

CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE
CONTROVERSIES & UPDATES
IN VASCULAR SURGERY



JANUARY 23-25 2014

MARRIOTT RIVE GAUCHE & CONFERENCE CENTER PARIS, FRANCE

Risk Stratification Methods for Asymptomatic Carotid Plaques

Méthodes de Stratification du Risque des Plaques Carotidiennes Asymptomatiques

Stavros Kakkos, Andrew Nicolaides

Ioannis Tsolakis

University of Patras, Medical School, Greece

Imperial College, London, UK



Randomised trials in asymptomatic carotid stenosis (ACS)

□ ACAS 1995; ACST 2004

Carotid endarterectomy reduced annual stroke risk from 2% to 1%

Perioperative stroke and death: 2.3%

Small net benefit after carotid endarterectomy for asymptomatic stenosis

Table 1 Five year risks of the main outcomes from ACAS and ACST, including the operative risk

	ACAS			ACST		
	BMT	CEA	ARR	BMT	CEA	ARR
Any stroke	17.5%	12.4%	5.1%	11.8%	6.4%	5.4%
No of 'any strokes' prevented per 1000 CEAs at 5 years		51			54	
Any major stroke	9.1%	6.4%	2.7%	6.1%	3.5%	2.6%
No of 'major strokes' prevented per 1000 CEAs at 5 years		27			26	
Ipsilateral stroke	11.0%	5.1%	5.9%	5.1%*	4.4%*	1.1%
No of ipsilateral strokes prevented per 1000 CEAs at 5 years		59				
Major ipsilateral stroke						n/a

“Up to 94% of interventions might not benefit the patient”

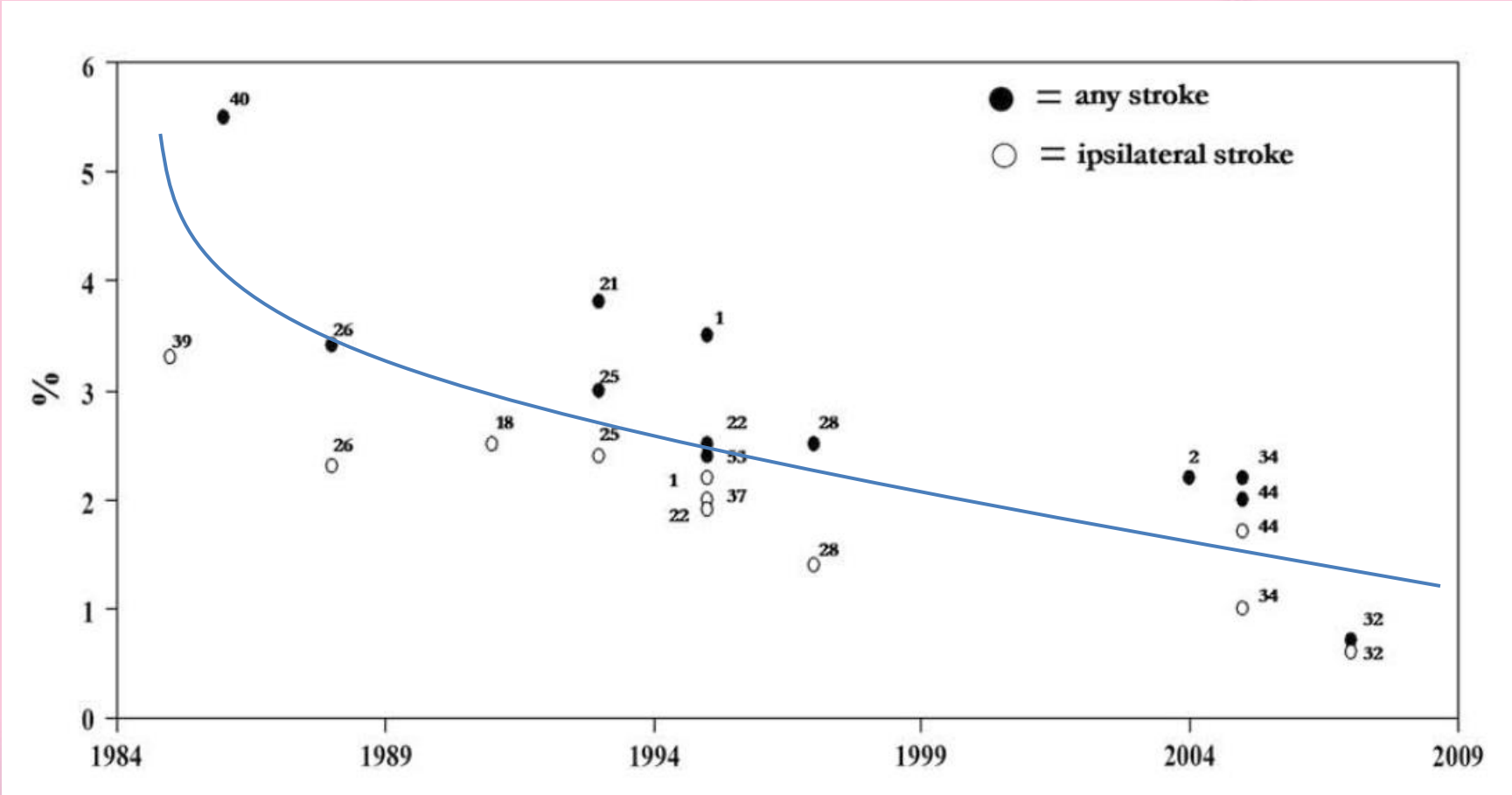
BMT = best medical therapy, CEA = carotid endarterectomy, * data derived from presentations about the 10 year ACST data. In the CEA group it includes a 2.8% operative risk, n/a = no data available, ARR = absolute risk reduction at 5 years.

Naylor 2009, EJVES

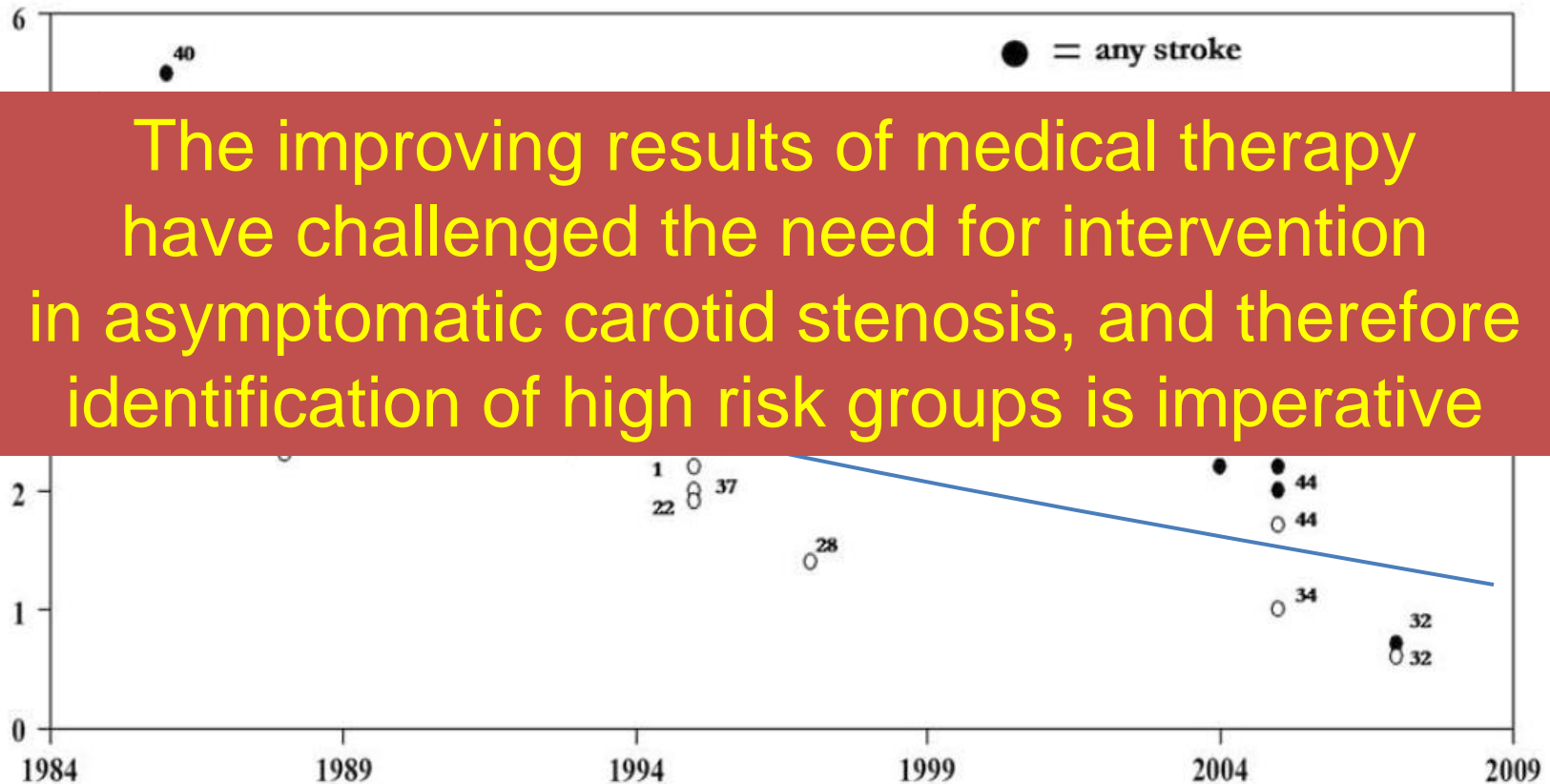
Therefore, a better risk stratification for ACS is urgently needed

