Ultrasound and plaque characterization

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Hopital de la Tour
Geneva-CH

Congresso nazionale SINV
2022

Carotid wall imaging

- fundamental goal of carotid wall imaging is to provide a better risk stratification for patients with advanced carotid atherosclerosis

Naylor AR, Eur J Endovasc Surg , 2003

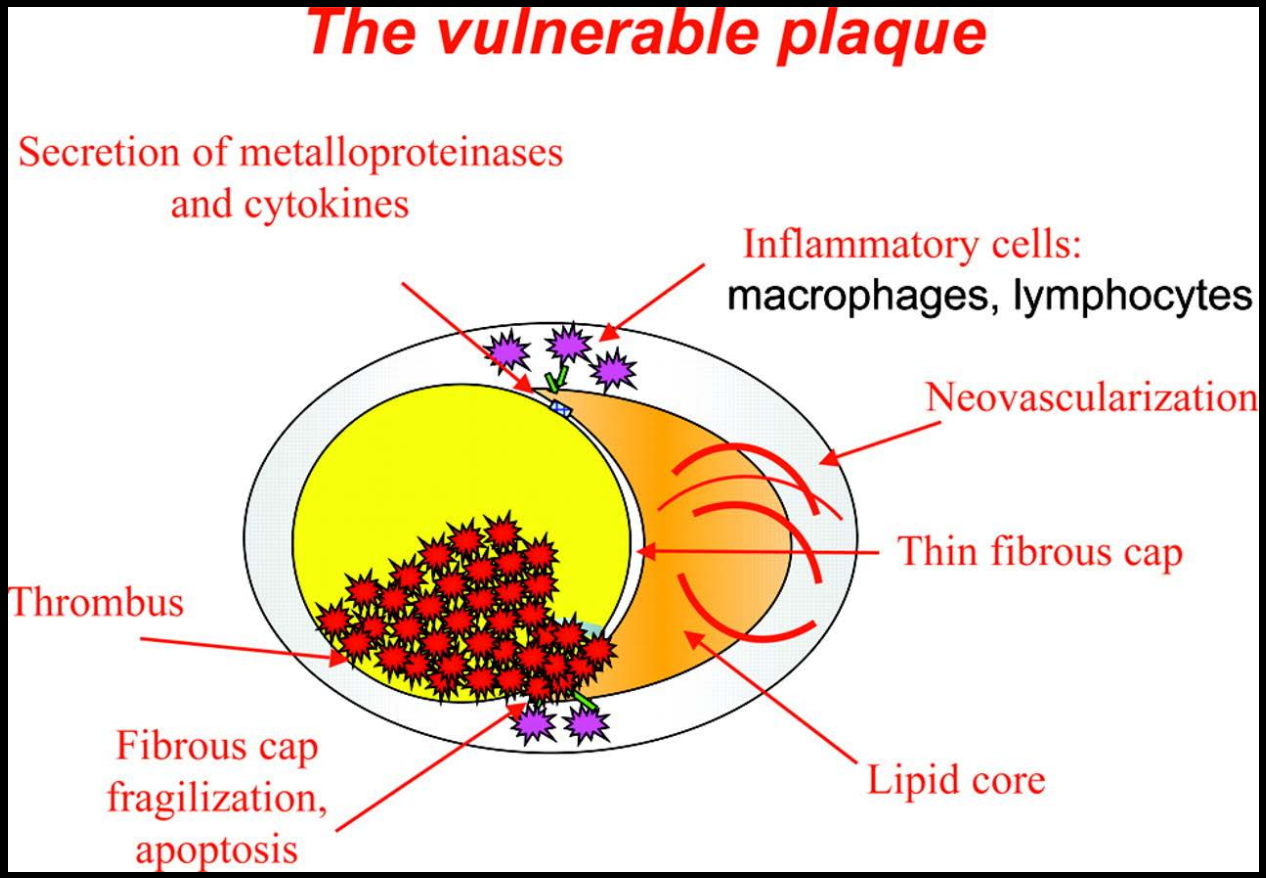
Carotid wall imaging

- approximately 20% of ischemic strokes are caused by rupture of carotid artey plaques
- currently stroke risk is assessed via percentage of dimater reduction
- stroke rates after guide-line achieved cartid endarterectomy for high grade stenosis in symptomatic patients are significantly lower than those observed with best medical therapy alone
- in asymptomatic patients majority of medically treated patients remain stoke free during follow-up
- in asymptomatic population, increasing degrees of stenosis have not been associated with increased risk of stroke/TIA
- degree of stenosis alone may therefore not be sufficient to evaluate the risk of stroke
- additional markers are needed to better identify subgroups of high risk patients who would benefit most from surgery or angioplasty/stent

Demirel S, Gefässchirurgie, 2018
Petty GW, Stroke 1999

Imaging methods of potential value in identifying high risk plaques

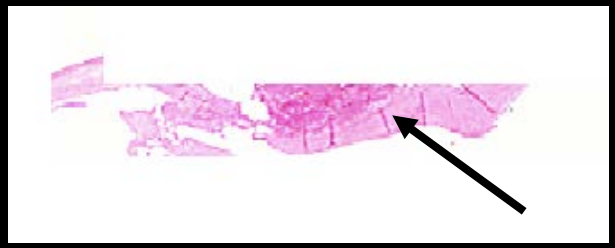
- **High resolution ultrasound:** echolucency, plaque heterogeneity, surface irregularity/ulcers
- **TCD:** microembolic signals
- **CT:** calcifications, hypodense plaques
- **MRI** (high resolution): thin fibrous cap, cap rupture, intraplaque heamorrhage, necrotic core
- **PET:** quantification of inflammation (SUV-TBR)
- **Molecular imaging:** MRI,ultrasound

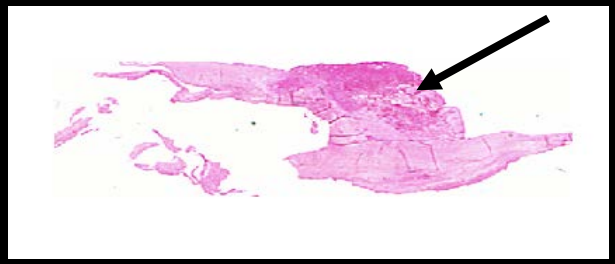


Nighoghossian, N. et al. Stroke 2005

Histological characteristics of an unstable plaque

- **Distance between necrotic core and surface increases the risk of presence of symptoms**





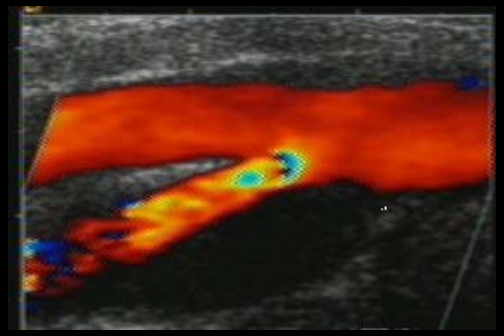
Bassiouny HS, J Vasc Surg,1997
Golledge J, Stroke,2000

ultrasonographic characteristics of carotid plaque morphology

- **Echogenicity (intensity of ultrasound reflection)**
- **texture (homogeneous/heterogeneous)**
- **surface (smooth, irregular/ulcerated)**

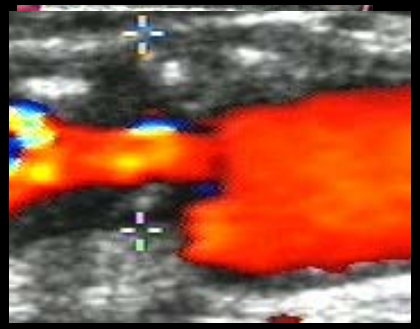
Plaque type classification:
according to Geroulakos et al, Br J Surg, 1993

Type I hypo- anechogenic, uniform (reference blood)

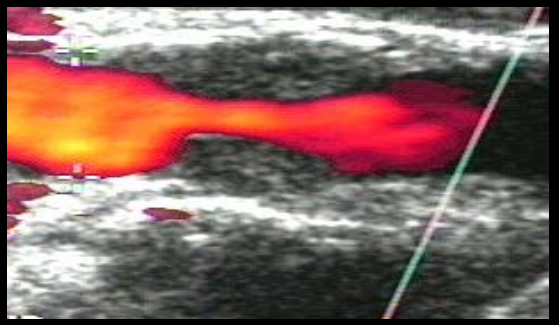


Type II predominant hypo, anechogenic

Type III predominant echogenic (reference adventitia)



Type IV echogenic, uniform (reference muscle)



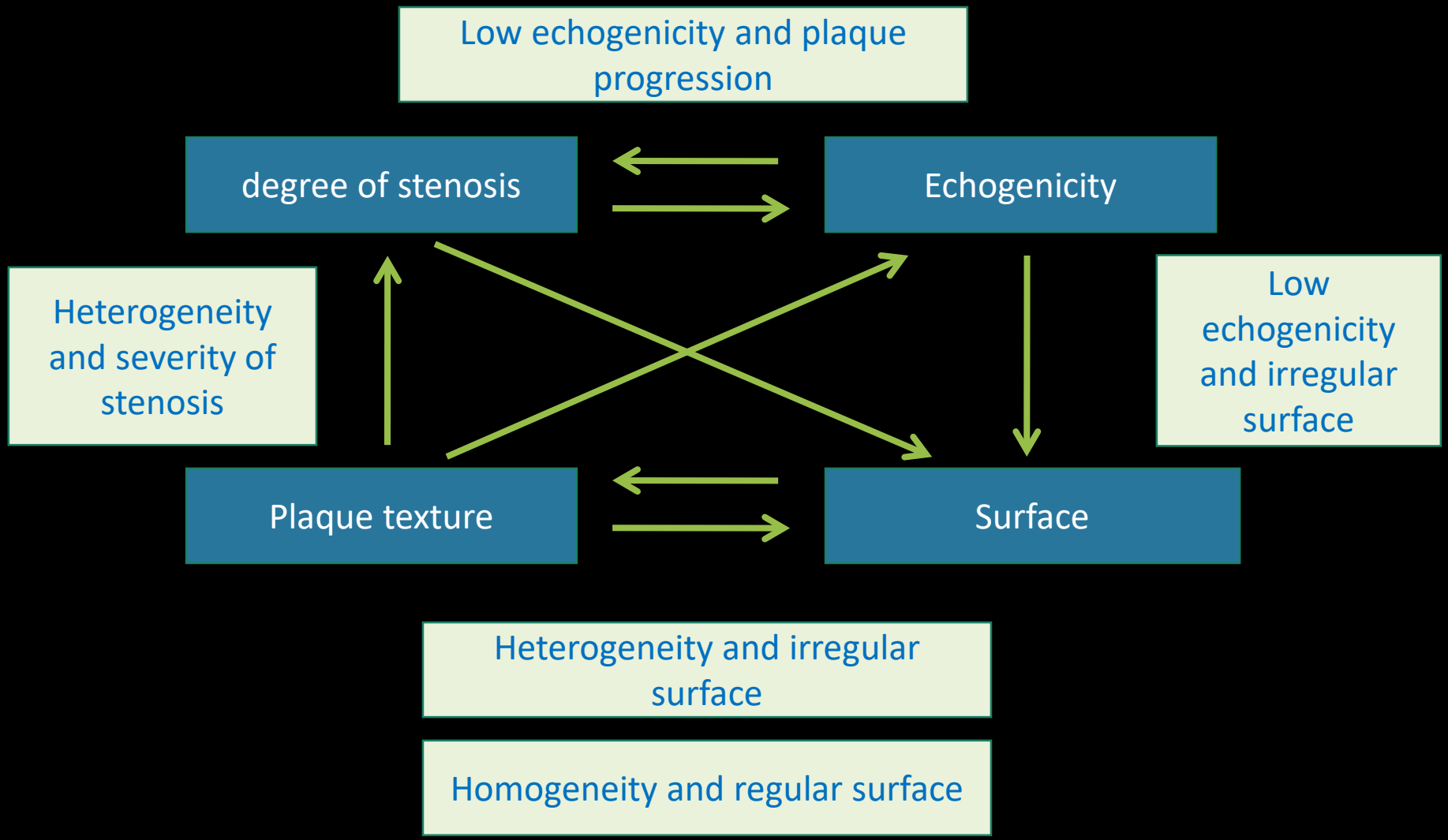
Plaque type classification:
according to Geroulakos et al, Br J Surg, 1993

