MEET 2015
MULTIDISCIPLINARY EUROPEAN
ENDOVASCULAR THERAPY

Results from the ROADSTER & EU Experience

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Disclosure

Isabelle Van Herzeele has the following potential conflicts of interest to report:

☑ Consulting

Silk Road Medical, Sunnyvale, CA, USA

Medtronic Academia, Tolochenaz, Swiss

☑ Research Grant

Simbionix, Cleveland, Ohio, USA

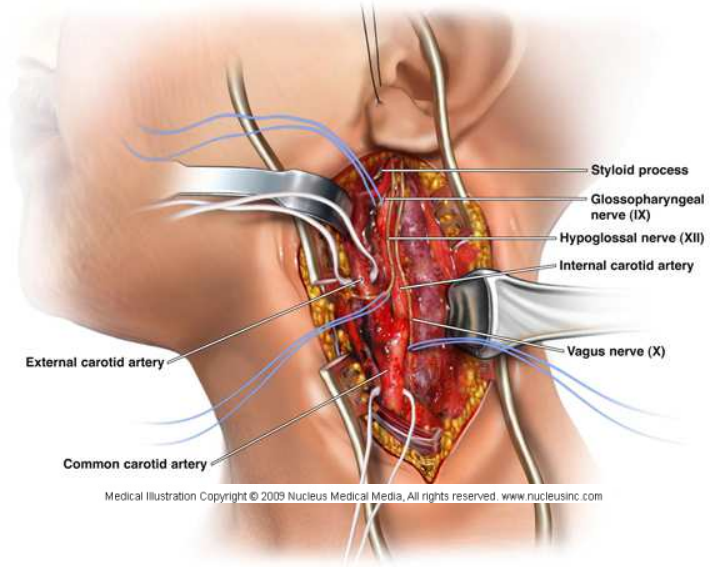
W.L. Gore & Associates, Inc., Flagstaff, USA

Medtronic Academia, Tolochenaz, Swiss

Silk Road Medical, Sunnyvale, CA, USA

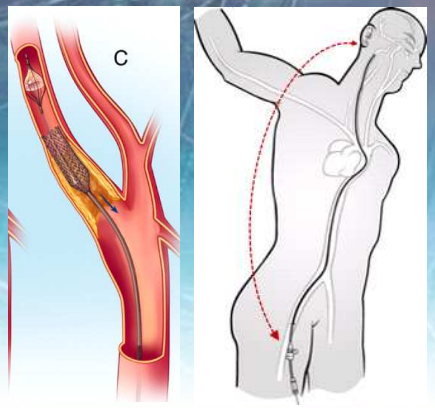
Gold Standard: CEA

Low stroke and death rates
Increased risk of MI and CNI



	CREST		p
	CEA	CAS	
Myocardial Infarction[1]	***2.3%***	1.1%	0.03
Cranial Nerve Injury[1]	***4.8%***	0.3%	<0.0001
Cranial Nerve Injury unresolved at 6 months[2]	2.0%	0.0%	

