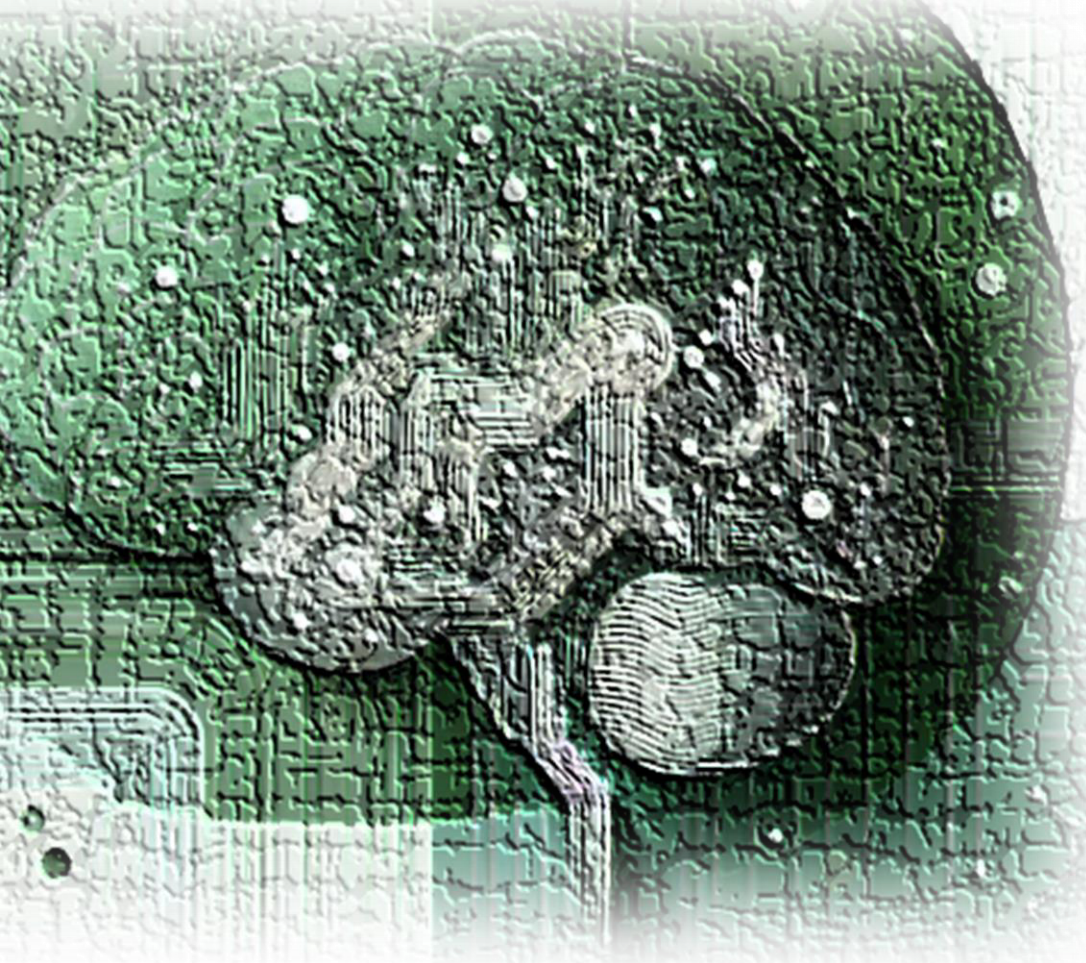


TOWARDS NOVEL INTRACEREBRAL HAEMORRHAGE STROKE MODELS USING ENDOVASCULAR APPROACH IN SWINE

Alexia García-Serran

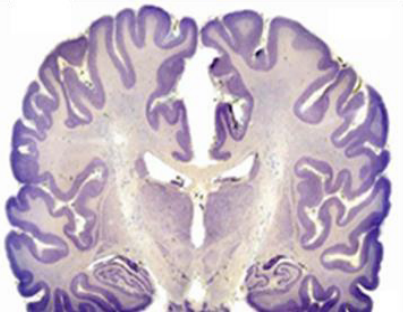
Teresa Gasull, CMN reserch group
Germans Trias i Pujol Research Institute
Barcelona, October 8th 2024
tgasull@igtp.cat

Background

ICH animal models

Small animals (rodents)

