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Houston, Texas

Noninvasive characterization of high-risk ICAS plaque & patient

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Presenter Disclosure Information

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Non-invasive characterization of high-risk ICAS plaque & patient

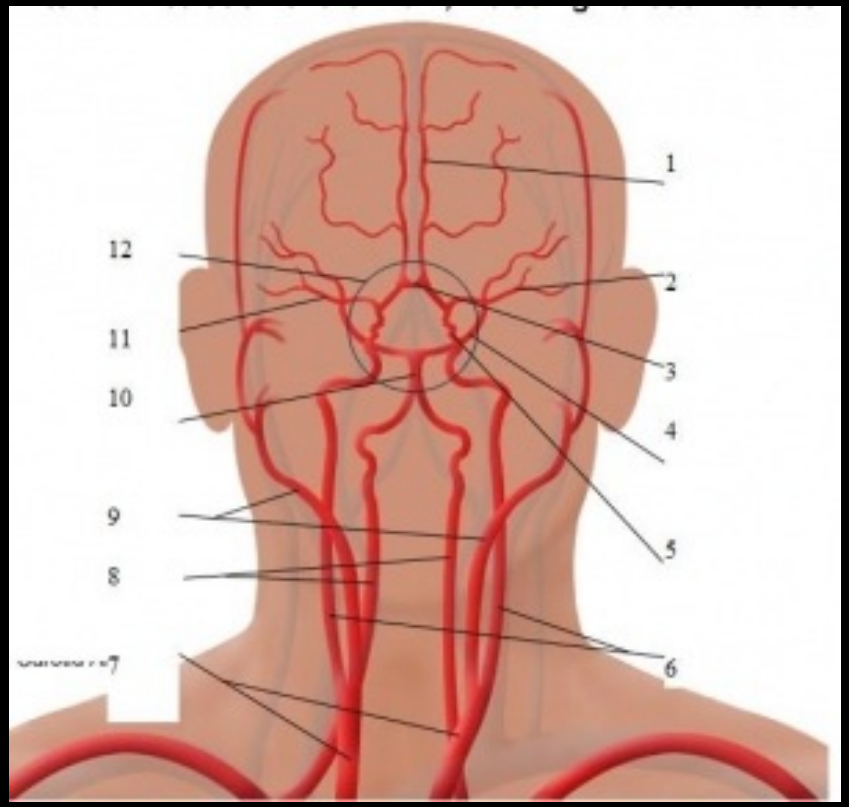
FINANCIAL DISCLOSURE:

No disclosures to be done relevant to attendance and content of talks in 2013 SVIN Conference.

UNLABELED/UNAPPROVED USES DISCLOSURE:

None

Intracranial Atherosclerosis



A major cause of stroke worldwide

Translational research priorities

- Intracranial vulnerable plaque characterization
- Vulnerable ICAS patient characterization
- Monitoring basic processes and response to therapies

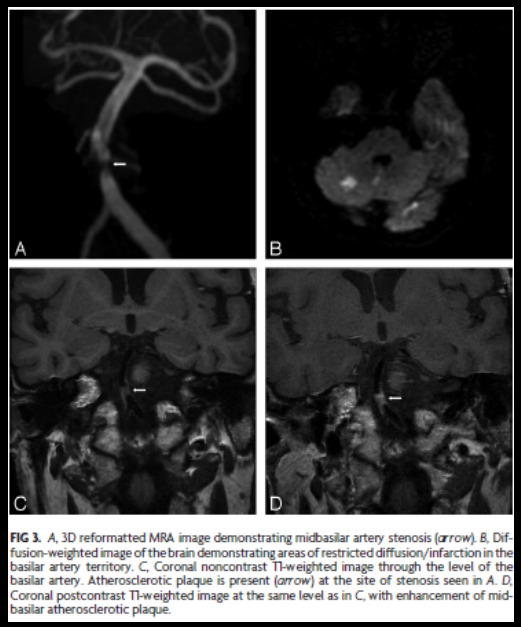
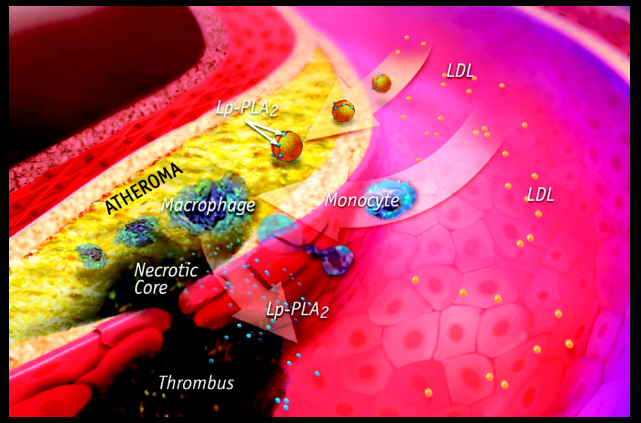
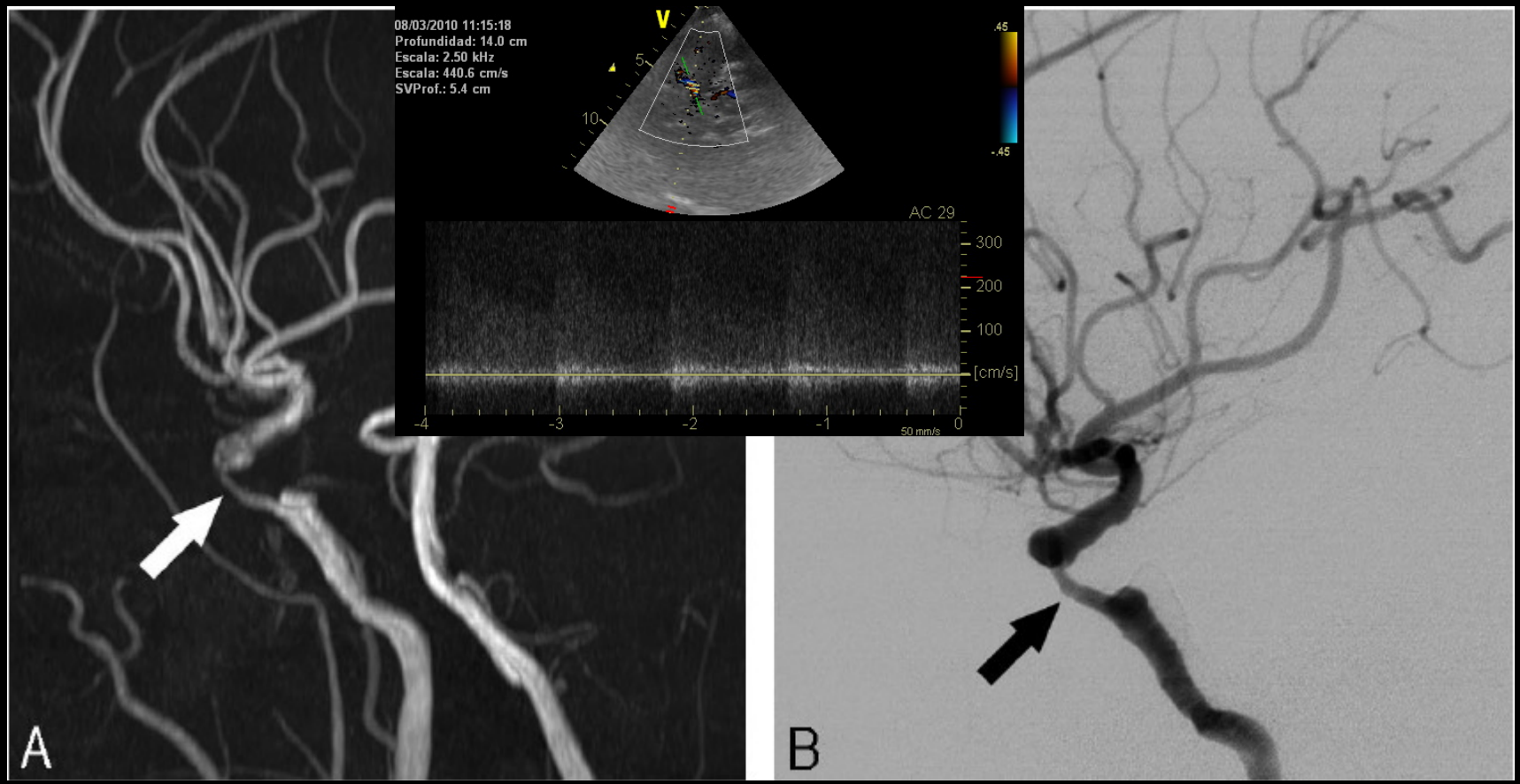