[1]N Engl J Med 2010;363:11-23
[2]FDA Panel Meeting, January 25, 2011



Transfemoral CAS

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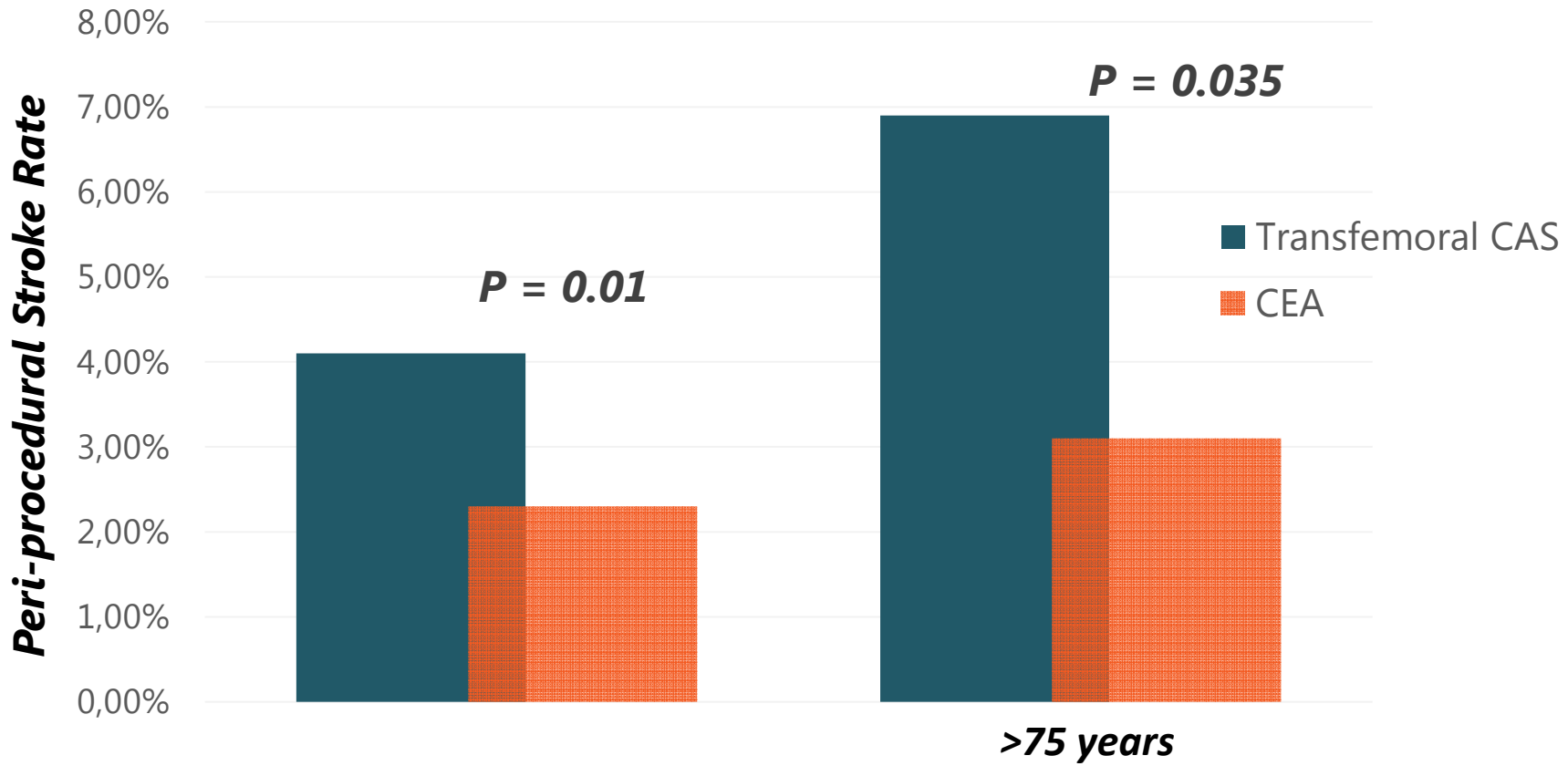
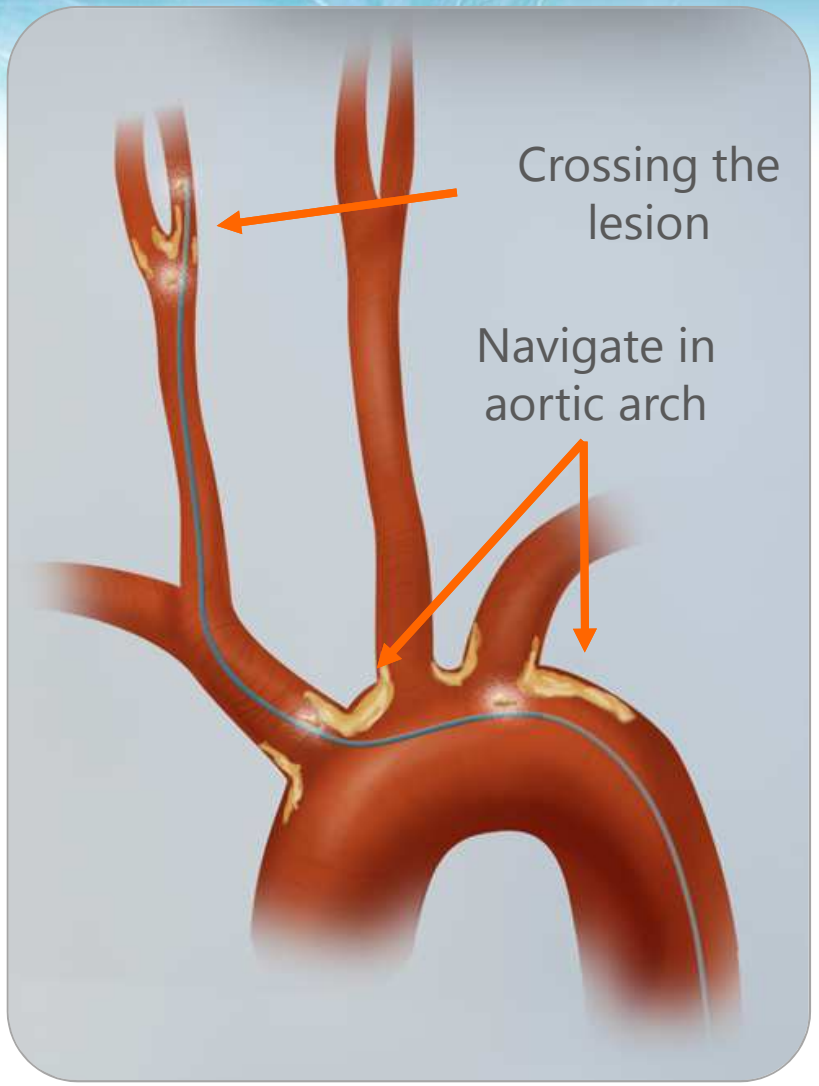


1. N Engl J Med 2010;363:11-23.

2. Stroke. 2011;42(12). 3484-90

Causes of Transfemoral Peri-procedural Stroke



Traditional Transfemoral CAS may cause embolic risk by

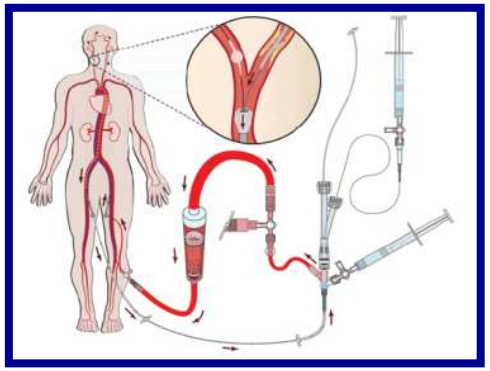
1. Manipulation of catheter in aortic arch
   - 18% Non-Ipsilateral stroke rate in CAPTURE Study*
2. Crossing lesion before neuroprotection in place
3. Inadequate neuroprotection
   - Misaligned filter
   - Inadequate manual aspiration of emboli

1. Ann Surg 2007;246: 551–558.

Aortic Arch Is Hostile Territory

The incidence of microemboli to the brain is less with endarterectomy than with percutaneous revascularization with distal filters or flow reversal

Procedure	N	Incidence MES	Procedural Stage
Carotid Endarterectomy	15	15.3 (±22)	Post-procedure
Filter protected CAS	20	319.3 (±110.3)	During protection
Flow reversal CAS	7	184.2 (±110.5)	Pre-protection

