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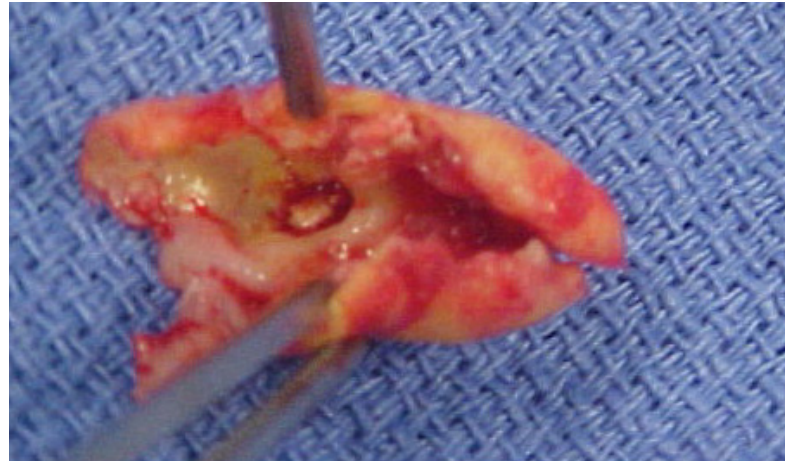
Carotid Plaque Characterization: Implications for CAS?

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Plaque is a complex biologic lesion. A partial list of its components includes fibrous tissue, calcium deposits, lipid deposits, thrombus, and necrotic regions.

Plaque characterization is the first step in a process that will help guide physicians to select patients with atherosclerotic carotid disease that is at risk for subsequent neurologic sequelae.

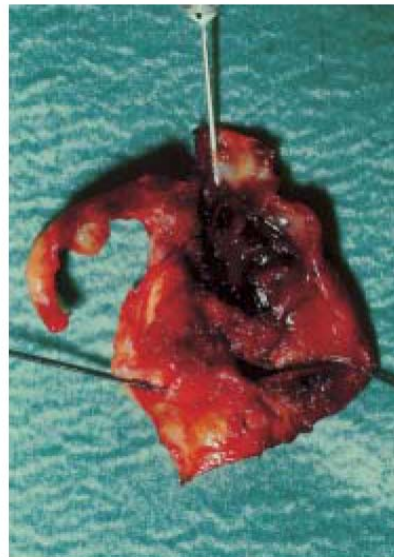


Carotid Plaque Characterization: Implications for CAS?

- **Among the panel of potential risk factors for CAS, plaque characteristics are suggested to play a potentially important role.**

Plaque morphology – Predictive value concerning risk of (future) events?

- * Natural history**
 - Influence on decision for invasive treatment**
- * Interventional risk**
 - Influence on choice of invasive treatment ?**



**Plaque morphology –
Predictive value concerning risk of (future) events?**

*** Natural history**

- Influence on decision for invasive treatment

**stable
asymptomatic**



**unstable
symptomatic**



Vulnerable lesions

High risk for

- * Intraplaque hemorrhage
- * Fibrous cap thinning
- * Rupture
- * Ulceration

Vulnerable lesions

Identification:

* MRI

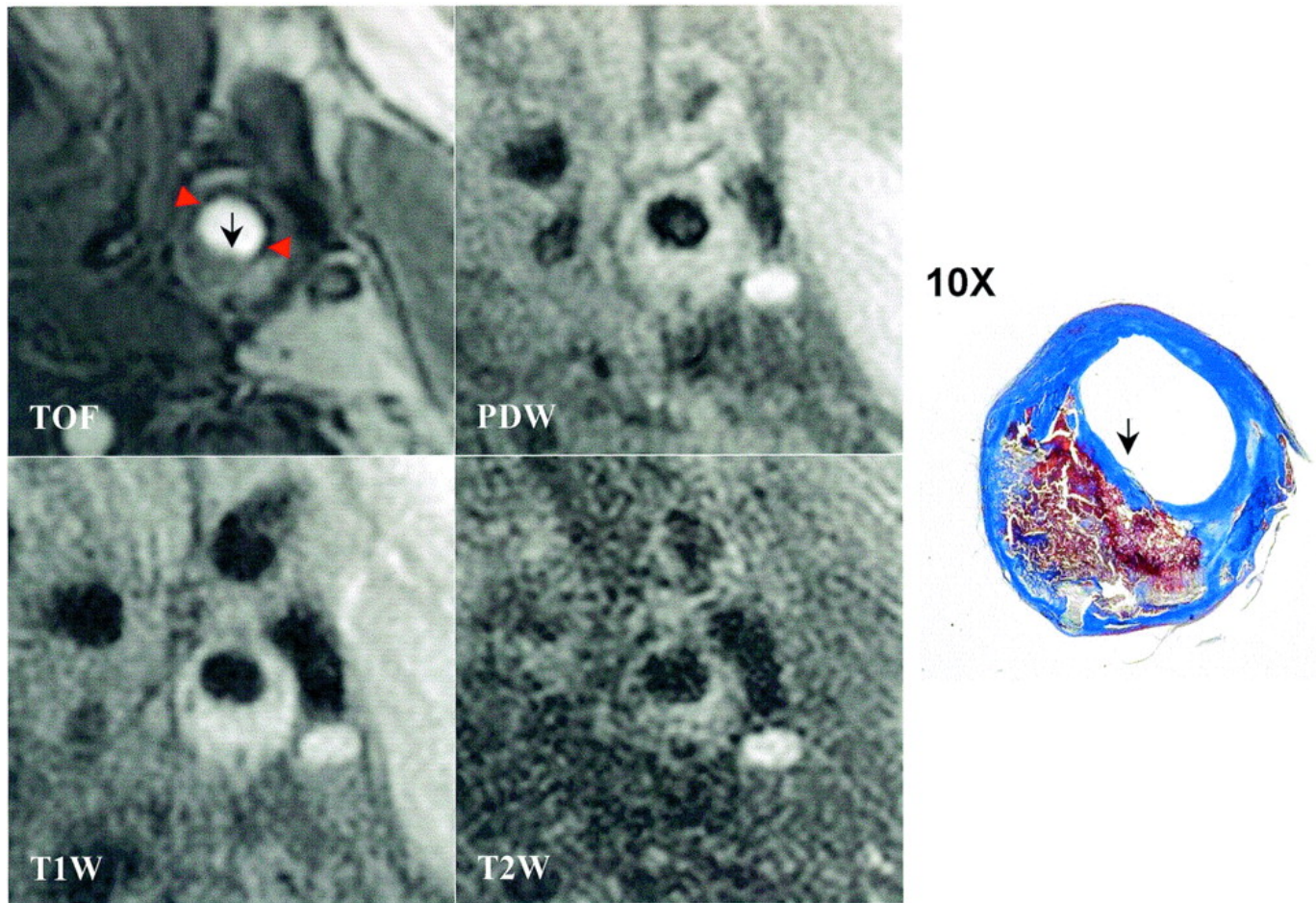
In vivo high-resolution MRI is capable of quantitatively measuring the dimensions of the intact **fibrous cap** and **lipid-rich necrotic core**.

(Cai J et al, Circulation 2005;112:3437)

Reproducibility of MRI for identifying and quantifying carotid plaque components is overall acceptable

Touze E; Stroke. 2007;38:1812-1819

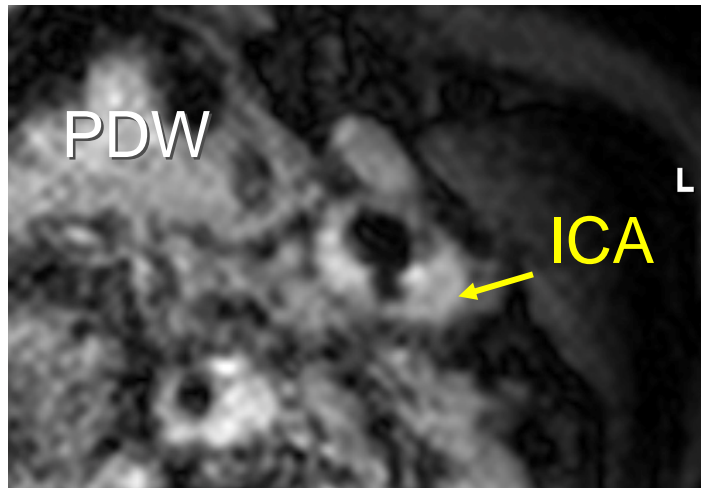
Thin intact fibrous cap and large lipid core on MRI and corresponding matched histological cross-section