FIG 3. *A*, 3D reformatted MRA image demonstrating midbasilar artery stenosis (*arrow*). *B*, Diffusion-weighted image of the brain demonstrating areas of restricted diffusion/infarction in the basilar artery territory. *C*, Coronal noncontrast TI-weighted image through the level of the basilar artery. Atherosclerotic plaque is present (*arrow*) at the site of stenosis seen in *A*. *D*, Coronal postcontrast TI-weighted image at the same level as in *C*, with enhancement of midbasilar atherosclerotic plaque.



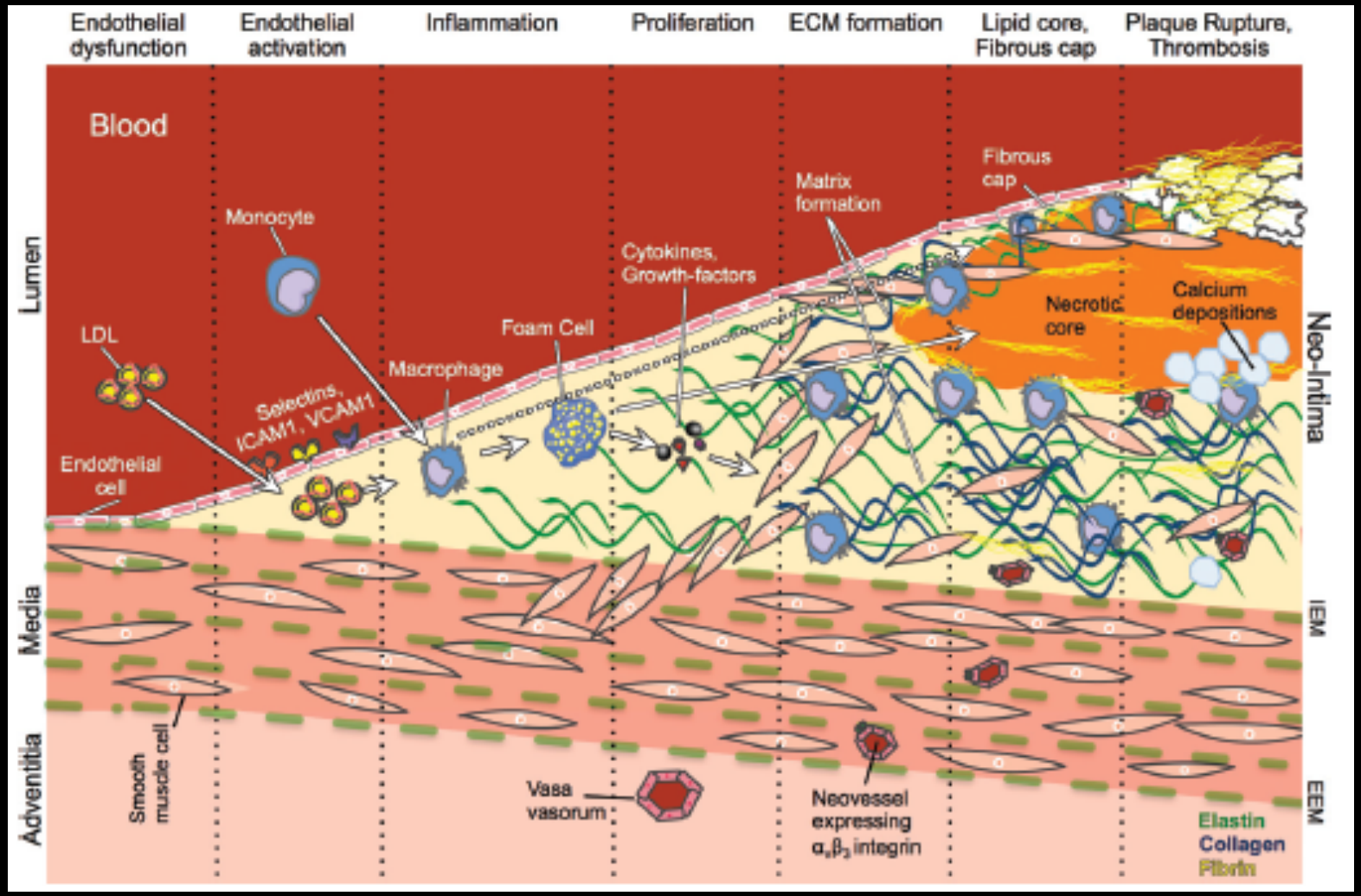
Classical approach

Focus on intracranial stenosis (Angiographic & Haemodinamic)



Limitations of classical approach

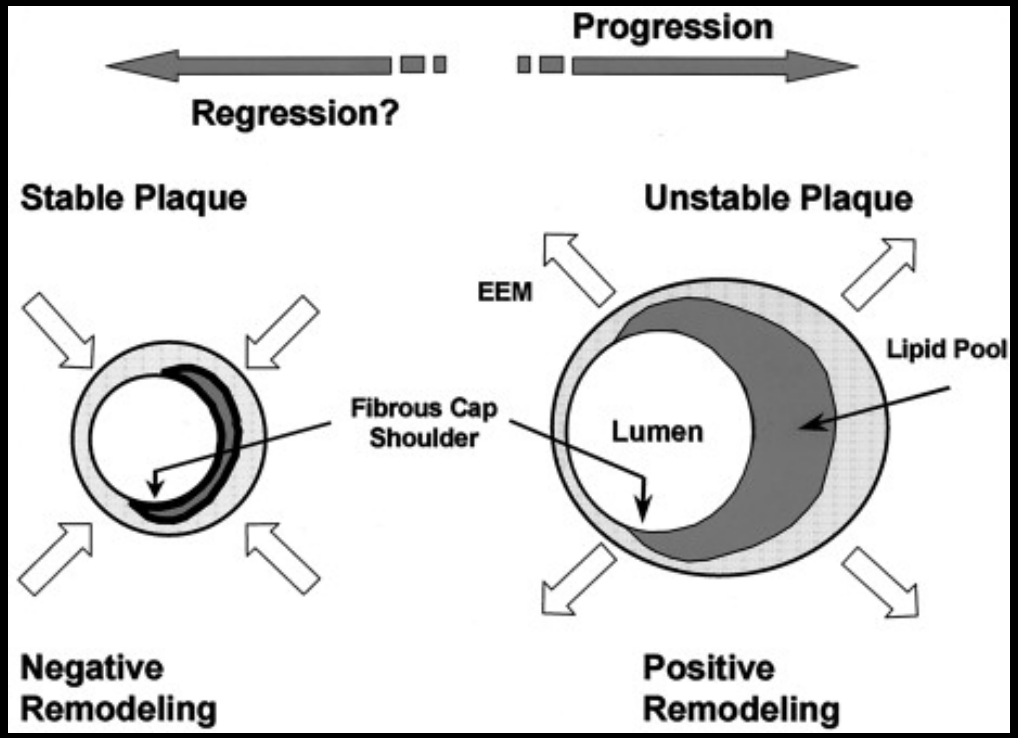
Restricted to advanced and stenoocclusive stage

