Should TRI be considered to reduce the risk of stroke?

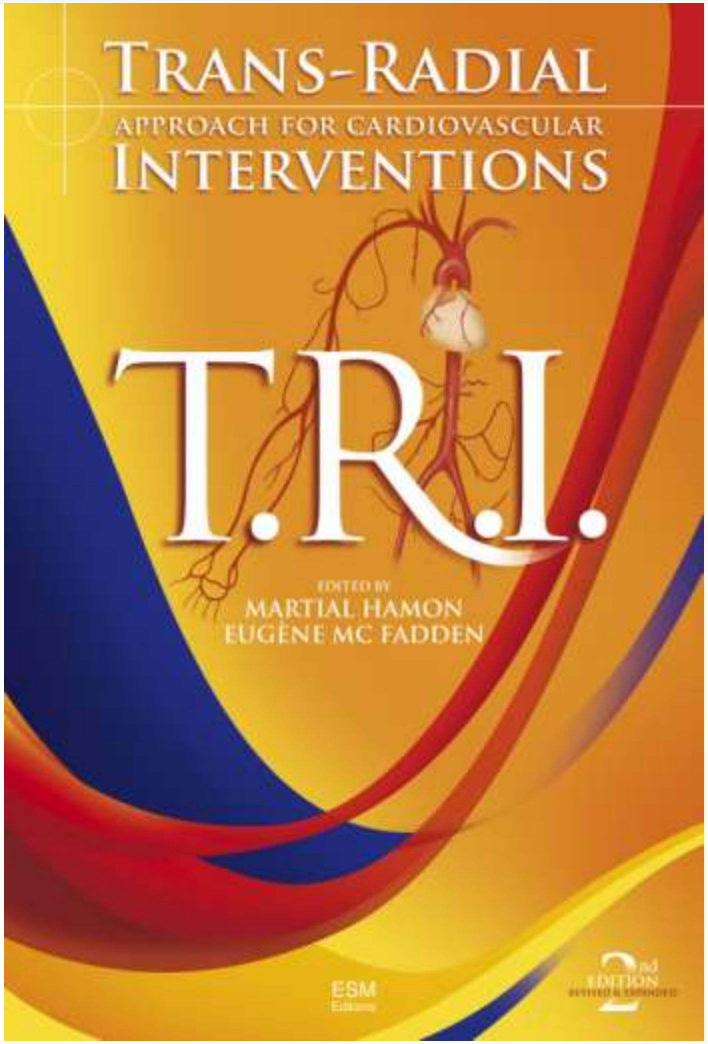
Impact of Arterial Access sites

On the risk of stroke

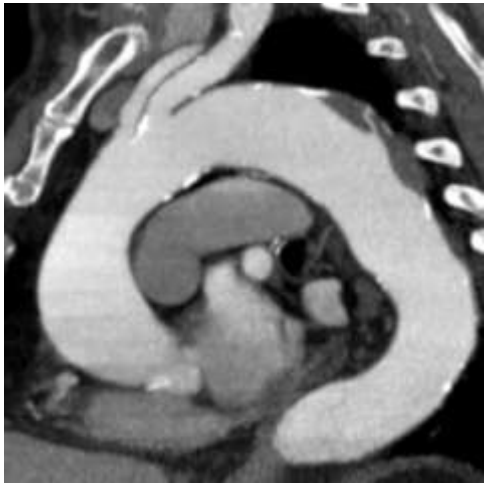
Martial Hamon, MD, FESC
Cardiology, CHU, Caen
Normandy, France

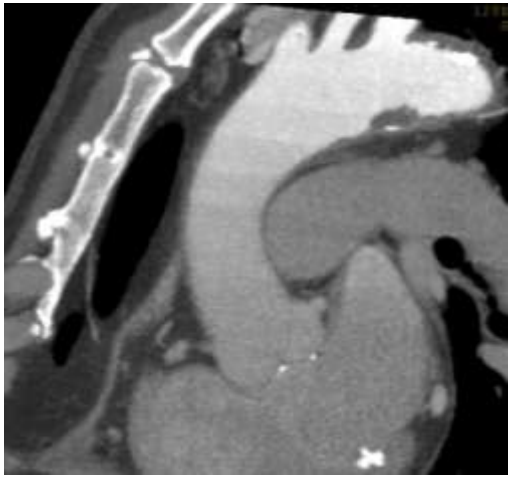
Disclosures

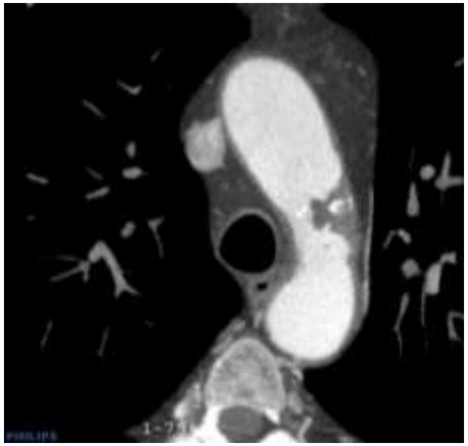
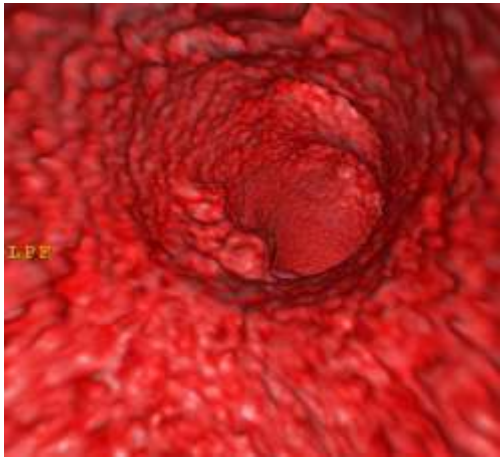
- Research grants: MSD, GSK, TMC, Lilly.
- Consultant:
  Terumo, Cordis



