

# cro<sup>m</sup>mis-2

Clinical Relevance Of Microbleeds In Stroke

Investigators meeting

Thursday 7 June 2012



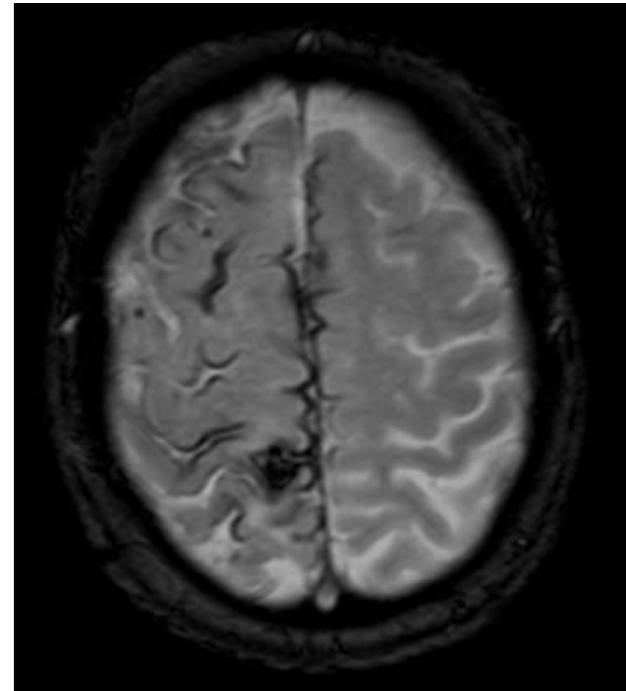
# Future plans

## Substudies

- Transient neurological episodes
- Genetics
- Biomarkers
- Retina changes
- Cognitive follow-up study
- Thrombolysis ICH

# Transient focal neurological episodes

- Dr A Charidimou
- Questionnaire
- Are they more common in lobar ICH than deep ICH?



## Genetics

- Genetics of Cerebral Haemorrhage on Anticoagulants (GOCHA) – lead: Dr J Rosand
- The GOCHA study is multi-site study funded by the National Institute of Health (NIH)
- Sample size 600 warfarin-related ICH
- Our UK target 300 cases of warfarin-related ICH
- Other genetic analyses in ICH (e.g. collagen genes, APOE) will also be possible at UCL depending on funding

# Biomarkers

- Dr A Banerjee, Prof G Lip and collaborators
- Biomarkers of thrombosis, endothelial function have potential utility in risk prediction in atrial fibrillation and stroke (1).
- Lp-PLA<sub>2</sub> and CRP are biomarkers of coronary atherosclerotic burden and atherosclerosis, and may be important for risk prediction in stroke patients (2,3).
- Inflammatory biomarkers (IL-6, CRP, fibrinogen and white cell count) are associated with recurrent cardiovascular events in acute stroke patients (4).
- VEGF has been associated with cerebral microbleeds (5)

1. Montoro-García S, Marín F, Lip GY. Thrombogenesis in lone atrial fibrillation: a role for soluble P-selectin? *Europace*. 2011;13:3-4.
2. Epps KC, Wilensky RL. Lp-PLA- a novel risk factor for high-risk coronary and carotid artery disease. *J Intern Med*. 2011;269:94-106.
3. Kim SJ, Choe YH, Bang OY; for the CHAOS-BIOMARKER Collaborators. Are Stroke Biomarkers Seeing Brain Vessels in Patients With Ischemic Stroke?: A C-Reactive Protein and Homocysteine Study. *Stroke*. 2011 Mar 24. [Epub ahead of print]
4. Whiteley W, Jackson C, Lewis S, Lowe G, Rumley A, Sandercock P, Wardlaw J, Dennis M, Sudlow C. Association of circulating inflammatory markers with recurrent vascular events after stroke: a prospective cohort study. *Stroke*. 2011;42:10-6.
5. Dassan P, Brown MM, Gregoire SM, Keir G, Werring DJ. Association of Cerebral Microbleeds in Acute Ischemic Stroke With High Serum Levels of Vascular Endothelial Growth Factor. *Arch Neurol*. 2012 May 28:1-4. [Epub ahead of print]

# Primary Questions

- (1) Are biomarkers of thrombosis, endothelial function or inflammation associated with ICH, stroke/TIA or death in patients with previous history of stroke/TIA and non-valvular AF?
- (2) Are biomarkers of thrombosis, endothelial function or inflammation associated with microbleeds?