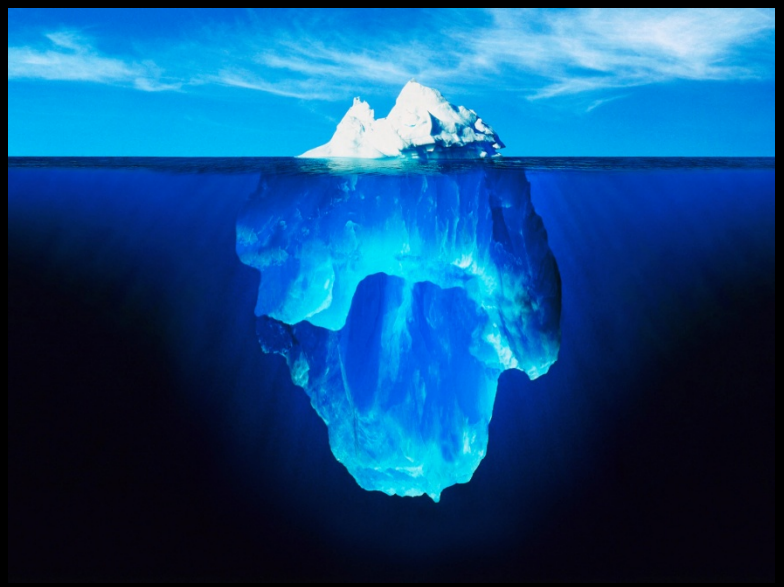


Makowski, Radiology 2013

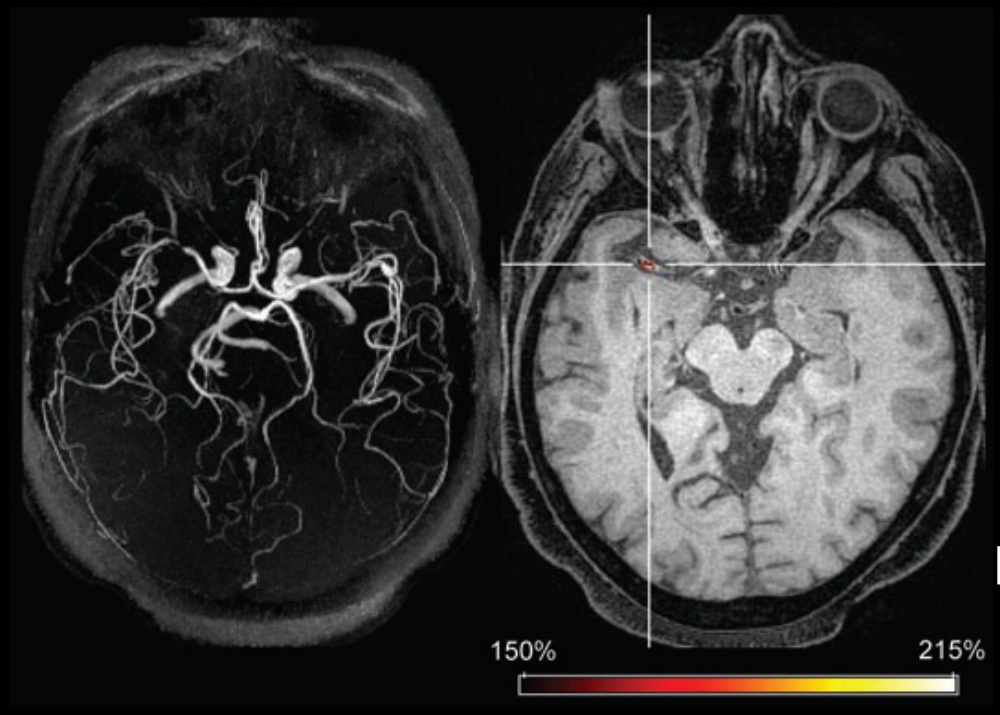
Limitations of classical approach

Arterial remodelling and plaque composition

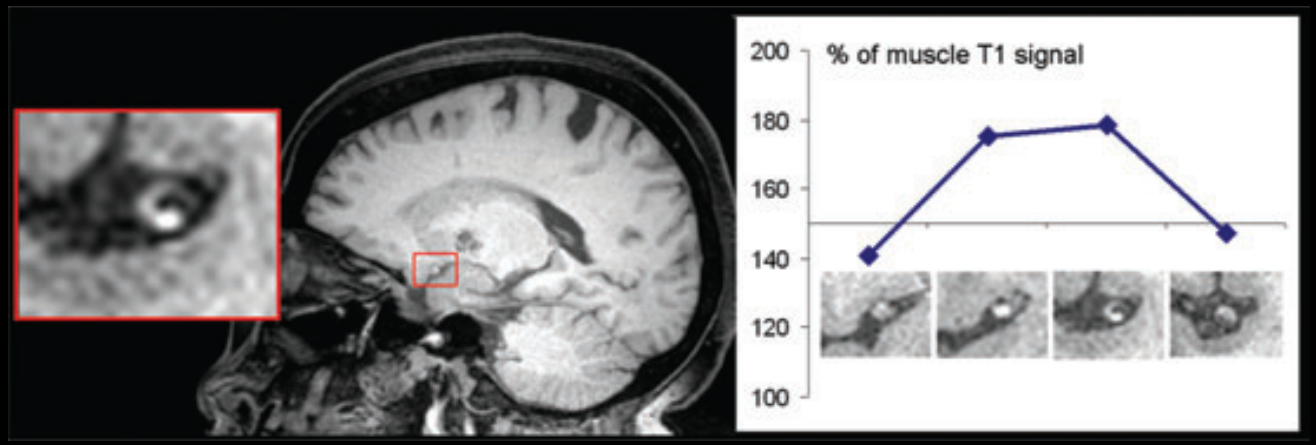




New approach to ICAS: Plaque imaging

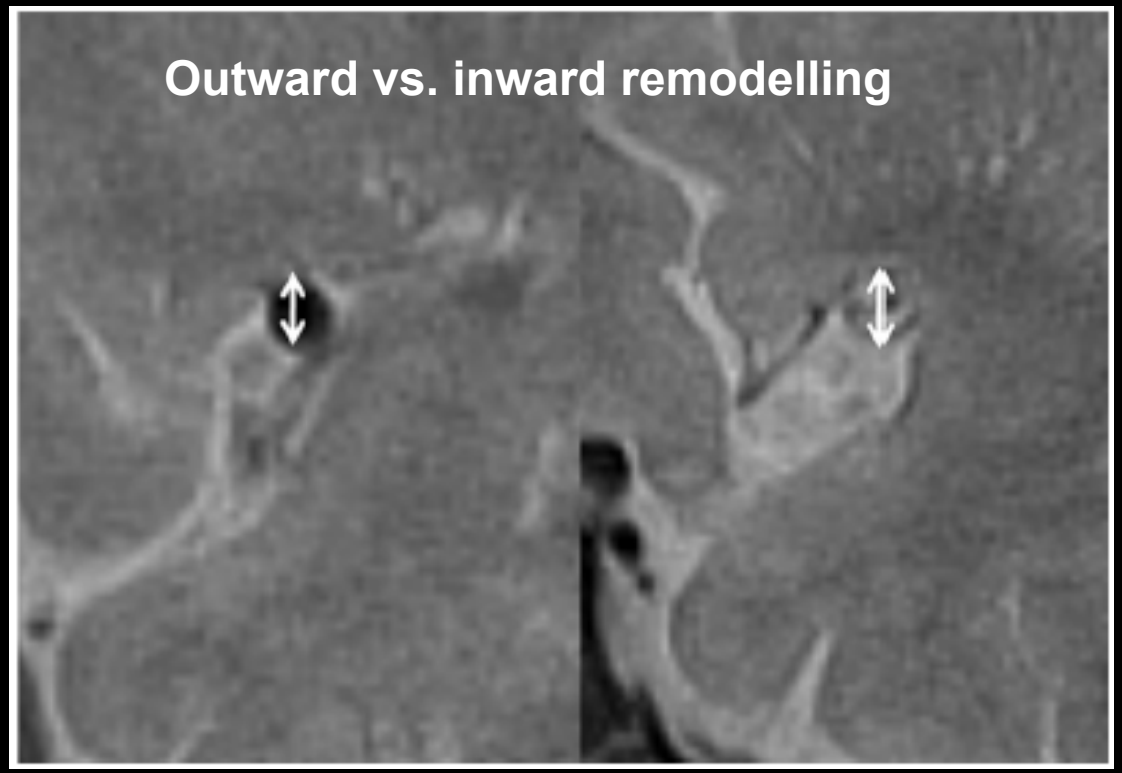


Plaque morphology & activity



Turan et al, J Neuroimaging 2010

Vulnerable plaque characterization



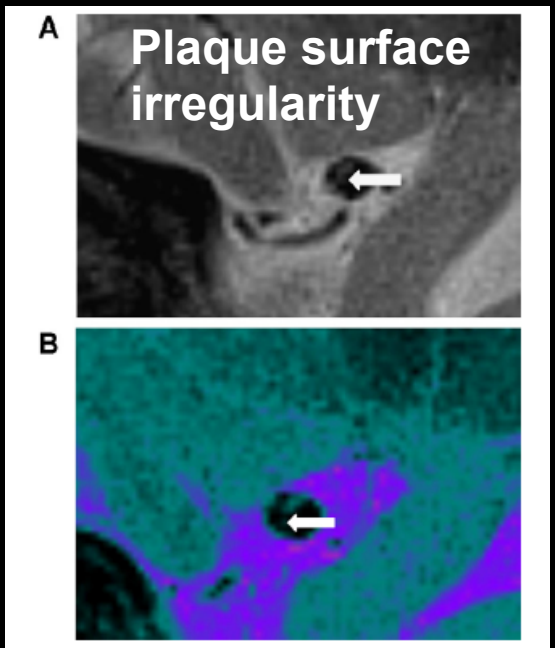


Fig. 4. Plaque surface irregularity on a color map of high resolution MRI in a 47-year-old man with multifocal infarctions of the right middle cerebral artery territory. (A) T2-weighted high resolution MR imaging shows the ill-defined