

**Advances in Cardiac arrhythmias and
great innovation in Cardiology**

Turin 2015

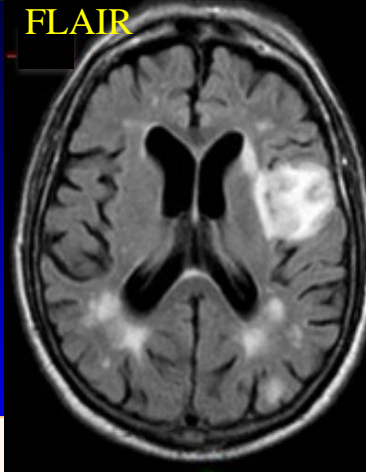
**Clinical and silent cerebral emboli
in AF: new insight**

Prof. Fiorenzo Gaita

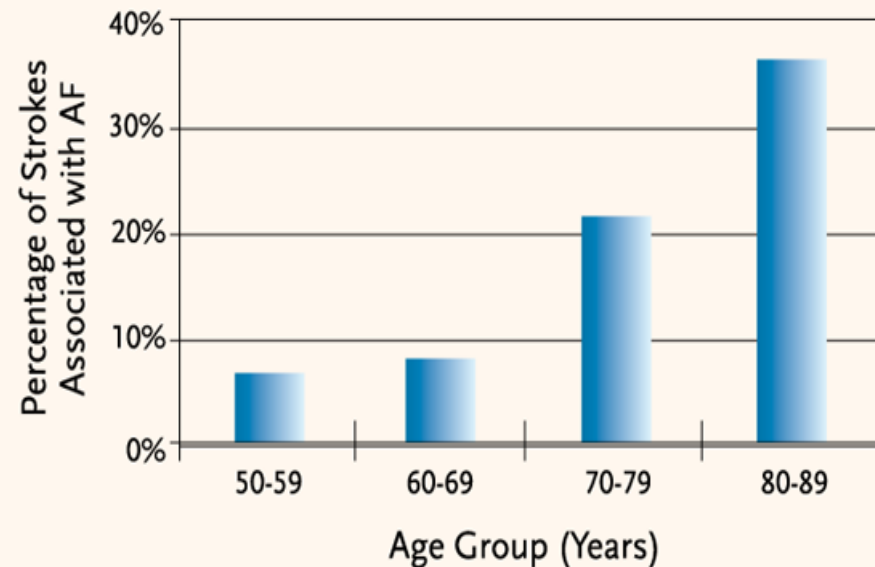
**Director of the School of Cardiology
University of Turin, Italy**

AF and risk of Stroke

AF patients have a higher risk of symptomatic cerebral events (**5 times higher**) that progressively increases with age.



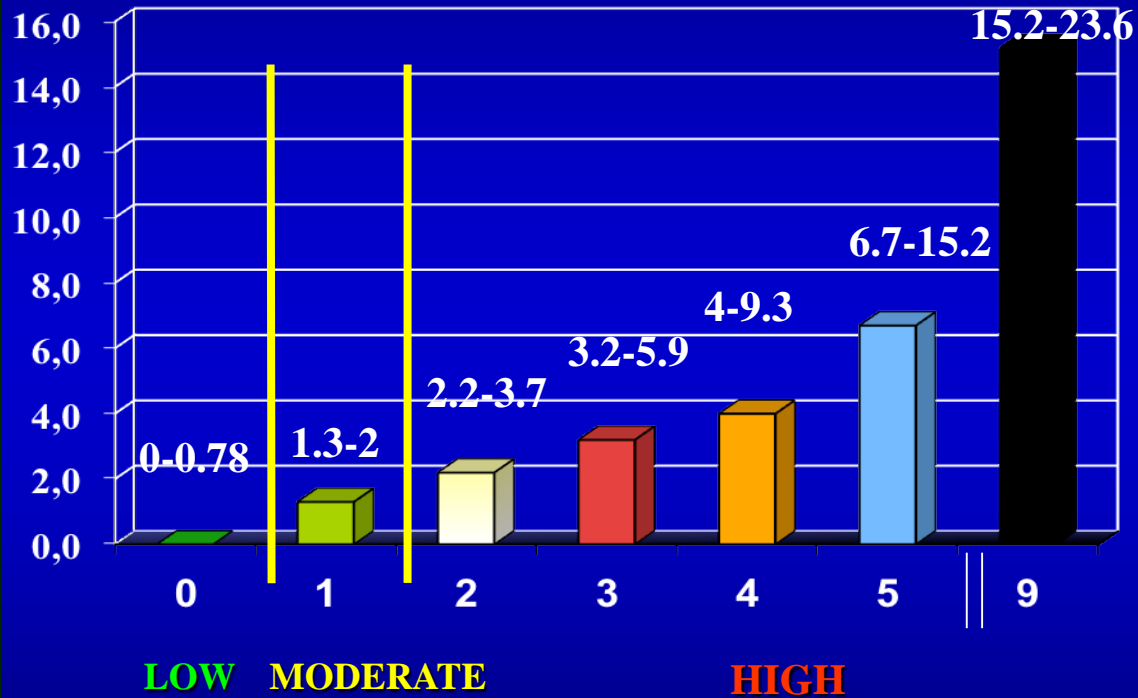
Percentage of Strokes Associated with Atrial Fibrillation



2010

Thromboembolic risk

CHA2DS2vasc score



Congestive heart failure	1
Hypertension	1
Age > 75 years	2
Diabetes mellitus	1
Prior Stroke or TIA	2
vasculopathy	1
age>65	1
sex	1