Outcome improvement over time, as a result of medical therapy

Annual ipsilateral and “any” stroke (50-99% stenosis)
by year of publication



Annual ipsilateral and “any” stroke (50-99% stenosis) by year of publication



The improving results of medical therapy have challenged the need for intervention in asymptomatic carotid stenosis, and therefore identification of high risk groups is imperative

Factors associated with a high risk of stroke in ACS

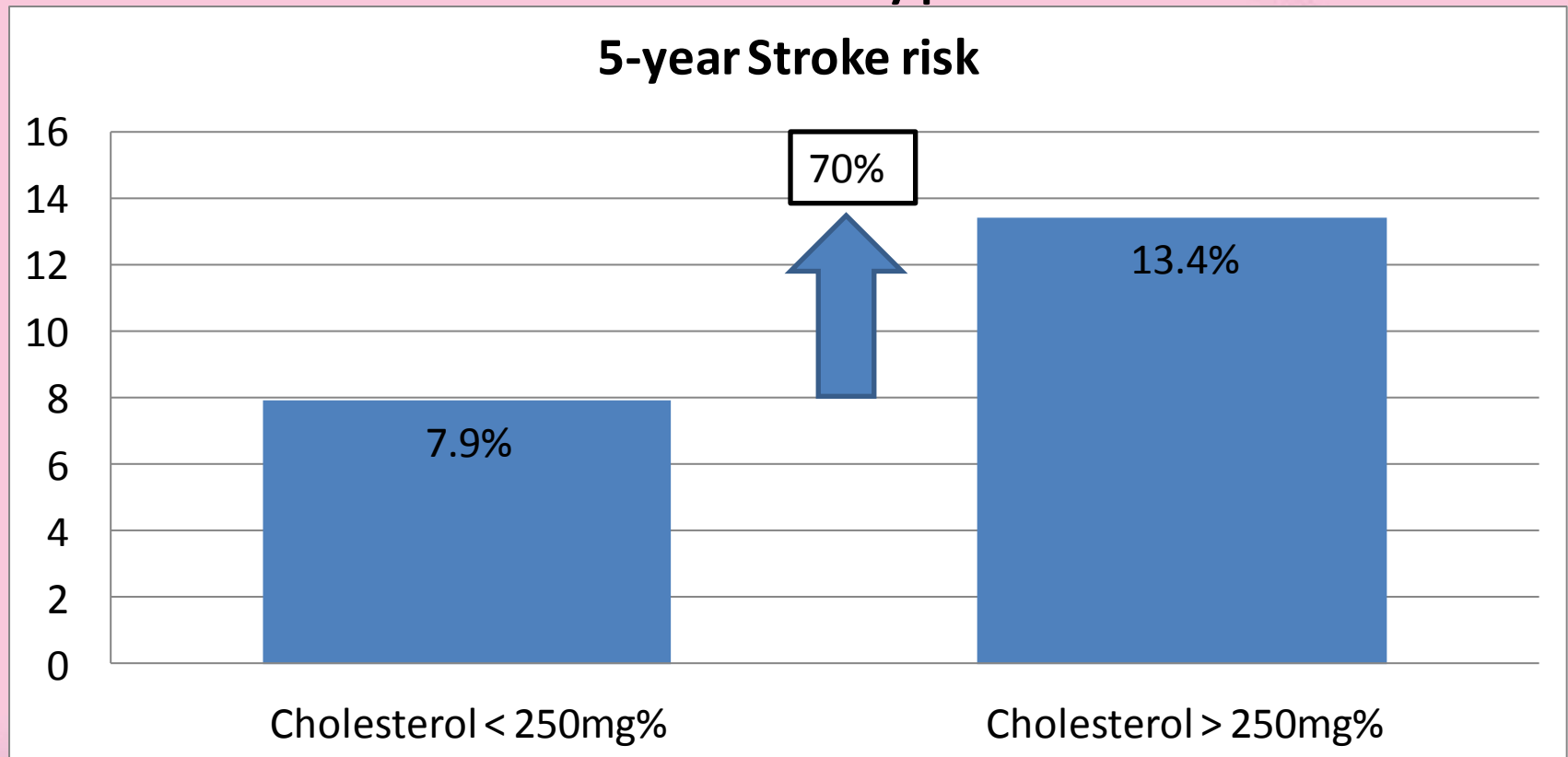
- Clinical characteristics
- Evidence of embolisation
 - Silent brain infarction
 - Embolic signals on TCD
- Lesion characteristics
 - Stenosis or characteristics
 - Plaque

Factors associated with a high risk of stroke in ACS

- **Clinical characteristics**
 - Hypertension (Moore D, Ann Surg 1985)
 - Hypercholesterolaemia (ACST 2004)
 - Age (> 70 years) (Moore D, Ann Surg 1985)
 - History of contralateral neurological symptoms (ACST 2004, ACSRS 2005)

Factors associated with a high risk of stroke in ACS

- **Clinical characteristics:** Hypercholesterolaemia



Factors associated with a high risk of stroke in ACS

- Clinical characteristics:** History of contralateral neurological symptoms

Study	<u>Risk estimate</u> (95%CI)	p value	Method
ACST 2004	<u>2.08</u> (1.35-3.18)*	0.001	Odds ratio
ACSRS 2013 (Kakkos, JVS, 2013)	<u>2.2</u> (1.27-3.79)	0.005	Hazard ratio- Cox regression

* calculated from the published data

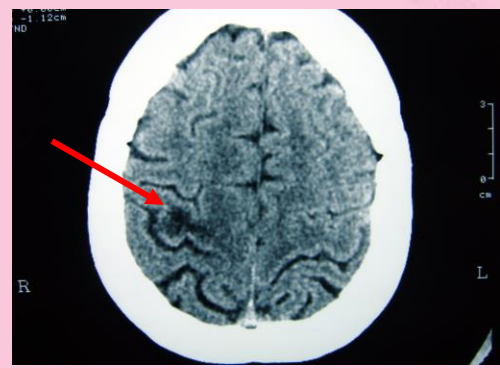
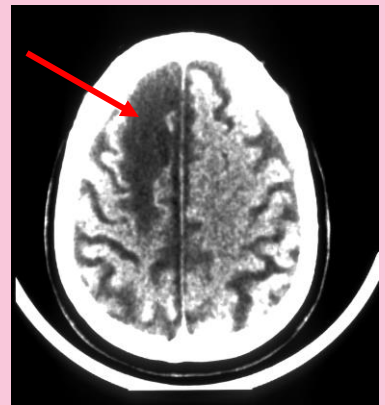
Factors associated

