

# WP 2 Scientific Coordination

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## Aim:

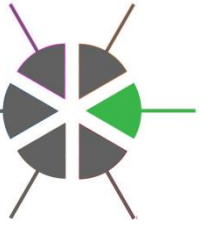
To establish:



the structures and procedures which allow a consortium of trialists to agree on specific investigational drugs or therapeutic principles worth testing by the group



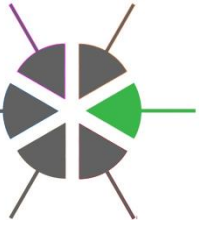
the models, experimental design, and protocols to be used.



# WP 2 Scientific Coordination

## Specifically, to establish

1. A core set of stroke models
2. SOPS and structure of study protocol
3. A system for monitoring standards of SOPs, protocols
4. The structure, remit, membership, powers of a *data monitoring committee*
5. The structure, remit, membership, powers of a *steering committee*
6. A process to exchange information on new therapy to be tested (including commissioning systematic review)



# WP 2 Scientific Coordination

## Deliverables

- D2.1 Month 6: Agreement around and definition of a core set of animal models
  - D2.2 Month 6: Template for designing the structure of a study protocol approved
  - D2.3 Month 12: Quality Standards Committee established
  - D2.4 Month 12: Data Monitoring Committee established
  - D2.5 Month 20: Steering Committee established along with the mechanism for initiating and approving preclinical stroke studies.
  - D2.6 Month 20: Task 2.6 Process for pre-trial information and knowledge exchange on therapy to be established
- } can we achieve these by Barcelona ?  
Hanno & Philip, Philip's statistician and an external person ?



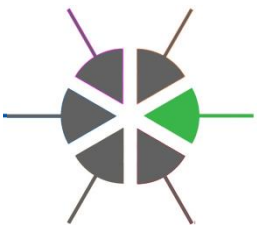
## D2.1 : Agreement around and definition of a core set of animal models

- Each centre provided feedback on the range of *“models they currently use”*
- Models they are not currently using but have *“Limited experience”* of .
- New models they are currently *“Setting up”*
- Models they have no experience of but *“would be willing to set up.”*



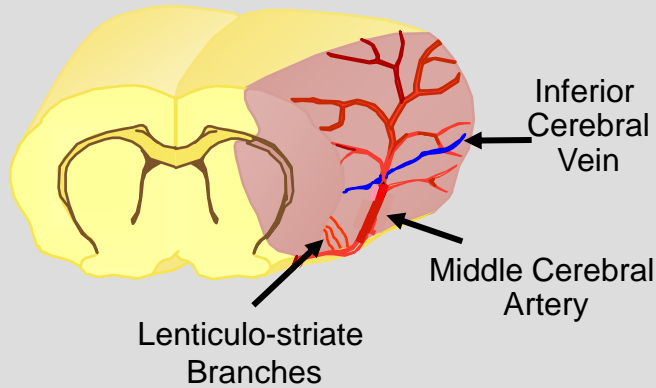
## **D2.1 : Agreement around and definition of a core set of animal models**