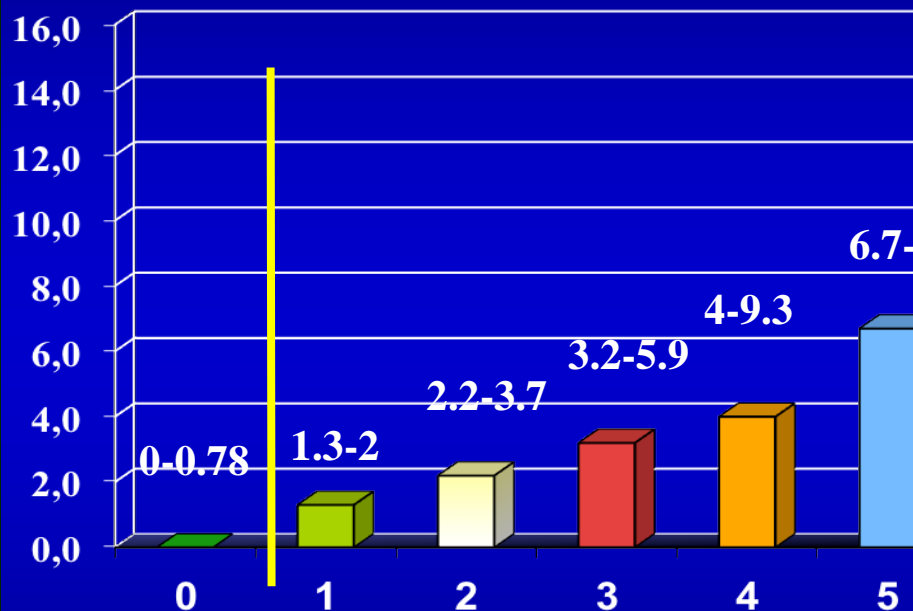
2012

Thromboembolic risk

TAO Guidelines

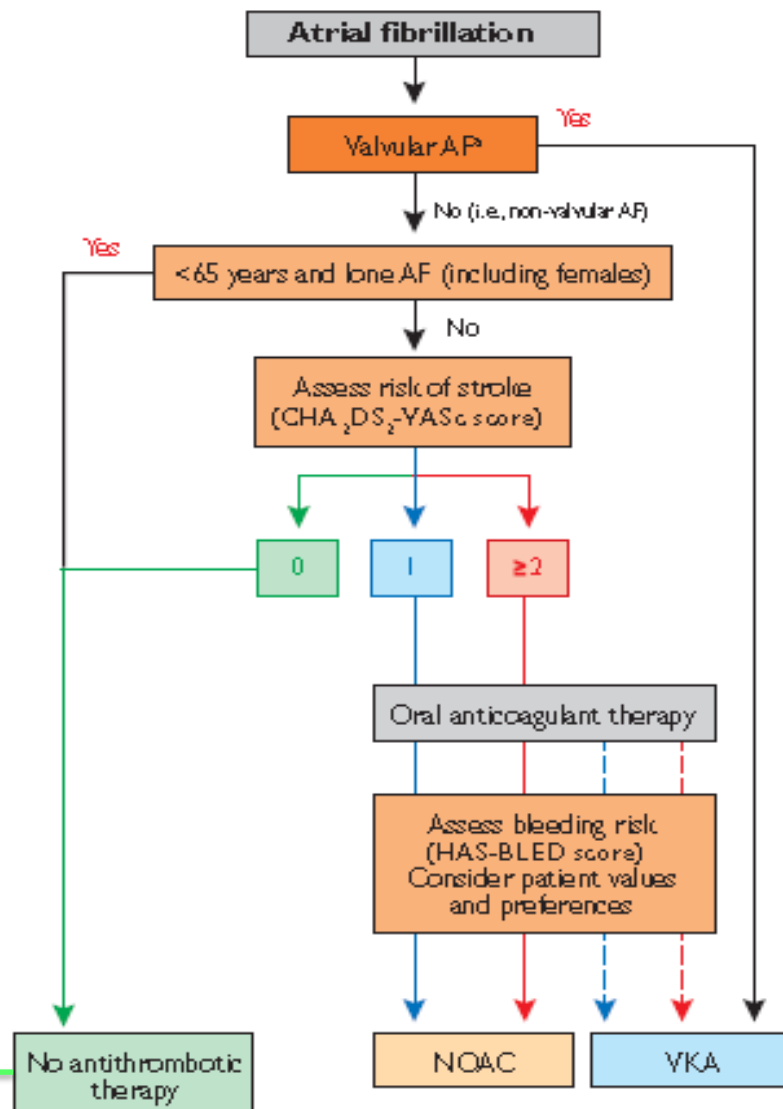


EUROPEAN SOCIETY OF CARDIOLOGY®



LOW MODERATE

HIGH

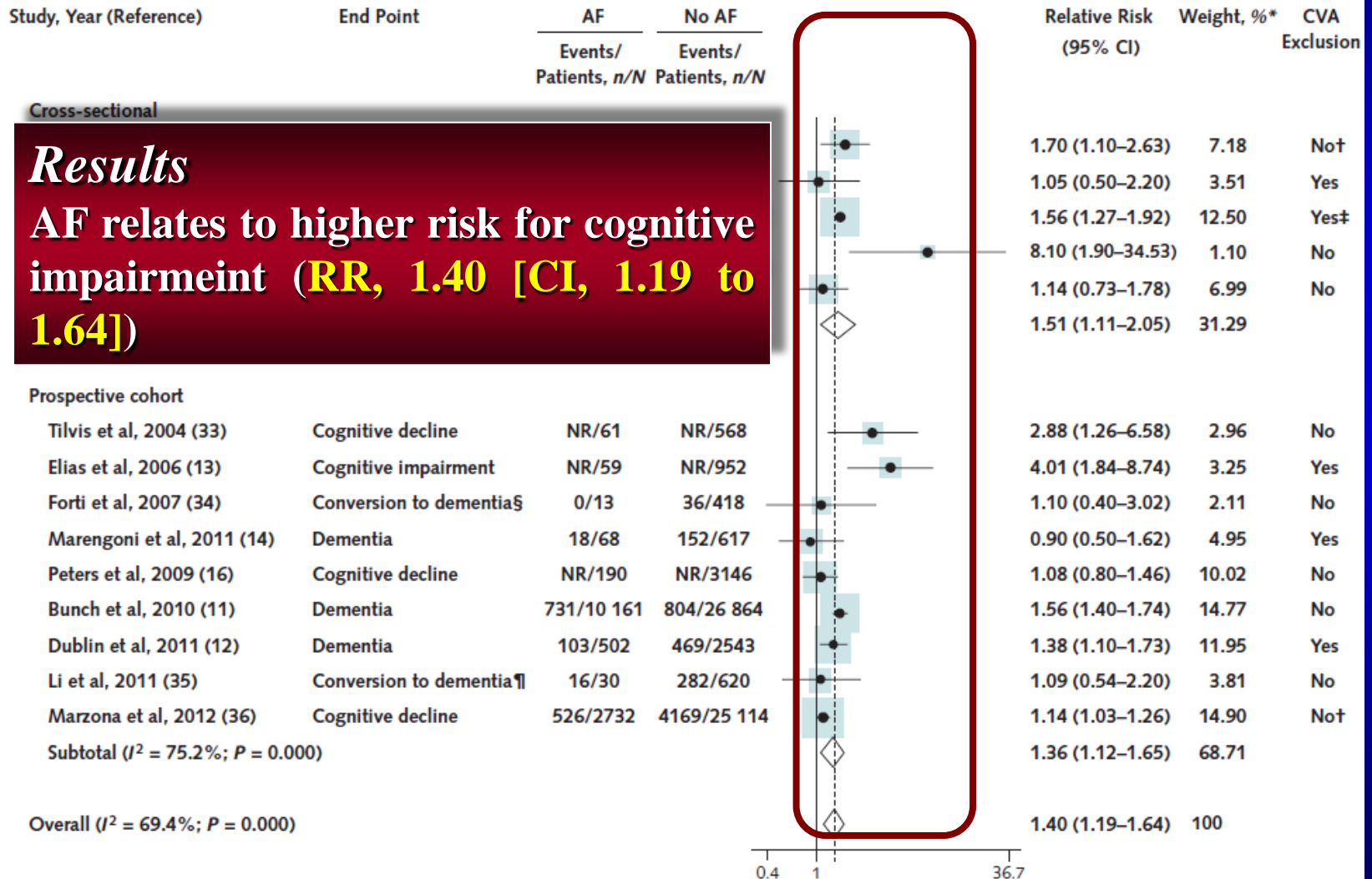


Cognitive impairment

While **Stroke/TIA** are regarded as clinically relevant events, **Cognitive Impairment** is less considered as a concern

