Brain MRIs Analisis in Taxinomisis project

Laura Ludovica Gramegna[1,2], MD - Luigi Cirillo[1,2], MD - David Neil Manners[1,2] (Engineer)

[1]Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[2]Functional and Molecular Neuroimaging Unit, IRCCS Istituto delle Scienze Neurologiche di Bologna

Neuroadiological imaging

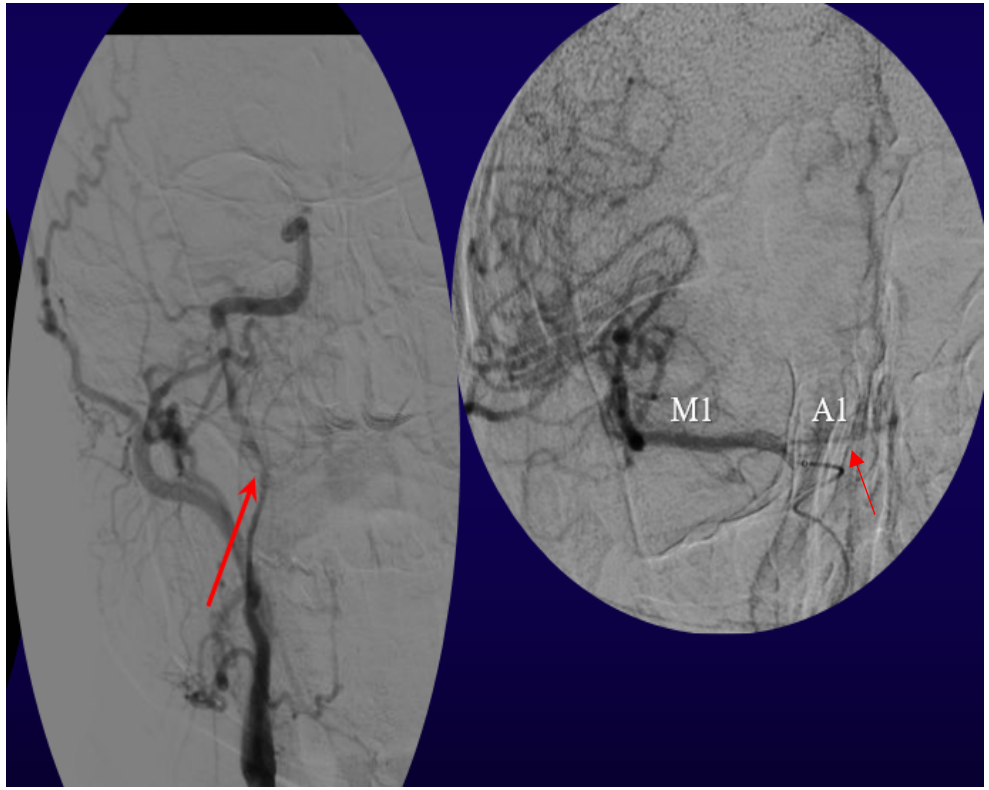
***Brain MRI** interpretation of ischemic lesions…*

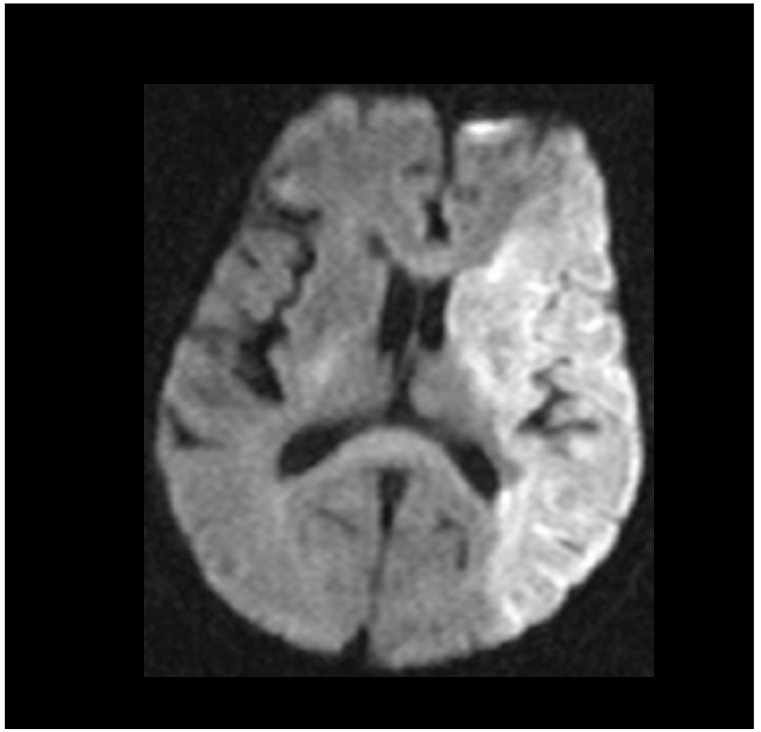
- *1) Cortical Infarct (Chronic ischemic lesions)*
- *2) Small Vessel Disease*
- *3) Silent brain ischemia*

… in Taxinomisis Project

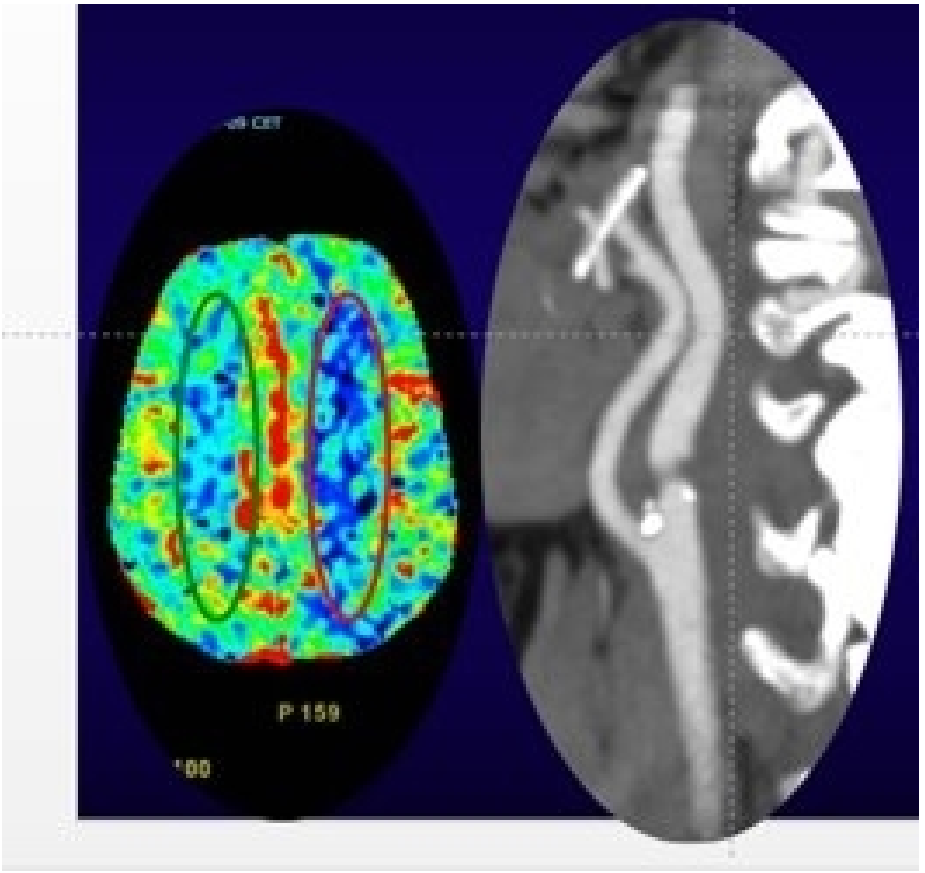
- *Baseline Brain MRI*
  - *Visual Inspection*
  - *Automated Segmentation*
- *Future perspective*

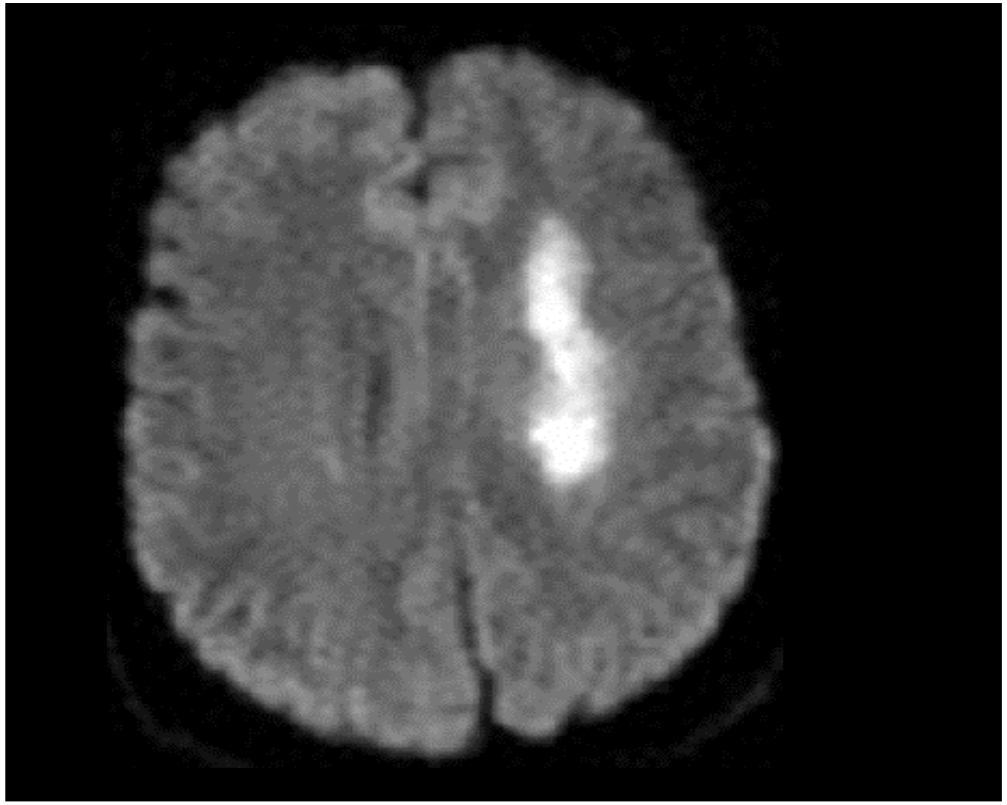
1) Cortical infarct = anterior circulation



