Proximal Protection vs. Distal Protection in CAS

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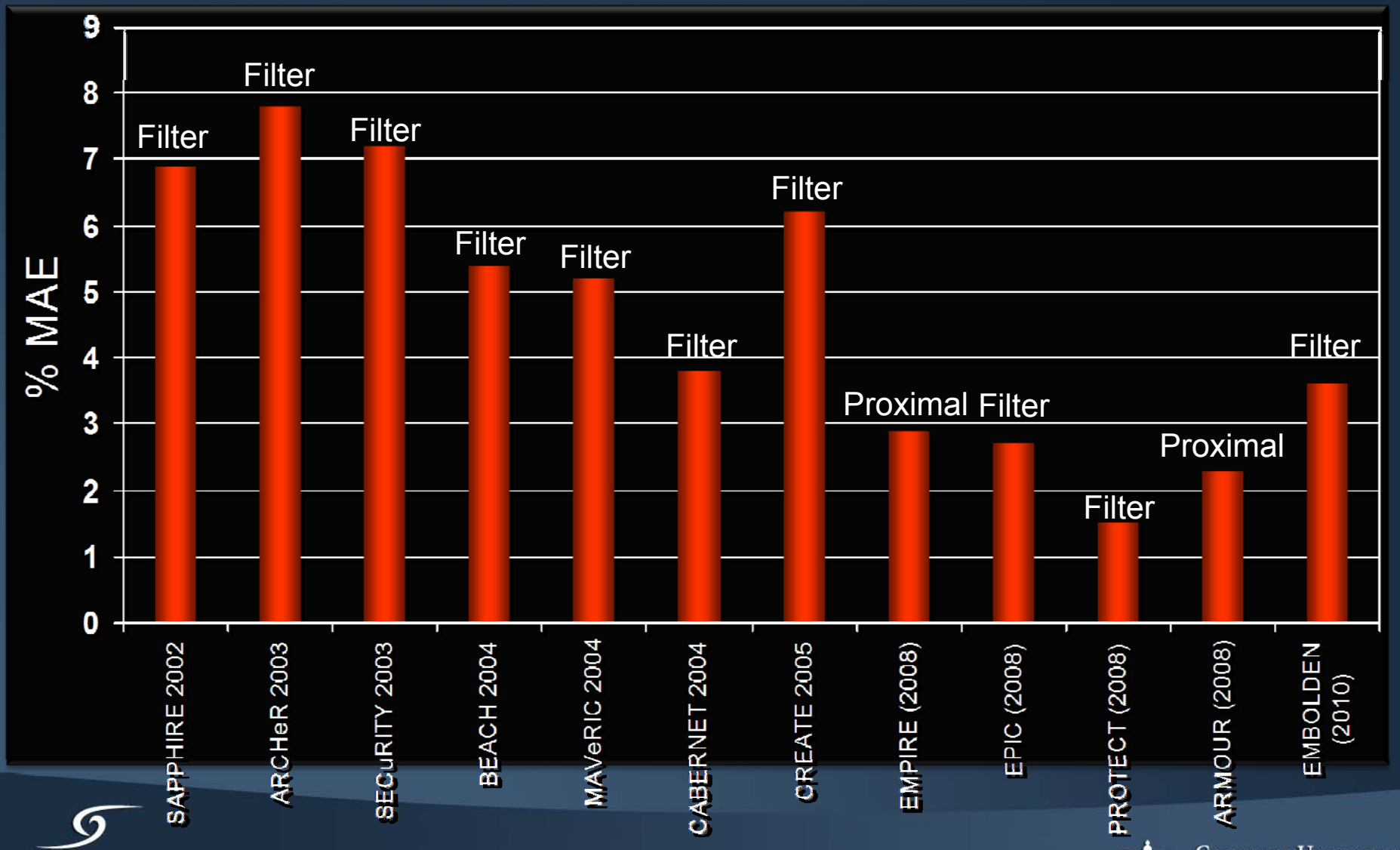
Improvement in CAS outcomes is unrelated to EPD type used



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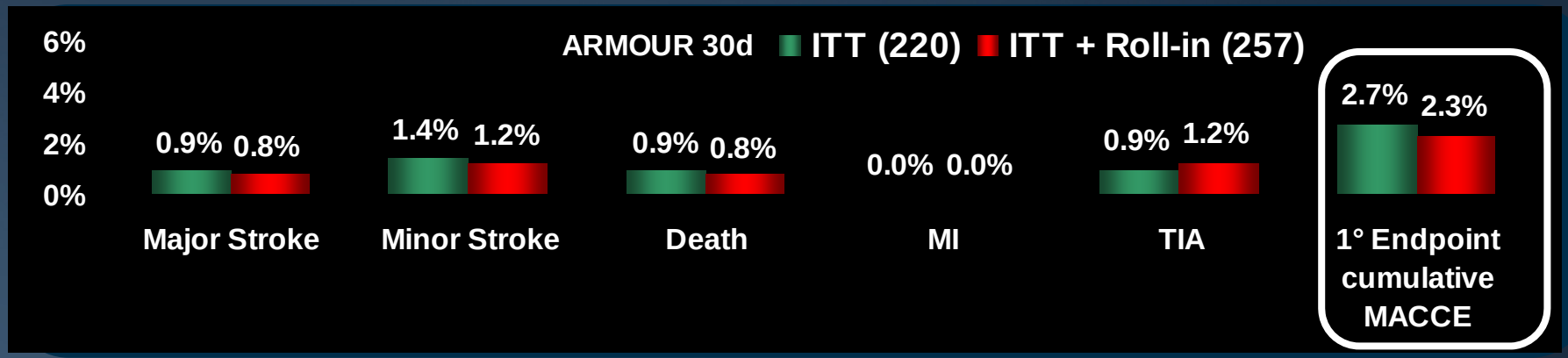
What about outcomes in the at-risk populations?

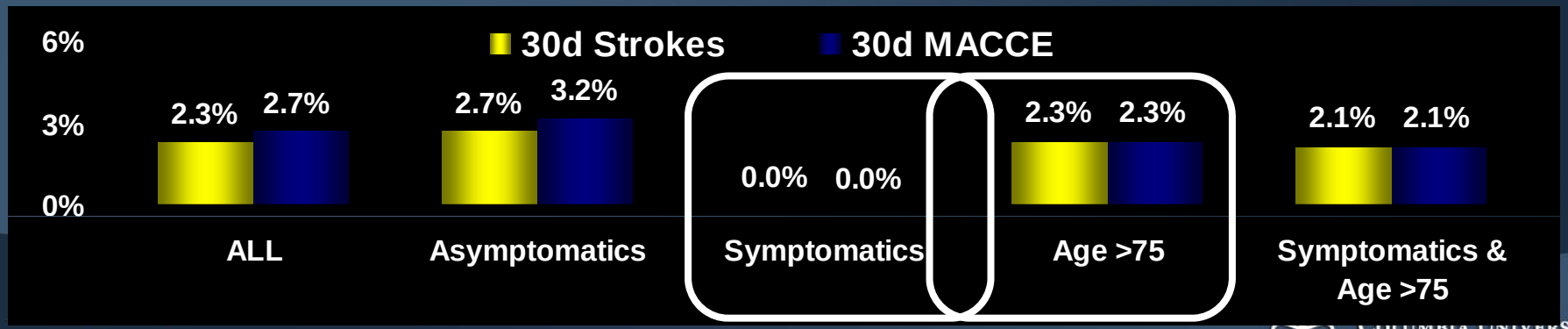
- Symptomatic
  - Expected 5%-6%
- Octogenarians
  - Expected >5%