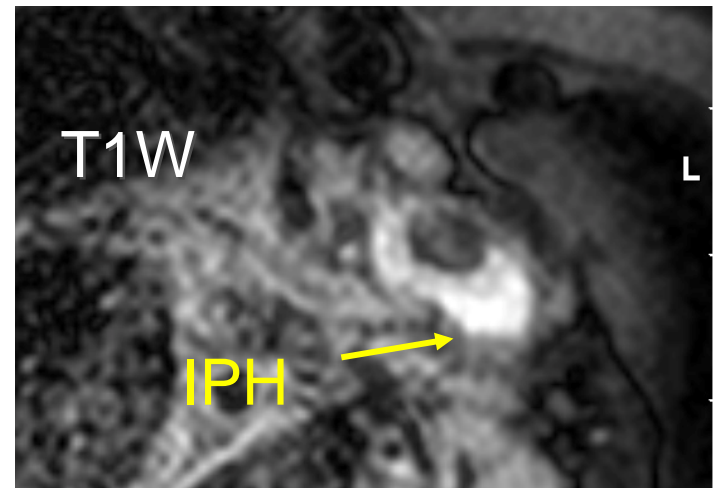
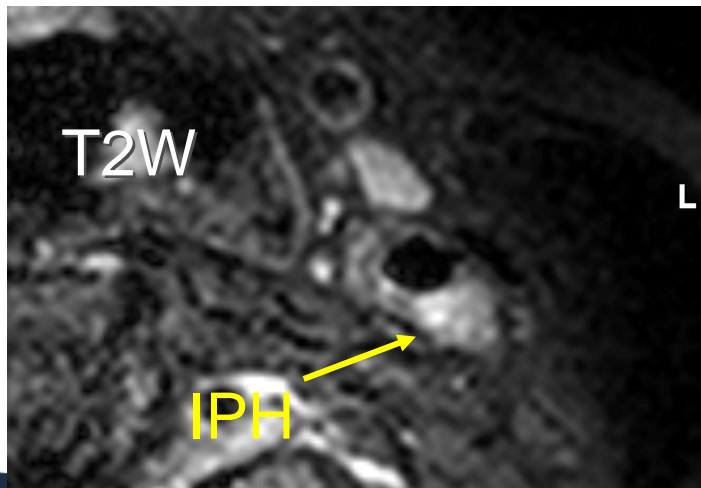
Yuan, C. et al. Circulation 2002;105:181-185

Intra-plaque hemorrhage

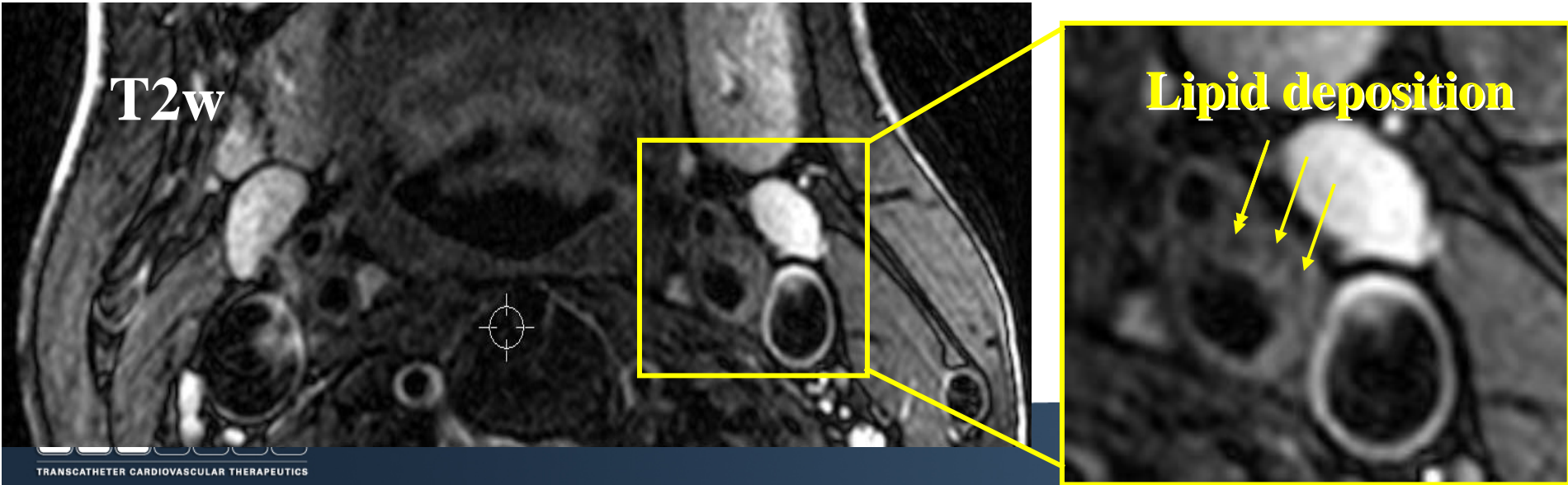
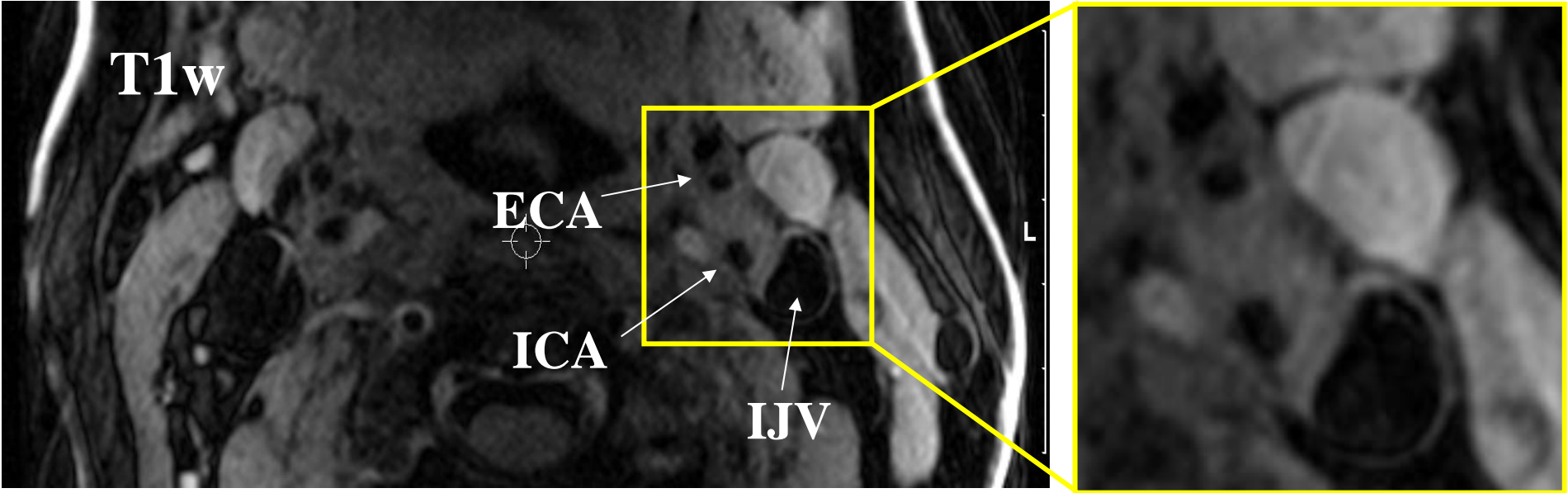
Left ICA: ruptured plaque with intraplaque hemorrhage (IPH)



64 years, female
Recent TIA



PLAQUE COMPOSITION BY MRI



**Association Between Carotid Plaque Characteristics and Subsequent Ischemic Cerebrovascular Events:
A Prospective Assessment With MRI—Initial Results**
Takaya N; Stroke 2006;37:818-823

Conclusion:

Arteries with thinned or ruptured fibrous caps, intraplaque hemorrhage, larger maximum %lipid-rich/necrotic cores, were associated with the occurrence of subsequent cerebrovascular events.

Plaque morphology – Predictive value ?

Natural history

Dense **plaque inflammation** (especially infiltration with macrophages) was the feature most strongly associated with cap rupture (OR 3.39, 95% CI 2.31 to 4.98, $P < 0.001$).