Type V undetermined (acoustic shadow)

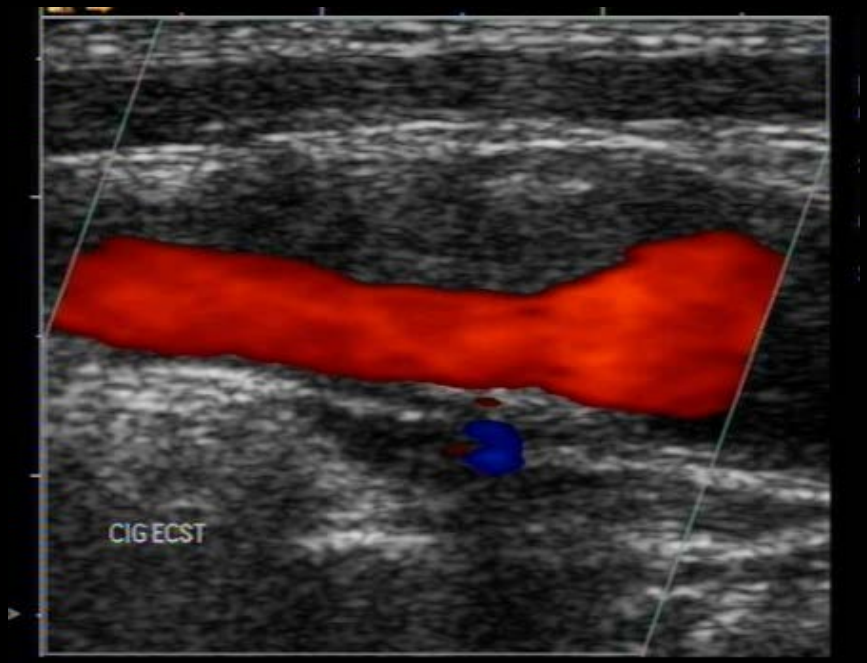
ultrasonographic characteristics of carotid plaque

- degree of stenosis: → progression/regression
- echogenicity → lower/higher
- texture → homogeneous/heterogenous
- surface mophology : → regular/irregular/ulcerated

Interactions between the different plaque components

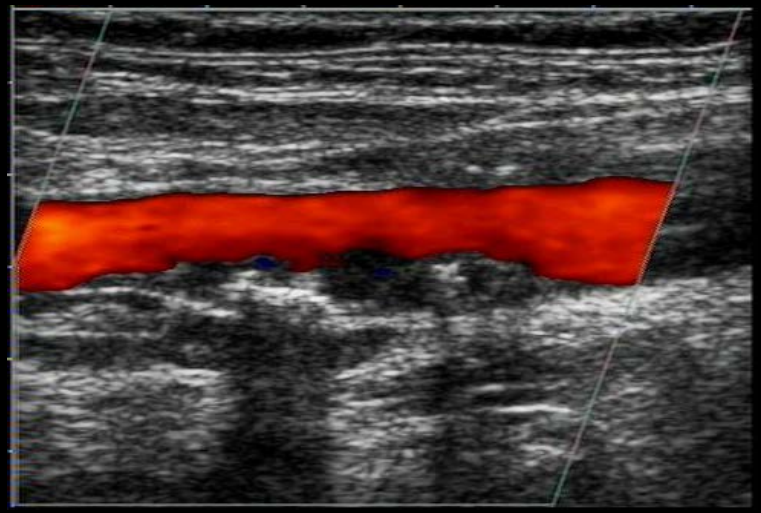


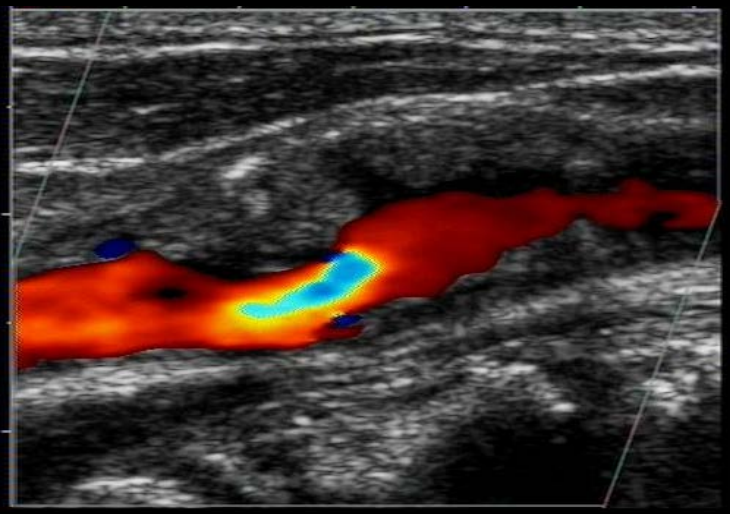
Homogeneous plaques tend to have more regular surface



Reilly LM, A J Sur 1997

Heterogeneous plaques are associated with more irregular surfaces





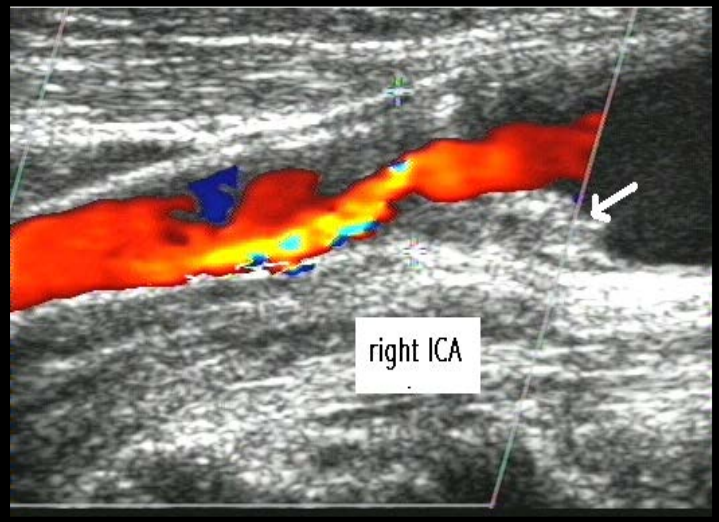
Reilly LM, A J Sur 1997

The higher the degree of carotid stenosis, the more likely it is associated with ultrasonic heterogeneous plaque

TABLE 2. Plaque Heterogeneity vs Severity of Stenosis

	Homogeneous, n (%)	Heterogeneous, n (%)	*P*	Odds Ratio (95% CI)
≥50% stenosis (N=1666)	678 (41)	988 (59)	<0.001	6.9 (5.6–8.6)
<50% stenosis (N=794)	656 (83)	138 (17)		
≥60% stenosis (N=1102)	305 (28)	797 (72)	<0.0001	8.2 (6.8–9.8)
<60% stenosis (N=1358)	1029 (76)	329 (24)		
≥70% stenosis (N=615)	119 (20)	496 (80)	<0.001	8.0 (6.4–10.1)
<70% stenosis (N=1845)	1215 (66)	630 (34)		

P values are for heterogeneous values within stenosis groups.

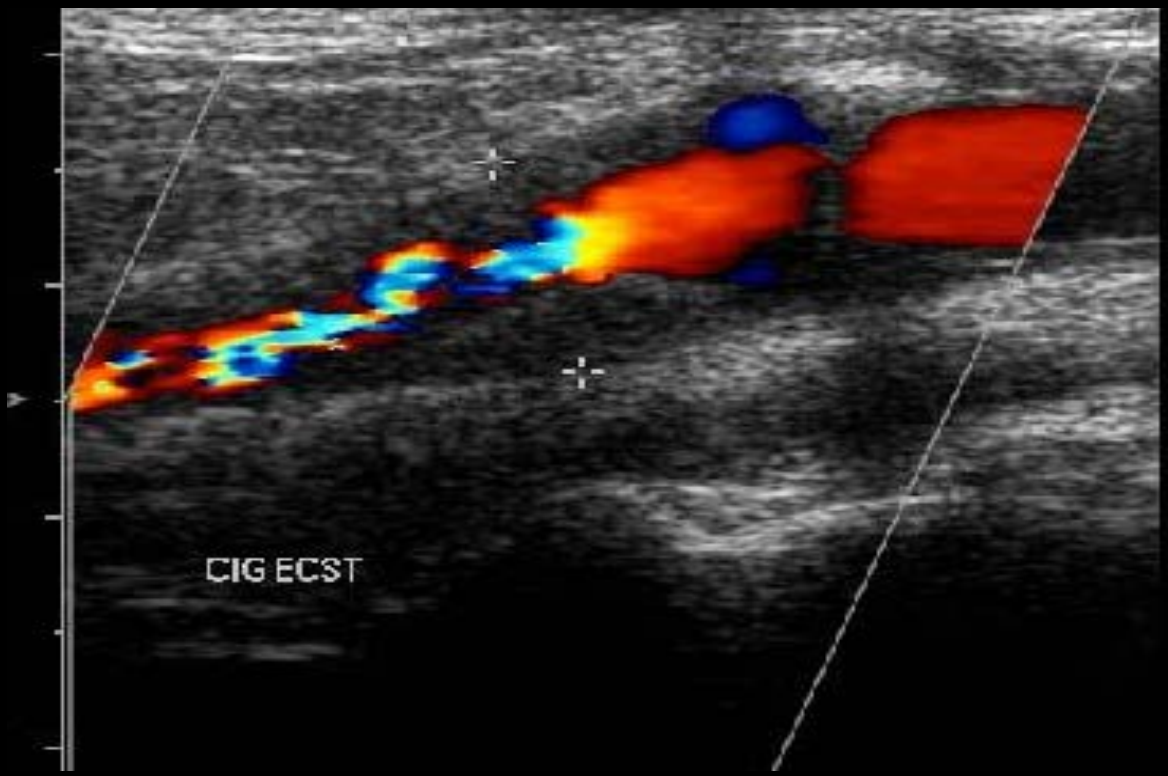


Ali F. AbuRahma, Stroke 2002

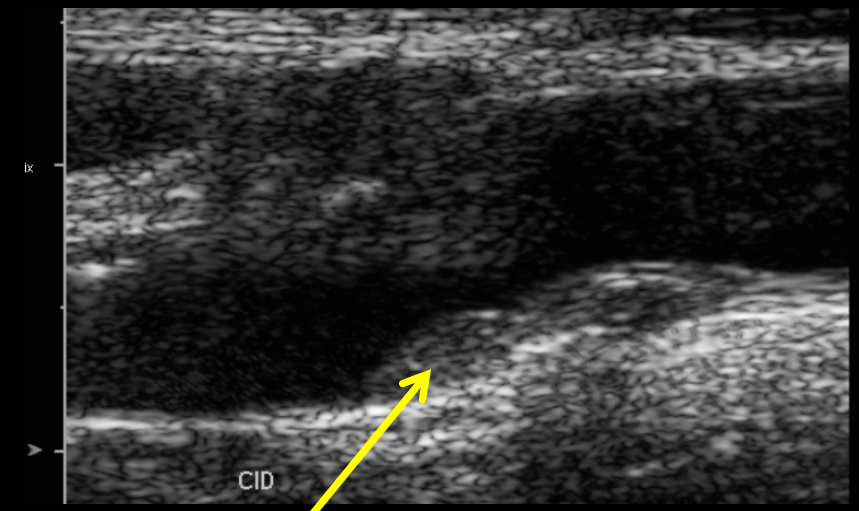
Ultrasonographic characteristics of the surface of the plaque