ARMOUR: Flow-arrest with compelling outcomes in at risk patients: *octogenarians and symptomatic patients*

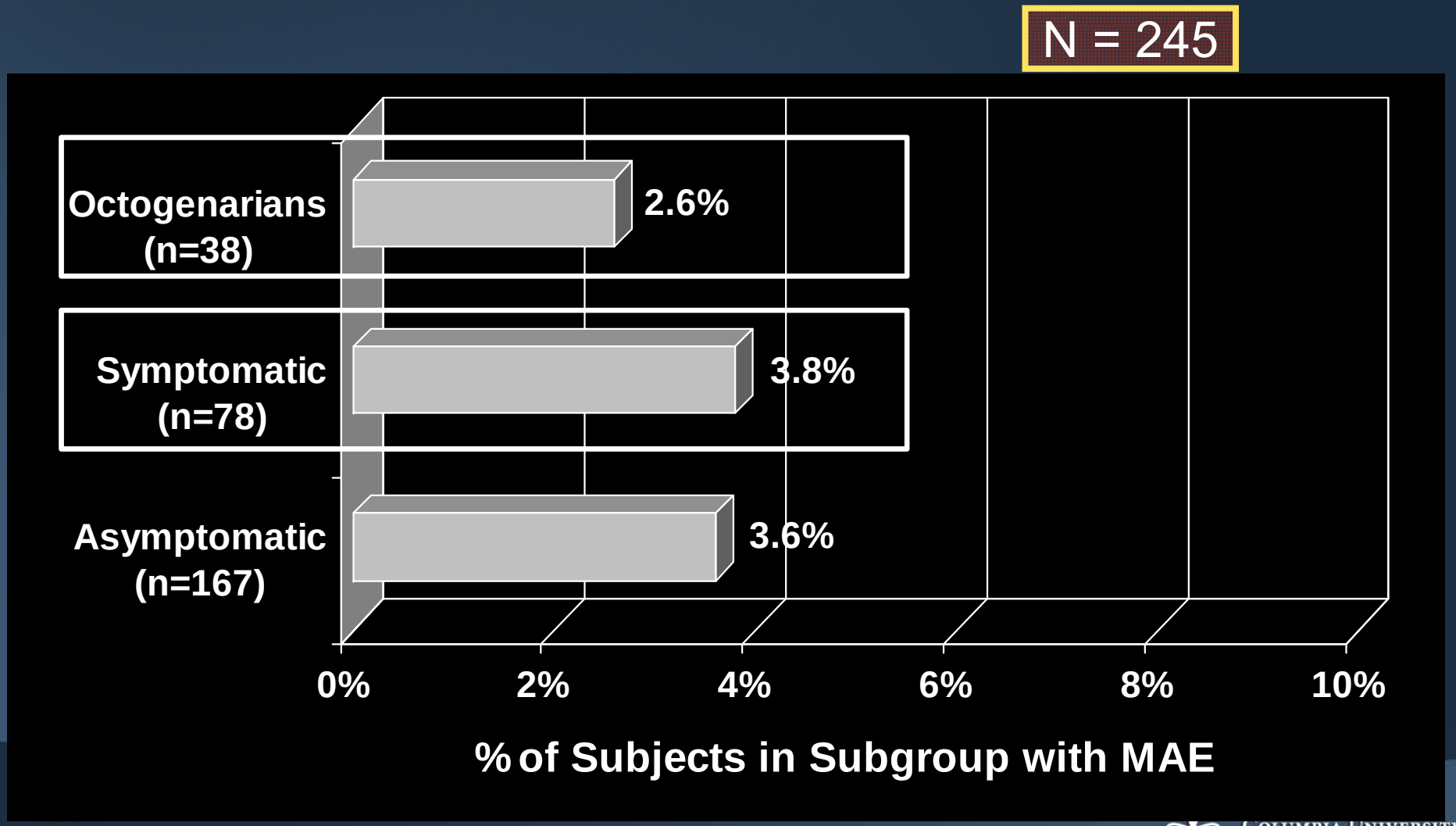
30d Results (ITT & Full Population)



30d Results by Symptoms and Age (ITT)



EMPiRE confirms proximal protection (flow reversal) is safe in at-risk patients: *octogenarians & symptomatic patients*



Clair DG et al. Catheter Cardiovasc Interv 2011;77:420-429

Embolic Protection:

Impact On Microembolic Burden

Filters

ICSS Primary Analysis CEA Vs. CAS in 1713 symptomatic patients

ICSS Substudy: N = 231

New white lesions on DWI:

62 of 124 (50%) transfemoral CAS

18 of 107 (17%) CEA

(OR 5.21, 2.78-9.79; *p < 0.0001*)

ICSS Substudy: N = 231

New white lesions on DWI

38 of 56 (68%) transfemoral distal filter CAS

24 0F 68 (35%) unprotected CAS

(OR 3.28, 1.50-7.20; *p < 0.03*)

PROXIMAL PROTECTION:

Trans-femoral Flow Arrest

(Medtronic MoMa)

Randomized Trials:

Filter Protected vs. Proximal Systems

MoMa

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Microembolization During Carotid Artery Stenting in Patients With High-Risk, Lipid-Rich Plaque: A Randomized Trial of Proximal Versus Distal Cerebral Protection

Patients With Detectable MES During the Different Phases of CAS

Steps	FilterWire EZ (n = 27)	MO.MA (n = 26)	p Value
Lesion wiring	26 (96%)	19 (73%)	0.145
Pre-dilation*	6/7 (86%)	4/10 (40%)	0.578
Stent crossing of the lesion	27 (100%)	7 (27%)	<0.0001
Stent deployment	27 (100%)	7 (27%)	<0.0001
Stent post-dilation	26 (96%)	7 (27%)	<0.0001
Device retrieval/deflation	22 (81%)	25 (96%)	0.721

Montorsi P et al. JACC 2011; 58: 1656-1663

MO.MA vs. Filters (DWMRI)

	DWMRI Subgroup	
	MO.MA	***Filter***
# new lesions	7	38
# pts with new lesions	14.2%	42.8%

*p NS**

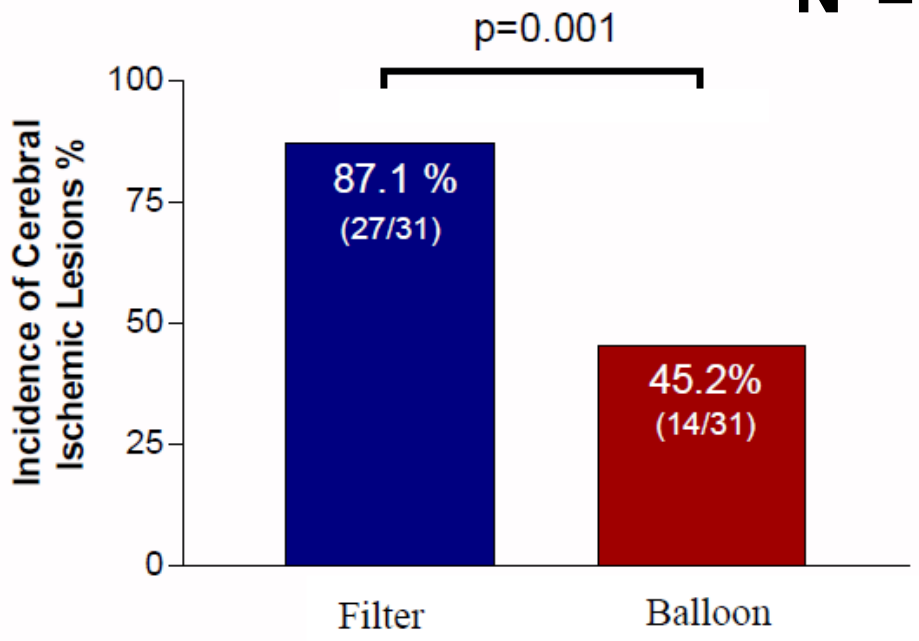
**Insufficient power*

PROFI: A Prospective, Randomized Trial of Proximal Balloon Occlusion vs. Filter Embolic Protection in Patients Undergoing Carotid Stenting

