ADVANCES IN CARDIAC ARRHYTHMIAS AND GREAT INNOVATIONS IN CARDIOLOGY

Turin, October 25-27, 2012

Cerebral ischemic pattern in patients with atrial fibrillation: the neuroradiologist point of view

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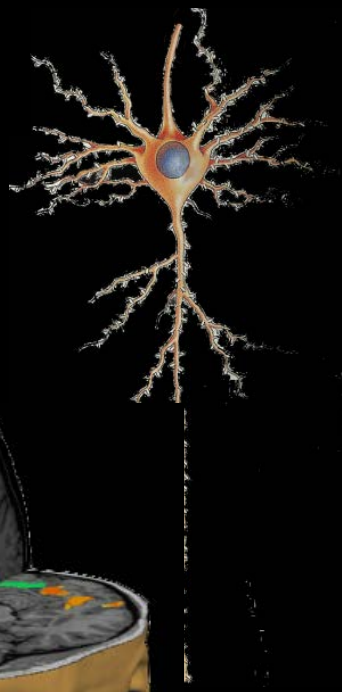
CITTA' DELLA SALUTE E DELLA SCIENZA

STROKE *EPIDEMIOLOGY*

Second cause of death worldwide

ITALY:

- 200.000 cases per year (80% are new)
- 1° cause of FUNTIONAL IMPAIRMENT
- 2° cause of DEMENTIA with disability

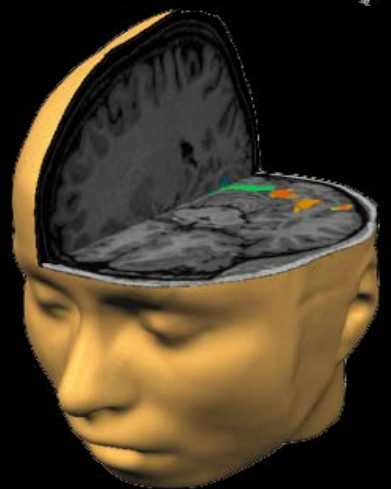


Lopez AD et al. Lancet (2006) 367:1747-1757

Rothwell PM et al. Lancet (2005) 366:1773-1783

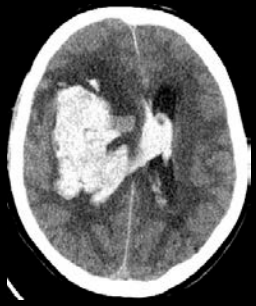
O'Brien JT et al. Lancet Neurol (2003) 2:89-98

- The brain metabolism is the most active in our body
- it exploits 17% of cardiac output
- it uses 20% of available oxygen

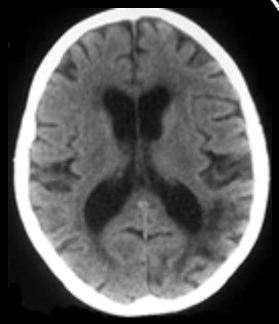


STROKE

⟹ *HAEMORRAGIC STROKE* 20%

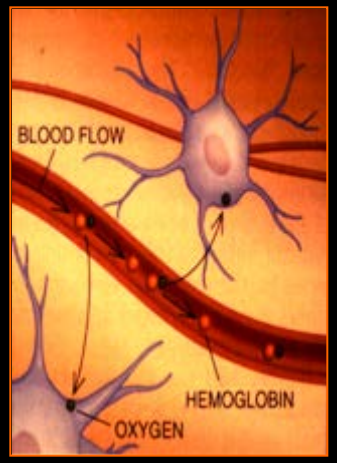


⟹ *ISCHEMIC STROKE* 80%



Time is brain !

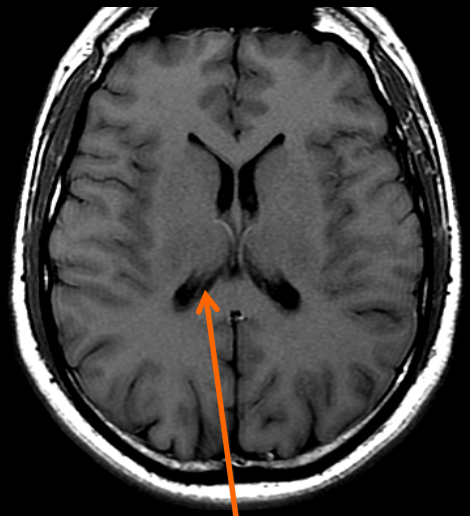
A portion of the brain dependent on blood flow from this vessel becomes deprived of oxygen. Within minutes, nerve cells begin to die, which results in permanent disability.



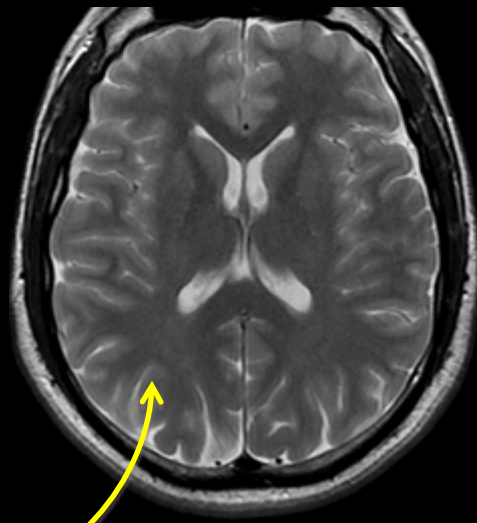
Conventional MRI

To have a morphological analysis must be acquired at least T1 and T2 sequences

Ax SE T1



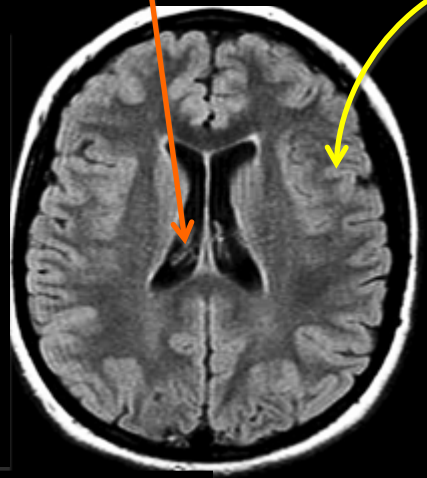
Ax SE T2



G.E.T2*

FLAIR

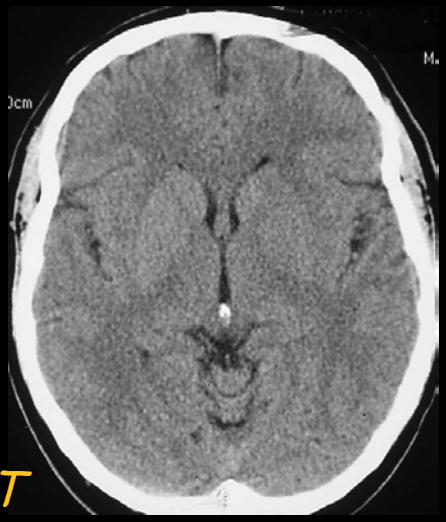
FLAIR



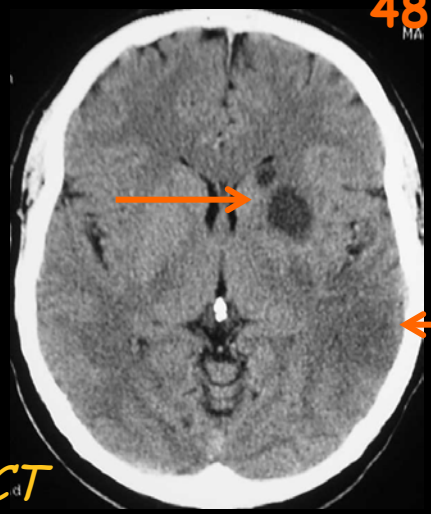
Fluid
Attenuation
Inversion
Recovery

ISCHEMIC STROKE

Hyperacute



CT

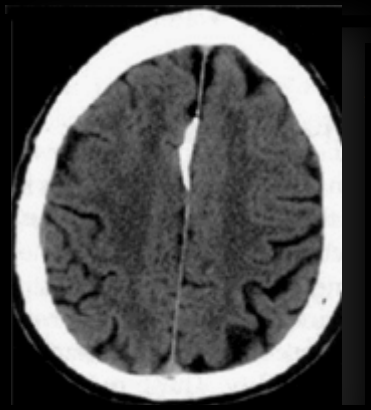


CT

Hyperacute (24H):

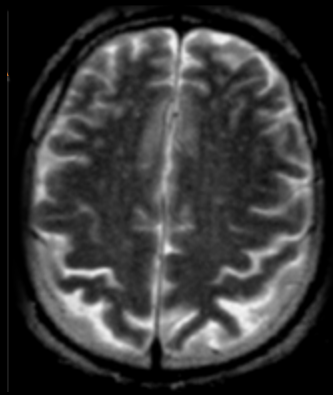
- symptoms , signs of stroke
- CT no abnormality > 50% cases
- there is delay in CT imaging

Conventional MRI after 8-12H:



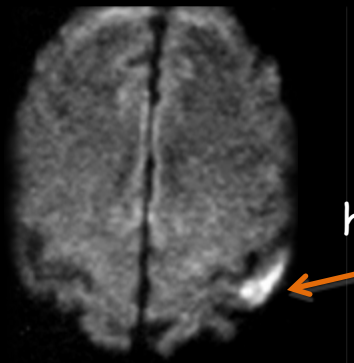
CT

normal



Rm T2

DIFFUSION (DWI)
shows area of ischemia



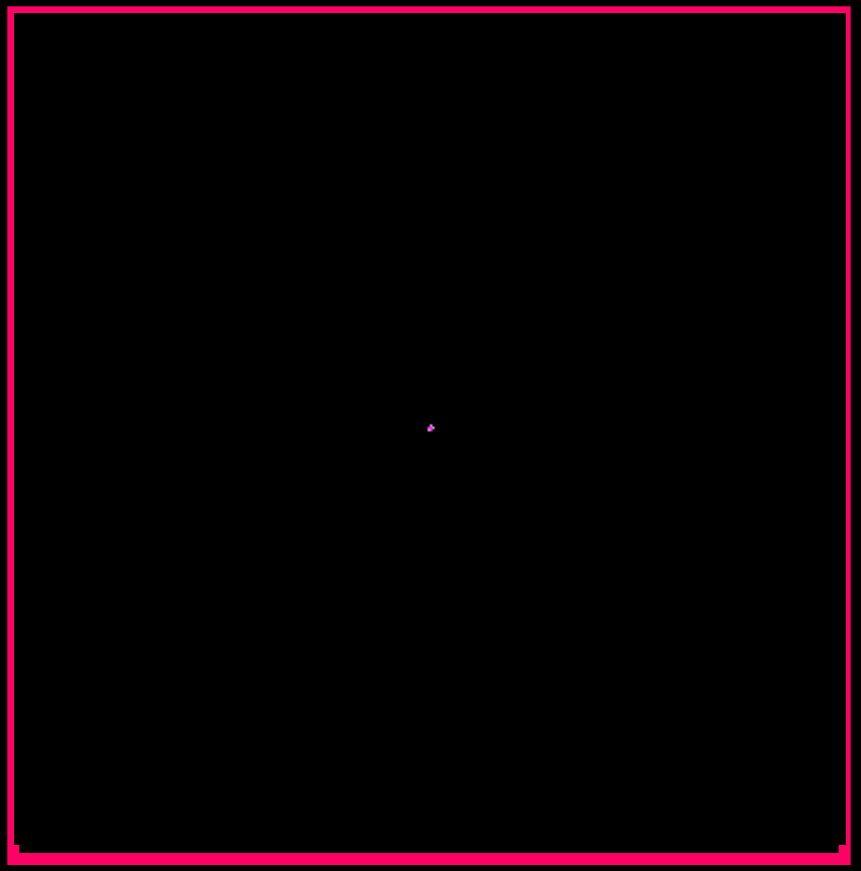
hyperintense lesion

DWI

DIFFUSION

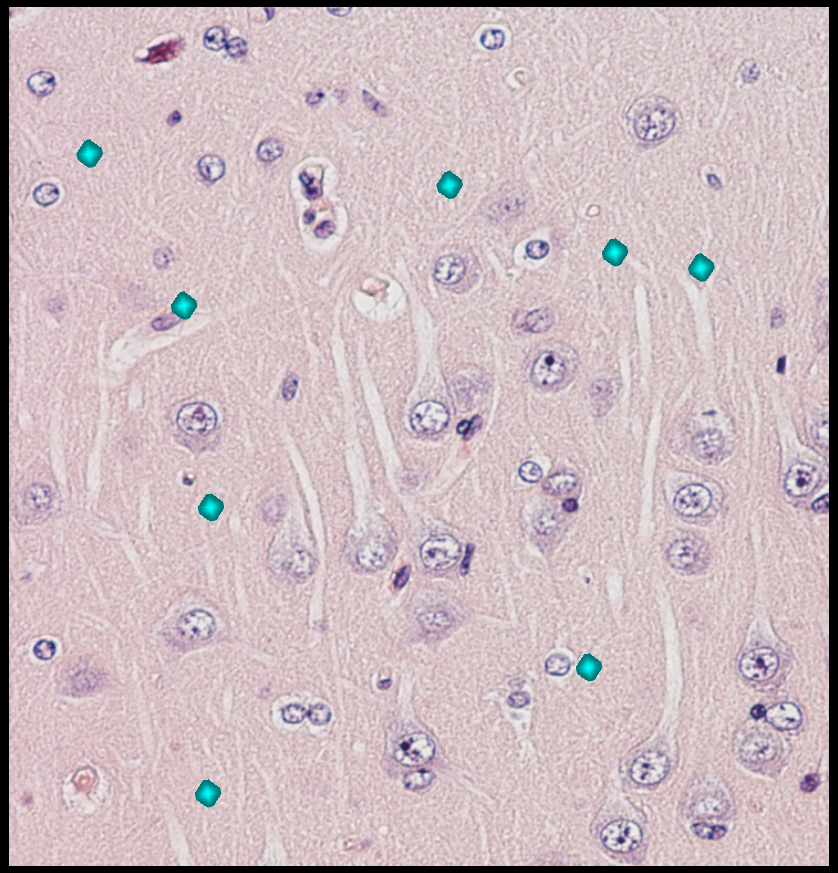
It 's a technique based on MR sensitivity to Brownian motion:

“Translational random movement of molecules in a fluid " observed for the first time by Robert Brown (1827)

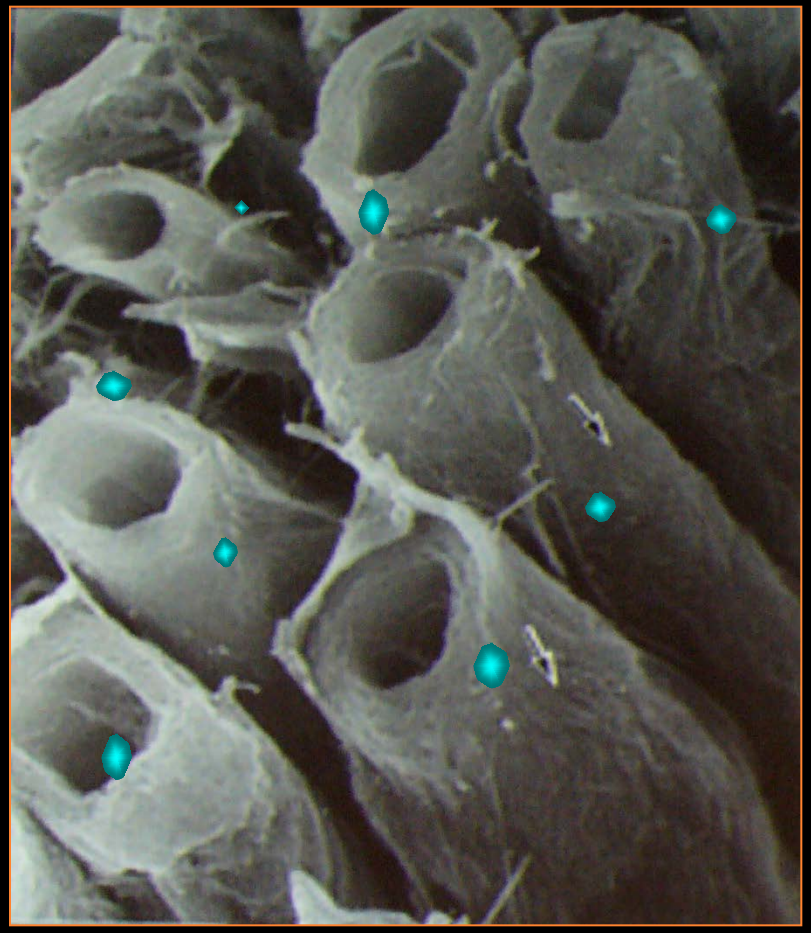


DIFFUSION

With MR it is possible to evaluate the entity and the direction of movement of the H2O molecules within tissues.



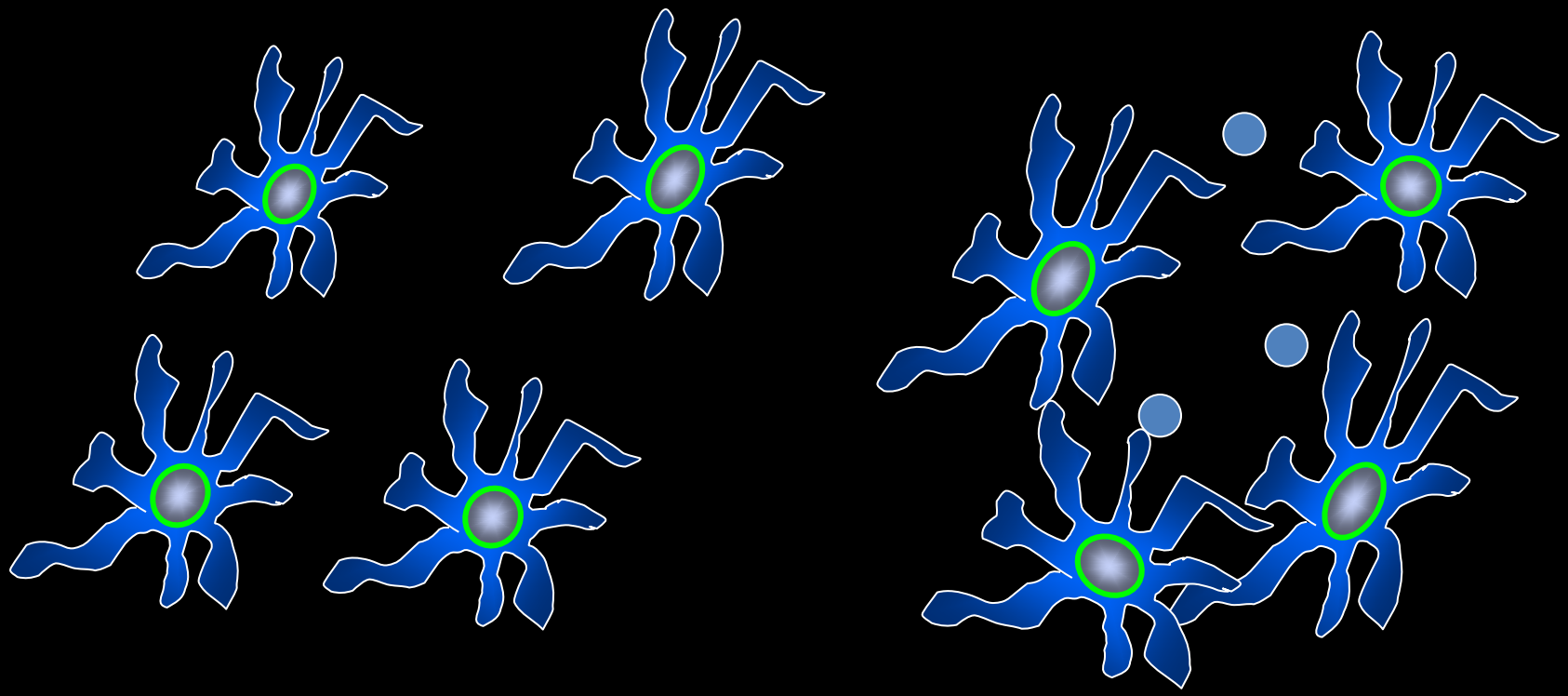
Isotropy



Anisotropy

Cerebral ischemia

Ischemia → intracellular Na + H20 → CYTOTOXIC EDEMA and CELLULAR SWELLING .