plaque margin (arrow). (B) Color map imaging of T2-weighted high resolution MR shows the luminal irregularity of the plaque's inner margin, suggestive of plaque surface irregularity (arrow).

Table 3
Predictors of symptomatic disease with MCA stenosis.

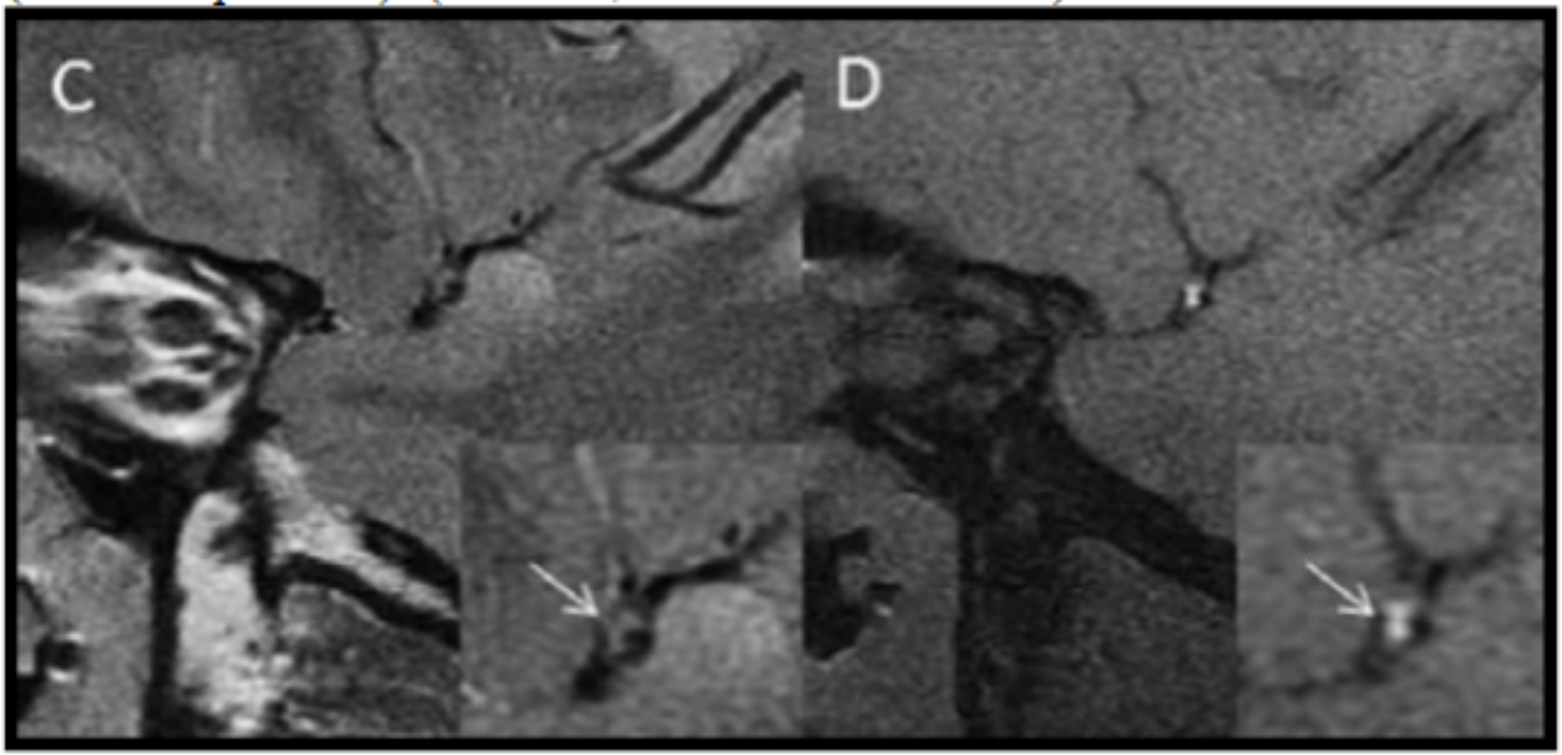
	Univariate regression		Multivariate regression	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Degree of MCA stenosis (%)	1.07 [1.01–1.15]	0.02	1.10 [1.00–1.22]	0.04
Remodeling ratio	1.11 [1.03–1.20]	<0.001	–	–
Outward remodeling	5.50 [1.15–26.41]	0.03	–	–
Inward remodeling	0.05 [0.01–0.45]	<0.001	0.02 [0.001–0.48]	0.01
Plaque surface irregularity	9.33 [1.52–57.66]	0.008	13.06 [0.84–203.84]	0.07