Oxford Plaque Study

Redgrave JN; Circulation. 2006;113:2320-2328

PET - Scan

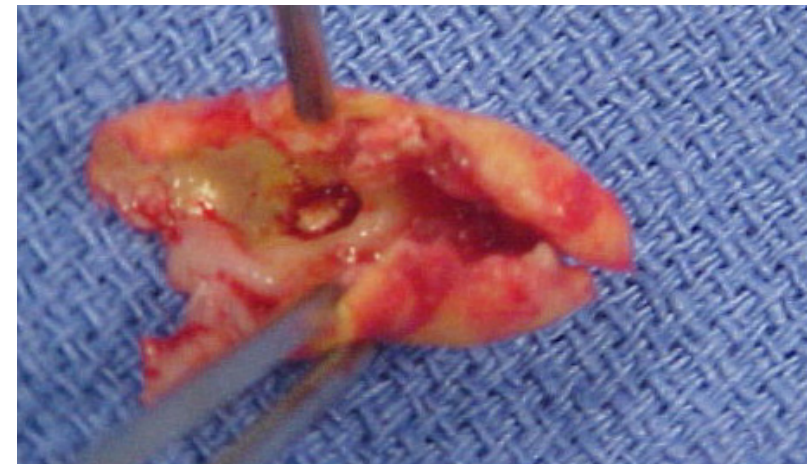
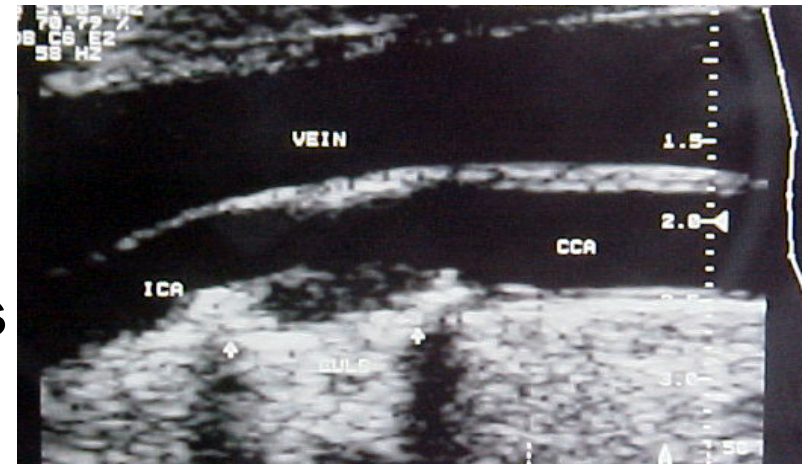
Fluorodeoxyglucose (FDG) **P**ositron **E**mission **T**omography

- * Highly sensitive method to measure inflammation in plaques
- * Higher inflammation related to more vulnerable lesion

Mohler ER; EV Today 2006; 8:79-82

Duplexsonography

- **Plaque-characterization**
 - * **homogenous vs heterogenous**
 - * **echolucent (hypoechoic) vs. echogen (hyperechoic)**
 - * **smooth vs. ulcerated**



**Plaque morphology at US of the carotid artery:
an independent risk factor for incident stroke**

N= 4 886; FU 3.3 years

Hypoechoic plaque: OR 2.53; 95% CI 1,42 - 4.53

Polak JF et al; Radiology 1998; 208: 649–54

Echolucent Plaques Are Associated With High Risk of Ischemic Cerebrovascular Events in Carotid Stenosis The Tromsø Study

Mathiesen EB et al; Circulation 2001;103:2171

The adjusted relative risk for cerebrovascular events in subjects with echolucent plaques was 4.6 (95% CI 1.1 to 18.9), and there was a significant linear trend ($P < 0.015$) for higher risk with increasing plaque echolucency.

Plaque morphology – Predictive value ?

Natural history

Asymptomatic Carotid Stenosis and Risk of Stroke (ACSRS) study

NASCET-stenosis 50-99%:

Type 1-3: 14% risk of stroke at 7 years (**2%/year**)

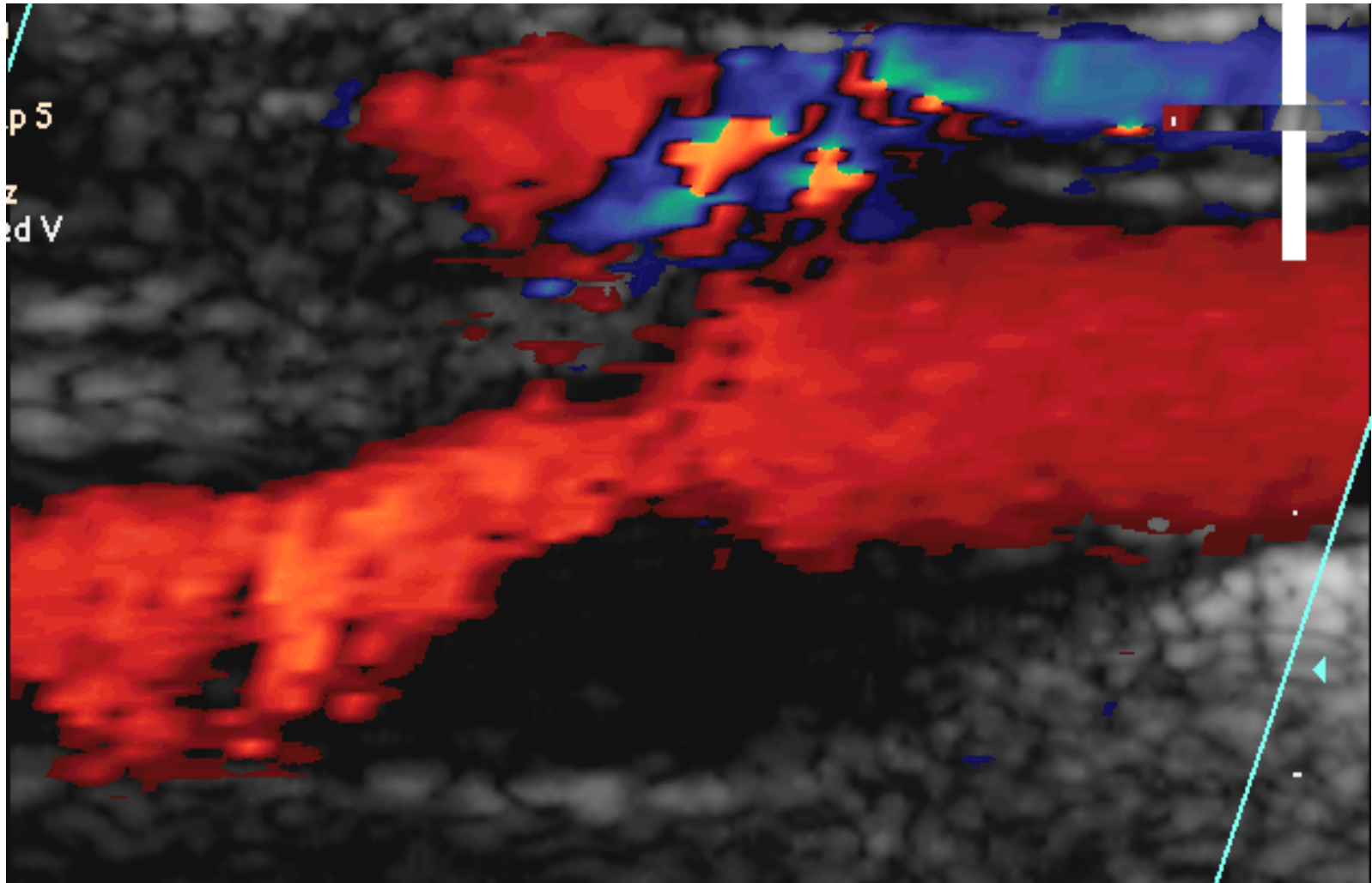
Type 4-5: 0.9% at 7 years (**0.14%/year**)