**9 preclinical stroke centres  
with expertise in  
15 (+) alternative stroke models**

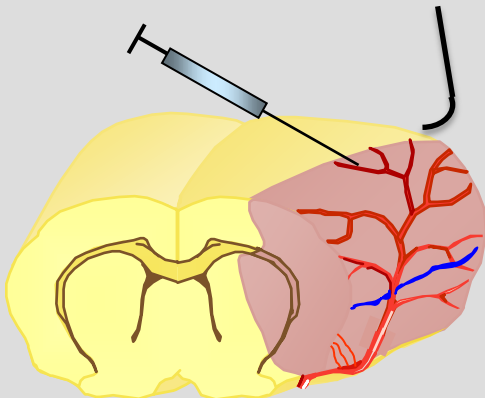


# WP 2 D2.1: Agreement around and definition of a core set of animal models

## MCA territory



## Intraluminal microinjection of thrombin (Orset) permanent or transient

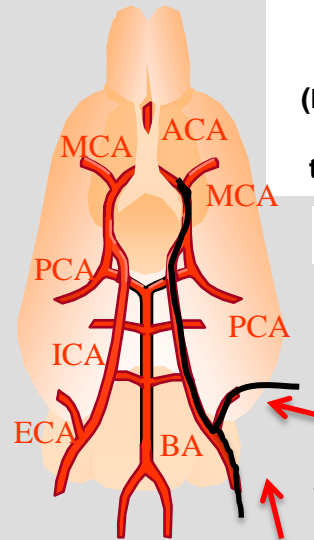


## Direct compression (Rosell) or elevation of branch (Brint) permanent or transient

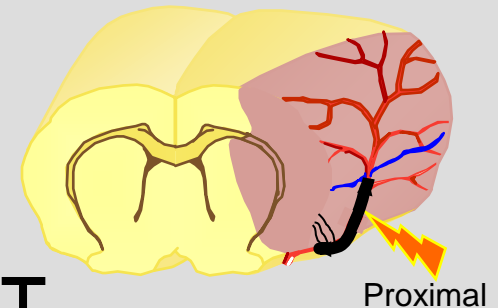
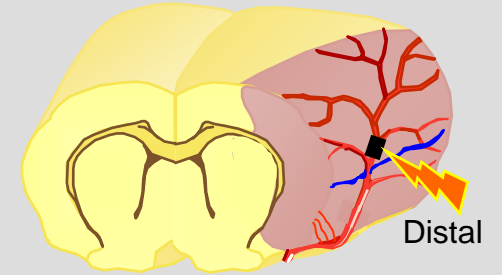
## Intraluminal Filament (Longa & Koizumi) permanent or transient MCAO

### Embolic

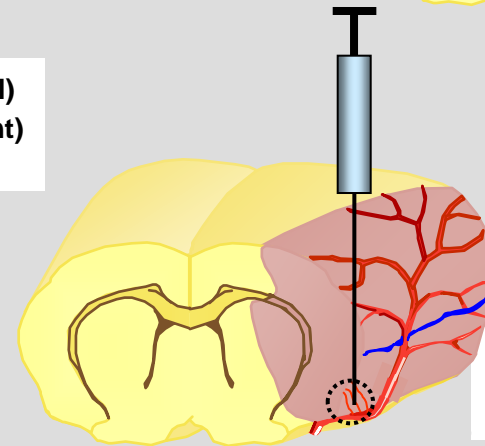
Filament or embolus introduced via ECA or CCA

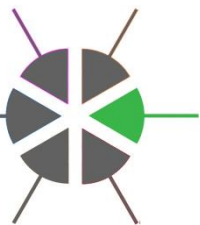


## Electrocoagulation (Tamura) permanent MCAO



## Intraparenchymal endothelin-1 microinjection (Sharkey) permanent MCAO





# WP 2 D2.1: Agreement around and definition of a core set of animal models

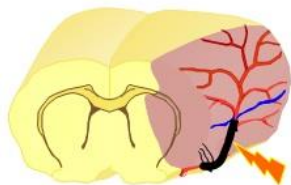
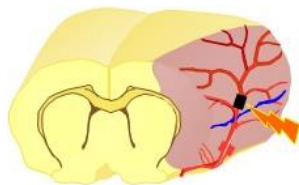
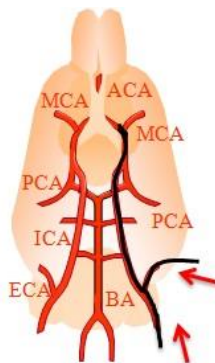
## 9 preclinical centres with expertise in 15 (+) alternative stroke models

Intraluminal filament: rats

Intraluminal filament: mice

Direct electrocoagulation of MCA: rats

Direct electrocoagulation of MCA: mice



Established in 7 centres, limited experience in 1

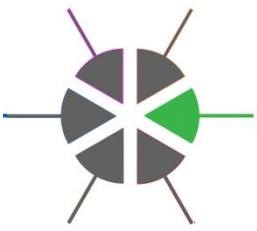
Established in 8 centres, limited experience in 1

Distal: Established in 2 centres, limited experience in 1, 2 centres willing to set up

Proximal: Established in 2 centres, limited experience in 1, 2 centres willing to set up

Distal: Established in 4 centres, limited experience in 1, 3 centres willing to set up

Proximal: Established in 1 centres, limited experience in 1, 4 centres willing to set up



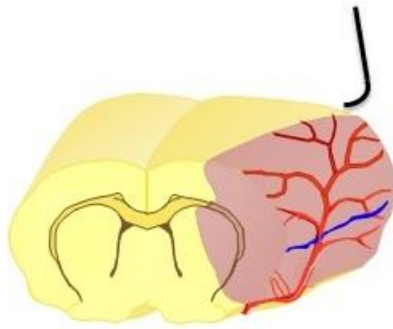
# WP 2 D2.1: Agreement around and definition of a core set of animal models

Direct compression of MCA: mice

Direct compression of MCA: rats

Direct occlusion of MCA by hook & elevation: rats

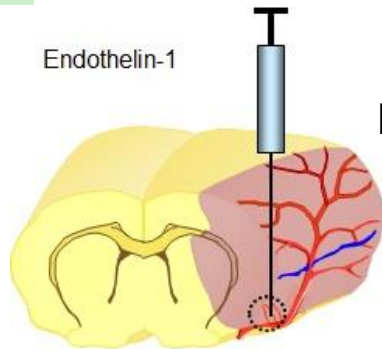
Endothelin-1 injection: rats



Distal: Established in 2 centres, 5 centres willing to set up

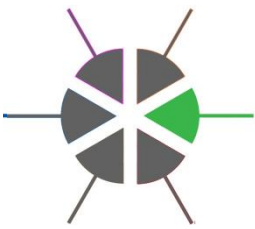
Distal: Established in 1 centres, 5 centres willing to set up