Impact of Arterial Access sites
On the risk of stroke





Stroke in Cadiac Catheterization: PCI subgroup analysis

0.2 to 0.4% & independent risk factors: Age, Atheroma extension, EF, ACS…

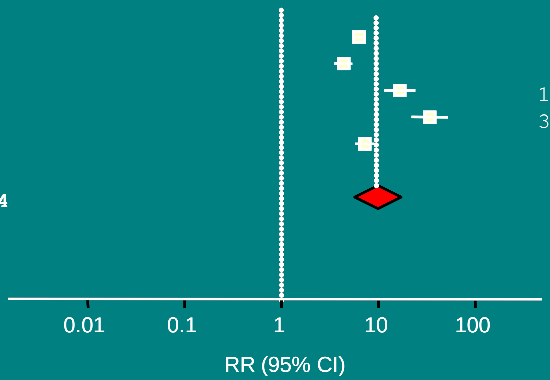
First Author	Patients & Fup	Incidence of Stroke In-hospital & postdischarge	N	%	95% CI	Independent Predictors of Stroke OR and 95% CI: Predictive variables	OR	95% CI	P
Lazar et al (1995)	**6,465 in-hospital**	Total	27	0.42%	[0.27-0.60]	Female gender	3.2	[1.4 - 7.4]	p < 0.01
		Ischemic	_	_	_	Vascular disease	3.1	[1.2 - 8.0]	p < 0.05
		Hemorrhagic	_	_	_	Extensive CAD	3.0	[1.2 - 7.4]	p < 0.05
		Uncertain	_	_	_	Ejection fraction	0.4	[0.2 - 1.0]	p < 0.05
						LVH	2.9	[1.2 - 7.3]	p < 0.05
Akkerhuis et al (2001)	**8,555 30 days**	Total	31	0..36%	[0.24-0.51]	Advanced age		NA	p < 0.001
		Ischemic	19	0.22%	[0.13-0.34]	Hypertension	2.9	[1.2-7.4]	p = 0.01
		Hemorrhagic	12	0.14%	[0.07-0.24]	PAD	2.2	[0.7-6.1]	p = 0.08
		Uncertain	1	0.01%	[0.00-0.06]				
Fuchs et al (2002)	**9,662 in-hospital**	Total	43	0.44%	[0.32-0.60]	IABP , emergency use	9.6	[3.9-23.9]	p < 0.001
		Ischemic	21	0.22%	[0.13-0.33]	IABP, prohylactic use	5.1	[1.8-14.0]	p = 0.002
		Hemorrhagic	20	0.21%	[0.13-0.32]	Age>80 years	3.2	[1.4-7.7]	p = 0.008
		Uncertain	2	0.02%	[0.00-0.07]	Vein graft intervention	2.7	[1.3-5.8]	p = 0.01
Dukkipati et al (2004)	**20,679 in-hospital**	Total	92	0.44%	[0.36-0.54]	Diabetes	1.8	[1.1-3.0]	p = 0.013
		Ischemic	43	0.21%	[0.15-0.28]	Hypertension	1.9	[1.1-1.3]	p =0.033
		Hemorrhagic	13	0.06%	[0.03-0.10]	Prior stroke	2.3	[1.3-4.0]	p < 0.006
		Uncertain	36	0.17%	[0.12-0.24]	Renal failure	3.1	[1.8-5.2]	p < 0.0001
						Urgent procedures	2.7	[1.3-5.5]	p <0.009
						IABP	2.2	[1.1-4.3]	p = 0.028
Wong et al (2005)	**76,903 in-hospital**	Total	140	0.18%	[0.15-0.21]	Age	1.0	[1.0-1.1]	p < 0.001
		Ischemic	_	_	_	GPI	1.5	[1.0-2.1]	p = 0.027
		Hemorrhagic	_	_	_	AMI	3.4	|2.6-5.8]	p < 0.001
		Uncertain	_	_	_	Carotid disease	3.4	[2.1-5.4]	p < 0.001
						Renal failure	2.0	[1.0-3.9]	p = 0.037
						Heart failure	2.9	[1.9-4.4]	p < 0.001
						IABP	3.5	[1.5-8.3]	p = 0.004

Mortality in patients with peri-procedural stroke in PCI

9.95 [95% CI: 5.73 to 17.27]

Deaths, No. / Patients, No

Study	STROKE (+)	STROKE (-)	RR (random) 95% CI
Budaj et al.	100/310	1782/34923	6.32 [5.35, 7.47]
Cronin et al.*	65/238	1123/17913	4.36 [3.51, 5.40]
Dukkipati et al.	23/92	309/20587	16.66 [11.50, 24.13]
Fuchs et al.	16/43	106/9619	33.77 [21.92, 52.01]
Westerhout et al.	56/228	1060/31162	7.22 [5.71, 9.13]
Total	**260/911**	**4380/114204**	**9.95 [5.73, 17.27]**



Test for heterogeneity: Chi² = 95.31, df = 4 (P < 0.00001), I² = 95.8%

Test for overall effect: Z = 8.16 (P < 0.00001)

Hamon M. et al Circulation 2008

Cerebrovascular accidents after diagnostic and interventional cardiac catheterization

Mechanisms of cerebrovascular accidents

Embolism of athero-thrombotic material (*causes & preventive actions*)

- Catheters (during procedure) (*appropriate heparinization/flushing*)
- Left ventricle (mural thrombus post MI) (*Echo/avoiding ventriculo*)
- Atherosclerotic aorto-femoral plaques (*manipulation of catheters*)

Air embolism (quite frequent) (*easily preventable: catheter filling/flushing*)

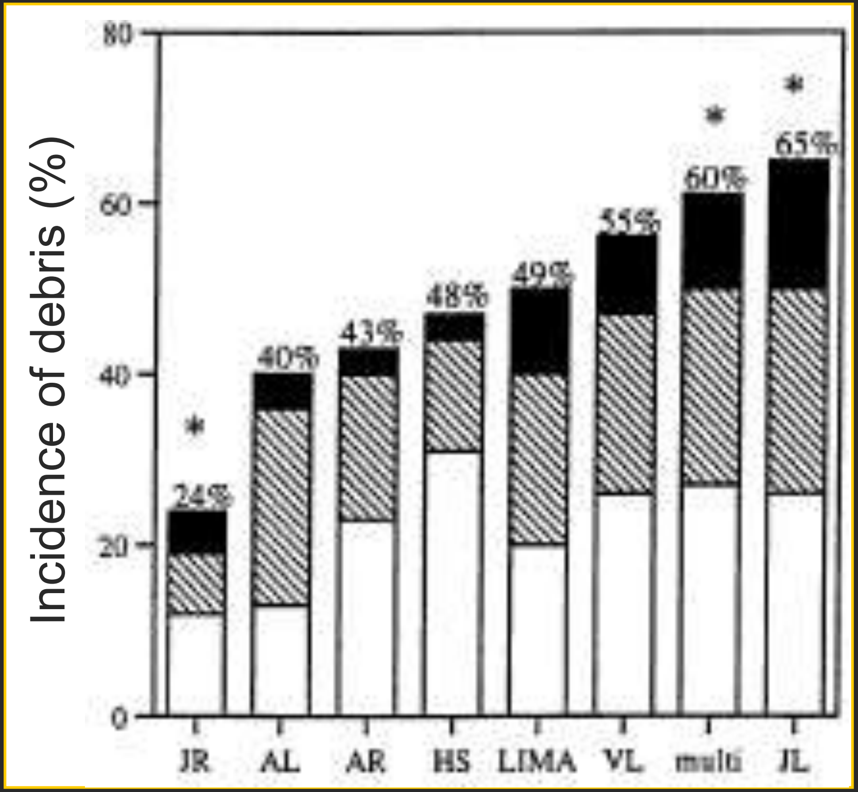
Contrast use (osmotic disruption of the blood-brain barrier) (*low osmotic agent*)

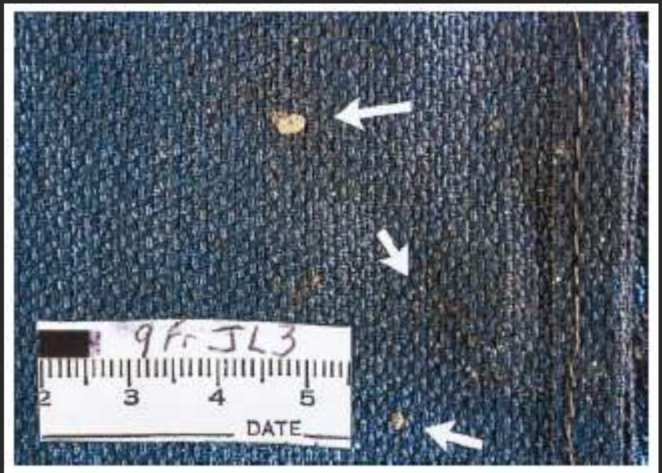
Miscellanous (intracranial bleeding in ACS, antithrombotic regimens…)