Cognitive Impairment Associated With Atrial Fibrillation

Tot pts 85118 AF patients 14147 No AF patients 70971



Atrial fibrillation and incident dementia

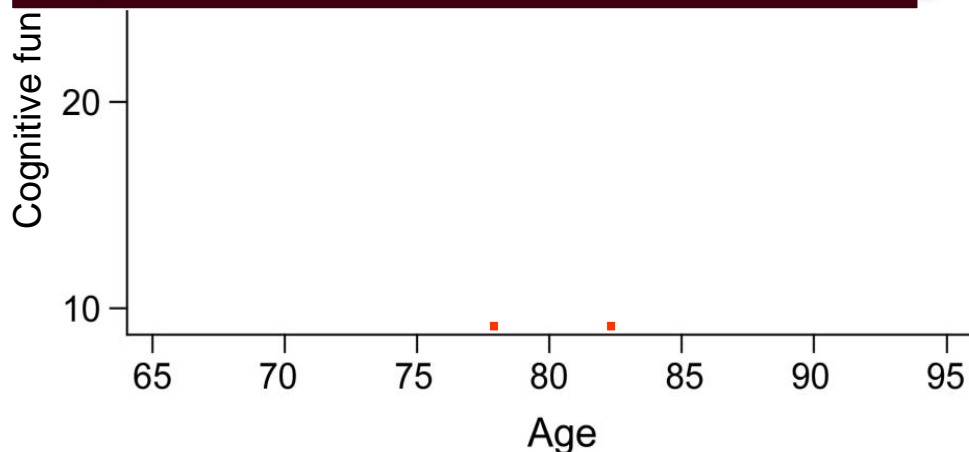
5.150 pts, mean age 73 yrs, Male 41%, Hypertension 57%
Not having atrial fibrillation or a history of stroke at baseline

Conclusion:

Cognitive function progressively decline with age, AF onset accelerates by above five years

Conclusion:

further studies are required to elucidate the cause of cognitive impairment



Mean follow-up 7 yrs

Cognitive test performed annually

New onset AF occurring in 552 (10.7%)

AF onset increases cognitive impairment

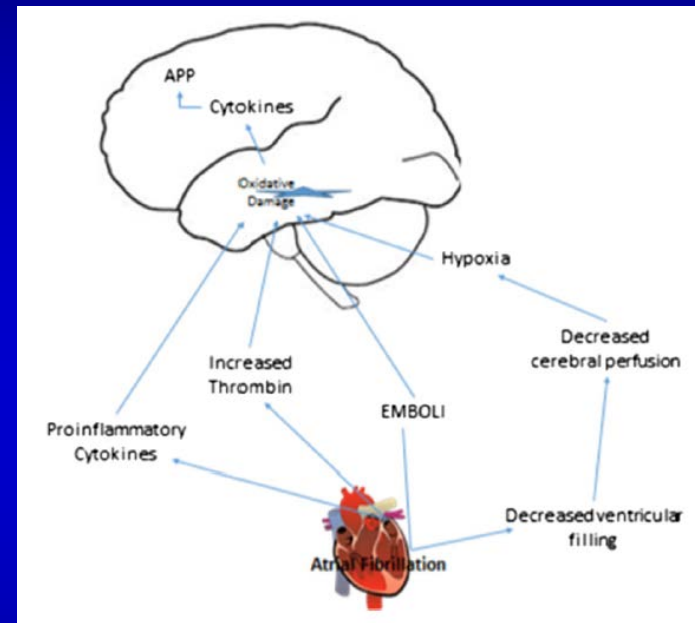
Hypothesis explaining cognitive impairment in AF

Reduced cerebral perfusion, due to beat to beat interval variability

Reduced cerebral perfusion, due to lower cardiac output

Increased Thrombin, Pro-inflammatory condition

“Silent” cerebral ischemia



Modified from Hui Am Heart J 2015

Lavy S. et al Stroke. 1980;11:35-8

Vermeer et al. Stroke. 2003 May;34(5):1126-9

Barber M et al J Thromb Haemost. 2004;2:1873-8

Anderson JL et al Am J Cardiol. 2004;94:1255-9

Kalantarian S et al *Ann Intern Med.* 2013;158:338-346

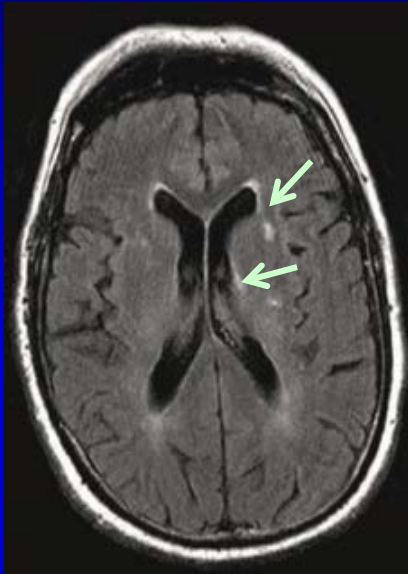
Tacker EL et al Neurology 2013;81:119–125

Hui Am Heart J 2015;169:448-56

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

1077 pts, 71 ± 7 yrs, 50% male,
46% hypertension, 4% AF

24% (259 pts) positive
for ischemic lesions at the cerebral MRI



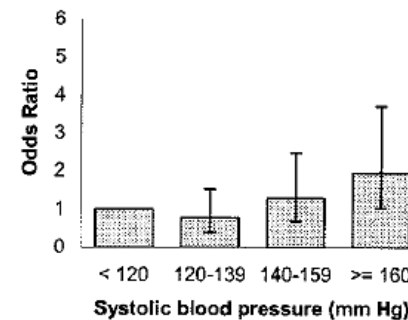
T2 Flair-MRI :
silent hyperintensities in left basal ganglia



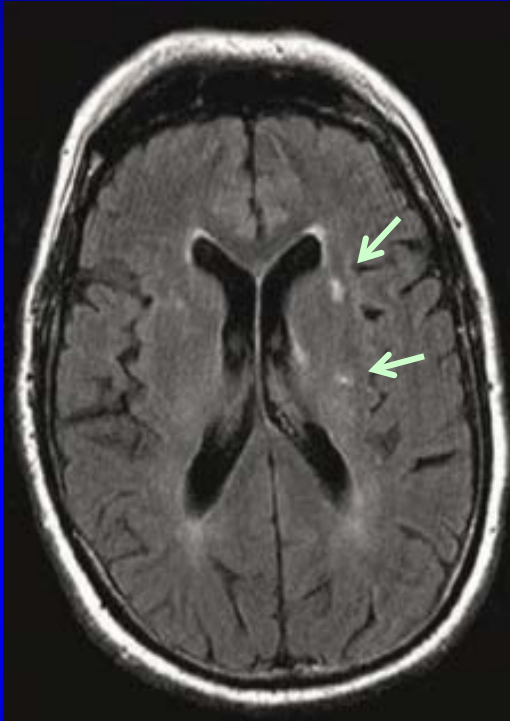
T1-weighted MRI :
silent lacunar infarct in the right thalamus

Factors associated with SCI:

Age
Hypertension
Gender



Silent brain infarcts and the risk of dementia and cognitive decline.



