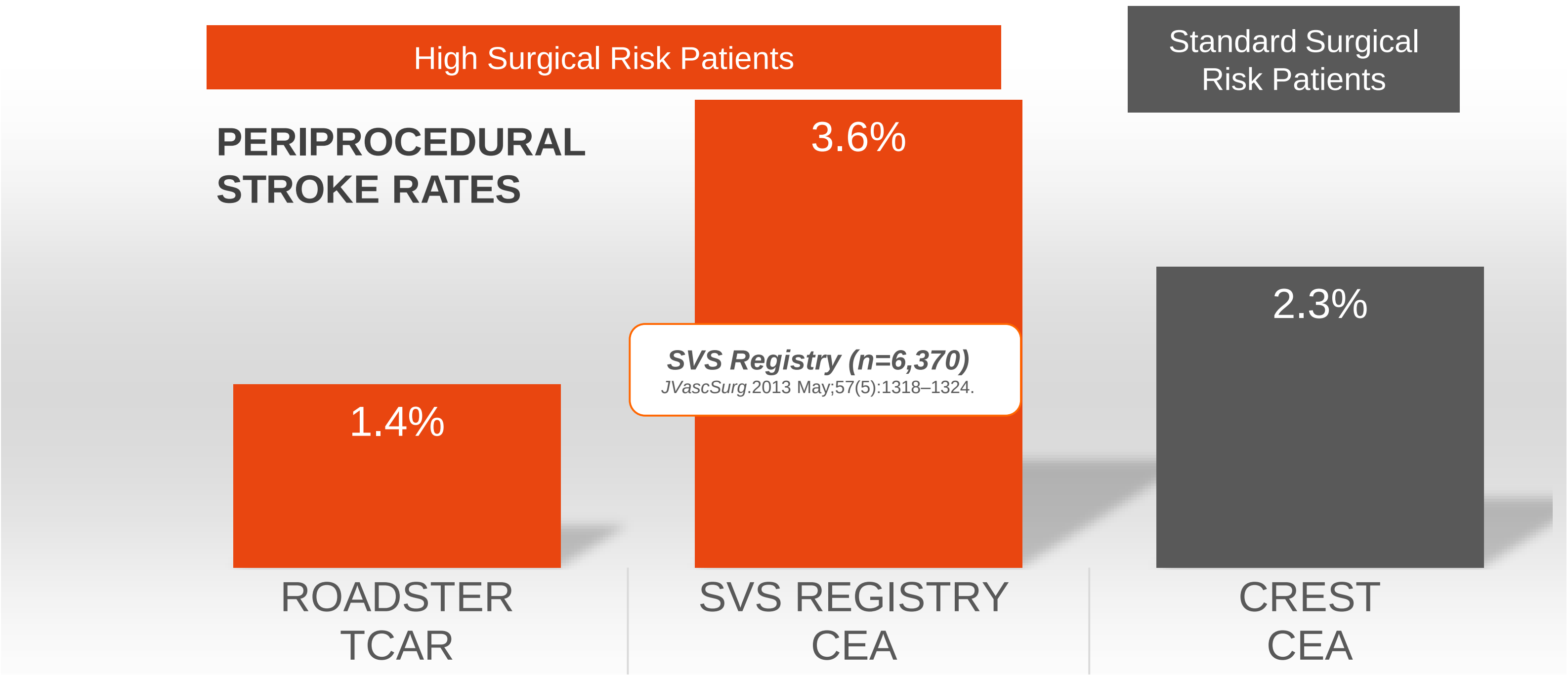
ROADSTER 30 Day All Stroke Per Protocol 0.7%

"The overall **stroke rate** of **1.4%** is the **lowest reported to date** for any prospective, multi-center trial of carotid stenting."