## Secondary Questions

(3) Are there ethnic differences in the associations with biomarkers among patients with previous stroke/TIA and AF?

(4) Are biomarkers of thrombosis, endothelial function and inflammation associated with genetic polymorphisms related to the integrity of brain small vessels or warfarin metabolism?

(5) Do biomarkers add any predictive value to existing risk scores for bleeding (HAS-BLED) and stroke (CHA<sub>2</sub>DS<sub>2</sub>-VASc, CHADS<sub>2</sub>) in the setting of AF?

# Substudy design

## *Inclusion criteria*

- All patients included in the main CROMIS-2(AF) study will be eligible for this substudy.

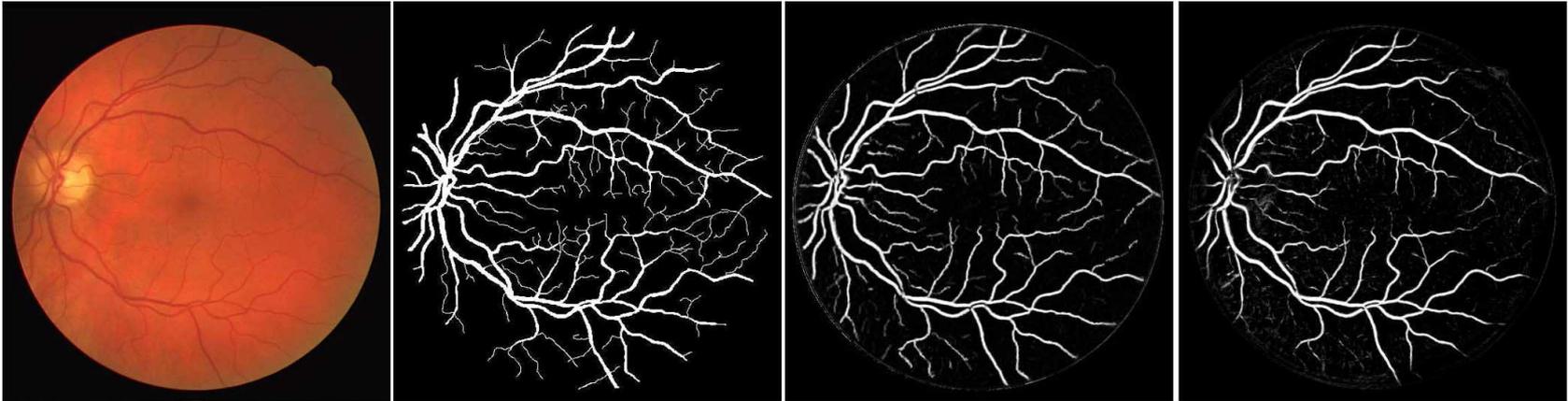
## *Addition to protocol*

- At baseline, the blood levels of lipoprotein-associated phospholipase A2 (Lp-PLA<sub>2</sub>) and C-reactive protein (CRP), IL-6, P-selectin, von Willebrand (VWF) and D-dimer.
- Bloods (frozen plasma) to be processed in Birmingham

# Progress

- To apply for BHF project grant in late July 2012

# Retinal changes in cerebral haemorrhage



- Dr Ahmed Toosy, Queen Square (Neurophthalmology)
- Could retinal changes (vessel size, branching angles, etc) relate to the underlying vasculopathy
- N=20 ICH, initially at UCL only