24% positive
for ischemic lesions at the
cerebral MRI

Elderly people with silent brain infarcts have an increased risk of dementia and a steeper decline in cognitive function

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

2040 pts, 58 ± 7 yrs, 47% male, 37% hypertension
3.1% AF (60 pts)

no evidence of prior clinical strokes

11% silent cerebral ischemias

Factors associated with silent ischemia were:

Age

Hypertension

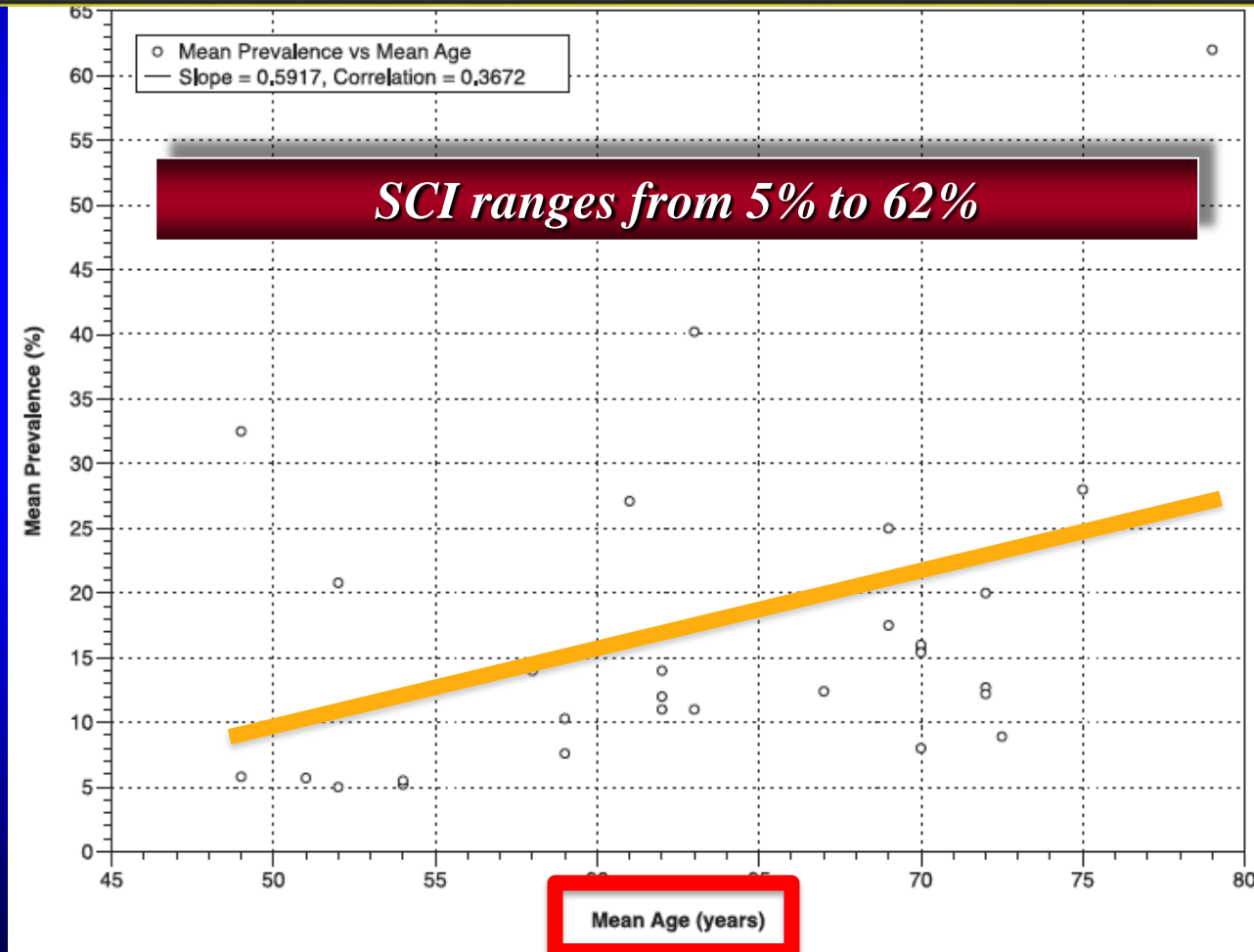
Plasma Homocysteine

Carotid Stenosis

Atrial Fibrillation

The epidemiology of silent brain infarction: a systematic review of population-based cohorts

Data from 32 studies from 1997 to 2013 on
33,671 patients underwent cerebral MRI examinations



The epidemiology of silent brain infarction: a systematic review of population-based cohorts

Strenght of association	Risk factors
Strong	Age Hypertension Carotid artery disease Chronic kidney disease
Unclear	Atrial fibrillation Dyslipidemia Diabetes

Prevalence of Silent Cerebral Ischemia in Paroxysmal and Persistent Atrial Fibrillation and Correlation With Cognitive Function