OR = odds ratio; CI = confidence interval; MCA = middle cerebral artery. The univariate columns show results for each variable fit separately while the multivariate columns show results from a single model fitting all variables simultaneously.

Chung et al, Eur J Radiol 2012

Vulnerable plaque characterization

Sagittal T2 (panel C) and T1-weighted fat-suppressed (panel D) imaging of symptomatic MCA. Lower right corner shows central region magnified. IPH is defined as bright signal on T1 fat-suppressed images (arrow in panel D). (Xu et al, Annals Neuro 2012)



Intraplaque hemorrhage more frequent in symptomatic MCA plaques (19.6% vs 3.2%)

Vulnerable plaque characterization

Intracranial Atherosclerotic Plaque Enhancement in Patients with Ischemic Stroke

M. Skarpathiotakis, D.M. Mandell, R.H. Swartz, G. Tomlinson, and D.J. Mikulis

AJNR Am J Neuroradiol 34:299–304 Feb 2013

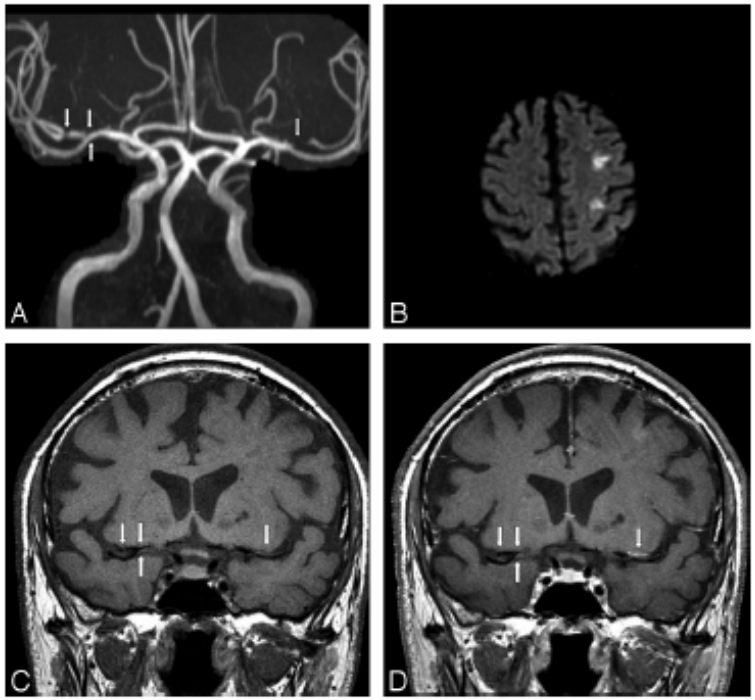


FIG 1. *A*, 3D reformatted MRA image demonstrating bilateral MCA stenoses (*arrows*). *B*, Diffusion-weighted image of the brain demonstrating areas of restricted diffusion/infarction in the left MCA territory. *C*, Coronal noncontrast T1-weighted image through the level of the MCAs. Atherosclerotic plaque is present in both the right MCA and left MCA (*arrows*) at the site of stenoses seen in *A*. *D*, Coronal postcontrast T1-weighted image at the same level as in *C*, with enhancement of the left MCA atherosclerotic plaque but not of the plaques on the right.

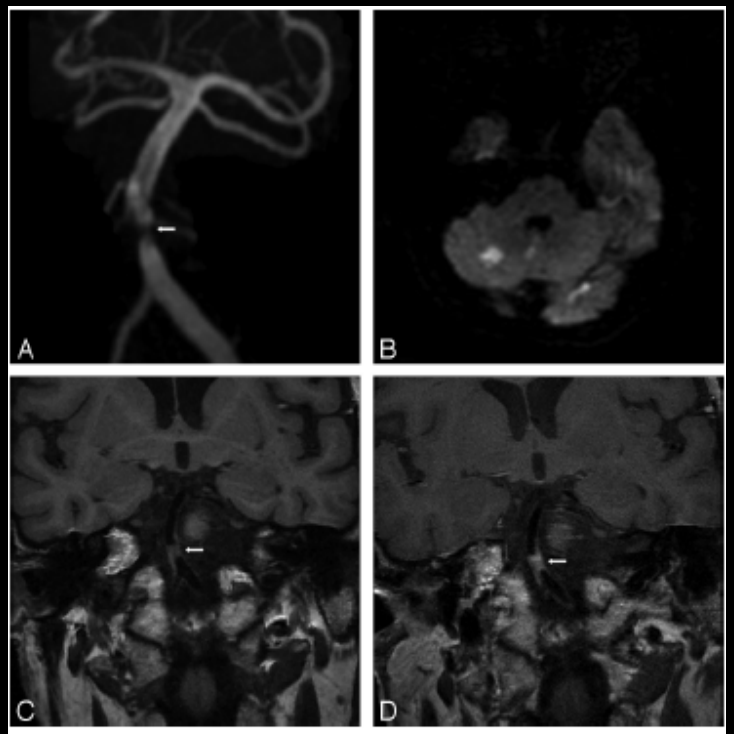


FIG 3. *A*, 3D reformatted MRA image demonstrating midbasilar artery stenosis (*arrow*). *B*, Diffusion-weighted image of the brain demonstrating areas of restricted diffusion/infarction in the basilar artery territory. *C*, Coronal noncontrast T1-weighted image through the level of the basilar artery. Atherosclerotic plaque is present (*arrow*) at the site of stenosis seen in *A*. *D*, Coronal postcontrast T1-weighted image at the same level as in *C*, with enhancement of midbasilar atherosclerotic plaque.