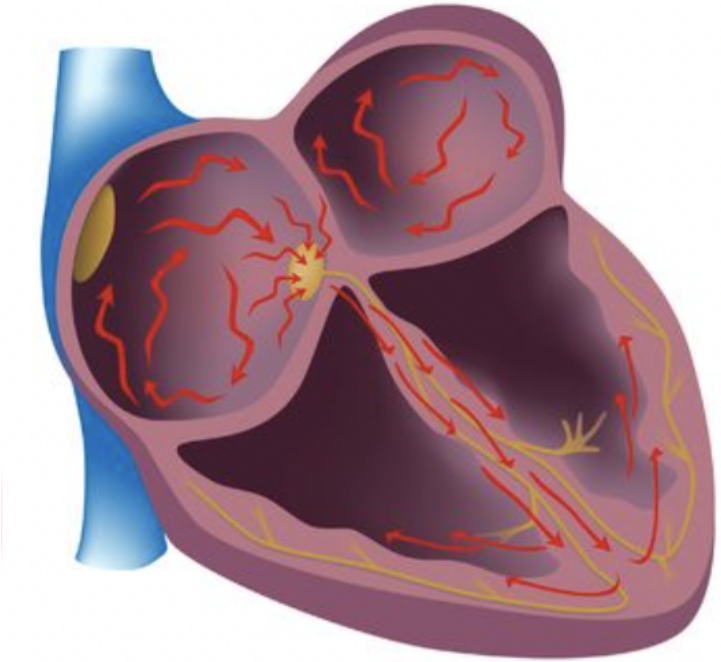


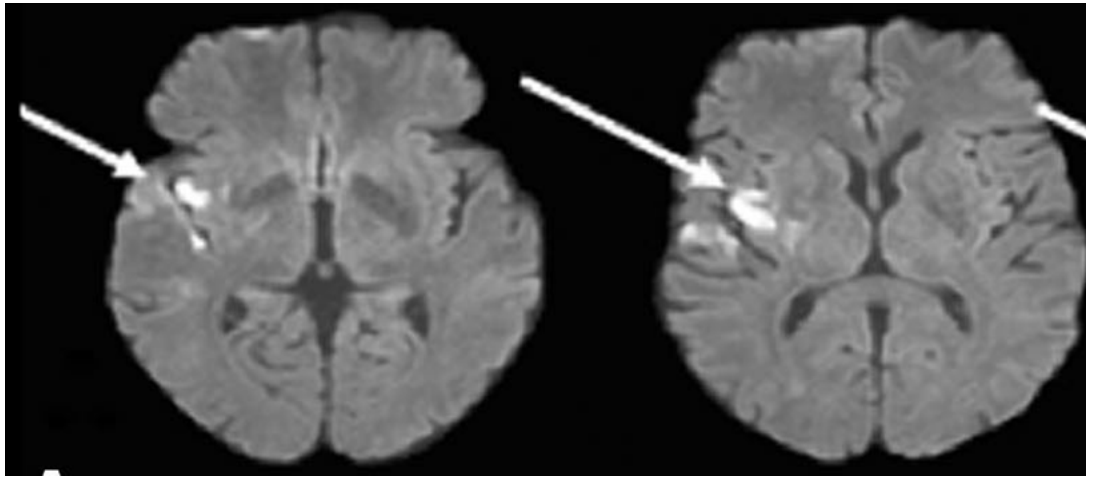
1) Cortical infarct = watershed infarct



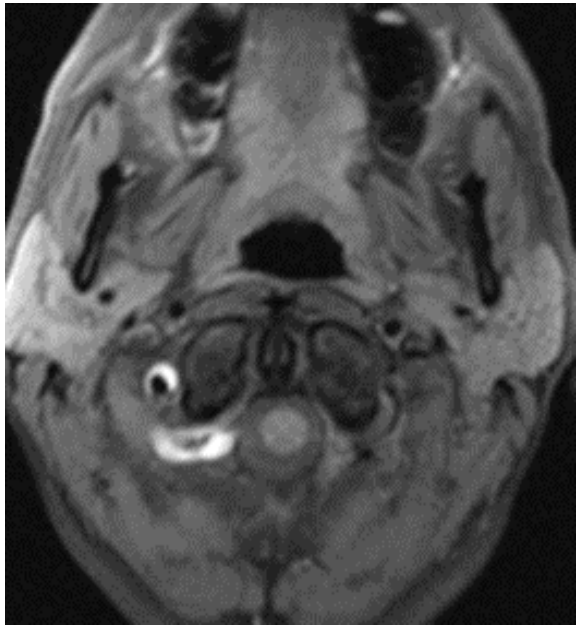


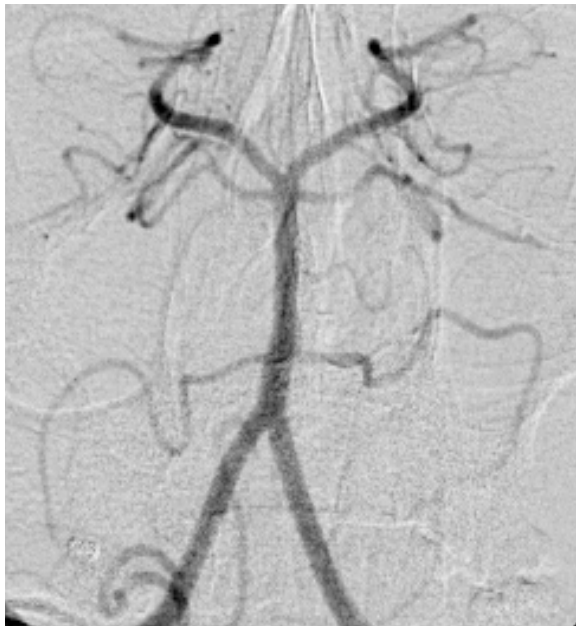
1) Cortical infarct = small cortical infarct





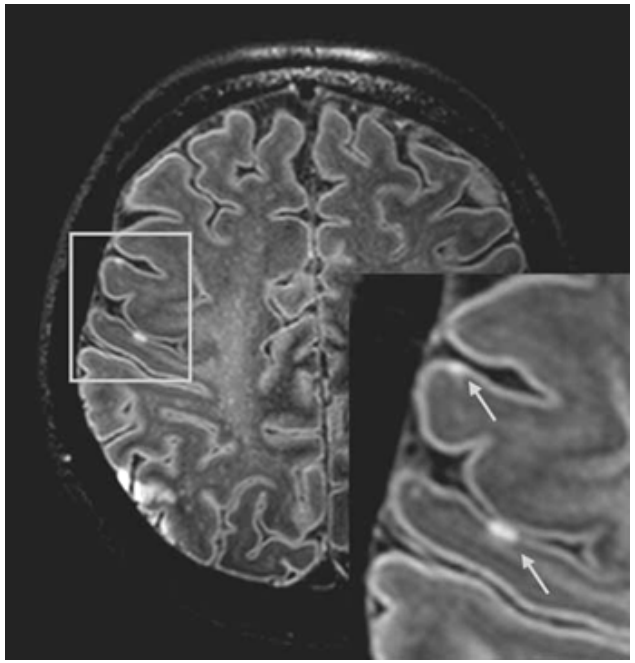
1) Cortical infarct = posterior circulation



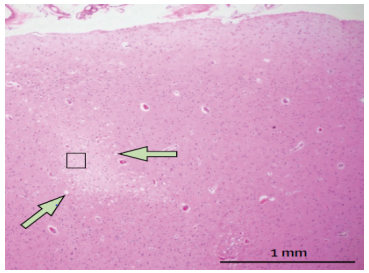


1) Cortical infarct = *Cortical micro-infarcts*

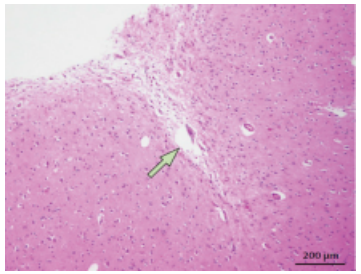
MRI 7 Testa



Neuropathology (>50 µm)



An acute microinfarct in the midfrontal cortex



Chronic microinfarct with cavitation in the inferior parietal cortex

Prevalence of cortical microinfarct on autopsy:

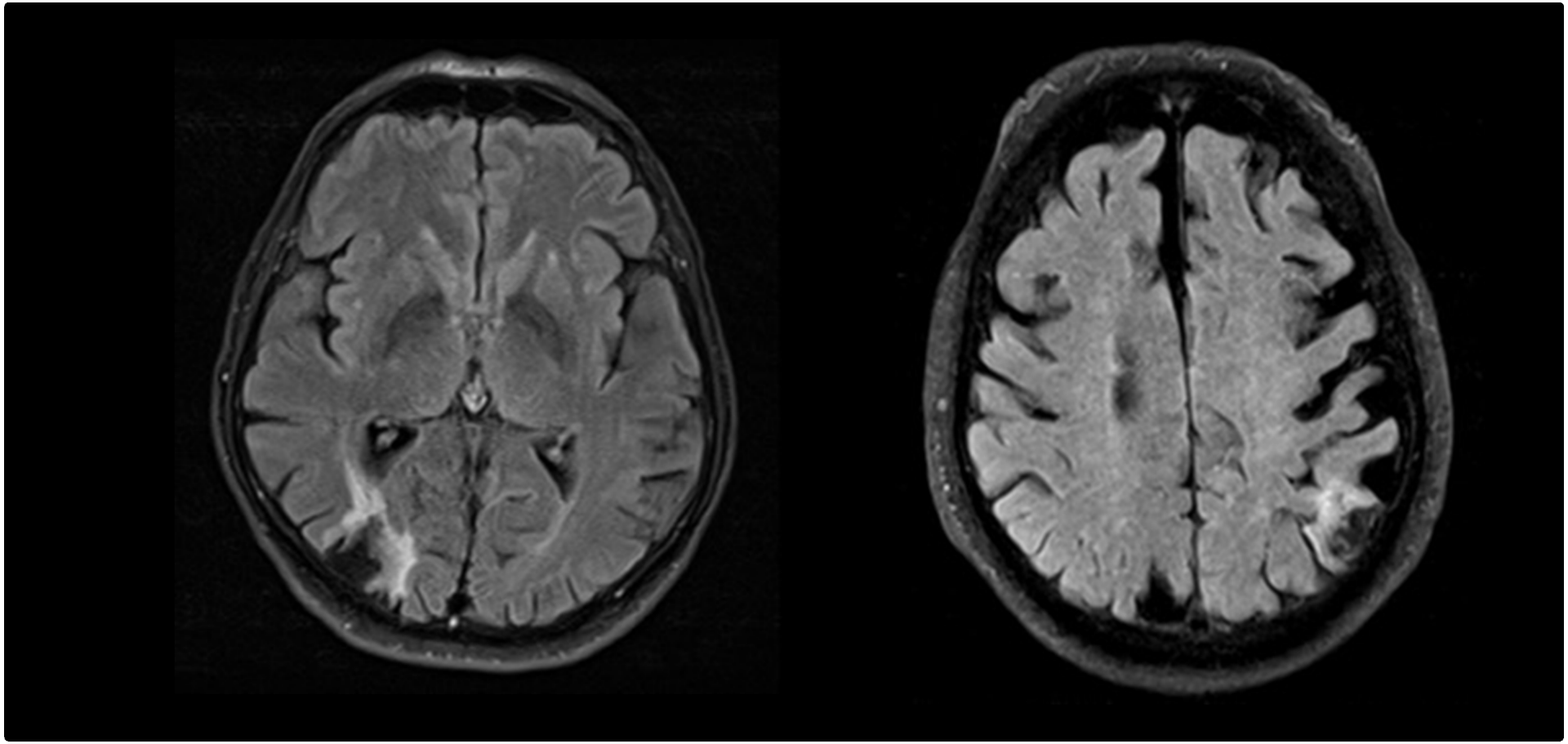
- 62% in patients with a diagnosis of vascular dementia
- 43% in Alzheimer's disease
- 24% in individuals aged around 75 years or older without a diagnosis of dementia before autopsy.
- Affected individuals are estimated to have hundreds to thousands of cerebral microinfarcts

Cortical ischemic lesions on magnetic resonance (MR) images obtained at 7 T

Fluid-attenuated inversion recovery (FLAIR) images from a 57-year-old woman with a **history of atrial fibrillation** who presented with left-sided hemiparesis based on cortical ischemia in the right middle cerebral artery territory.

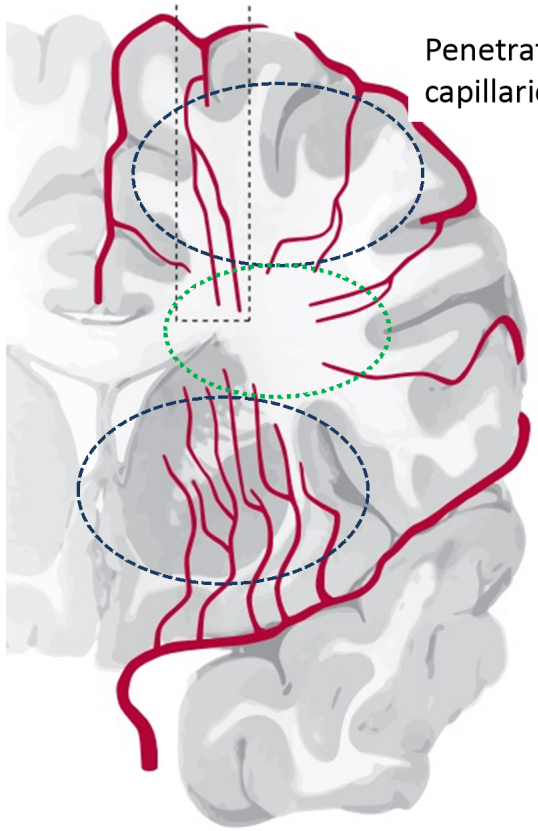
Brundel M et al. J Cereb Blood Flow Metab 2012