with a high risk of stroke in ACS

“Embolic” infarction on CT brain scanning

Large cortical

Small cortical

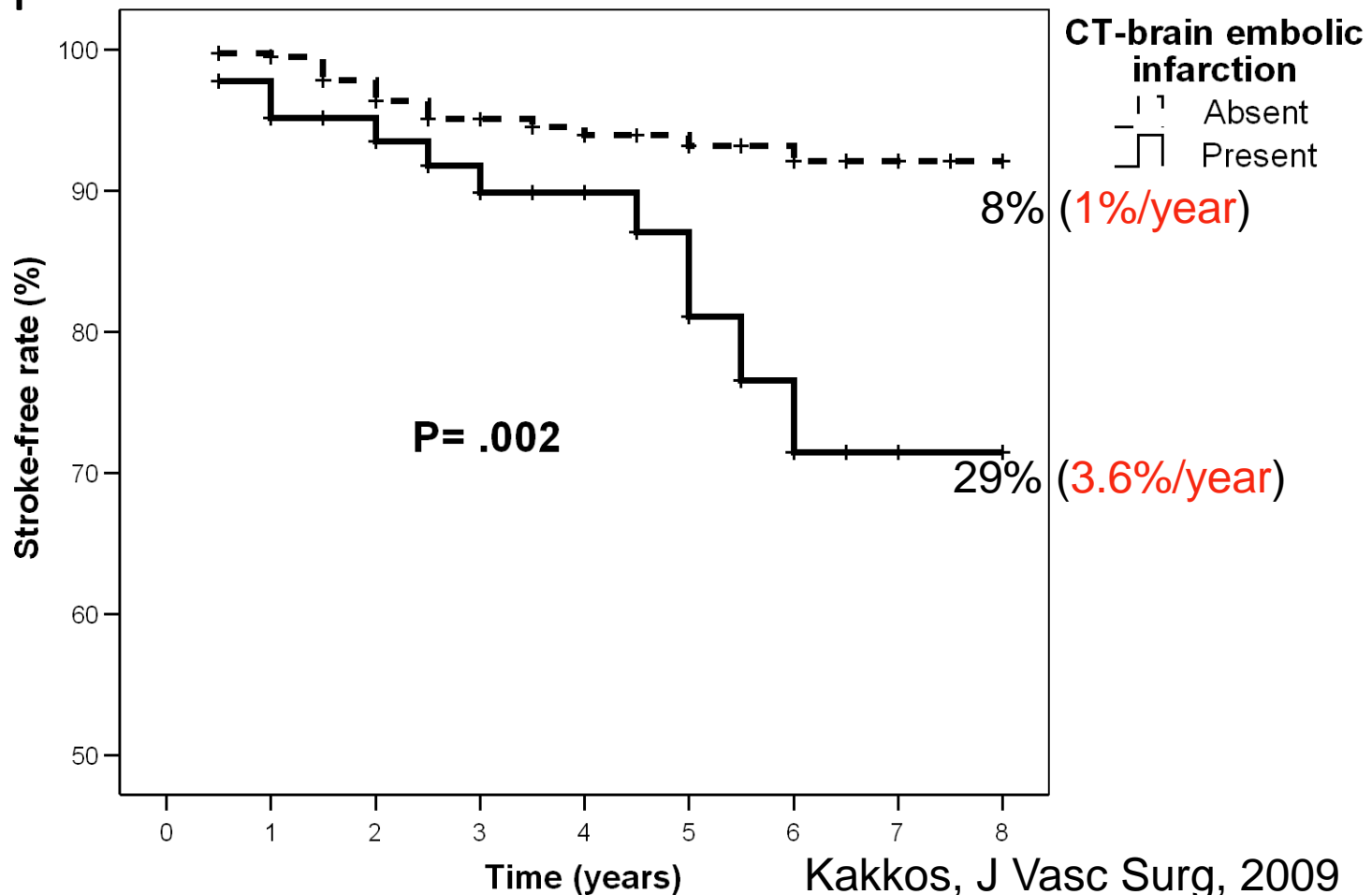


Discrete subcortical

Basal ganglia (non-lacunar) lesions

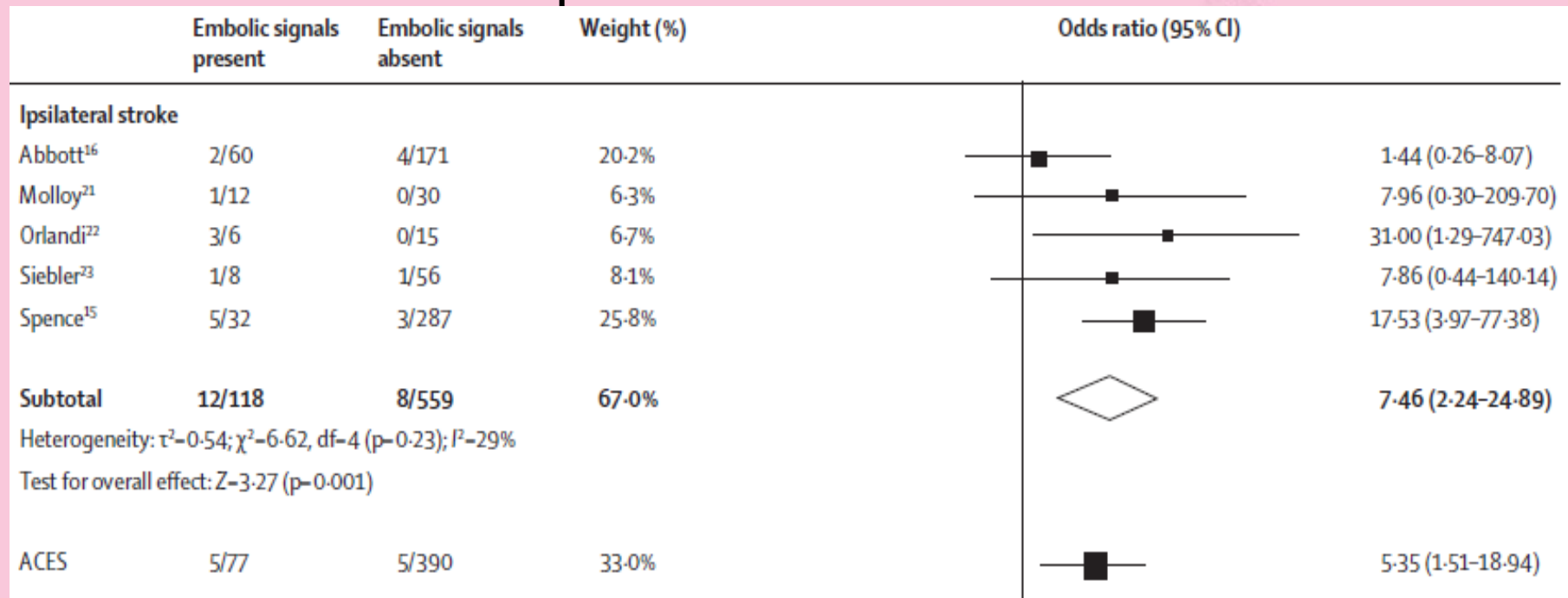


Ipsilateral stroke-free rate in patients with 60-99% (NASCET) ACS (n=462) in relation to “embolic” infarction: 70% of the plaques that will produce a stroke are missed



Factors associated with a high risk of stroke in ACS

Embotic signals on TCD: 43% of the plaques that will produce a stroke are missed



Meta-analysis of ACES and Previous Studies

Factors associated with a high risk of stroke in ACS

- **Stenosis characteristics**
 - Increasing severity of carotid stenosis (ACSRS 2010)
 - Progression of carotid stenosis over time
(Aburahma, J Vasc Surg 2002)
 - Occluded contralateral internal carotid artery
(Aburahma, Ann Surg 2003)

Stenosis severity and risk of stroke

ACSRS study

<i>ECST</i> <i>stenosis (%)</i>	<i>NASCET</i> <i>stenosis (%)</i>	<i>No.</i>	<i>CORI events</i>	<i>Strokes</i>
All patients		1121	130 (11.6%)	59 (5.3%)
50-69 ^a	<50	198	16 (8.1%)	5 (2.5%)
70-89 ^a	50-82	598	65 (10.9%)	29 (4.8%)
90-99 ^a	83-99	325	49 (15.1%)	25 (7.7%)
			<i>P</i> = .01	<i>P</i> = .008

Factors associated with a high risk of stroke in ACS

- **Plaque characteristics**

- Plaque ulceration (Handa, Stroke 1995)
- Unstable carotid plaque morphology on ultrasound