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Marco Scaglione, MD¶

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Controls

Paroxysmal AF

Persistent AF

Undergone to cerebral MRI



SCI

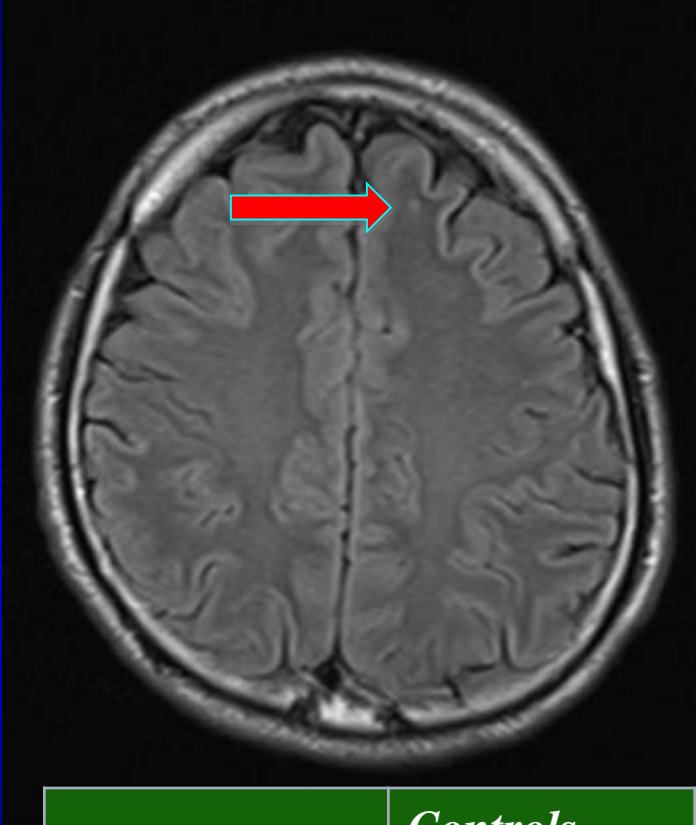
Cognitive test



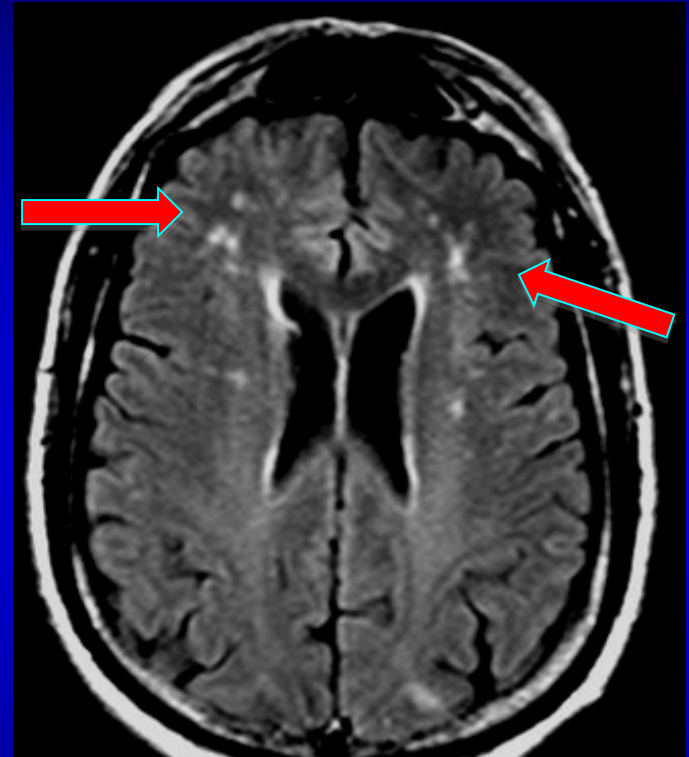
Cognitive decline

Prevalence of Silent Cerebral Ischemia in Controls and AF patients

Controls 90 pts: 48% SCI



180 AF pts 90% SCI



	<i>Controls</i>
Age	59
Hypertension	45 (50%)
Diabetes	12 (6%)

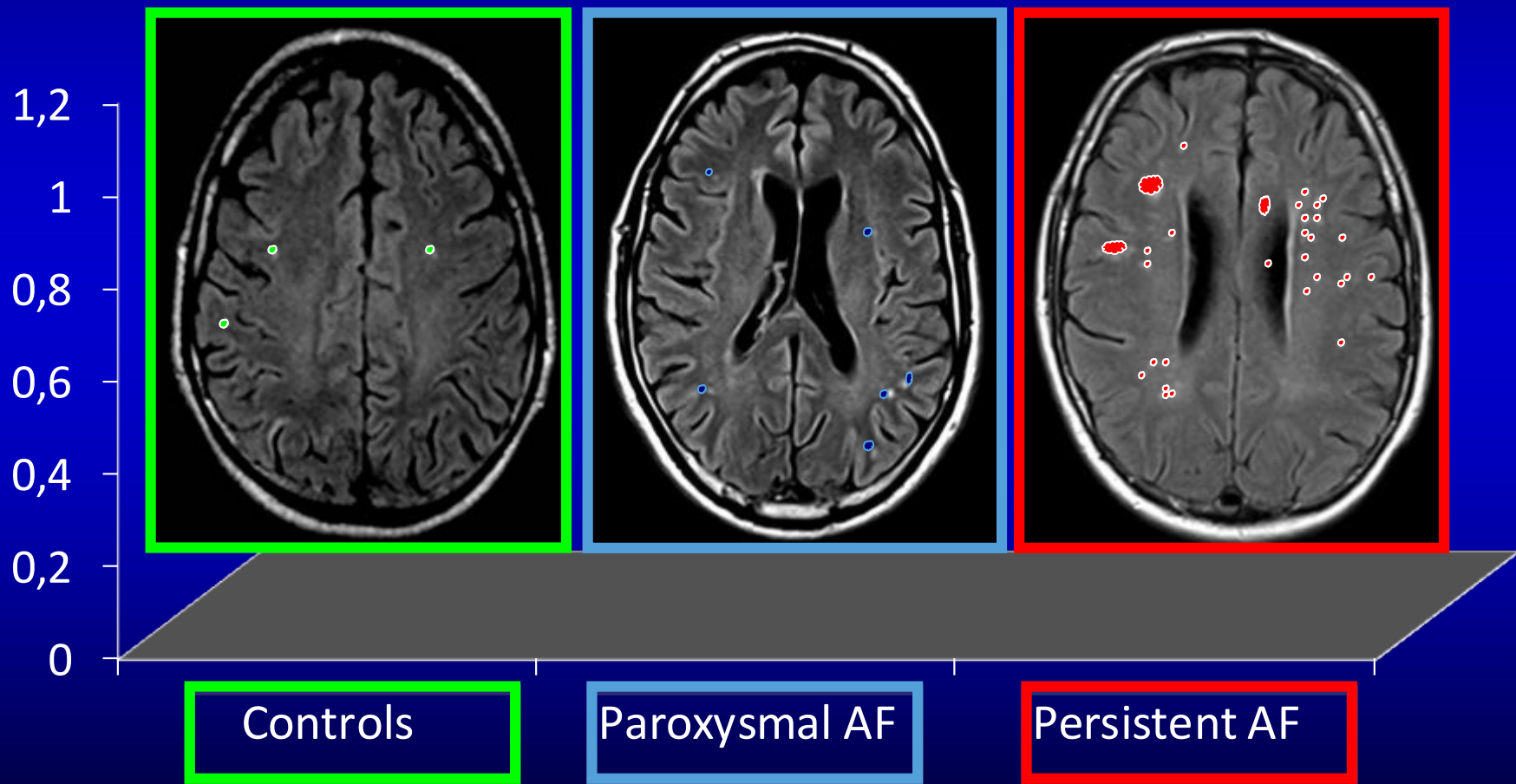
	<i>AF</i>	P value
Age	60	0.31
Hypertension	46 (51%)	0.96
Diabetes	5 (6%)	0.78