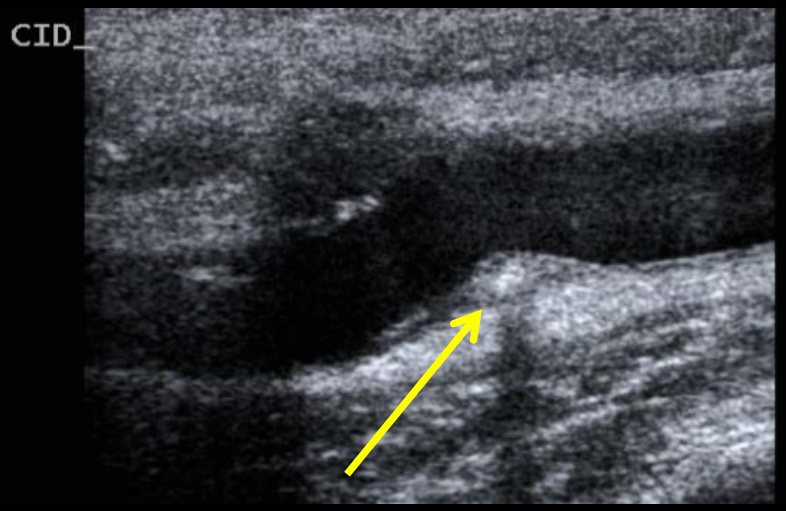
Ulcerations meet 3 criteria:

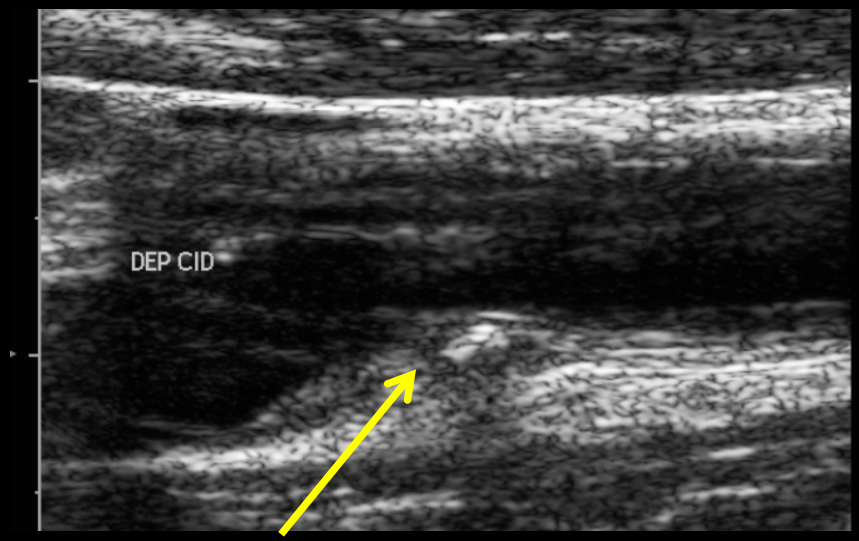
- **t**he recess is at least 2 mm deep and 2 mm long
- it has a well defined wall at its base
- area of reversed flow within the recess or a zone of low flow signal



Increase of plaque echogenicity and plaque regression from dec 2009-march 2011







From our center

Correlations between ultrasonographic characteristics
and histological studies:
echogenicity and structure

AUTHOR	YEAR	N	ANECHOGENIC	ECHOGENIC	HOMOGENEOUS	HETEROGENEOUS
Reilly LM	1983	54	Hemorrhage Lipids	Calcification	Fibrous tissue	Hemorrhage
O´Donnell TG	1985	54	Lipids Hemorrhage	Fibrous tissue Calcifications	Fibrous tissue	Hemorrhage
Bluth EI	1986	50	Hemorrhage	Fibrous tissue	Fibrous tissue	Intraplaque hemorrhage
Ratliff DA	1985	39	No correlation	Calcifications	No correlation	No correlation
Aldoori MI	1987	27	Hemorrhage	Fibrous tissue	Fibrous tissue	Hemorrhage
Gray-Weale AC	1988	220	Hemorrhage	Fibrous tissue	Fibrous tissue	Hemorrhage
Spagnoli LG	1988	43	Hemorrhage Lipids	Fibrous tissue Calcifications	Fibrous tissue	NI
Widder B	1989	169	Hemorrhage Lipids	Fibrous tissue	Fibrous tissue	NI
Feeley T	1991	52	Hemorrhage Lipids	Fibrous tissue	Fibrous tissue	NI
*ECPSP	1995	270	Hemorrhage Lipids	Fibrous tissue Calcification	NI	Calcifications
Droste DW	1997	29	Hemorrhage Thrombosis Fibrous tissue	Hemorrhage	Hemorrhage Thrombosis Fibrous tissue	Hemorrhage Thrombosis
Gronholdt MLM	1997	78	Lipids	Fibrous tissue Calcifications	NI	Calcifications
Schulte-Altedorneburg	2000	44	Lipids Hemorrhage Thrombosis	Fibrous tissue	Lipids Hemorrhage	Lipids Calcifications

presence of discrete white areas (DWAs) on carotid plaque n=38)

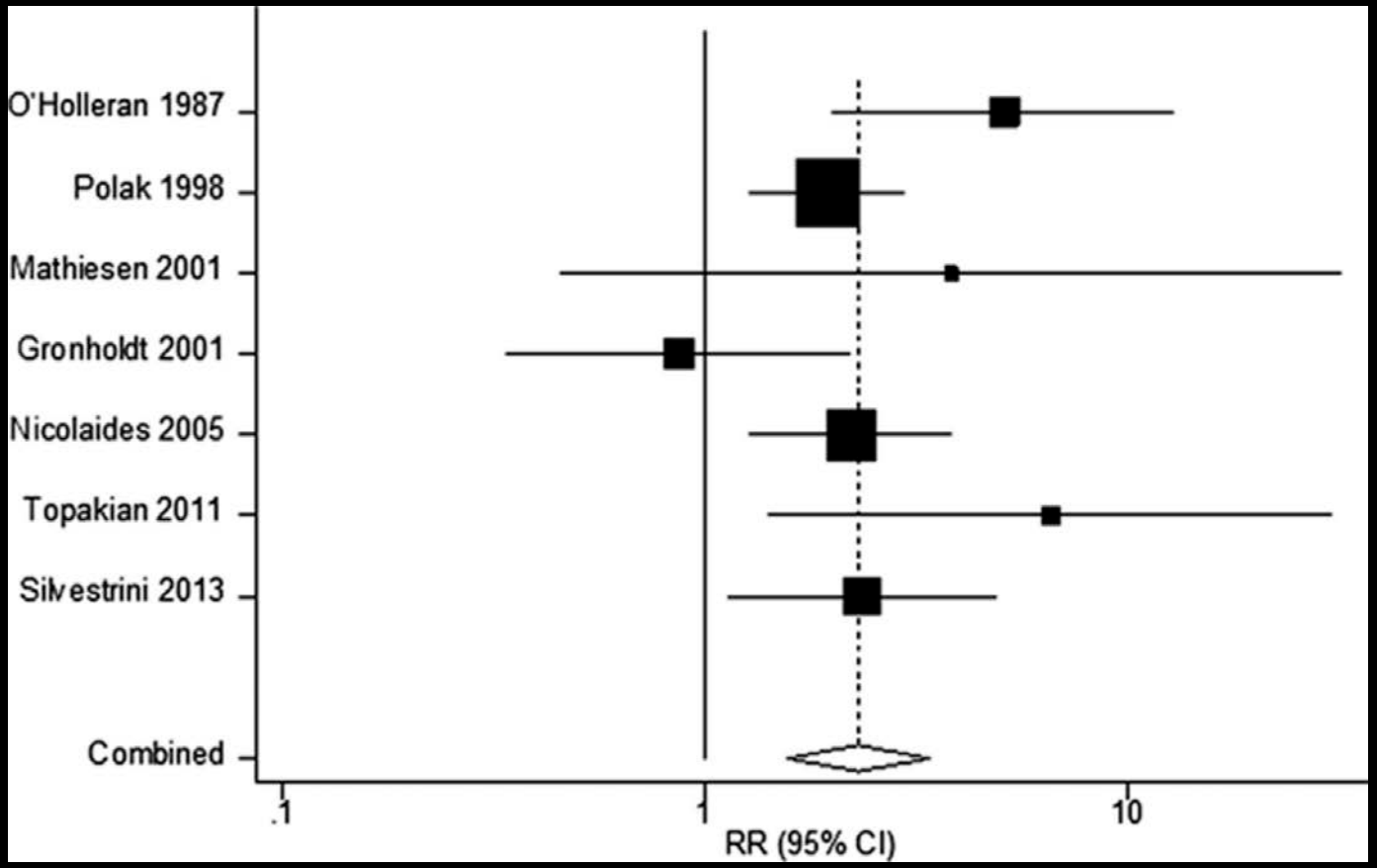
Presence on ultrasound of DWA was associated with more plaque hemosiderin ($p = 0.0005$) and inflammation ($p = 0.019$) on histopathology examination

Mitchell,Utrasound in Med and Biol 2017

High resolution ultrasound ,characteristics of the carotid plaque and the risk of stroke

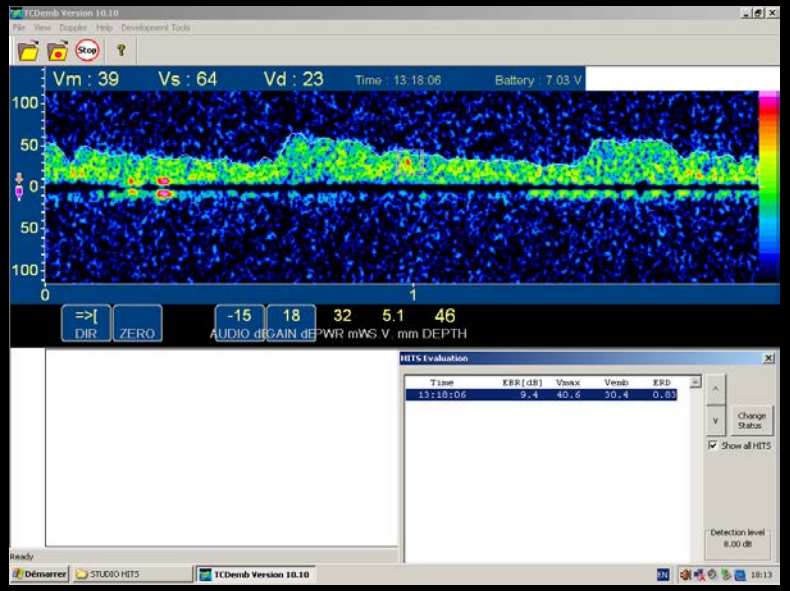
Association between carotid plaque echolucency and risk of stroke

data from 7 studies on 7557 subjects with a mean follow-up of 37.2 months



Gupta, Stroke 2015

Micro-embolic signals (MES)



- **MES and carotid stenosis: increased risk of recurrence (Markus H, Brain 1995, Lancet 2010)**
- **Presence of MES in asymptomatic stenoses predicts stroke occurrence (Spence JD, Stroke 2005)**
- **MES and ulcerated plaques (Sitzer M, Stroke 1995, Mitchell US in Med and Biology 2015)**

Correlation MES (micro-embolic signals) and plaque morphology (echogenicity): 71 patients with 93 carotid stenoses between 50-99%

	MES+ N = 17	MES- N= 76
Type I/II	**13 (76%) ***	**27 (36%)**
Type III/IV	**4 (25%)**	**39 (51%)**
Type V	**1(excluded)**	**10 (excluded)**

***p<0.009**

Momjian-Mayor I, Acta Scandinavica 2002

Heterogeneous plaques and the risk of stroke

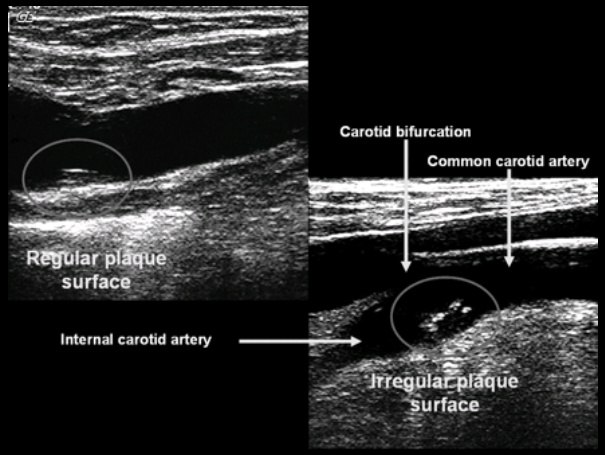
	Sympt N %	Asympt N %	Odds Ratio (95% CI)
All heterogeneous* (N=1126)	904 (80)	222 (20)	
All 50% stenosis (N=1666)	968 (58)	698 (42)	0.3 (0.3–0.4)
All 60% stenosis (N=1102)	745 (68)	357 (32)	0.5 (0.4–0.6)
All 70% stenosis (N=615)	464 (75)	151 (25)	0.8 (0.6–1.0)

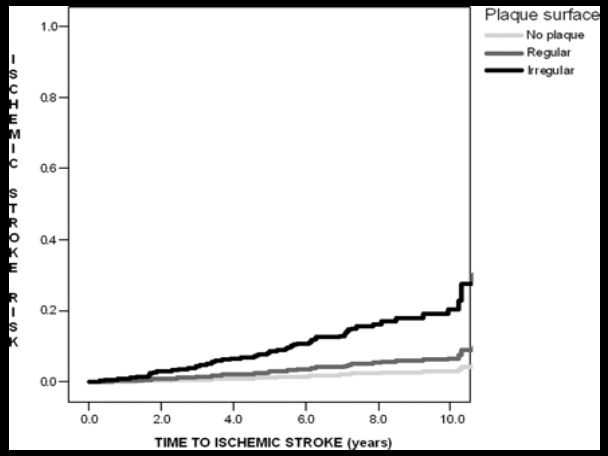
*Includes all stenoses (including <50% stenosis).