# Predictors of dementia in AF-related stroke

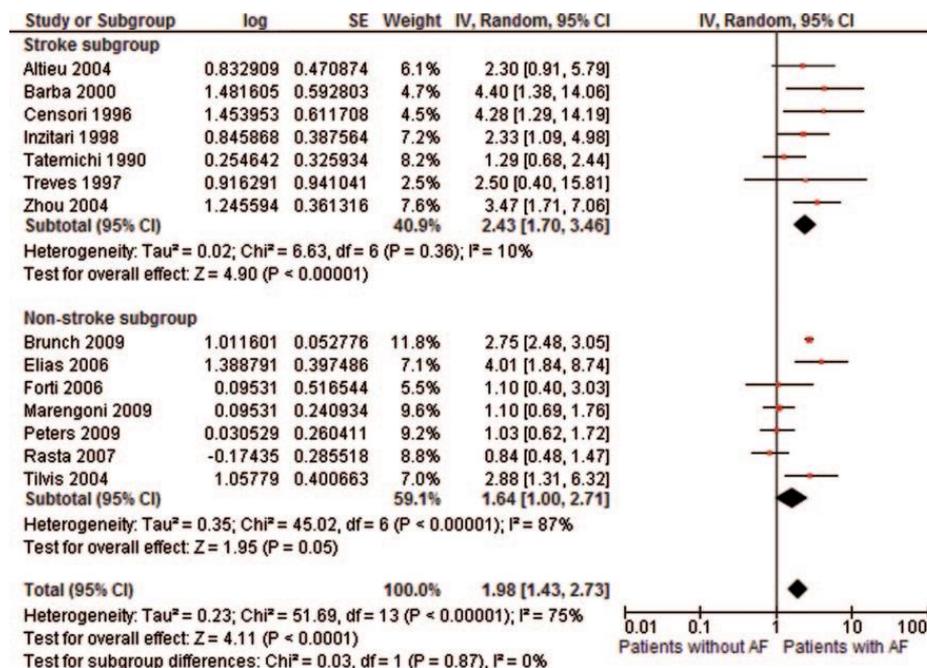
## Atrial fibrillation and incidence of dementia

A systematic review and meta-analysis

Kwok et al, *Neurology* 2011

- AF-related stroke carries a high risk of future dementia

Figure 2 Meta-analysis of risk of dementia in patients with and those without atrial fibrillation



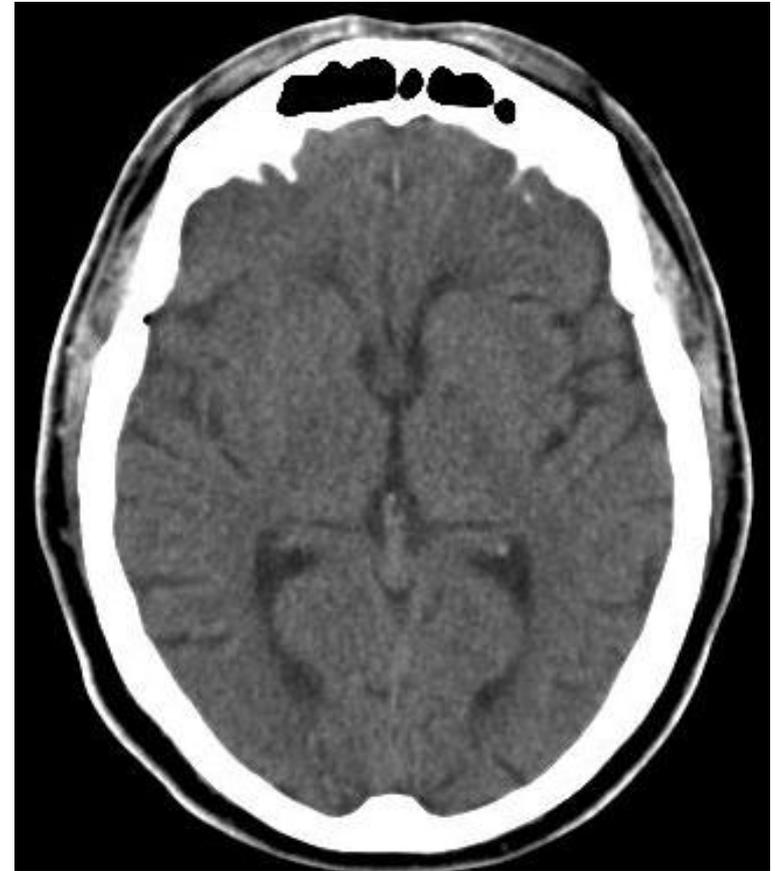
## **Predictors of dementia in AF-related stroke**