The number of SCI varies according to AF type

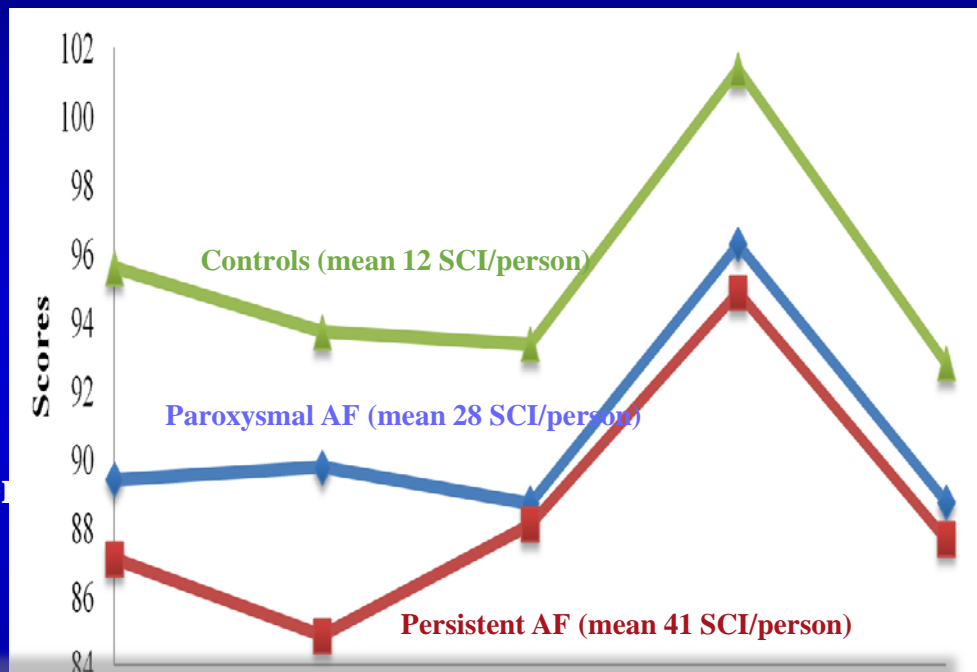
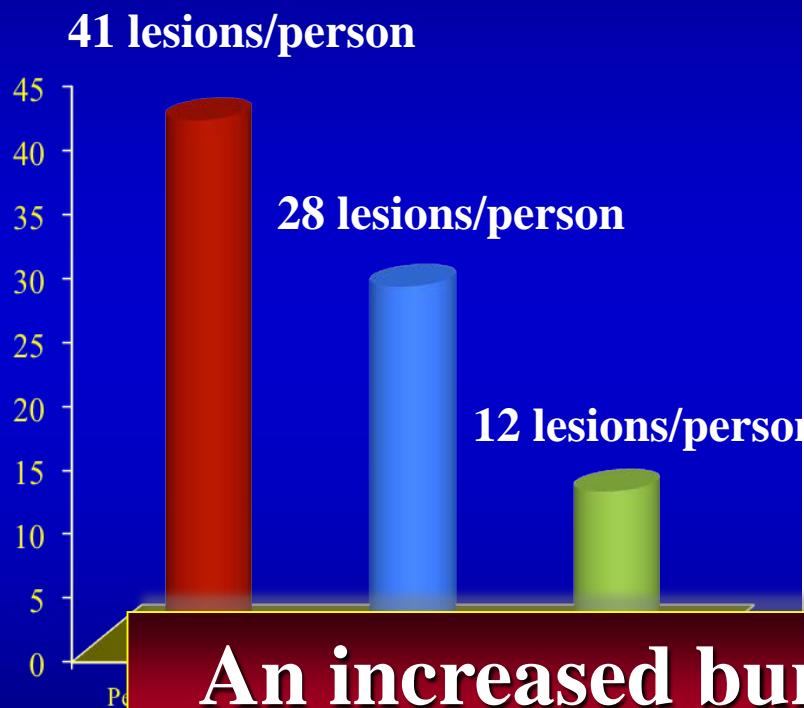
12 lesions/person

28 lesions/person

41 lesions/person



Correlation between AF type, SCI number and cognitive function



An increased burden of SCI relates with worse cognitive performance

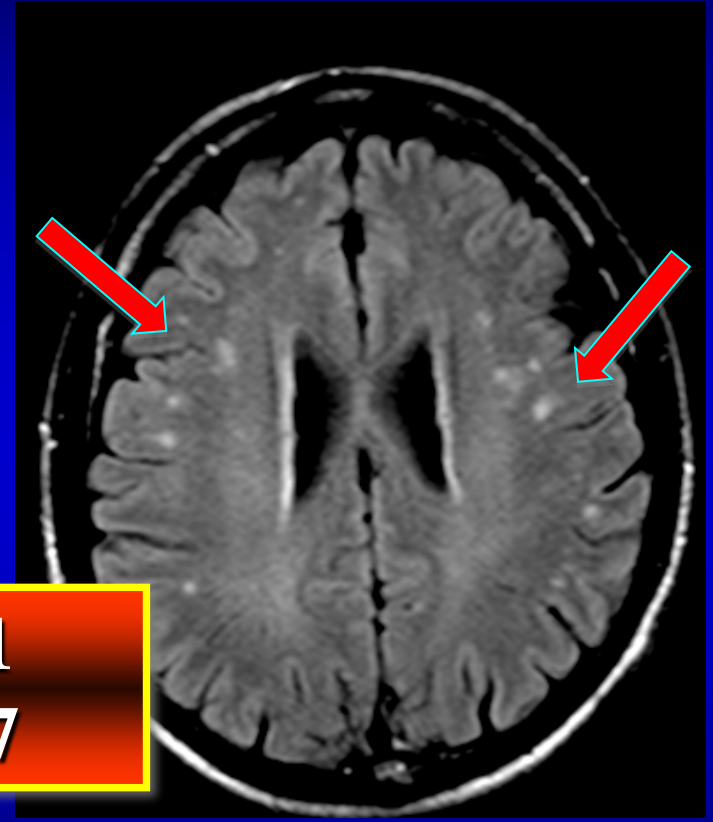
1-Immediate Memory 2-Visuo-spatial abilities 3-Language 4-Attention 5- Delayed memory

SCI prevalence in patients without risk factors: Controls versus AF

Controls 16% SCI



AF 76% SCI



**$P < 0.001$
OR: 4,77**

**In the absence of cardiovascular risk factors (ChadsVasc 0),
AF related to five fold increase of SCI**

Selective Vulnerability of Cortical Border Zone between Anterior, Middle and Posterior Cerebral Arteries