Events associated with plaques type 1-3

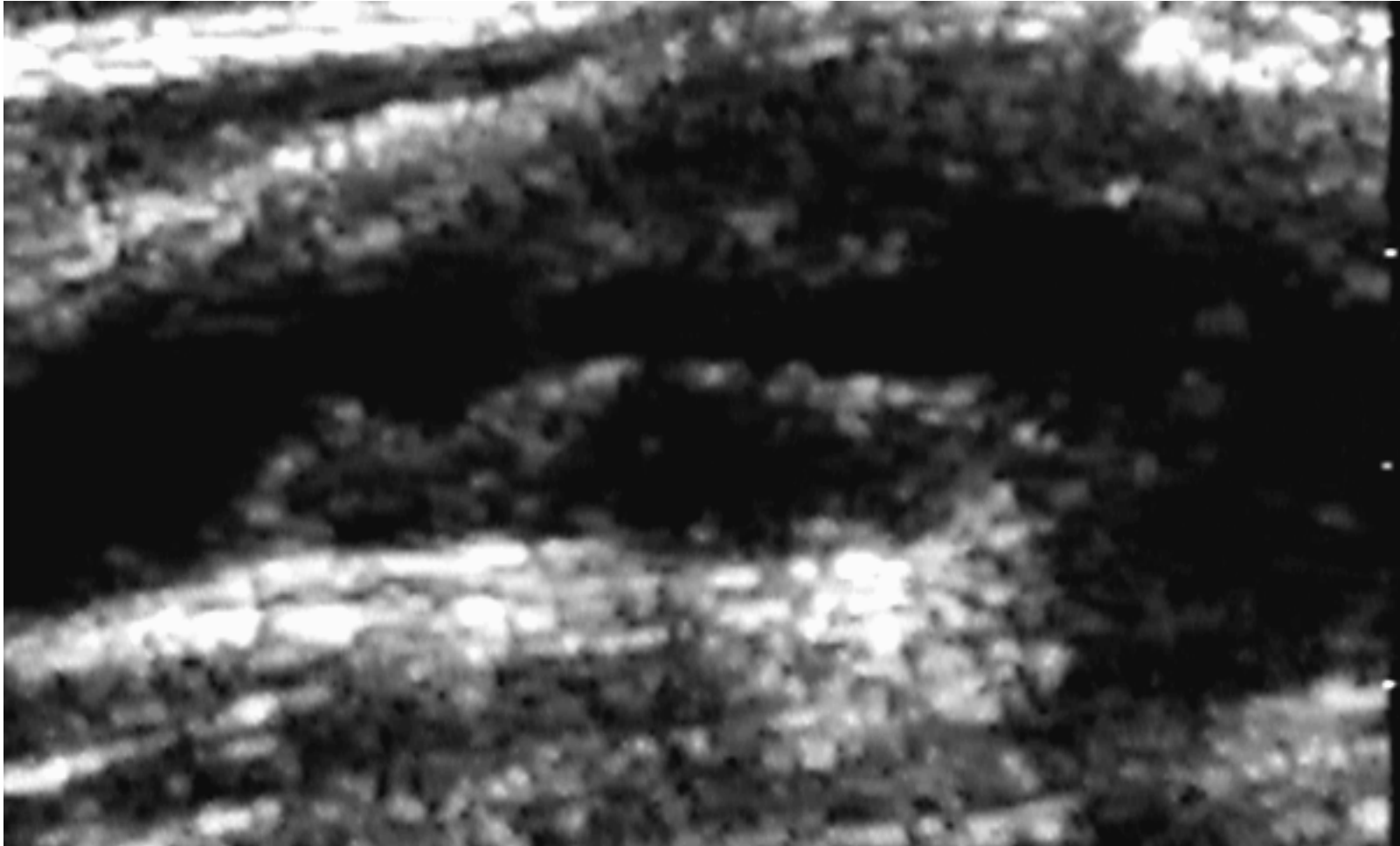
Type 4-5 plaques are at low risk of stroke irrespective of the degree of stenosis