TCD: ***Digital Power M-mode Doppler***
Cardiac Catheterization Monitorring

Scraping of Aortic Debris by Coronary Guiding Catheters

Results of a prospective evaluation in 1,000 cases

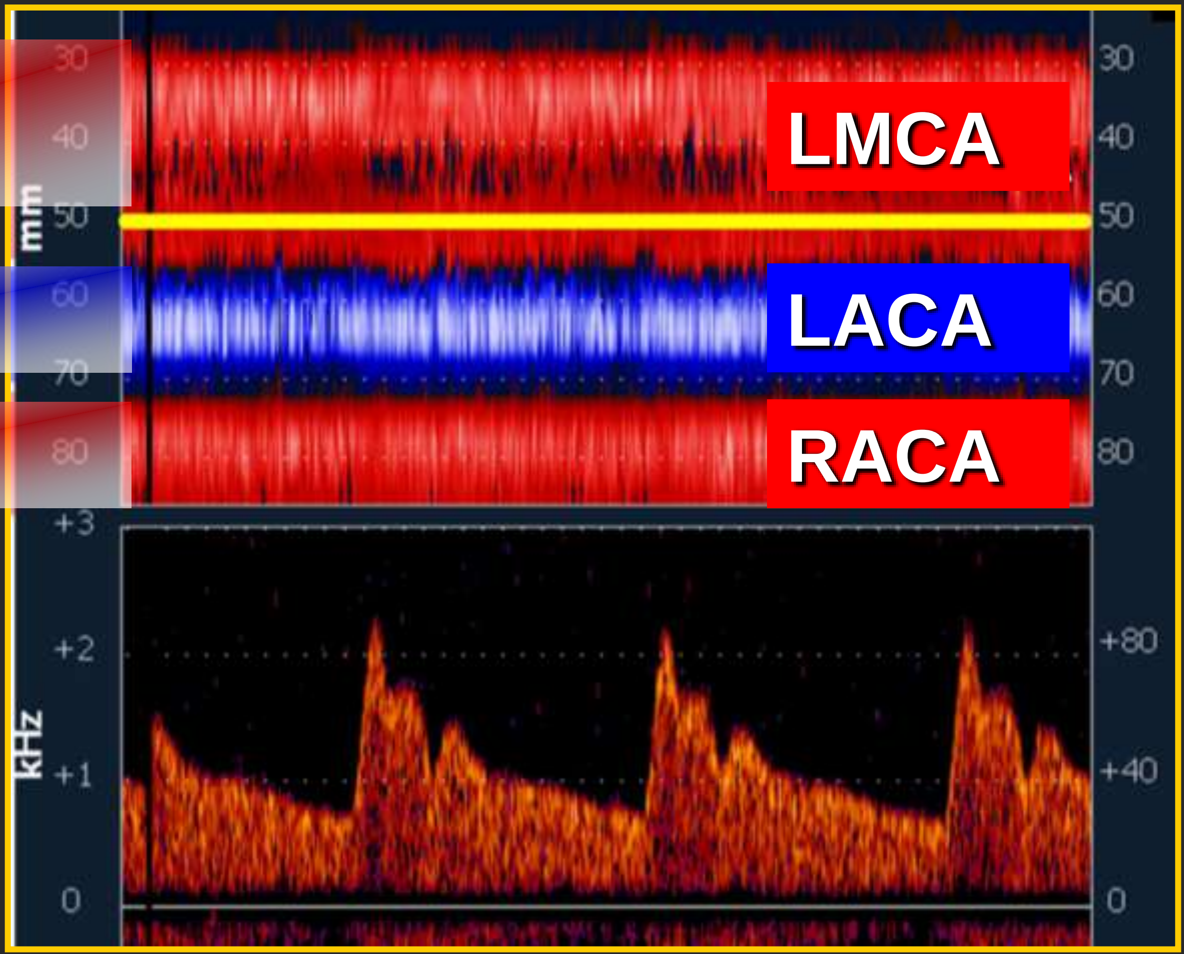




Keeley EC et al. J Am Coll Cardiol 1998;1861-5

Digital Power M-Mode TCD

Easy Signal Acquisition & Vessel Identification



Microembolism in cardiac catheterization: TCD studies

- Cerebral Microembolism detected by TCD during percutaneous transvenous mitral commisurotomy.

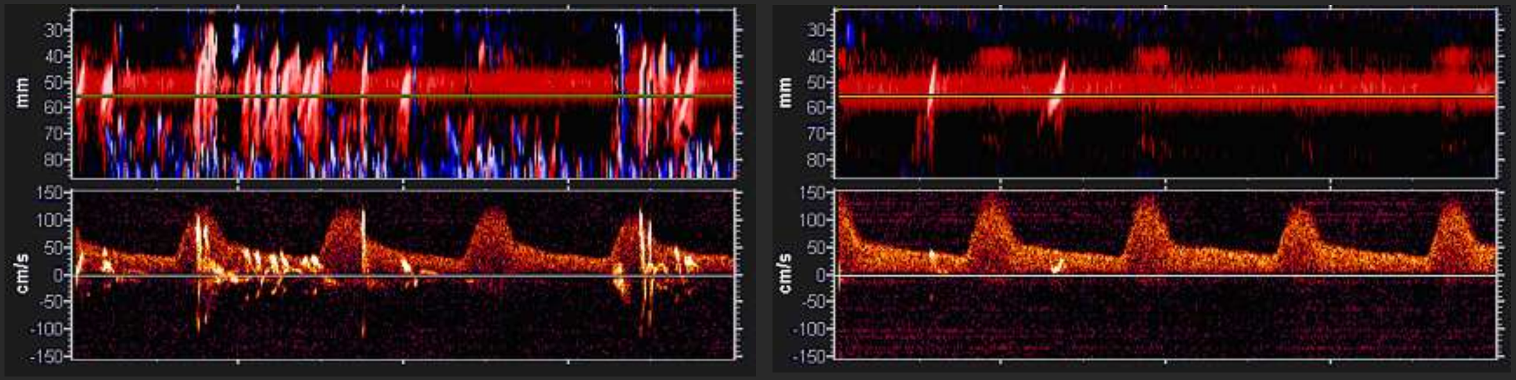
Kay et al. Am J Cardiol 1995;75:189-190.

- TCD detection of microemboli during percutaneous transluminal coronary angioplasty.

Bladin et al. Stroke 1998;29:2367-2370.

- TCD detection of cerebral microemboli during left heart catheterization.

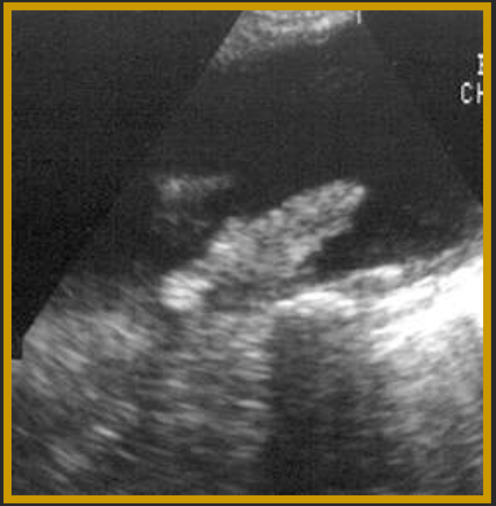
Leclercq et al. Cerebrovasc Dis 2001;12:59-65.