With cellular swelling, there is reduced extracellular space volume → restricted diffusion

Diffusion Diffusion-Weighted Imaging or DWI

DWI allows the measurement of the diffusion distance of water molecules.

The shorter is this distance, more hyperintense is the lesion

Immagine D

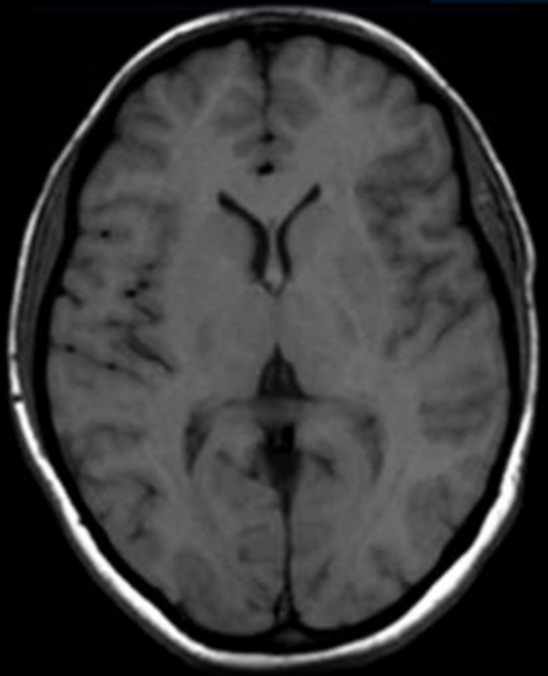
T1

Low signal

High speed diffusion

High signal

Low diffusion velocity



PLAIR

1: 0,009

2: 0,005

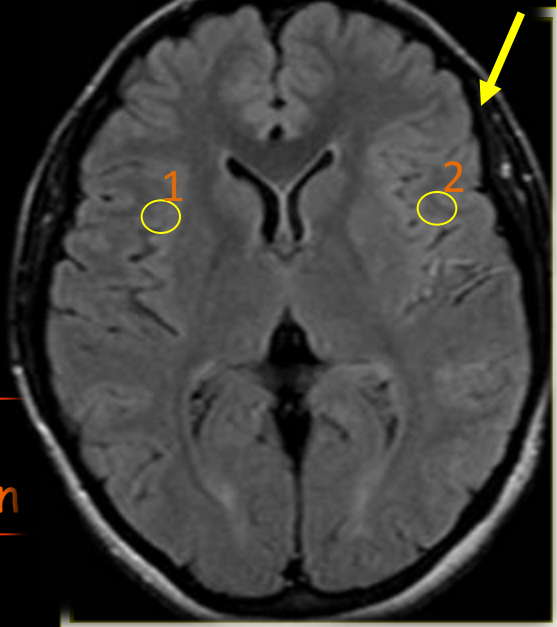
tricted

Diffusion

ADC map:

apparent diffusion coefficient

average diffusion value of H_2O molecules



Free Diffusion

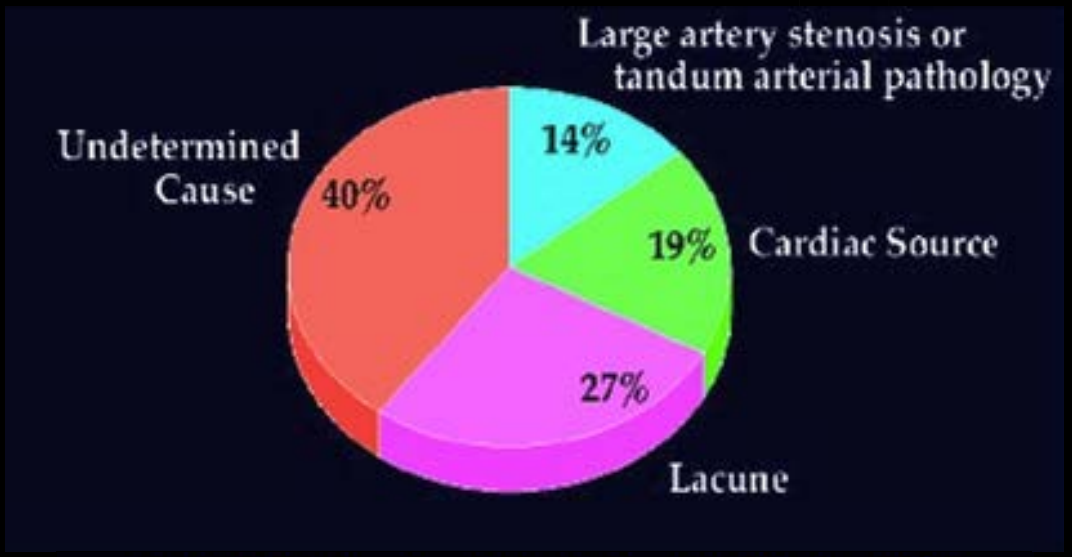
S.E. conventional images are normal

Ischemic Stroke

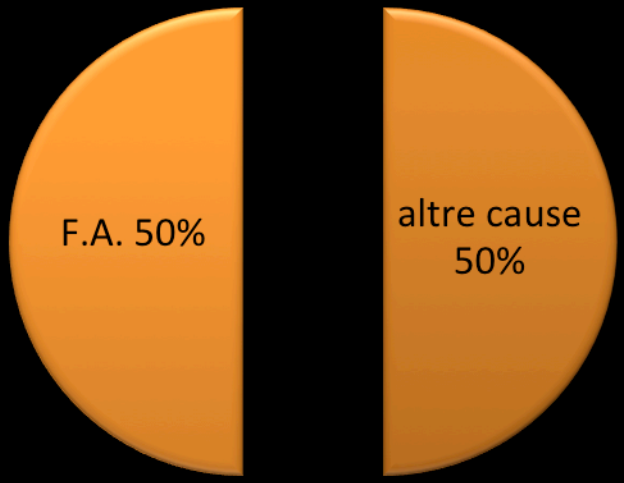
1. Thrombosis (local vessel obstruction caused by an blood clot originated in situ)
2. Embolism (local vessel obstruction caused by an embolus originated elsewhere)
3. Systemic Hypoperfusion
4. Other not known causes: cryptogenetic or not thoroughly investigated

25 to 30% of stroks are secondary to heart disease

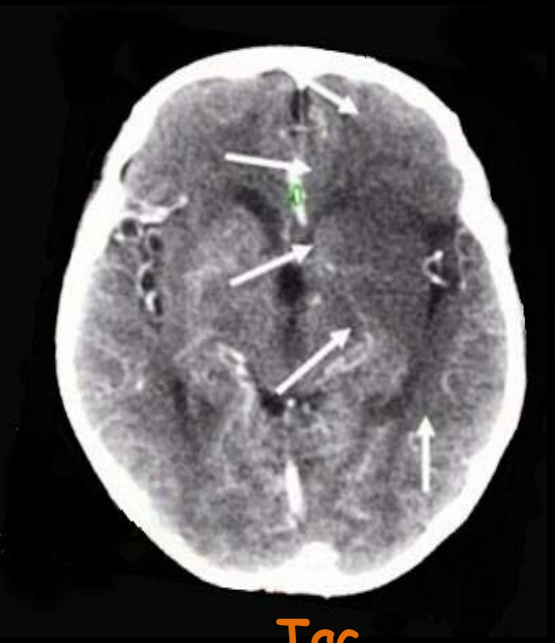
Cervera et al. 2001



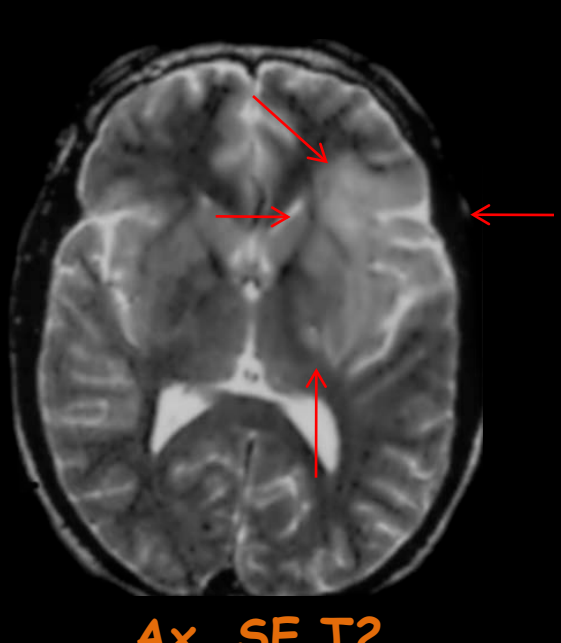
NINDS Stroke Data Bank
Classification of Ischemic Stroke (N = 1,273)



Risk Factors for Stroke



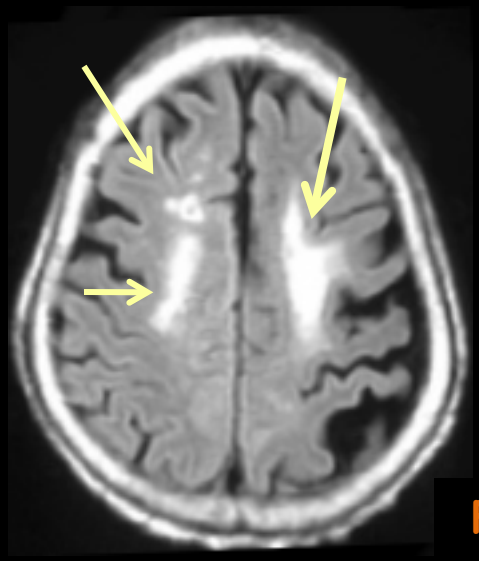
Tac



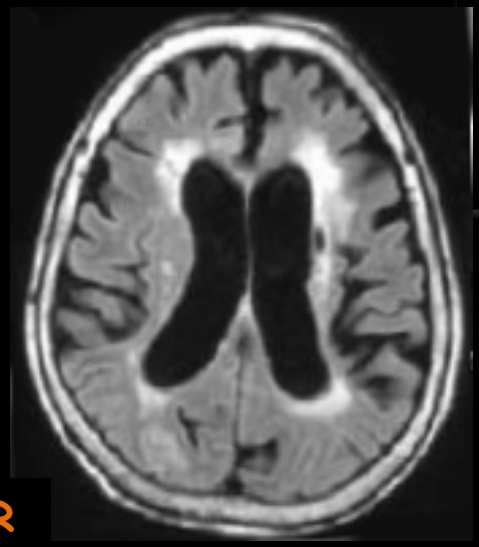
Ax SE T2

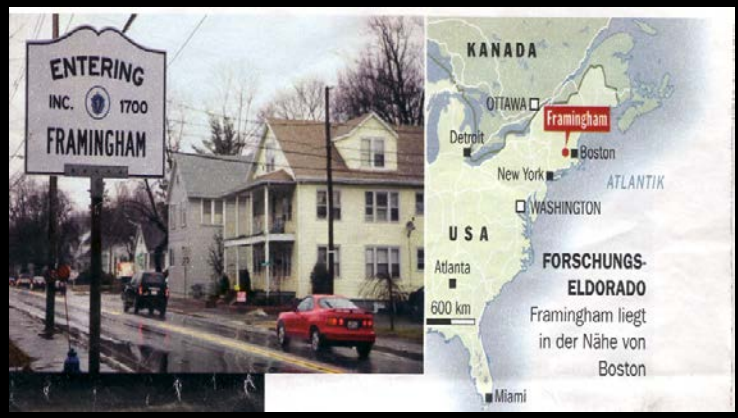
- Hypertension
- Atherosclerosis
- Cardio embolism
- Amyloidosis
- Diabetes
- Age
- Smoke .....

Framingham Risk Score



FLAIR





Stroke 1991;22:312-318

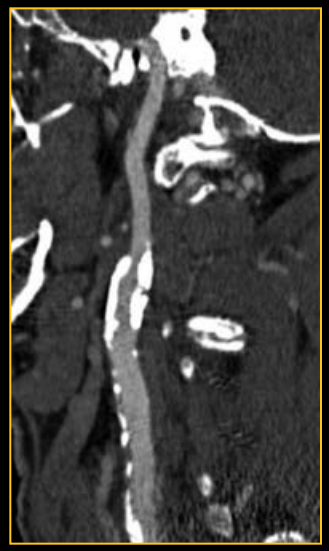
10 yr risk for Stroke in Adults 55 -84 yrs old according to basic Risk Factor (Framingham Heart Study)

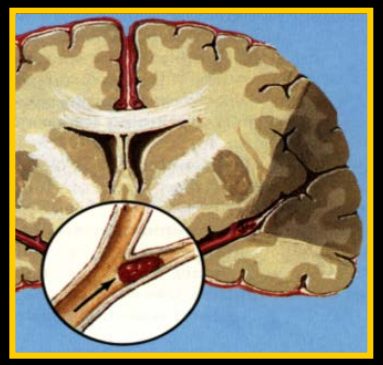
Silent Ischemic Lesions (S.C.I.)

Silent Ischemic Lesions without clinical or neurological signs

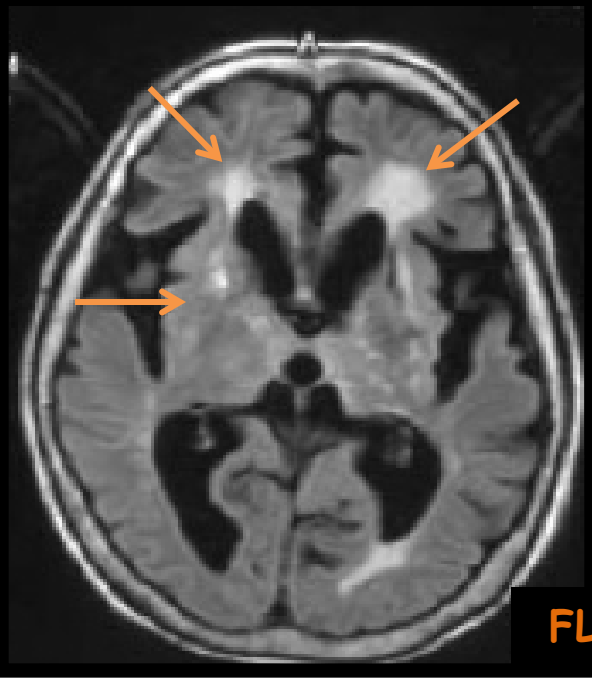
Silent brain infarcts: a systematic review
Sarah Vermeer et al.- Lancet Neurol 2007

Prevalence and risk factors of silent brain infarcts in the population- based Rotterdam Scan study
Vermeer SE et al. Stroke 2002; 33: 21–25.





Angio TC



FLAIR

Subcortical silent brain infarction as a risk factor for clinical stroke. Kobayashi S et al. Stroke 1997; 28: 1932–39.

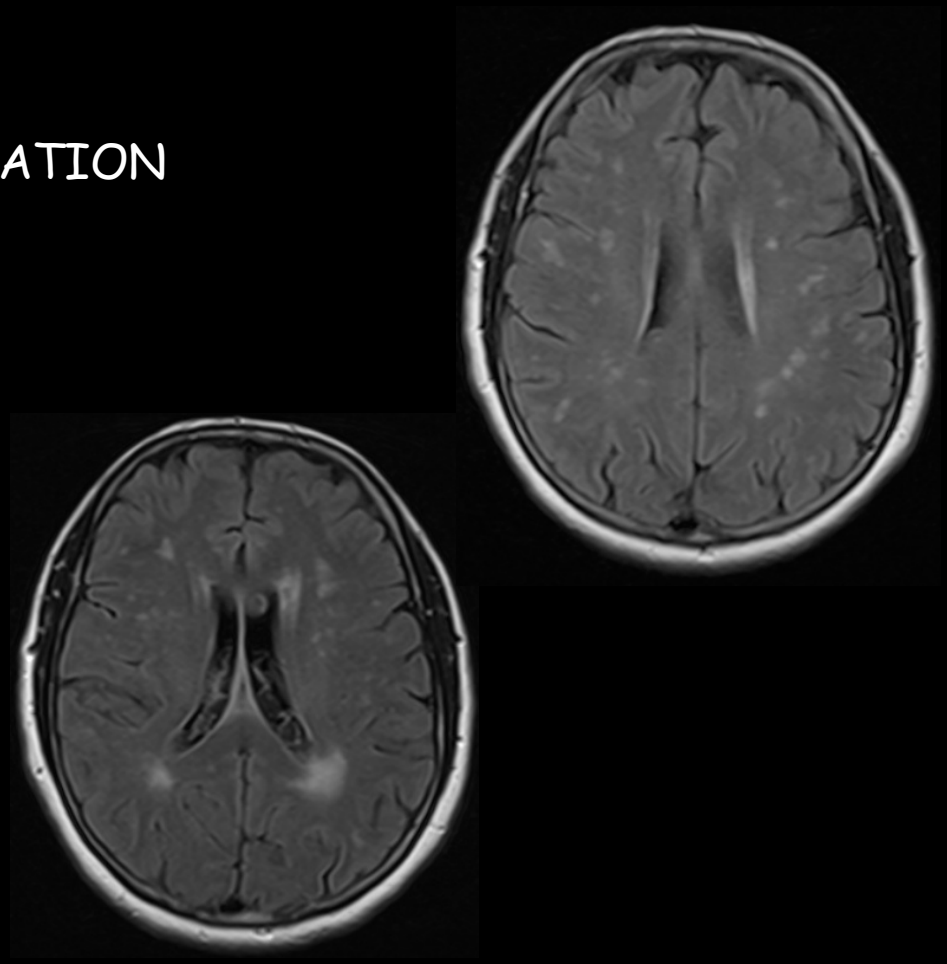
Kotani K, Osaki Y, Sakane N, Adachi S, Ishimaru Y. Risk factors for silent cerebral infarction in the elderly. Arch Med Res 2004; 35: 522–24.

Prevalence of stroke in the general population: the Rotterdam Study. Bots ML et al , Stroke 1996; 27: 1499–501.