Nicolaides AN et al; Vascular 2005;13:211

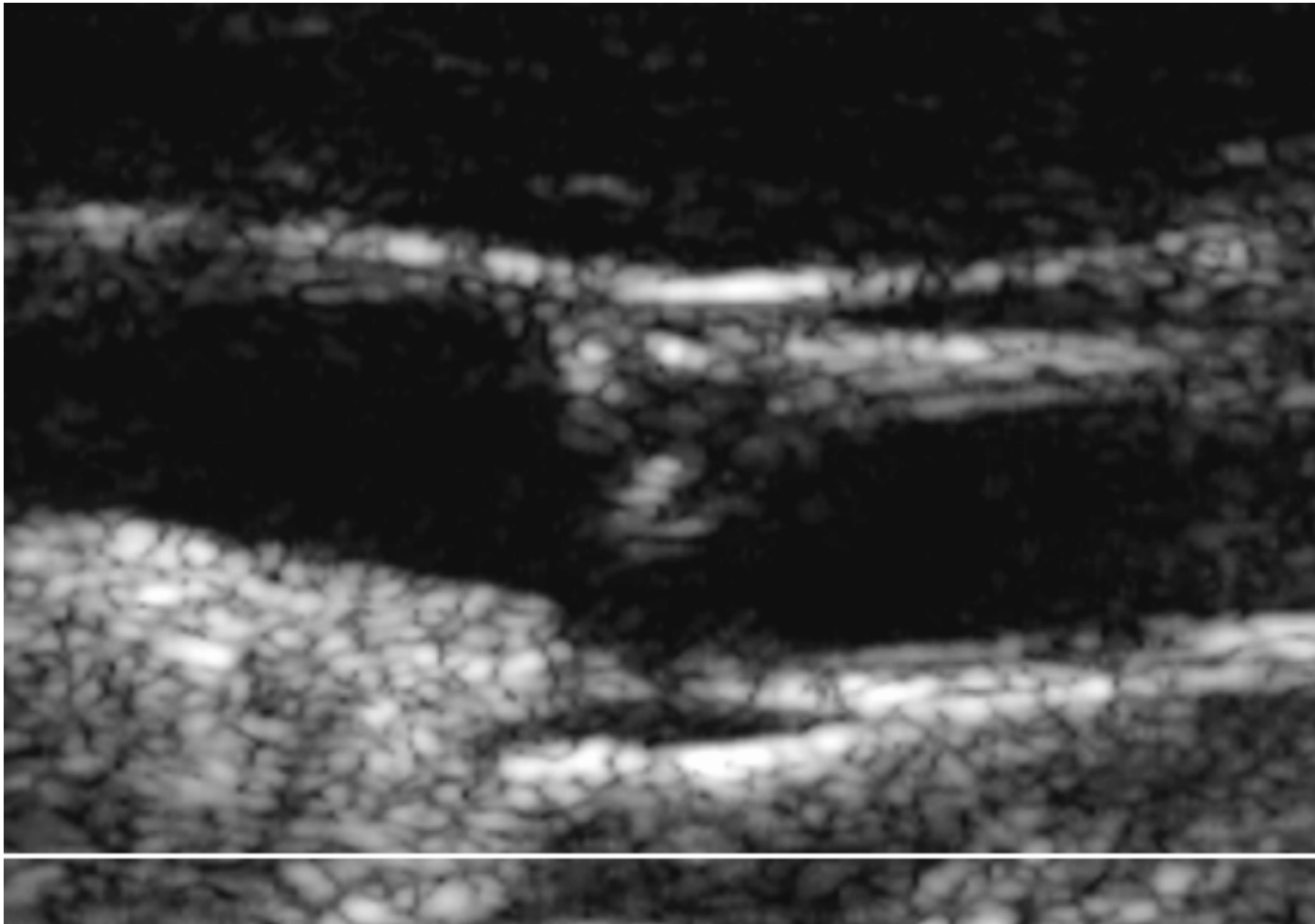
Plaque type 1



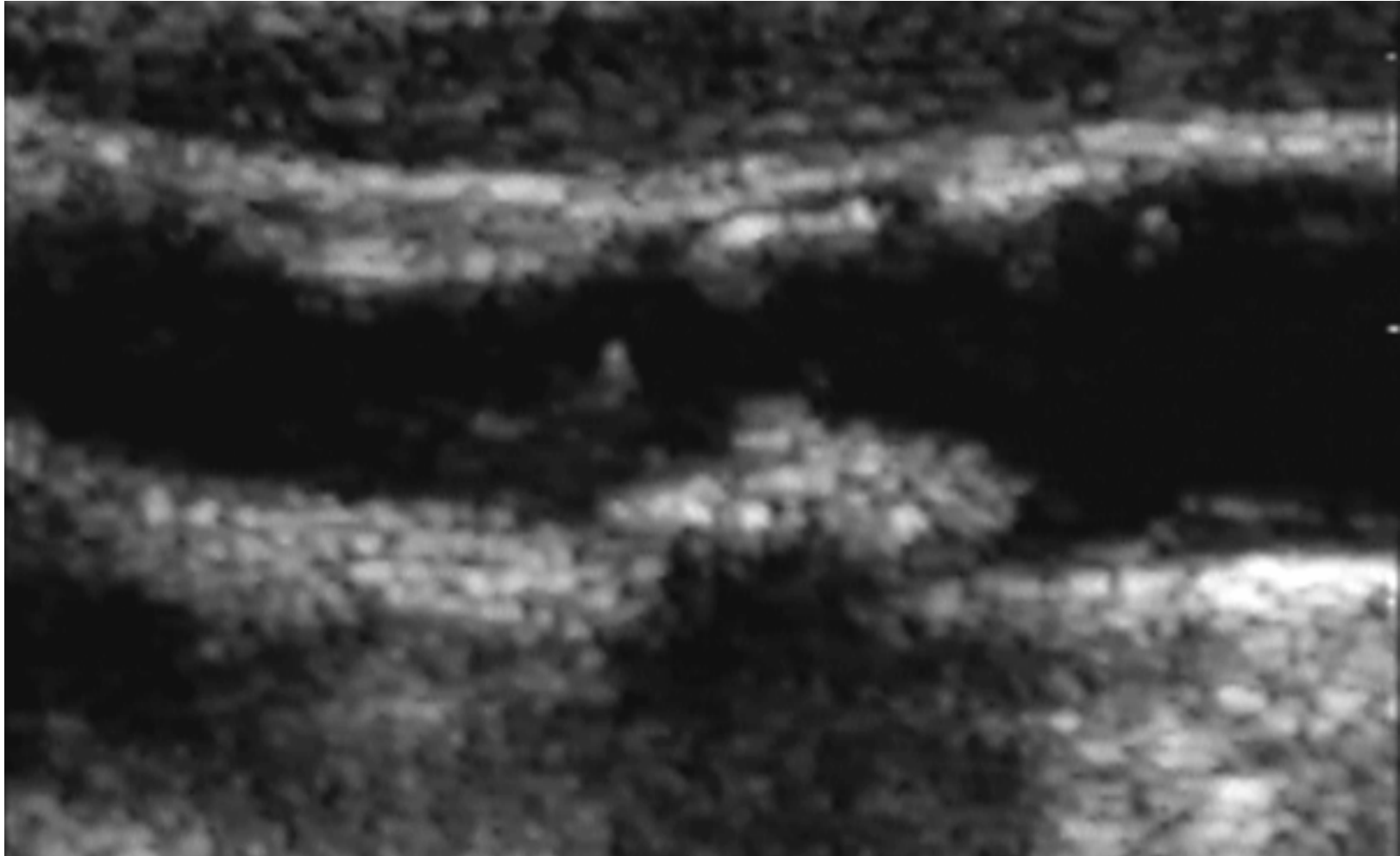
Plaque Type 2



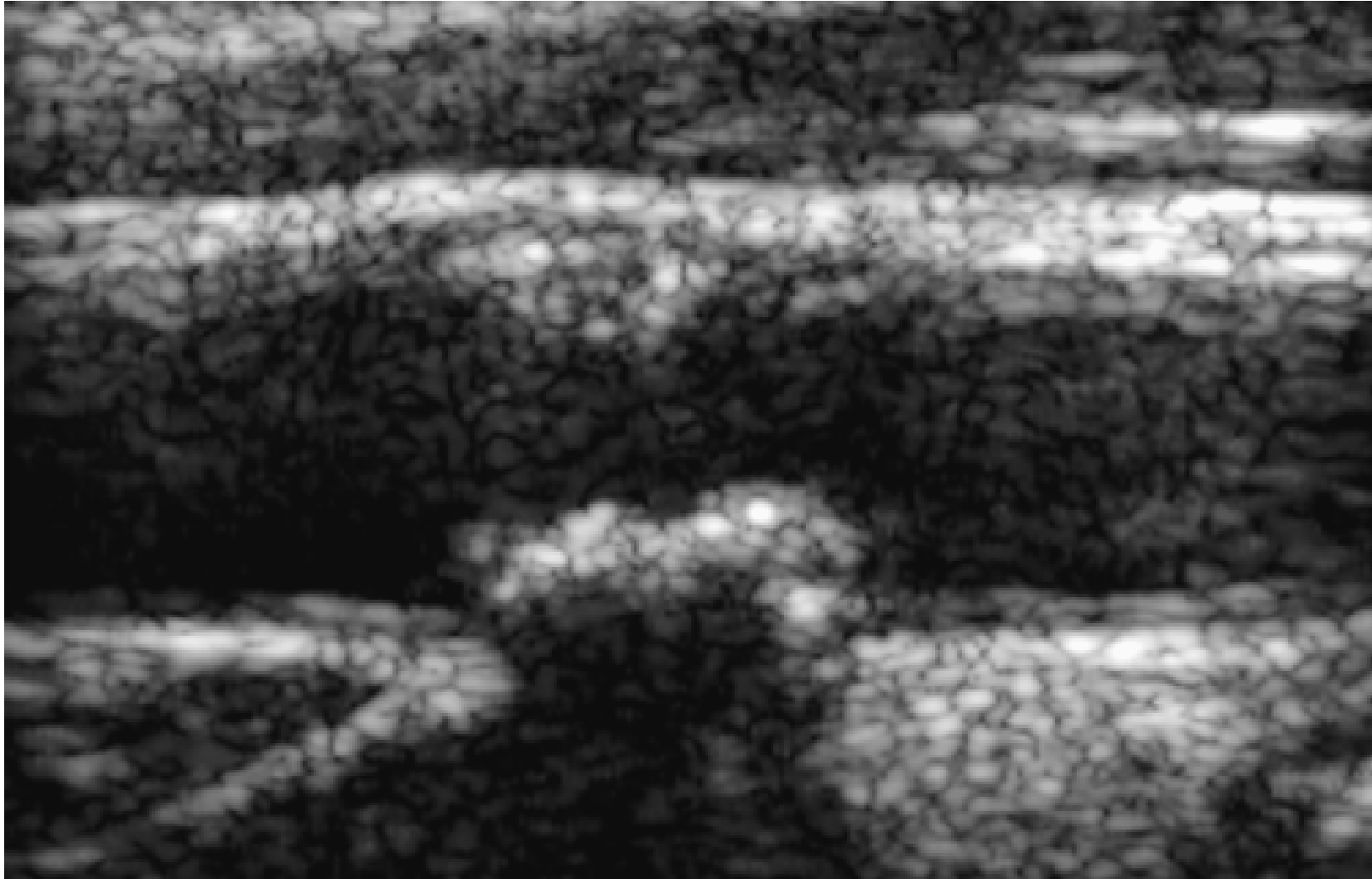
Plaque Type 3



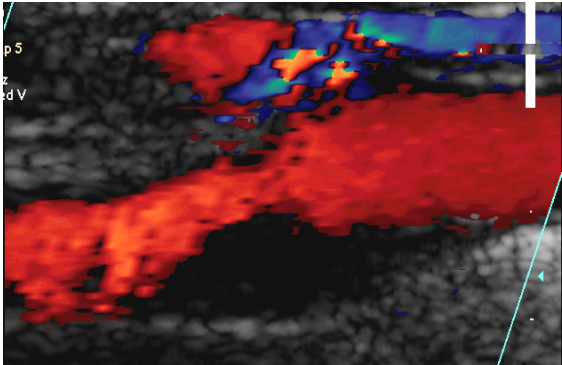
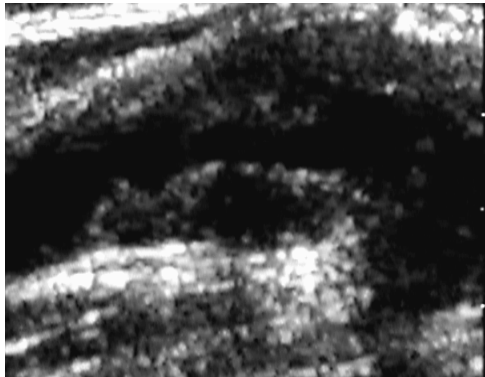
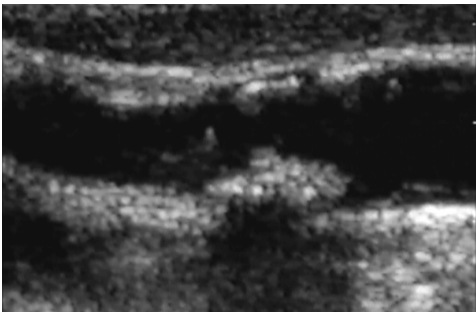
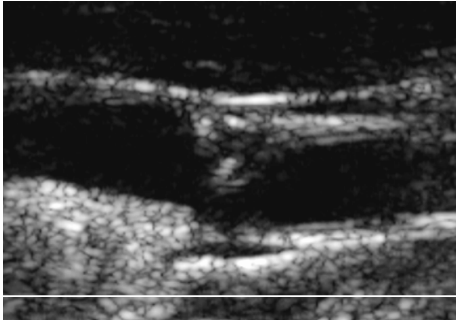
Plaque Type 4



Plaque Type 5



Echodensity vs Homogeneity/Heterogeneity and Risk of Symptoms

	<i>Homogenous</i>	<i>Heterogenous</i>
<i>Hypoechoic</i>	<p style="text-align: center;">Type I (6%) : OR 3.8</p> 	<p style="text-align: center;">Type II (28%) : OR 4.5</p> 
<i>Hyperchoic</i>	<p style="text-align: center;">Type IV (21%) : OR 1.0</p> 	<p style="text-align: center;">Type III (45%) : OR 3.3</p> 

Plaque morphology – Predictive value concerning risk of (future) events?