Correlation with histology

Intracranial-Derived Atherosclerosis Assessment: An In Vitro Comparison between Virtual Histology by Intravascular Ultrasonography, 7T MRI, and Histopathologic Findings

S. Majidi, J. Sein, M. Watanabe, A.E. Hassan, P.-F. Van de Moortele, M.F.K. Suri, H.B. Clark, and A.J. Qureshi

AJNR 2013

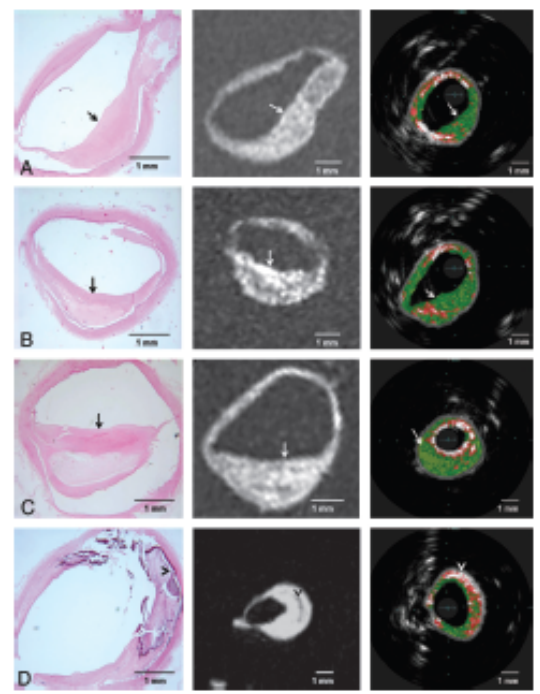


FIG 3. Four different histopathologic sections of intracranial vessels with atherosclerotic plaque and their corresponding 3D SPACE MR imaging (in the middle) and VH-IVUS (on the right) images. Fibrous areas (arrows) and attenuated calcium (arrowheads) consistently visualized as areas with hyperintense and hypointense signals in MR imaging, respectively.

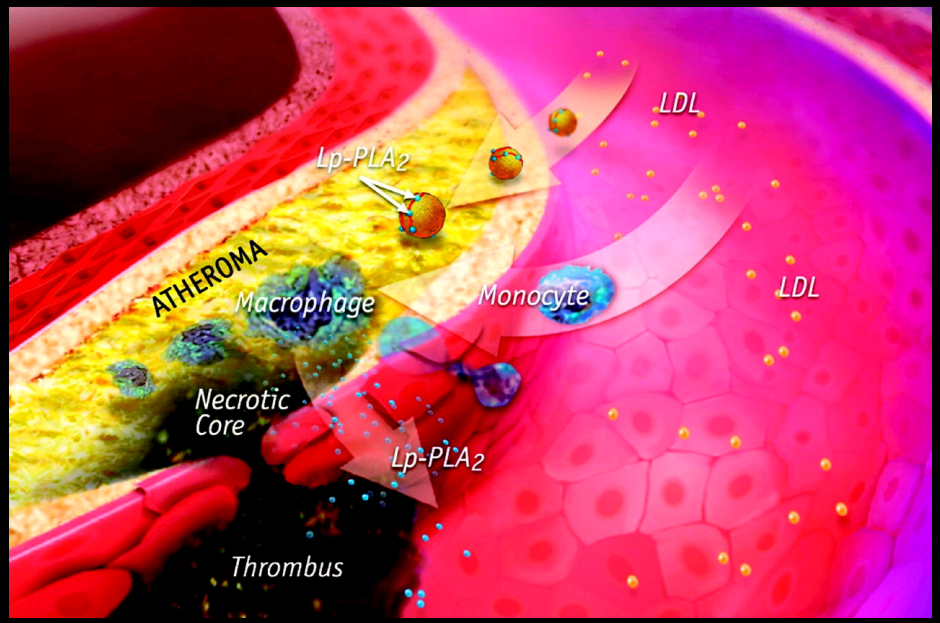
Very good identifying presence of plaque

Still limitations regarding plaque components

Basic mechanisms?

In vivo monitoring of basic mechanisms and molecular pathways determining high-risk ICAS

- Inflammatory infiltration, Thrombogenic potential
- Response to therapies: Plaque stabilization and regression
- Development of collateral circulation (Angiogenesis, Arteriogenesis)



Biomarkers: Inflammation

C-Reactive Protein Predicts Further Ischemic Events in First-Ever Transient Ischemic Attack or Stroke Patients With Intracranial Large-Artery Occlusive Disease

Juan F. Arenillas, MD; José Álvarez-Sabín, MD, PhD; Carlos A. Molina, MD, PhD; Pilar Chacón, MD, PhD; Joan Montaner, MD, PhD; Álex Rovira, MD; Bernardo Ibarra, MD; Manuel Quintana

Stroke 2003

Progression of Symptomatic Intracranial Large Artery Atherosclerosis Is Associated With a Proinflammatory State and Impaired Fibrinolysis

Juan F. Arenillas, MD, PhD; José Álvarez-Sabín, MD, PhD; Carlos A. Molina, MD, PhD; Pilar Chacón, MD, PhD; Israel Fernández-Cadenas, PhD; Marc Ribó, MD, PhD; Pilar Delgado, MD, PhD; Marta Rubiera MD, PhD; Anna Penalba; Alex Rovira, MD; Joan Montaner, MD, PhD

Stroke 2008

Association between Inflammatory Biomarkers and Progression of Intracranial Large Artery Stenosis after Ischemic Stroke

Kanako Shimizu, MD, Kana Shimomura, MD, Yoshiaki Tokuyama, MD, Kenzo Sakurai, MD, PhD, Kenji Isahaya, MD, PhD, Satoshi Takaishi, MD, PhD, Bunta Kato, MD, PhD, Noriko Usuki, MD, Takahiro Shimizu, MD, Koji Yamada, MD, PhD, and Yasuhiro Hasegawa, MD, PhD

Journal of Stroke and Cerebrovascular Diseases, Vol. 22, No. 3 (April), 2013: pp 211-217