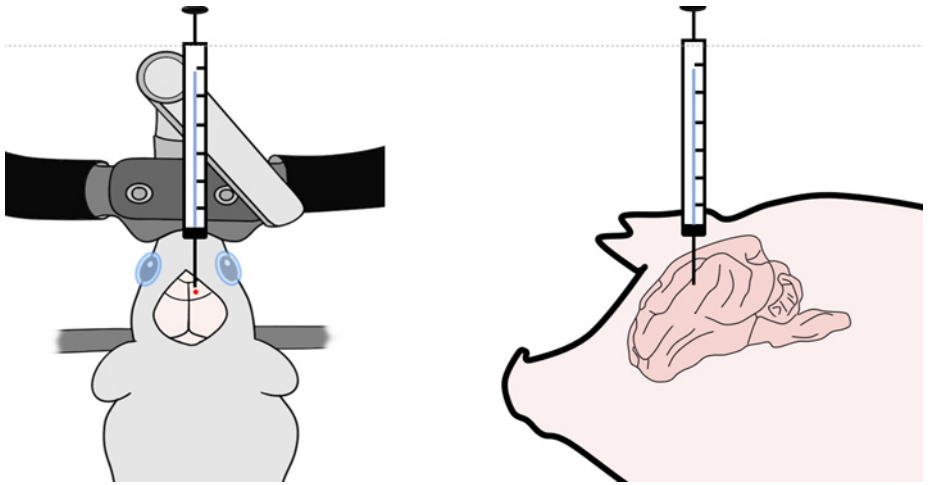
- ✓ Manageable.
- x Lissencephalic brains.
- x Low white matter proportion.
- x Nocturnal animals (a concern regarding performance of neurological t working hours nocturnal phas
- x Low samp s



Human

x Ethical concerns & expensive

Background



What will be the best possible ICH animal model?

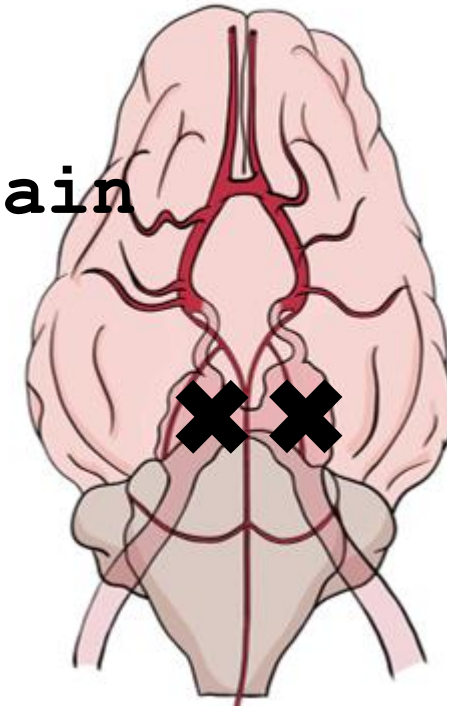
- ✓ Gyrencephalic brains.
- ✓ White matter proportion and distribution similar to that in human
- ✓ That do not need to burr a hole or damage the cranium
- ✓ That recapitulate the arterial blood spill over observed in the clinics
- ✓ Brains that can be imaged with multimodal MRI using same methods used in stroke patients (longitudinal studies)
- ✓ Model in which we could use similar techniques of those used in humans (catheters to access endovascularly specific brain areas)
- ✓ No significant ethical concerns
- ✓ Diurnal animals to determine outcome in tests during the active period.