**Subjective
features**

- plaque echolucency (Nicolaidis, Kakkos, 2005)
- discrete echogenic plaque components (Nicolaidis, 2010)
- plaque heterogeneity (Sterpetti, 1988)

**Objective
features**

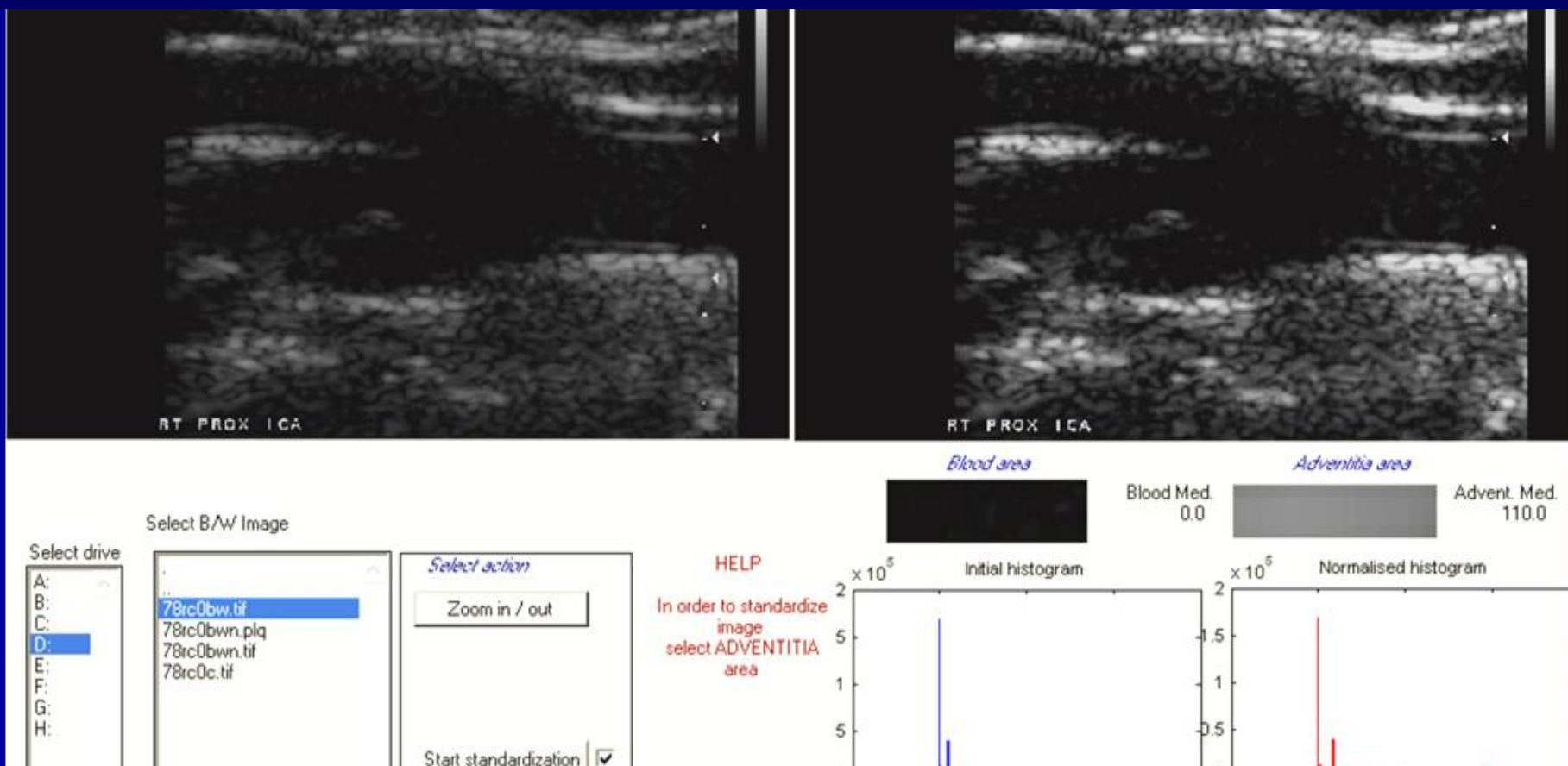
- low gray scale median (GSM) (Nicolaidis, 2010)
- large plaque area (Nicolaidis, 2010)
- juxtaluminal black (echolucent) areas (JBA) (Kakkos, 2013)

Juxtaluminal Black Area (JBA): a U/S marker of plaque instability

- ✓ A juxtaluminal black (hypoechoic) area is observed more frequently in symptomatic compared to asymptomatic carotid plaques (Pedro, EJVES 2002)

Measurement of JBA

Images transferred to PC for processing

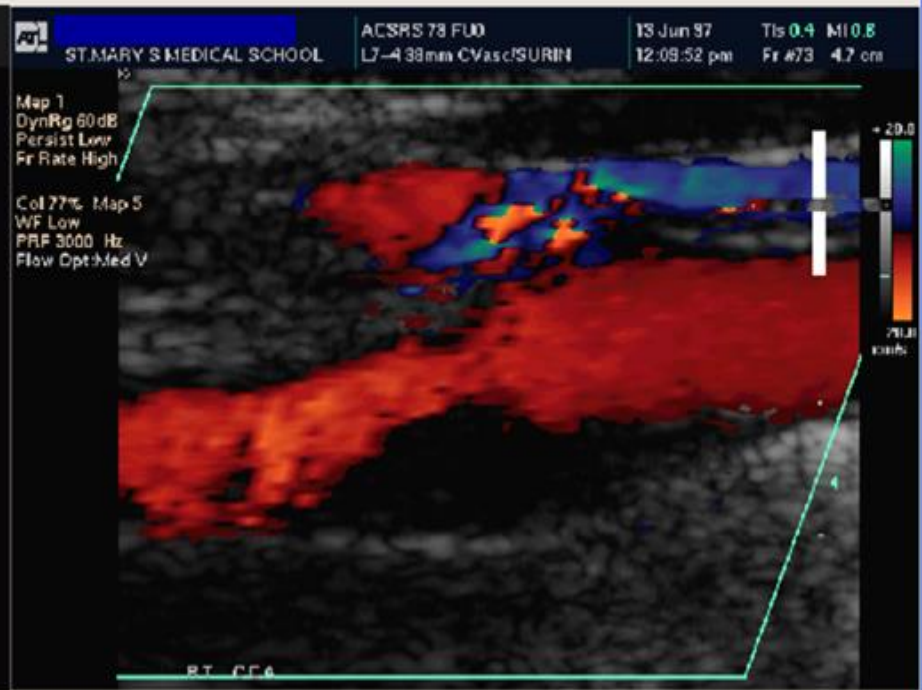


Images normalised for grey scale using two reference points:
blood=0; adventitia=190

Plaque / Region Of Interest selection

Gray Scale Image

Colour Image



Log image

Erase selections

Select Grayscale Image

Image region

Select colour Image

Select drive

- A: ..
- B: 78rc0bw.tif
- C: 78rc0bwn.plq
- D: 78rc0bwn.scl
- E: 78rc0bwn.tif
- F: 78rc0c.tif
- G:
- H:

Select action

Zoom in / out

Image region

Def.Im.scale

HELP

In order to load:
Grayscale image, double click on the image at the left hand side listbox
Colour image, double click on the right hand side listbox