1) Chronic ischemic lesions

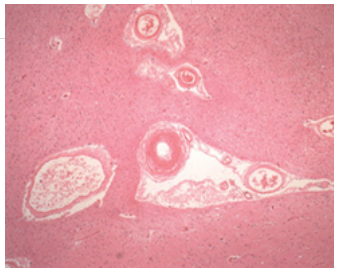


Cortical-subcortical FLAIR-hypointense and hyperintense lesions

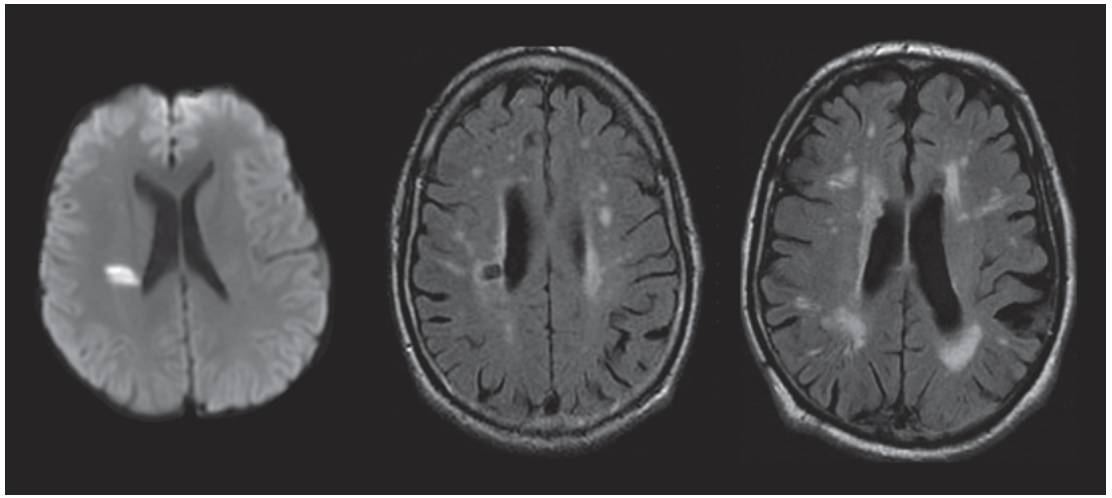
2) Small vessel disease (SVD)



Penetrating arterioles (medullary), capillaries and venules



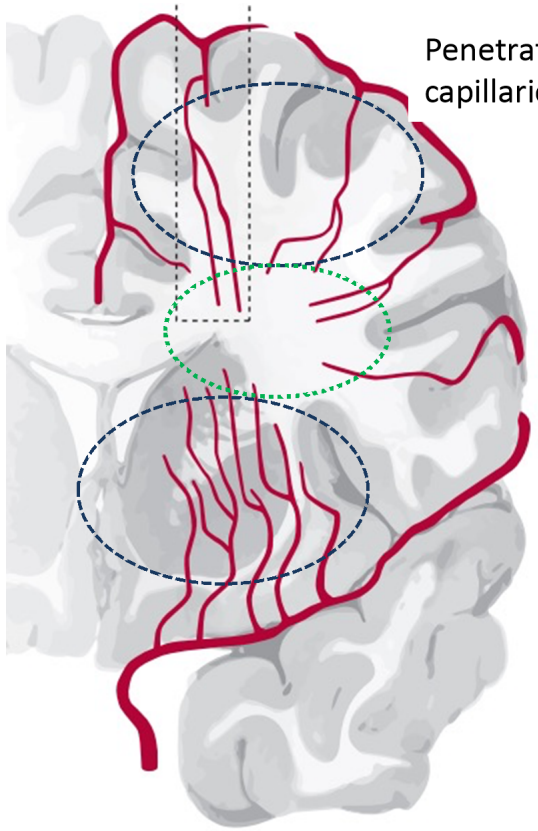
Penetrating arterioles (perforating), capillaries and venules



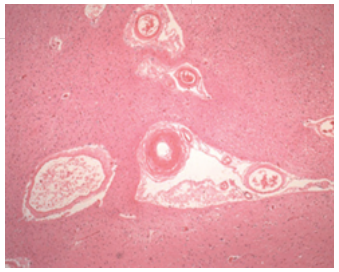
Lacunar infarcts

White matter Hyperintesities
Of presumed vascular origin

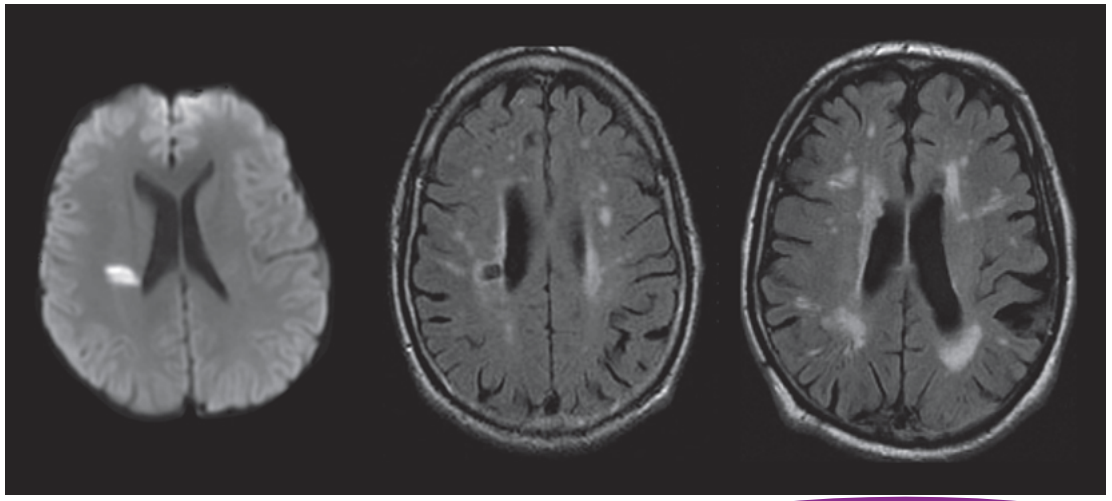
2) Small vessel disease (SVD)



Penetrating arterioles (medullary), capillaries and venules



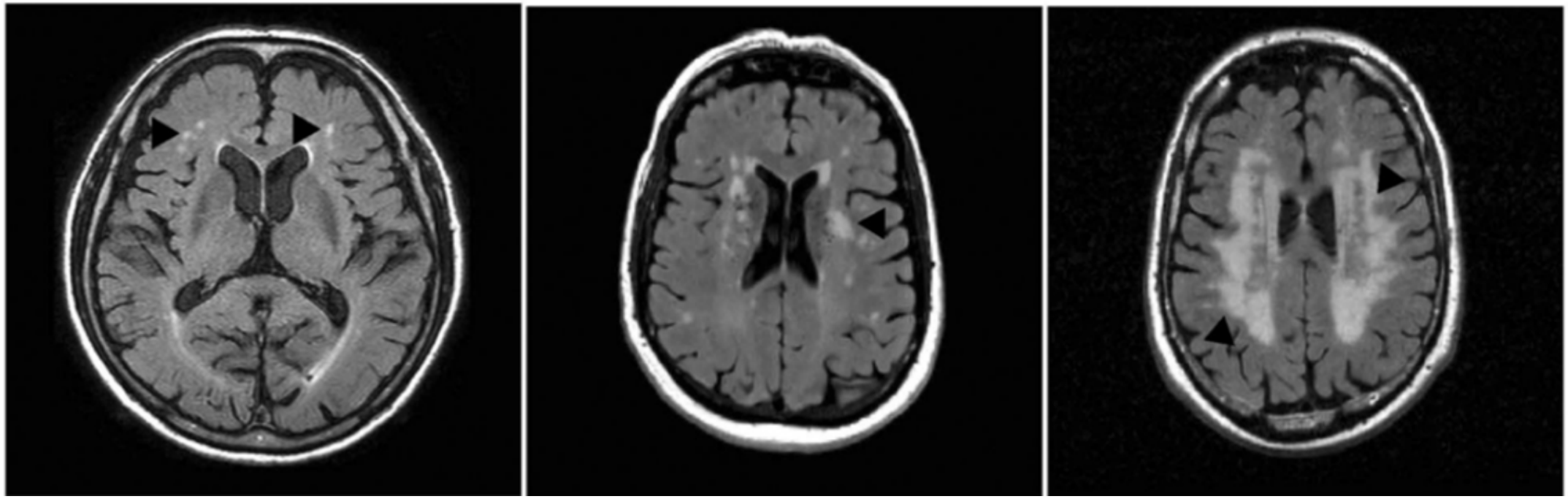
Penetrating arterioles (perforating), capillaries and venules



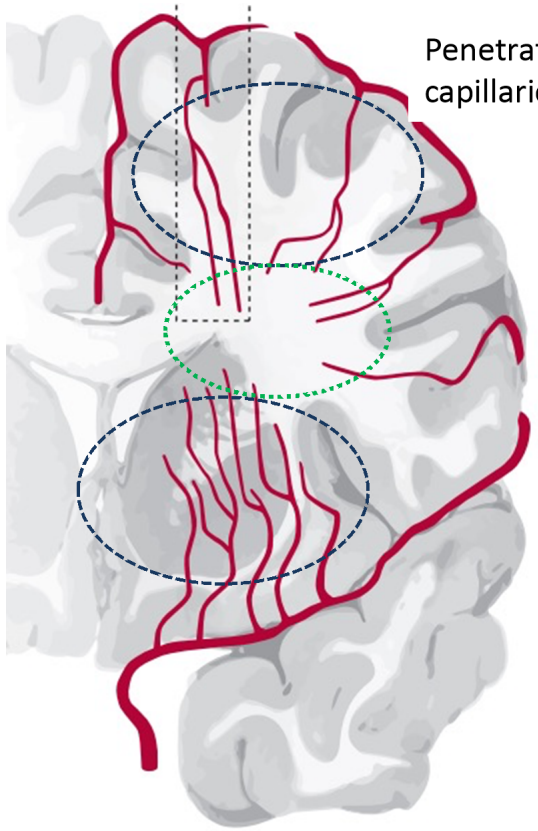
Lacunar infarcts

White matter Hyperintesities
Of presumed vascular origin

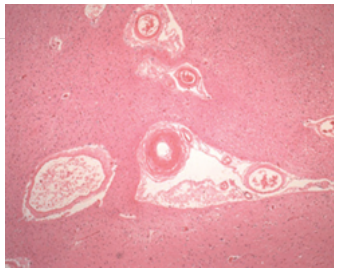
2) SVD= White matter Hyperintesities Of presumed vascular origin



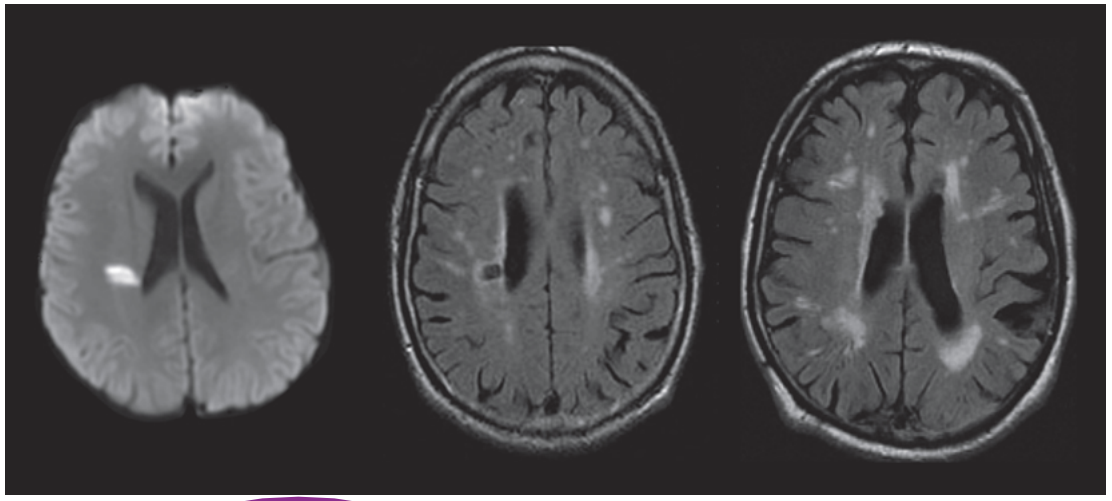
2) Small vessel disease (SVD)