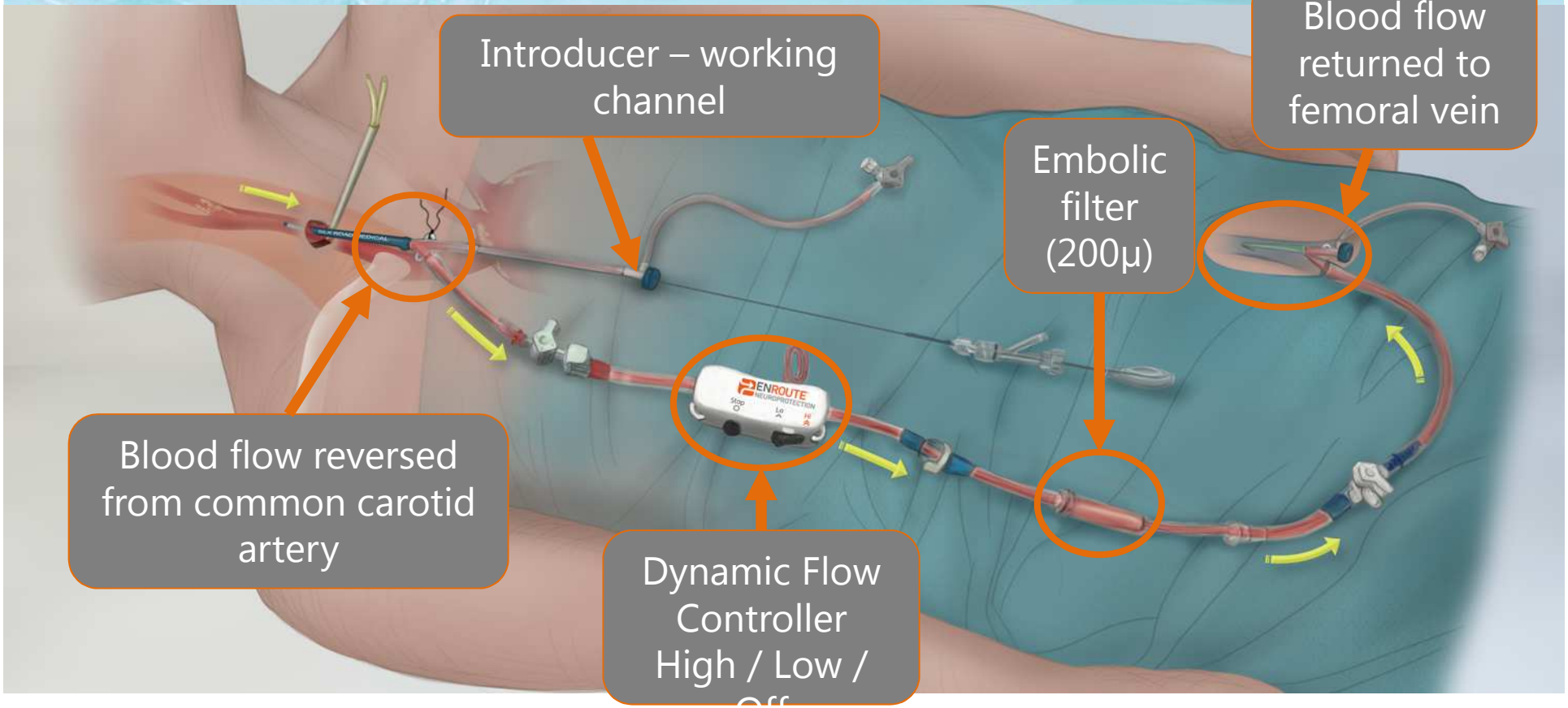


Gupta N et al. J Vasc Surg. 2011;53:316-322

Study	Procedure	Embolic Protection	# subjects	% w/ New DWI Lesions
ICSS[1]	Transfemoral CAS	Distal filter (various)	51	73
ICSS[1]	CEA	Clamp, backbleed	107	17
PROFI[2]	Transfemoral CAS	Distal filter (Emboshield)	31	87
Leal[4]	Transfemoral	Distal Filter (FilterWire)	33	33
PROFI[2]	Transfemoral CAS	Proximal occlusion (MoMa)	31	45
DESERVE[5]	Transfemoral CAS	Proximal occlusion (MoMa)	127	26
PROOF[3]	Transervical CAS	High-flow rate flow reversal	48	16.7
Leal[4]	Transervical CAS	Flow Reversal	31	12.9

1 Lancet Neurol. 2010 Apr;9(4):353-62
2. J Am Coll Cardiol. 2012;59:1383-89
3. JVS 2011;54:1317-23
4. JVS 2012 ;56:1585-90
5. Int J Cardiol 2014;15: 174(2):382-3

Enroute Transcarotid and Neuroprotection System



	CE Mark	***FDA Approval***
ENROUTE Transcarotid Neuroprotection System	January 2012	February 2015
ENROUTE Transcarotid Stent System	July 2013	May 2015

How Can We Achieve CEA-Like Neuroprotection Less Invasively?