Biomarkers: Inflammation

Bio iS

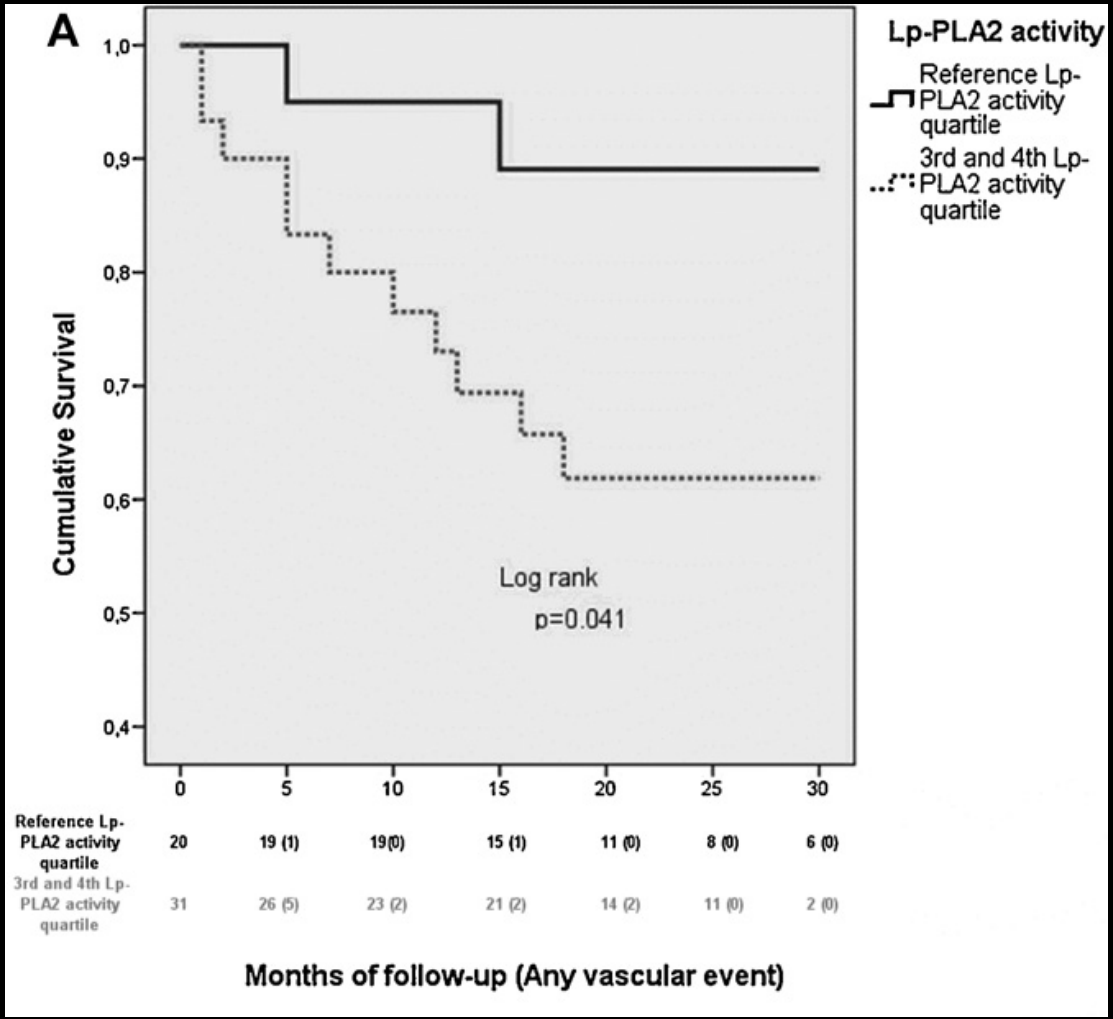
BIOSIS

Biomarkers of Ischemic Outcomes in Symptomatic Intracranial Stenosis

NIH Grant# 1 R01 NS064162

PI: Michael Frankel, MD
Institution: Emory University

Biomarkers: Inflammation LpPLA2



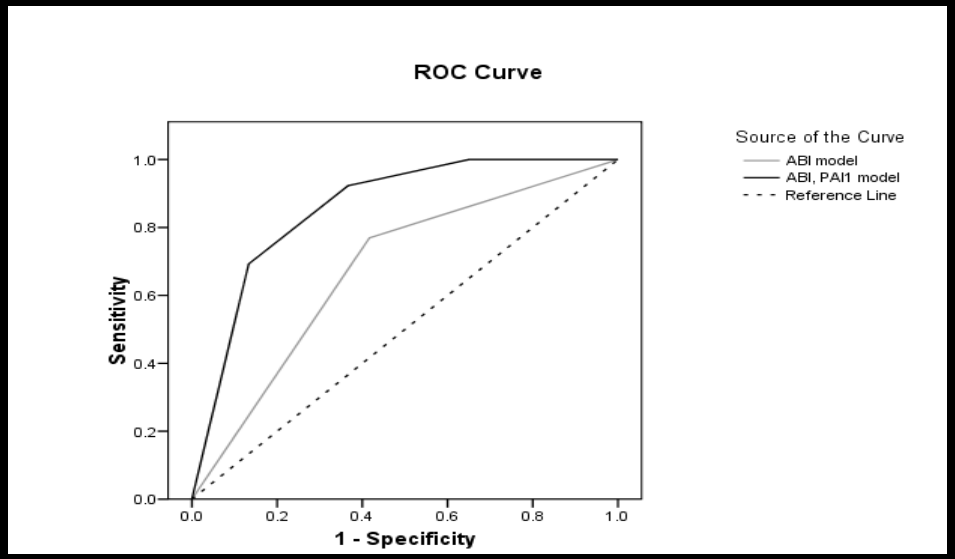
N= 75

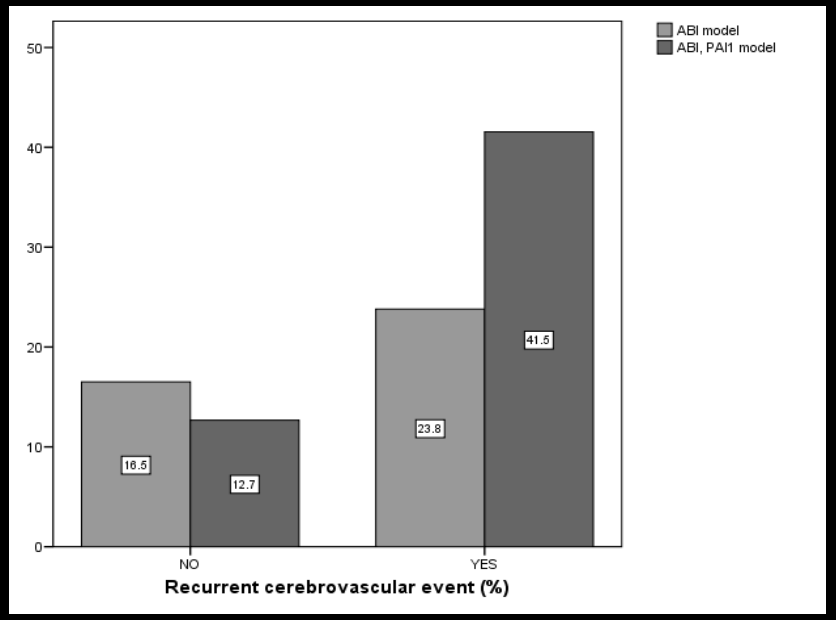
18 recurrent events

(10 ischemic stroke)

Massot A, Vall d'Hebron ICAS investigators, *Atherosclerosis* 2011

Biomarkers: PAI-1

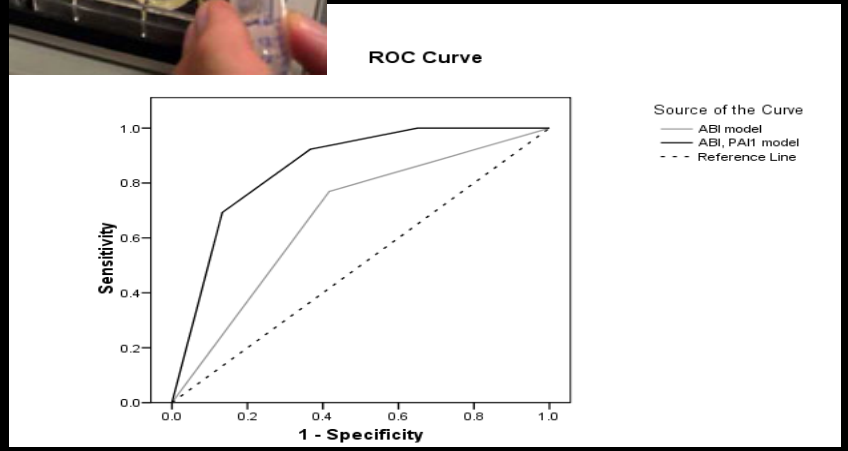




Predictive value of ankle-brachial index and PAI-1 in symptomatic intracranial atherosclerotic disease recurrence (new ischemic stroke)