Silent Ischemic Lesions

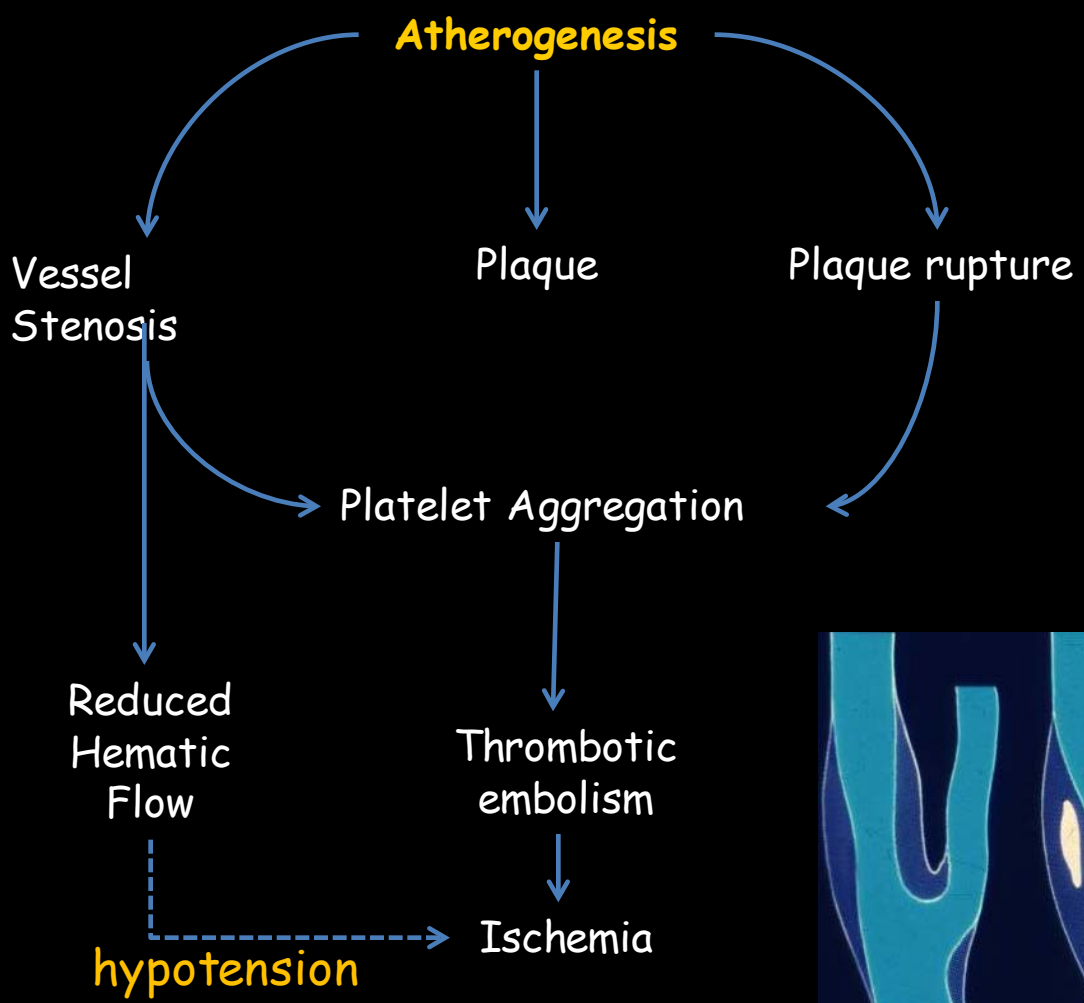
ETHIOLOGY (42 KNOWN CAUSES)

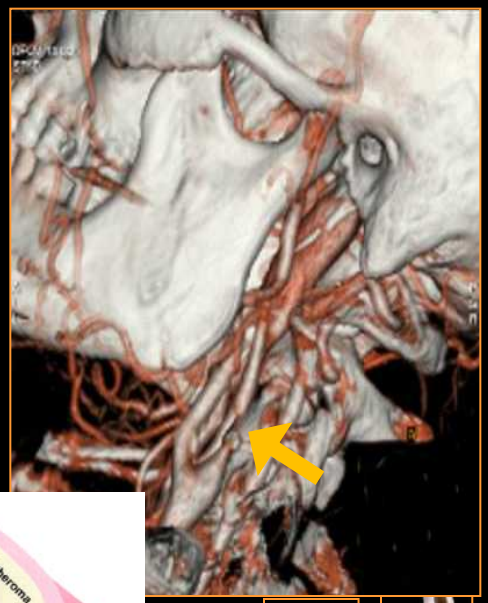
- Atherosclerosis VESSEL WALL ALTERATION
- Hypertension (acute and chronic)
- Amyloidotic angiopathy
- Cardio-embolic
- Vasculitis
- Systemic lupus erythematosus
- Antiphospholipid syndrome
- Migraine …

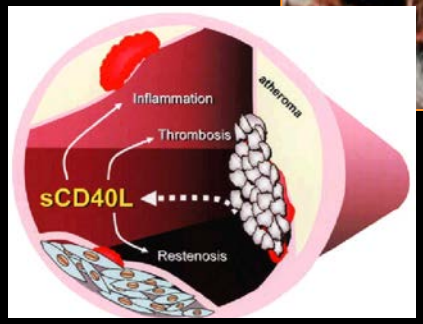


Atherosclerosis

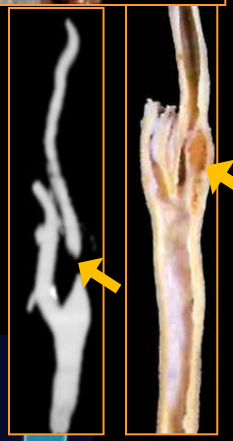
Flowchart of athero thrombotic stroke

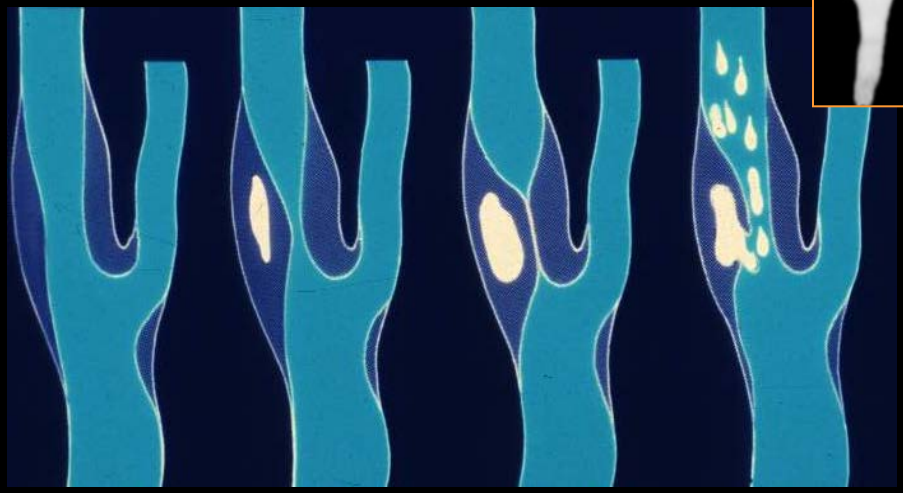






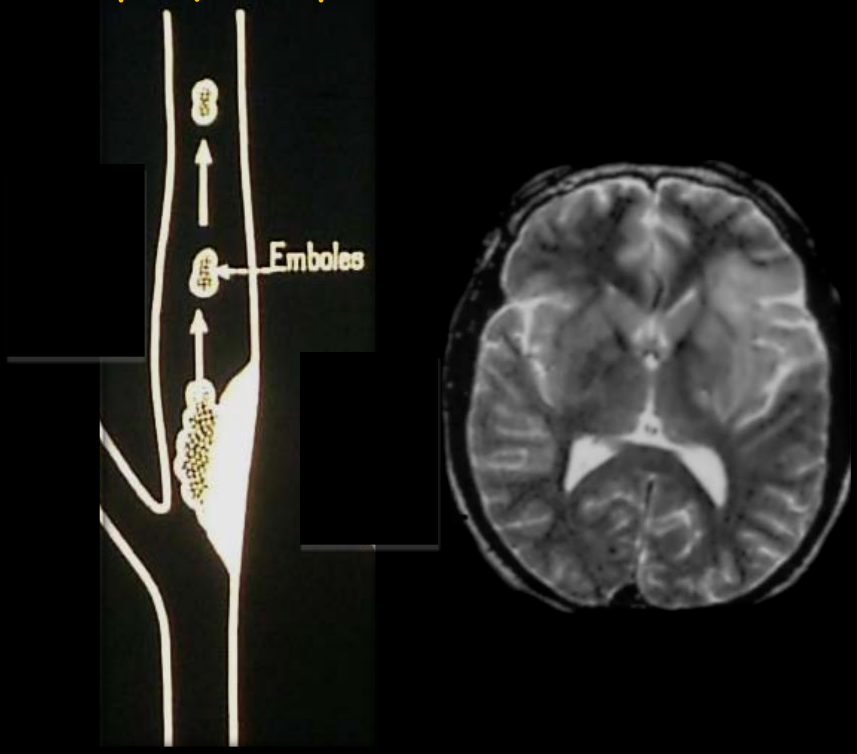
Circulation. 2002:106:896-899.



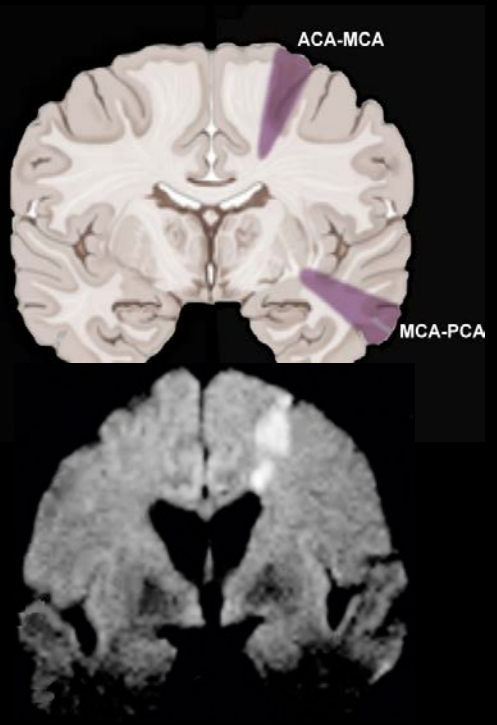


Atherosclerosis of main vessels

- Embolism "artery-to-artery" caused by fragments generated by plaque rupture



- Hemodynamic Ischemia in a boundary area withstanding an excessive hypotension.

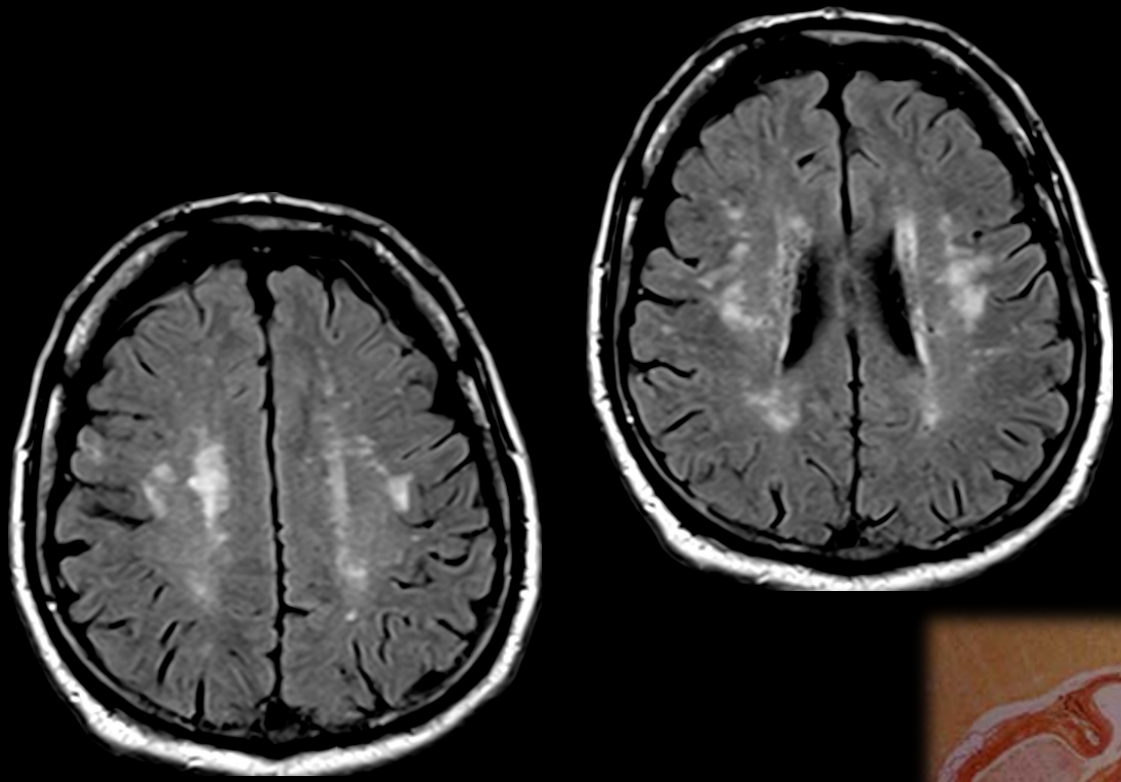


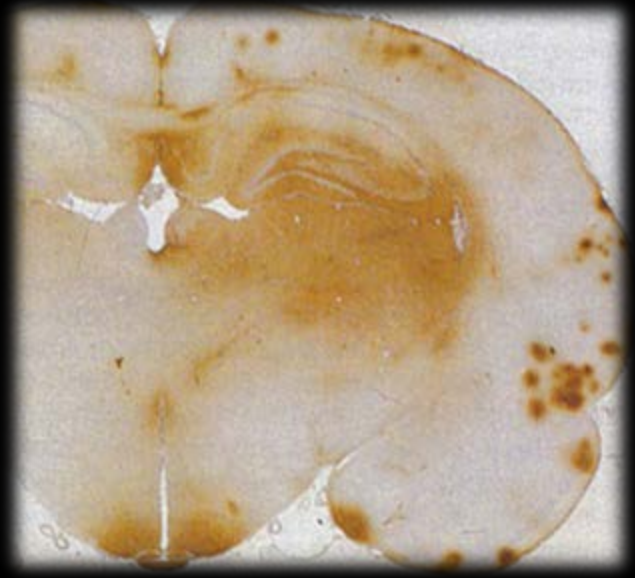
Silent ischemic lesions: ARTERIOLOSCLEROSIS

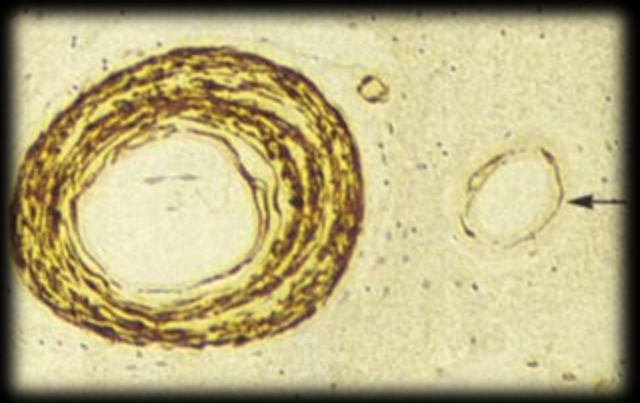
Small vessel disease/microangiopathy

Sclerosis of small arteries (arterioles), common in chronic hypertension or DM

Fisher (1965): vessel occlusion in case of arteries wall lipohyalinosis





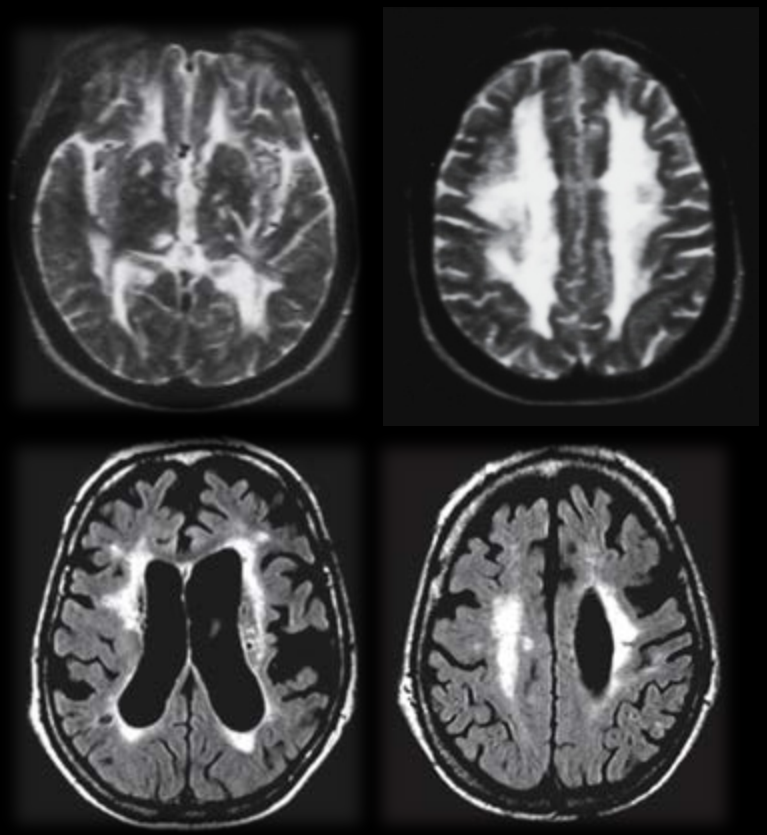


Silent ischemic lesions: Atherosclerotic Microangiopathy

Hypertensive encephalopathy

Atherosclerotic subcortical encephalopathy or Binswanger encephalopathy

- Leucoaraiosis
- Lacunar infarcts
- Intracerebral hemorrhages (microbleeds)



Amyloid deposits and fibrinoid necrosis in the cortical and leptomeningeal wall vessels

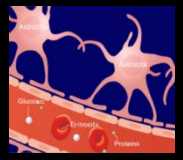
Hypertensive encephalopaty pathogenesis

Hypertension

Perforating arteries

Lypoialinosis microatheroma

Loss of Regulation Blood-brain barrier



- ✓ tight junctions openings
- ✓ increased pinocitosis
- ✓ Alterations of cell membrane channels

Sistemic factors: **hypotension**

Worsening of small vessel disease → Leucoaraiosis

Perforating arteries occlusion → Lacunas

Silent ischemic lesions:

Small vessels disease

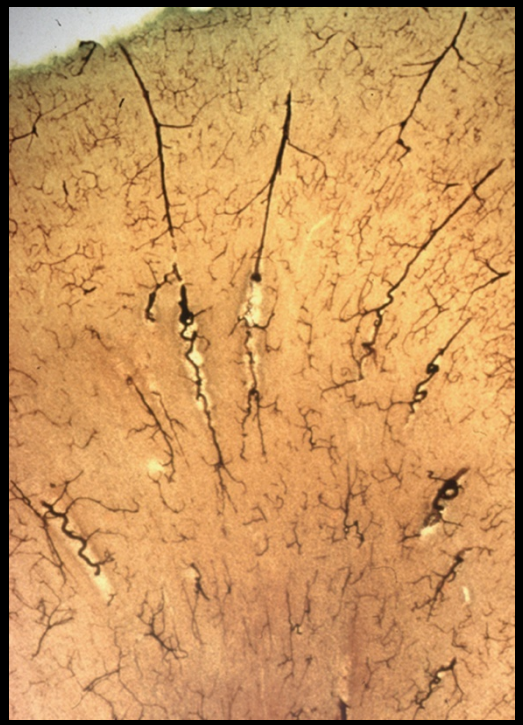
LEUCOARAIOSIS

Arteriolosclerotic microangiopathy

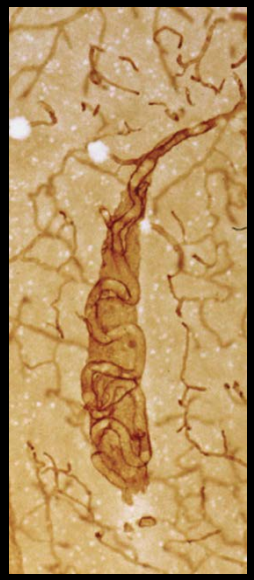
Hypertensive angiopathy

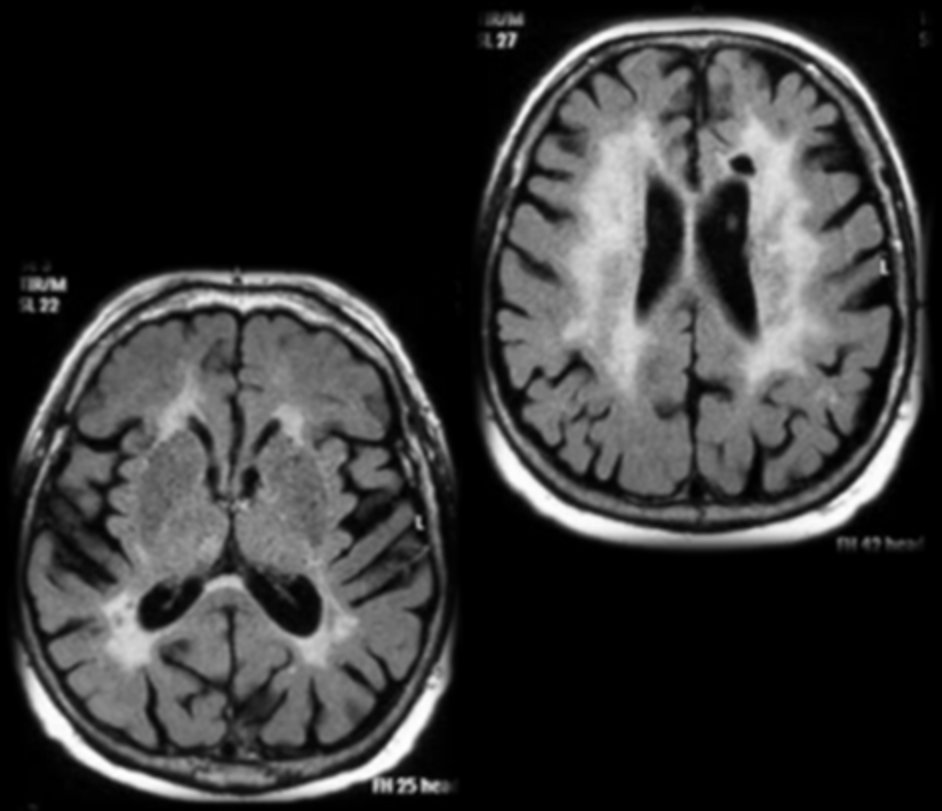
White matter widespread rarefaction:

- myelin degeneration
- astrocyte gliosis
- small vessels wall fibrosis



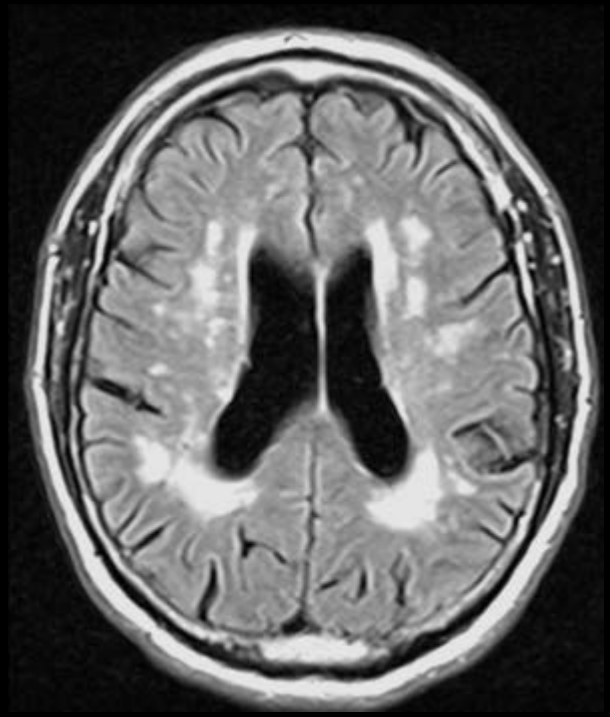
Elongated and winding vessels



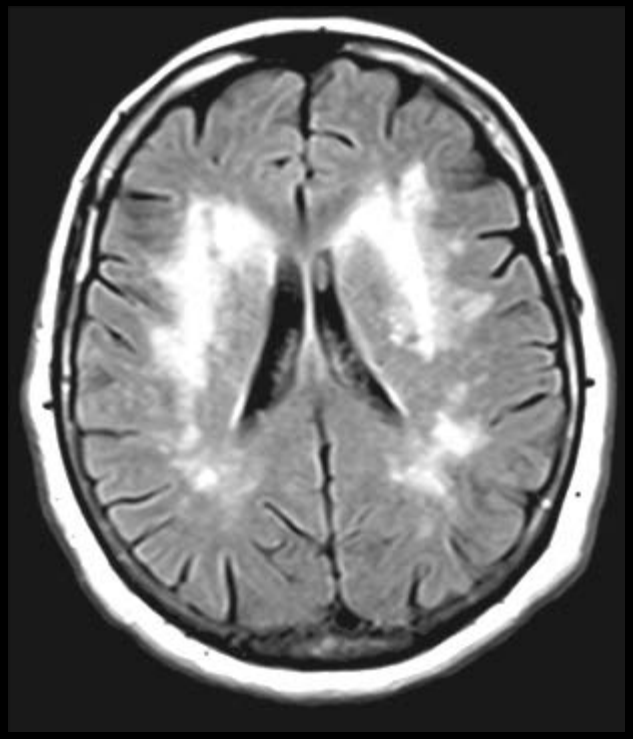


MR features

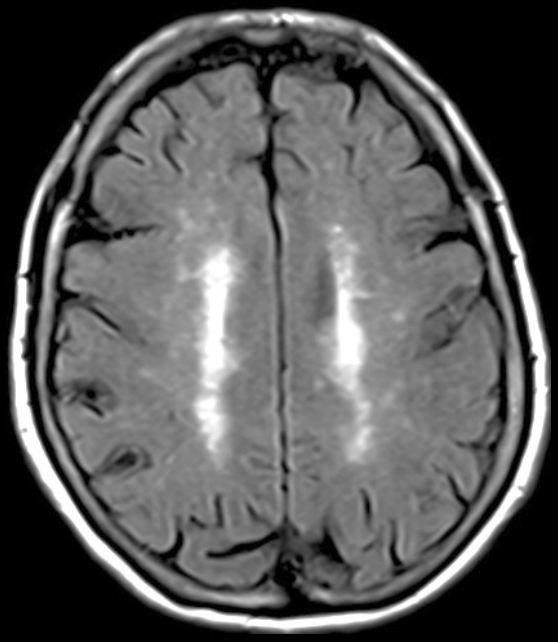
Bilateral patchy or diffuse hyperintense signal in T2 and hypointense in T1 sequences with ill-defined margins



periventricular



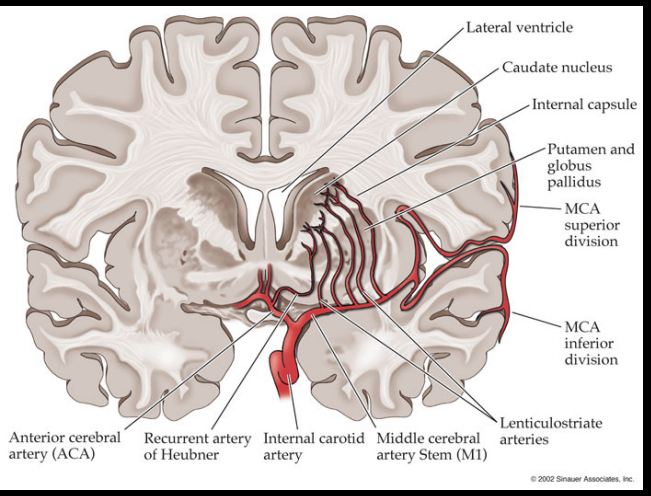
corona
radiata

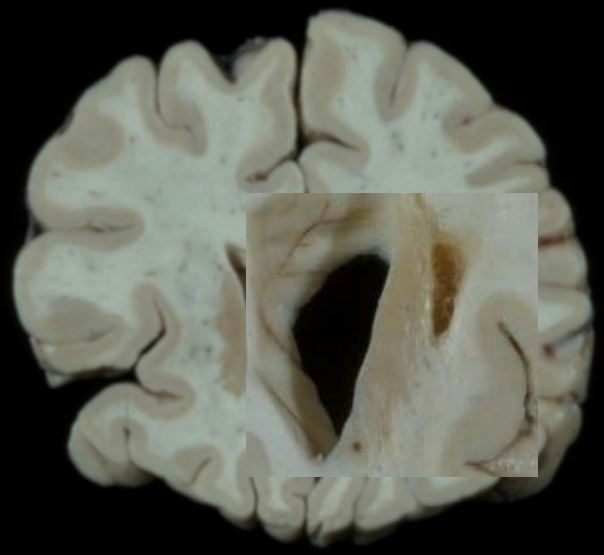


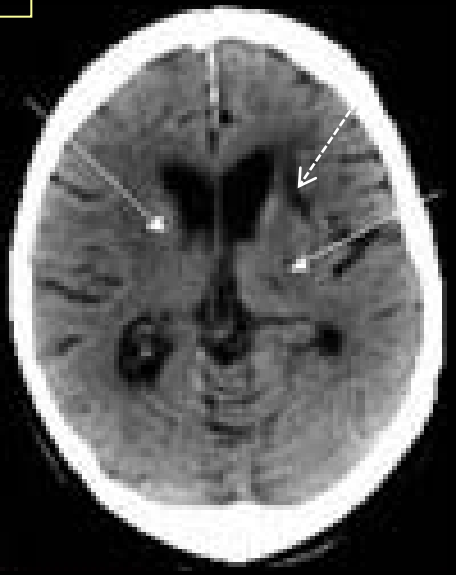
centrum
semiovale

Silent ischemic lesions: # LACUNAR INFARCTIONS

1883: Dechambre first anatomical-pathological description : Small cavity <15 mm, with liquor, located in basal ganglia, thalamus, centrum semiovale and brain stem







Lacunes: Small, deep cerebral infarcts

C. Miller Fisher, M.D.

Caused by the occlusion of perforating arteries originating from:

- Middle cerebral artery
- Posterior cerebral artery
- Basilar artery

- Ischemic infarct in a small and deep area in the "brain".
- No in cerebral and cerebellum cortex
- Mostly in basal ganglia and pons.

Silent ischemic lesions:

"Les lacunes Cérébrales"

C. Derousné, J. Poirier
Rev. Neurol. 1999

Type I lacunas

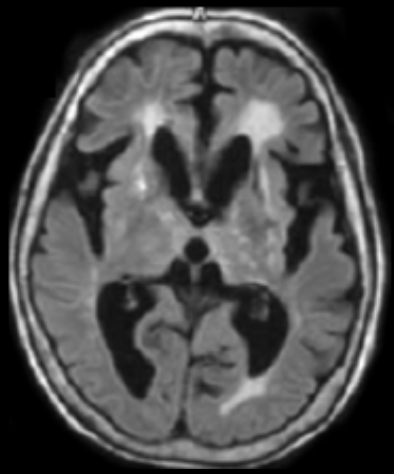
- Occlusion of perforating arteries or their main branches

Type II lacunas

- microhemorragic content: hemosiderin and macrofages

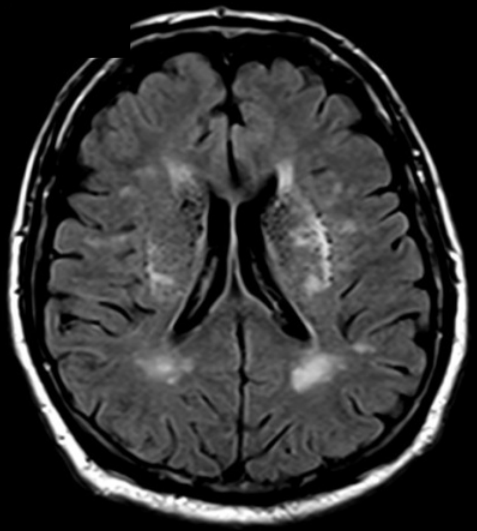
Type III lacunas

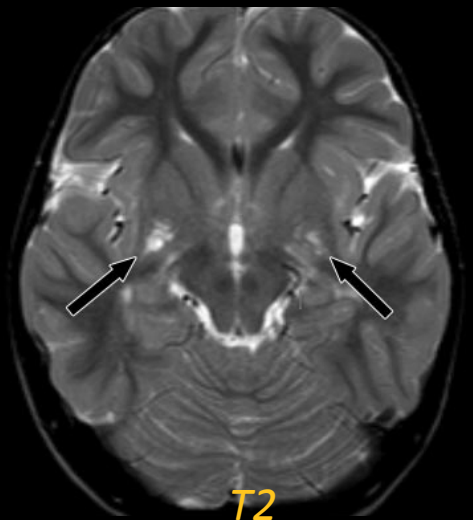
- enlargement of perivascular spaces



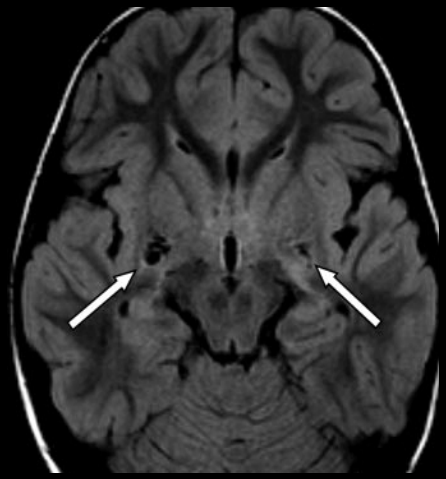
flair

flair





T2

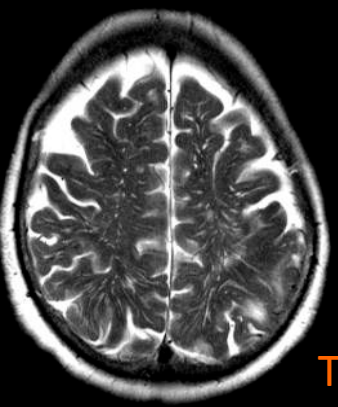


FLAIR

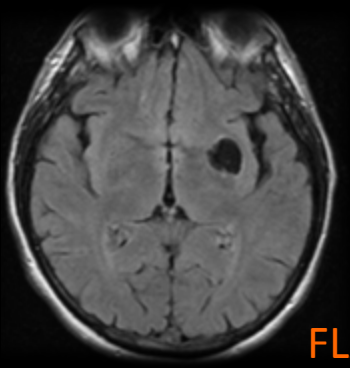
Type III Lacunas

Perivascular space dilatation

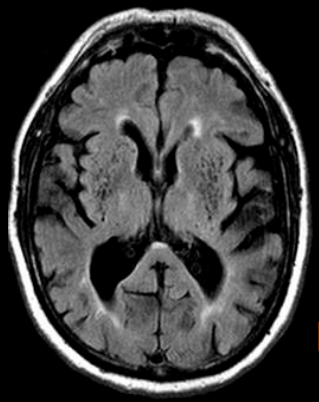
Extracellular water in Virchov-Robin spaces



T2



FLAIR

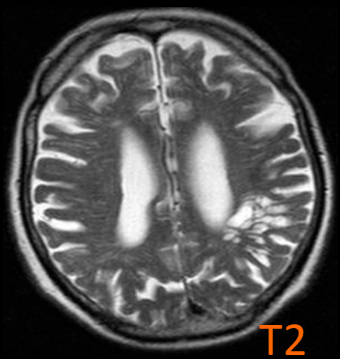


FLAIR

- ✓ Abnormal vessel permeability
- ✓ Parenchimal atrophy all around the vessels
- ✓ Mechanical stress due to vessel pulsatility

Increases:

- ➢ With advancing age
- ➢ With hypertension
- ➢ Elongated and **winding arterioles**



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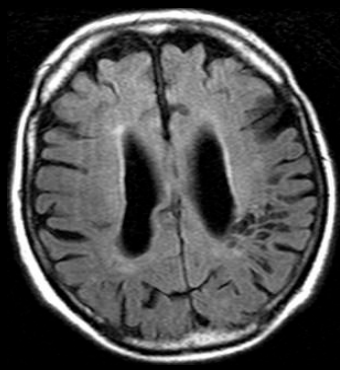
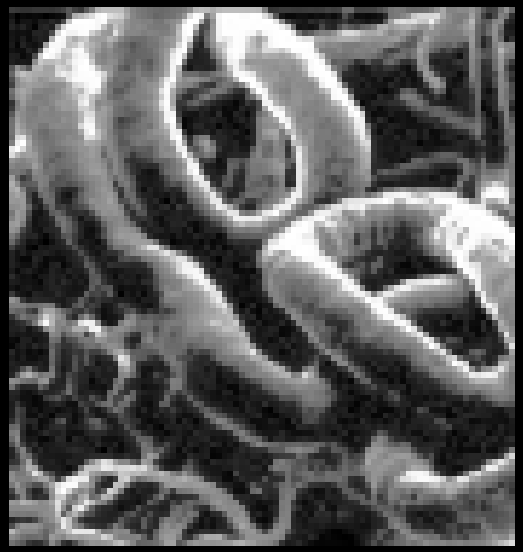


FLAIR

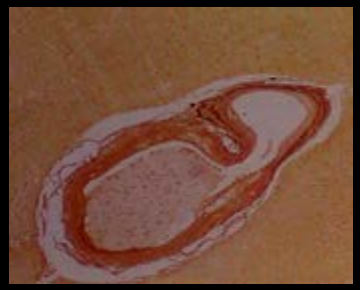


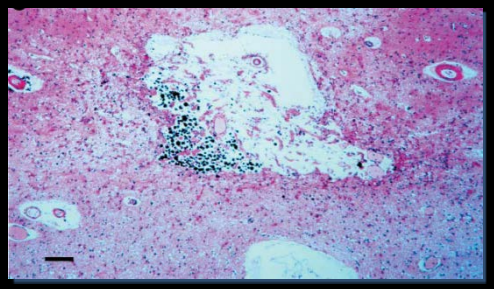
Distinguishing silent lacunar infarction from enlarged Virchow-Robin spaces
Hirokazu Bokura et al –J.Neurol. 1998

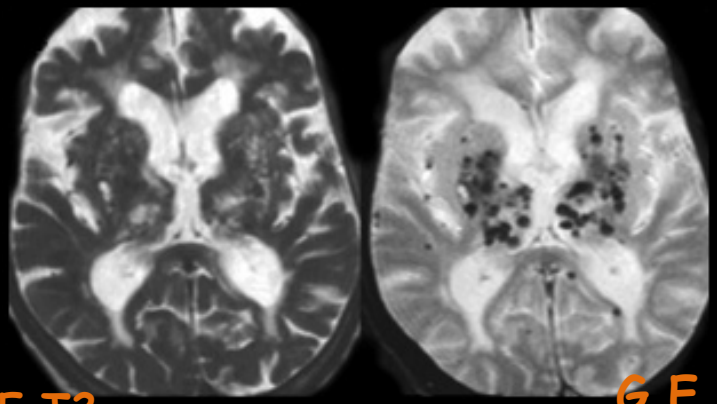
Types II Lacunas

Silent ischemic lesions:

Arteriolosclerosis: pseudoaneurism rupture
lipohyalinosis of vessel wall







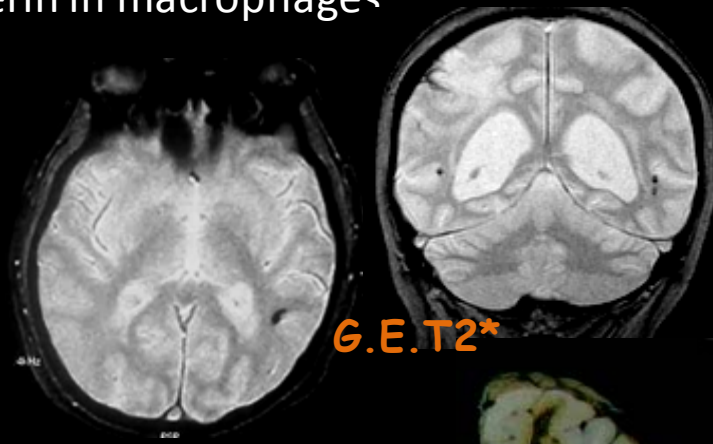
S.E.T2 G.E.T2*

- deep lacunes: microhemorrhagic content, hemosiderin in macrophages

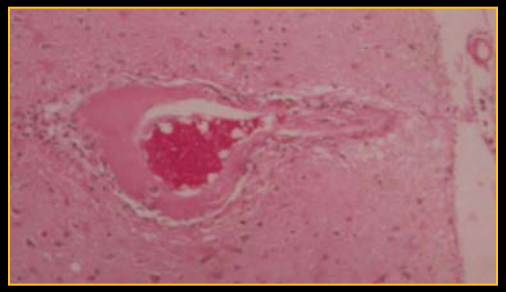
D.D. amyloidotic angiopathy

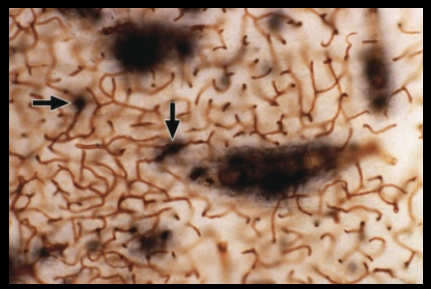
Amyloidotic deposits and fibrinoid necrosis in vessels wall (cerebral cortical and leptomeningeal)