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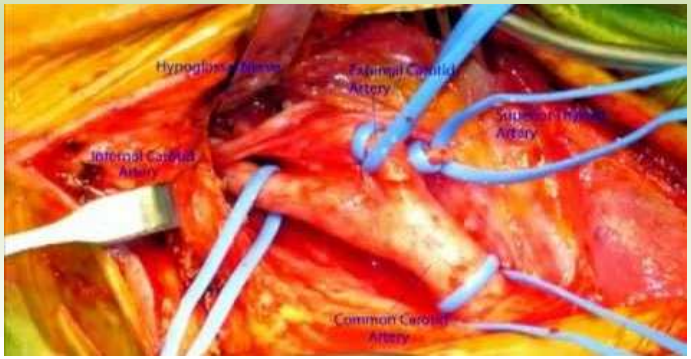
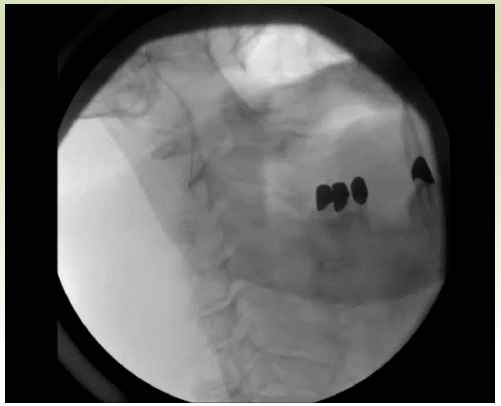
Direct Carotid Access
CCA Clamp & Loop Control



Direct Carotid Access (avoid arch)
CCA Rummel Loop Control

Backbleed to Clear Debris

Backbleed to Clear Debris



“Robust” Flow Reversal SIMILAR to CEA Backbleed

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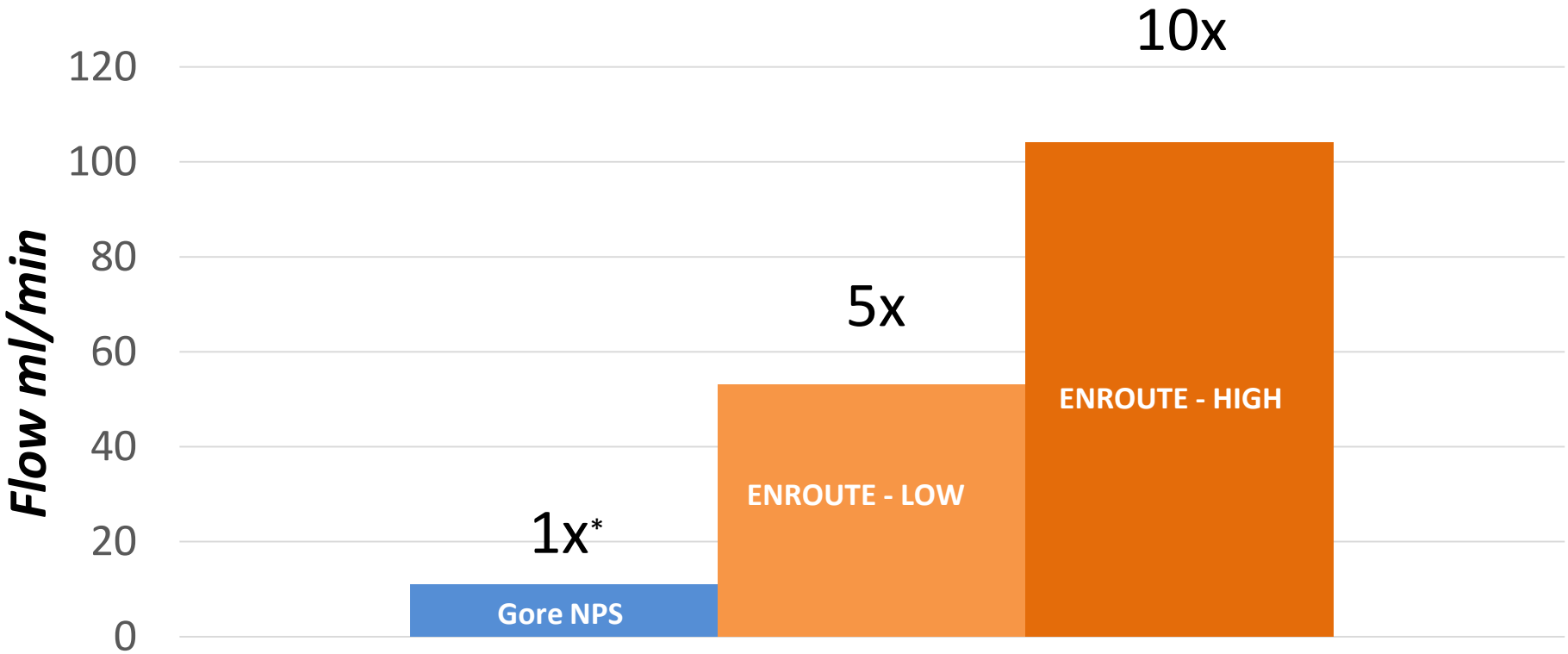
Bench: AV Shunt Flow Rates at 60 mmHg with Cordis Precise RX Pro Stent Delivery System in the Flow Reversal Circuit