J Vasc Surg 2015;62:1227-35

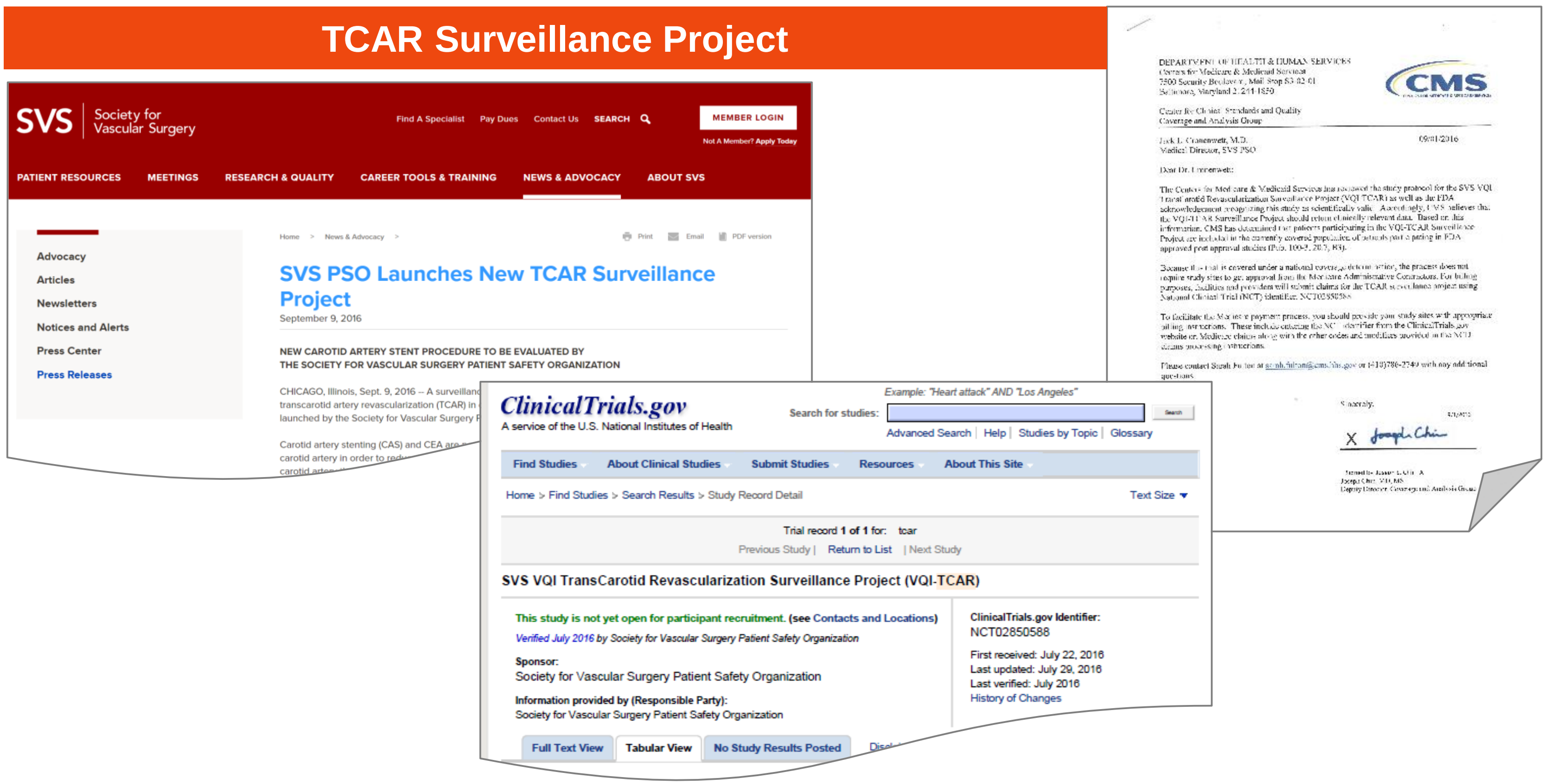
CREST: N Engl J Med. 2016 Mar 17;374(11):1011-20.
ROADSTER: J Vasc Surg. 2015 Nov;62(5):1227-35.

CEA Periprocedural stroke rates significantly worse in High Surgical Risk patients



ROADSTER: J Vasc Surg. 2015 Nov;62(5):1227-35.
SVS Registry: Schermerhorn, et al. The impact of Centers for Medicare and Medicaid Services high-risk criteria on outcome after carotid endarterectomy and carotid artery stenting in the SVS Vascular Registry. J Vasc Surg. 2013 May;57(5):1318-24.
CREST: N Engl J Med. 2016 Mar 17;374(11):1011-20.

September 1, 2016
CMS Grants Coverage for TCAR!



TCAR Coverage

Carotid Artery Stenting National Coverage Determination (NCD) 20.7

1. High Surgical Risk, Symptomatic & ≥70% Stenosis › **Covered under NCD**

2. HSR, Symptomatic >50% stenosis
3. HSR, Asymptomatic ≥80% stenosis

› **Covered through CMS Approved Studies***

Studies Providing TCAR Coverage Under NCD 20.7

CREST 2: Registry

Standard & High Surgical Risk
Symptomatic >50%
Asymptomatic >70%

TCAR Surveillance Project

High Surgical Risk:
Symptomatic >50%
Asymptomatic ≥80%

VQI CAS Registry Participants

ROADSTER 2: Post-Approval

High Surgical Risk:
Symptomatic >50%
Asymptomatic ≥80%

* https://www.cms.gov/Medicare/Medicare-General-Information/MedicareApprovedFacilitie/Carotid-Artery-Stenting-CAS-Investigational-Studies.html

TCAR - Covered Patient Population

~2/3 of All

ONE Risk Factor Qualifies Patient for CMS High Surgical Risk Status

- **Age ≥75**
- Congestive Heart Failure w/NYHA Class III or IV
- Left Ventricular Ejection Fraction ≤35%
- ≥2 diseased coronaries with ≥70% stenosis
- Unstable angina
- MI >72hr & <6 weeks prior to procedure
- Abnormal stress test
- Need for open heart surgery
- Need for major surgery (including vascular)
- Uncontrolled diabetes
- Severe pulmonary disease
  - FEV1 <50%, chronic O2 therapy or resting PO2 <60mmHg