Heterogeneous plaques were associated with an incidence of symptoms that was higher than that for homogeneous plaques for all grades of stenoses

Ali F. AbuRahma, Stroke 2002

Carotid Plaque Surface Irregularity Predicts Ischemic Stroke





1939 subjects, mean follow up of 6.2 years,
69 ischemic strokes occurred
Unadjusted cumulative 5-year risks of ischemic stroke were:
1.3%, 3.0%, and 8.5% for no plaque, regular plaque, and irregular plaque

After adjusting for demographics (risk factors, degree of stenosis, and plaque thickness) presence of irregular plaque (vs no plaque) was independently associated with ischemic stroke
HR: 3.1; 95% CI, 1.1 to 8.5
Plaque surface irregularities assessed by B-mode ultrasonography may help identify intermediate- to high-risk individuals beyond their vascular risk factors

Shyam Prabhakaran, Stroke 2006

Reproducibility of carotid ultrasound: (intra- and interobserver)

AUTHORS AND YEAR	CLASSIFICATION ECHOGENICITY HETEROGENEITY	NUMBER OF PLAQUES	INTEROB-SERVER VALUES κ	INTRAOB-SERVER VALUES κ	REFERENCE STRUCTURES
Widder 1990	8	30	0.6	-	no information
Geroulakos 1993	5	147	0.79	-	no information
Joakimsen 1997	4	107	0.72	0.76	blood/media-adventitia
DeBray 1998	5	53	0.31	0.47	blood/media-adventitia
Van Swijndregt 1998	3	46	0.38	0.44	blood/media-adventitia
Arnold 1999	4	114	0.52 0.62	0.53 0.49	blood/adventitia
Mathiesen 2000	4	60	0.56	- -	no information
Hartmann 2000	4	114	0.18	-	no information
Tegos 2001	3	192	0.95	-	Blood /adventitia

Maior-Momjian I Ultrasound, Med and Biol, 2003

Reproducibility of three-dimensional (3D) ultrasound (US) over two-dimensional (2D) US in characterizing atherosclerotic carotid plaques using inter- and intra-observer agreement metrics

- 51 patients with 105 carotid artery plaques were screened using 3D and 2D US probes attached to the same US scanner
- echotexture, echogenicity and surface characteristics
- intra-observer agreements:
- using three morphological features :
  - 1st observer: 2D US showed fair (k=0.4-0.59) /3D very strong(k>0.8)
  - 2nd observer: 2D US moderate strong (k=0.6-0.79)/ /3D very strong(k>0.8)
- inter-observer agreements:
  - 2D moderate strong (k=0.6-0.79) /3D very strong (k>0.8) moderate strong (k=0.6-0.79) with 2D US and very strong with 3D US (k>0.8) intra-observer performances. Moderate strong (k=0.6-0
- 2D and 3D US were correlated 62% using only echotexture and 56% using surface morphology coupled with echogenicity
- **Conclusion:** High reproducibility in carotid plaque characterization was obtained using 3D US rather than 2D US.

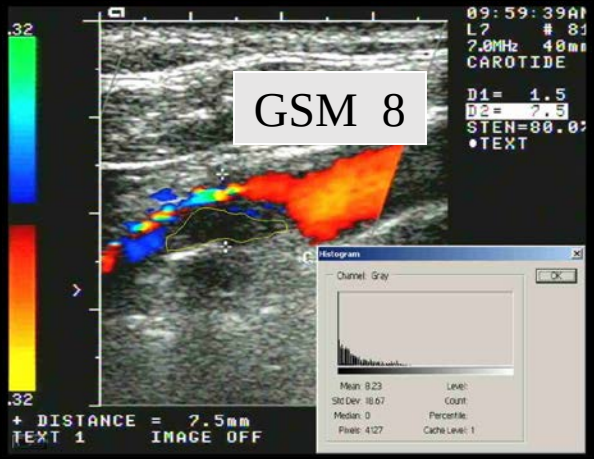
Leong , Comput Biol Med 2016

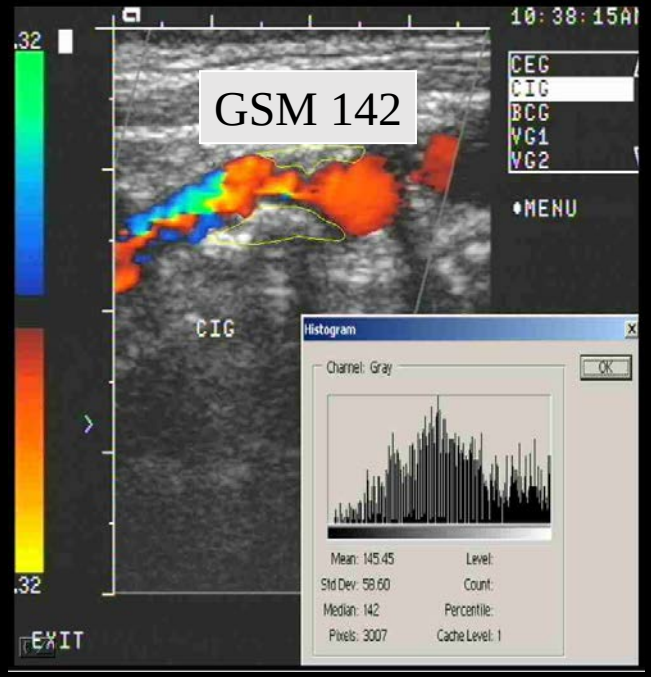
ultrasound developments

- **computerized analysis of the carotid plaque by ultrasound (GSM)**
- **colour mapping of plaque/surface**
- **ultrasound contrast enhanced method to assess neoangiogenesis**

Carotid plaque evaluation by grey-scale-median (GSM)

(El-Barghouty. Eur J Vasc Endovasc Surg 1995)





GSM value: depends on frequency of distribution of the grey scale of the different pixels;

normalisation on ground of reference values : GSM blood :0 and GSM adventitia :190

Asymptomatic Carotid Stenosis and Risk of Stroke (ACSRS)

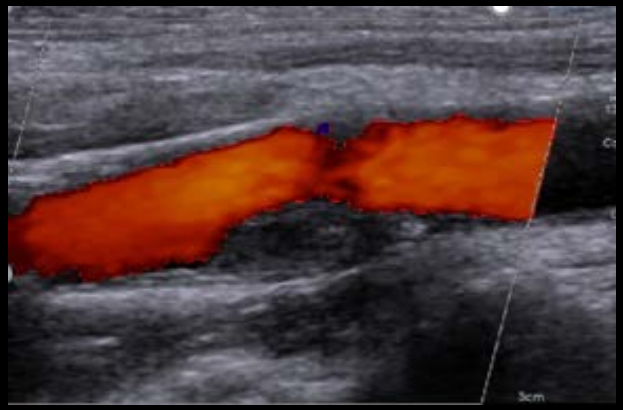
- 1115 patients with asymptomatic stenosis were categorized according to echolucency on ultrasound (Type I-V)
- **image normalization resulted in 60% of plaques being reclassified.**
- before image normalization, a high event rate was associated with all types of plaque
- after image normalization, 109 (94%) of the events occurred in patients with plaque types I-III
  - For patients with 50-99% diameter stenosis (NASCET) plaque types I-III, the cumulative stroke rate was 14% at 7 years (2% per year),
  - and for patients with plaque types IV-V, the cumulative stroke rate was 0.9% at 7 years (0.14% per year).

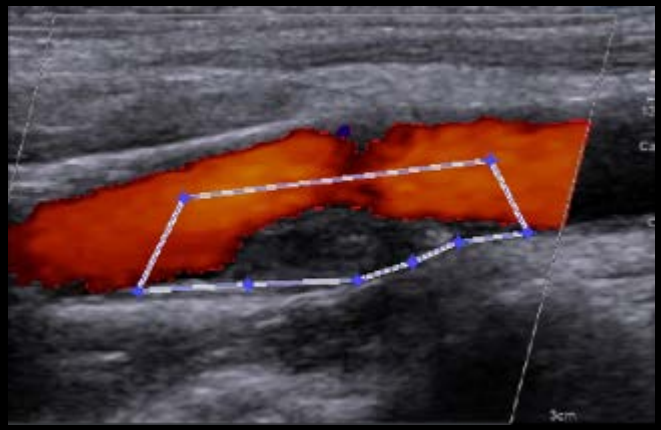
Nicolaides AN, Vasc surg ,2010

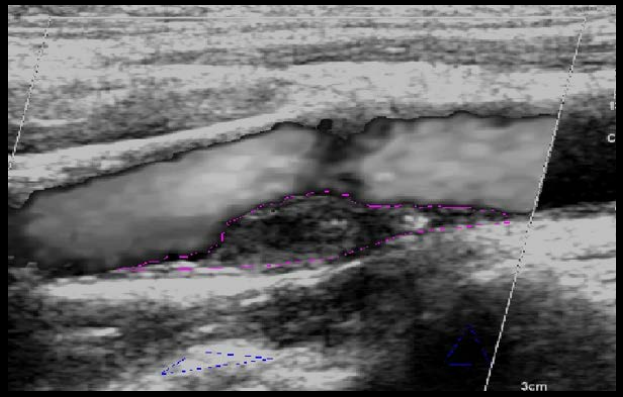
Evaluation of plaque echogenicity by means of GSM method
(inter- and intraobserver κ values > 0.75)

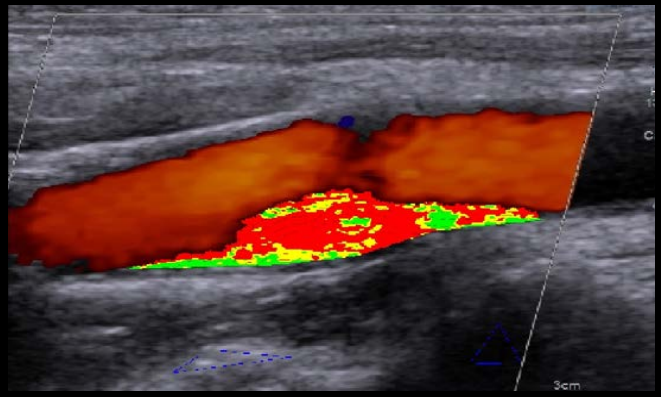
Author and year	N	Stroke/TIA	P values and RR
El-Barghouty 1995	87 <50% stenosis	Plaques with GSM<32 associated with an incidence of 55% of CT infarction vs 11% if GSM>32	P<0.001 RR 2.2 (95%CI 4.7 to 108
Biasi 1999	96 with a carotid stenosis 50-99%	Incidence of stroke 40% if GSM <50 and 9% if GSM>50	RR 4.6 (95%CI 1.8 to 11.6) P<0.001
Matsagas 2000	38 with a carotid stenosis 50-99%	GSM< 35 associated with a higher incidence of symptoms and cerebral infarction than GSM >35	P<0.0001 and P<0.004
Gronholdt 2001	135 symptomatic and 111 asymptomatic patients with >50% stenosis follow-up 4.4 y	Incidence of stroke was elevated in symptomatic patients with low GSM values in comparison with high GSM	RR 3.1 with high GSM and 80-99% stenosis RR 4.2 with low GSM and 50-79% stenosis RR 7.9 with low GSM and 80-99% stenosis

colour mapping of the whole plaque and of the surface
3 colours according to intensity of plaque echogenicity:
red for low, yellow for intermediate and green for high