Penetrating arterioles (medullary), capillaries and venules



Penetrating arterioles (perforating), capillaries and venules

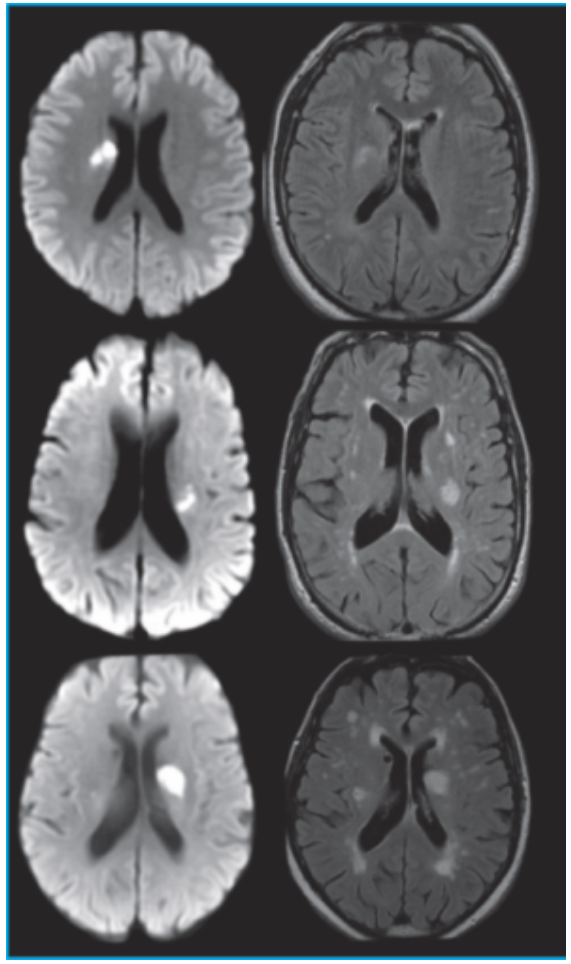


Lacunar infarcts

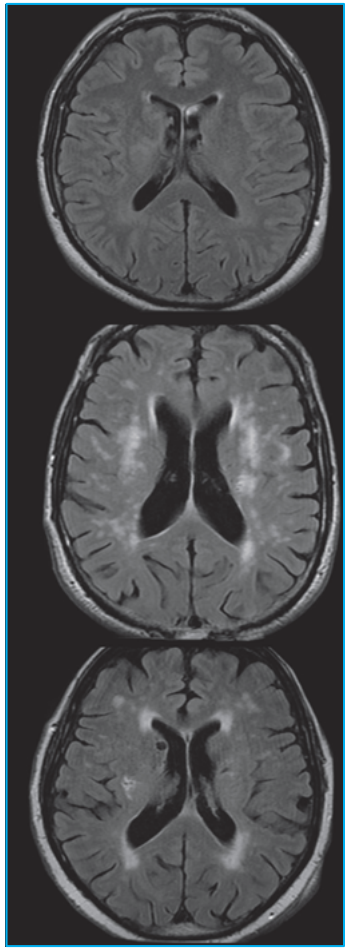
White matter Hyperintesities
Of presumed vascular origin

2) SVD= Lacunar infarct

Acute MRI scan



~ 1 year later

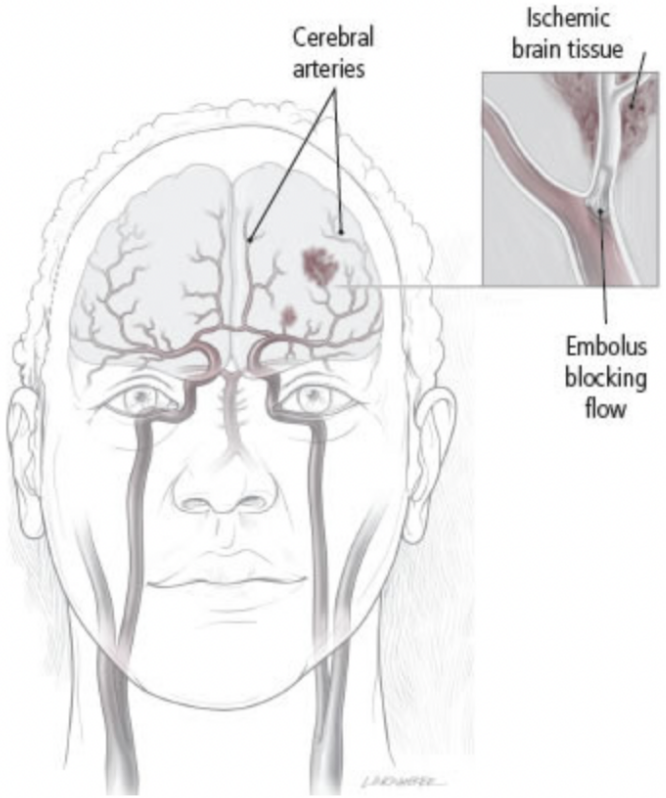


Almost **disappeared**

White matter hyperintensity

Small CSF-containing lacuna

3) SVD= Silent Brain Ischemia

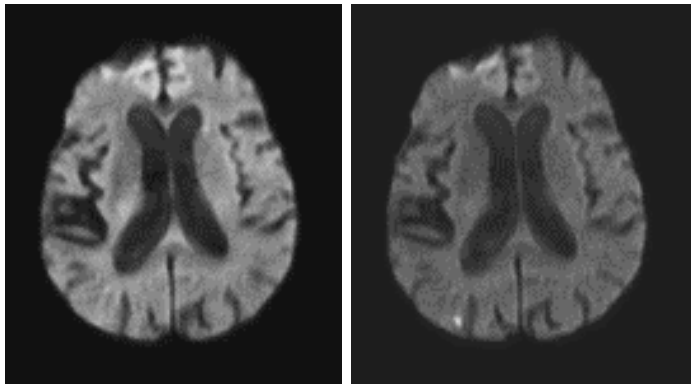


MIND & MOOD

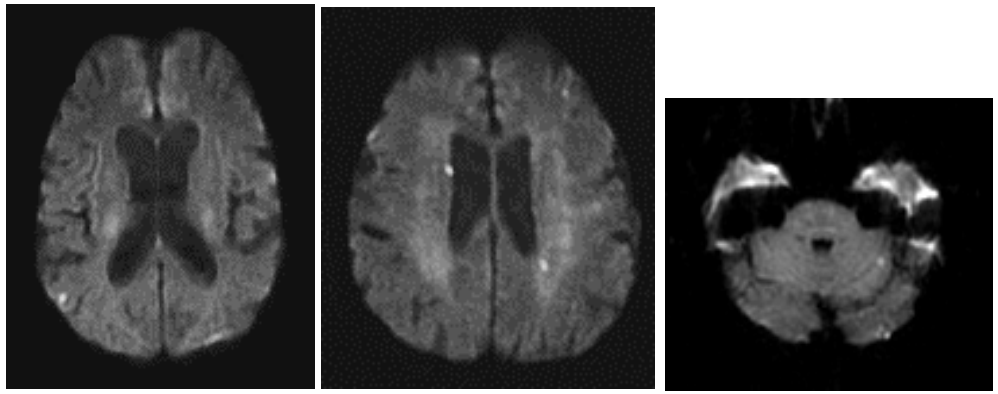
Could a silent stroke erode your memory?

Harvard Health Publishing
HARVARD MEDICAL SCHOOL

3) SVD= Silent Brain Ischemia



Pre-CAS Post-CAS



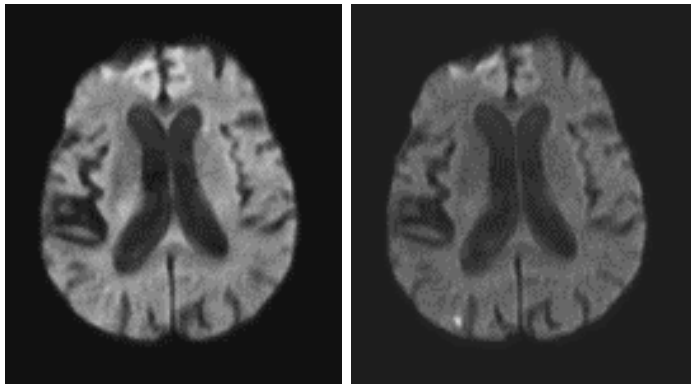
Post-CAS Post-CAS Post-CAS

Atherosclerotic aortic lesions increase the risk of cerebral embolism during carotid stenting in patients with complex aortic arch anatomy

GianLuca Faggioli, MD,[a] Monica Ferri, MD,[a] Claudio Rapezzi, MD,[b] Caterina Tonon, MD,[c] Lamberto Manzoli, MD,[d] and Andrea Stella, MD,[a] *Bologna and Chieti, Italy*

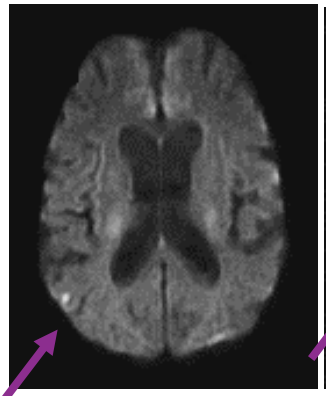
- After CAS, new DWI focal lesions were detected in 34/59 pts (58%)
- Median number of lesions: 3 (range 1 to 23)
- Median volume: 0.35 cc (range 0.06 to 12 cc)
- Only two patients experienced a transitory ischemic attack in the ipsilateral hemisphere

3) SVD= Silent Brain Ischemia

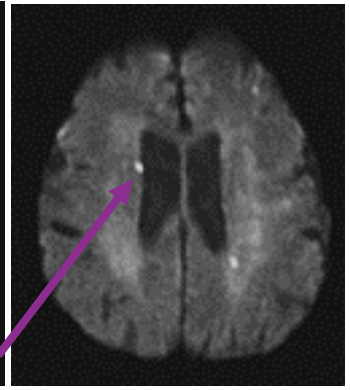


Pre-CAS

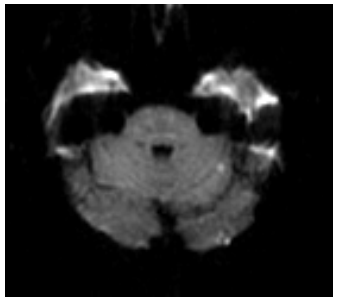
Post-CAS



Post-CAS



Post-CAS



Post-CAS

- After CAS, new DWI focal lesions were detected in 34/59 pts (58%)
- Median number of lesions: 3 (range 1 to 23)
- Median volume: 0.35 cc (range 0.06 to 12 cc)
- Only two patients experienced a transitory ischemic attack in the ipsilateral hemisphere

Atherosclerotic aortic lesions increase the risk of cerebral embolism during carotid stenting in patients with complex aortic arch anatomy

GianLuca Faggioli, MD,[a] Monica Ferri, MD,[a] Claudio Rapezzi, MD,[b] Caterina Tonon, MD,[c] Lamberto Manzoli, MD,[d] and Andrea Stella, MD,[a] *Bologna and Chieti, Italy*

3) SVD= Silent Brain Ischemia

Silent Brain Infarction and Risk of Future Stroke: A Systematic Review and Meta-Analysis

Ajay Gupta, MD[1,2,*], Ashley E. Giambrone, PhD[3], Gino Gialdini, MD[2], Caitlin Finn, BS[1], Diana Delgado, MLS[4], Jose Gutierrez, MD, MPH[5], Clinton Wright, MD, MS[6], Alexa S. Beiser, PhD[7], Sudha Seshadri, MD[8], Ankur Pandya, PhD[9], and Hooman Kamel, MD[2,10]

Conclusions—SBI is present in approximately one in five stroke-free older adults and is associated with a 2-fold increased risk of future stroke. Future studies of in-depth stroke risk evaluations and intensive prevention measures are warranted in patients with clinically unrecognized radiologically evident brain infarctions.

Gupta, Stroke 2016

Silent Brain Ischemia

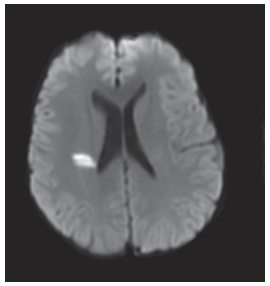
Supplemental Table III: Silent Brain Infarction Definitions