Incidence of new Cerebral Ischemic Lesions

(Primary Endpoint)

N = 62



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Bijuklic K et al. JACC Epub 2012 Jan 19th

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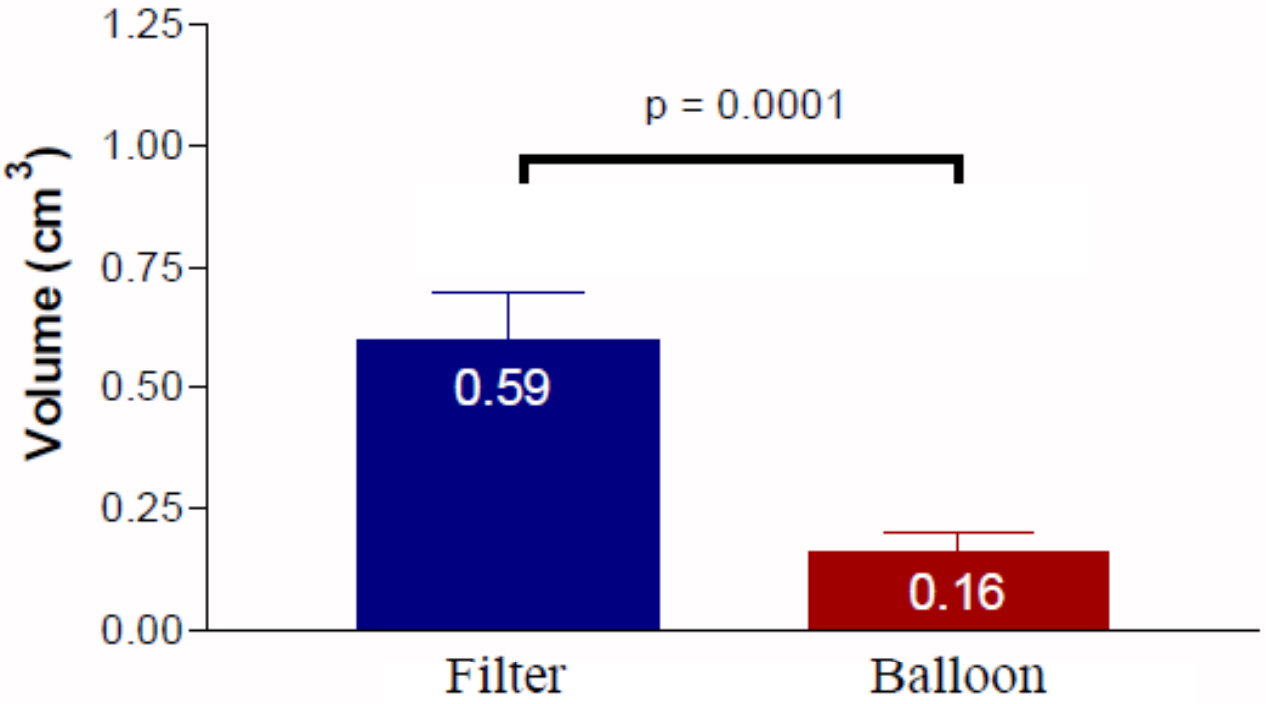
Mean Volume of new Cerebral Ischemic Lesions

(Secondary Endpoint)



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Case Series Data:

Filter Protected vs. *MoMa*

MoMa Vs. Filters (TCD)

CLINICAL RESEARCH **Interventional Cardiology**

Effect of Two Different Neuroprotection Systems on Microembolization During Carotid Artery Stenting

Single center *non randomized* study of MoMa Vs. Filters to assess microembolization with TCD

	MoMa	***Filter***
# Patients	21	21
Symptomatic	7 (33%)	6 (29%)
Degree of Stenosis	86±9%	85±8%
Evidence of Macroscopic Debris	18 (89%)	14 (67%)
Stroke & Deaths procedural	0	0
Total MES Counts	57±41	196 ±84
	p <.0.0001	

Schmidt et al. JACC 2004

Columbia University Medical Center

MoMa Vs. Filters (TCD)

Number of Patients (%) with Detectable MES During the Different Phases of CAS

	Filter Group	MO.MA Group	p Value
Sheath placement-protection device placement	21 (100%)	21 (100%)	NS
Wiring of the stenosis	20 (95%)	6 (29%)	< 0.0001
Stent deployment	21 (100%)	11 (52%)	0.0003
Balloon dilation	21 (100%)	15 (71%)	0.008
Retrieval of the protection device	21 (100%)	21 (100%)	NS

Data are mean values ± SD or n (%).
CAS = carotid artery stenting; MES = microembolic signals; NS = not significant.

Establishment & retrieval of EPD – universally emboligenic

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Schmidt et al. JACC 2004

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DESERVE: DWI study of Mo.Ma transfemoral proximal protection

DESERVE: N = 127

New white lesions on DWI

38 of 127 (30%)

2.4% MACCE

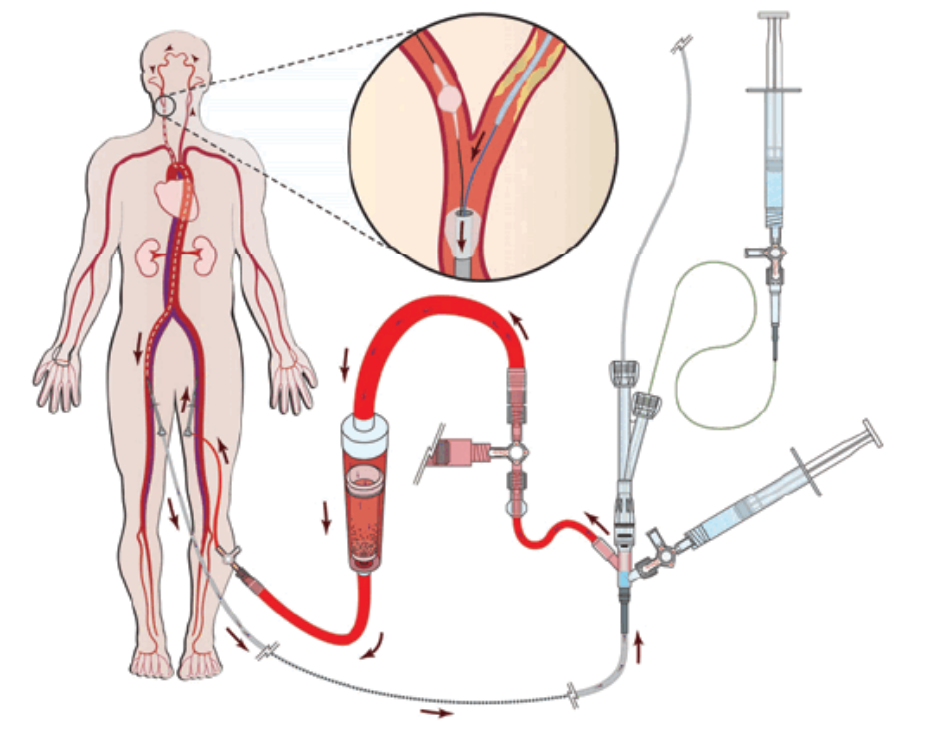
3 of 127 (2.4%) minor stroke

1 of 127 (0.8%) TIA

PROXIMAL PROTECTION:

Trans-femoral Flow Reversal

(Gore Flow Reversal System)



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Diffusion-Weighted MR Imaging in Carotid Angioplasty and Stenting with Protection by the Reversed Carotid Arterial Flow

Procedure	N	DWI lesion incidence (%)
Diagnostic angiography	26	3/26 (11.5)
CAS with flow reversal	11	2/11 (18.2)

CONCLUSIONS: Protection results obtained with the Parodi system were excellent and comparable with conventional angiography.

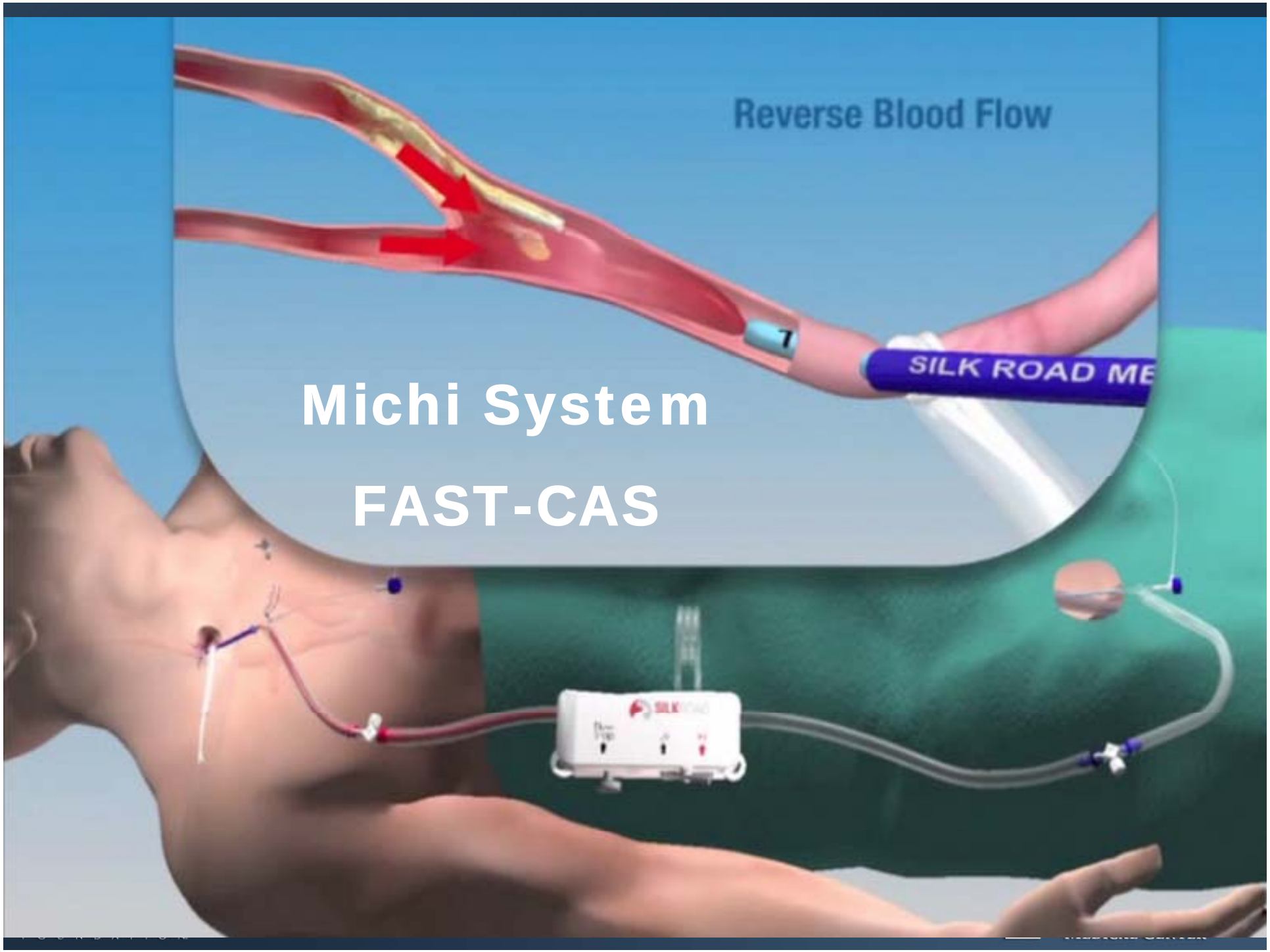
Results: MES on TCD

	Reverse Flow Patients	Filter Protected
Total MES count	192	*469* *P=0.01*
Total MES during deployment of protection device	87	*220* *P=0.009*
Total MES during embologenic stage of CAS – pre and post dilatation and stent insertion	46	*169* *P=0.004*

PROXIMAL PROTECTION:

Transcervical Access with High Flow Rate Flow Reversal

(Silk Road Michi NPS)


Reverse Blood Flow
SILK ROAD ME
Michi System
FAST-CAS

PROOF Safety Results

Parameter	Value (n=65)
Subjects completing 30-day follow up	61 (94%)
Composite of major stroke, myocardial infarction and death from the index procedure through the 30-day post procedural period	0 (0%)
Minor Stroke	1 (1.5%)[1]
Cranial Nerve Injury	1 (1.5%)[2]

[1]One minor contralateral stroke was reported at 30 days in a patient who had a negative post-procedural DW-MRI scan

[2]Data monitored but not adjudicated.

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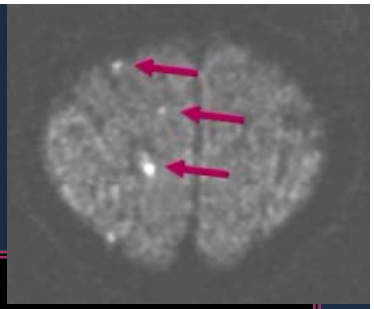
PROOF DWI Sub Study

- Baseline scan within 72 hours
- Post-procedure scan within 12-48 hours
- Submitted to core laboratory for blinded evaluation by two independent neuroradiologists

Parameter	Value (n=48)
Subjects with new DW-MRI lesion(s)	8 (16.7%)

Prospective DW-MRI studies



Comparison of New White Lesion Rate

Study	Procedure	Embolic Protection	# subjects	% 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%
DESERVE[3]	Transfemoral CAS	Proximal occlusion (MoMa)	127	30%
ICSS[2]	**CEA**	**Clamp, backbleed**	**107**	**17%**