- ..
- 78rc0bw.tif
- 78rc0bwn.plq
- 78rc0bwn.scl
- 78rc0bwn.tif
- 78rc0c.tif

Save plaque file

File saved

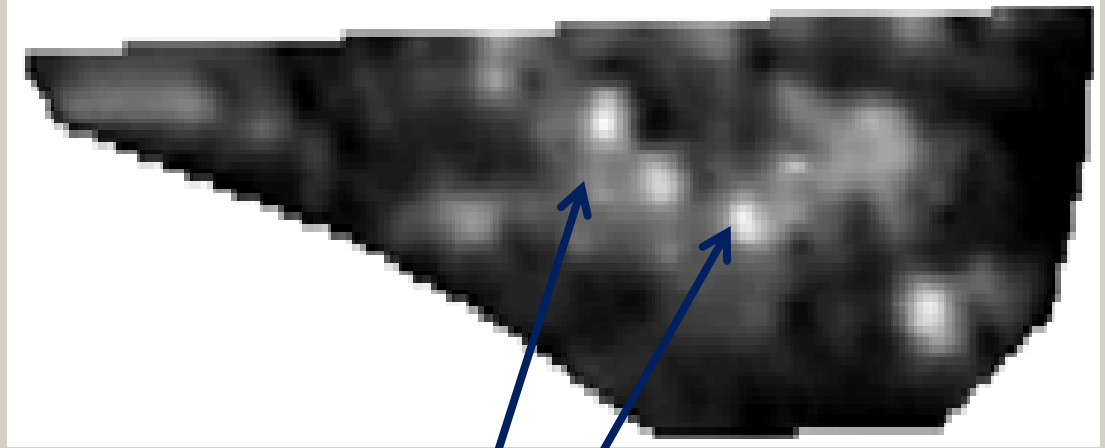
Features Extraction

Close

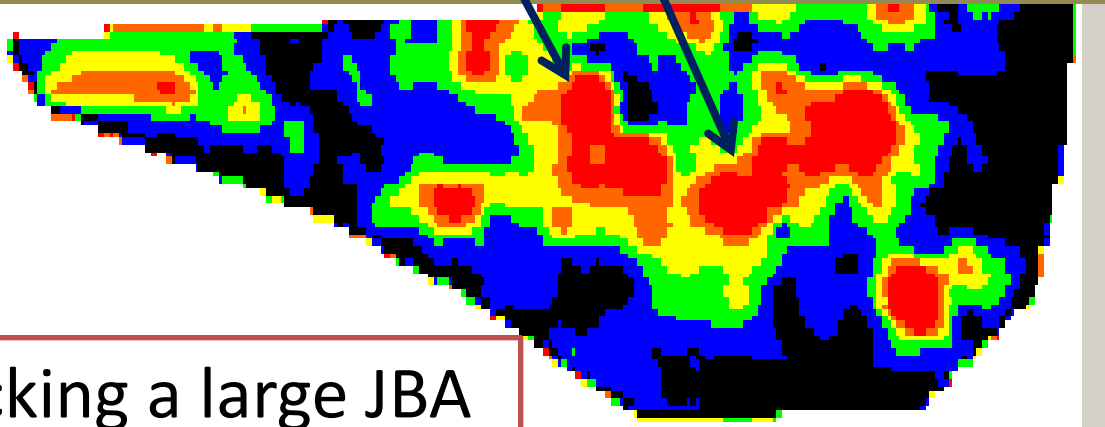
Plaque outlines were normalised to a pixel resolution of 20/mm

Image contouring

Grey scale	Colour
0-25	black
25-50	blue
50-75	green
75-100	yellow
100-125	orange
>125	red



Discrete plaque white areas (DWAs)



Example of a plaque lacking a large JBA

Example of a plaque with a large JBA

PHILIPS

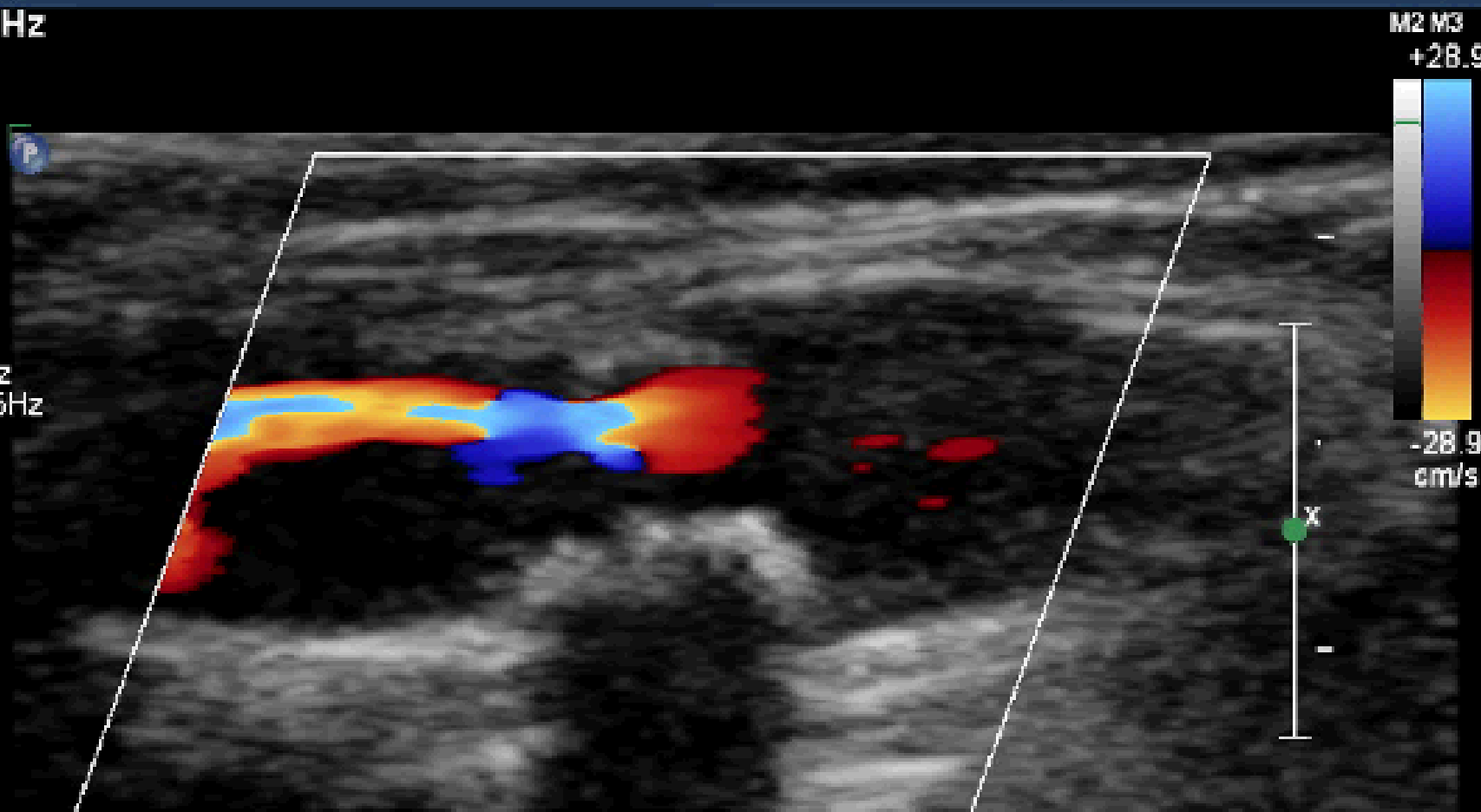
27/10/2009 02:07:07PM TIS0.5 MI 1.2

L9-3/Vasc Car

FR 29Hz
R1

2D
62%
C 52
P Low
Gen

CF
68%
3000Hz
WF 165Hz
Med



M2 M3
+28.9

-28.9
cm/s

Image region

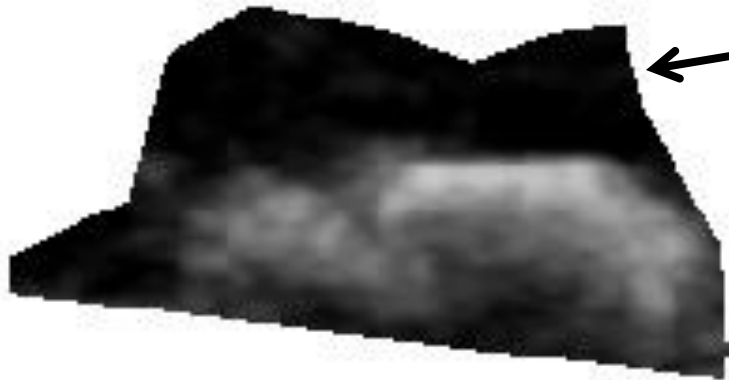
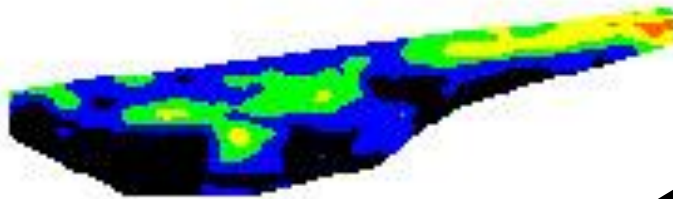
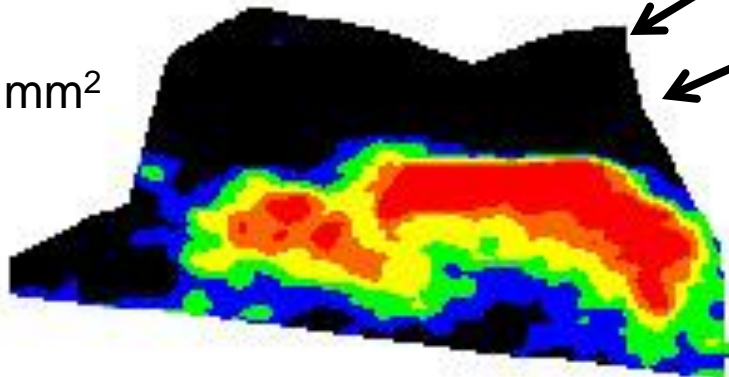