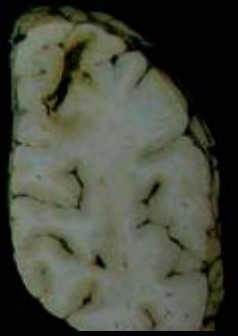
- wall segmentary thickening
- microaneurism formation



G.E.T2*



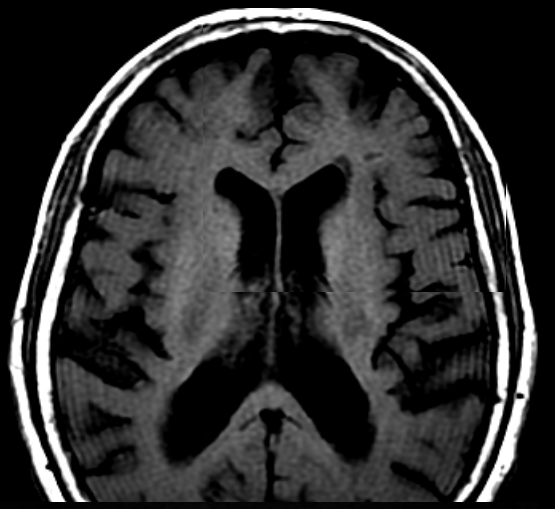


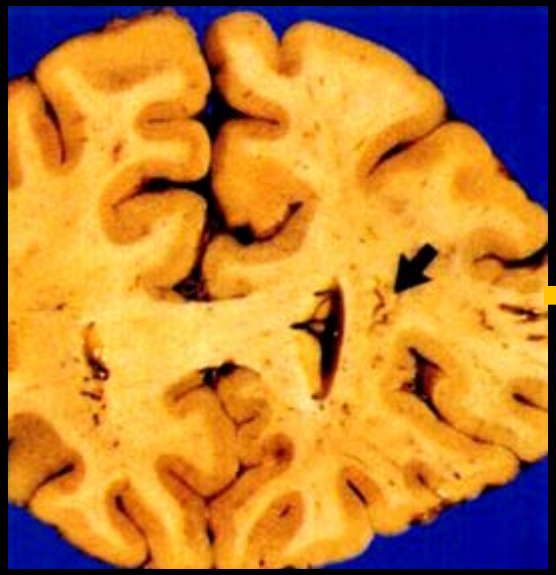


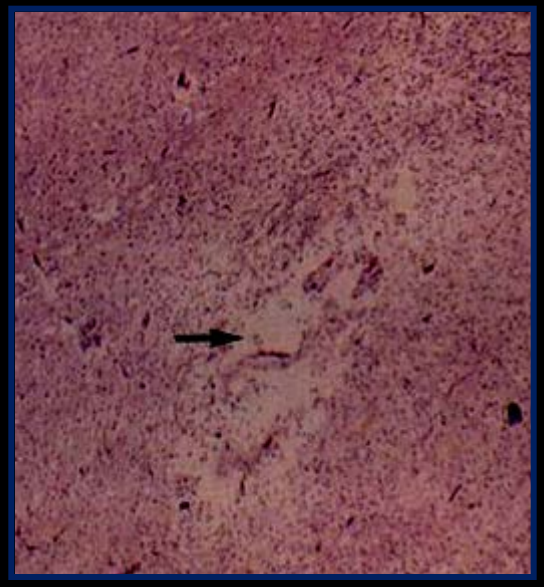
Silent ischemic lesions:

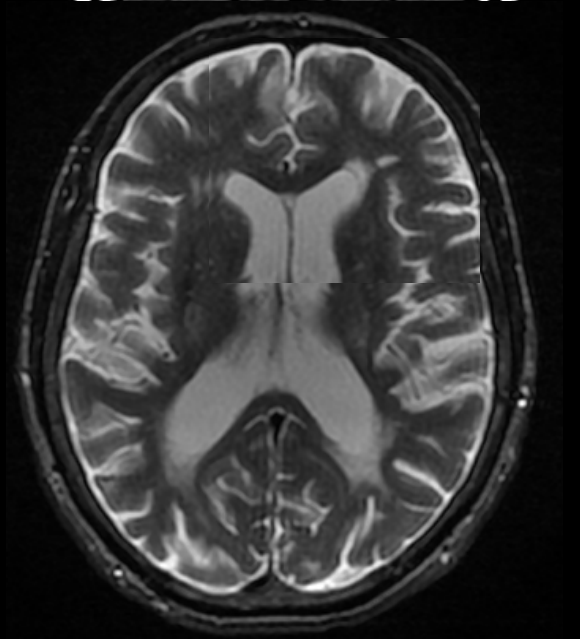
Type 1a Lacunas *"complete infarction"*

- **Central necrosis: LIQUOR (hypointensity in T1 and in FLAIR)**
- Axonal loss
- Demyelination
- Astrocyte reaction all around
- Isomorphic gliosis (reactive astrocytes oriented along the damaged axon)









Vaughn G. Marshall, MD • William G. Bradley, Jr., MD, PhD • Charles E. Marshall, MD • Tanin Bhoopat, MD • Roy H. Rhodes, MD, PhD

Deep White Matter Infarction: Correlation of MR Imaging and Histopathologic Findings[1]

Radiology 1988; 167:517–522

In T2 images, the isomorphic gliosis around the infarction increases its dimension

Silent ischemic lesions:

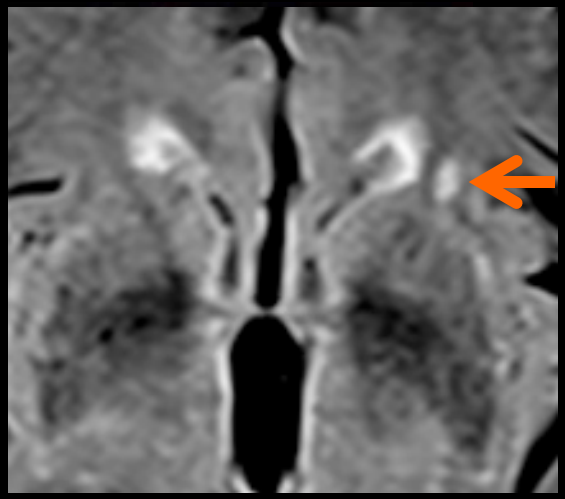
Lacunas Type 1b "incomplete infarction"

A White Matter Disorder in Dementia of the Alzheimer Type: A Pathoanatomical Study
A. Brun – E. Englund *Ann Neurol 19:253-262, 1986*

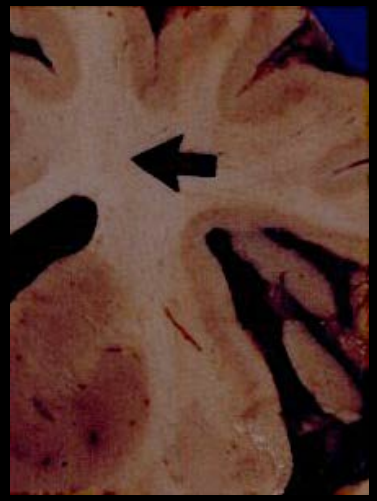
- **Axonal loss and oligodendroglial loss**
- Demyelination
- Macrophages with associated arteriolar hyaline fibrosis
- Reactive astrocytes all around
- Isomorphic gliosis of moderate degree (reactive astrocytes oriented along the damaged axon)

NO CENTRAL NECROSIY

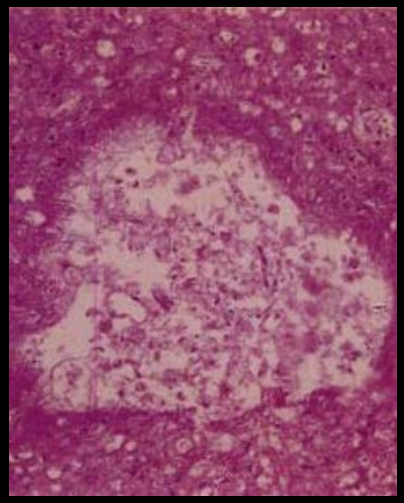
NO HYPOINTENSITY IN T1 AND in FLAIR
IPER-INTENSITY IN FLAIR

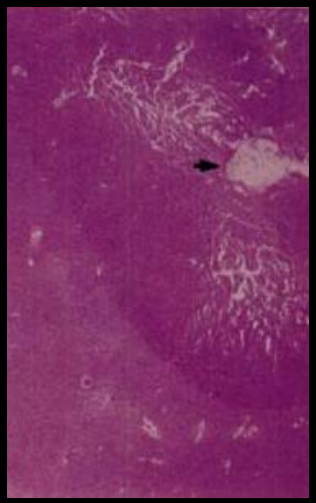


Small area of hyperintensity in FLAIR



Small area of myelinic paleness





hematoxylin and eosin : area of axonal and oligondroglial loss surrounded by reactive gliosis

Silent ischemic lesions: Lacunas Type 1b *"incomplete infarction"*

VESSEL OCCLUSION

Deep white matter infarction: Correlation of Mr imaging and Histopathologic Findings

Vaughn G.Marshall – William G.Bradley et all
RADIOLOGY 1988;167:517-522

BLOOD-BRAIN BARRRIER RUPTURE

Cerebral Microvascular Alterations in Aging, Leukoaraiosis, and Alzheimer's Disease

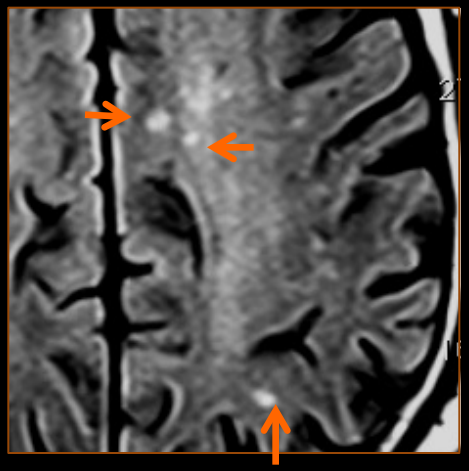
DIXON M. MOODY B
ANNALS NEW YORK ACADEMY OF SCIENCES 103-116 1996

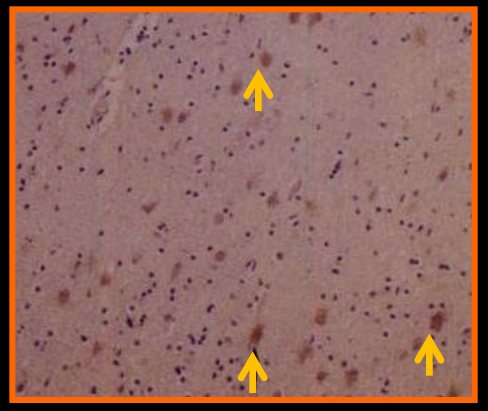
CHEMOTAXIS AND ACTIVATION OF ASTROCYTES

RE-UPTAKE OF SERUM PROTEINS

SWOLLEN ASTROCYTES WITH INCREASED INTRACELLULAR WATER

ISOMORPHIC GLIOSIS

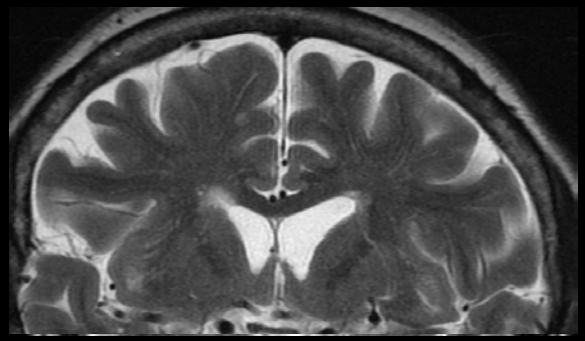


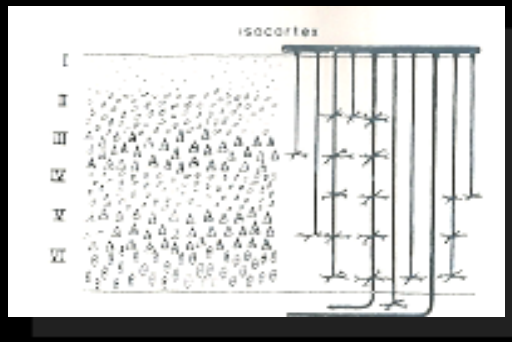


CORTICAL AND SUBCORTICAL VASCULARIZATION ANGIO-ARCHITECTURE

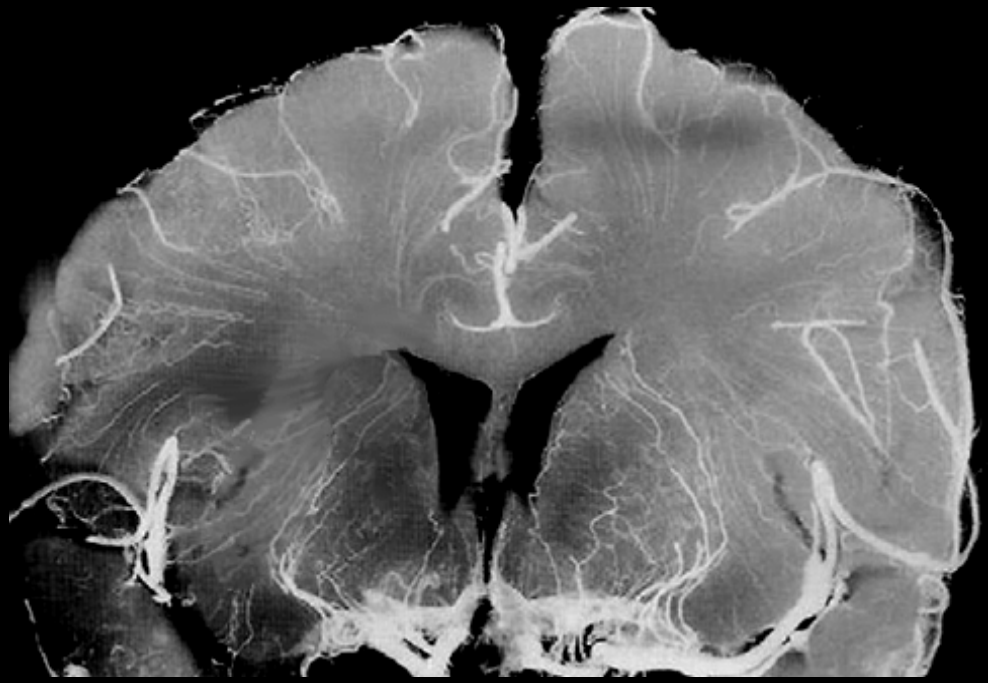
3 TYPES OF perforanting LEPTOMENINGEAL ARTERIES

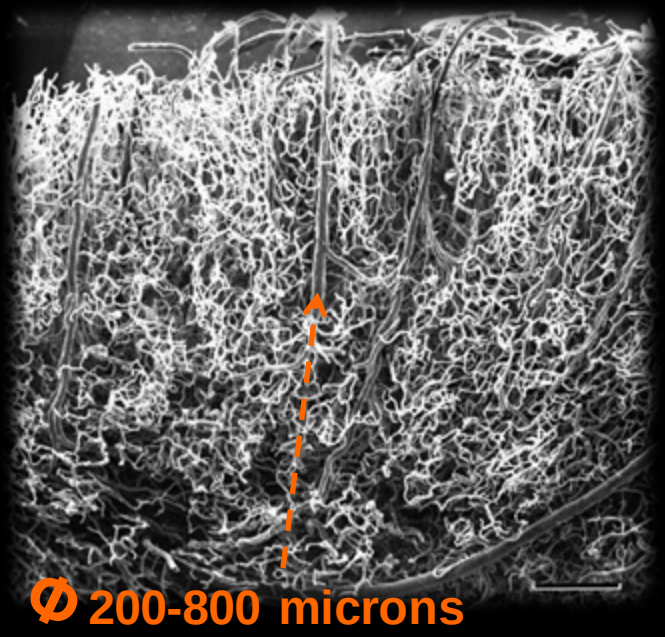
1. CORTICAL
2. CORTICO-MEDULLARY
3. MEDULLARY





PENETRANTING BRANCHES : NO ANASTOMOSIS → SINGLE VASCULAR TERMINAL AREAS





The aim of our study

To compare the
prevalence and the characteristics of silent cerebral lesions in patients with paroxysmal and persistent atrial fibrillation
versus
a control population without evidence of atrial fibrillation

MR and silent ischemic lesions: literature analysis

MR POPOLATION STUDIES

"silent lesions are focally defined, sharply demarcated areas hyperintense in T2, hypointense in T1"

Prevalence and Risk Factors of Silent Cerebral Infarction in Apparently Normal Adults

Sang-Chol Lee, Sang-Joon Park, Hyun-Kyun Ki, Hyeon-Cheol Gwon, Chin-Sang Chung, Hong Sik Byun, Kyung-Ja Shin, Myung-Hee Shin and Won Ro Lee

Hypertension 2000;36;73-77

Prevalence and Risk Factors of Silent Brain Infarcts in the Population-Based Rotterdam Scan Study

Sarah E. Vermeer, Peter J. Koudstaal, Matthijs Oudkerk, Albert Hofman and Monique M.B. Breteler

Stroke 2002;33;21-25

Prevalence and Correlates of Silent Cerebral Infarcts in the Framingham Offspring Study

Rohit R. Das, Sudha Seshadri, Alexa S. Beiser, Margaret Kelly-Hayes, Rhoda Au, Jayandra J. Himali, Carlos S. Kase, Emelia J. Benjamin, Joseph F. Polak, Christopher J. O'Donnell, Mitsuhiro Yoshita, Ralph B. D'Agostino, Sr, Charles DeCarli and Philip A. Wolf

Stroke 2008;39;2929-2935; originally published online Jun 26, 2008;

MR AF PATIENTS STUDIES

"silent lesions are focally defined, sharply demarcated areas hyperintense in T2"

Silent Cerebral Infarcts and Cerebral White Matter Lesions in Patients with Nonvalvular Atrial Fibrillation

Circulation - Sato H. 2004

Aspirin Attenuates the Incidence of Silent Brain Lesions in Patients With Nonvalvular Atrial Fibrillation

Kobayashi A. 2010

Material and methods

1. Field Intensity: 0.5 T - 1.5 T
2. T1, T2 and DP
3. Thick: 5 - 7 mm
4. Dimensional criterium ≥ a 3 mm
5. "...At Least One.."