1 J Am Coll Cardiol. 2012;59:1383-1389
2 Lancet Neurol. 2010 Apr;9(4):353-62
3 P Rubino, 2011 EuroPCR

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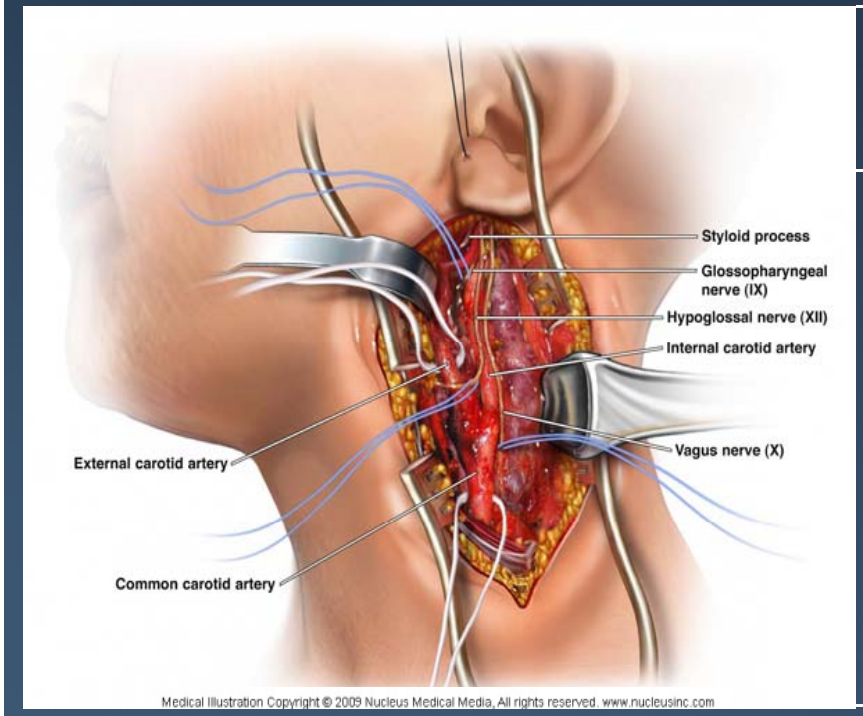
The clinical relevance of microembolic burden?

Conclusions

- No clinical difference in stroke or death can be identified by EPD type
  - Perhaps in the at-risk populations?
- Proximal EPD are significantly better than filters at controlling the microembolic burden of CAS
  - The clinical relevance of this is unclear, but intuitively makes sense and puts CAS on par with CEA in this regard

Gold standard: CEA

Low stroke and death rates but morbid procedure

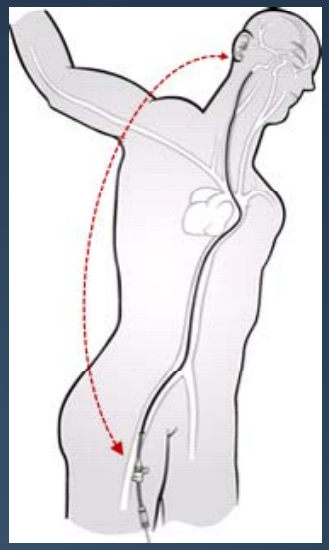


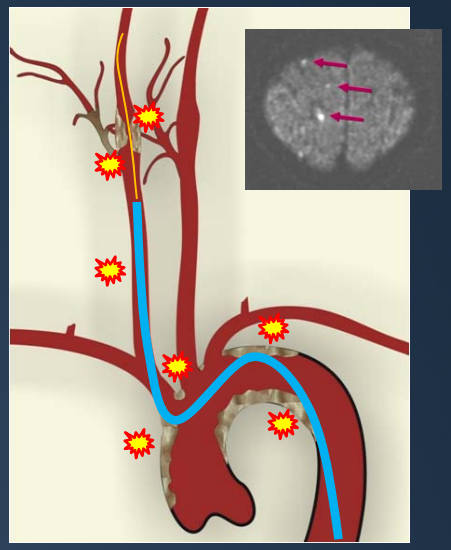
Major Unmet Needs	CREST		p
	CEA	CAS	
Myocardial Infarction[1]	2.3%	1.1%	0.03
Cranial Nerve Injury[1]	4.8%	0.3%	<0.0001
Cranial Nerve Injury unresolved (6 months)[2]	2.0%	0.0%	

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

Transfemoral CAS

Patient friendly but increased peri-procedural stroke risk





Major Unmet Needs	CEA	CAS	p
CREST Peri-procedural Stroke[1]	2.3%	4.1%	0.01
CREST Peri-procedural Stroke, ≥ 75 years[2]	3.1%	6.9%	0.035

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

[2] Stroke. 2011;42:00-00.

EPD:
In Favour of Differential Outcomes;
Clinical

PROOF: First In Man

Michi Neuroprotection System:

Transcervical Access With High Flow Rate Flow Reversal

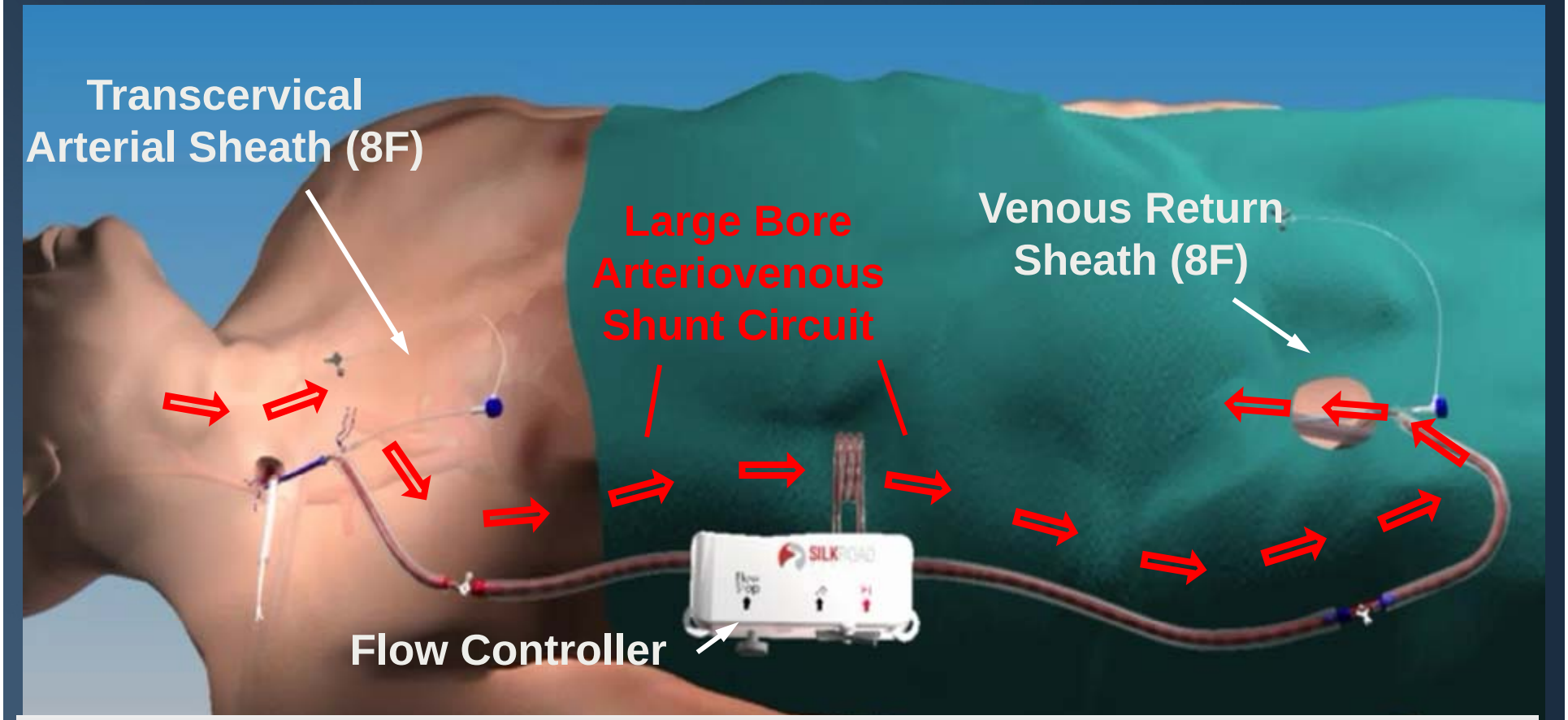
N = 65

Presented at VIVA 2011

Columbia University Medical Center

FAST-CAS

Flow Altered Short Transcervical Carotid Artery Stenting



MICHI™ Neuroprotection System

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A Meta-Analysis of Proximal Occlusion Device Outcomes in CAS

N = 2,397

All stroke 1.71%

MI 0.02%

Death 0.4%

S/D/MI 2.25%

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Bersin RM et al JACC 2012 In Press

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Stent Design:
In Favour of Differential Outcomes;
" Subclinical "

New Brain Lesions After Carotid Stenting Versus Carotid Endarterectomy: A Systematic Review of the Literature

Sonja Schnaudigel, Klaus Gröschel, Sara M. Pilgram and Andreas Kastrup

32 studies: 1363 CAS & 754 CEA

Ipsilateral DWI lesions:

51% open cell stents

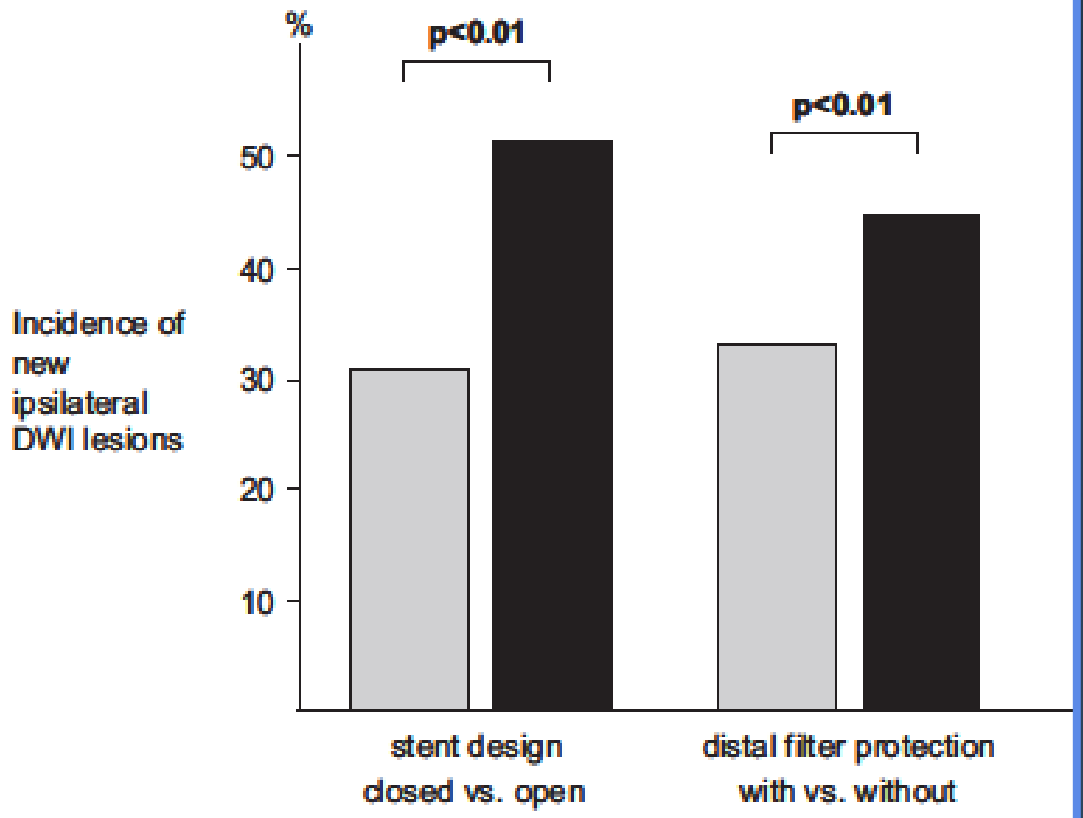
31% closed cell stents

p < 0.01

(*Stroke*. 2008;39:1911-1919.)

New Brain Lesions After Carotid Stenting Versus Carotid Endarterectomy: A Systematic Review of the Literature

Sonja Schnaudigel, Klaus Gröschel, Sara M. Pilgram and Andreas Kastrup



Black = Open Cell

Grey = Closed Cell

(*Stroke*. 2008;39:1911-1919.)

Randomized clinical trial of open-cell vs closed-cell stents for carotid stenting and effects of stent design on cerebral embolization

Carlos H. Timaran, MD,[a,b] Eric B. Rosero, MD,[b] Adriana Higuera, MD,[b] Adriana Ilarraza, BS,[b] J. Gregory Modrall, MD,[a,b] and G. Patrick Clagett, MD,[b] *Dallas, Tex*

N = 40; 20 XAct, 20 Acculink

Acculink EPD

Primary endpoint subclinical (DWMRI & MES on TCD)

43% symptomatic, 57% asymptomatic

JVS 2011; 54:1310-1316

MES Endpoint:

	MEDIAN MES (total)	p	MEDIAN MES (post stent ***i.e. filter retrieval***)	p
OPEN	264*	0.56	48	0.56
CLOSED	339*		53	

Filter effects:

Macdonald S, Cerebrovascular diseases, 2010;29:282-289

Covered Versus Bare Self-Expanding Stents for Endovascular Treatment of Carotid Artery Stenosis: A Stopped Randomized Trial

14 asymptomatic patients

1:1 RCT ePTFE covered membrane stent (symbiot) vs. Wallstent

Microembolisation (TCD) and DWI

Schillinger et al JEVT 2006;13:312-319

Covered Versus Bare Self-Expanding Stents for Endovascular Treatment of Carotid Artery Stenosis: A Stopped Randomized Trial

Symbiot: median 1 MES / patient (IQR 0-4)

Wallstent: median 6 MES / patient (IQR 3-8)