Image colouring



13.6 mm²



DEFINITION

JBA is defined as an area of pixels adjacent to the lumen with gray scale value <25 and without a visible echogenic cap

JBA area is quantified in mm²

Texture feature extraction

Plaque parameters

File Help

Image region


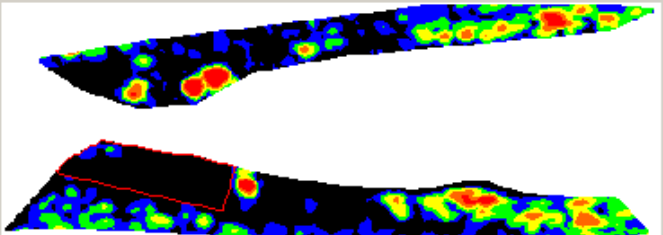


Image colouring (10 contours)



Zoom

% Stenosis

ECST	NASCET
50	12
55	20
60	30
65	40
70	47
75	50
77	60
80	65
83	70
86	80
89	87
90	90
95	90
99	99

Histogram measures

Kurtosis	
1.69901	
Total number of pixels	
20702	
Plaque area mm2	71.91
Perc. of pix below lev.30	54.24%
Perc. of pix below lev.50	72.49%
Contours	
Black	48.01%
	24.48%
	14.85%
	7.809%
	3.056%
	1.175%
	0.4033%
	0.2156%
White	0%
	0%

Dark area
Close to lumen

Patient status
A (Asym)

Discrete white areas
Yes

Type of plaque
Type 3

Percent Stenosis 1-99%
90

Meas. Dark area close to lumen
1 comp. All plaque

Perc. of dark area:

Dark area mm2:

Select drive

A:	10rc0bw.tif
B:	10rc0bwn.tif
C:	10rc0bwnr.plq
D:	10rc0bwnr.scl
E:	10rc0bwnr.tif
F:	10rc0bwnrr10.plq
G:	10rc0bwnrr20.plq
H:	10rc0bwnrr20_plq.tif
	10rc0bwnrr20r15.plq

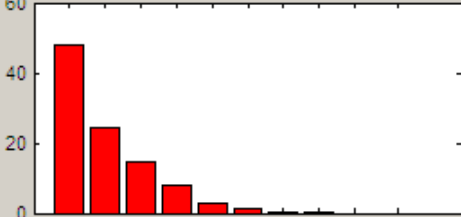
HELP

In order to calculate the parameters for a plaque file, double click on the appropriate ...pl (version 1.x) or ...plq(version2.x) file

Texture measures

SGLDM measures	First ord. stats	GLDM measures			
Ang.S.Mom	0.00749869	Mean	35.4664	Homog.	0.275695
Contrast	49.6491	Variance	1096.58	Contr.	49.4785
Correl	0.977644	Median	26.9169	Energy	0.0921141
Variance	1108.61	Skewn.	1.21057	Entropy	2.66801
Homoge.	0.275297	Energy	0.0198508	Mean	4.81659
Sum Aver.	73.1522	Entropy	4.49302		
Sum Var.	4384.8				
Sum Entr.	5.1589				
Entropy	7.38066				
Diff.	25.3631				
Diff. Entr.	2.64608				
Inf.Meas1	-0.358678				
Inf.Meas2	0.978652				

Intensity image - colour percent.



Runlength meas.

SRE	0.931959
LRE	1.66927
GLD	280.081
RLD	20389.3
RP	23.6423

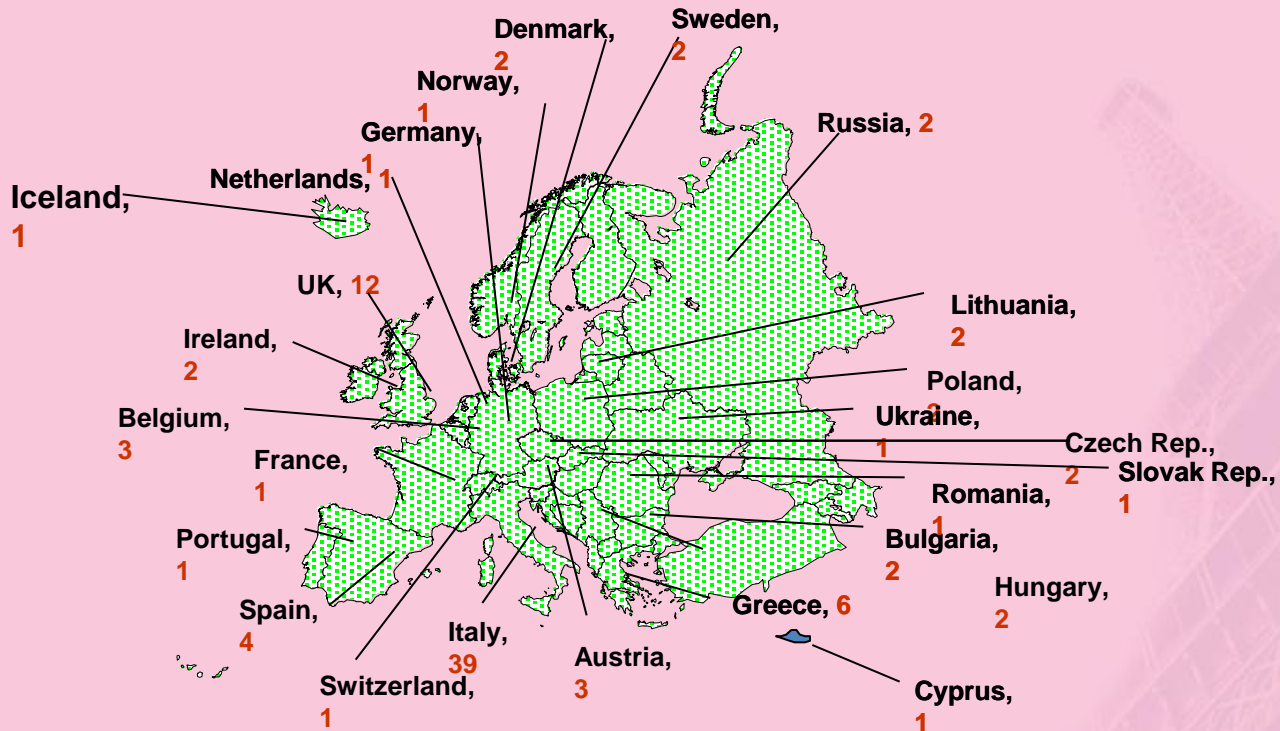
Fourier power spec.