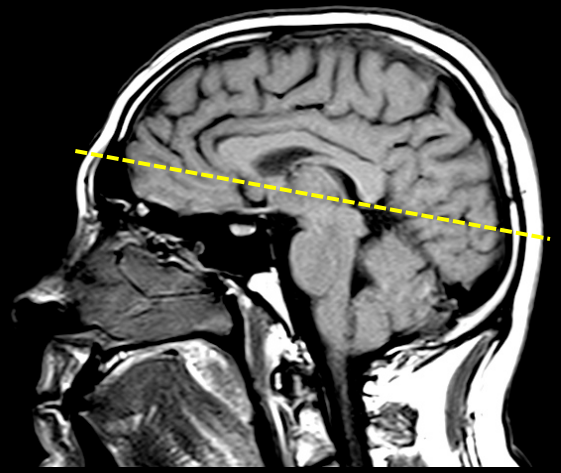
Material and methods

368 AF patients
119 controls

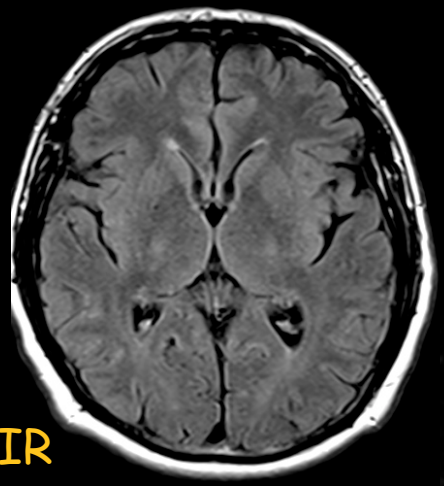
Patients and controls were matched for age, gender, socio-cultural profile and cardiovascular risk factors

MR PROTOCOL

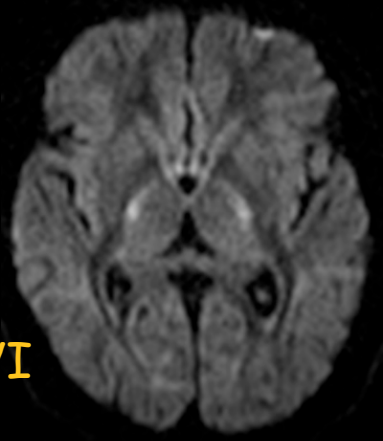
- RM 1.5T
- Sagittal T1
- DWI (Diffusion)
- Axial FLAIR T2
- Slice thickness 5 mm



T1



FLAIR



DWI

Materials and Methods

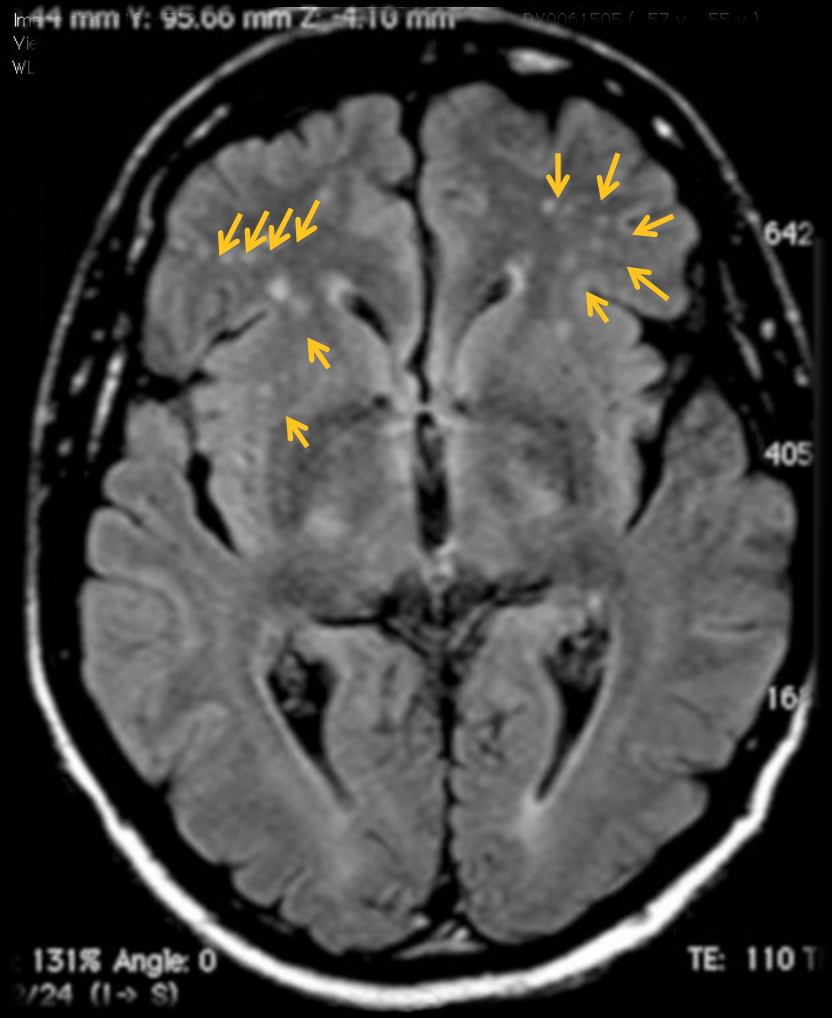
SILENT ISCHEMIC LESION

- Hyperintense Area in T2 Flair
  Iso or Hypointense Area in T1

- Lesion Number / Burden of Lesions
- Mono or Bilateral
- Dimensions
  - < 3 mm
  - between 3 and 5 mm
  - > 5 mm

- Leucoaraiosis
  - Grade 1 2 3 (Fazekas scale)

- Dilatation of Perivascular Spaces

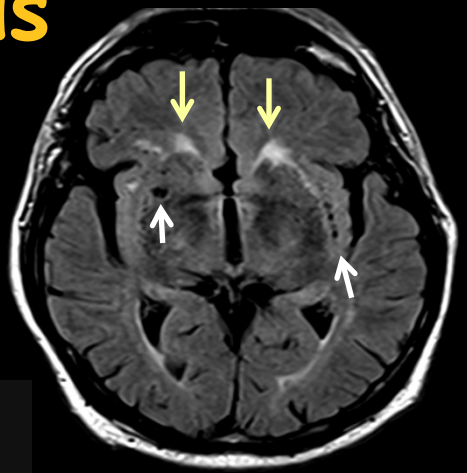


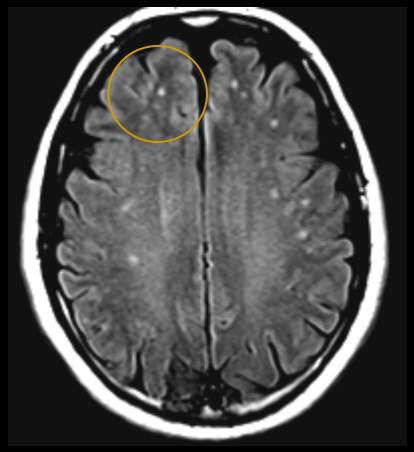
Materials and Methods

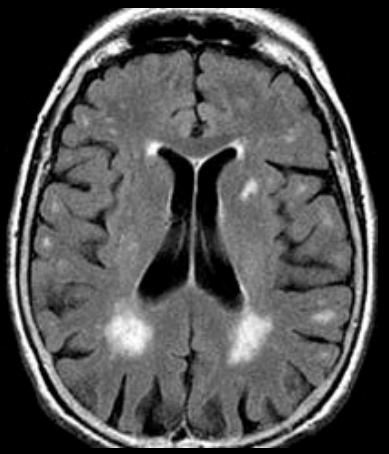
CLASSIFICATION OF LESIONS

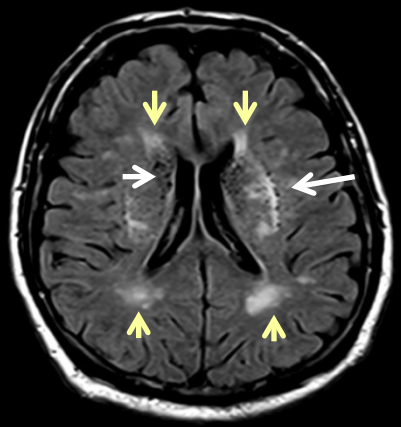
- Cortical
- Cortical-subcortical junction
- Subcortical white matter
- Deep white matter

- Frontal Lobe
- Parietal Lobe
- Temporal Lobe
- Occipital Lobe
- Insula
- Basal Ganglia
- Cerebellum, Brain stem

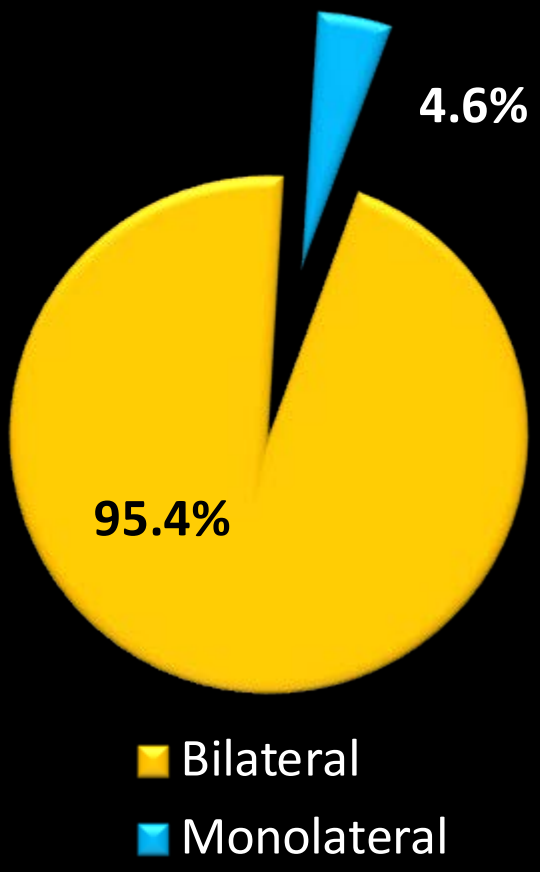




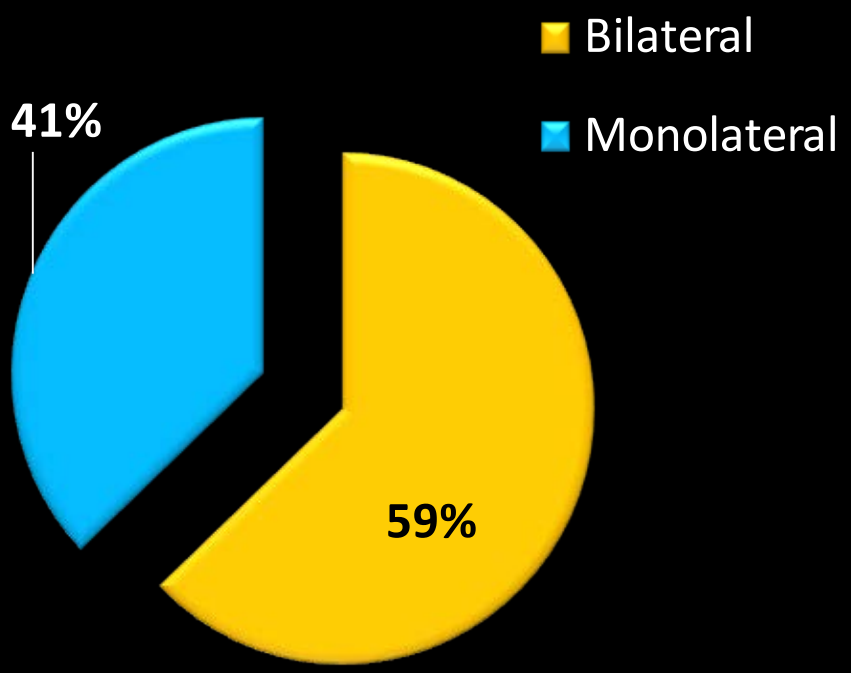




A.F. patient

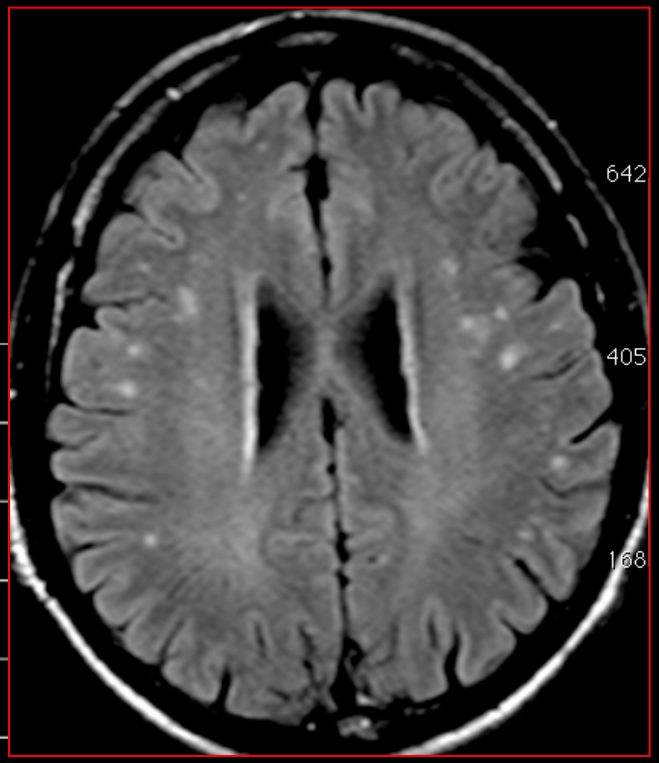


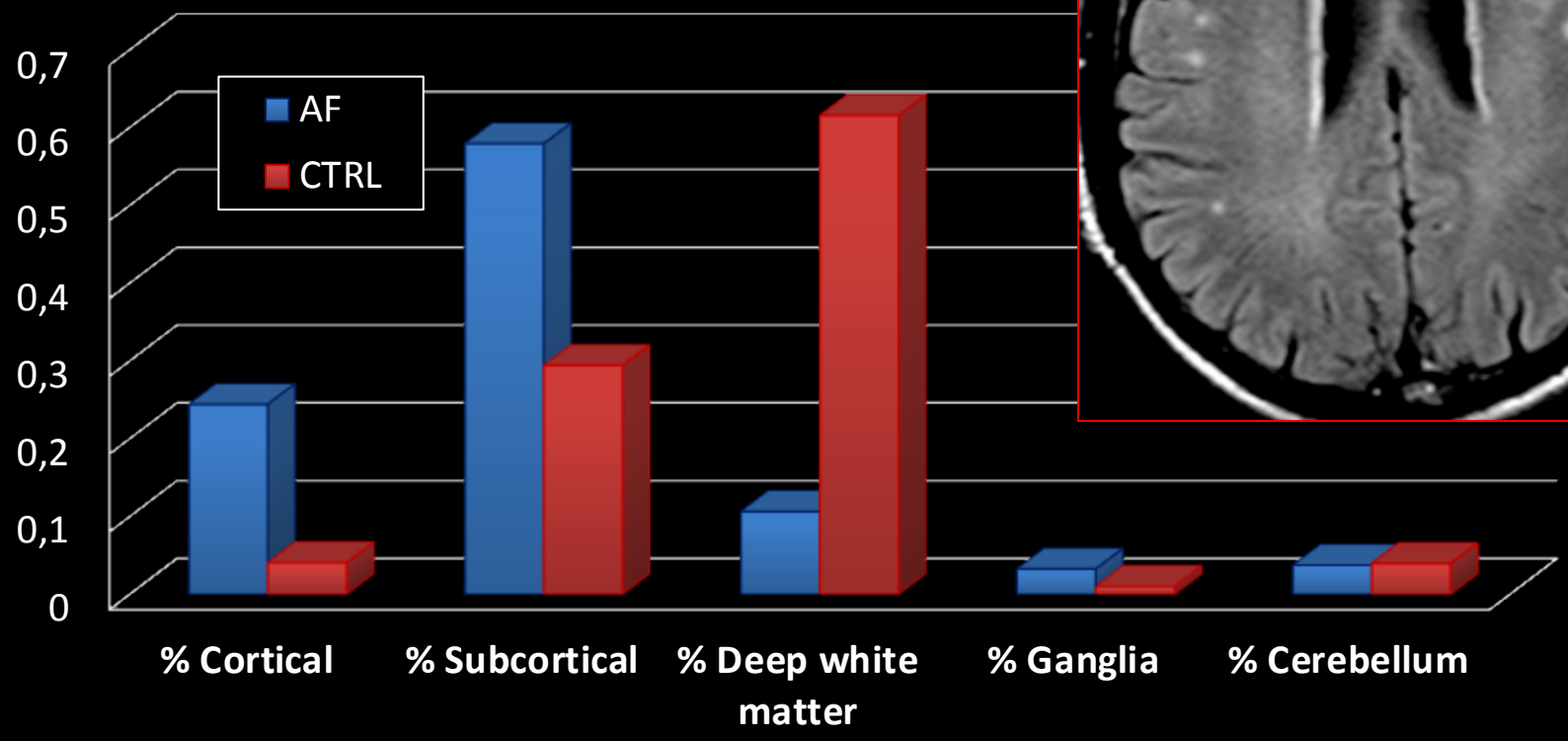
Control Group



In AF patients the lesions are mainly bilateral .
In the Control group the lesions are bilateral just in 59% of subjects.

Anatomic distribution of Silent Cerebral Ischemia (SCI) in controls and in A.F. patients



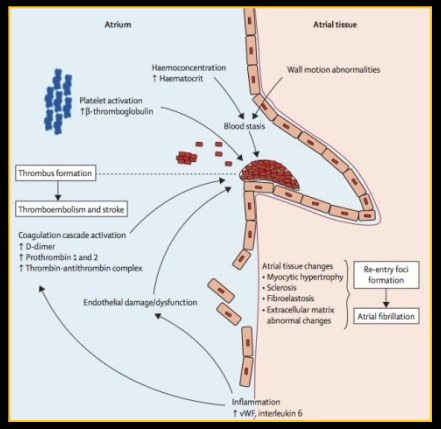


The three conditions identified as an indicator of the AF related SCIL presence

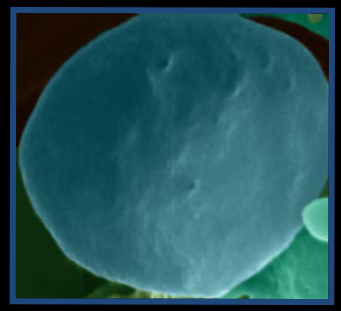
	< 3mm	Bilateral lesions	Sub-cortical spot pattern
AF subjects	366 (99.5%)	351 (95.4%)	309 (84.0%)
CTRL subjects	83 (70.3%)	75(63.5%)	5(4.1%)
p	< 10e-7	< 10e-7	< 10e-7
OR (95%CI)	77 (18-339)	12 (6-23)	124 (38-407)

Atrial Fibrillation

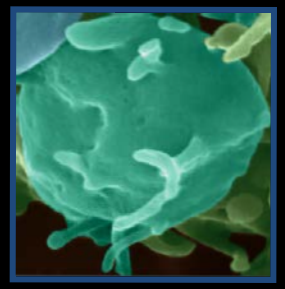
The hematic stasis : turbulent flows, eddies, cause the summing up of pro-thrombotic factors and the activation of surface receptors



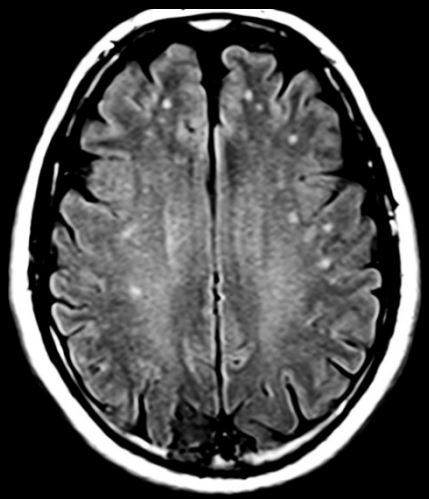
Watson T et al. Lancet 2009; 373: 155-66