Distal: Established in 1 centres, 4 centres willing to set up



Not established in any centres, but 4 centres willing to set up





# WP 2 D2.1: Agreement around and definition of a core set of animal models

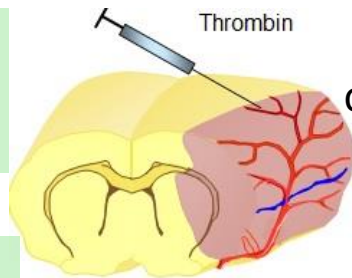
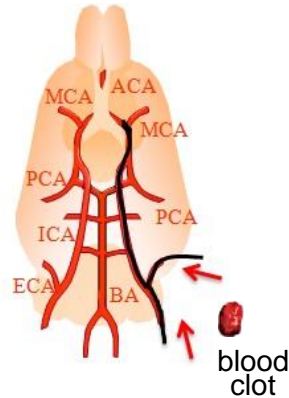
Embolitic stroke  
blood clot: rats

Embolitic stroke  
blood clot: mice

Thrombin injection  
into MCA  
branch: mice

Thrombin injection  
into MCA  
branch: rats

Thrombin injection  
into MCA branch: macaques



Established in 2 centres, limited experience in 2 centres 1 centre setting it up and 2 centres willing to set up

Not established in any centres, limited experience in 1 centre and 5 centres willing to set up

Distal: Established in 1 centre, limited experience in 1 centre and 5 centres willing to set up

Distal: Established in 1 centre, 5 centres willing to set up

Distal: Established in 1 centre

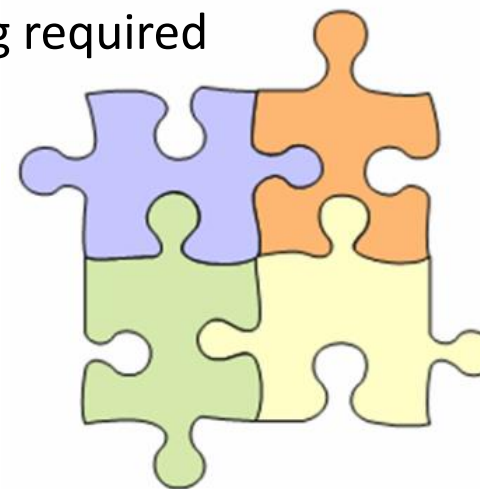


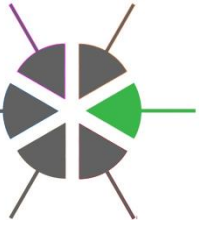
## D2.2 Month 6: Template for designing the structure of a study protocol approved

**Proposal:** Study protocol will be generated from a portfolio of approved SOPs  
A number of SOPs will together cover everything required to make up a study protocol.

Some SOPs will be general and included in all study protocols  
e.g. randomisation & blinding, estimation of group size,  
post-op care of animals

Other SOPs will relate to specific features of a particular study protocol  
e.g. a specific behavioural test, MRI, specific brain assay, etc.





## D2.2 Month 6: Template for designing the structure of a study protocol approved

Formsheets will be used to generate SOPs which, once approved by the consortium, will be held on the central data base.

A study protocol will be put together from SOPs plus additional details

Animal specifics

Details of species, strain & sex , comorbidities

Therapy specifics

Available pharmacology, pharmacokinetics, pharmacodynamics

Randomisation & Blinding SOP

Sample size SOP

Statistical Analysis plan

Stroke model SOPs: including details of anaesthesia, monitoring, local analgesia, etc

Inclusion/Exclusion criteria

SOP for behaviour assessment

SOP for LD flowmetry

Therapy administration plan

Details route, dose, frequency etc

when to euthanise

Post-stroke care SOP

GO/NOGO points once study underway

Primary outcome SOP

Secondary outcome SOP



## D2.2 Month 6: Template for designing the structure of a study protocol approved

### Next steps:

- Group to provide feedback to optimise the study design protocol
- Reach agreement on and establish the SOPs.  
Share out draft writing and optimisation  
(e.g. the main users of each stroke model, to write the relevant SOP)
- **WP 3 leads** Randomisation & Blinding SOP      Sample size SOP
- **WP2 leads** to collect information on existing expertise in:
  - co-morbid models
  - behavioural tests and neurological scores