*** Gore recommends Manual Aspiration during interventional device delivery.**

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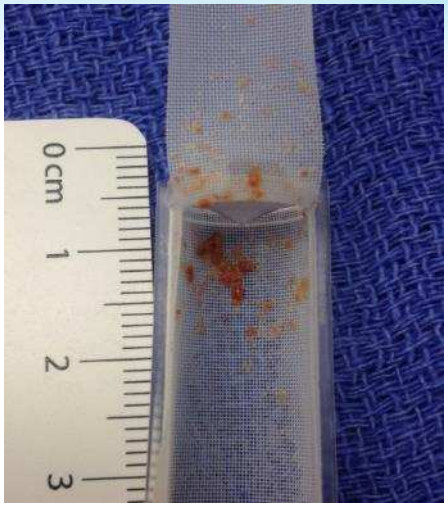
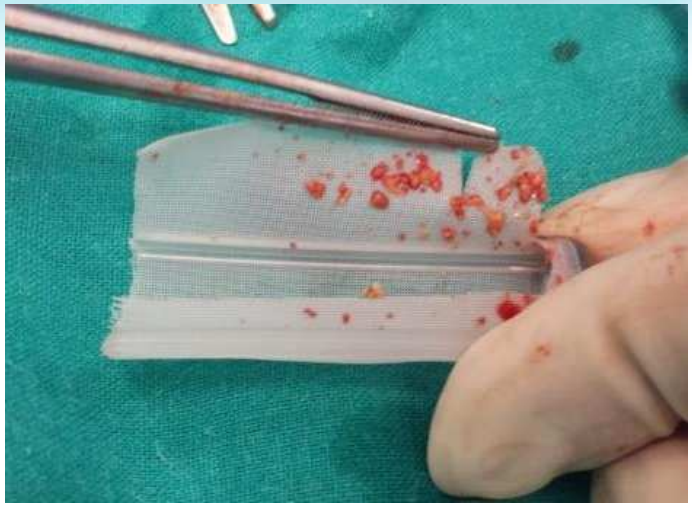
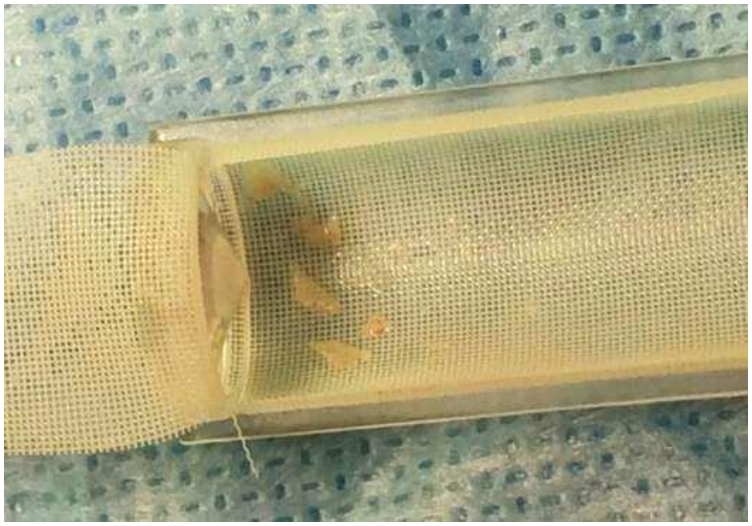
PROOF = IN THE FILTER

Macro & Micro emboli in ENROUTE® NPS FILTERS







Transcarotid Artery Revascularization and Stroke Reduction

Silk Road Clinical Studies				
	PROOF	***TESLA***	***ROADSTER***	***ENROUTE DW-MRI study***
Study type	First In Man EU	Multicenter EU Post-Market Registry	US Pivotal IDE	European registry
Number of Patients	75	58	208	30
Profile	All-comers	All-comers	High Surgical Risk: Symptomatic & Asymptomatic	Symptomatic <6 weeks
Status	Complete	Complete	Complete	Enrolling

THE PROOF STUDY: FIRST IN MAN

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Prof Ralf Kolvenbach, Dusseldorf, Germany

Safety Results[1,2]

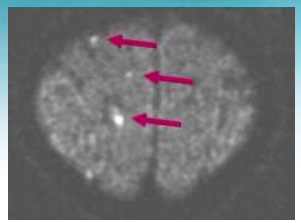
Primary Endpoint: Major stroke, MI, and death through 30 days	0/71 (0%)
Minor stroke	
Minor contralateral stroke adjudicated as not device or procedure-related	1/71 (1.3%)

1. J Vasc Surg 2011;54:1317-23

2. Kolvenbach, Ralf, MD PhD. " Transcervical Carotid Revascularization with Flow Reversal Neuroprotection: Final Results from the Silk Road Medical Neuroprotection System: First-In-Man PROOF Study." VEITH Meeting, Nov 2012

The PROOF Study

Micro-Emboli Measurement



DW-MRI Studies – A More Sensitive Marker

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

1 J Am Coll Cardiol. 2012 Jan 19.
2 Lancet Neurol. 2010 Apr;9(4):353-62
3 Kolvenbach, Ralf, MD PhD. " Transcervical Carotid Revascularization with Flow Reversal Neuroprotection: Final Results from the Silk Road Medical Neuroprotection System: First-In-Man PROOF Study." VEITH Meeting, Nov 2012

Tesla: Multi-Center EU registry

0% - DAY 0 STROKE

TESLA - DEMOGRAPHICS & RESULTS	Value (n=58)
Neurological Status	
Symptomatic	38 (65.5%)
Asymptomatic	20 (34.5%)
Outcomes	
Procedural Success	57 (98.3%)
Major Adverse Event Rate – Day 0 (Stroke, Death and Myocardial Infarction)	0 (0%)
Cranial Nerve Injury	0 (0%)