Study Number	Study First Author and Year	Magnet Field Strength	Section Thickness (mm)	Section Gap (mm)	Size classification	SBI MRI Signal Characteristics	Means of differentiating SBI from perivascular spaces	Means of detecting SBI in patients with documented prior stroke
1	Bernick 2001[1]	0.35 and 1.5 Tesla	5 mm	0	3 mm or greater	brighter lesions on spin density and T2 sequences than normal grav matter (for cortical and deep grey matter); brighter at spin density and T1 hypointense (for white matter)	spin density brigthness used to distinguish SBI from perivascular spaces	NA
2	Kario 2001[2]	1.5 Tesla	7.8 to 8.0 mm	not specified	3 to 15 mm	low signal intensity area on T1-weighted images that was also visible as a hyperintense lesion on T2-weighted images	not specified	NA
3	Naganuma 2005[3]	1.5 Tesla	10 mm	not specified	>3 mm	focal area on both T1 and T2-weighted images that was visible as low-intensity areas on T1 weighted image and as high signal intensity area on T2 weighted images.	not specified	NA
4	Bokura 2006[4]	0.15, 0.2 and 1.5 Tesla	10 mm, 7 mm	not specified	>3 mm	focal hyperintensity lesion on T2WI corresponding to a hypointensity lesion on T1WI	proton density weighted or FLAIR images used to distinguish infarcts from dilated perivascular spaces	NA
5	Debette 2010[5]	1 or 1.5 Tesla	4 mm	not specified	>3 mm	area of abnormal signal intensity in a vascular distribution, at least 3 mm in size with a cerebrospinal fluid density on the subtraction image and, for lesions in the basal ganglia area, distinct separation from the circle of Willis vessels	size, location, shape, and tissue contrast to distinguish SBI from dilated perivascular spaces	NA
6	Putaala 2011[6]	1.0 to 1.5 Tesla	not specified	not specified	≥ 3 mm	focal hyperintensity on T2-weighted images without a corresponding history of neurologic symptoms or signs	simultaneous hyperintensity on T2-weighted images and hypointensity on FLAIR images for perivascular spaces as opposed to SBI	MRI of the brain studies acquired at the initial presentation for acute ischemic stroke were reinterpreted by study stroke neurologists and a senior neuroradiologist. SBI classification required appropriate imaging criteria as well as no corresponding history of neurologic symptoms or signs.
7	Umemura 2011[7]	1.5 Tesla	5 mm	2 mm	>3 mm	areas of focal hyperintensity larger than 3 mm in diameter detected on T2-weighted images, hypointensity areas on T1-weighted images and areas of hypointensity surrounded by hyperintense rim on FLAIR images.	lesions less than 3 mm in diameter or with a signal intensity similar to that of cerebrospinal fluid on FLAIR images excluded because of the high possibility of enlarged perivascular spaces, even if hyperintensity on T2-weighted images and hypointensity on T1-weighted images	NA
8	Gioia 2012[8]	1.5 T or 3 Tesla	not specified	not specified	≥ 3 mm	focal hyperintensities on T2-weighted and FLAIR-weighted sequences, 3 mm in diameter, without corresponding neurologic symptoms; leukoaraiosis defined as multifocal or confluent hyperintensities located in periventicular or subcortical regions or in the pontine white matter on T2-weighted or FLAIR sequences. Differentiated from SBIs based on lesion morphology and localization	hyperintensity of T2-FLAIR images used to distinguish SBI from dilated perivascular space	SBI determined on imaging performed during the patient's initial workup for acute ischemic stroke; consensus of 2 neurologists needed to establish a lesion as an asymptomatic brain infarction using all available clinical data
9	Poels 2012[9]	1.5 Tesla	5 or 6 mm	1 or 2 mm	at least 3 mm	evidence of one or more infarcts on MRI, without a history of (corresponding) stroke or TIA (focal hyperintensities on T2 weighted images); white matter lesions (rather than SBIs) were considered to be present if hyperintensities were visible on proton-density and T2-weighted images, without prominent hypointensities on T1-weighted scans	proton density scans were used to distinguish infarcts from dilated perivascular spaces	NA
10	Weber 2012[10]	Not specified	not specified	not specified	≥ 3 mm	focal hyperintense lesion on T2-weighted images and/or fluid-attenuated inversion recovery with no corresponding symptoms in the clinical history of the patient that could be attributed to the lesion; SBI were distinguished from nonspecific subcortical and periventricular white matter lesions by the presence of a corresponding hypointense lesion on T1-weighted images	hyperintensity of T2-FLAIR images used to distinguish SBI from dilated perivascular space	Two study investigators defined SBI on the baseline imaging performed for acute ischemic stroke as chronic lesions with no corresponding symptoms in the clinical history of the patient that could be attributed the presumed SBI; Information about symptoms of the qualifying ischemic stroke was collected using baseline case report forms
11	Di Tullio 2013[11]	1.5 Tesla	FLAIR=3 mm; T1=1.3 mm	0 mm	≥ 3 mm	(1) CSF density on the subtraction image and (2) if the stroke was in the basal ganglia area, distinct separation from the circle of Willis vessels and perivascular spaces.	lesion morphology used to distinguish SBI from perivascular spaces	NA
12	Miwa 2013[12]	Not specified	Not specified	not specified	>3 and <15 mm	hypointense lesion and hyperintense rim on FLAIR images when located supratentorially, according to the corresponding hyperintensity and hypointensity on T2- and T1-weighted images, respectively, without stroke history.	hyperintensity of T2-FLAIR images used to distinguish SBI from dilated perivascular space	NA
13	Windham 2015[13]	1.5 Tesla	5 mm	0	≥ 3 mm	lesions 3 mm in size and visible on both T1- and proton-density/T2-weighted images were classified as infarcts; an additional analysis was performed on putative vascular lesions <3 mm which were too small to definitely characterize as SBI	spin density brigthness used to distinguish SBI from perivascular spaces	NA

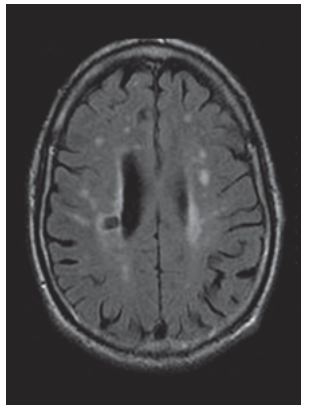
MRI = magnetic resonance imaging; SBI = silent brain infarction; FLAIR = fluid attenuated inversion recovery; NA = not applicable

Supplemental Table III: Silent Brain Infarction Definitions

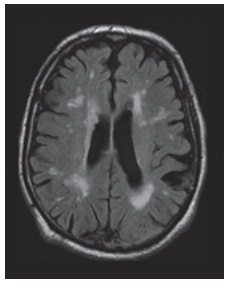
focal hyperintensity on T2-weighted images without a corresponding history of neurologic symptoms or signs



areas of focal hyperintensity larger than 3 mm in diameter detected on T2-weighted images, hypointensity areas on T1-weighted images and areas of hypointensity surrounded by hyperintense rim on FLAIR images.



focal hyperintensities on T2-weighted and FLAIR-weighted sequences, 3 mm in diameter, without corresponding neurologic symptoms; leukoaraiosis defined as multifocal or confluent hyperintensities located in periventicular or subcortical regions or in the pontine white matter on T2-weighted or FLAIR sequences. Differentiated from SBIs based on lesion morphology and localization



Neuroadiological imaging

Brain MRI interpretation of ischemic lesions…

- *1) Cortical Infarct (Chronic ischemic lesions)*
- *2) Small Vessel Disease*
- *3) Silent brain ischemia*

*… in **Taxinomisis Project***

- *Baseline Brain MRI*
  - *Visual Inspection of chronic infarcts*
  - *Automatic Segmentation*
- *Future perspective*

Baseline Brain MRI of Taxinomisis project

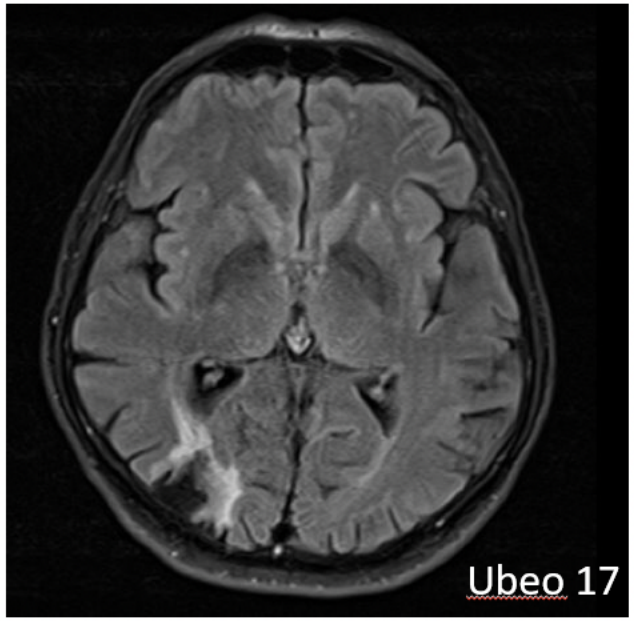
TAXINOMISIS

Site	Location	Scanner	N of baseline studies
FCRB	Barcelona	Siemens Vida 3T	25
NKUA	Athens	GE SIGNA Explorer 1.5T	62
TUM	Munich	Philips Ingenia 3T	57
UBEO	Belgrade	Siemens Skyra 3T	115
UMC	Utrecht	Philips Ingenia 3T	37
USMI	Genova	Siemens Prisma 3T	24

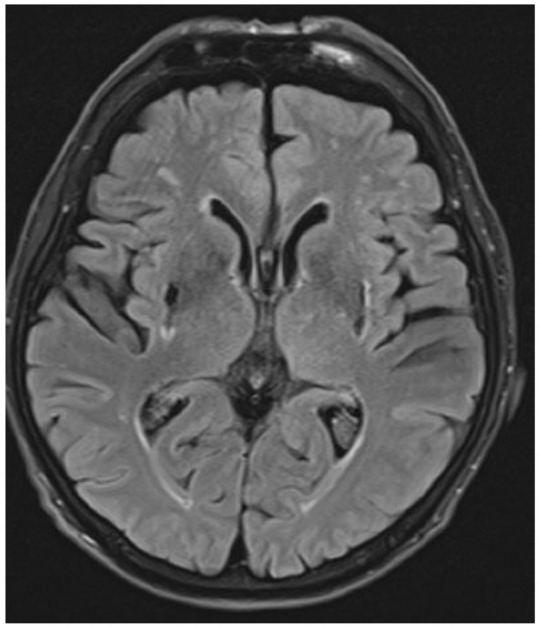
FLAIR-DWI

1) Visual inspection: chronic infarcts

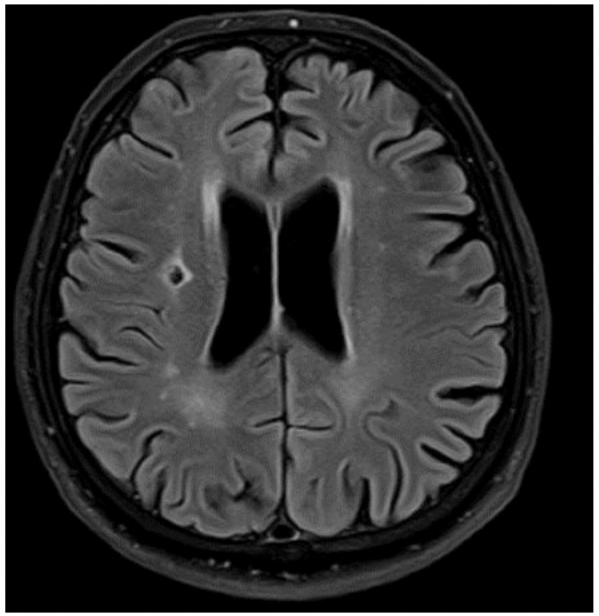
Chronic cortical infarcts



Basal Ganglia



Lacune

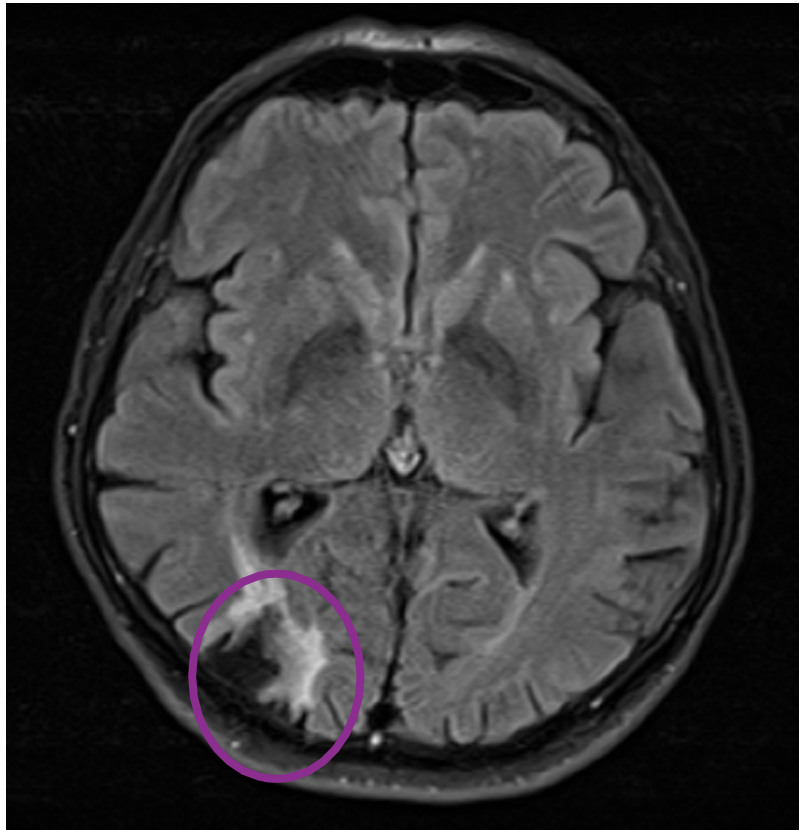


Consensus by two expert vascular neuroradiologist

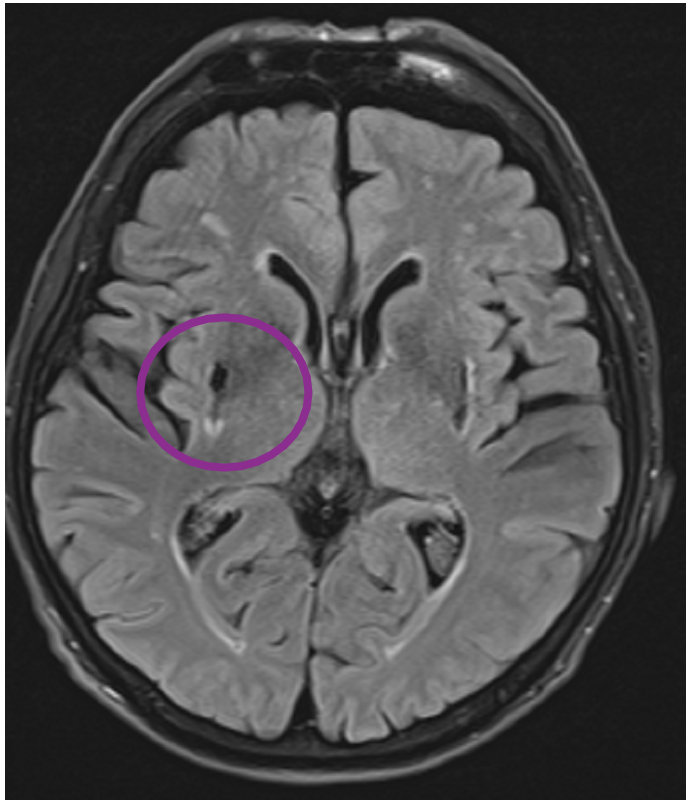
Preliminary UBEO data (n=114) – Visual Inspection