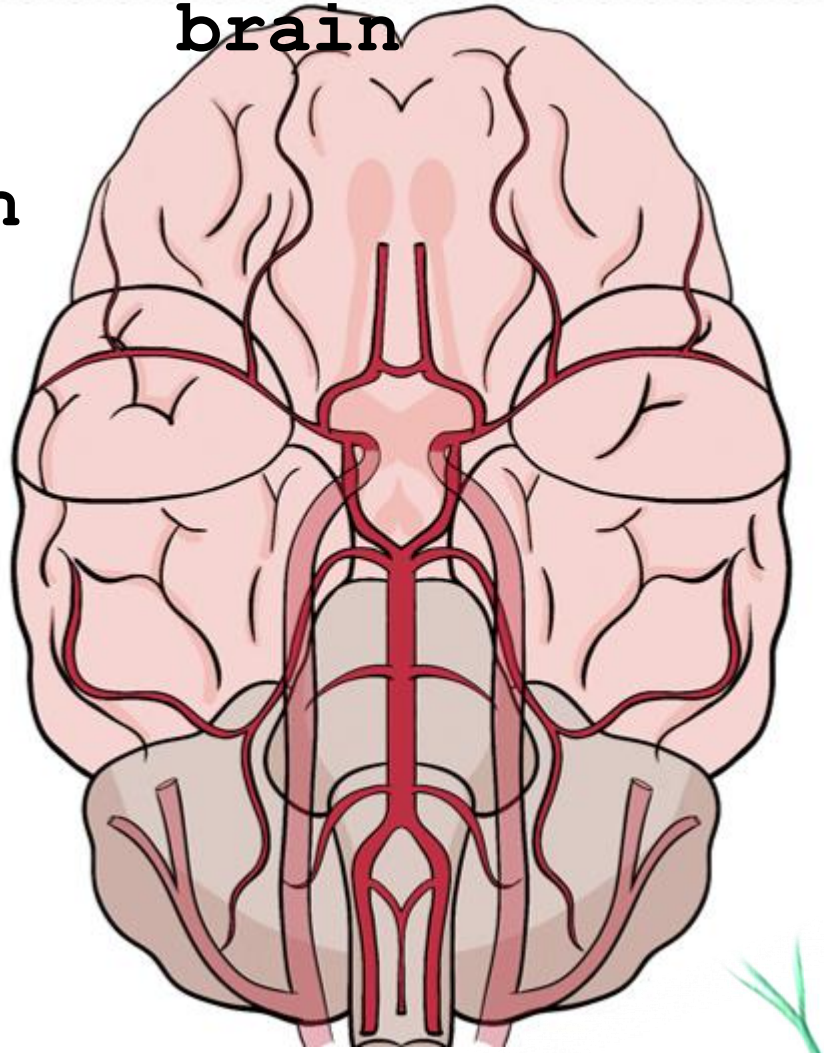
Background

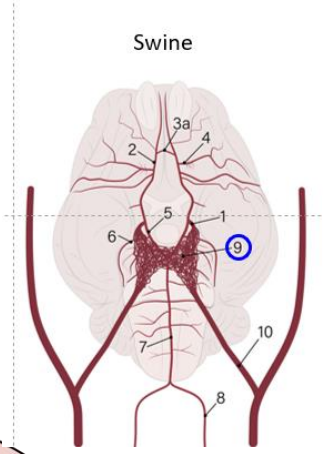
Human brain

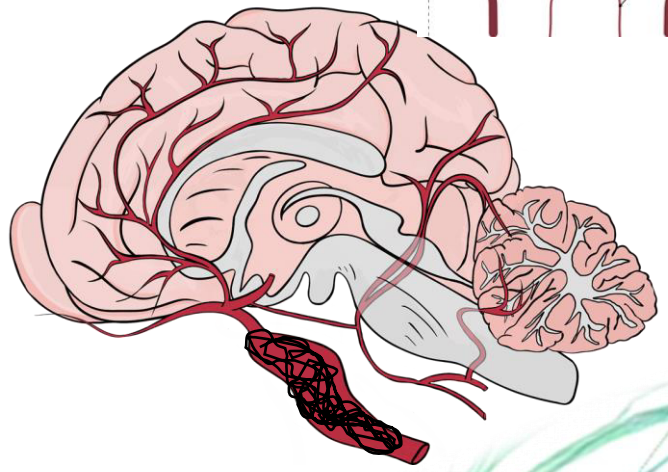
Pig brain

Mouse brain









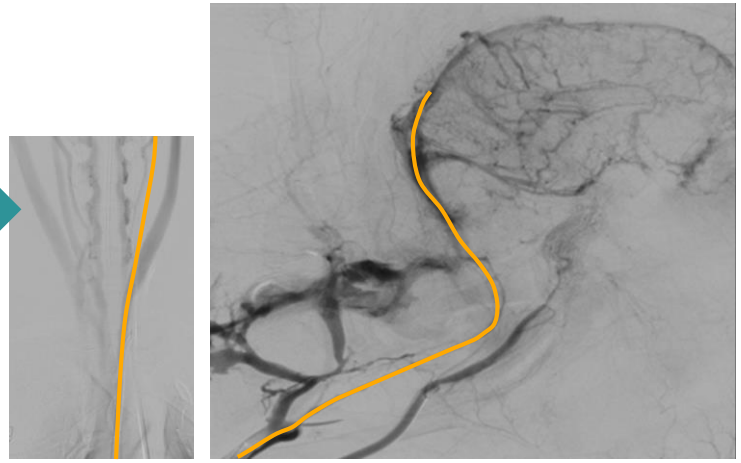
Rete Mirabile (RM)