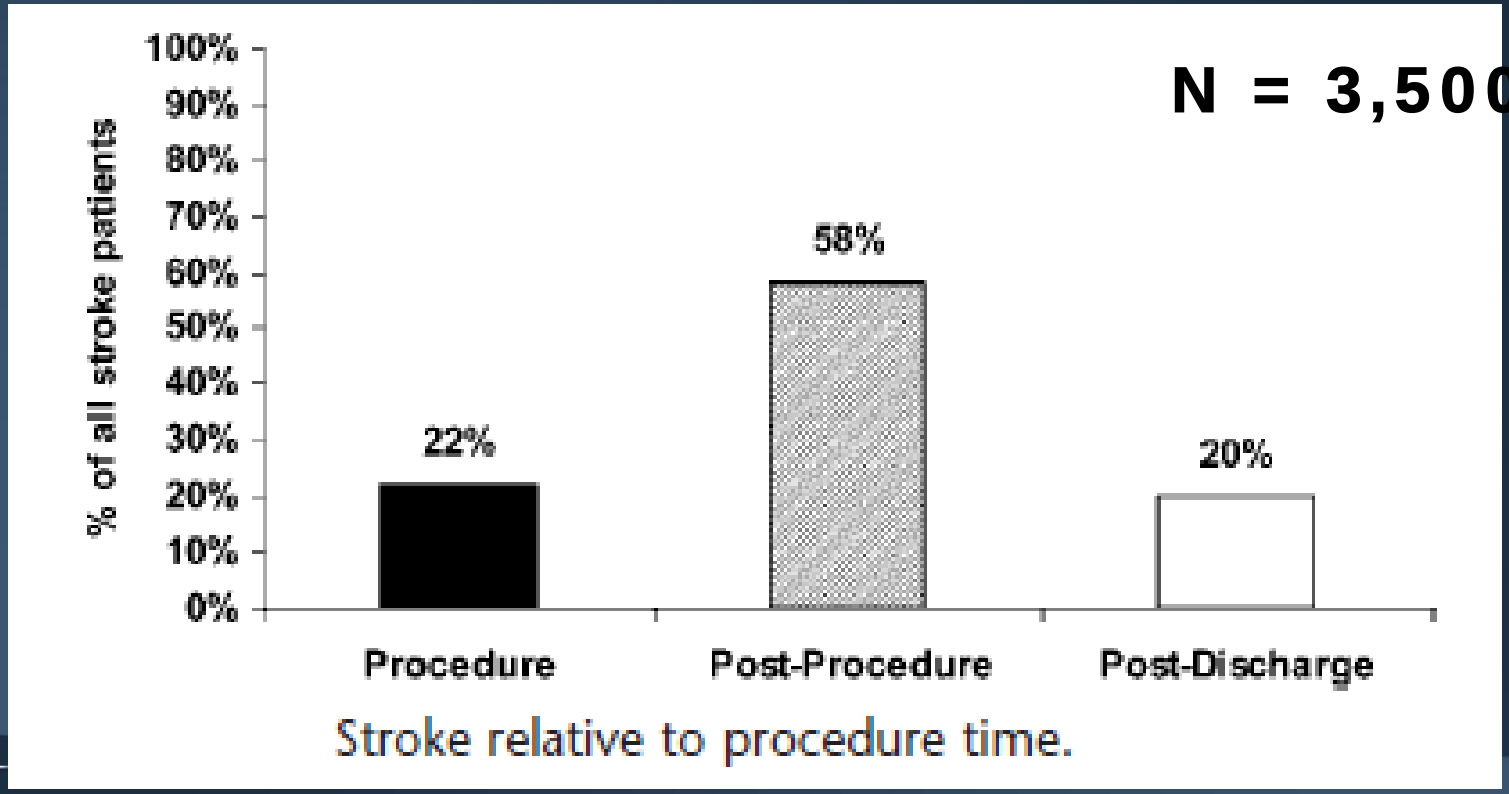
p = 0.04

Stent Design:
In Favour of Differential Outcomes;
Clinical

The CAPTURE Registry

Analysis of Strokes Resulting From Carotid Artery Stenting in the Post Approval Setting: Timing, Location, Severity, and Type

Ronald Fairman, MD, William A. Gray, MD,† Andrea P. Scicli, PhD,‡ Olivia Wilburn, MD, PhD,‡ Patrick Verta, MD,‡ Richard Atkinson, MD,§ Jay S. Yadav, MD,¶ Mark Wholey, MD,‖ L. Nelson Hopkins, MD,** Rod Raabe, MD,†† Stanley Barnwell, MD,‡‡ and Richard Green, MD,§§ for the CAPTURE Trial Collaborators*



Stroke relative to procedure time.

Ann Surg 2007;246:551-558

Phase 1: Catheterisation of arch / great vessels*

Phase 2: Lesion crossing / EPD

Phase 3: Stent deployment / postdilatation*

Phase 4: 24 hours post CAS*

Phase 5: 30 days post CAS*

*30 – day **major stroke** = 10 (4 phase 1, 6 phase 3)*

*30 – day **minor stroke** = 18 (Phase 4 & 5)*

“ Off – table ” strokes may be due to plaque prolapse

" Free Cell Area " & Outcome
N =3,179

Stent name	Precise
X-act	Protégé
Nexstent	Acculink
Wallstent	Exponent

Table 5. *P*-values for the test that event rates differ between stents

Population	Outcome	*p*-value
Total	All events	0.018
	Post-procedural events	0.002
Symptomatic	All events	0.006
	Post-procedural events	<0.0001
Asymptomatic	All events	0.248
	Post-procedural events	0.790

Bosiers M e al. Does Free Cell Area Influence the Outcome in Carotid

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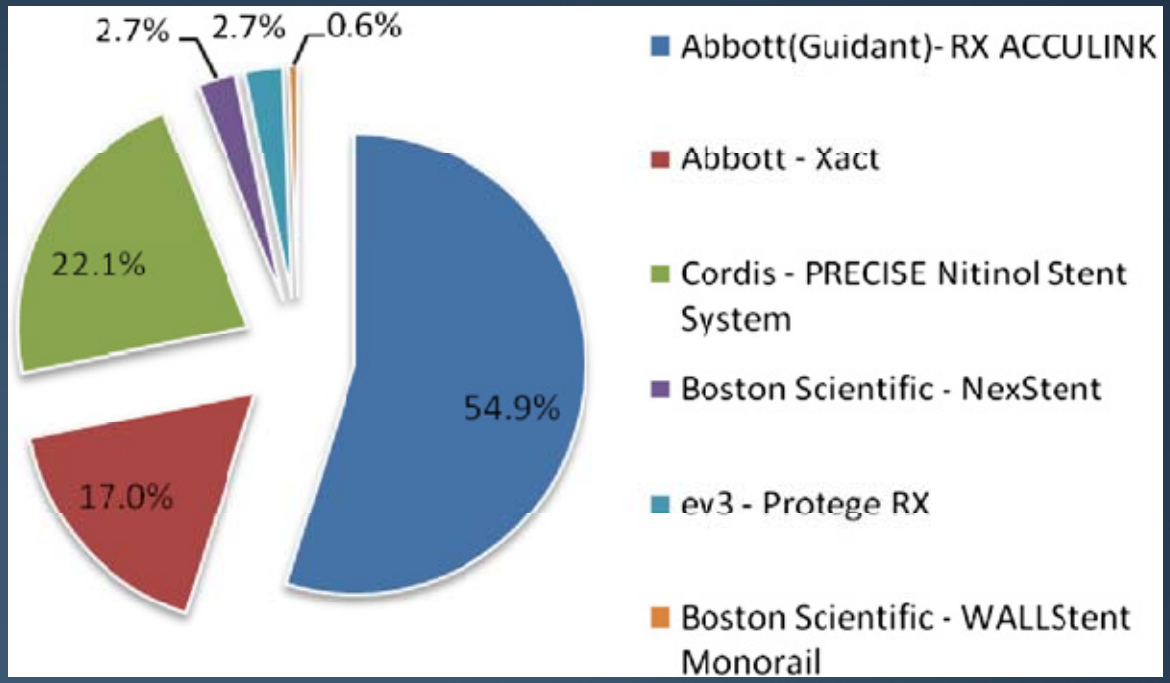
Society for Vascular Surgery Vascular Registry evaluation of stent cell design on carotid artery stenting outcomes