Transesophageal Echocardiography

Case control study
(152 strokes, 152 control)

Aortic Arch Atheroma and Stroke



Aortic atheroma:
complex plaques
protruding atheroma

OR = 21.3 [2.4-193.2]

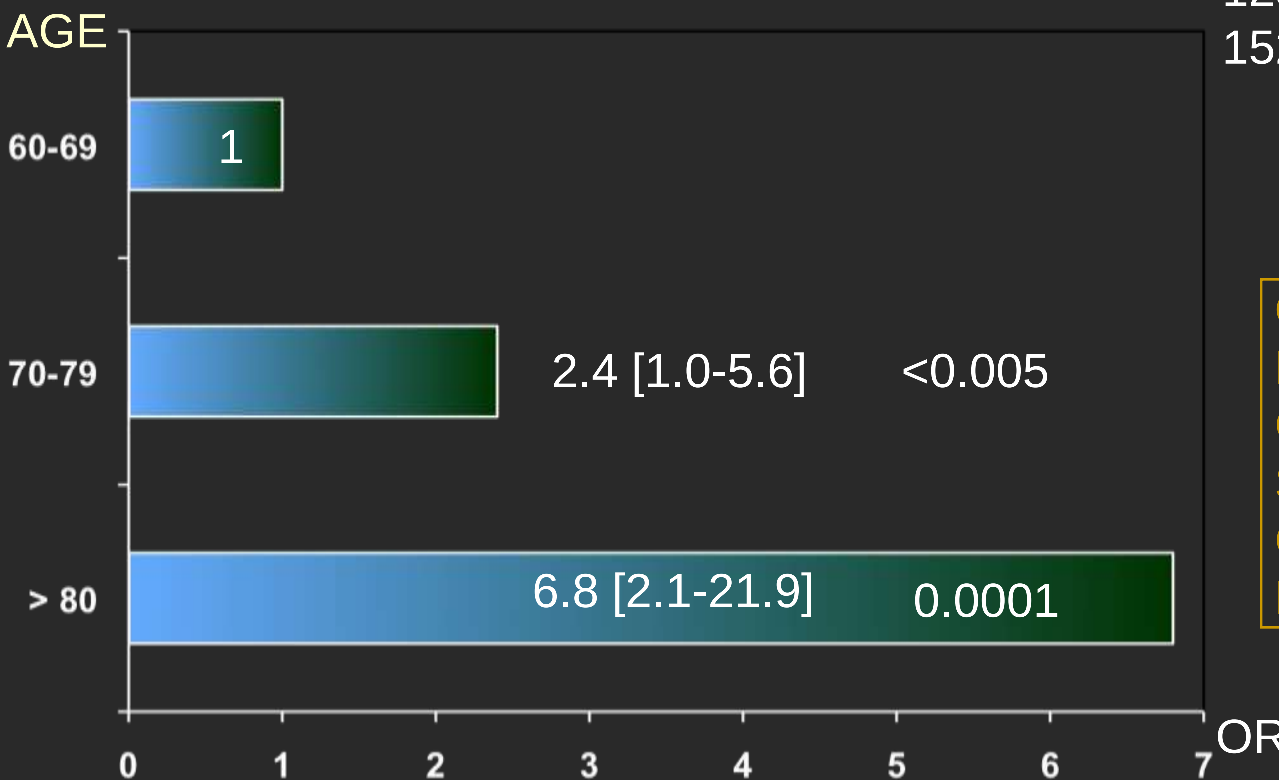
Location of aortic plaques	Patients with Stroke (n = 152)	Control patients (n = 152)	Adjusted OR (95% CI)
No Atheroma	28 (18.4%)	55 (36.2%)	-
Small atheroma (<4mm)	56 (36.8%)	68 (44.7%)	1.9 [1.0-3.6]
Large Atheroma (>4mm)	68 (44.8%)	29 (19.1%)	4.3 [2.1-8.7]
- Non complex	34 (22.4%)	25 (16.5%)	2.4 [1.1-5.1]
- Complex	34 (22.4%)	4 (2.6%)	17.1 [5.1-57.3]
- Ulcerated	24 (15.8%)	3 (2.0%)	15.8 [4.1-61.4]
- Mobile	10 (6.6%)	1 (0.7%)	21.3 [2.4-193.2]

Di Tullio Am Heart J 2000; 139:329-36

Catheter-related peripheral embolism

Predictors of aortic debris

Case-control Study
125 aortic debris
152 no debris

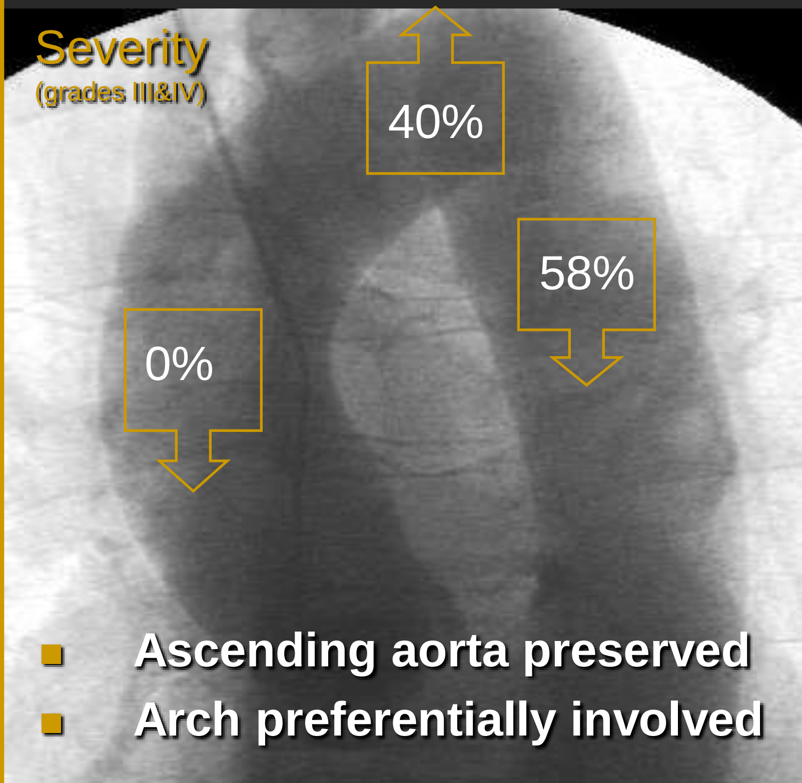


Other predictors :
- HT (OR 2.5)
- Chol (OR 3.8)
- Smoking (OR 2.9)
- CAD (OR 2.3)
- PAD (OR 6.3)

Karalis et al. Am Heart J 1996 ; 131 : 1149-56

Aortic atheroma and arterial access issue

Frequency and distribution of atherosclerotic plaques within the thoracic aorta in patients with CAD



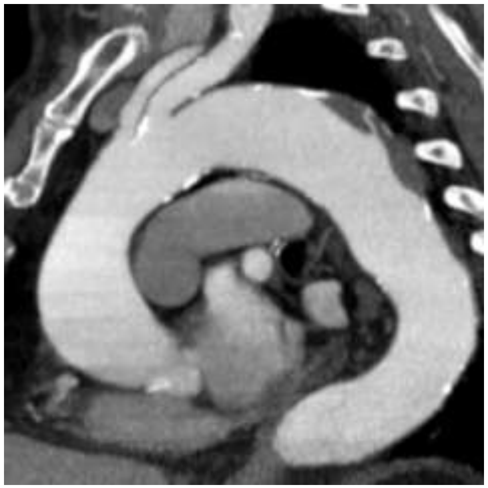
Location of aortic plaques	CAD (n = 97)
Descending Aorta	90 (93%)
Aortic Arch	77 (80%)
Ascending Aorta	36 (37%)

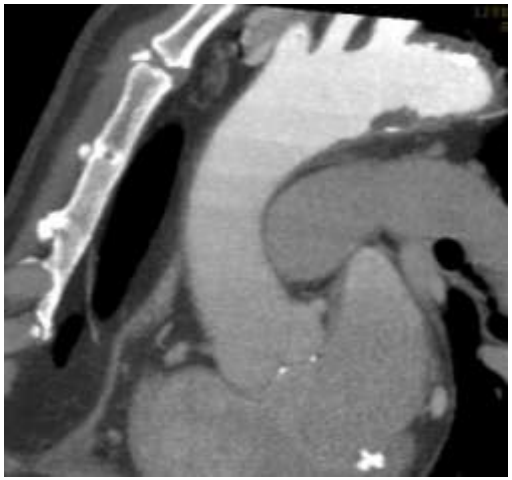
Severity of atheroscleotic plaques / CAD	No plaques (grade I)	Simple (grade II)	Complex (grades III&IV)
Descending Aorta	7(7%)	34 (35%)	56 (58%) [47-68]
Aortic Arch	20 (21%)	38 (39%)	39 (40%) [30-51]
Ascending Aorta	61 (63%)	36 (37%)	0 [0-4]