- * Natural history
 - Influence on decision for invasive treatment
- * **Interventional risk**
 - **Influence on choice of invasive treatment ?**

Is carotid plaque morphology a risk indicator for embolism during CAS ?

No plaques are safe from embolism

Is there a relationship between echolucency quantification (GSM) and neurological complications after CAS ?

YES

Biasi GM et al; Circulation 2004;110:756

Carotid Plaque Echolucency Increases the Risk of Stroke in Carotid Stenting: The Imaging in Carotid Angioplasty and Risk of Stroke

(ICAROS) Study

Plaque morphology

Subjective ultrasound characterization of carotid plaque morphology may be associated with unacceptable levels of reproducibility.



Importance of normalization of B-mode values to allow interscan comparisons.

Gray Scale Median (GSM)

Standardized computerized characterization of carotid plaque

Each shade of grey is numbered from 0 (black) and 255 (white)

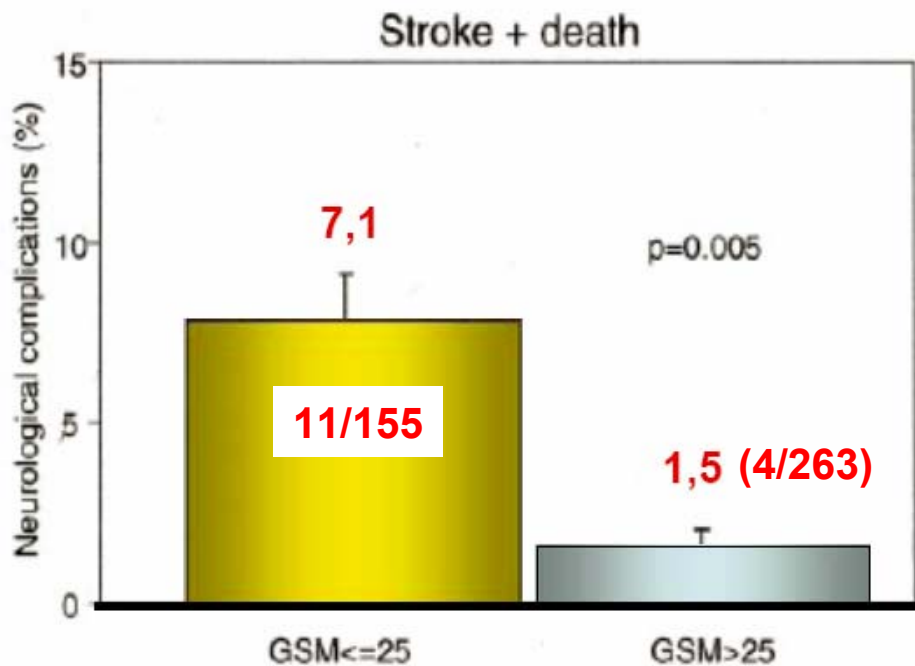
GSM (gray-scale median): index of echogenicity



Carotid Plaque Echolucency Increases the Risk of Stroke in Carotid Stenting

The Imaging in Carotid Angioplasty and Risk of Stroke (ICAROS) Study

Biasi GM; Circulation 2004; 110;756-762



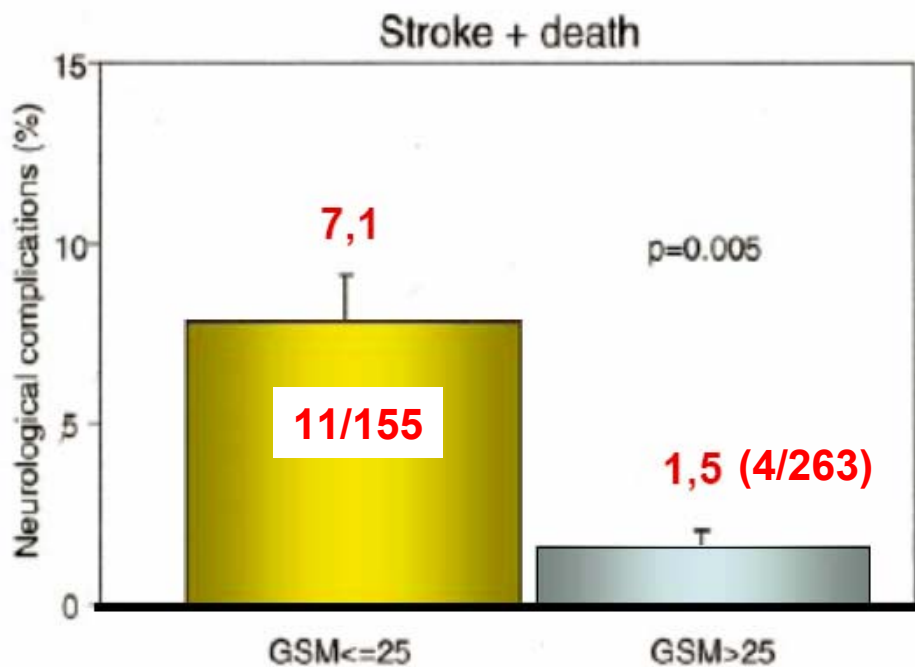
Multivariate analysis revealed that **GSM** (OR, 7.11; P< 0.002) and **rate of stenosis** (OR, 5.76; P<0.010) are independent predictors of stroke

418 patients; 11 international centers

Carotid Plaque Echolucency Increases the Risk of Stroke in Carotid Stenting

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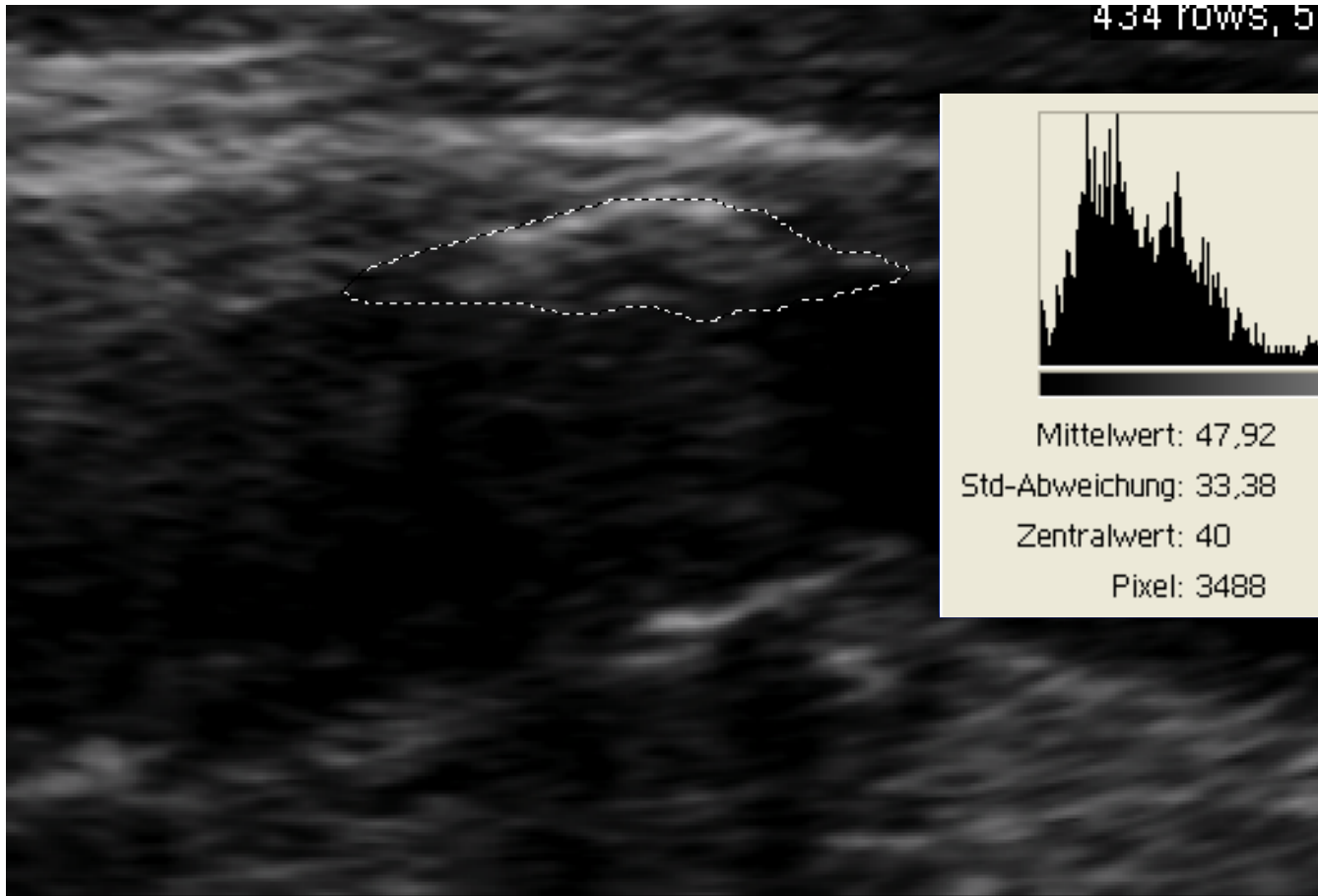


The **effectiveness** of brain protection devices was confirmed in those with GSM > 25 (P < 0.01) but not in those with GSM ≤ 25

418 patients; 11 international centers

GSM: Gray-scale intensity of the entire plaque

Problem: GSM measures the median brightness of the entire plaque. Regional instability may exist within a plaque even with a high GSM value.