ROADSTER Study

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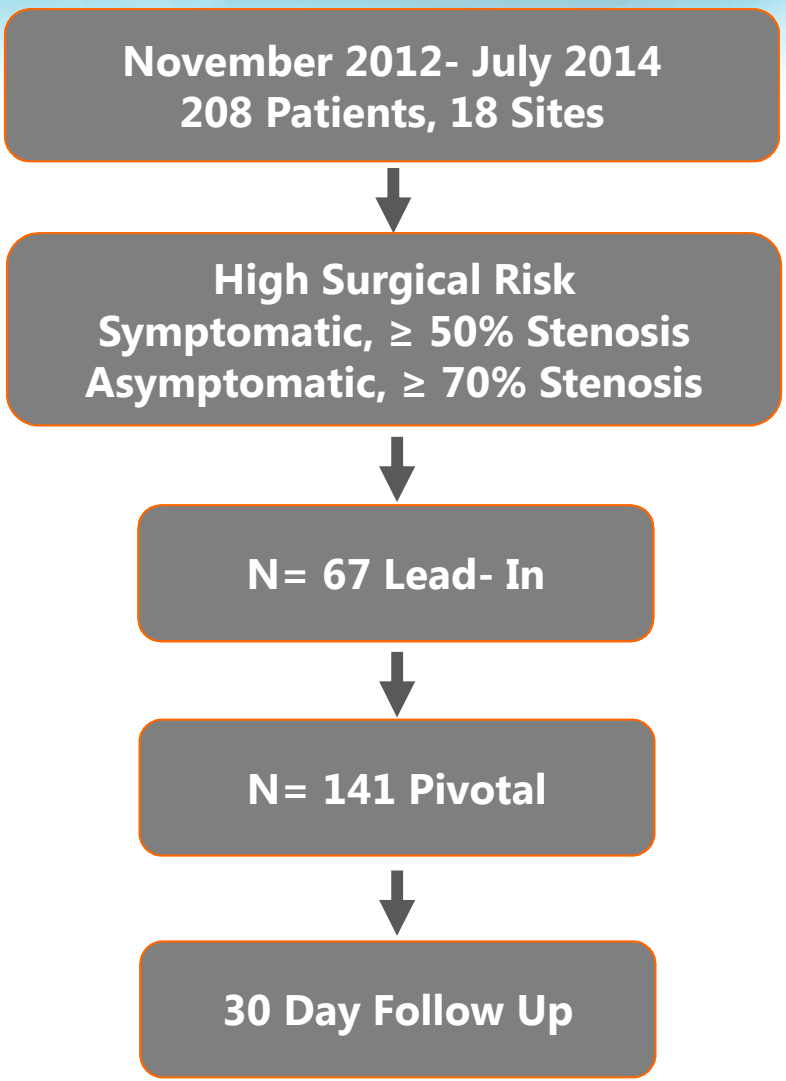
- **DESIGN**: IDE study with OPC of 11% S/D/MI
- **OBJECTIVE**: Evaluate safety and efficacy of CAS with ENROUTE Transcarotid Neuroprotection System
- **INDEPENDENT REVIEW:** CEC, DSMB, Core labs (angiography, duplex ultrasound, cardiology)

- **PRIMARY ENDPOINT**
  - Composite of S/D/MI at 30-days post-procedure
- **SECONDARY ENDPOINTS**
  - Cranial nerve injury (CNI)
  - Stroke and death (S/D)
  - Procedural and technical success



ROADSTER
Patient Population

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Physiologic HSR Inclusion

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

Anatomic HSR Inclusion

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

Exclusion: Common to CAS

- Atrial fibrillation
- Recent valve or MI
- 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 Study
Baseline Characteristics

High Surgical Risk	Pivotal Group (N=141)
Age	72.9 ±9 (40,90)
Age ≥75	47%
Age ≥ 80	28%
Female	35%
Symptomatic	26%
Physiologic Risk Factors	56%
Anatomic Risk Factors	
Hostile Neck	16%
Restenosis post CEA	21%
Physiologic & Anatomic Risk Factors	40%

ROADSTER Study Outcomes

Intention to Treat & Per Protocol Groups

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 Mo	0	0%	0	0%

ROADSTER Study
Subgroup Outcomes

High Surgical Risk Pivotal Intention to Treat	Age ≥ 75	Symptomatic
N	N=66 (47%)	N=36 (26%)
S/D/MI	3 (4.5%)	1 (2.8%)
Major Stroke	0%	0%
Minor Stroke	0%	0%
Death	3.0%	2.8%
MI	1.5%	0%
Stroke & Death	3.0%	2.8%

Physician-Friendly

Silk Road Procedure Time <1/2 That Of CEA

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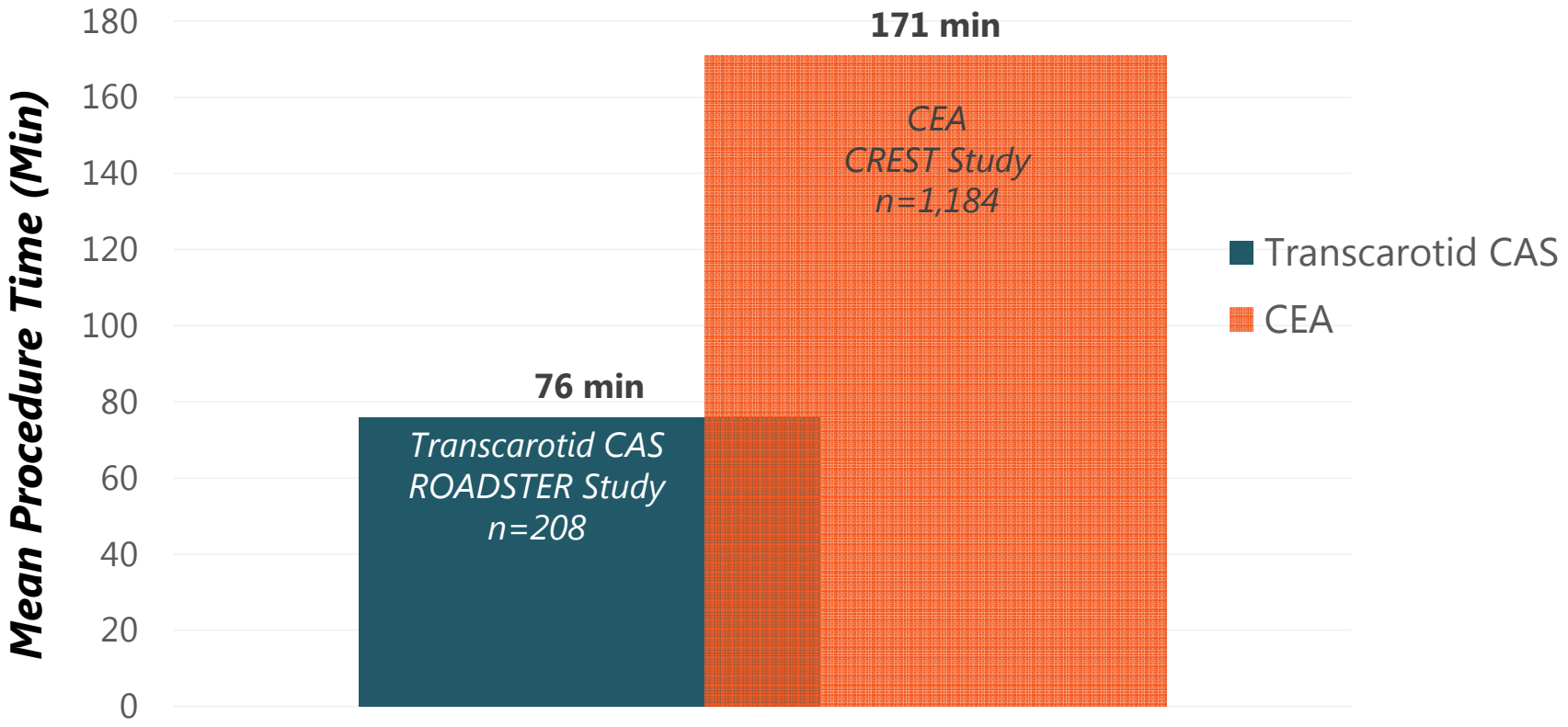
ROADSTER vs. CREST