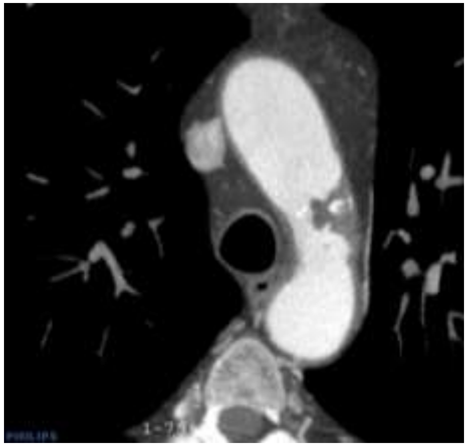
Khoury Z Am J Cardiol 1997; 79: 23-27

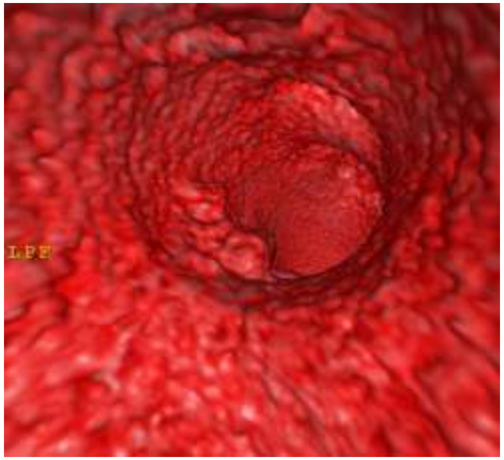
Retrograde progression of aortic atheroma with age

From Descending Aorta to the Arch and Ascending Aorta









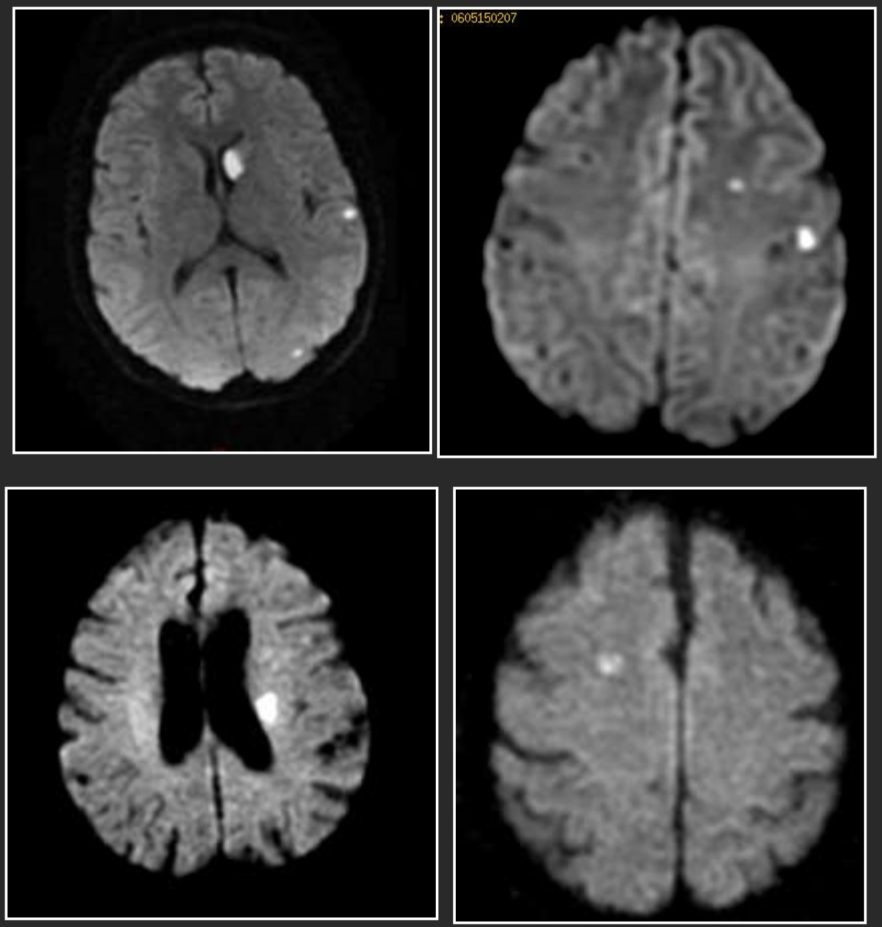
Comparison of femoral and radial approaches for the occurrence of stroke

Sample size calculation:

- 0.2% risk of stroke by femoral approach
- 0.4% risk of stroke by radial approach
- 50% increase in risk
- Alpha level of 0.05
- Beta level of 0.20
- Randomized 1:1
- 25 000 patients are necessary

Surrogates endpoints?

DW MRI and stroke detection



Diffusion weighted
Magnetic Resonance Imaging

DW-MRI

Allowing the detection of subclinical brain injury

Silent stroke in cardiac catheterization: Diffusion-Weighted MRI studies

- Silent and apparent cerebral embolism after retrograde catheterization of the aortic valve in valvular stenosis: a prospective, randomized study.
  Omran et al. Lancet 2003;361:1241-1246.

- Cerebral infarction incidence and risk factors after diagnosis and interventional cardiac catheterization-prospective evaluation at DW MRI.
  Busing et al. Radiology 2005;235:177-183.

- Cerebral emboli during left heart catheterization may cause acute brain injury.
  Lund et al. Eur Heart J 2005;26:1269-1275.

- Cerebral Microembolism during Cardiac catheterization and risk of acute brain injury. A prospective DW MRI study.
  Hamon et al. Stroke 2006;37:2035-2038.

- Risk of acute brain injury related to cerebral microembolism during cardiac catheterization performed by right upper lim arterial access.
  Hamon et al. Stroke 2007;38:2176-2179.

Cerebral emboli during left heart catheterization may cause acute brain injury

47 pts, left catheterization (5 PCI), transcranial Doppler, Cerebral MRI
754 cerebral microemboli: 92.1% gaseous , 7.9% solid

	Transradial	Transfemoral	p
%	78.7	21.3	
Solid microemboli: median (range)	57 (18-372)	36 (12-66)	0.012
New cerebral lesions MRI* (%)	15.2	0	0.567
*associated with			
- solid microemboli: median (range)	90 (60–372)	42 (12–246)	0.016
- longer fluoroscopy time	11.3 (3.8–14.8)	5.2 (1.4–33.6)	0.039

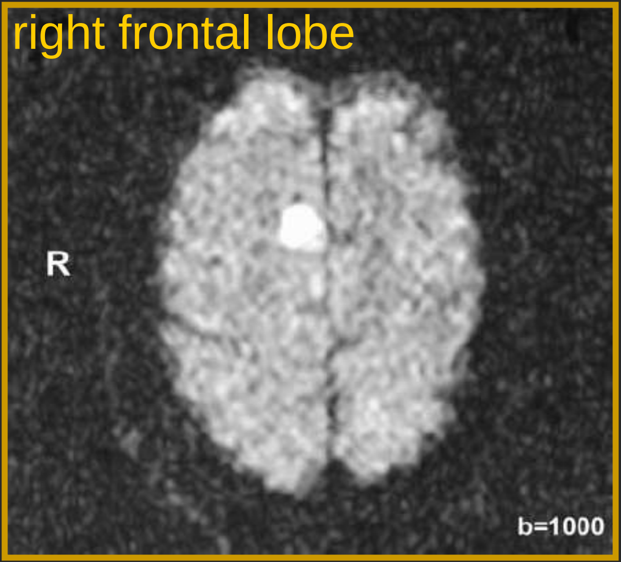
6F diagnostic catheters + 0.038'', J tip, 220 cm guidewire