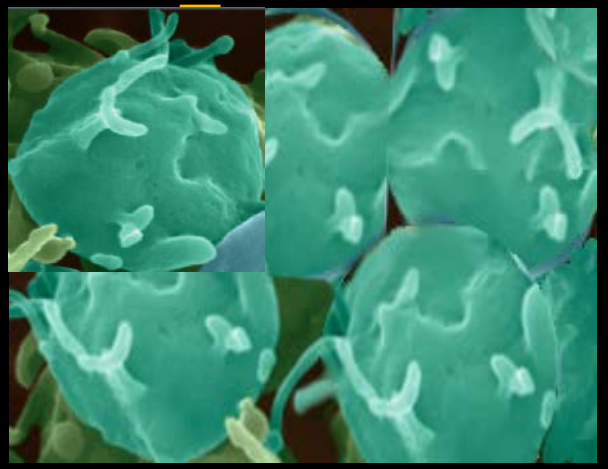


activation



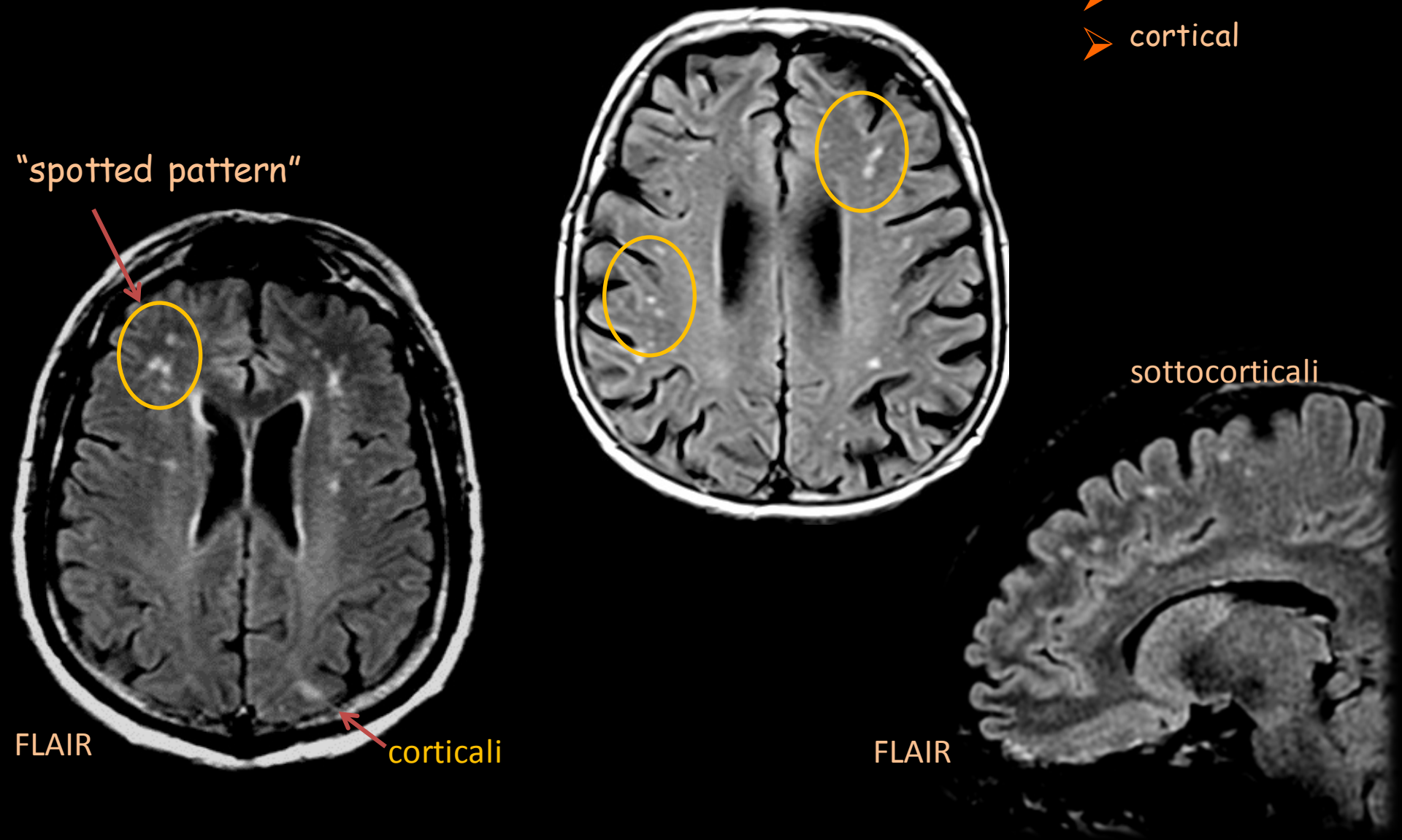
The activated platelets aggregate and, transported by the flow, reach the perforating leptomeningeal cortical, cortico-medullary and medullary vessels

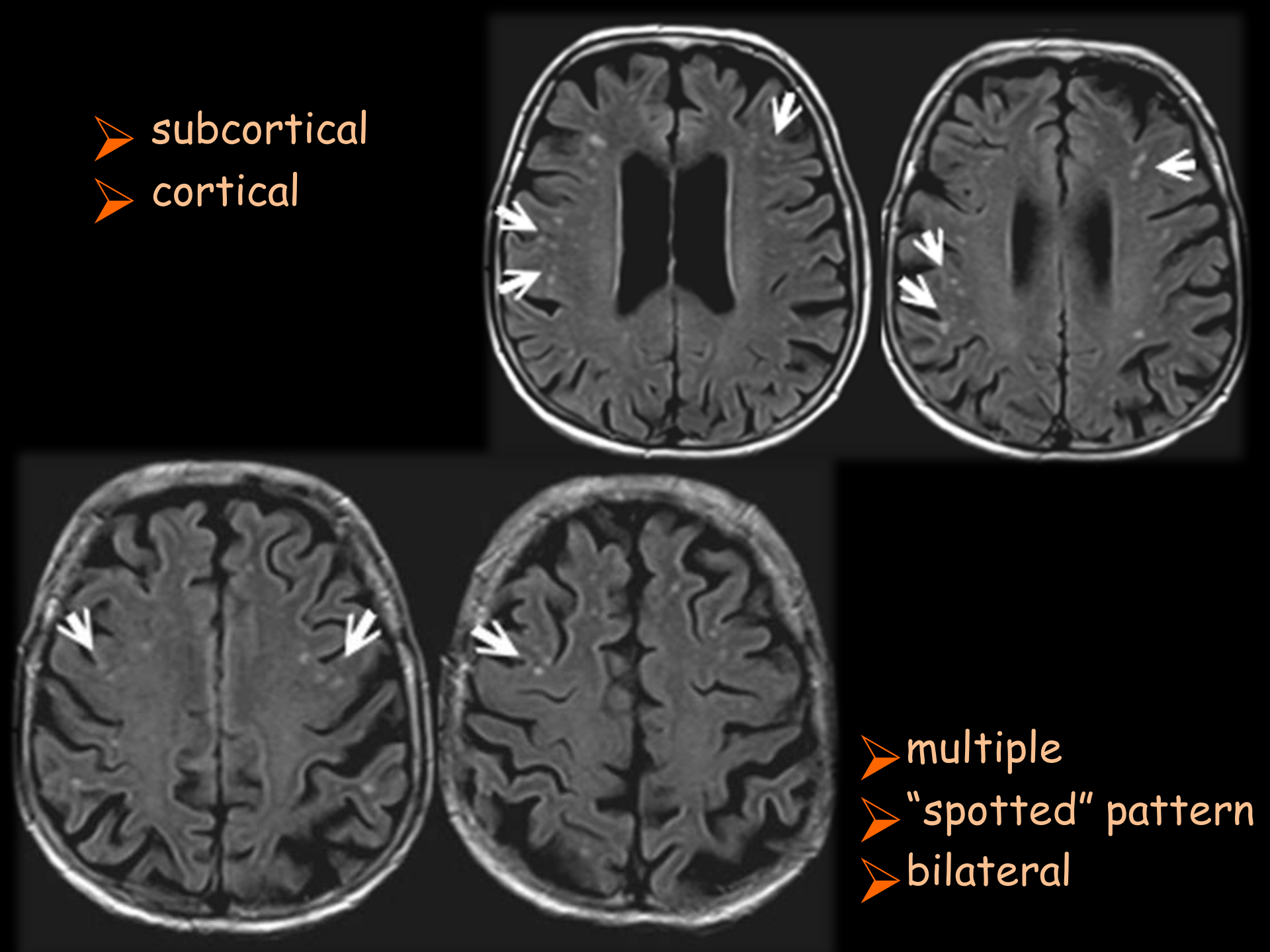


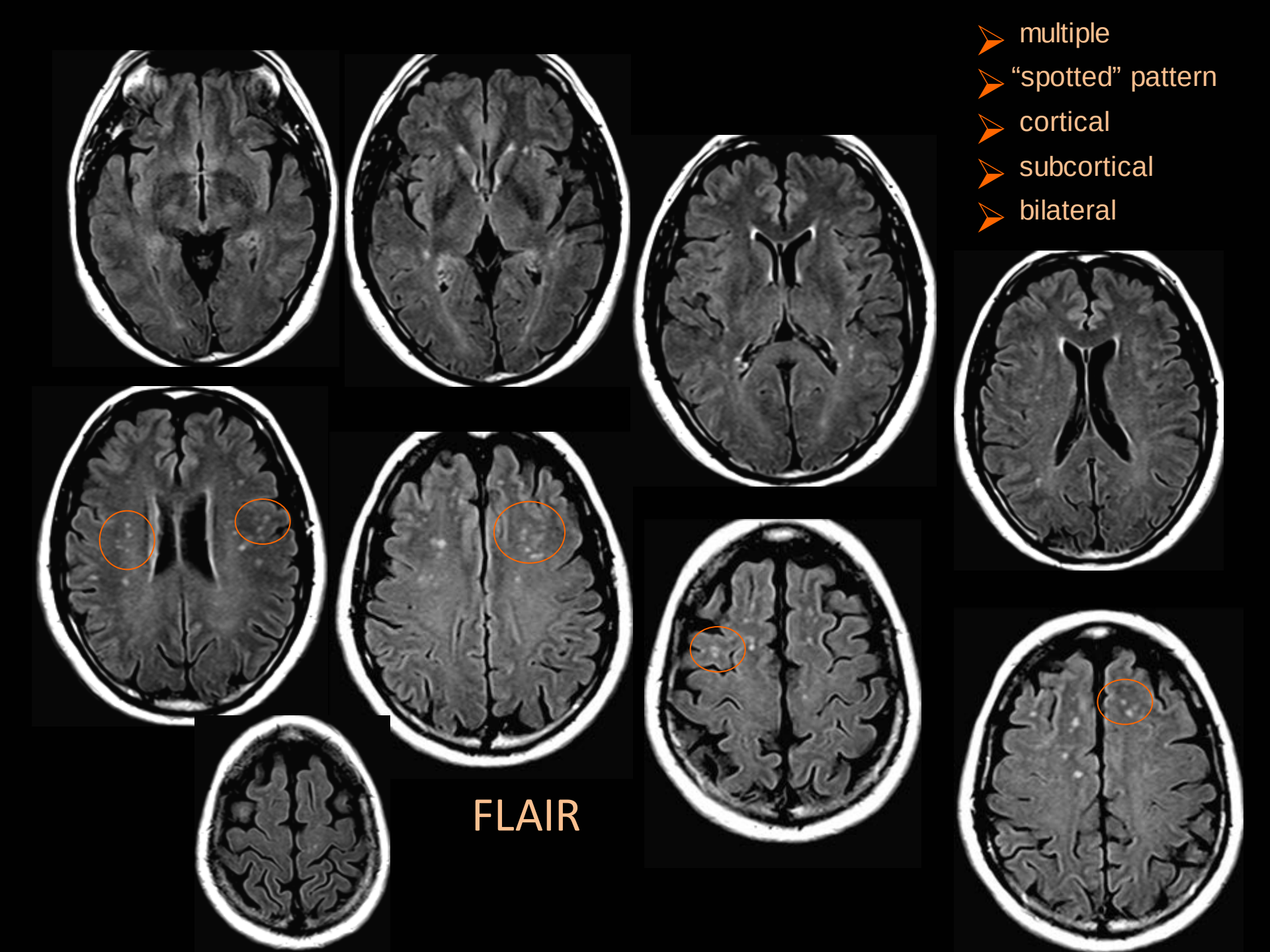


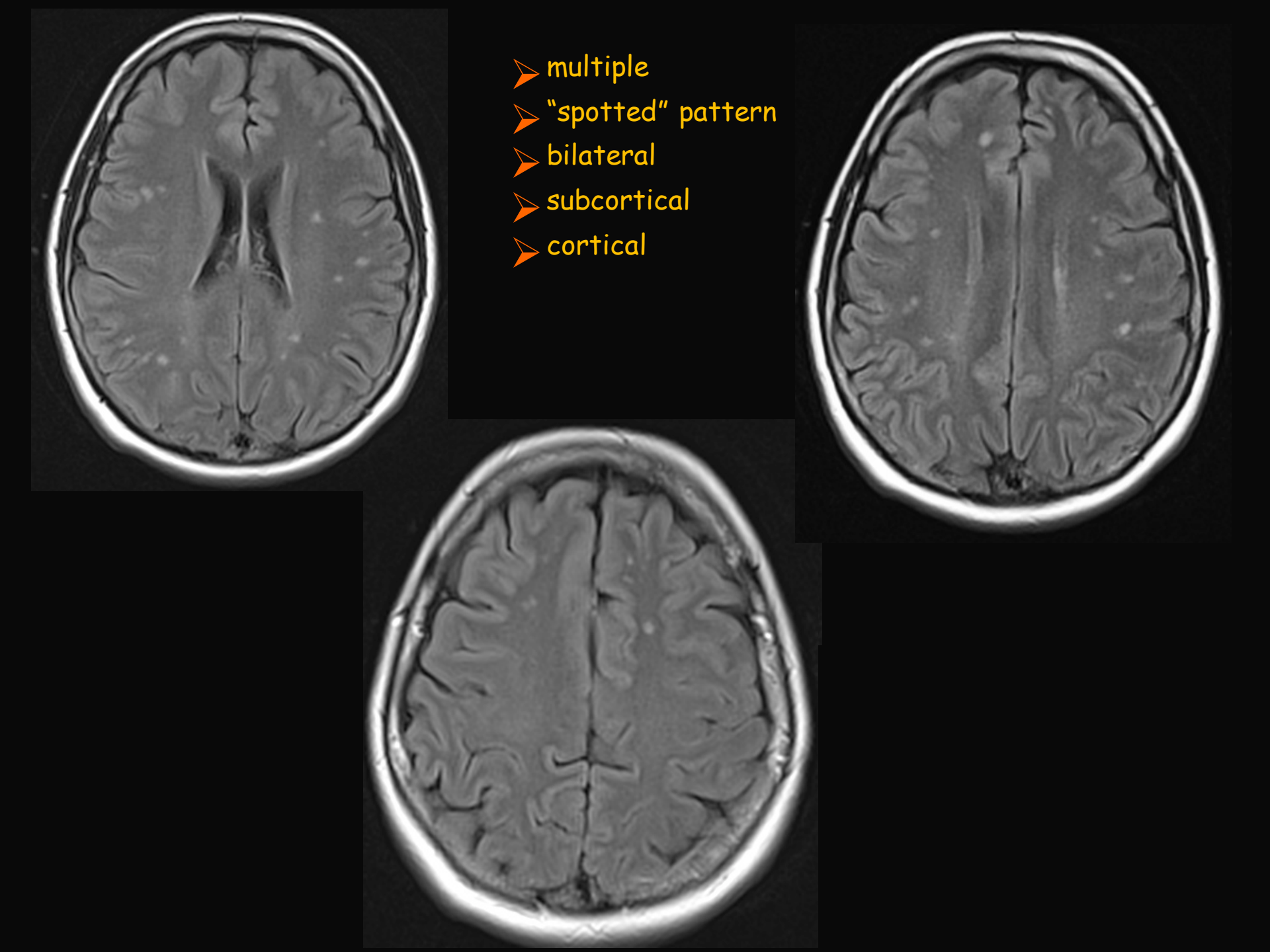
In atrial fibrillation lesions are:

- multiple
- "spotted" pattern
- bilateral
- subcortical
- cortical




subcortical
cortical
multiple
"spotted" pattern
bilateral

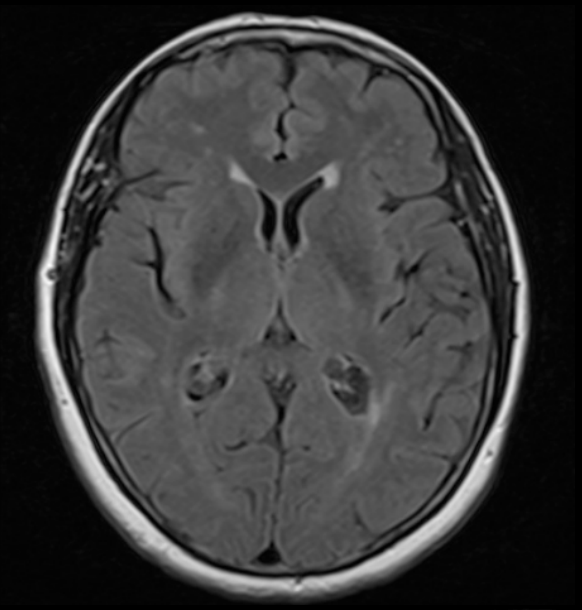

multiple
“spotted” pattern
cortical
subcortical
bilateral
FLAIR

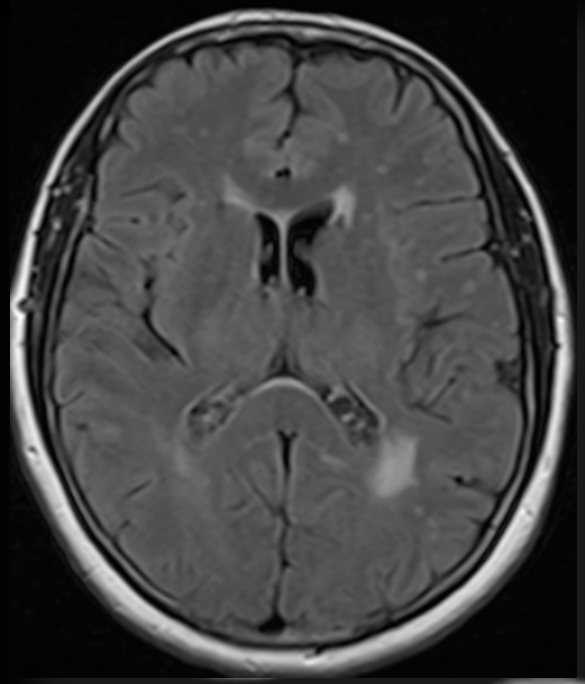

multiple
"spotted" pattern
bilateral
subcortical
cortical

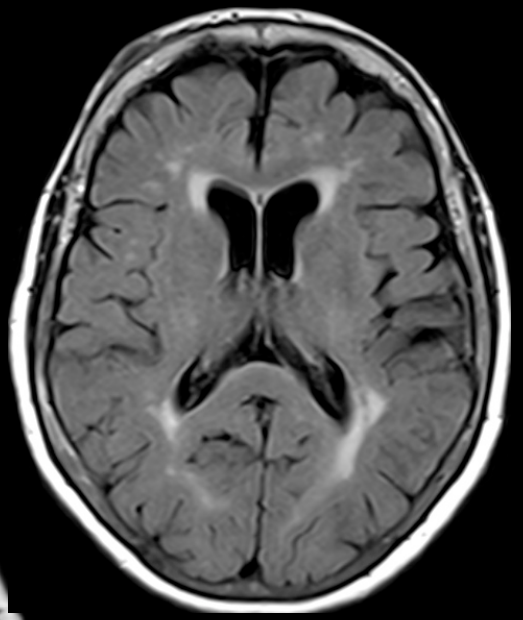
Atherosclerosis
Hypertension

Leucoaraiosis

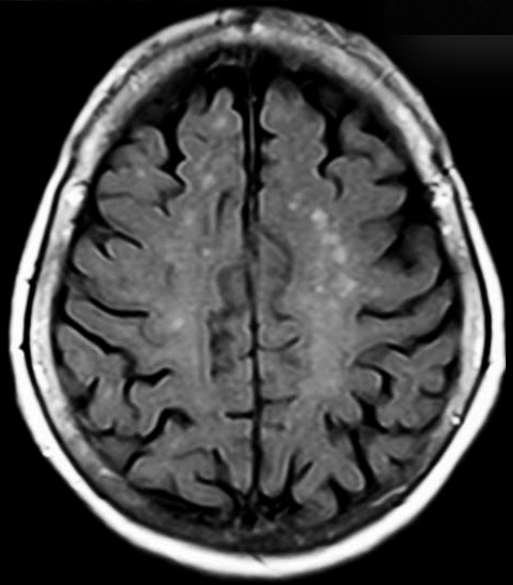
- multiple
- "spotted" pattern
- cortical
- subcortical
- bilateral