- Mechanisms not known
- ? Due to pre-existing neurodegenerative disease or ongoing embolization
- We have a unique opportunity to prospectively study this in CROMIS-2
- We would like to obtain follow-up cognitive data on as the complete AF cohort if possible
- Telephone (short) version of MOCA at 1 year from recruitment

***Please let Clare know if you are interested!***

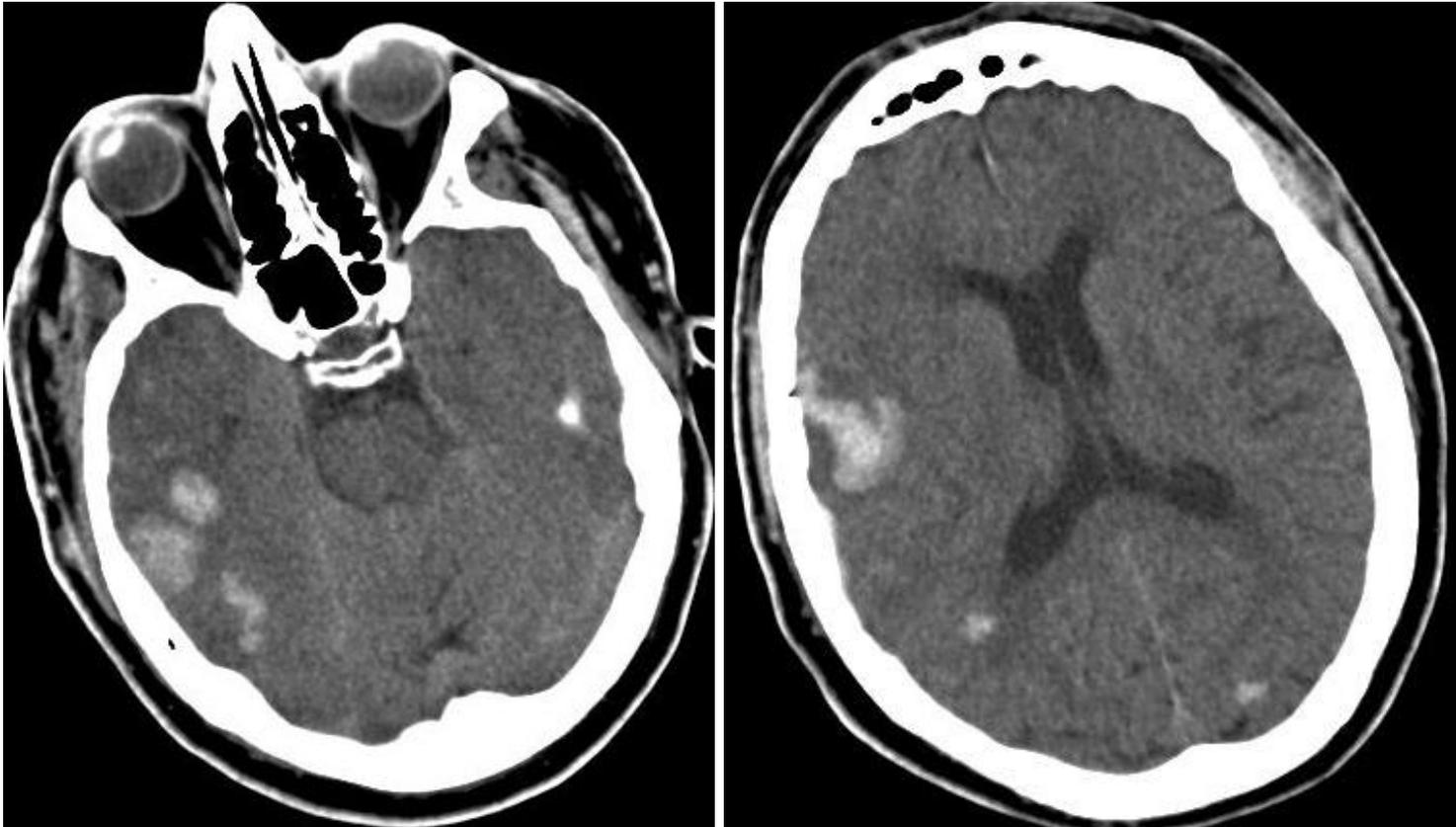
# Thrombolysis-related ICH

- 70 year old man
- Presented with sudden left face and arm weakness
- Hypertensive, previous AF
- NIHSS 6
- BP 200/100

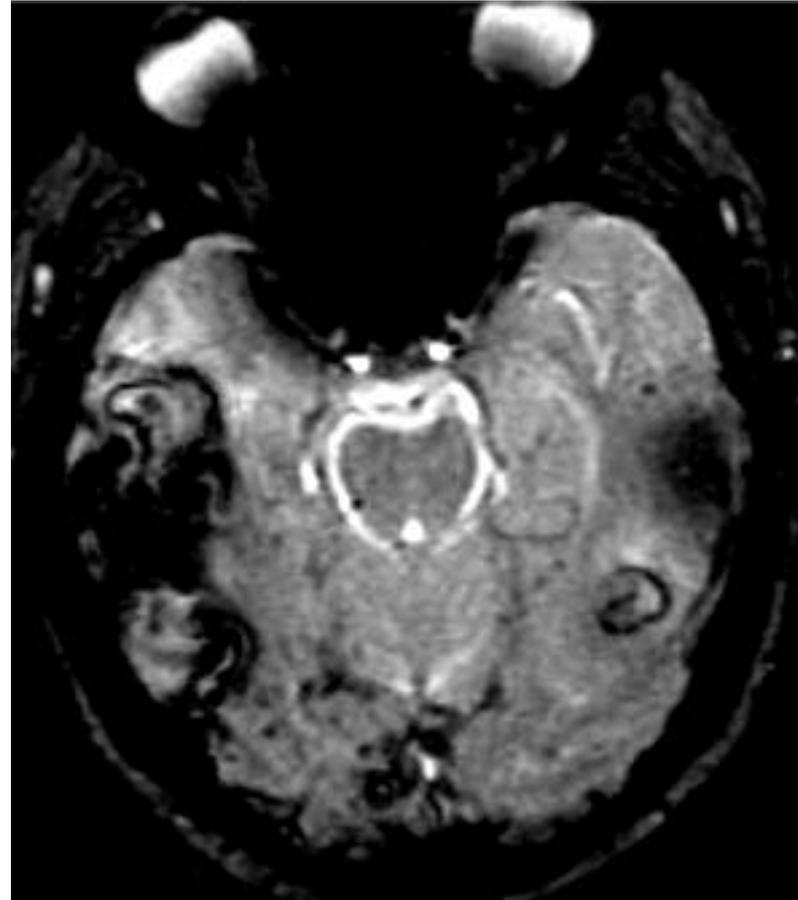
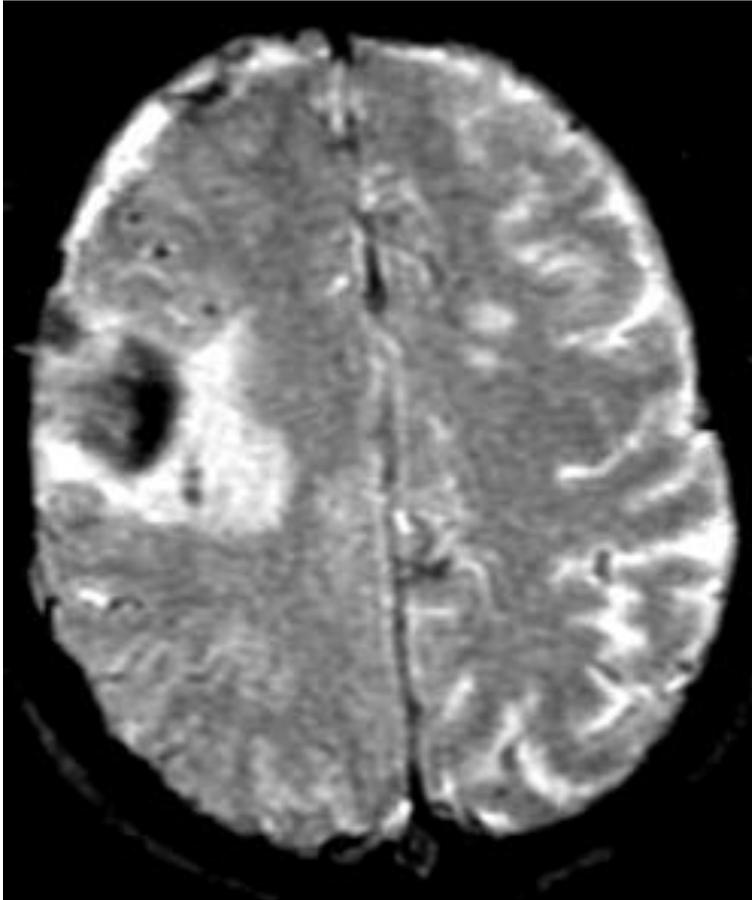