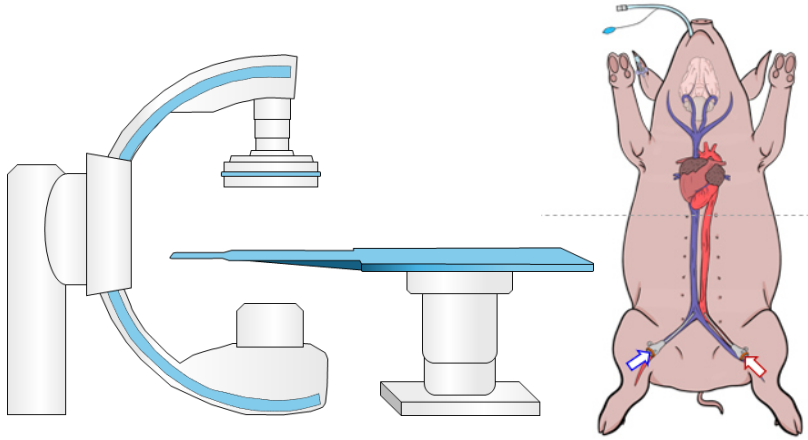
Hypothesis and Objective

Hypothesis

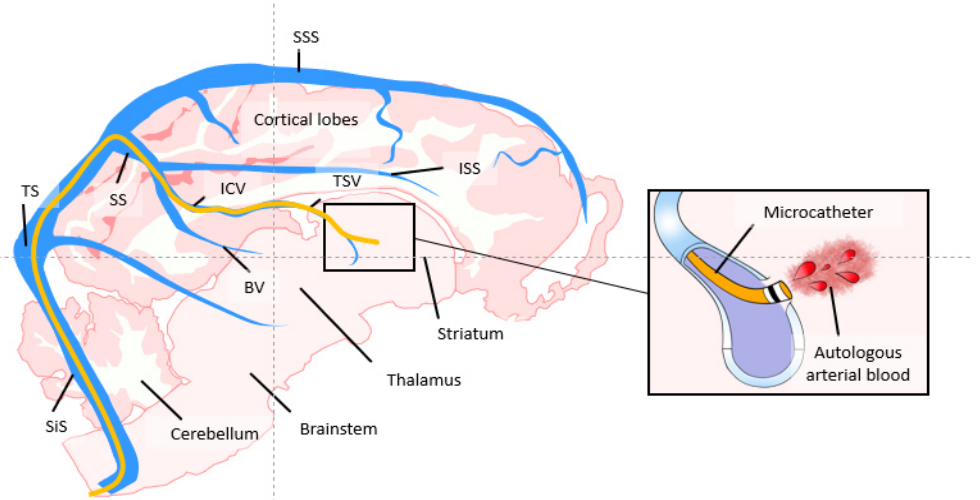
Specific brain regions of interest can be accessed endovascularly by a catheter through the pig's cerebral veins to reach different sinuses and once in there we can induce a small rupture and inject autologous arterial blood to create a new ICH model.