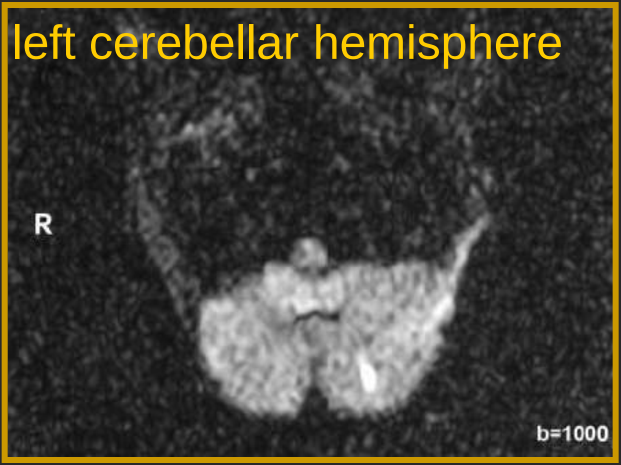
(Non randomized, non consecutive series, monocentric, small sample, no adjustment)

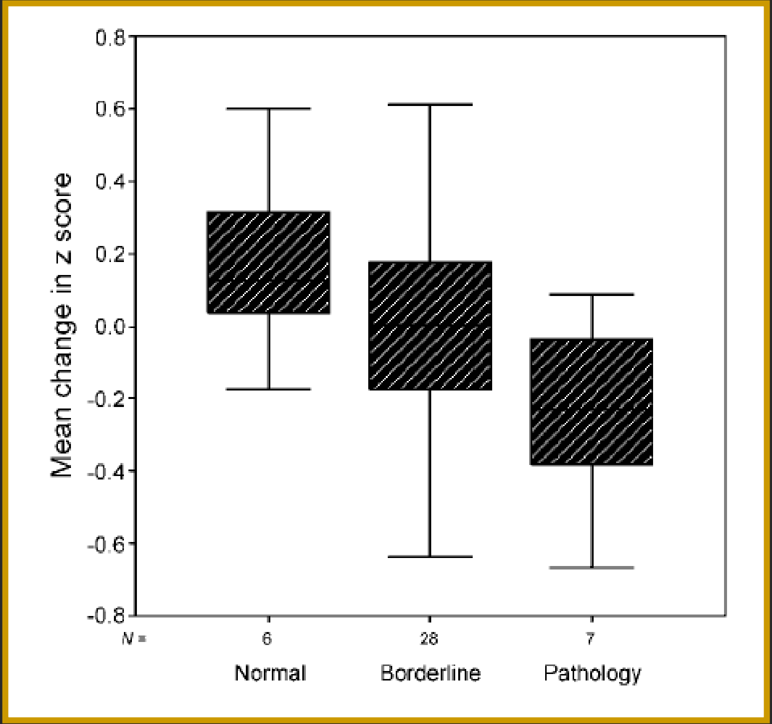
Lund, European Heart Journal 2005

Cerebral emboli during left heart catheterization may cause acute brain injury

Post-catheterization cerebral DWI







Cognitive impairment associated with degree of cerebral MRI injury (P = 0.03)

Lund, European Heart Journal 2005

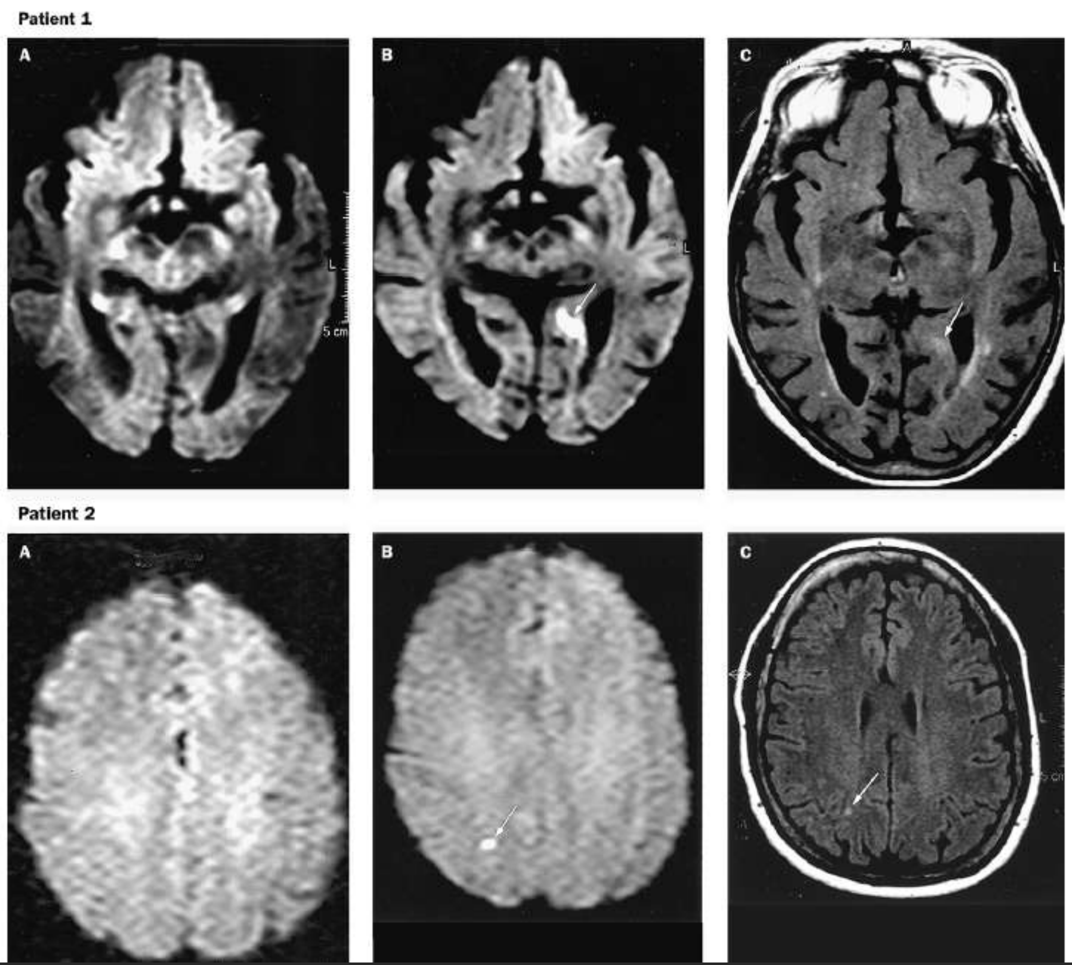
Cereral infarction: Incidence and risk factors after diagnosis and interventional cardiac catheterization

Prospective evaluation at diffusion-weighted MRI

- 52 patients referred for cardiac catheterization
- MRI before (3-26h) and after procedure (12-48h)
- 11 experimented cardiologists
- 7 patients (15%) presented cerebral infarcts
- Patients remained asymptomatic: SBI
- Only duration of the procedure was independent predictor for cerebral infarction ($p<.05$)
- All femoral approach+++