1. ROADSTER Presentation – Late Breaking Trials, VIVA 2014, C. Kwolek, MD
2. Stroke. 2012;43:00-00.

Patient-Friendly

Reverse Flow Time 1/3 That of CEA Clamp Time

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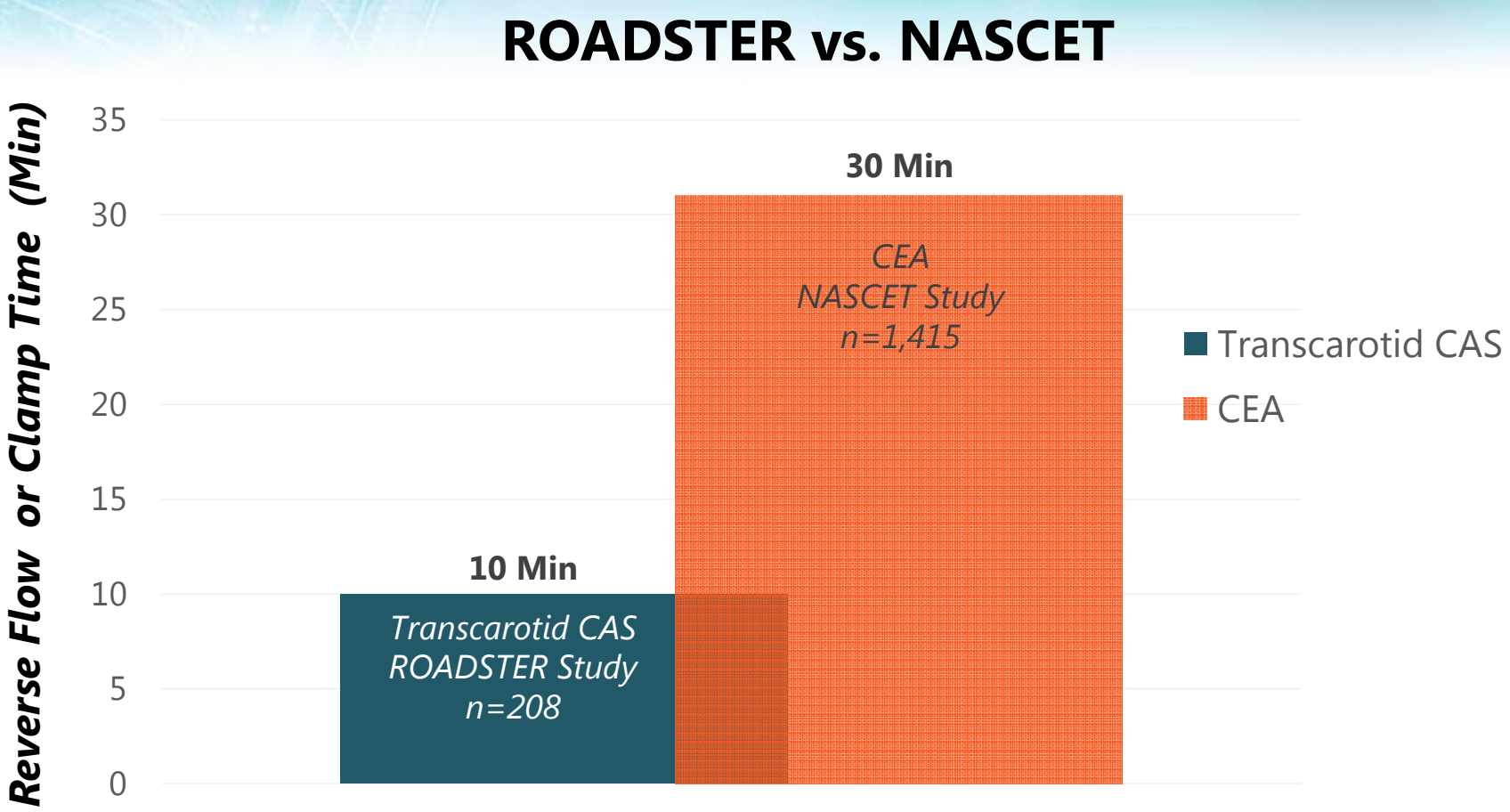

1. ROADSTER Presentation – Late Breaking Trials, VIVA 2014, C. Kwolek, MD
2. Stroke. 1999;30:1751-1758

ROADSTER Study
Summary

- The ROADSTER study met the primary endpoint S/D/MI (3.5%)