A catheter may access through the brain's venous system

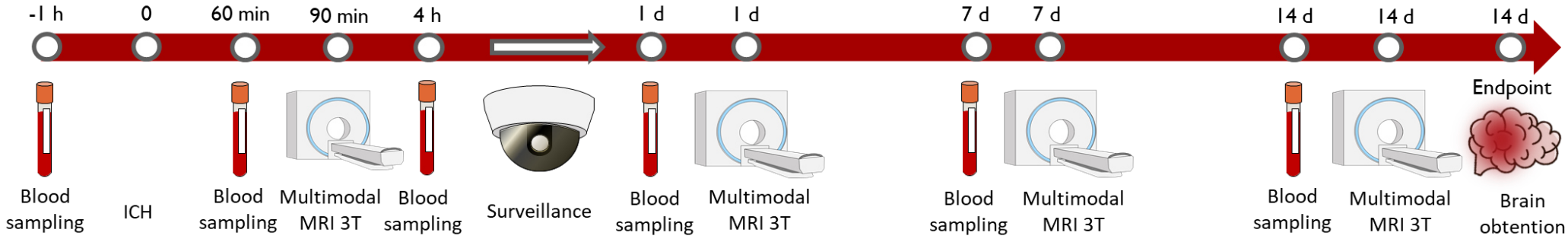


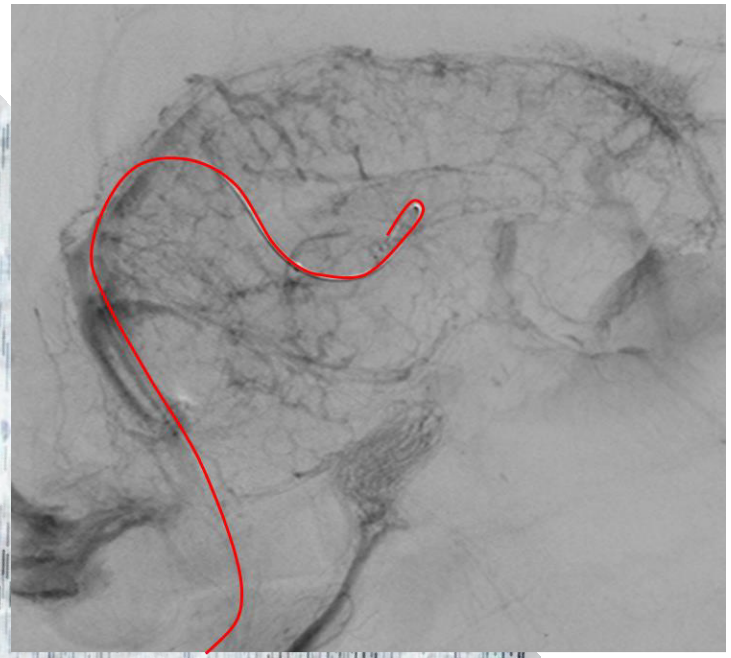


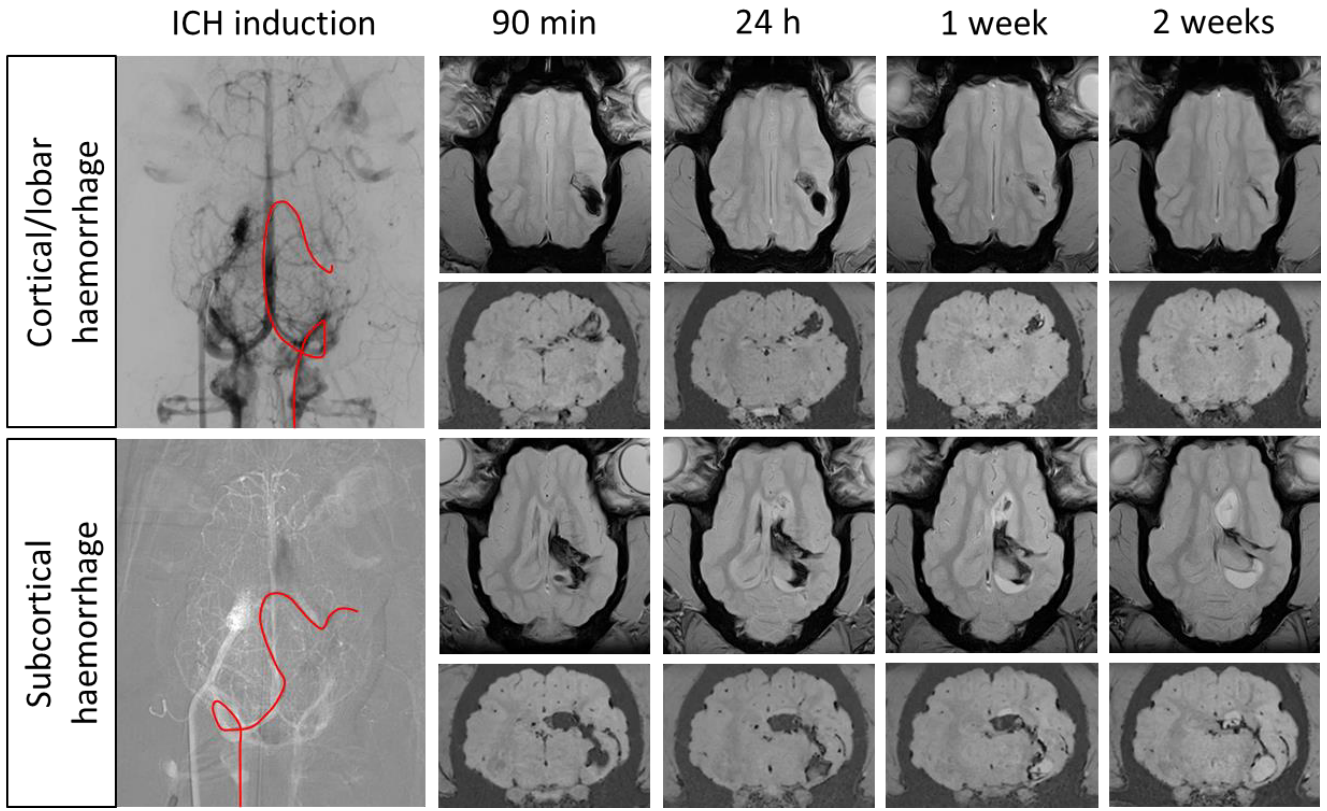
Access to pig's brain venous system through the right internal jugular vein (IJV). The SSS (Superior sagittal sinus), ISS (Inferior sagittal sinus), TS (Transverse sinus), and SS (Sigmoid sinus).