Mittelwert: 47,92	Tonwert:
Std-Abweichung: 33,38	Häufigkeit:
Zentralwert: 40	Spreizung:
Pixel: 3488	Cache-Stufe: 1

Endovascular Treatment of Soft Carotid Plaques: A Single-Center Carotid Stent Experience

**84 consecutive patients (63 men; mean age 71 years)
Soft echolucent (gray scale median <25) carotid lesions**

**Total neurological events at 30-day FU included 3 TIAs
and 1 minor stroke (4.8% neurological event rate).**

The 30-day all death/stroke rate was 2.4%.

Cremonesi A; Journal of Endovascular Therapy 2006; 13: 190–195

Is carotid plaque morphology a risk indicator for embolism during CAS ?

Is there a relationship between echolucency quantification (GSM) and neurological complications after CAS ?

NO

Reiter M et al; Stroke 2006;37:2378-2380

698 consecutive patients - 3 experienced operators

Objective

Evaluation of association between

- plaque morphology measured by **GSM** and **visual scores**
- and occurrence of neurological events and mortality after elective CAS

Is carotid plaque morphology a risk indicator for embolism during CAS ?

	Odds Ratio	95% Confidence interval	p-value
Risk for neurological complications			
GSM below 25	0.39	0.12 to 1.12	0.079
GSM (continuous)	1.01	1.0 to 1.02	0.059
Beletsky	1.42	0.80 to 2.54	0.24
Gray-Weale	1.17	0.87 to 1.57	0.31
Risk for stroke			
GSM below 25	0.59	0.14 to 2.41	0.46
GSM (continuous)	1.01	1.00 to 1.03	0.054
Beletsky	1.42	0.62 to 3.26	0.41
Gray-Weale	1.17	0.76 to 1.76	0.48

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Is carotid plaque morphology a risk indicator for embolism during CAS ?

Conclusion:

Plaque echolucency measured by objective and subjective grading did not identify patients with an increased risk of peri-interventional neurological events.

Evaluation of plaque echolucency with actual methods therefore cannot be recommended for risk stratification in CAS patients.

Reiter M et al; Stroke 2006;37:2378-2380

Carotid Plaque Echolucency Predicts the Risk of Stroke in Carotid Stenting

Biasi et al; Stroke 2007;38:e67(letter)

For few centers with excellent results, carotid plaque morphology could not be a predictor of stroke,

but for most centers not performing hundreds of cases per year (or starting a CAS program!), GSM is a strong predictor of stroke.

IVUS

COMPUTER DEFINED OBSTRUCTION ANALYSIS

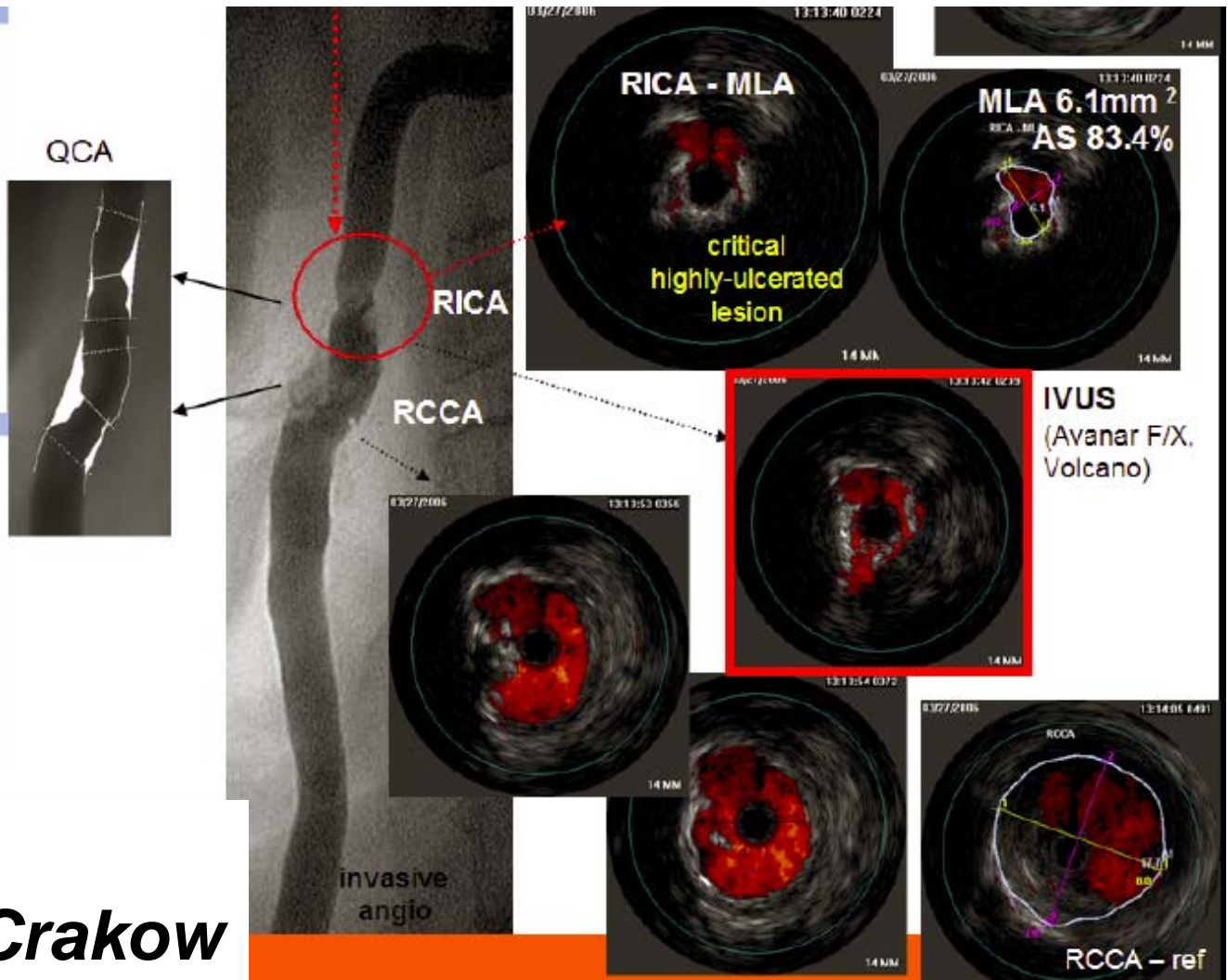
MLD	RICA	: 3.73 mm
% diameter stenosis		: 30 %
Reference diameter		: 5.31 mm
Length stenotic segment		: 10.20 mm
Position of proximal border		: 1.78 mm

MLA densitometry		: 7.88 mm ²
MLA circular		: 10.93 mm ²
% area stenosis densitometry		: 64 %
% area stenosis circular		: 51 %
Reference area		: 22.18 mm ²

COMPUTER DEFINED OBSTRUCTION ANALYSIS

MLD	RCCA	: 4.04 mm
% diameter stenosis		: 32 %
Reference diameter		: 5.98 mm
Length stenotic segment		: 11.32 mm
Position of proximal border		: 1.60 mm