Selective embolization may be due to:
Peculiar anatomy of pial arteries

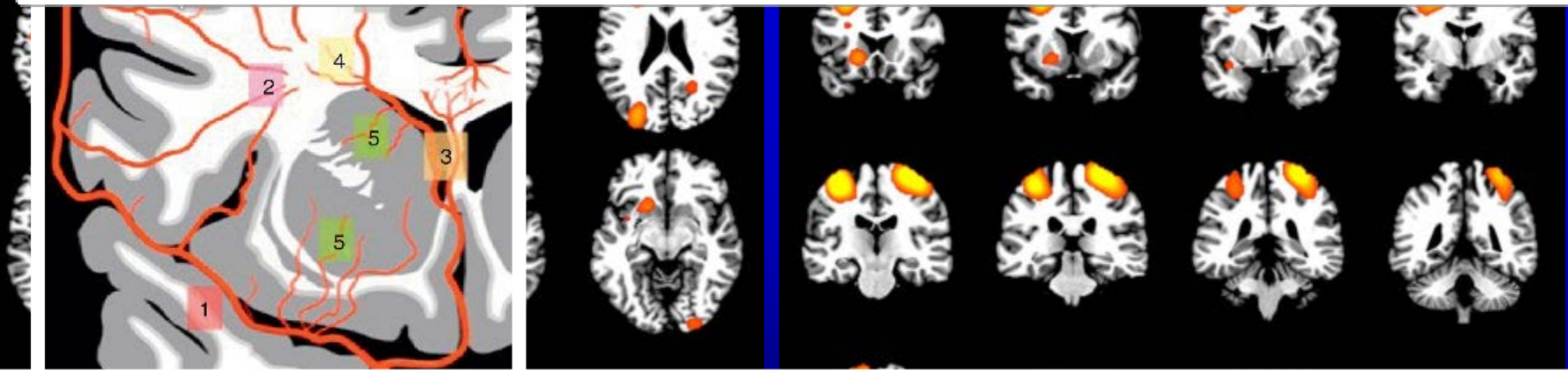
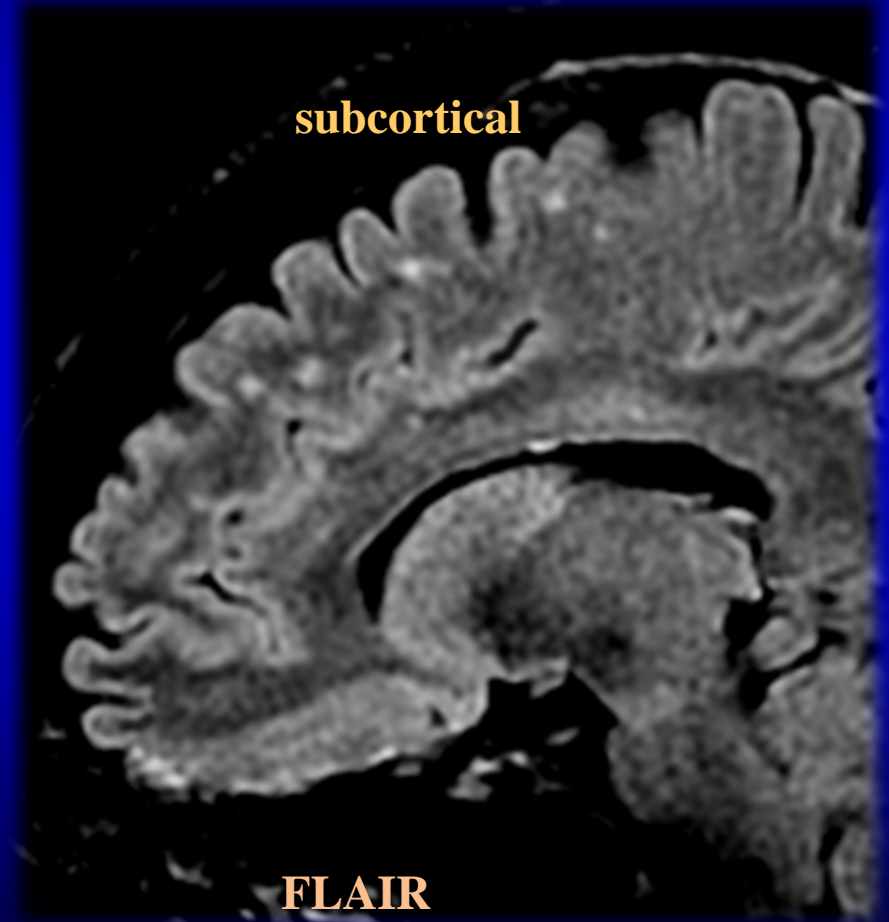
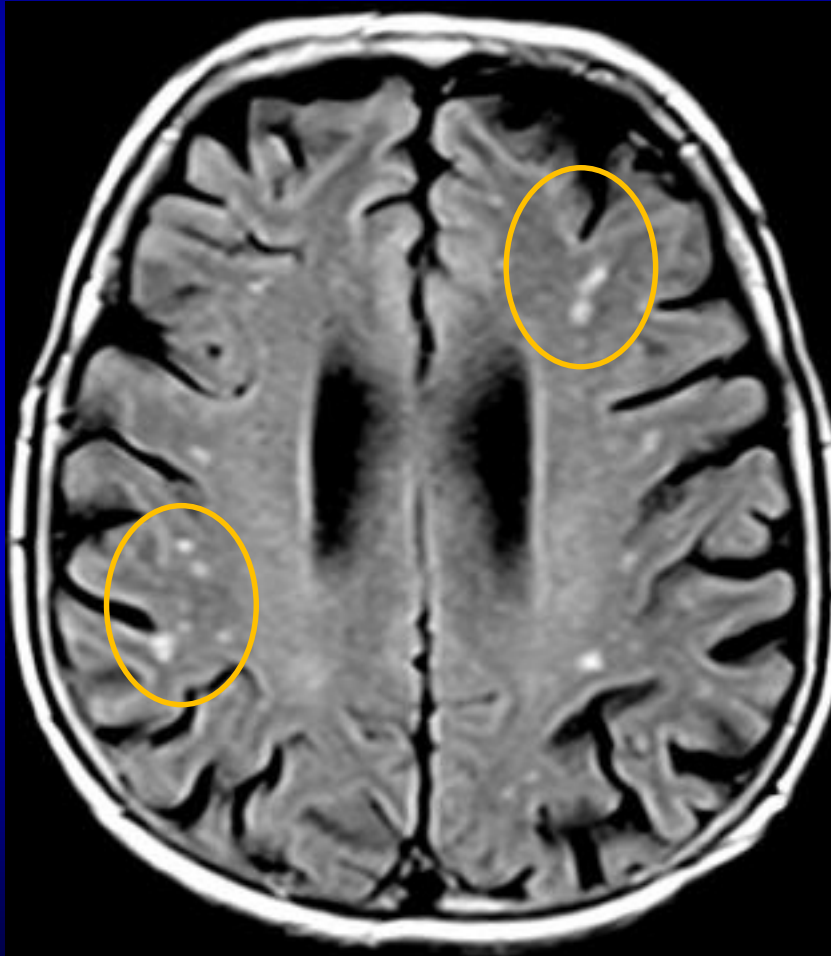


Figure 1. **Cerebral arterial microcirculation.** 1: cortical arteries; 2: pial arteries; 2.1: short branches; 3: subependymal arteries; 4: subependymal perforating arterioles; 5: lenticulostriated and thalamic perforating arterioles; 6: transcerebral arterioles.