47 chronic infarcts **(38 asymptomatic)**

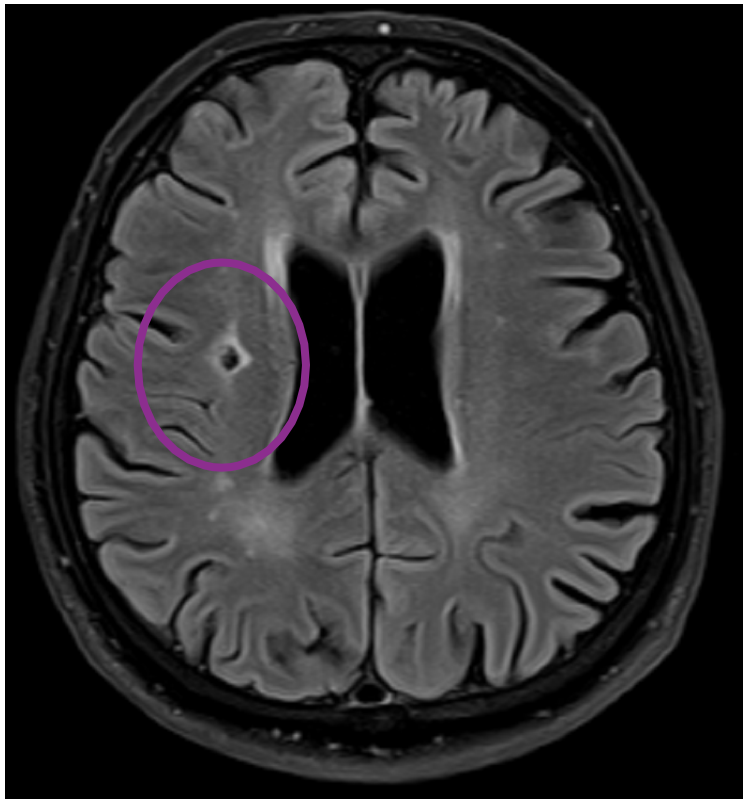
25 cortical infarcts



6 lacunae basal ganglia



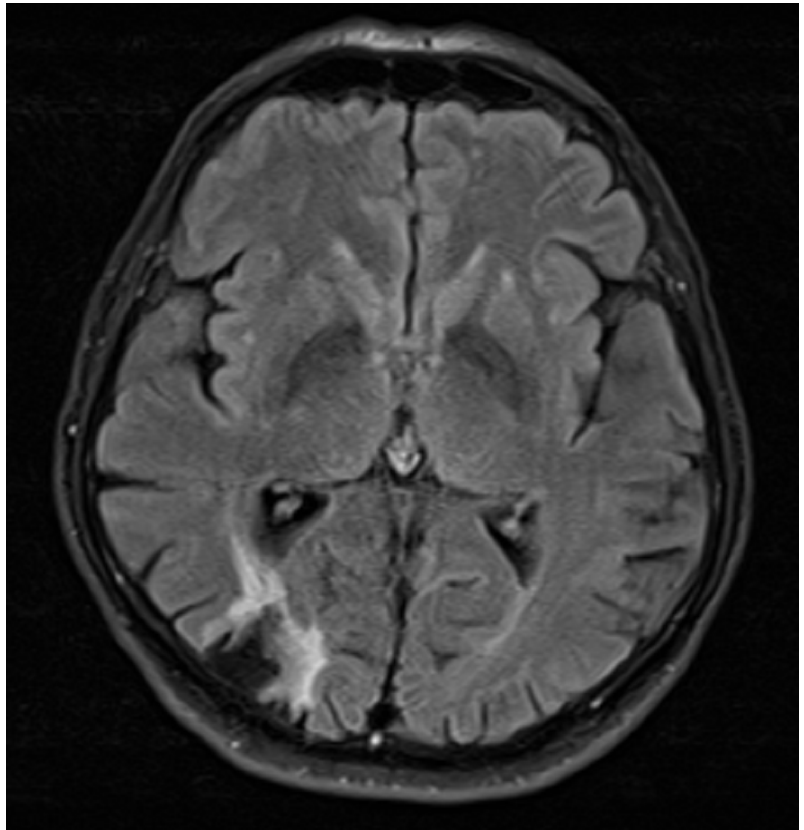
16 lacunae deep white matter



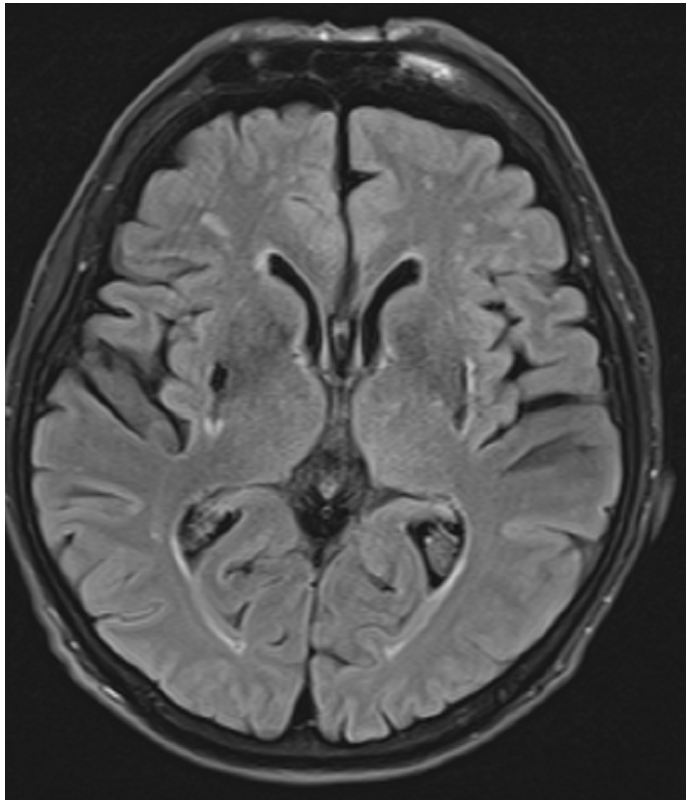
Preliminary UBEO data – Visual Inspection

38/114 (33%) of total population (mean age 67± 6 y) has silent brain infarction

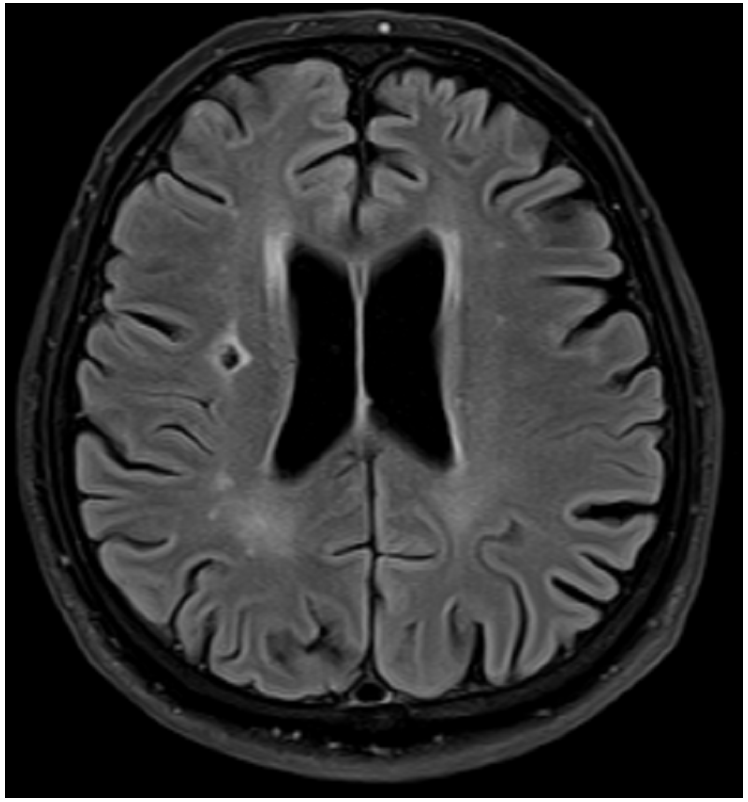
25 cortical infarcts



6 lacunae basal ganglia



16 lacunae deep white matter



Preliminary UBEO data – Visual Inspection

Higher prevalence of silent brain infarct in comparison to the literature

Silent brain infarcts: a systematic review

Sarah E Vermeer, William T Longstreth Jr, Peter J Koudstaal

	General population	N	Mean age (range), years	SBI, %
Helsinki Aging Brain Study (HABS), 1995[9]	Finland, elderly oversampled, not institutionalised, no neurological disease	128	72 (56–88)	16
Cardiovascular Health Study (CHS), 1997[10]	USA, African-Americans oversampled, not institutionalised, no stroke	3397	75 (65–97)	28
Atherosclerosis Risk in Communities (ARIC) Study, 1998[11]	USA, African-Americans oversampled, no stroke or transient ischaemic attack	1538	63 (55–72)	11
Rotterdam Scan Study (RSS), 2002[12]	Netherlands, elderly oversampled, no dementia	1077	72 (60–90)	20
National Institute for Longevity Sciences - Longitudinal Study of Aging (NILS-LSA), 2003[13]	Japan, no stroke or transient ischaemic attack	1721	59 (40–79)	10
Memory and Morbidity in Augsburg Elderly (MEMO) study, 2004[14]	Germany, participants of MONICA survey, not institutionalised, no stroke	267	72 (65–83)	13
Framingham Heart Study (FHS), 2005[15]	USA, original participants and their offspring, no stroke or dementia	2081	62 (34–97)	12
Austrian Stroke Prevention Study (ASPS), 2006[16]	Austria, not institutionalised, no stroke or dementia	505	64 (50–75)	8

Table 1: **Studies of prevalence of MRI-defined silent brain infarcts (SBIs) in the general population**