N = 4,377

Jim J et al SVS Outcomes Committee. Society for Vasc registry evaluation of stent design on carotid artery s JVS 2011;54:71-78

Table III. In-hospital outcomes in OPEN versus CLOSED patients

In-hospital outcomes	*OPEN (n = 3451)* n (%)	*CLOSED (n = 886)* n (%)	P *value*
Death, stroke, or MI	85 (2.46)	28 (3.16)	.2386
Death, stroke, or TIA	111 (3.22)	38 (4.29)	.1213
Mortality	18 (0.52)	8 (0.90)	.2192
Stroke	64 (1.85)	19 (2.14)	.5825
MI	15 (0.43)	5 (0.56)	.5816
TIA	36 (1.04)	14 (1.58)	.2146
TMB	7 (0.20)	3 (0.34)	.4366

CLOSED, Closed cell stent; *MI*, myocardial infarction; *OPEN*, open cell stent; *TIA*, transient ischemic attack; *TMB*, transient monocular blindness. *P* values were based on Fisher exact test. Outcomes are defined as any event intraoperatively or predischarge. Rates are per patient.

Jim J et al SVS Outcomes Committee. Society for Vas
registry evaluation of stent design on carotid artery
outcome. JVS 2011;54:71-79

The ***Open Cell*** group had (a non-significantly) higher rate of Death / Stroke / MI at 30-days

" Suggesting the benefit of ***Closed Cell*** stents in later follow-up "

Jim J et al SVS Outcomes Committee. Society for Vas
registry evaluation of stent design on carotid artery s
outcome. JVS 2011;54:71-79

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SPACE: PURELY SYMPTOMATIC POPULATION

Table 1. Interventional Devices (stents; protection devices) Approved for Use Within the SPACE Trial if the Interventionalist Was Certified for the Specific Device

Stent		Protection Device
Closed cell stent	Wallstent (Boston Scientific)	GuardWire (PercuSurge)
Open cell stent	Precise (Cordis)	Epifilter (Boston Scientific)
	Acculink (Guidant)	AngioGuard (Cordis)
		NeuroShield (MedNova)
		Trap NFS (Microvena)

Jansen O et al. Protection or Nonprotection in Carotid Stent Angioplasty: The Influence of Interventional

SPACE:

(OE *30-day* ipsilateral / stroke / death)

Table 4. Influence of Different Stent Types on OE Rate

Stent	Wallstent	Acculink	Precise
No. of patients	436	92	35
Pat. with OE	24	9	5
OE rate (95% CI)	5.5% (3.6–8.1%)	9.8% (4.6–17.8%)	14.3% (4.8–30.3%)

Combined OE rate: 11.0% (6.2–17.8%)

NB: More pronounced difference without EPD – hinting at the inherent protective properties of closed-cell stents.

Conclusions:

How Do We Advance CAS Technique Meaningfully?

- Use proximal protection
- Avoid the arch
- Consider stent design

Microscopic air embolism during cerebral angiography and strategies for its avoidance

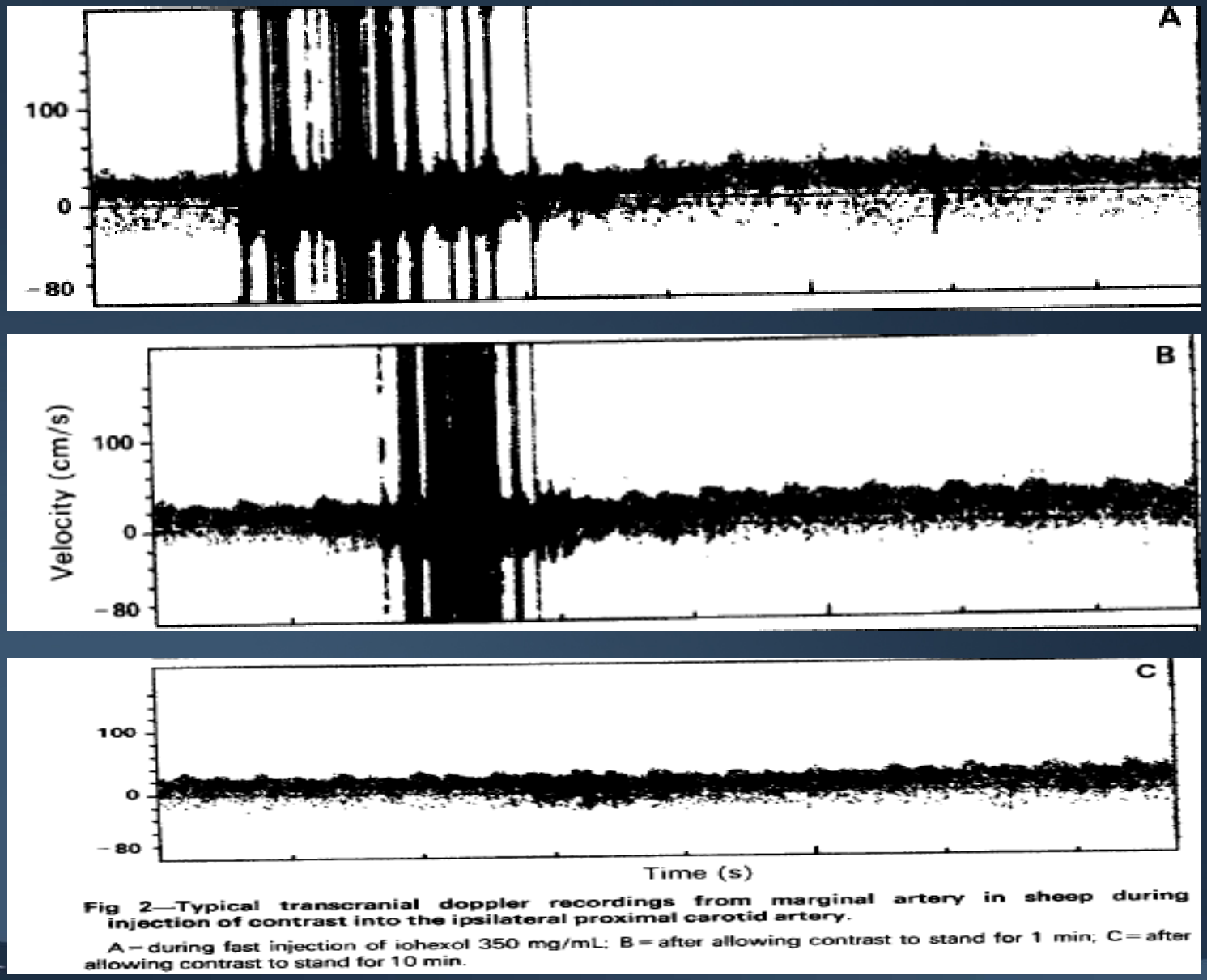

Fig 2—Typical transcranial doppler recordings from marginal artery in sheep during injection of contrast into the ipsilateral proximal carotid artery.

A—during fast injection of iohexol 350 mg/mL; B = after allowing contrast to stand for 1 min; C = after allowing contrast to stand for 10 min.

Markus H et al The Lancet 1993;341:784 - 787