Busing KA Radiology 2005; 235: 177-183

Silent and apparent cerebral embolism after retrograde catheterisation of the aortic valve in valvular stenosis: a prospective, randomised study



N=101 patients
22% of silent embolism
3% clinically apparent

Fluoroscopy time
6.1 vs 2.9 min (p<0.0001)

Contrast media volume
N° of catheter exchanges

Omran et al. Lancet 2003; 361: 1241–46

SCIPION

(**S**ilent **C**erebral **I**nfarct and **P**CI Evaluat**ION**)

Cerebral Microembolism During Cardiac Catheterization and Risk of Acute Brain Injury

A Prospective Diffusion-Weighted Magnetic Resonance Imaging Study

Michèle Hamon, MD; Sophie Gomes, MD; Catherine Oppenheim, MD, PhD;
Rémy Morello, MD, MPH; Rémi Sabatier, MD; Thérèse Lognoné, MD; Gilles Grollier, MD;
Patrick Courtheoux, MD; Martial Hamon, MD

TABLE 2. Comparison of Recent Studies Exploring Brain Injury Using Serial DW at MRI After Cardiac Catheterization.

	n	Heparin	Fluoroscopy Time (min) DWI+/DWI−	Catheter Size (French)	Serial DW MRI	New Cerebral Infarction Observed %	New Cerebral Infarction Mid-Point [95% CI]	Indication
Omran 2003[3]	101	5000 IU	6.1/2.9	6 F-7 F	100%	22%	23% [15–31]	Aortic stenosis
Lund 2005[5]	47	5000 IU	11.3/5.2	6 F	89%	13.5%	15.7% [6–26]	CAD
Busing 2005[4]	48	2500 IU	10.1/7.4	5 F-6 F-7 F	94%	15%	17% [7–28]	CAD
Hamon 2006	46	5000 IU	7.0/5.4	5 F	100%	2.2%	5.9%* [0.01–12.5]	Aortic stenosis

CAD indicates coronary artery disease.

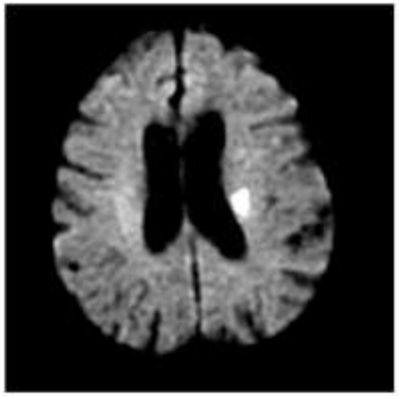
*Only 1 new cerebral infarction in our consecutive series of 46 patients was documented (2.2%, observed proportion). The mid-point of the adjusted Wald interval and 95% CI is calculated for all studies. It is noteworthy that by comparison to previous studies a lower rate of new cerebral infarction was documented by DW MRI in our series ($P<0.02$) and especially by comparison with the results of Omran et al[3] ($P<0.002$).

SCIPION study

(**S**ilent **C**erebral **I**nfarct and **P**CI Evaluat**ION**)

Silent cerebral infarct after cardiac catheterization as detected by diffusion weighted Magnetic Resonance Imaging: a randomized comparison of radial and femoral arterial approaches

Michèle Hamon[1], Francesco Burzotta[2], Catherine Oppenheim[3], Rémy Morello[4], Fausto Viader[5], Martial Hamon*[6] for the SCIPION Investigators[7]



Primary endpoint:

-SBI as detected by DW-MRI

Sample size:

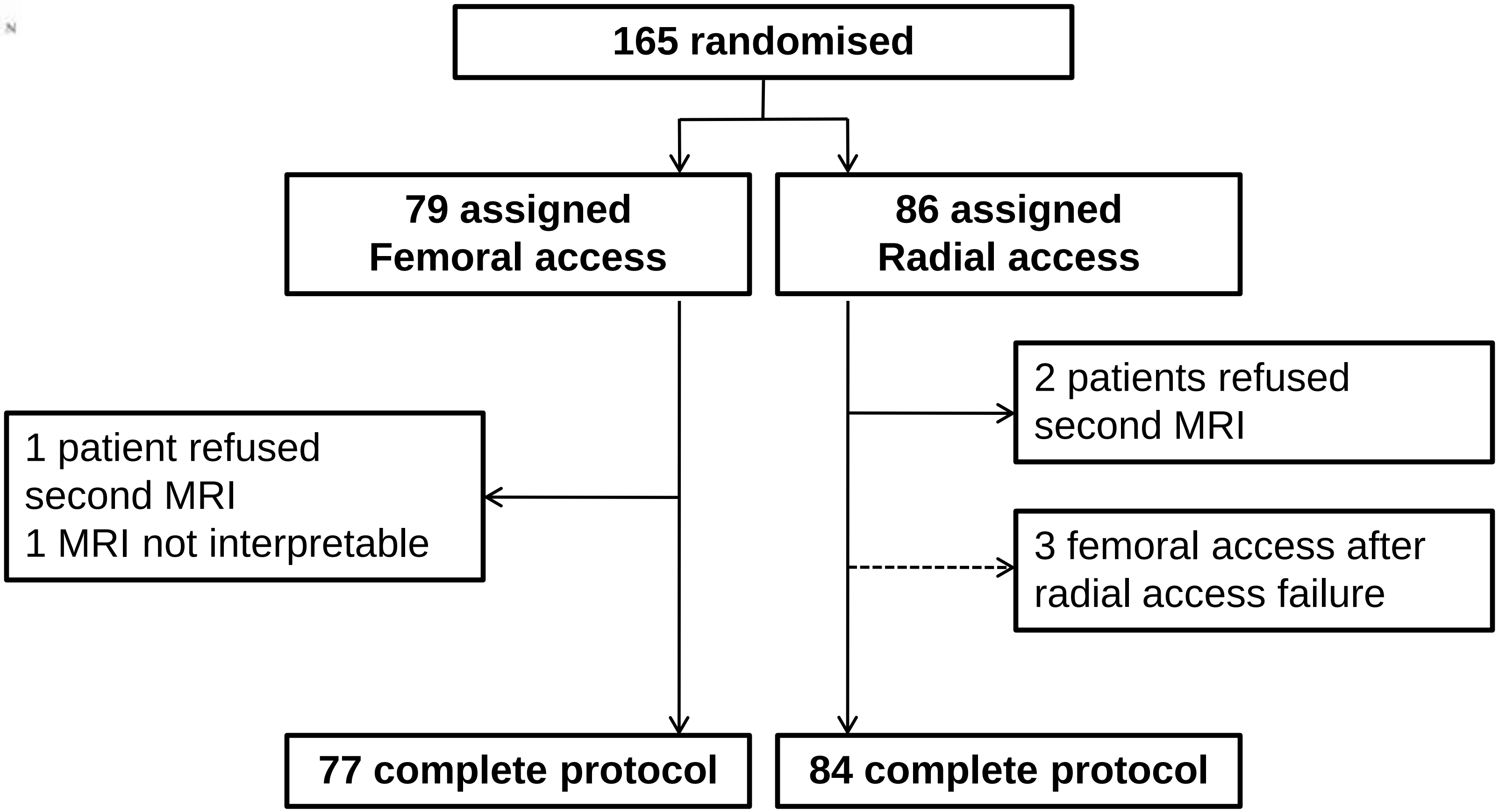
-152 pts, Randomized 1/1, Power 80%, P<0.05

(Lund et al. Lancet 2005 vs Hamon et al Stroke 2006)

Prospective Randomized Study in 4 centers:

- Janus Lipiecki, Clermont Ferrand, France
- Didier Carrié, Toulouse, France
- Francesco Burzotta, Roma, Italy
- Martial Hamon, Caen, France