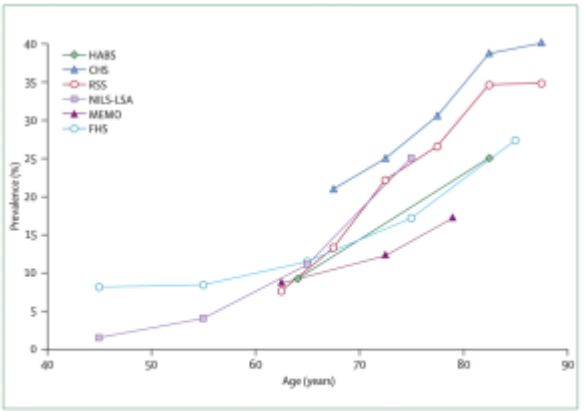
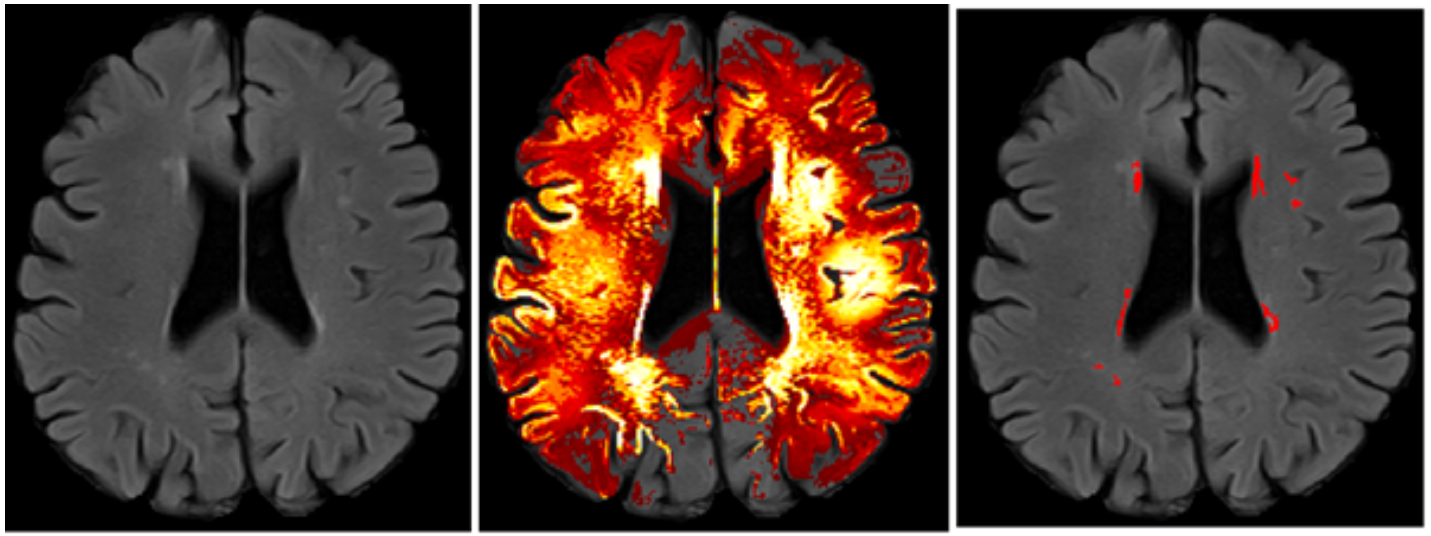


Figure 2: Prevalence of silent brain infarcts with increasing age, as reported in six population-based studies
HABS, Helsinki (Finland) Aging Brain Study;[9] CHS, Cardiovascular Health Study;[10] RSS, Rotterdam Scan Study;[12] NILS-LSA, National Institute for Longevity Sciences-Longitudinal Study of Aging;[13] MEMO, Memory and Morbidity in Augsburg Elderly study;[14] and FHS, Framingham Heart Study.[15]

Vermeer SE, Longstreth WT Jr, Koudstaal PJ. Silent brain infarcts: a systematic review. Lancet Neurol. 2007

Preliminary UBEO data – Automatic segmentation



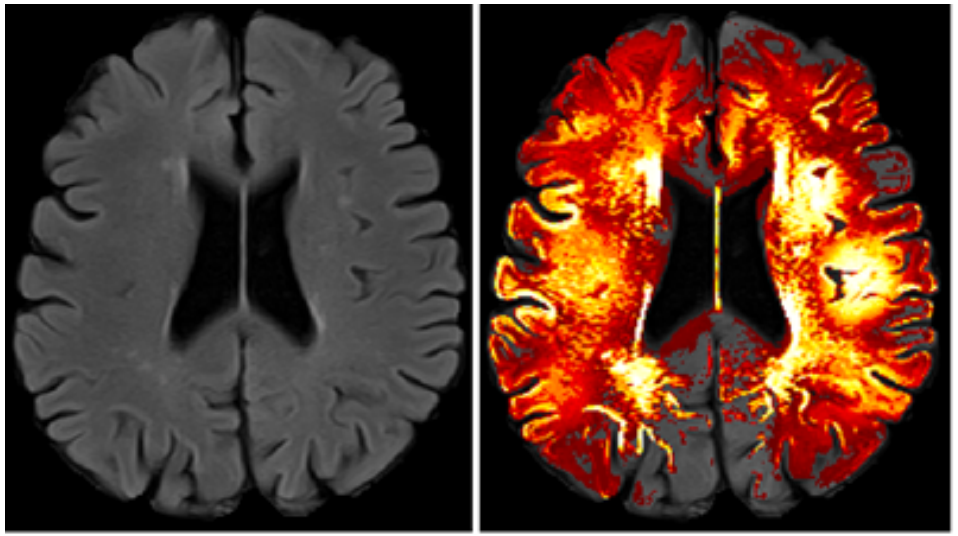
FLAIR image

Lesion probability

Probability threshold 98%
Minimum cluster 5 voxels

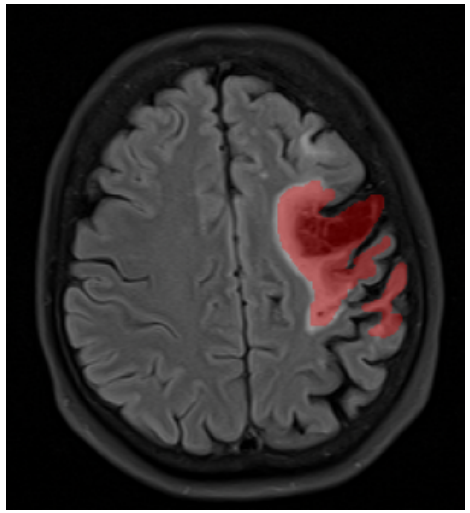
Automatic quantification of «white matter lesion of presumed vascular origin»
lesion load

Preliminary UBEO data – Automatic segmentation



FLAIR image

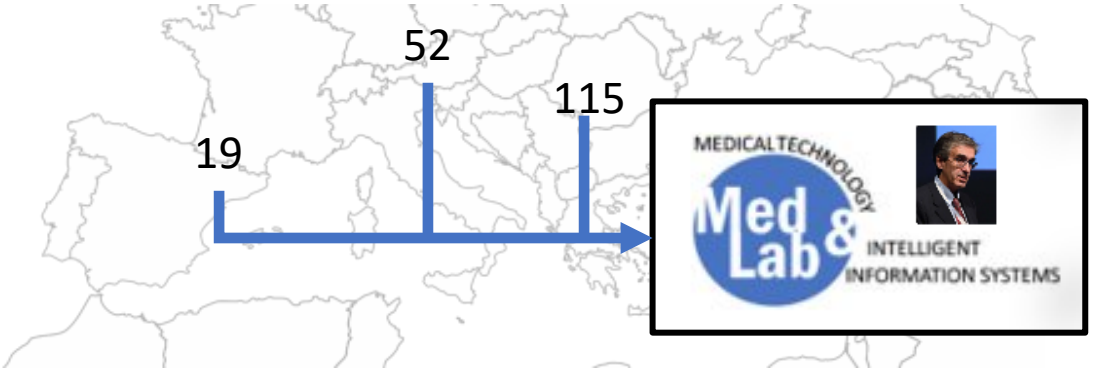
Lesion probability

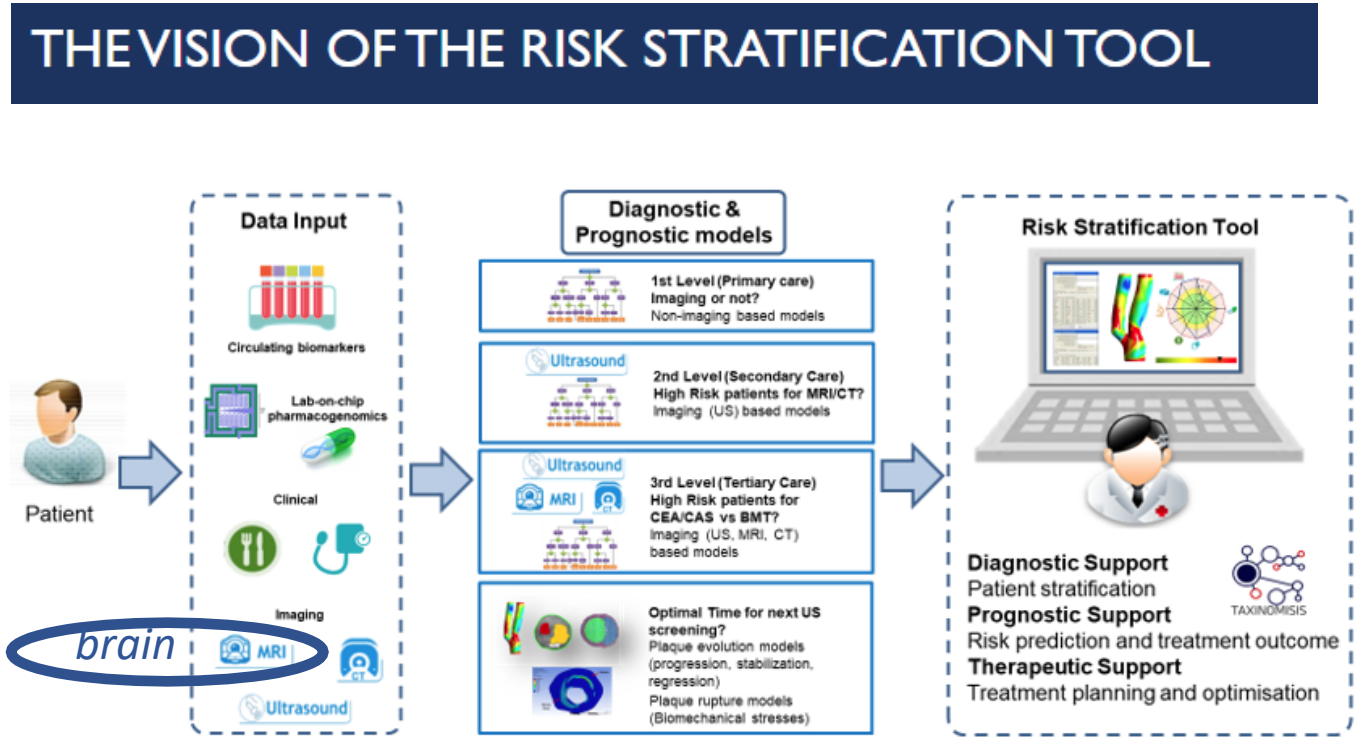


Semi- Automatic

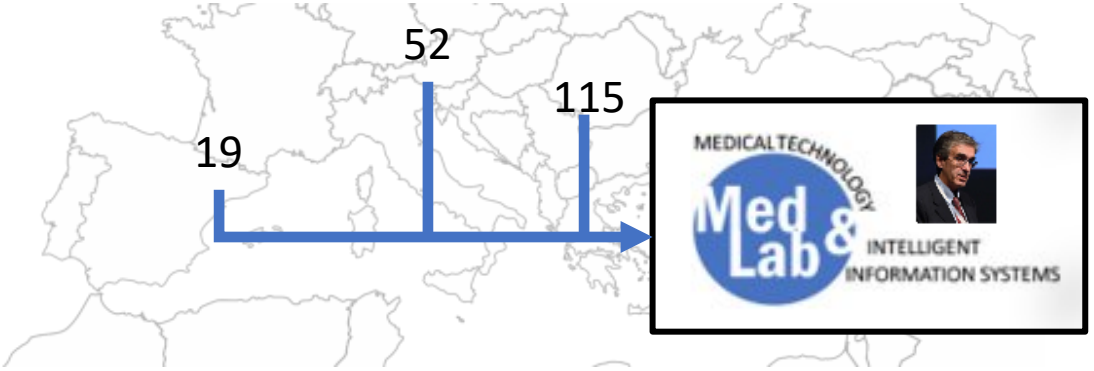
Segmentation of chronic cortical and subcortical infarcts

Step 1 = Brain MRI data *for risk stratification model*





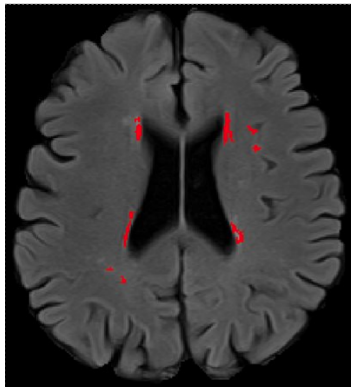
Step 1 = Brain MRI data *for risk stratification model*