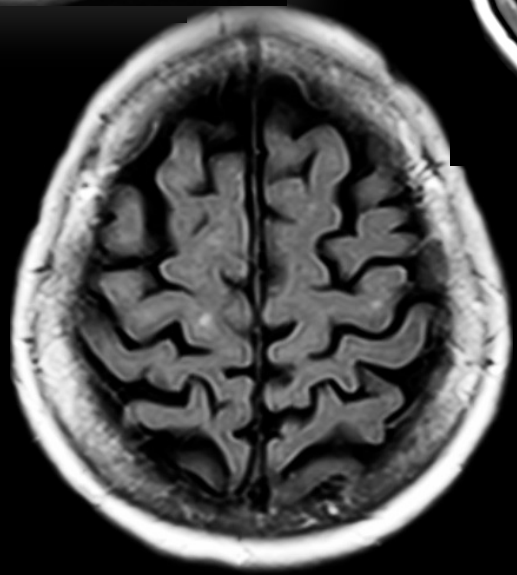






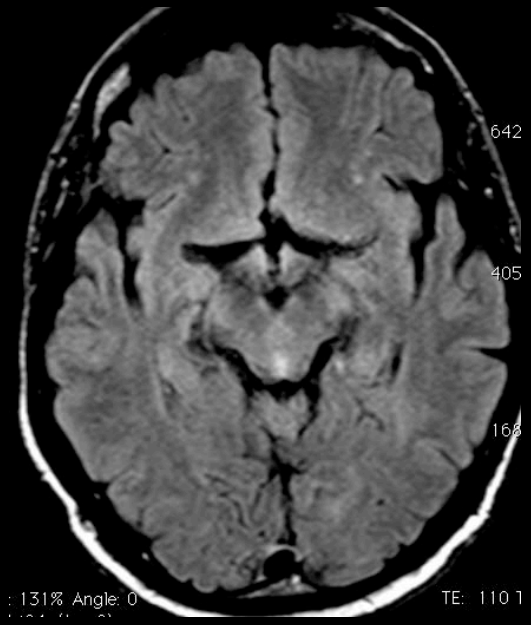
FLAIR

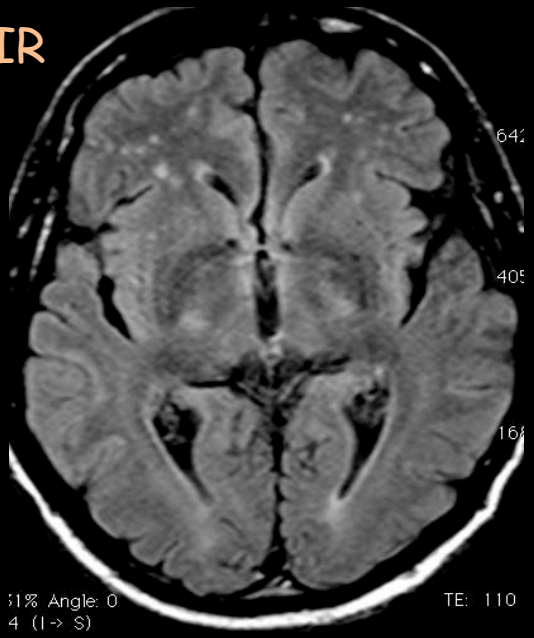


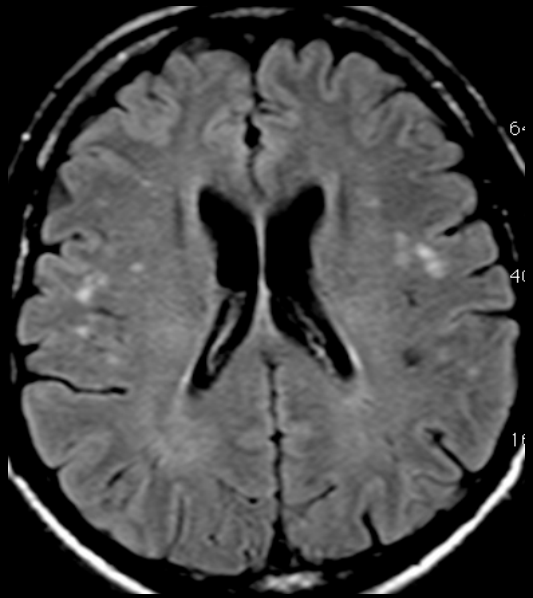


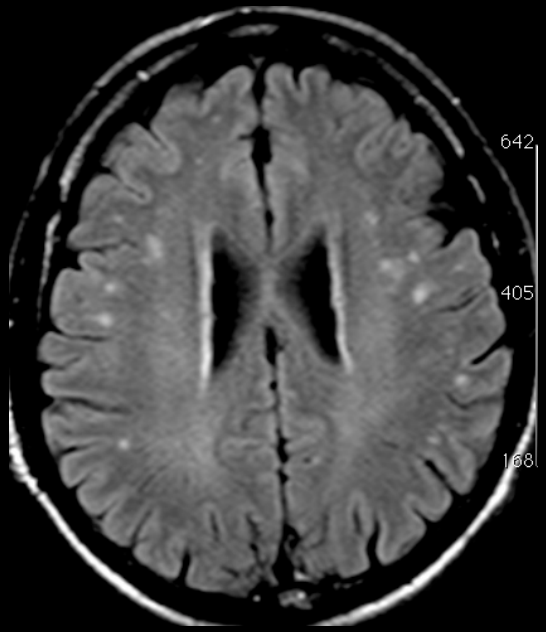
- multiple
- "spotted" pattern
- cortical
- subcortical
- bilateral

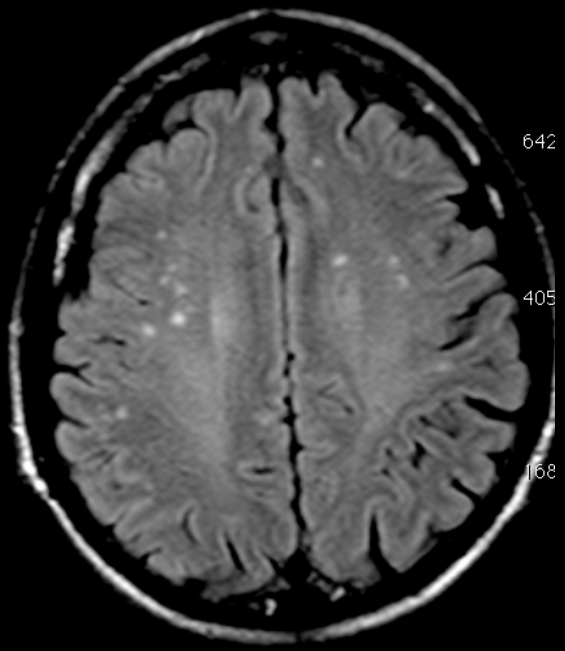
FLAIR

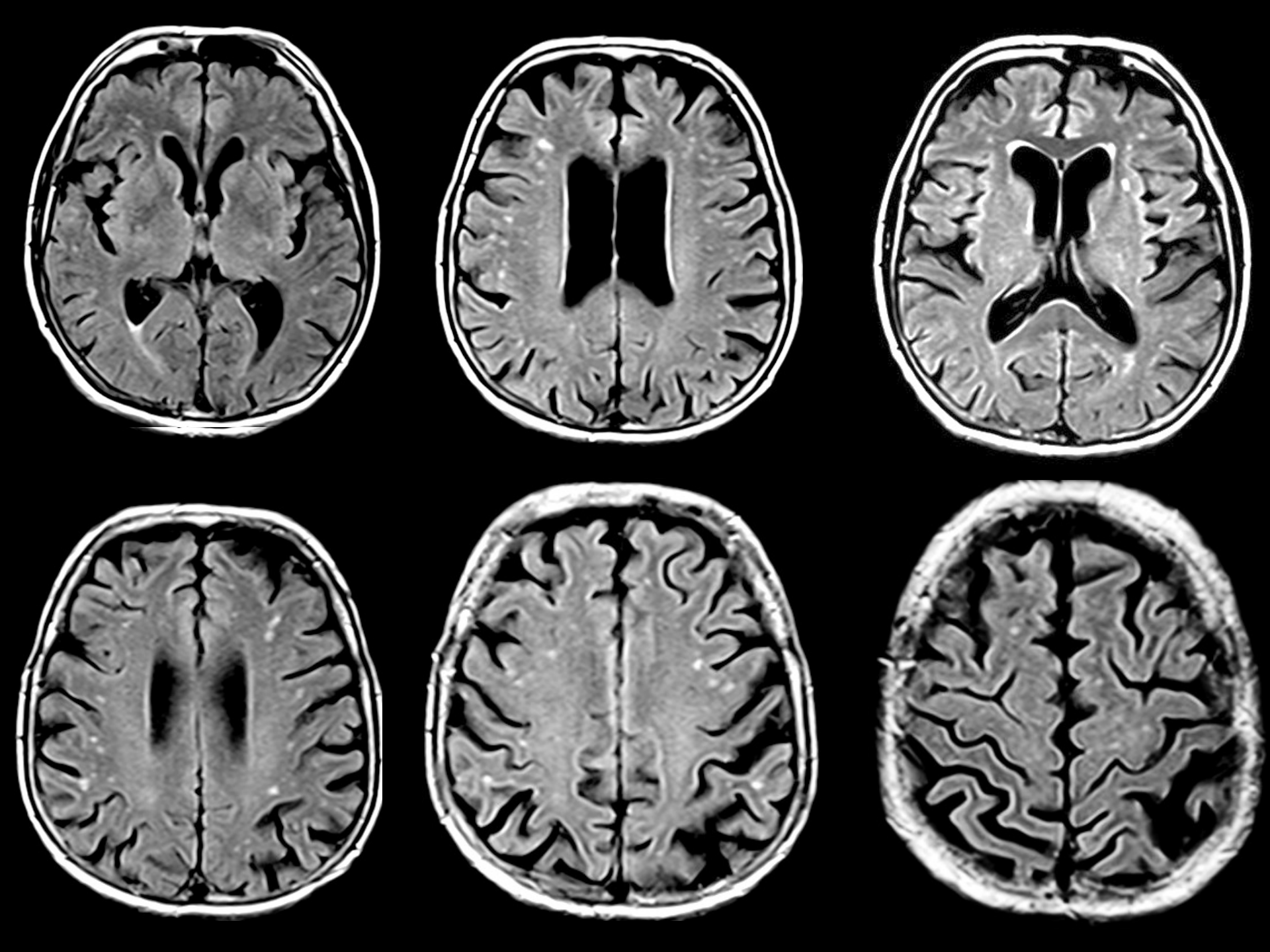


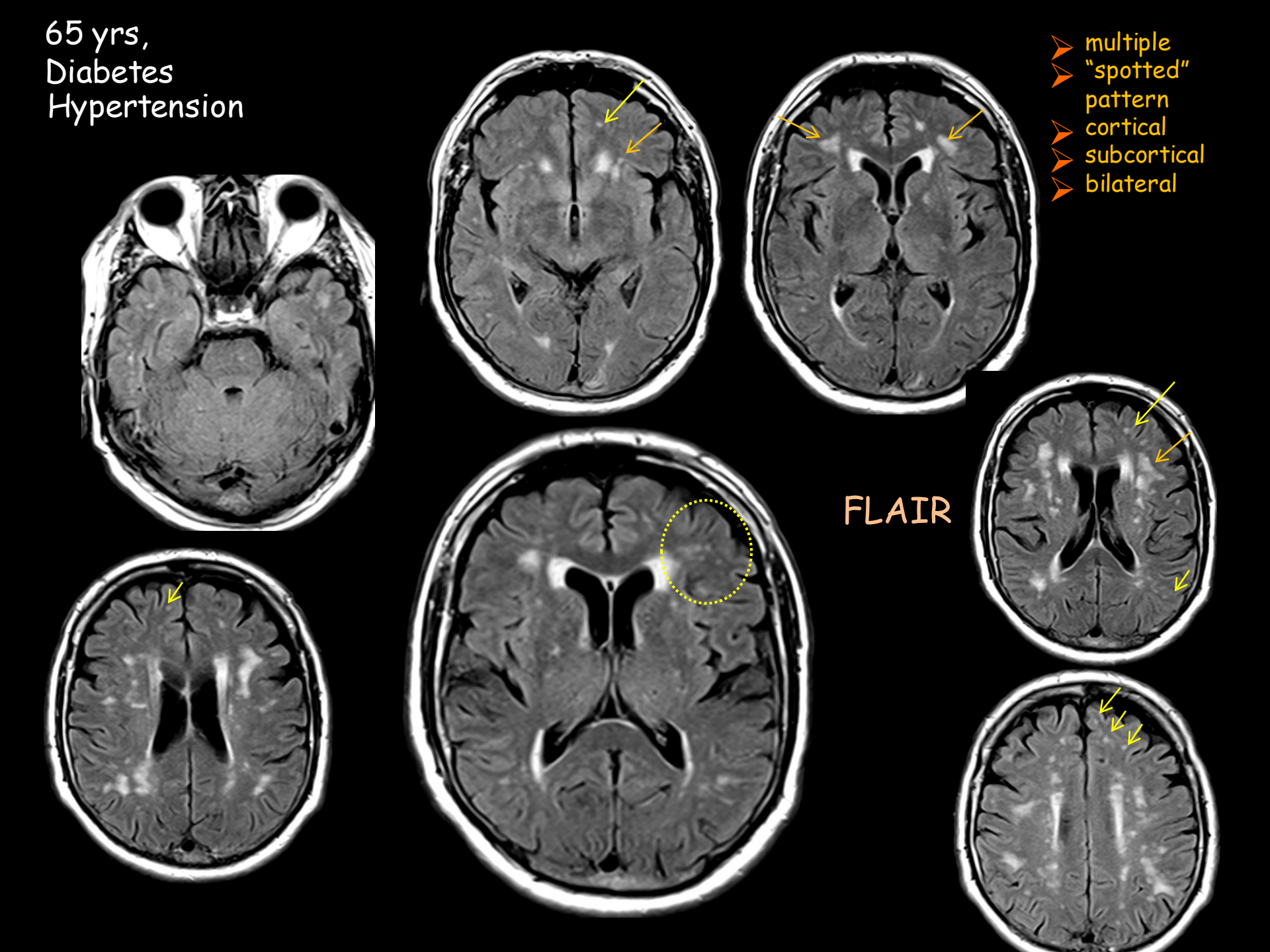




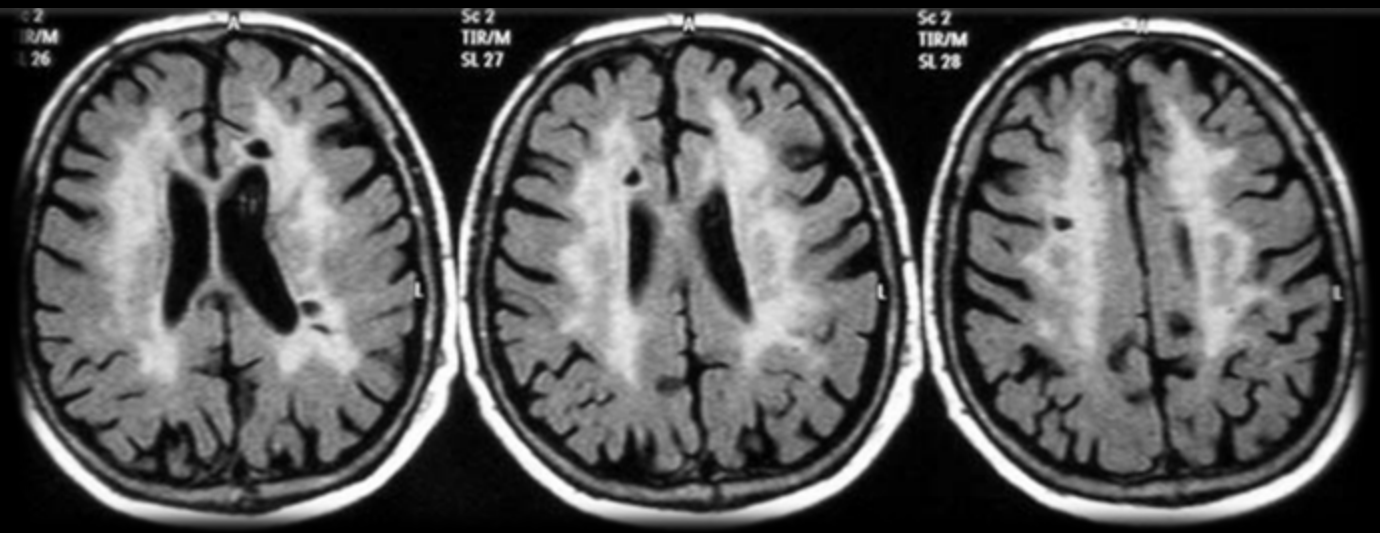




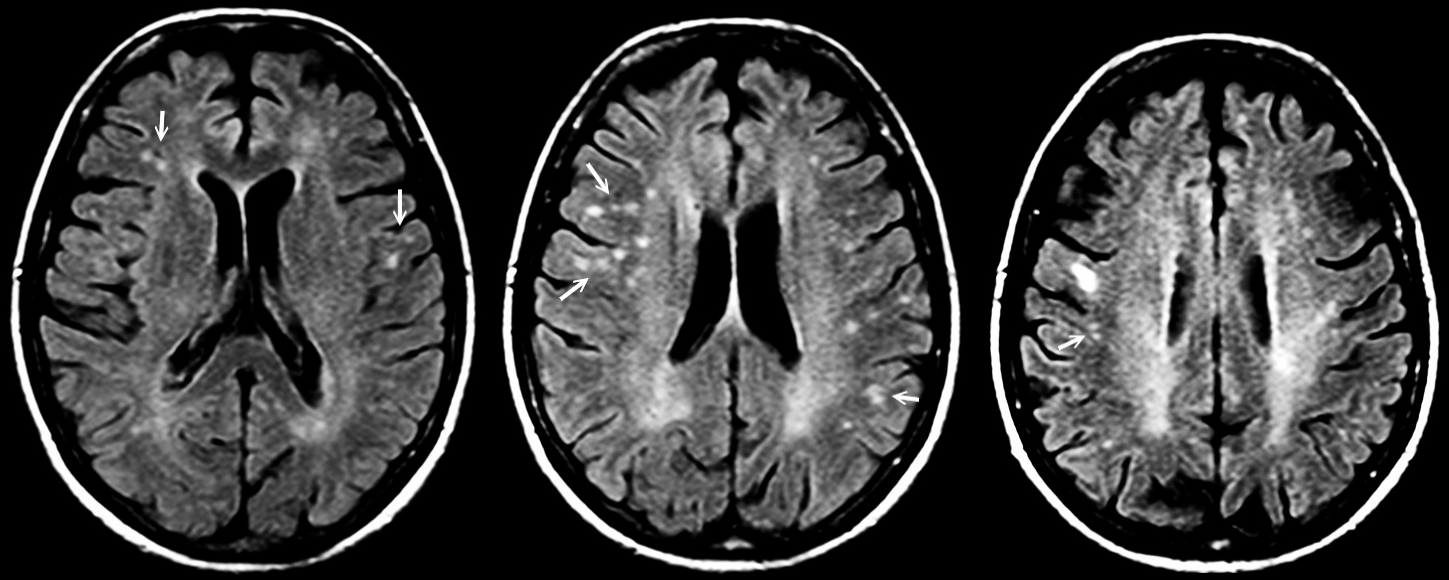



65 yrs,
Diabetes
Hypertension
multiple
"spotted"
pattern
cortical
subcortical
bilateral
FLAIR

Control



AF



Thank you for your attention