# Thrombolysed

- Deteriorated ~7 hours later
- Drowsy, worsening weakness



## MRI done 5 days later



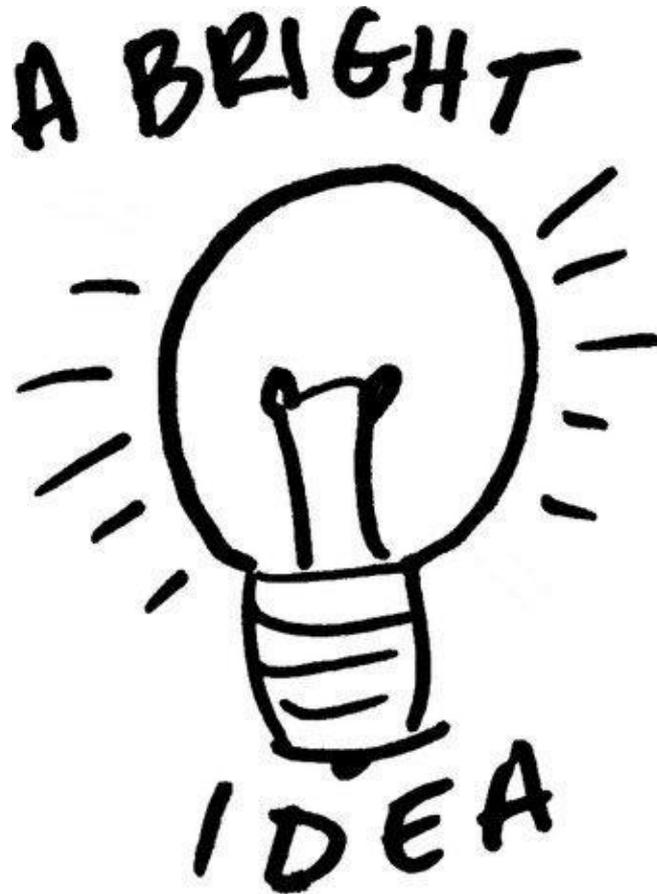
Diagnosis ??

# Thrombolysis-related ICH

- Devastating complication
- Not well understood
- Currently excluded from CROMIS-2
- We would like to include such patients (prospectively and retrospectively) to allow their characteristics to be better defined
- Is CAA a common cause?

***Please let Clare know if you are interested!***

**Ideas for further CROMIS-2 substudies are welcome!**



**Thank you for coming!**

***Next CROMIS-2 Investigators meeting planned for UKSF, December 2012, Harrogate***

*Details to be confirmed*



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