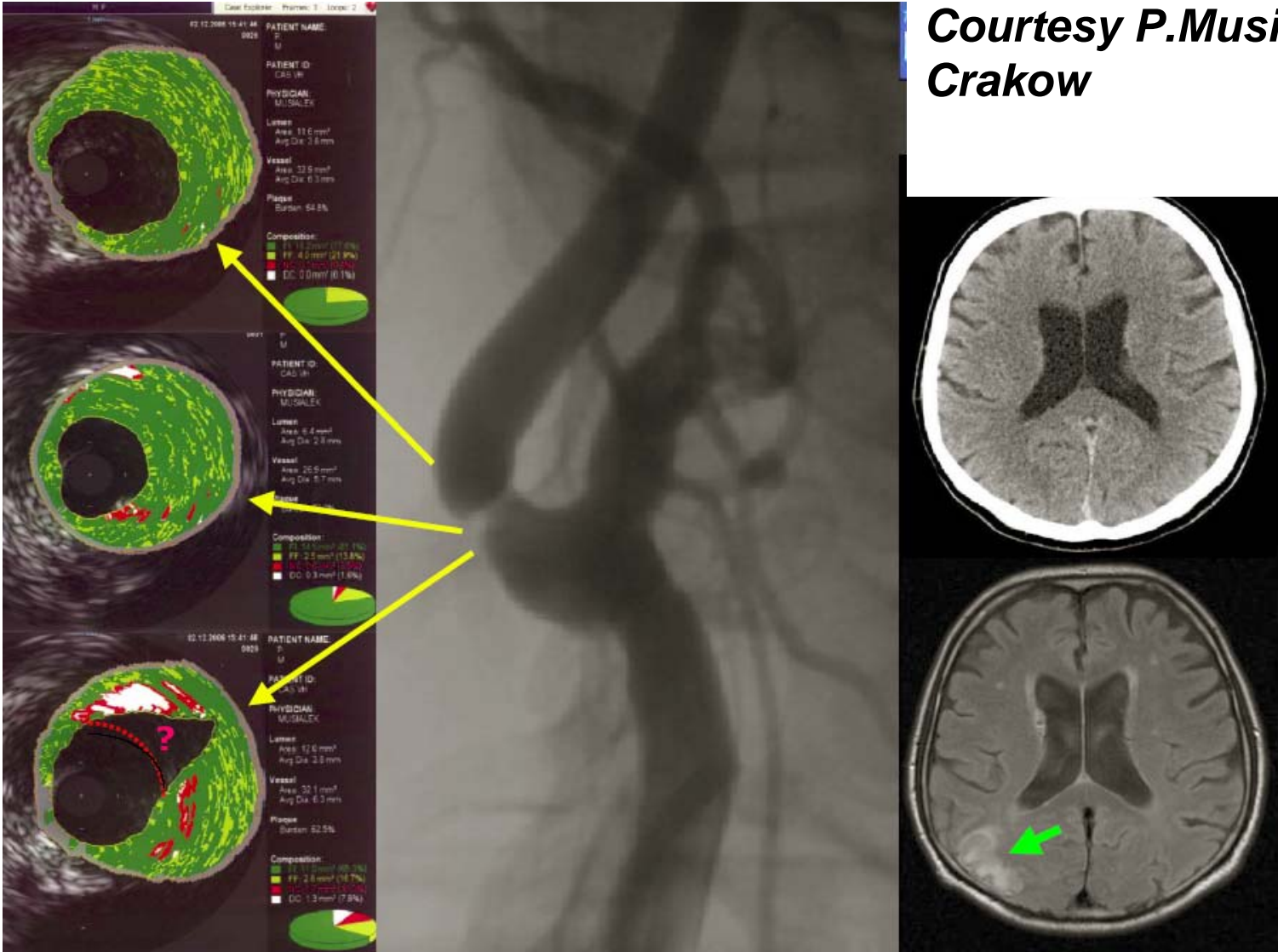
MLA densitometry		: 23.89 mm ²
MLA circular		: 12.83 mm ²
% area stenosis densitometry		: 15 %
% area stenosis circular		: 54 %
Reference area		: 28.10 mm ²



**Courtesy
P.Musialek; Crakow**

Virtual histology

Courtesy P. Musialek;
Crakow



Virtual Histology Intravascular Ultrasound Assessment of Carotid Artery Disease: The Carotid Artery Plaque Virtual Histology Evaluation (CAPITAL) Study

Diethrich E et al; J Endovasc Ther 2007;14:676–686

The diagnostic accuracy of VH IVUS to agree with true histology in different carotid plaque types depends on the type of plaque; e.g.

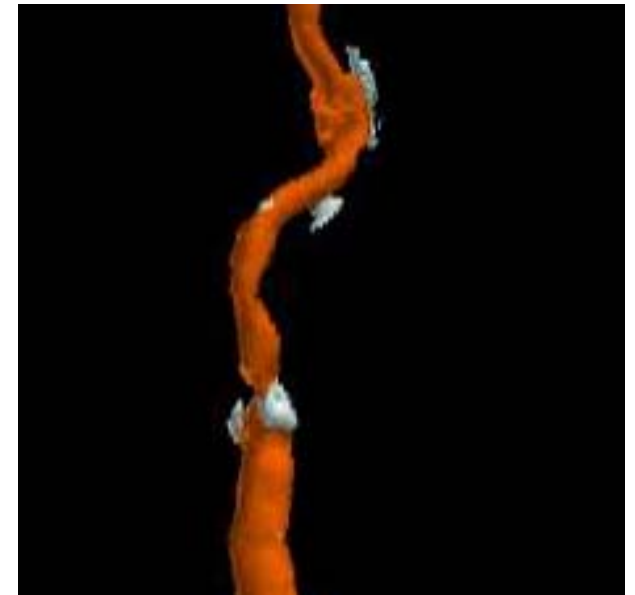
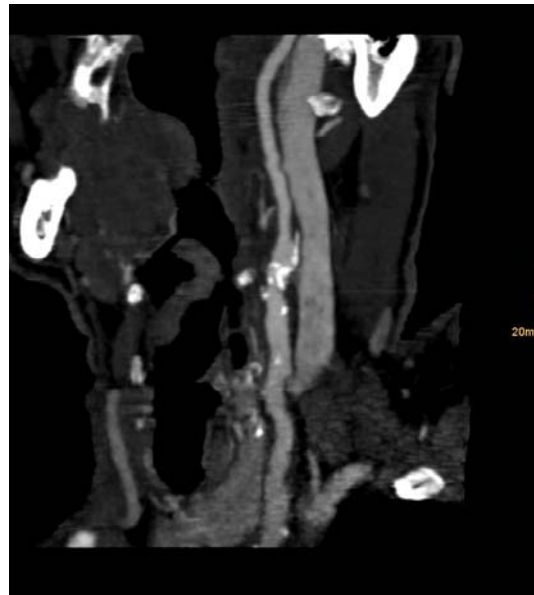
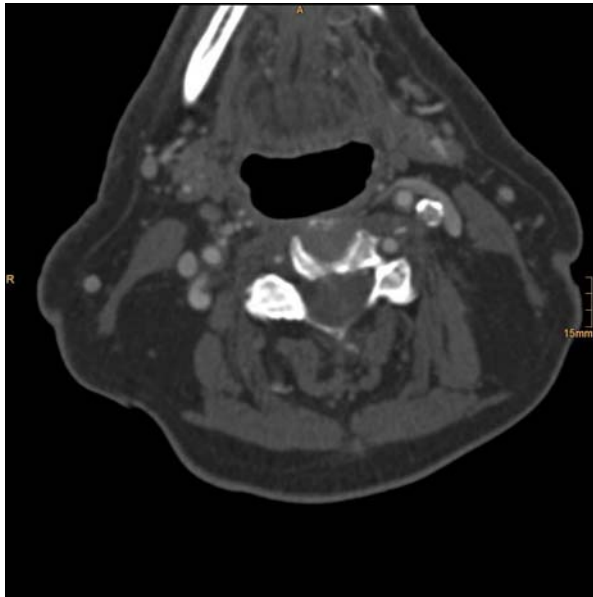
99.4% in thin-cap fibroatheroma

85.9% in fibroatheroma

72.4% for calcified fibroatheroma.

Multislice computed tomography

Good visibility of calcifications, but lack of tissue definition



Carotid Plaque Characterization: Implications for CAS?

Further studies of the potential clinical utility of plaque morphology to predict outcome are planned.

**B-mode ultrasound studies before carotid intervention:
Plaque characterization data in asymptomatic patients
will be a secondary endpoint of the**

Transatlantic Asymptomatic Carotid Intervention Trial

Carotid Plaque Characterization: Implications for CAS?

Conclusion:

- * Plaque morphology determined by duplexsonography has definitely a predictive value concerning the risk of carotid lesions for future symptomatic events in the spontaneous course.
- * Currently there are only few and divergent data concerning the value of duplexsonography for risk stratification in CAS patients.
- * The importance of newer technology (such as MRI and VH) for identification of plaque types prone to complications has to be evaluated in future studies.