- **Stroke Rates are CEA- LIKE**

	ROADSTER	*CREST CEA*
– All stroke rate in patients PP	0.7%	*2,3%*
– Stroke rate in ***symptomatic*** patients	0%	*3,2%*
– Stroke rate in patients ***≥75 yrs.***	0%	*3,1%*
– Stroke rate in ***women***	0%	*2,2 %*

- Mean Procedure Time <1/2 of CREST CEA
  Flow reversal time < 1/3 of NASCET CEA clamp time

- **No permanent Cranial Nerve Injuries**

FDA cleared the ENROUTE Transcarotid NPS

ENROUTE
DW- MRI study

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- ***Symptomatic*** carotid artery stenosis < 6 weeks
  - TIA, amaurosis fugax, minor, non-disabling stroke
  - mRS ≤ 2, NIH<4
- Primary endpoint:
  Incidence of new white lesions by DW-MRI post procedure

	Preop	Periop	24H	48-60H	1M
Clinical neurological examination	✔		✔		✔
DW-MRI	✔			✔	✔
TCD	✔	✔			
Duplex carotid arteries	✔			✔	✔

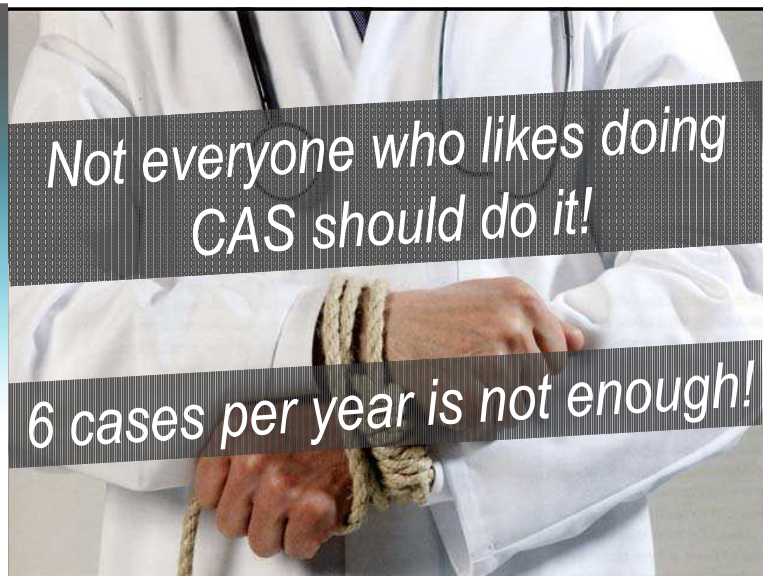
TransCarotid Artery Revascularization Procedure Experience in EU

322 Cases – 30 d Stroke/Death rate ***1.5%***

Study	F/U	Status	Total Enrollment
PROOF	30-DAY	CLOSED	75
LOTUS	30-DAY	CLOSED	12
PROOF EC	30-DAY	CLOSED	6
TESLA	30-DAY	CLOSED	75
F-1 (Filter Debris)	30-DAY	CLOSED	24
ROADSTER	30-DAY	CLOSED	29*
MINI (KOBI)	ACUTE	ENROLLING	39
DW-MRI	30-DAY	ENROLLING	9
Other	ACUTE	COMMERCIAL	53
		TOTAL	322

Endpoints	SILK ROAD PROCEDURE
Stroke/Death (30-day)	5/322 (1.5%)*
Intraprocedural	0/322 (0.0%)
CNI (periprocedural)	2/322 (0.6%)

Conclusion



Courtesy K Matthias

- Transcarotid CAS with dynamic flow reversal may improve the less than optimal CAS results.
- CEA-trained vascular surgeons and CAS-trained physicians rapidly adopt the ***hybrid*** technique
- Low stroke, death and MI rate even in ***elderly*** and in ***symptomatic*** cases

Carotid Management
Cognitive and Technical Skills

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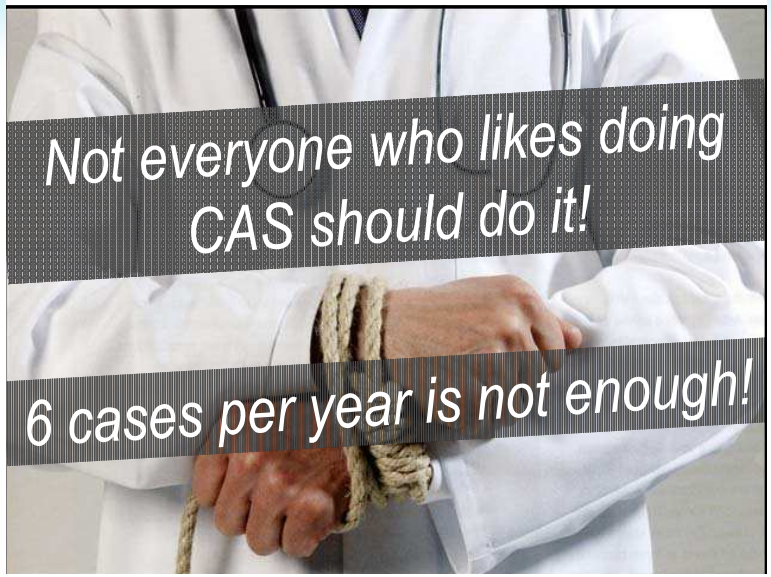
- Patient selection!
- Probing of CCA in aortic arch = atraumatic or skipped
- Tip of sheath in CCA + tip of 0.014 wire always in view
- Use adequate devices (in difficult anatomy)
- Be patient when crossing the lesion
- Place stent properly
- Monitor BP, HR, ACT…
- Use intelligence, not force!



Courtesy of K Matthias