SCIPION Trial
Flow-chart



Baseline characteristics of patients

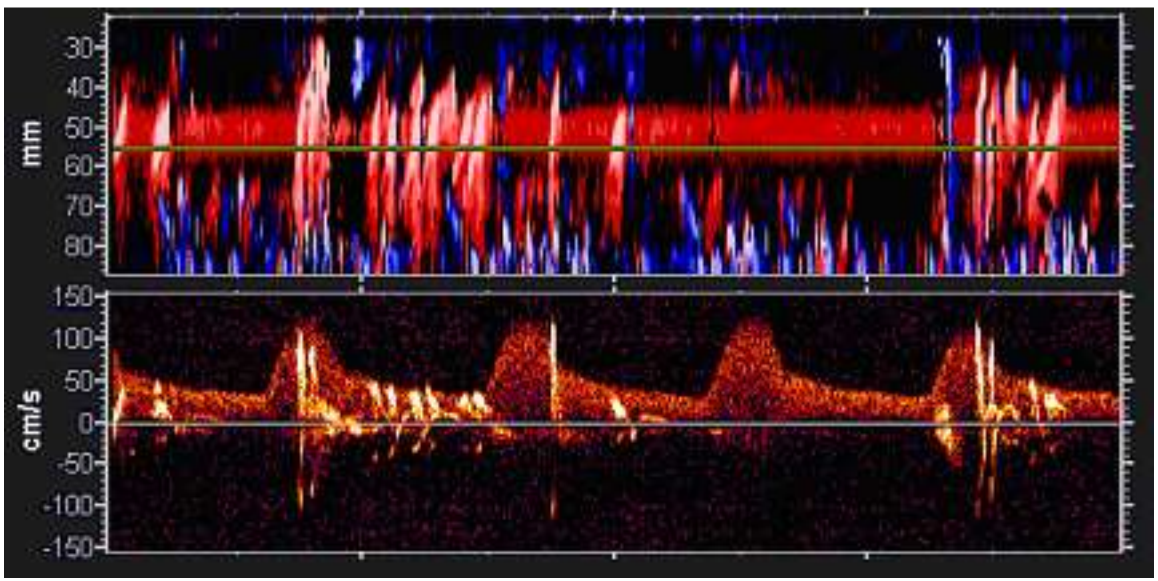
%	Femoral (n=79)	Radial (n=86)	p
Age (yrs)	73.7 (2.5)	75.2 (1.8)	0.34
Men (%)	53.2 (11)	55.8(10.5)	0.73
Smoking	31.6	32.5	0.90
Hypertension	74.6	76.7	0.75
Dyslipidemia	46.8	53.5	0.41
Diabetes	35.4	26.7	0.23
BMI > 30	32.3	28	0.48
Heredity	11.4	12.8	0.78
Prior AF	21.5	16.3	0.39
Prior stroke	3.8	4.6	0.91

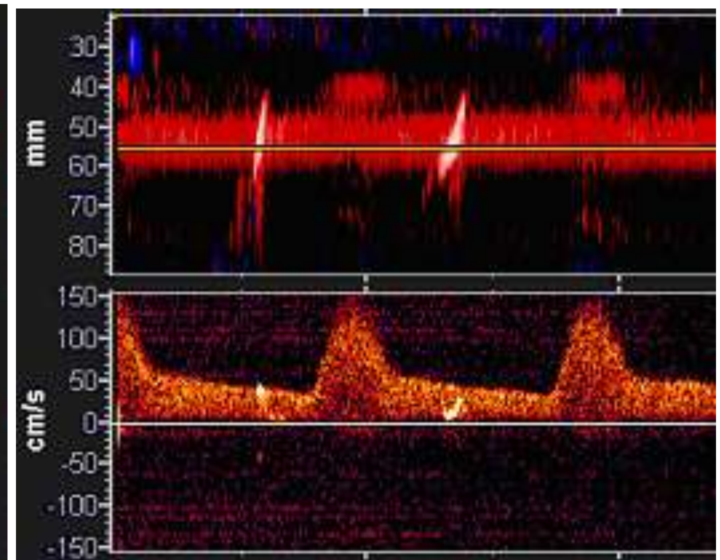
Procedural characterisctics

	Femoral (n=79)	Radial (n=86)	p
Procedural time (min)	25.2 (2.8)	24.7 (2.8)	0.81
Fluoroscopy (min)	7.24 (1.2)	7.77 (0.93)	0.49
CAD (%)	56.9	40.7	0.03
EF%	62.6 (2.7)	61.1 (2.6)	0.44
Gradient	46.1 (3.2)	48.4 (3.1)	0.31
AS crossed (%)	96.2	91.8	0.40
N catheters	4.07 (0.2)	3.79 (0.19)	0.052
1st MRI/Cath (h)	12.3 (2.8)	13.4 (3.6)	0.63
2nd MRI (h)	16.1 (3.5)	16 (2.9)	0.97

High Intensity Transient Signals

	Femoral	Radial	p
HITS	52.7 (11)	56.2 (29)	0.78

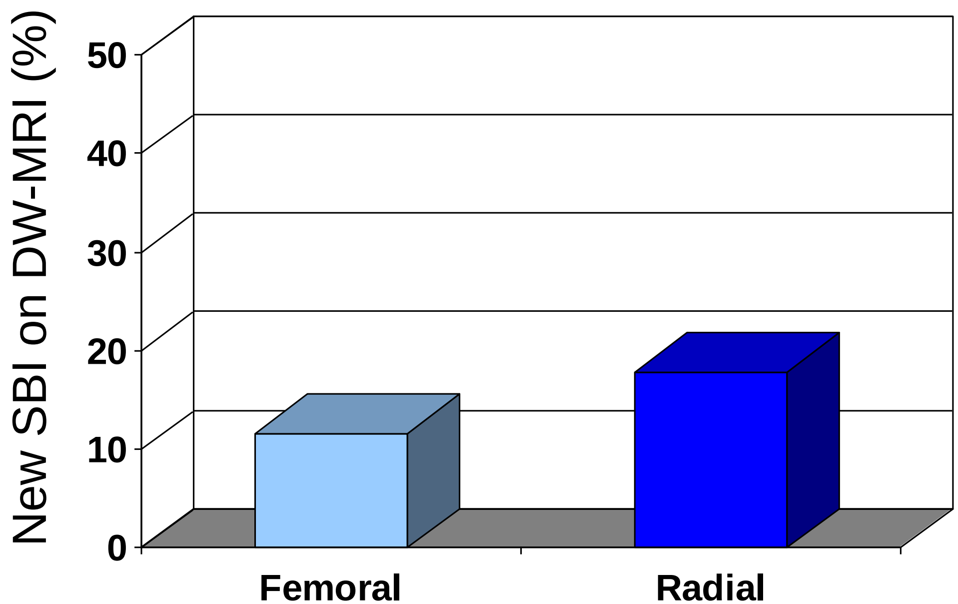




Primary Endpoint

New SBI on serial DW-MRI

New SBI – MRI (%)	**Femoral (n=77)**	**Radial (n=84)**	**p**
Observed (%,n) And Exact 95% CI	11.6% (9) (5.4 to 21.0)	17.8% (15) (10.3 to 27.7)	0.27
Mid point of Adjusted Wald 95% CI	12.6% (6.0 to 20.9)	18.6% (11.02 to 27.5)	



Conclusions

- Clinically apparent stroke are uncommon
- Unsuspected SBI in PCI up to 15-22% of cases!
- Risk factor : Duration of the procedure
- Both radial and Femoral approaches concerned: SCIPION
- High risk patients: Antithrombotics, Materials, Technical issues

- DWI, TCD, neuro-psychological tests: useful tools