Radial	2925.06
Angular	2699.94

C:\Documents and Settings\Andreas\My Documents\ACSRS Images\1110
 Filename:10rc0bwnrr20.plq

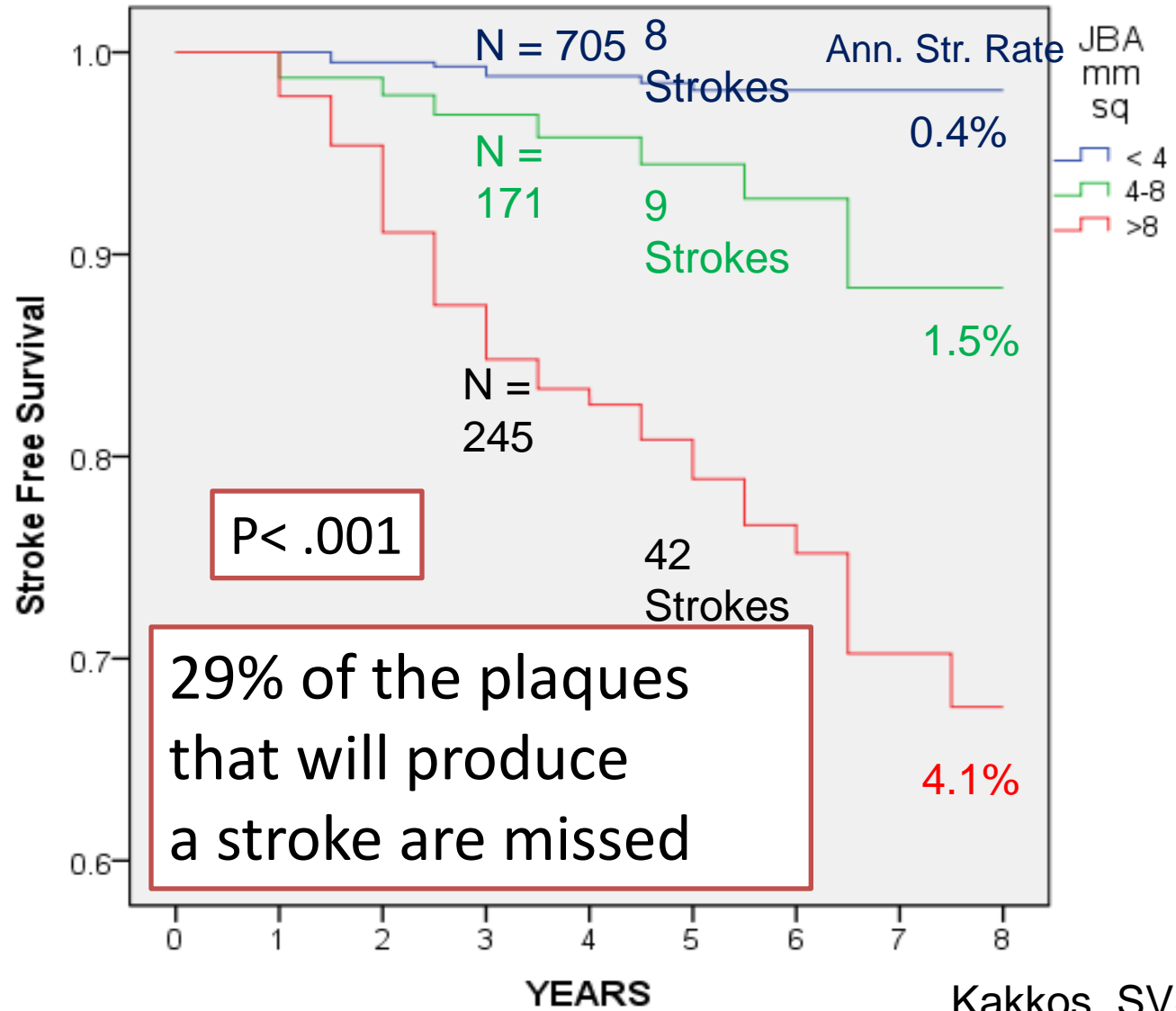
Europe

ACSRS Study: 1121 patients with > 50% ACS

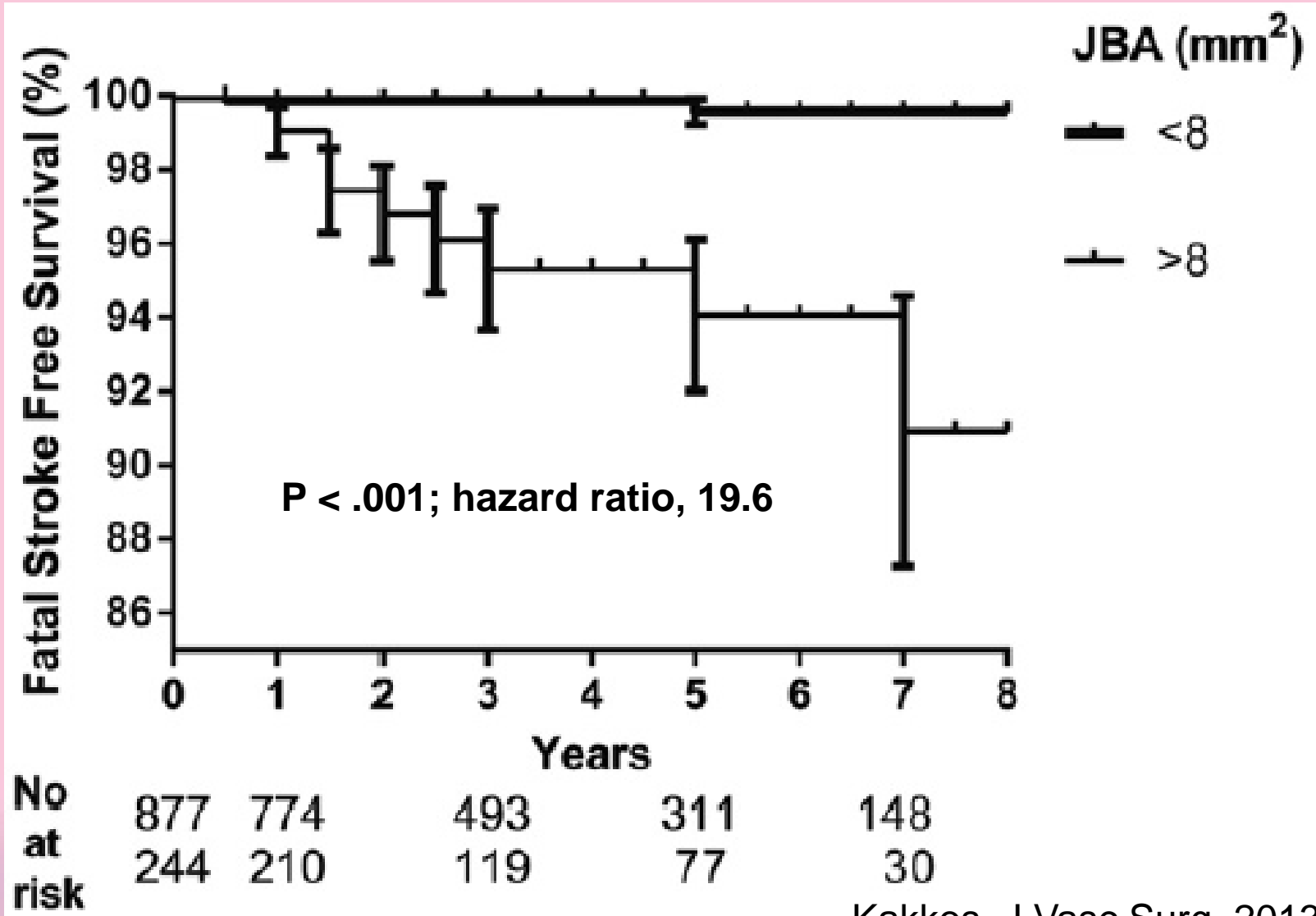


mean follow-up 4 years

Ipsilateral ischemic stroke in relation to JBA size in the ACSRS study



Fatal ipsilateral ischemic stroke in relation to JBA in the ACSRS study



Predictors of ipsilateral ischemic stroke on Cox Multivariate Analysis in ACSRS: risk stratification is possible

Independent predictors of risk	HR	95% CI	P value
JBA (4, 4-8, 8-10, >10) in mm ²	2.34	1.89-2.91	<0.001
Stenosis (50-69, 70-89, 90-99) (%)	1.59	1.06-2.37	0.023
DWA (present, absent)	1.90	0.98-3.27	0.059
History of contr. TIA or stroke (present, absent)	2.20	1.27-3.79	0.005