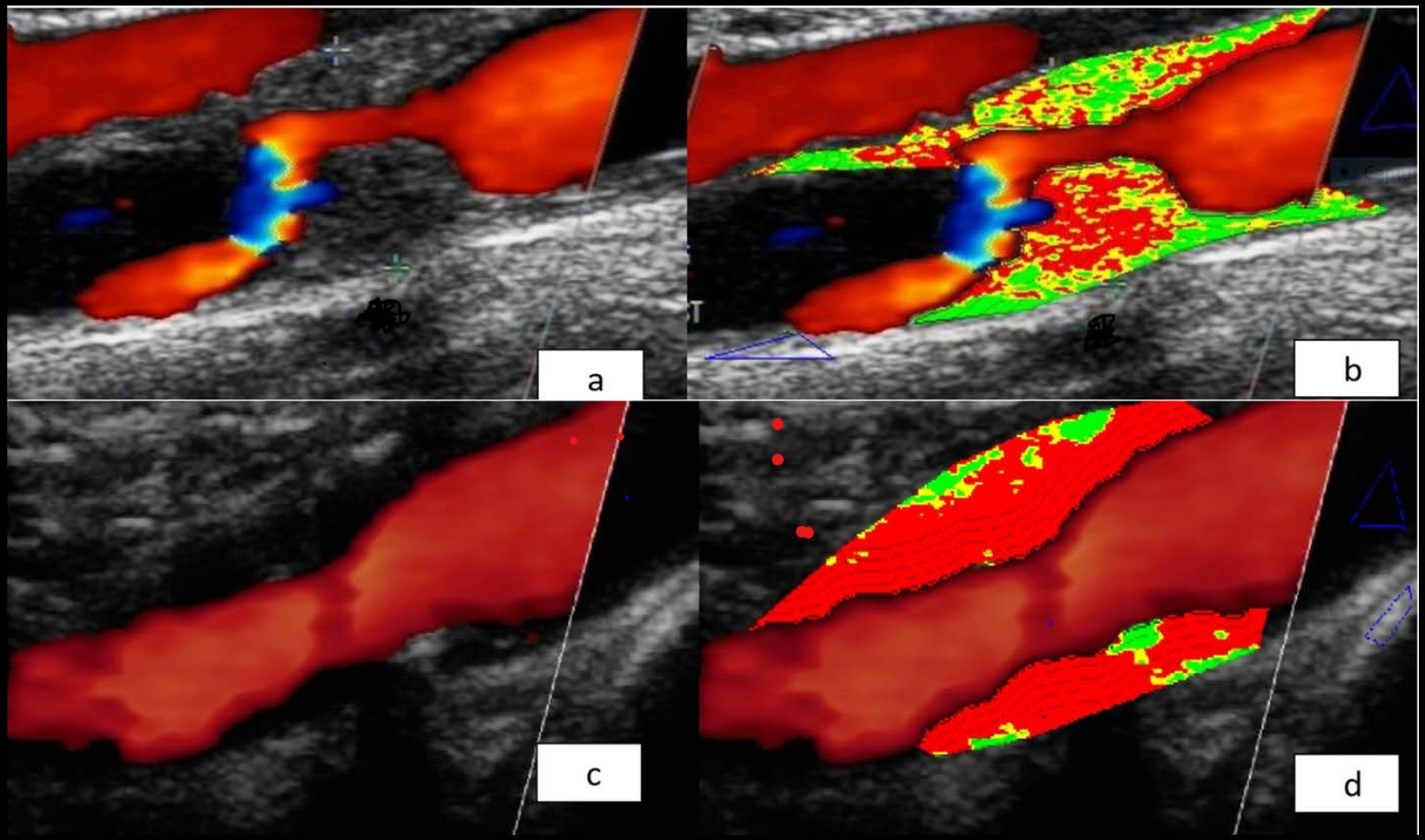




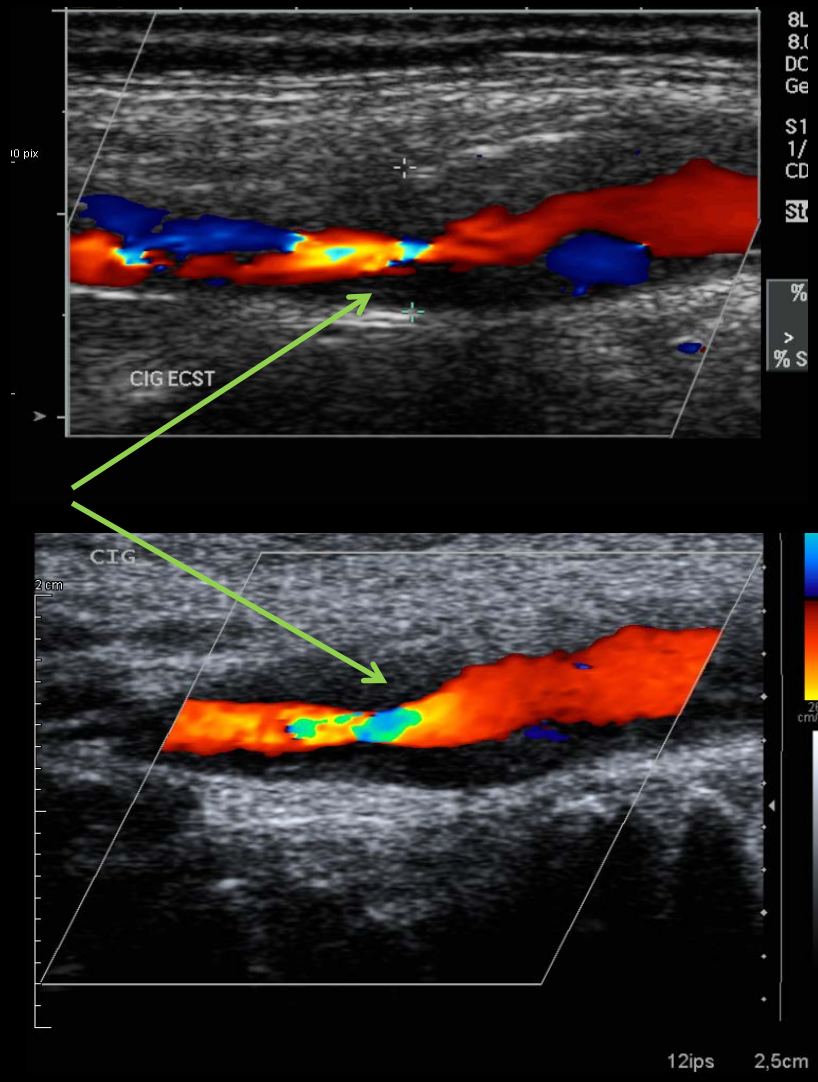


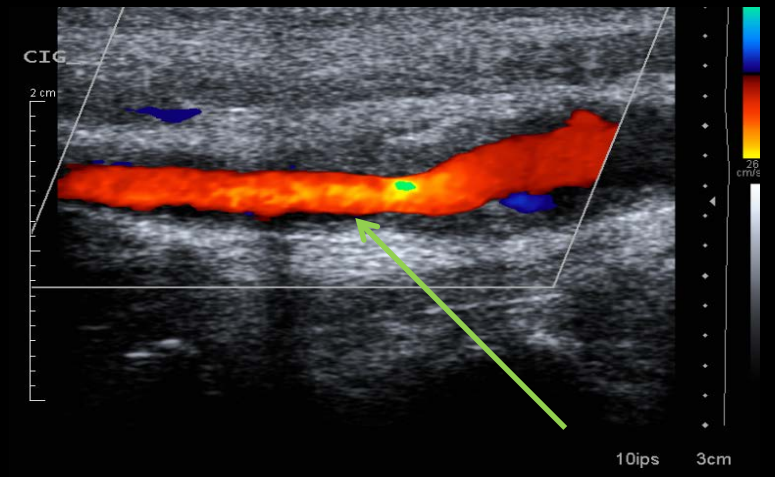


colour mapping of the plaque



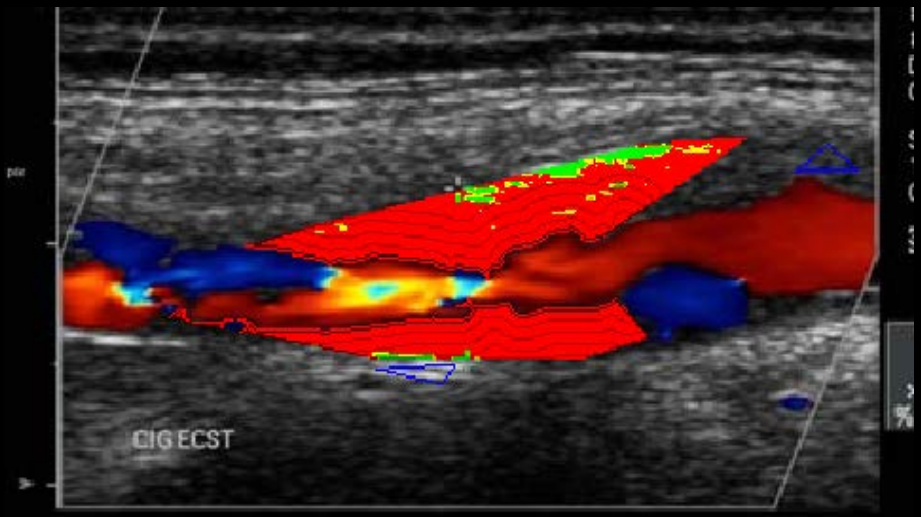
Increase of plaque echogenicity and plaque regression