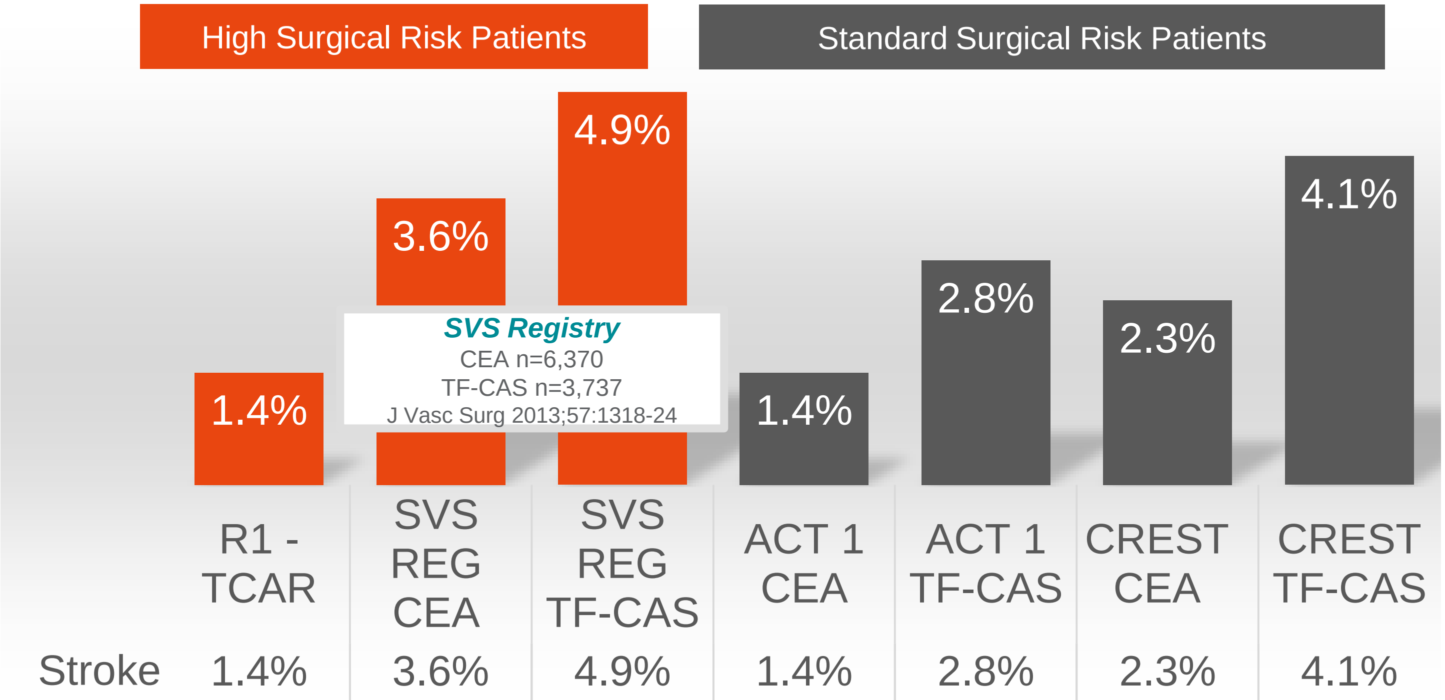
- **Prior head/neck surgery or irradiation**
- Cervical spine immobility
- **Restenosis post CEA**
- **Surgically inaccessible lesion**
- Laryngeal palsy; Laryngectomy;
- **Permanent contralateral cranial nerve injury**
- **Contralateral occlusion**
- Severe tandem lesions
- Bilateral stenosis requiring treatment

These criteria are considered reimbursement eligible for the TCAR Procedure
per the Medicare National Coverage Determination (20.7) on PTA including CAS.

Above list is a compendium of risk factors across all carotid stent and embolic protection device IDE trials.

Periprocedural Stroke Rates

Contemporaneous Publications of TCAR, CEA & TF-CAS



ROADSTER: J Vasc Surg. 2015 Nov;62(5):1227-34.
SVS Registry: Schermerhorn, et al. The impact of Centers for Medicare and Medicaid Services high-risk criteria on outcome after carotid endarterectomy and carotid artery stenting in the SVS Vascular Registry. J Vasc Surg. 2013 May;57(5):1318-24.
ACT 1: N Engl J Med. 2010;363:11-23.
CREST: N Engl J Med. 2016 Mar 17;374(11):1011-20.

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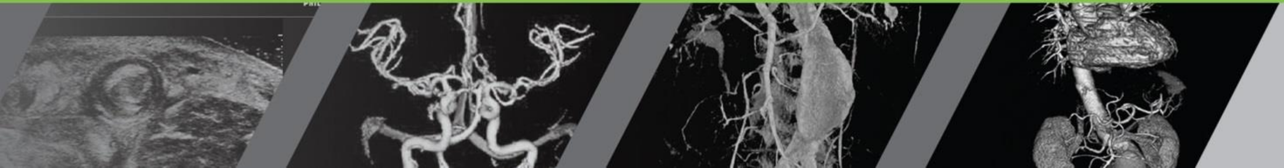

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