In atrial fibrillation lesions are:

- bilateral
- multiple
- “spotted” pattern
- Cortical border zone



Open Issues

**Can oral anticoagulation prevent
AF related cognitive impairment?**

Blinded Randomized Trial of Anticoagulation to Prevent Ischemic Stroke and Neurocognitive Impairment in Atrial Fibrillation



Prospective, multicenter, randomized, blinded clinical trial

Rivaroxaban compared to aspirin or acetylsalicylic acid

ONGOING

Inclusion criteria:
Age 30-60, Non-valvular AF, CHADS score 0

Primary endpoint

- Stroke, TIA and neurocognitive decline

Open Issues

**Can rhythm control strategy
(antiarrhythmic tx or TC ablation)
reduce the progression
of cognitive impairment?**

AF and Cognitive performance long term follow-up (183 subject)

Sinus Rhythm:
55

Rhythm
control:69

Rate control:
59

All subjects underwent
cognitive test at baseline

Cognitive test repetition
at 2,6 y follow up



IMMEDIATE MEMORY

VISUOSPATIAL ABILITIES

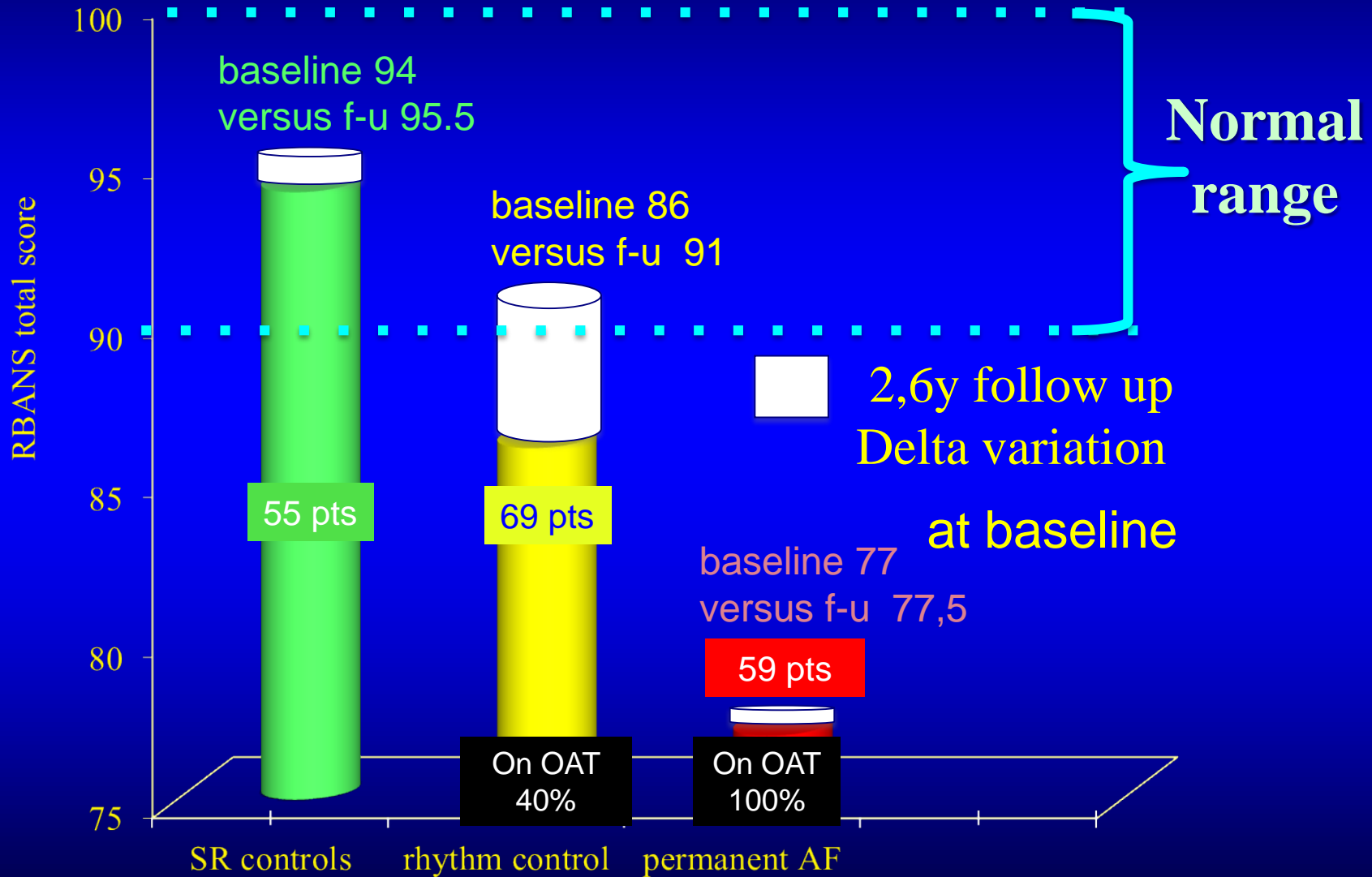
LANGUAGE

ATTENTION

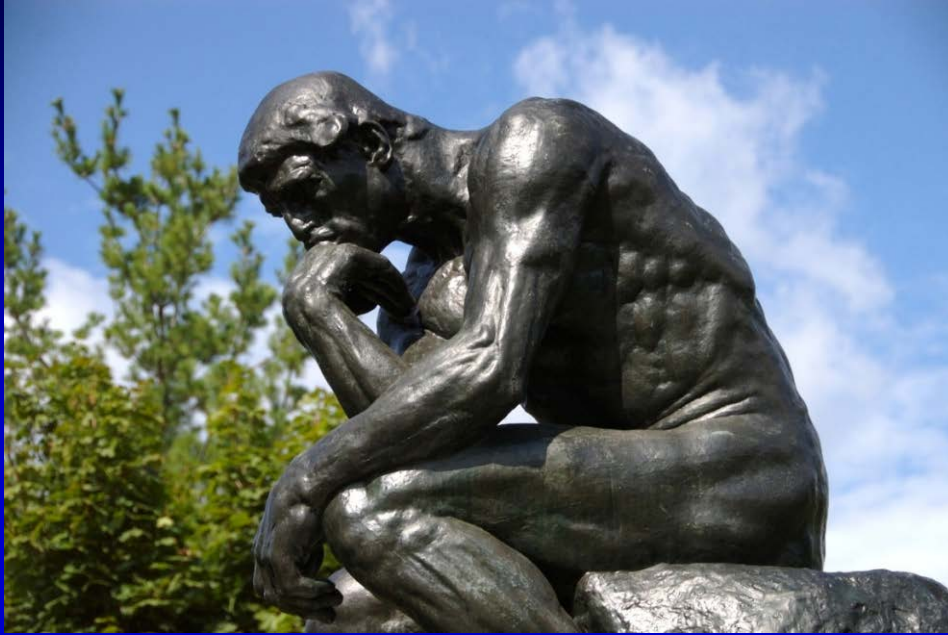
DELAYED MEMORY

Investigated
subdomain

Long term Cognitive performance follow-up: results



Conclusions



For **normal people**
if God gave us
sinus rhythm there
should be a reason

For **physician** the fact
that sinus rhythm is
better than cronic A Fib
must be proved in
randomized clinical trial