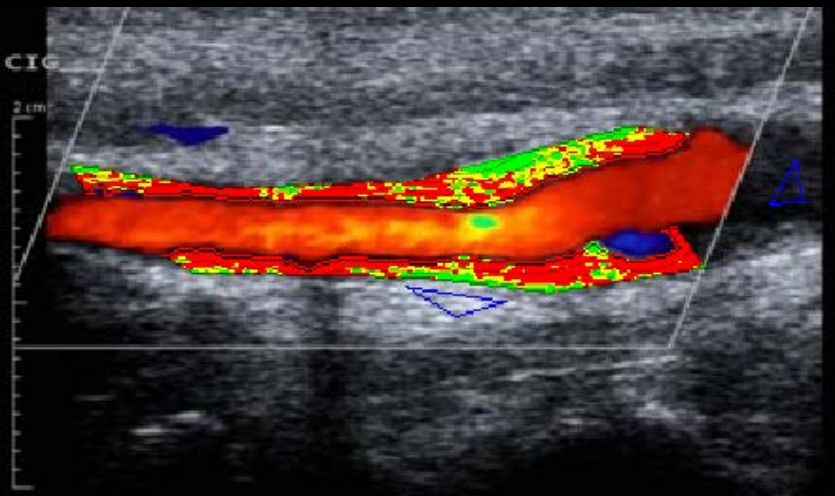


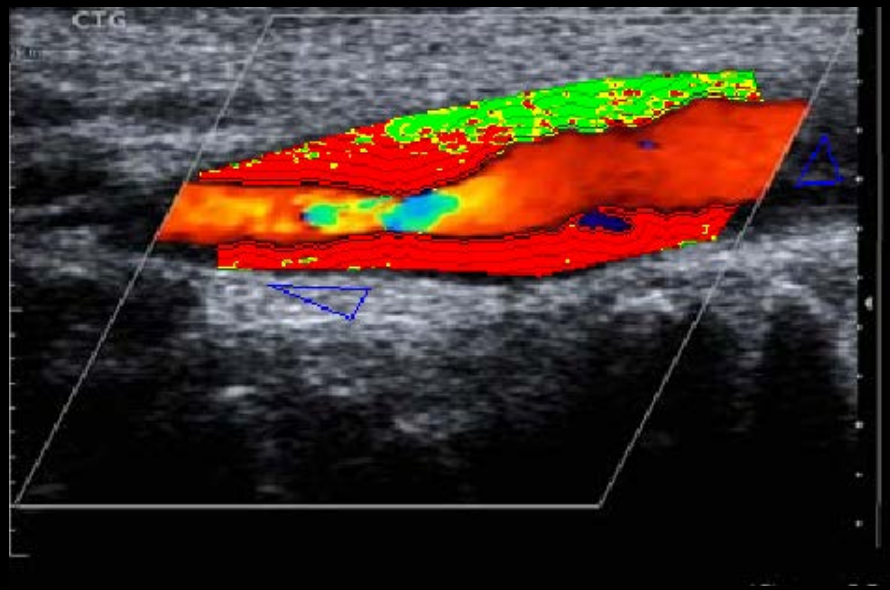


From our center

Increase of plaque echogenicity and plaque regression

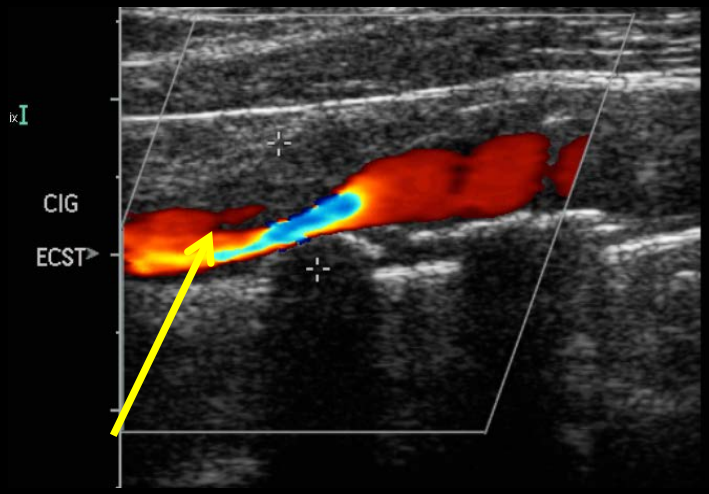


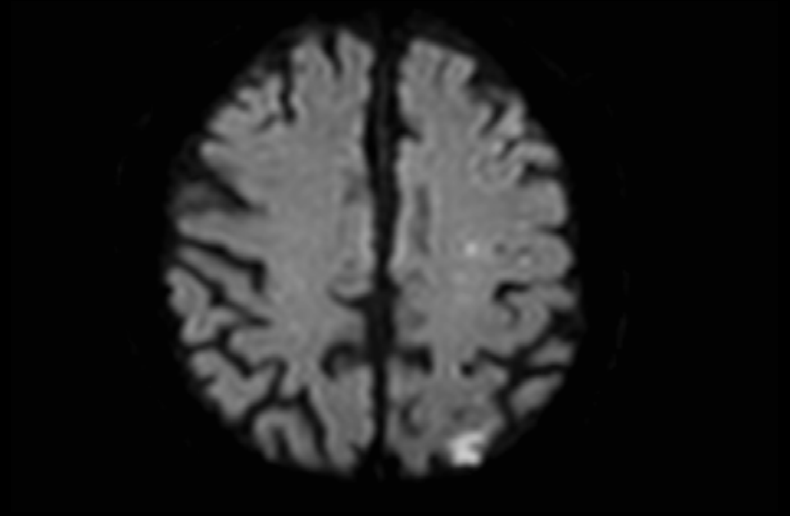




GSM 0 red 92%
GSM 20 red 66%
GSM 52 red 57%

Decrease of plaque echogenicity and plaque progression low echogenicity from feb 2007- oct 2010





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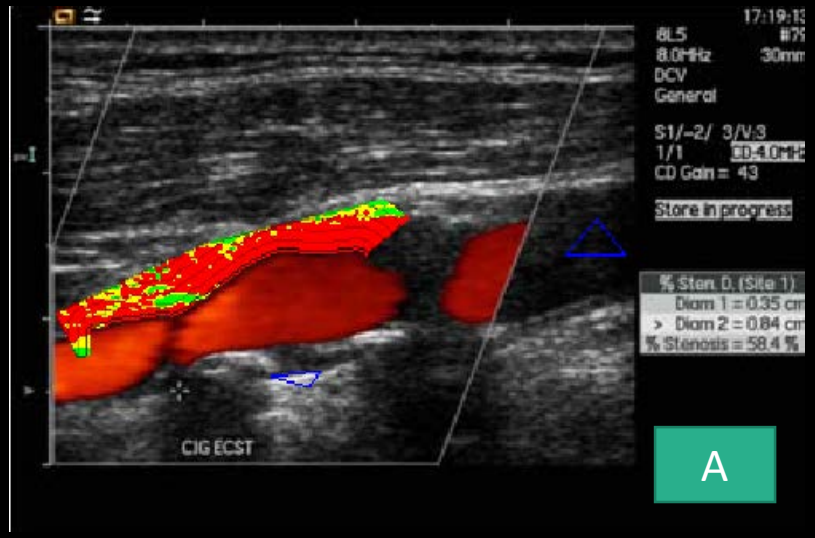
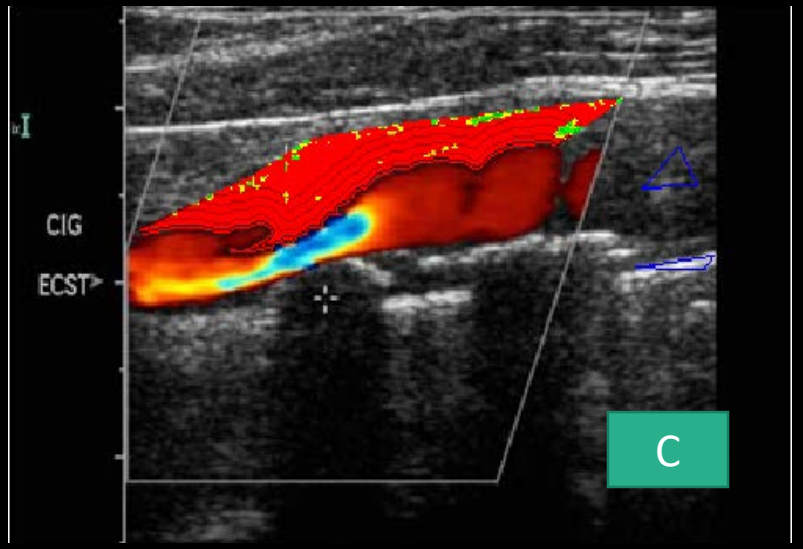
from feb 2007- oct 2010





Plaque A: GSM 41 73% red colour

Plaque B: GSM 0 93% red colour

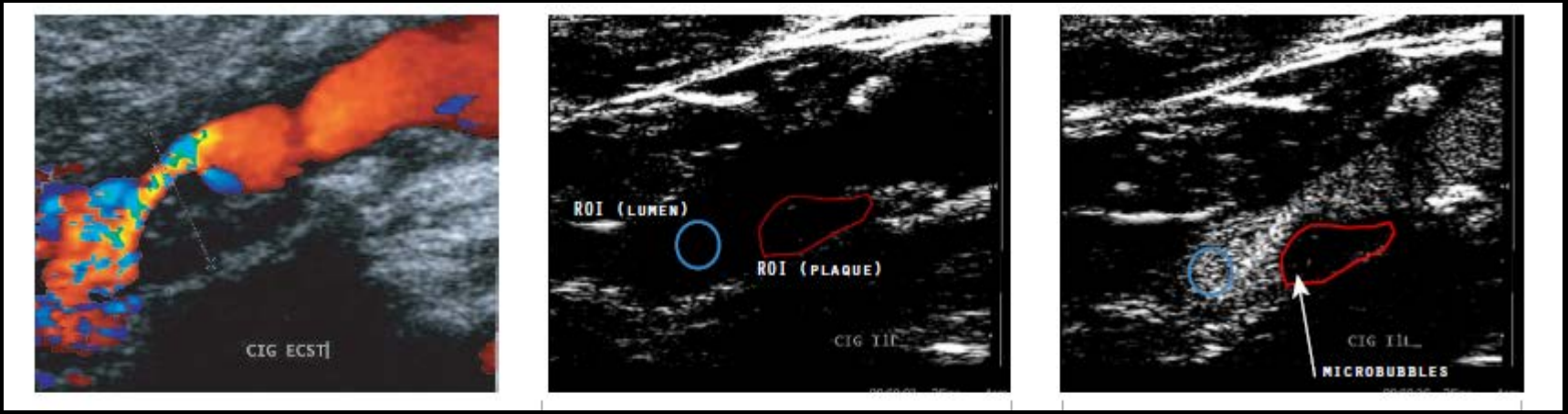
Assessment of plaque neoangiogenesis by means of ultrasound

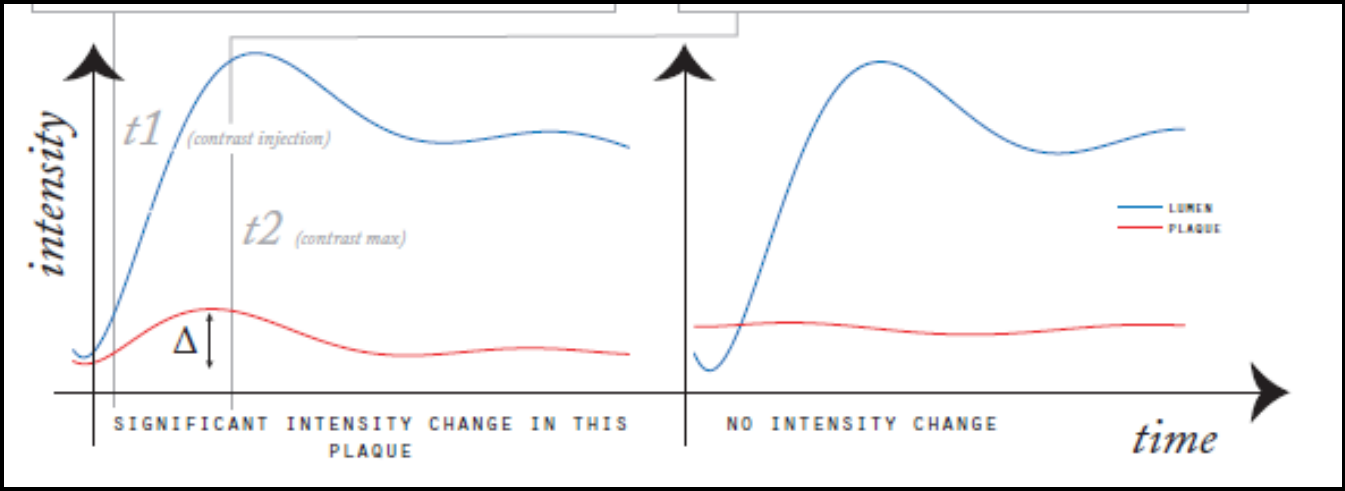
Detection of Carotid Adventitial Vasa Vasorum and Plaque Vascularization With Ultrasound Cadence Contrast Pulse Sequencing Technique and Echo-Contrast Agent

- Adventitial vasa vasorum and plaque vascularization have been established as predictors of unstable lesions in cerebro- and cardiovascular patients.
- Ultrasound contrast agents provide reliable information on tissue perfusion and microcirculation.