Results

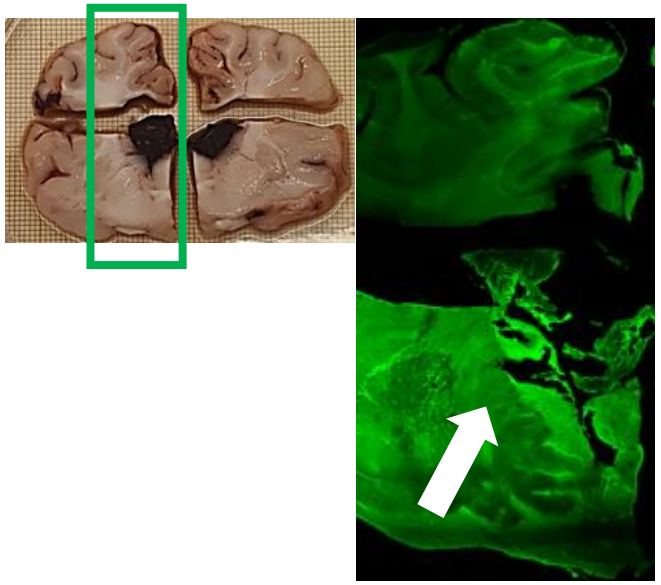

-1 h
0
60 min
90 min
4 h
1 d
1 d
7 d
7 d
14 d
14 d
14 d
Endpoint
Blood sampling
ICH
Blood sampling
Multimodal MRI 3T
Blood sampling
Surveillance
Blood sampling
Multimodal MRI 3T
Blood sampling
Multimodal MRI 3T
Blood sampling
Multimodal MRI 3T
Brain obtention



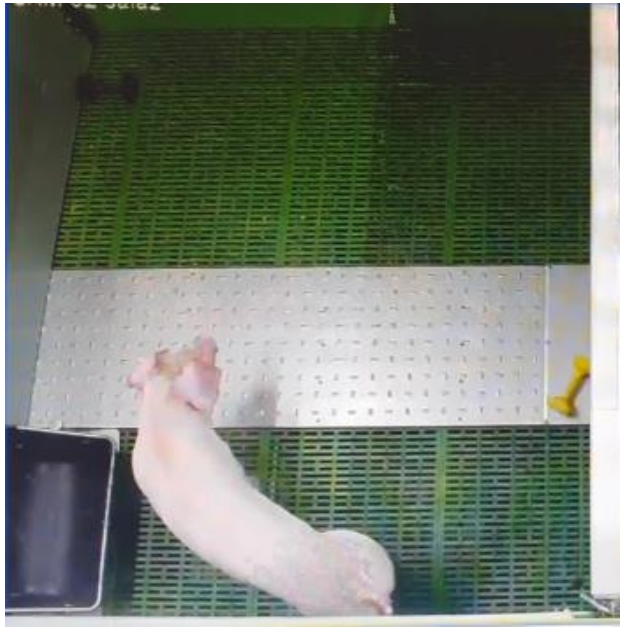

ICH induction
90 min
24 h
1 week
2 weeks
Cortical/lobar haemorrhage
Subcortical haemorrhage