GSM and plaque area: Non significant

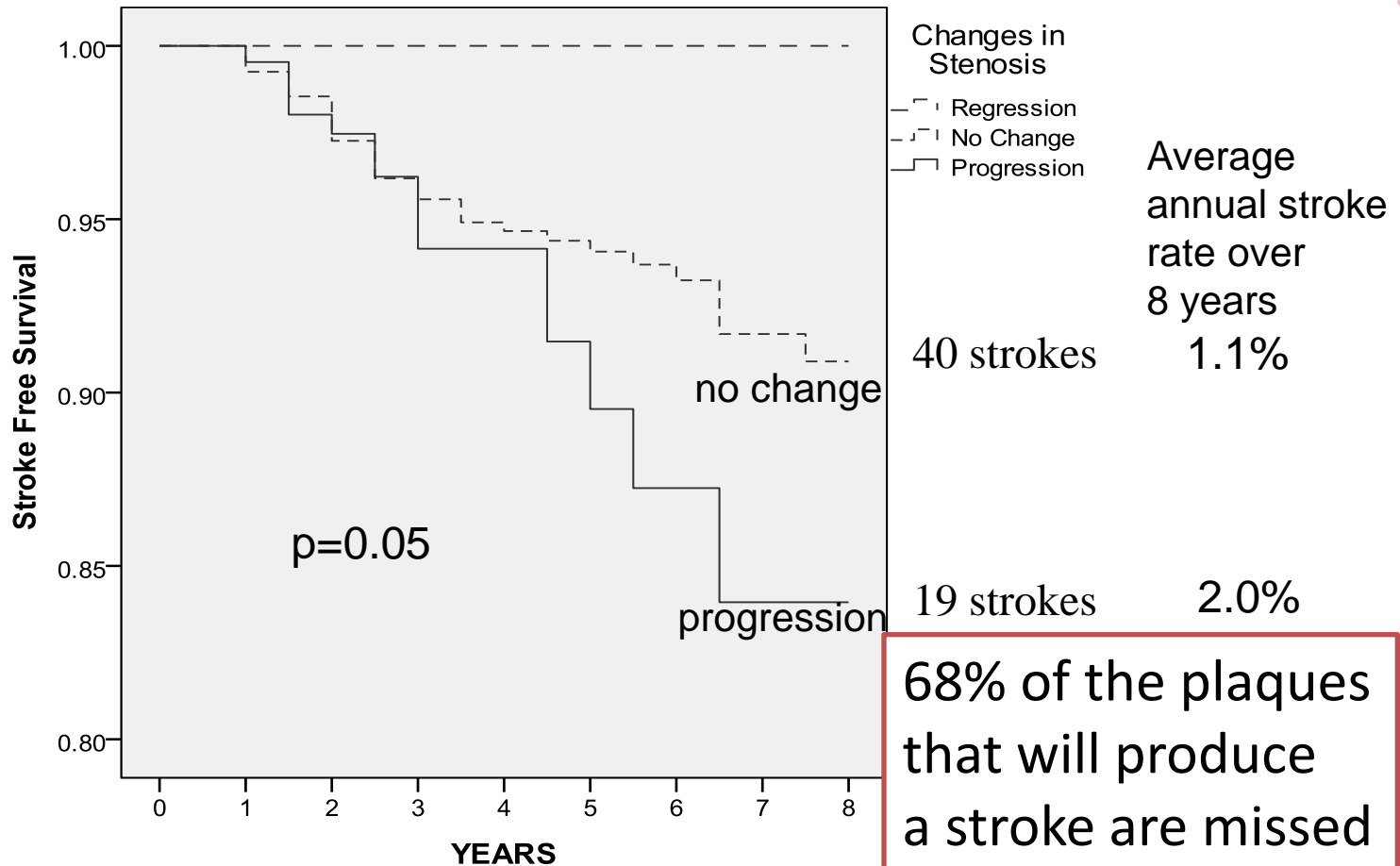
Stenosis 70-89% ECST (50-82% NASCET) (n=598) and predicted annual stroke risk

		History of Contralateral TIAs or Stroke Absent				History of Contralateral TIAs or Stroke Present				Annual Stroke Rate %
		< 4	4-8	8-10	≥ 10	< 4	4-8	8-10	≥ 10	
DWA	Present n =	0.6% 220	1.4% 50	2.8% 20	4.4% 44	0.8% 25	2.6% 7	5.8% 2	8.4% 15	≥ 6
	Absent n =	0.4% 129	0.9% 19	1.4% 3	2.6% 40	0.5% 12	1.6% 1	3.4% 2	5.4% 8	4.0-5.9
		< 4	4-8	8-10	≥ 10	< 4	4-8	8-10	≥ 10	2.0-3.9
			JBA mm ²				JBA mm ²			1.0-1.9
										< 1.0

Stenosis 90-99% ECST (83-99% NASCET) (n=325) and predicted annual stroke risk

		History of Contralateral TIAs or Stroke Absent				History of Contralateral TIAs or Stroke Present				Annual Stroke Rate %		
DWA												
DWA	Present n =	0.8% 101	2.0% 39	4.1% 8	6.2% 30			1.0% 19	3.6% 9	7.6% 4	10.0% 8	≥ 6
	Absent n =	0.6% 44	1.2% 16	3.0% 2	3.8% 24			0.7% 14	2.6% 2	5.2% 4	7.4% 0	4.0-5.9
		< 4	4-8	8-10	≥ 10			< 4	4-8	8-10	≥ 10	2.0-3.9
			JBA mm ²						JBA mm ²			1.0-1.9
												< 1.0

Effect of changes in stenosis on ipsilateral ischemic stroke in the ACSRS study



Numbers at risk

	0	1	2	3	4	5	6	7	8
Regression	38	28	19	5					
No change	740	455	282	134					
Progression	205	129	87	39					

Kakkos S et al, JVS, in press

Progression of stenosis added as covariate in a proportional hazards model previously published* that could predict the risk of future events (ACSRS study)

Variable	β	HR	95% CI	p value
<u>Ipsilateral stenosis (10% increase)</u>	0.017	1.017	1.002-1.032	0.023
Log (GSM+40)	-2.464	0.085	0.042-0.171	< 0.001
Plaque area ^{1/3} (mm ²)	0.630	1.878	1.463-2.413	< 0.001
DWA	0.725	2.065	1.292-3.302	0.002
History of contr. TIAs or stroke	0.661	1.938	1.321-2.842	0.001
Progression	0.353	1.424	0.980-2.067	0.064

*Nicolaidis et al, J Vasc Surg 2010

Kakkos S et al, JVS, in press

Conclusions

- ❑ Effective risk stratification methods in asymptomatic carotid artery stenosis has been reported in recent years, and this has improved the selection of patients in need of a carotid intervention.
- ❑ Not only the severity of stenosis, but also history of contralateral neurological symptoms, plaque features like JBA and DWA, and CT brain infarcts have all emerged as powerful predictors of stroke occurrence.

Where we go from here?

1. User friendly software for image analysis for vascular labs
2. Doctors who like a number
 They should ask for
 (a) % Stenosis
 (b) Annual stroke risk

Print preview

Plaque Classification and Stroke Risk

Image name: CARBULB40n
 Image region

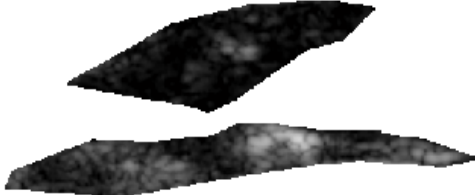
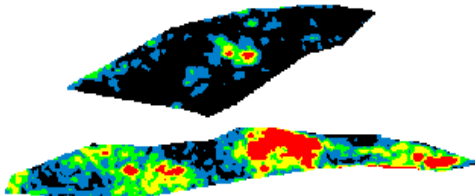


Image colouring (10 contours)



% Stenosis	
ECST	NASCET
50	12
55	20
60	30
65	40
70	50
75	60
80	70
85	80
90	90
95	90
99	99

Input Measurements		Plaque Characteristics	
ECST Stenosis % :	90	Pl. Type (Geroulakos):	Type 3
GSM :	32	Consistency:	Heterogenous
JBA mm ² :	9.15	Echodensity:	Intermediate
DWA in 1-3 pl. type :	Yes	JBA > 6mm ² :	Yes
Plaque area mm ² :	0	Classification (A-0) :	K
Hemispheric status:	Asymptomatic	Plaque stability :	Unstable

Stroke Risk for Stenosis Present (if Asymptomatic)

High risk group
 4.5% per year
 (95% CI 2.75% to 7.0%)

Print Print to a file Close

Thanks!