Moreno PR,Curr Molecular Medicine, 2006

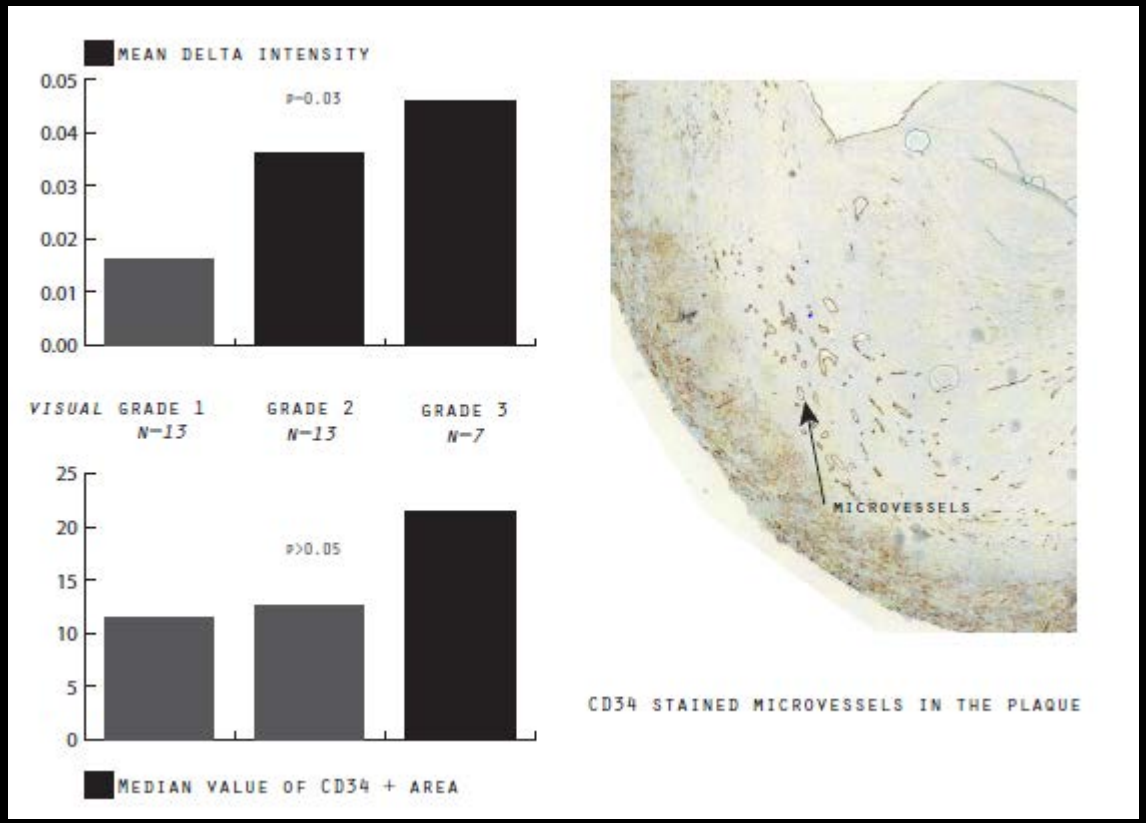
neovascularisation
(specific mode: pulse inverision, use of low mechanical index)





Muller H et al, Ultrasound in Med and Biol 2014

neovascularisation: accuracy of visual analysis



Muller H et al, Ultrasound in Med and Biol 2014

Detection of Carotid Adventitial Vasa Vasorum and Plaque Vascularization With Ultrasound Cadence Contrast Pulse Sequencing Technique and Echo-Contrast Agent

- Carotid contrast ultrasound imaging appears to be an emerging technic for identifying plaque angiogenesis

Multimodal ultrasound (n=98)

- plaque surface morphology (smooth, irregular, ulcerated), intraplaque neovascularization and degree of stenosis
- follow-up of one year , each parameter predicted independently the occurrence of ischemic vascular events.
- 98 patients (75 men, mean age 67 ± 8 years) were included
    - 50 were symptomatic and 48 were asymptomatic
    - plaque surface morphology (PSM): OR 2.99, 95% CI 1.26-7.12, *P* = 0.013
    - intraplaque neovascularization (IPN) grades: OR 3.23, 95% CI 1.77-5.89, *P*<0.001
    - carotid stenosis degree (CSD): OR 4.12, 95% CI 1.47-11.55, *P* = 0.007
    - →Nomogram: area under the ROC curve was 0.85 (95% CI 0.77-0.92)

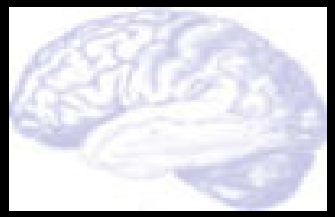
Li, Acta Radiol 2022

Conclusions

- High resolution ultrasound and new ultrasound developments provide detailed information regarding different aspects of the plaque
- all these methods have the ability to distinguish between stable and unstable plaques

Conclusions

- overall computerised methods provide a more accurate and a more operator-independant assessment of plaque morphology with better inter- and intraobserver κ values
- the challenge of these techniques is to reach a level of accuracy to dictate treatment options for the individual patient
- for this more prospective large studies are still needed in particular these studies should consider the different aspects (echogenicity/structure and surface) of plaque morphoglogy as variables in order to determine independant predictive factors

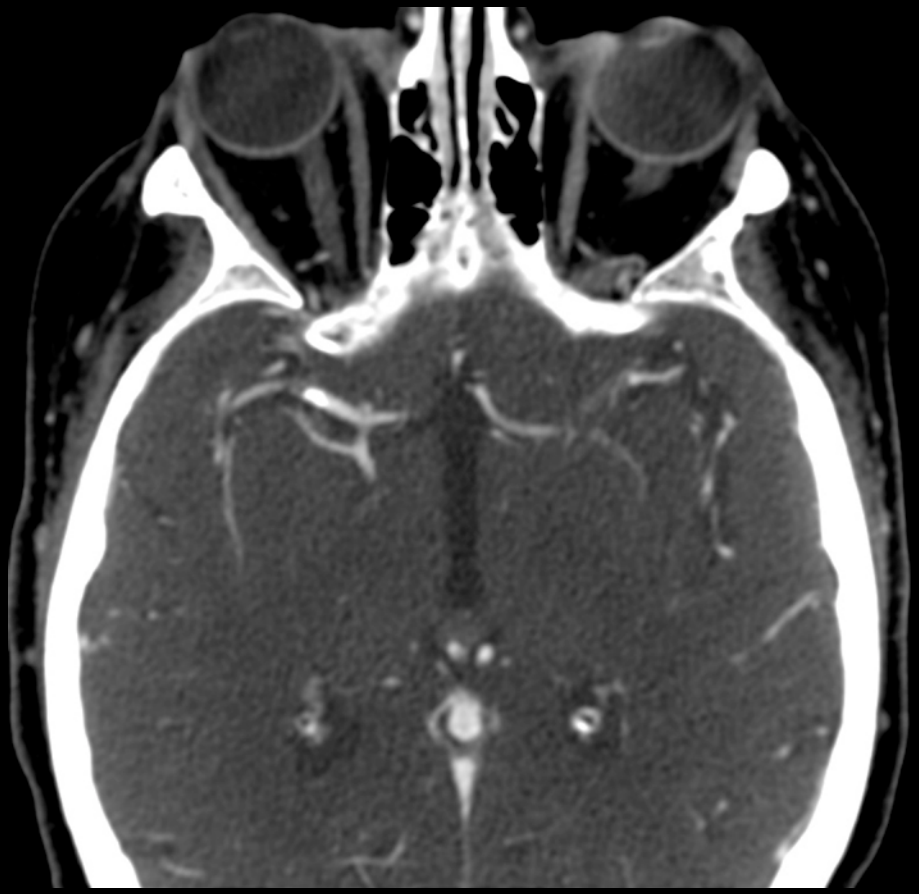


thank you for your attention

1st case

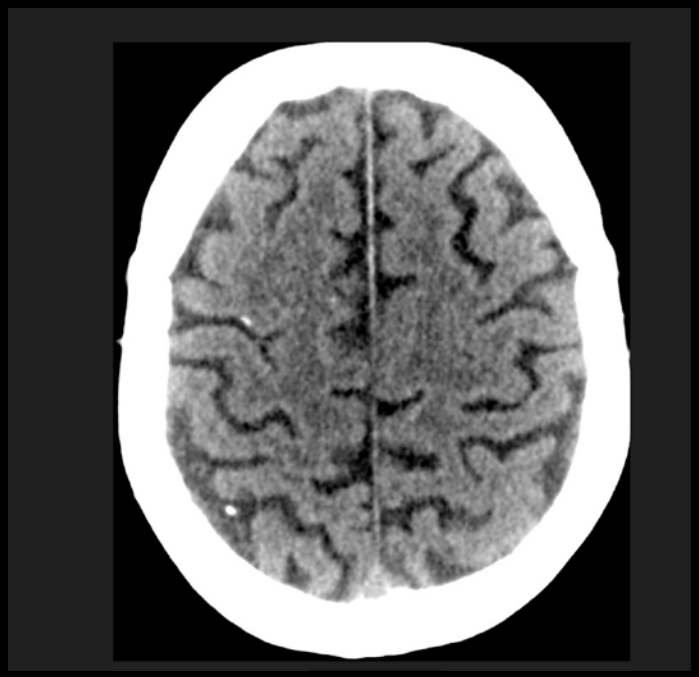
- A 66-year old female with a history of arterial hypertension and hypercholesterolemia presents to the emergency department because of acute onset of vertigo associated with dysarthria and left-sided hemiparesis.
- computed tomography is performed after 2 hours after beginning of symptoms

Brain Ct-scan

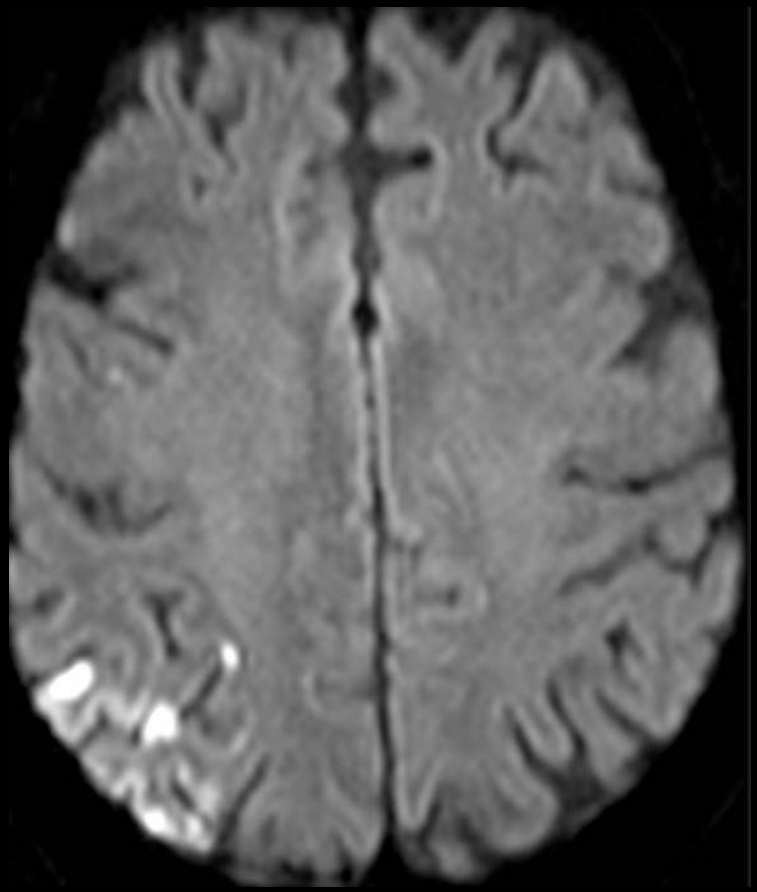


Brain CT-scan

«salted bretzel sign»



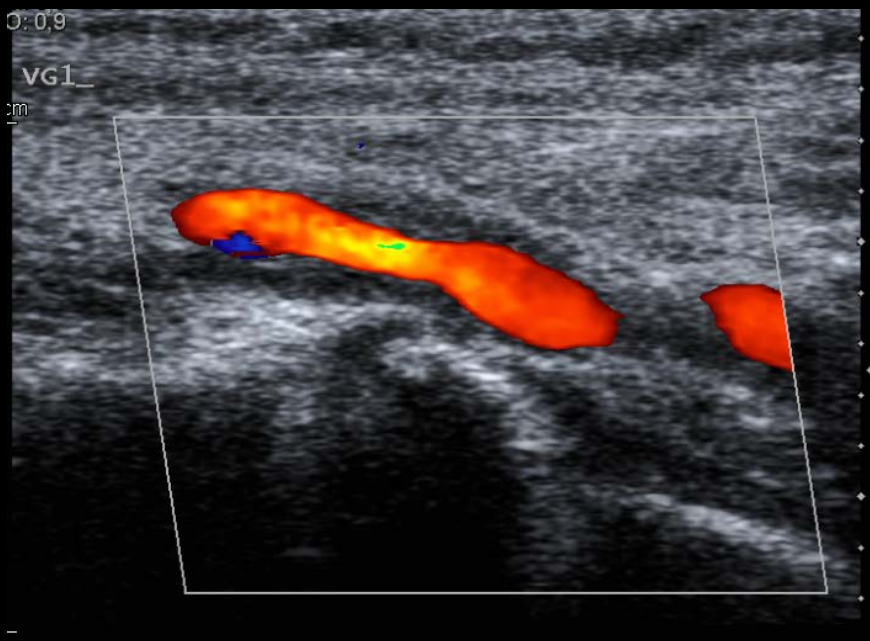
Brain MRI



2nd case

- 84 years old patient, with a history of high bloood pressure, reports several episodes of diplopia
- Brain MRI showas signs of leucoencephalopathy
- Exocranial vessels were not investigated

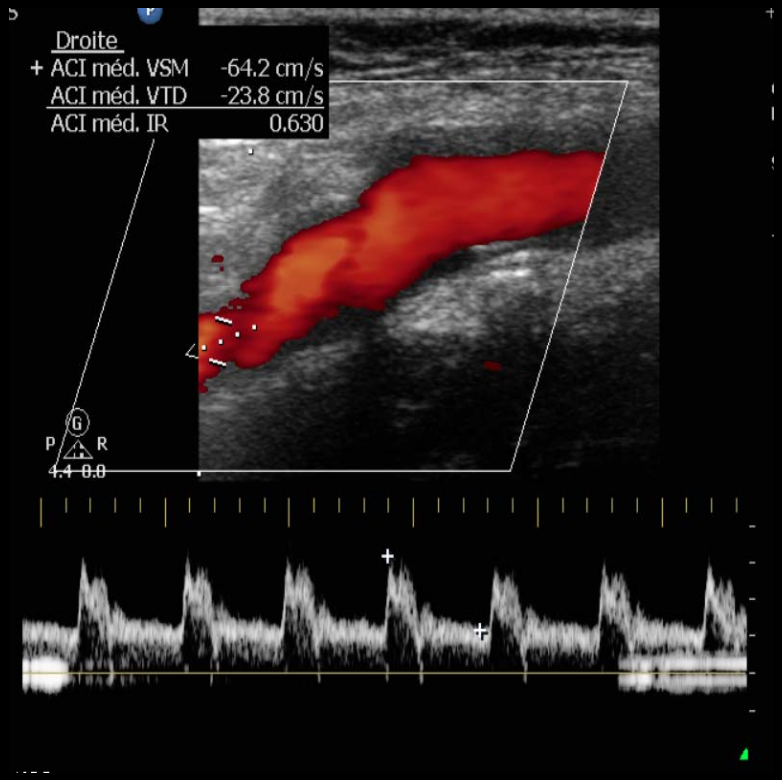
left vertebral artery

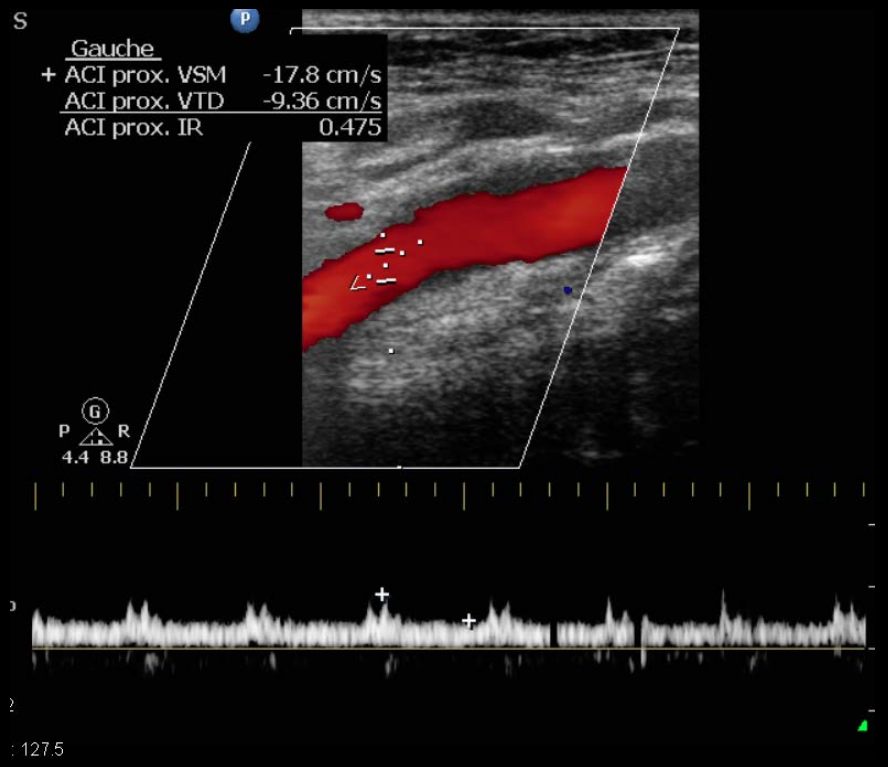


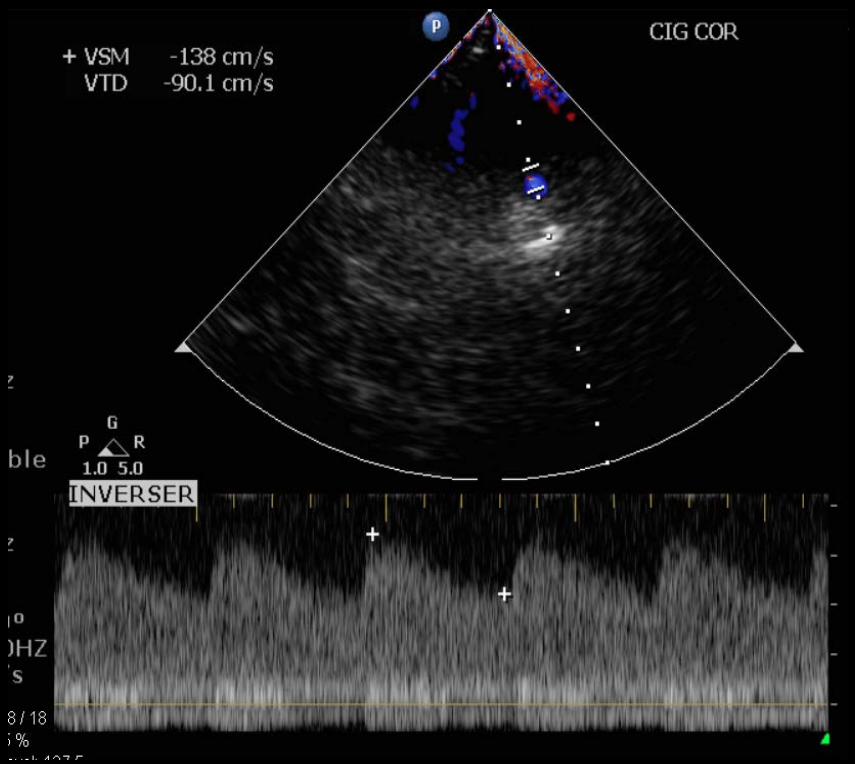
3rd case

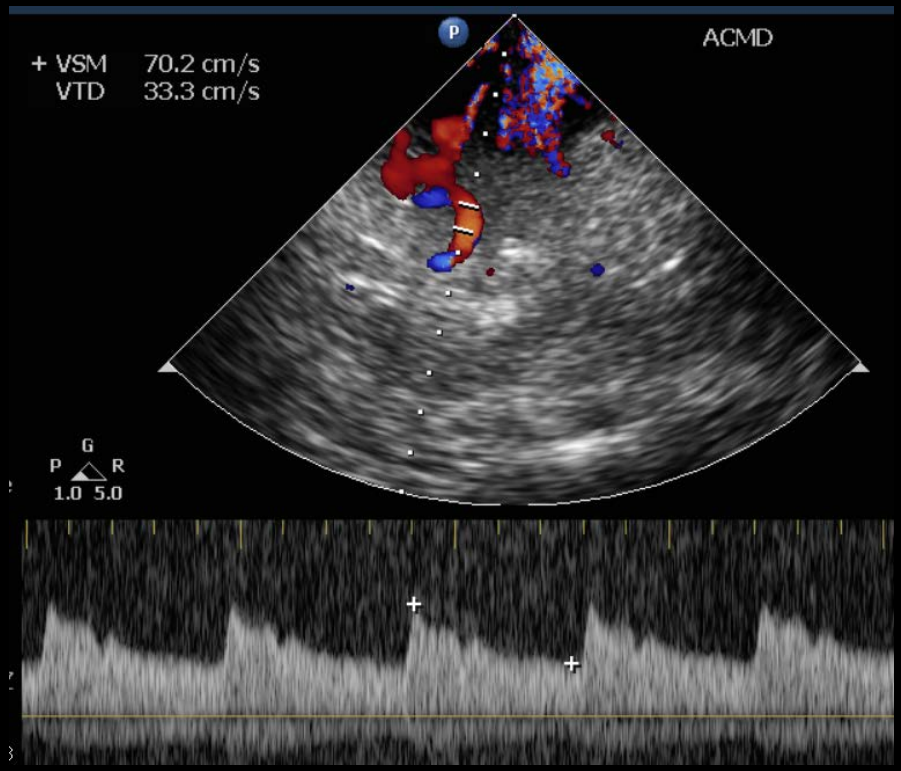
24 years old lady, with no medical history, develops several episode of peresthesia on her right face and arm .

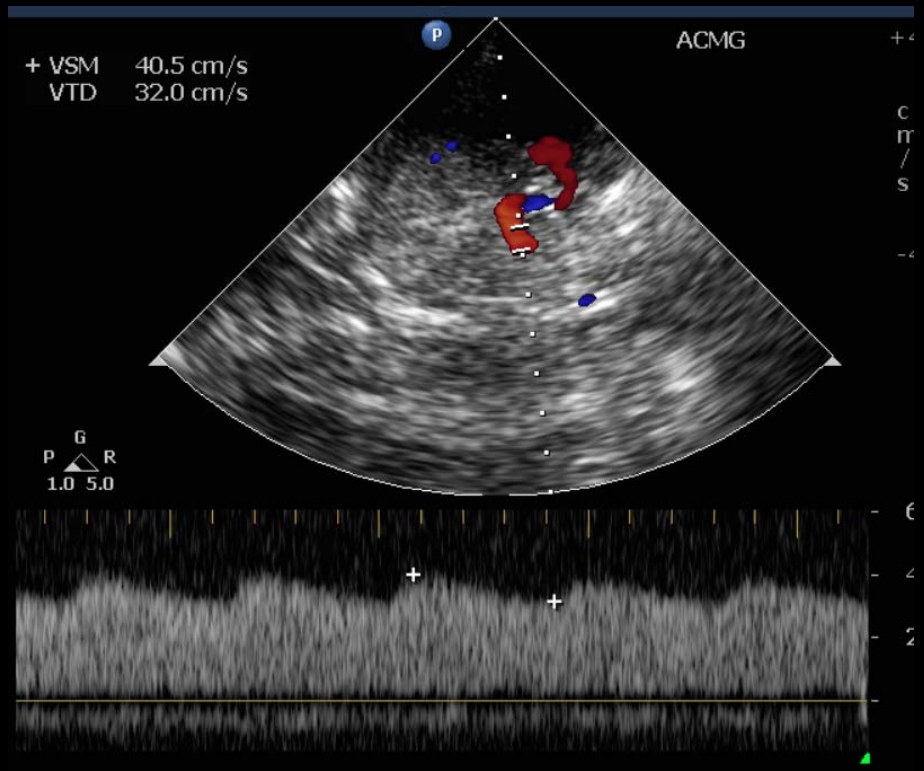
She feels some discomfort on her right orbital region


Droite
+ ACI méd. VSM -64.2 cm/s
ACI méd. VTD -23.8 cm/s
ACI méd. IR 0.630
P R
4.4 8.8


Gauche
+ ACI prox. VSM -17.8 cm/s
ACI prox. VTD -9.36 cm/s
ACI prox. IR 0.475
P R
4.4 8.8
127.5


+ VSM -138 cm/s
VTD -90.1 cm/s
CIG COR
P
G
P R
1.0 5.0
INVERSER


+ VSM 70.2 cm/s
VTD 33.3 cm/s
ACMD
P
G
P R
1.0 5.0


+ VSM 40.5 cm/s
VTD 32.0 cm/s
ACMG
P
G
P R
1.0 5.0

Thank you for your attention