Results

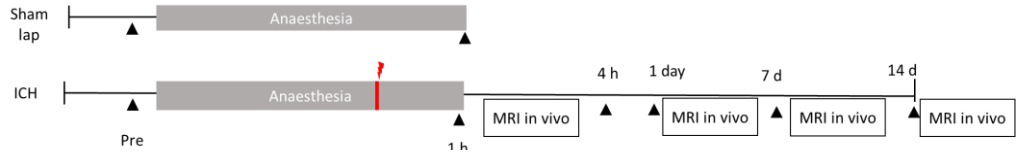
4 h post ICH

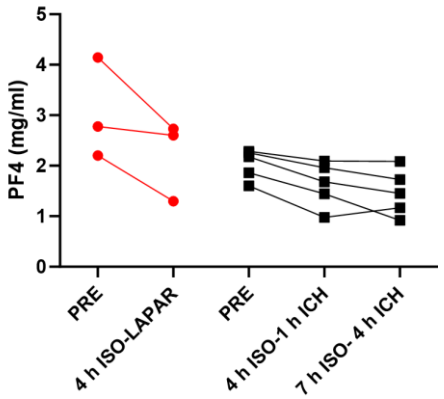


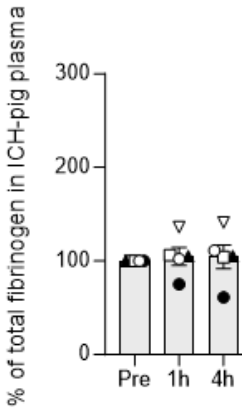
ICH-right cortical hemisphere

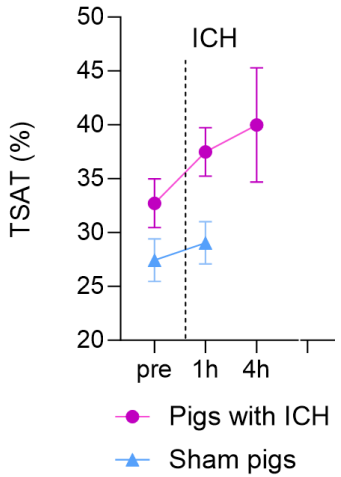


Early changes in the systemic circulation after ICH induction









Conclusions

1) We developed a model of ICH using an intravascular approach through the venous system in a large animal that has a brain similar to humans
2) The survival is good
3) We can view the hemorrhage area and the clot reabsorption by MRI
4) ICH-exposed pigs show neurological impairment that can be quantified
5) We are currently characterizing systemic factors associated to the coagulation cascade in the model
6) We are determining molecules of interest in brain slices in the areas nearby the hematoma by IHC

Thank you

RICORS-ICTUS

Instituto de Salud Carlos III

IGTP Germans Trias i Pujol Research Institute

CMCiB Comparative Medicine & Bioimage Centre of Catalonia

Germans Trias i Pujol Hospital
Institut Català de la Salut

INc Institut de Neurociències

UAB Universitat Autònoma de Barcelona

Cellular and Molecular Neurobiology group (CMN)

Teresa Gasull
Octavi Martí-Sistac
Núria DeGregorio-Rocasolano
Alexia García-Serran
Diego Sahuquillo

Jesús Ordoño
Marina Mas-Argemí

Neurovascular Research Group

Antoni Dávalos
Carlos Castaño
Maria Rosa García-Sort
María Hernández-Pérez
Adrián Valls-Carbó

Proteomics and Metabolomics platform

José María Hernández

Comparative Medicine and Bioimage Center of Catalonia (CMCiB)

Jordi Grífols
Osvaldo Pino
Gemma Monté-Rubio
Josep Puig
Marta Margalef
Osmany Hernández
Juan Ricardo González
Montse Ochando
Vanessa Figueredo

Canon CANON MEDICAL SYSTEMS S.A.

Canon Medical Systems

Alba Iruela
Alicia Palomar

IRBLleida Institut de Recerca Biomèdica

Biomedical Research Institute of Lleida Fundació Dr. Pifarré (IRBLleida)

Francisco Purroy
Glòria Arqué
Cristina Pereira

UKE HAMBURG

Universitätsklinikum Hamburg-Eppendorf (UKE)

Eva Tolosa

West Laboratory

University of Georgia, Athens, US

Prof. Franklin West lab

UNIVERSITY of MARYLAND SCHOOL OF MEDICINE

University of Maryland, Baltimore,

Prof. Piotr Walczak lab

ALMA MATER STUDIORUM UNIVERSITÀ DI BOLOGNA

University of Bologna, I

Maria Laura Bacci's Lab