Massot A, Arenillas J et al, under review

Biomarkers & advanced imaging



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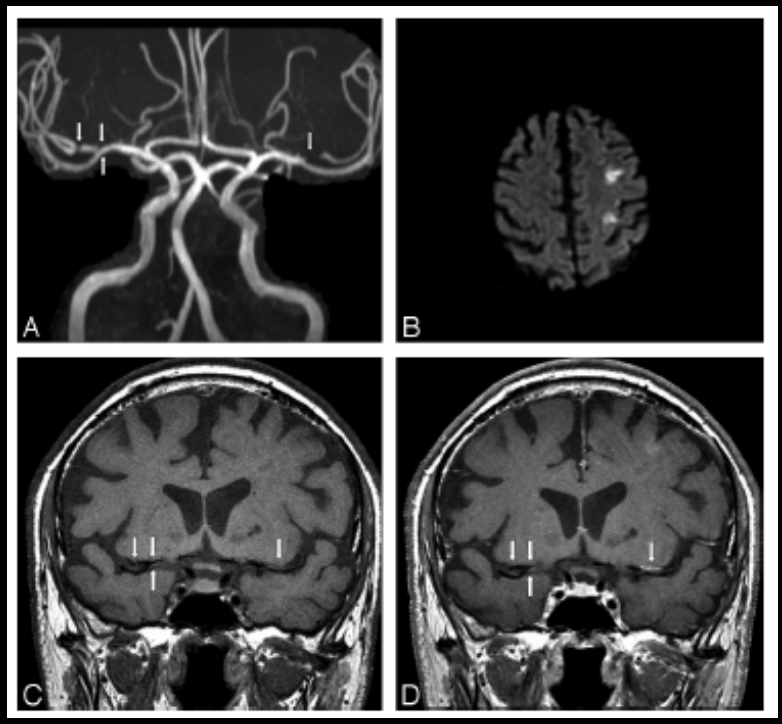


Omics approach

Refine statistical analysis to improve predictive power

Next step: Molecular imaging in ICAS

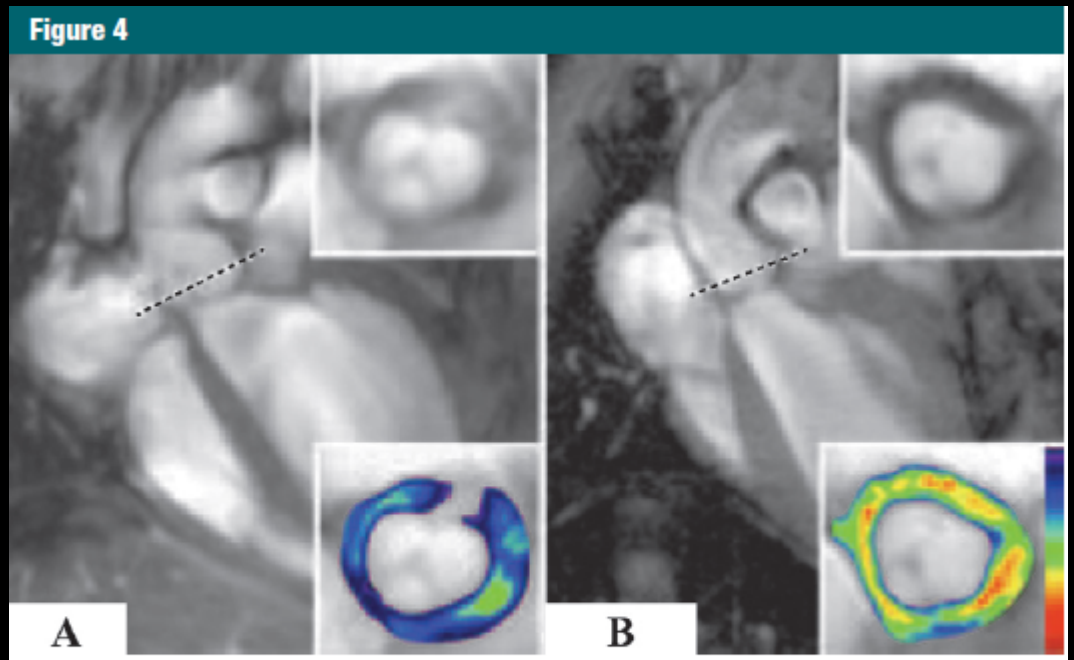


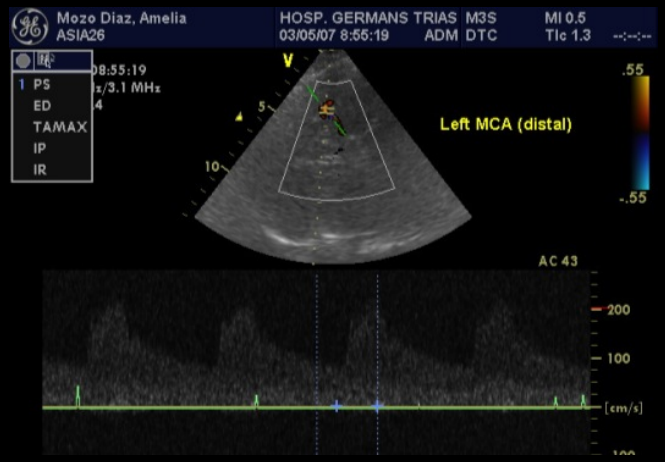
Figure 4: In vivo imaging of atherosclerotic inflammation by using a specific marker for VCAM-1 (VINP-28) performed in the aortic root of apolipoprotein E–knockout mice prior to, *A*, and after, *B*, administration of VINP-28. Considerable decrease in signal intensity is seen on the transverse MR images (repetition time, 7.0–8.0 msec; echo time, 2.7 and 4.7 msec) of the aortic root wall (grayscale insets). The contrast-to-noise ratio is significantly increased after the administration of the probe (color insets), demonstrating noninvasive imaging of VCAM-1–expression on endothelial cells and macrophages of atherosclerotic vessel segments. (Adapted and adapted, with permission, from reference 53.)

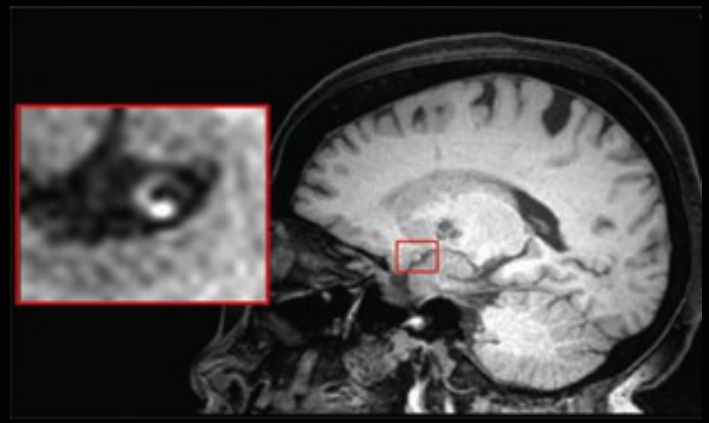
Following coronary & carotid literature

Makowski et al, Radiology 2013

Conclusion

- Noninvasive identification of high-risk ICAS plaque & patient as a main research priority
- HRMIR shows first evidence of differential ultraestructural characteristics of symptomatic intracranial ath plaque in vivo
- Biomarker studies suggest involvement of inflammation and PAI-1, further studies needed





Intracranial stenosis

Intracranial ath PLAQUE

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