Excel file for each center

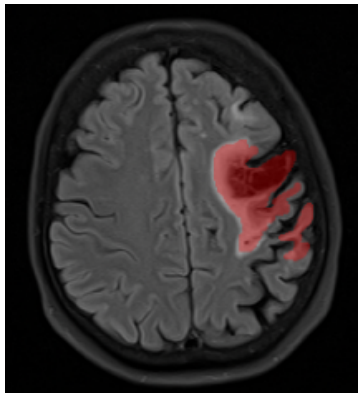
Visual inspection	***score***
Fazekas score	1-3
Cortical_infarct_present	1-0
L_cortical_infarct	1-0
R_cortical_infarct	1-0
Posterior_cortical_infarct	1-0
Lacunar_infarct	1-0
Site of Lacunar Infarct	L-R
Small subcortical infarct	1-0
Site of the small infarct	L-R

Automatic WMHPVO score



(software BIANCA)

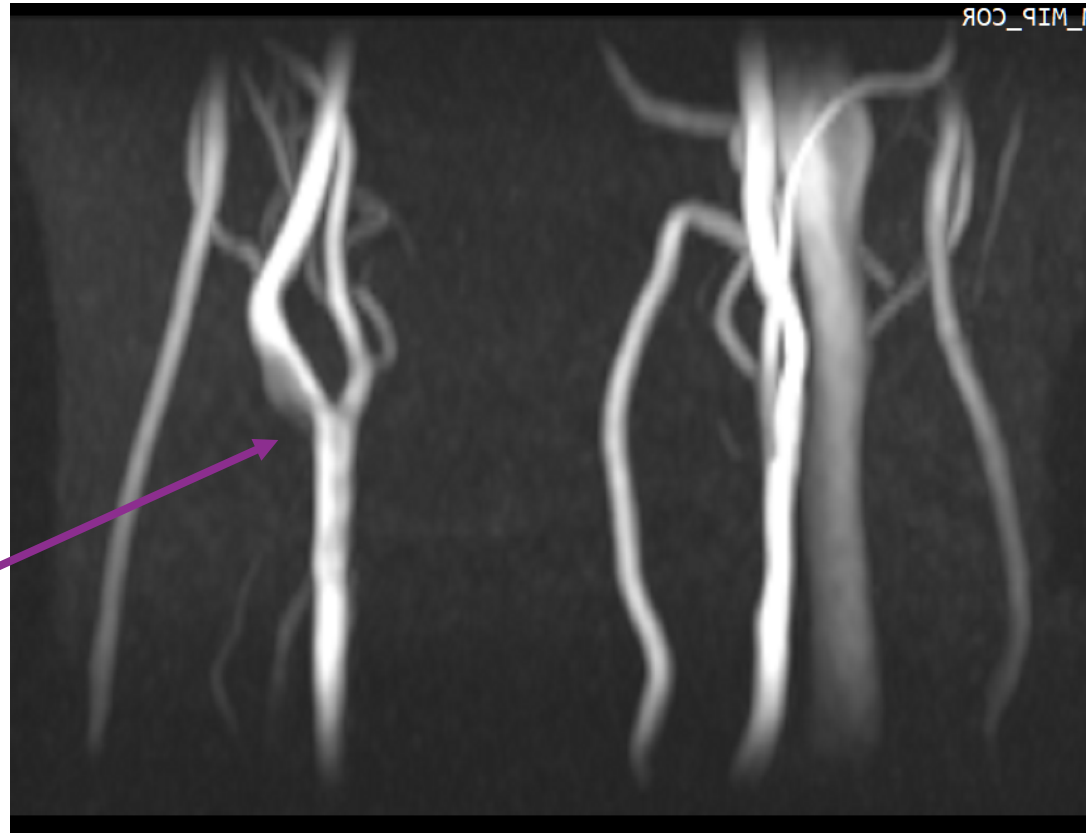
Segmentation map of the cortical, subcortical, lacunar infarcts

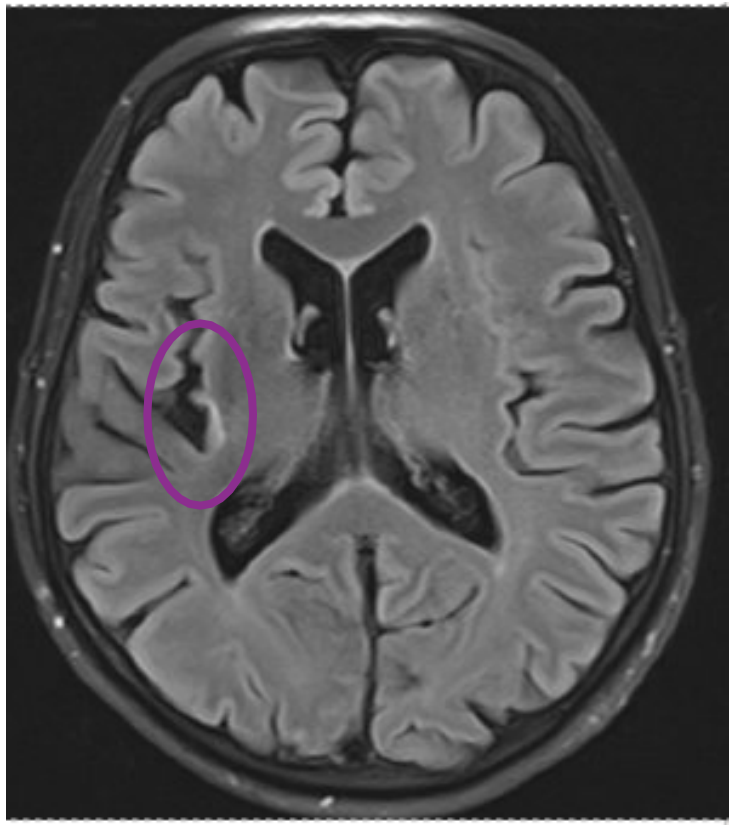


(manually drawn two expert neuroradiologist)

Step 2 = Description of the Brain MRI data?

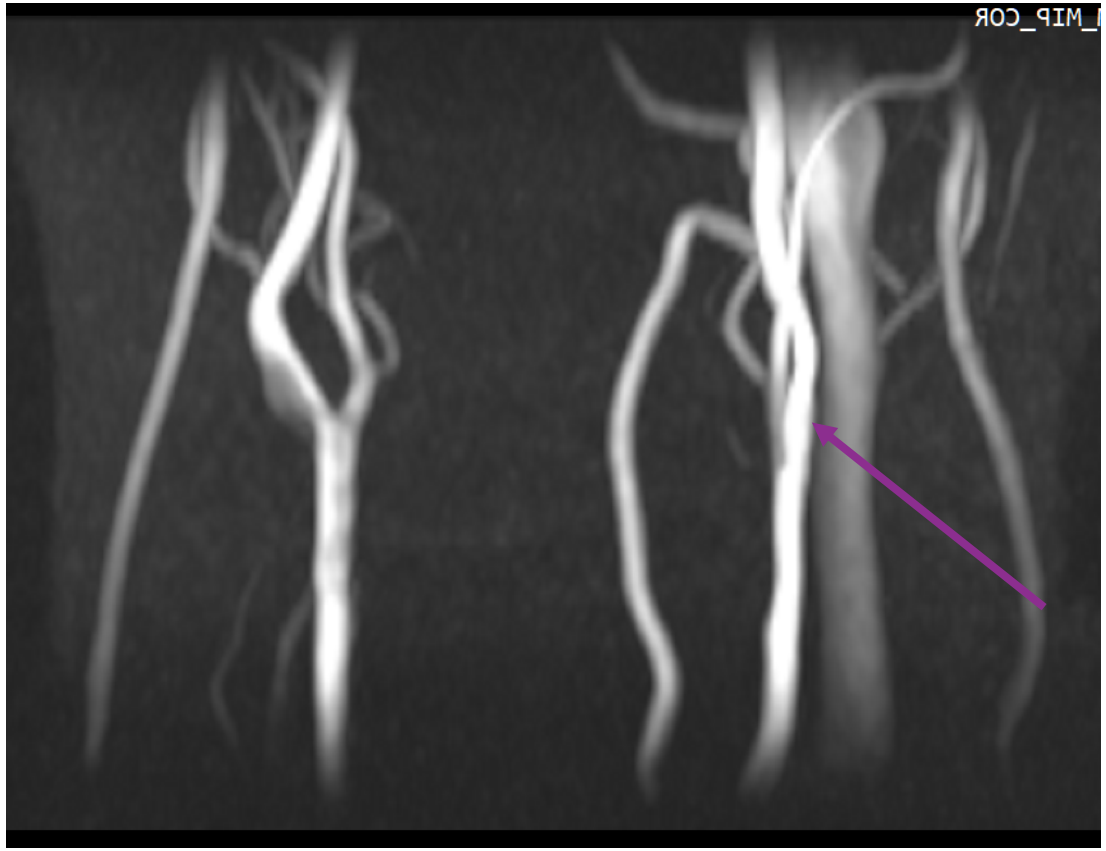
Carotid-plaque classification = **active** (cortical infarct) and symptomatic

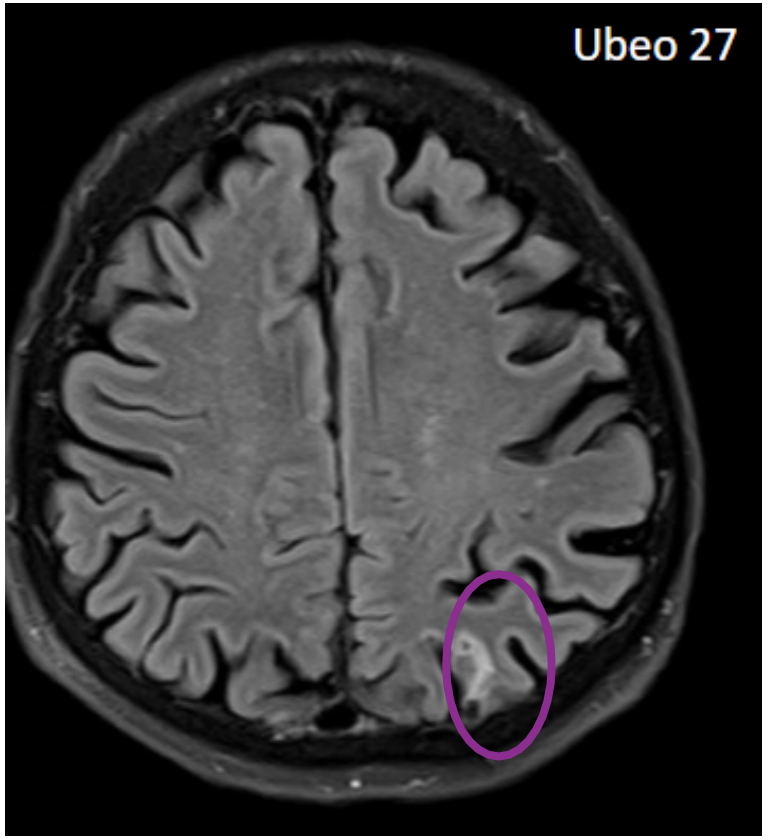




Step 2 = Description of the Brain MRI data?

Carotid-plaque classification = **active** (cortical infarct) and **a**symptomatic





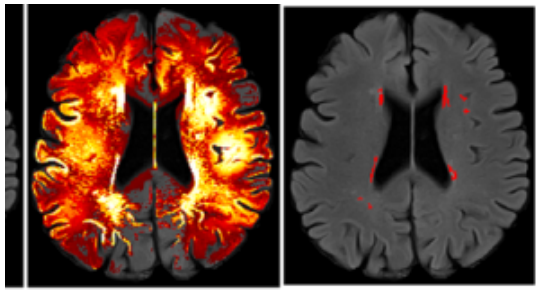
Step 2 = Description of the Brain MRI data?

Carotid-plaque classification = **active** (cortical infarct) and **a**symptomatic

Left active	Left symtpomatic	Right active	Right symtpomatic
25 (22%)	9 (8%)	27 (23%)	4 (5%)
4 treated	6 treated	4 treated	none

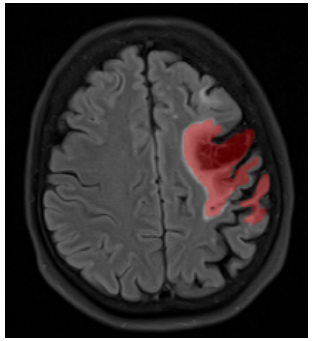
Future perspective

- Discuss the data analysis after sharing



Lesion probability

Probability threshold 98%
Minimum cluster 5 voxels



- Find association of US and clinical data with status of the plaque at baseline

Analisis proposal:

- Left active carotid vs left non active carotid
  US and clinical characteristic
  (if any, which are independent)
- Right active carotid vs right non active carotid
  US and clinical characteristic
  (if any, which are independent)
- Patients with at least one active carotis vs without
  clinical characteristic
  (if any, which are independent)

Thank you for your attention!

Simplicity Is The Ultimate Sophistication - Leonardo Da Vinci

TAXINOMISIS

ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA