Instituto de Salud Carlos III

Funded by the European Union
NextGenerationEU

Plan de Recuperación, Transformación y Resiliencia

Animal models of hemorrhage: challenges and successes

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Barcelona, October 8th 2024

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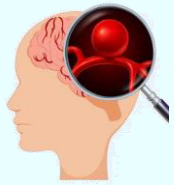
Types and main causes of brain hemorrhages

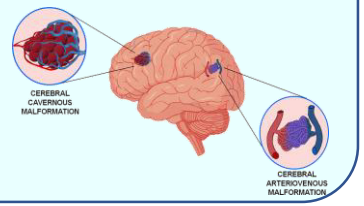
Trauma

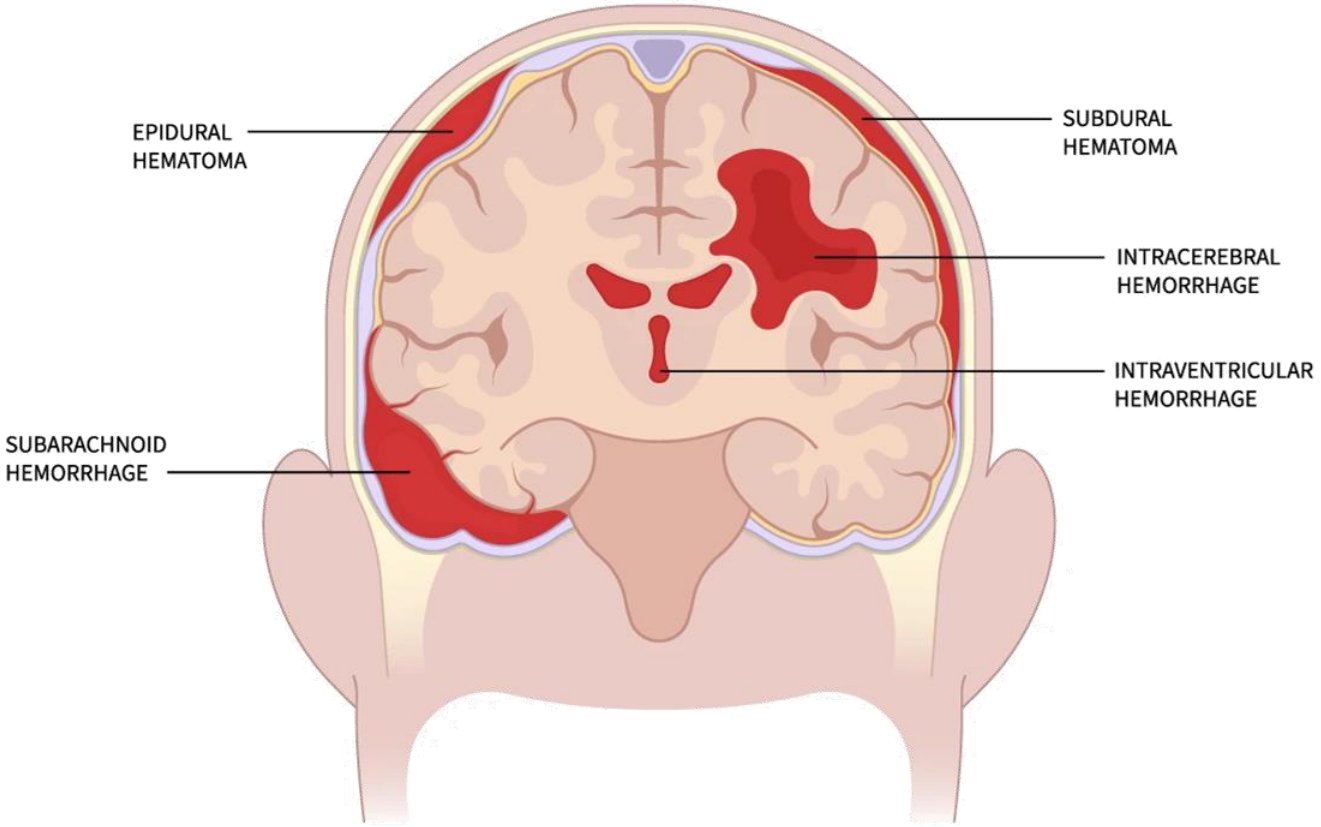
Tumor

Aneurysm

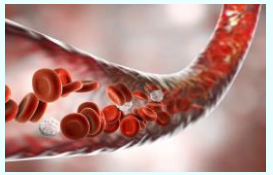


Vascular malformation





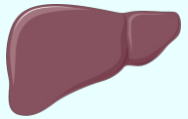
Blood or bleeding disorders



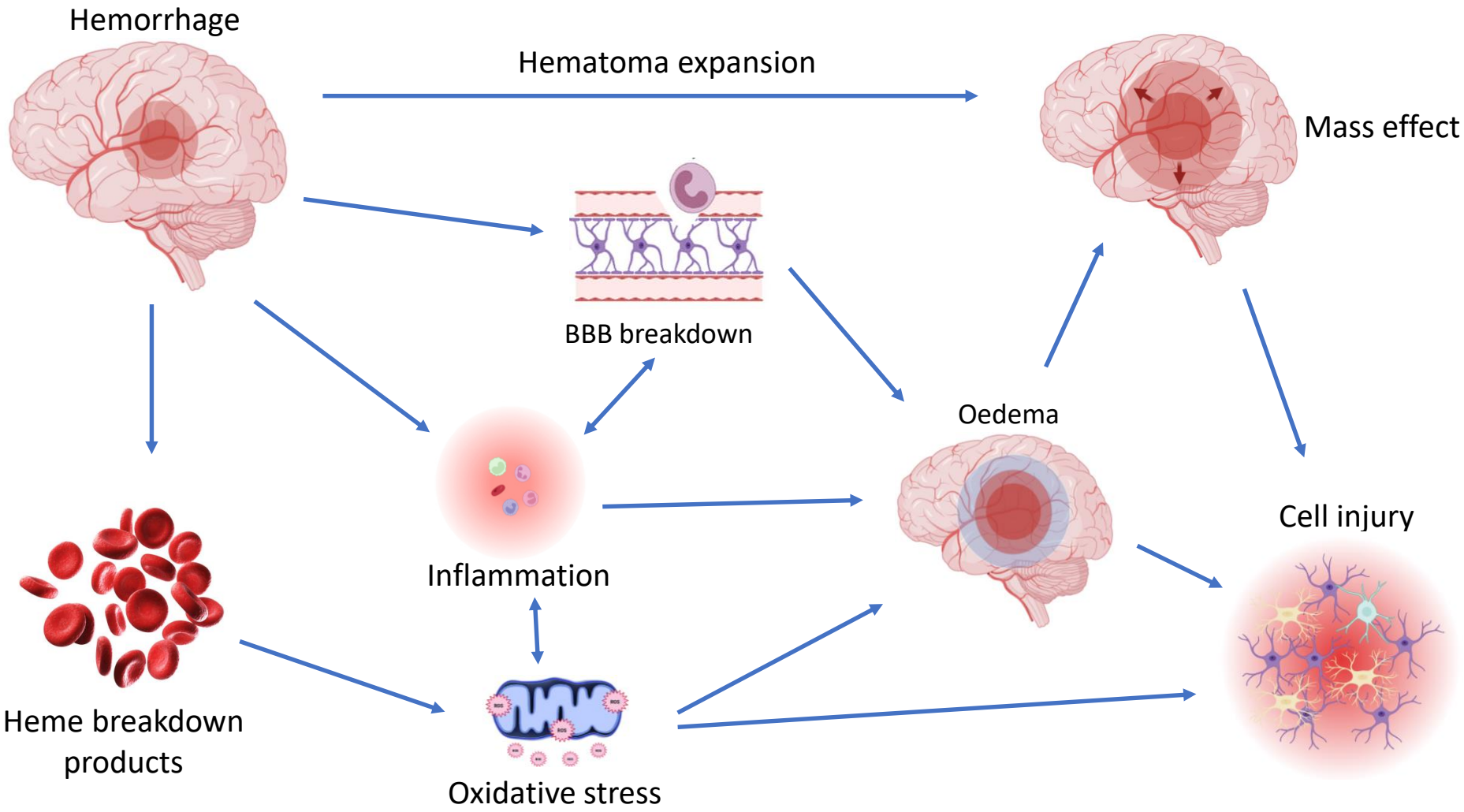
Amyloid angiopathy

Hght blood pressure

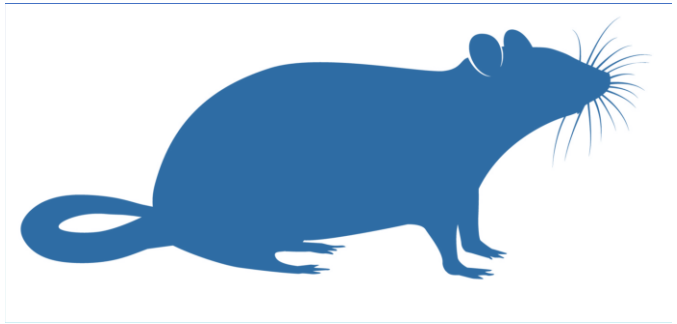
Liver disease

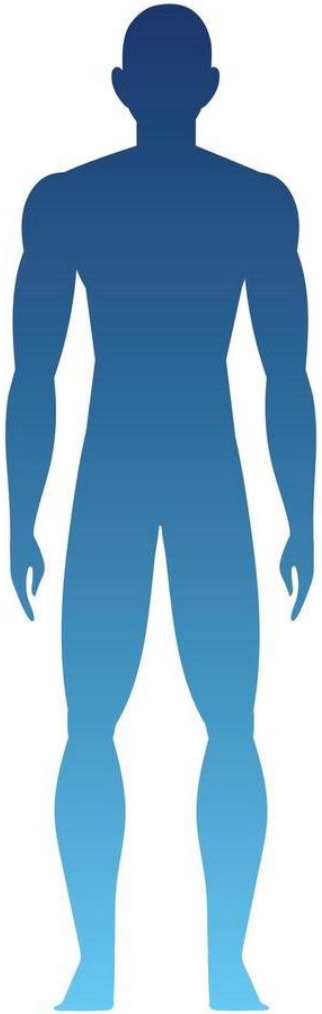


Consequences of brain hemorrhages



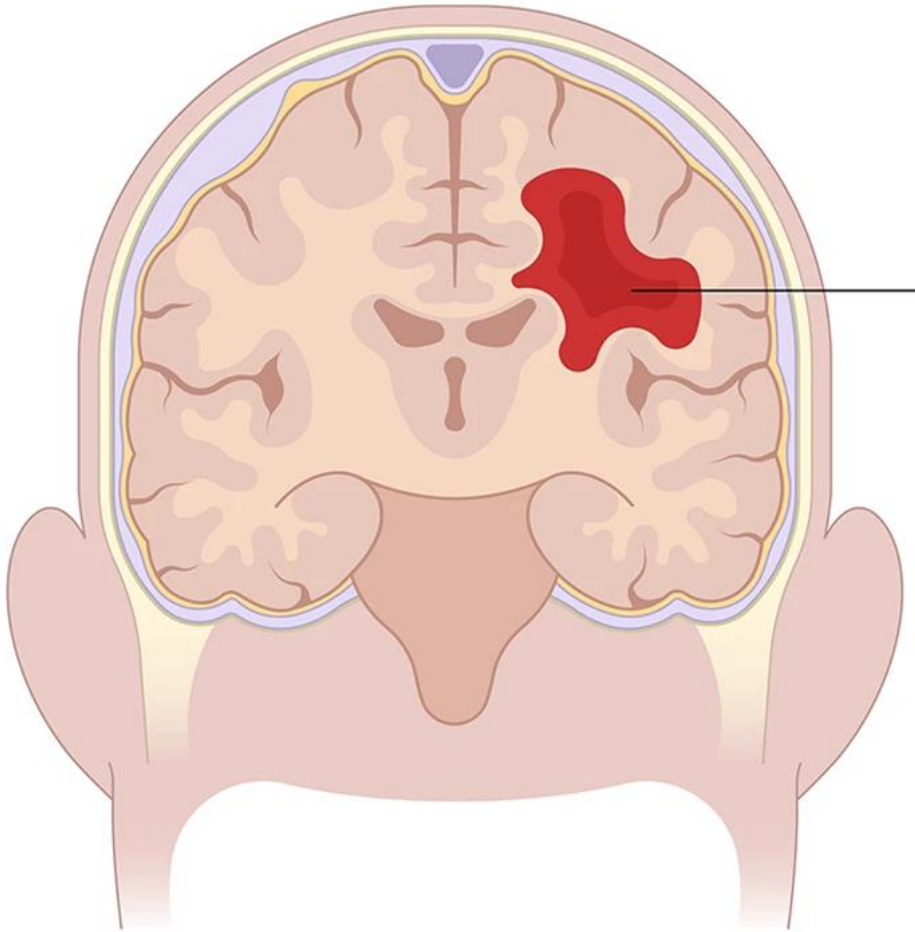
Translational chalenges



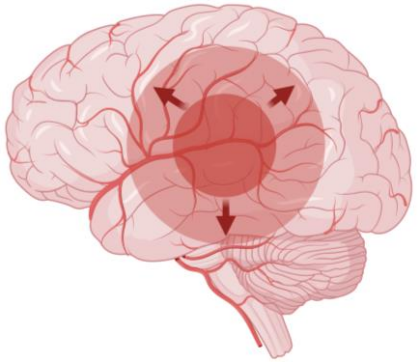


Intracerebral hemorrhages

Modeling intracerebral hemorrhages



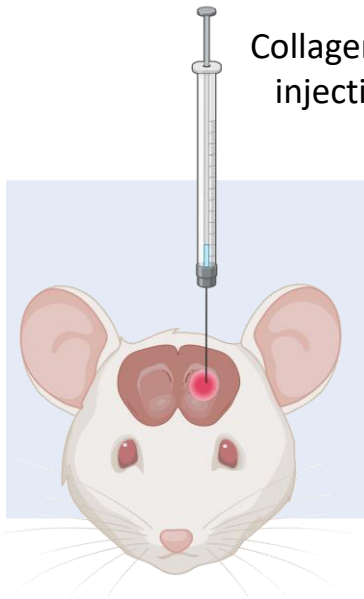
Mass effect



Heme breakdown products

Intracerebral hemorrhages

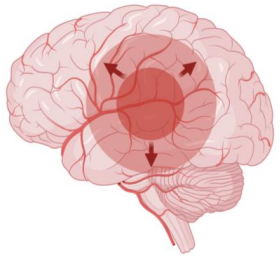
❖ Intracerebral hemorrhage : injection of collagenase



Collagenase injection

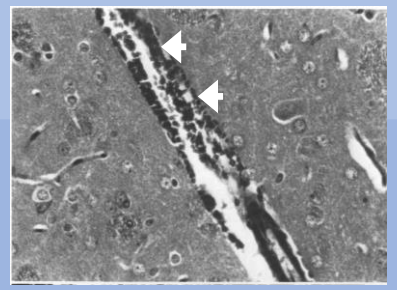
Rosenberg et al. 1990, Stroke

Vessel rupture

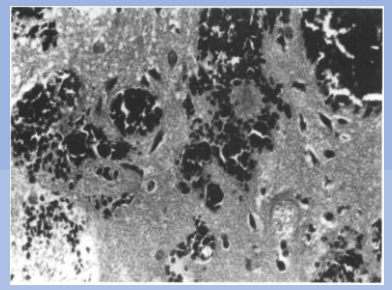


Bleeding

+10 min



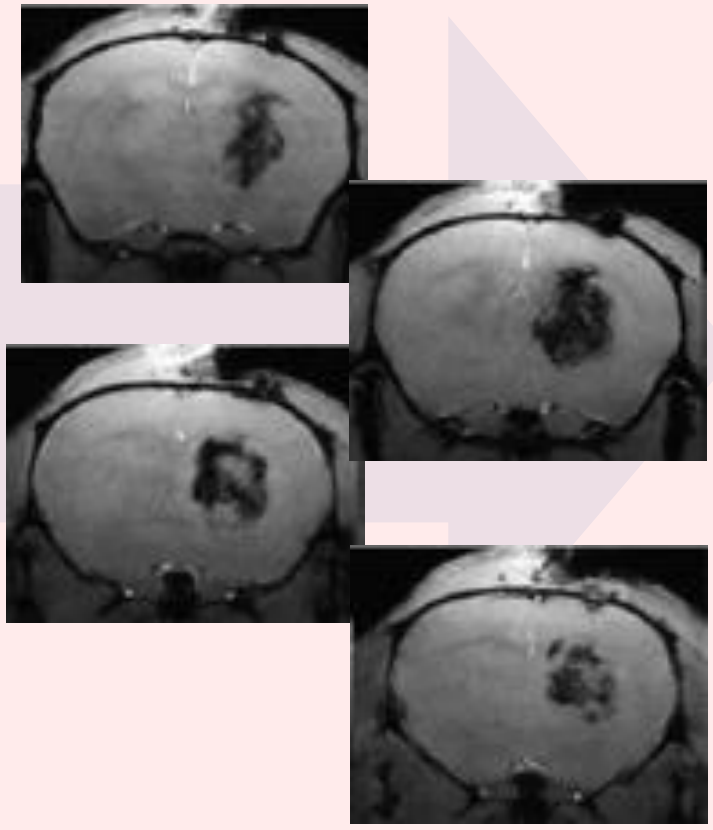
+45 min



Rosenberg et al. 1990, Stroke

Hematoma

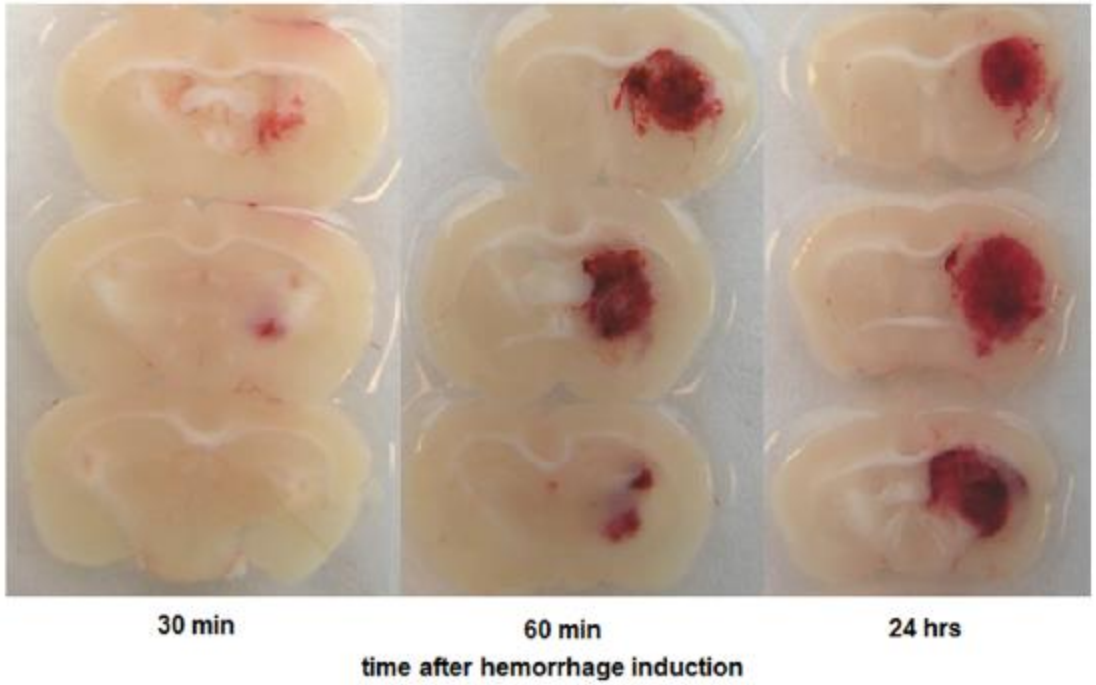
MRI – T2*WI +24h

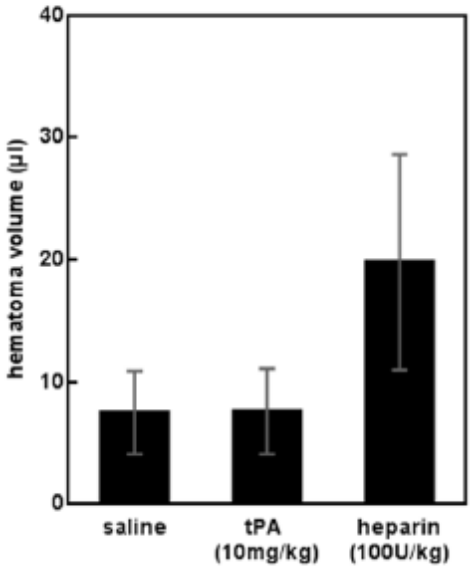


Intracerebral hemorrhages

Usefull for rebleeding studies

Effect of tPA on intracerebral hemorrhage in mice

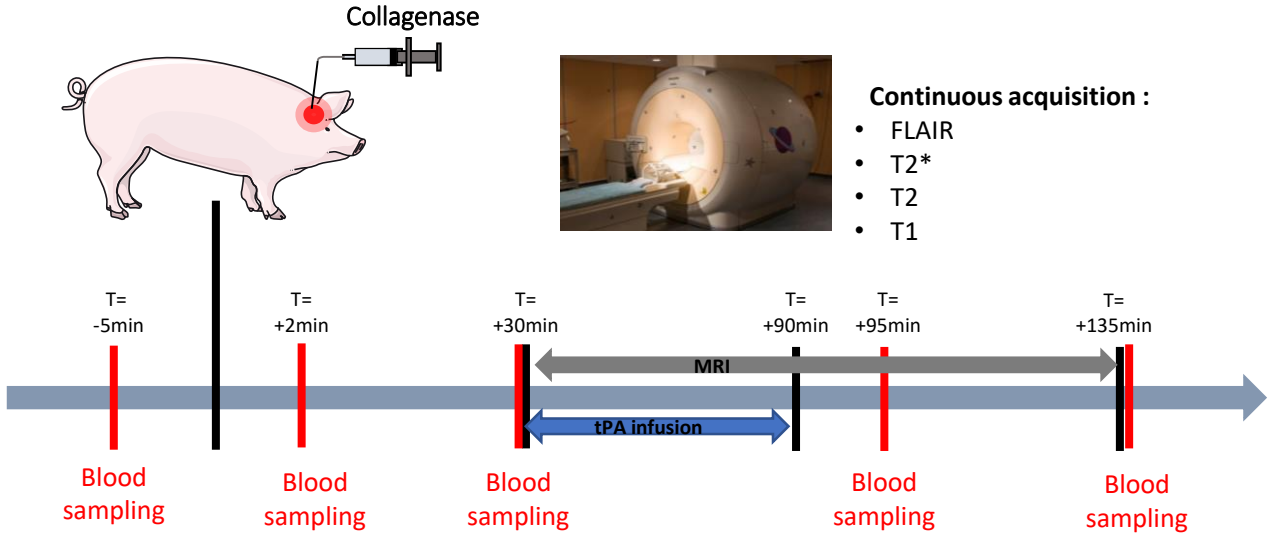


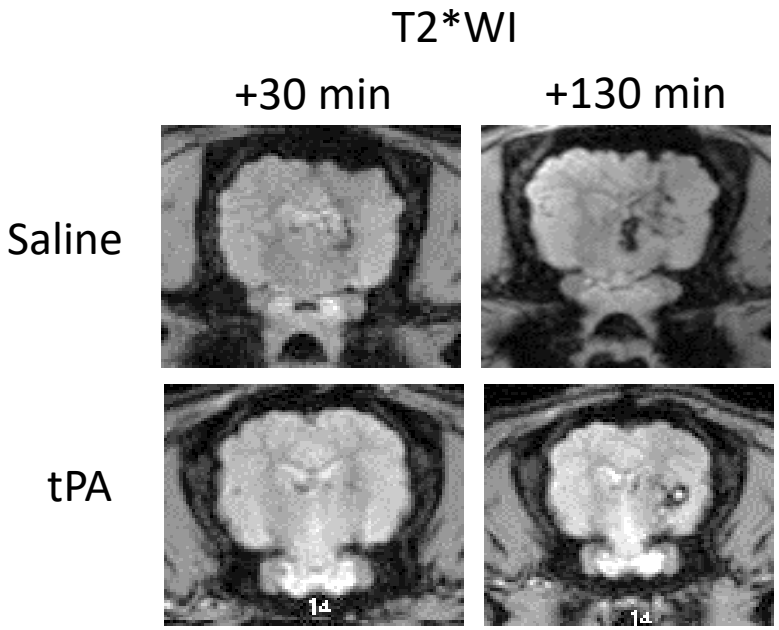


Foerch et al. Plosone, 2013

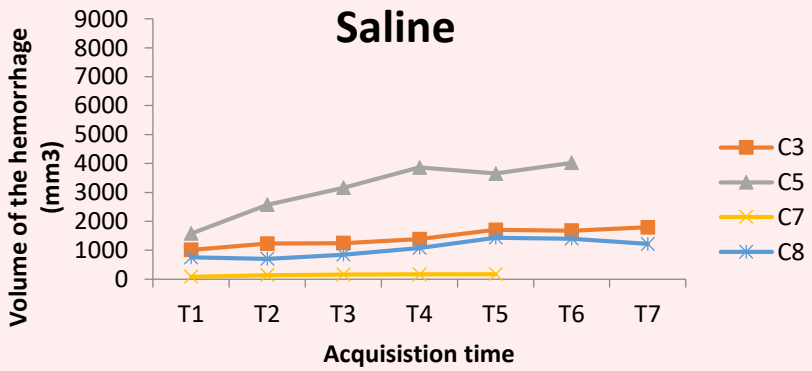
Intracerebral hemorrhages

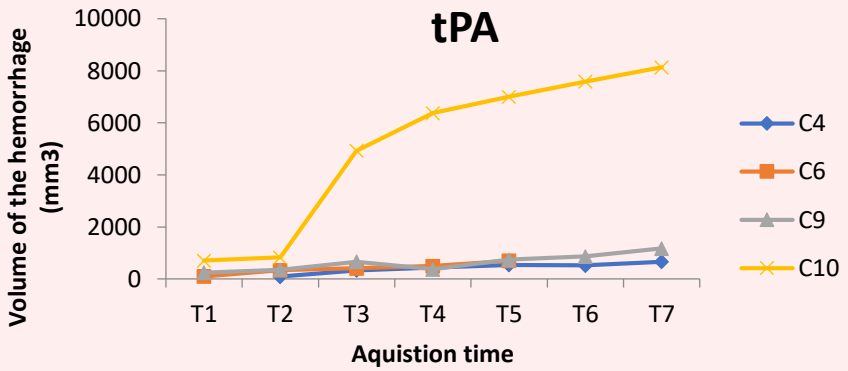
Effect of tPA on intracerebral hemorrhage in swine





Hematoma volume

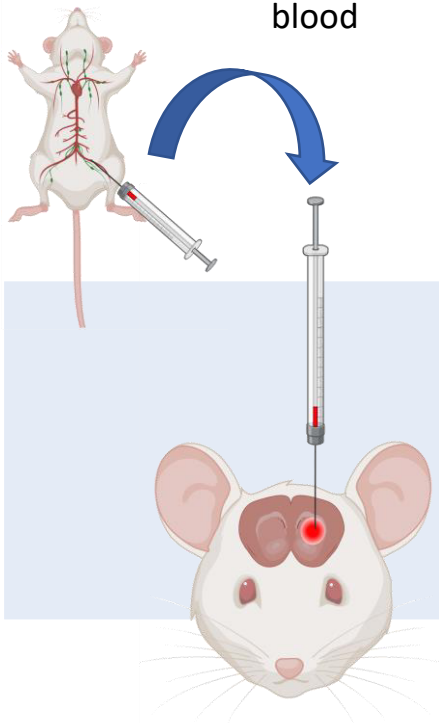




Intracerebral hemorrhages

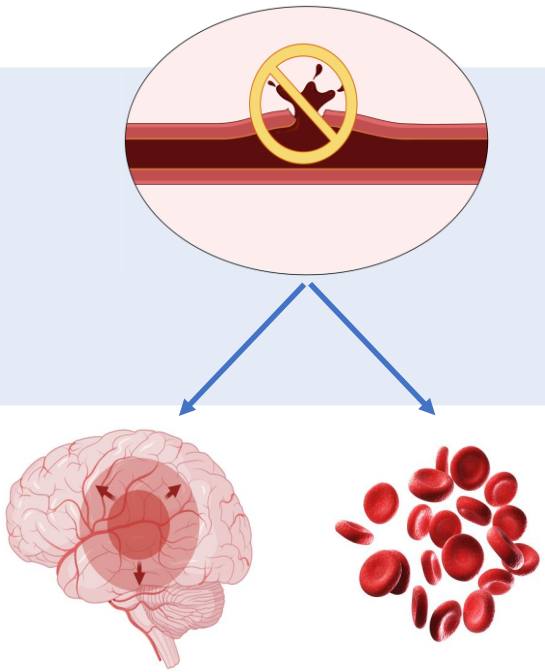
❖ Intracerebral hemorrhage : injection of blood

Autologous/heterologous blood

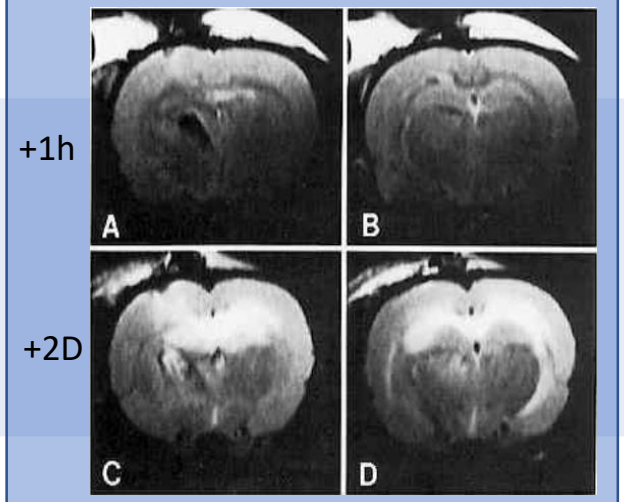


Yang G-Y et al. 1994, J Neurosurg

No vessel rupture



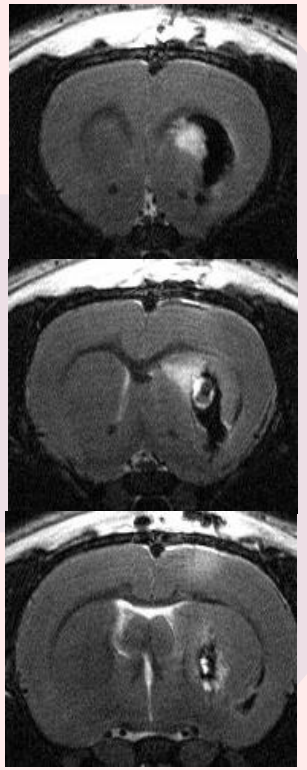
Hematoma



Yang G-Y et al. 1994, J Neurosurg

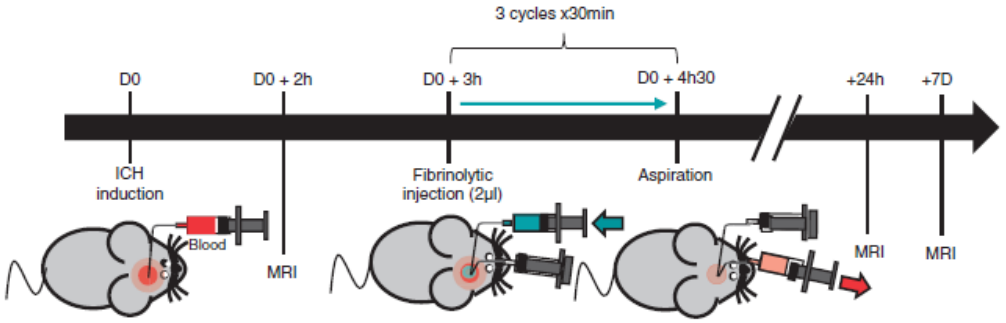
Hematoma

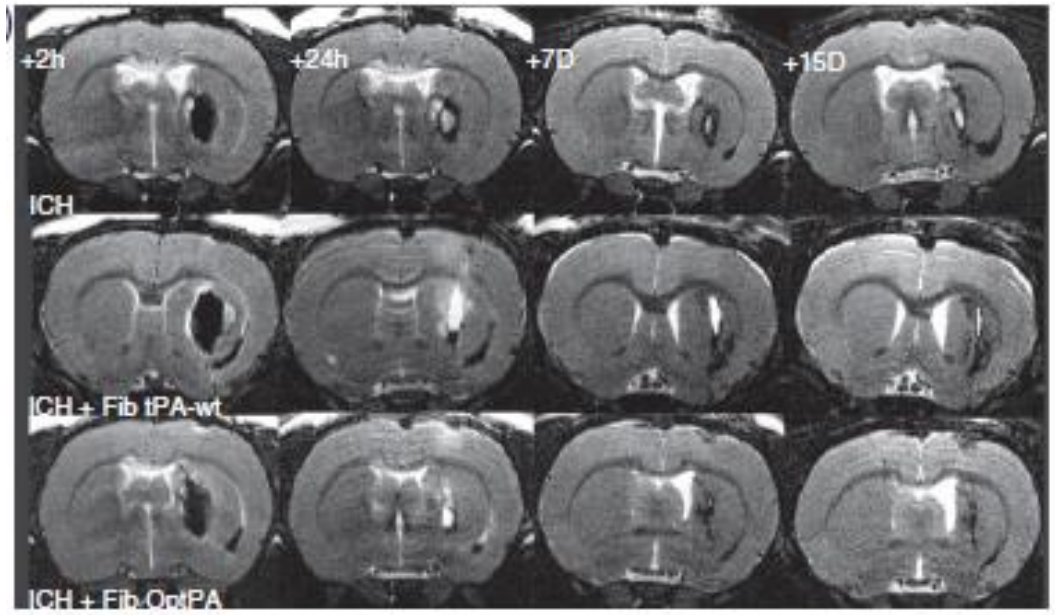
MRI – T2WI +24h

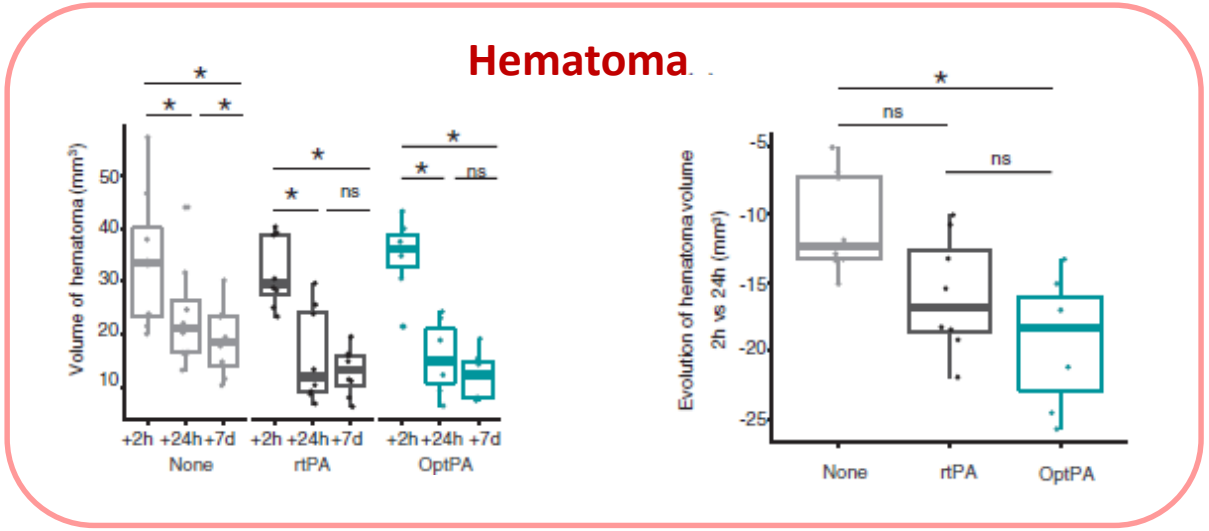


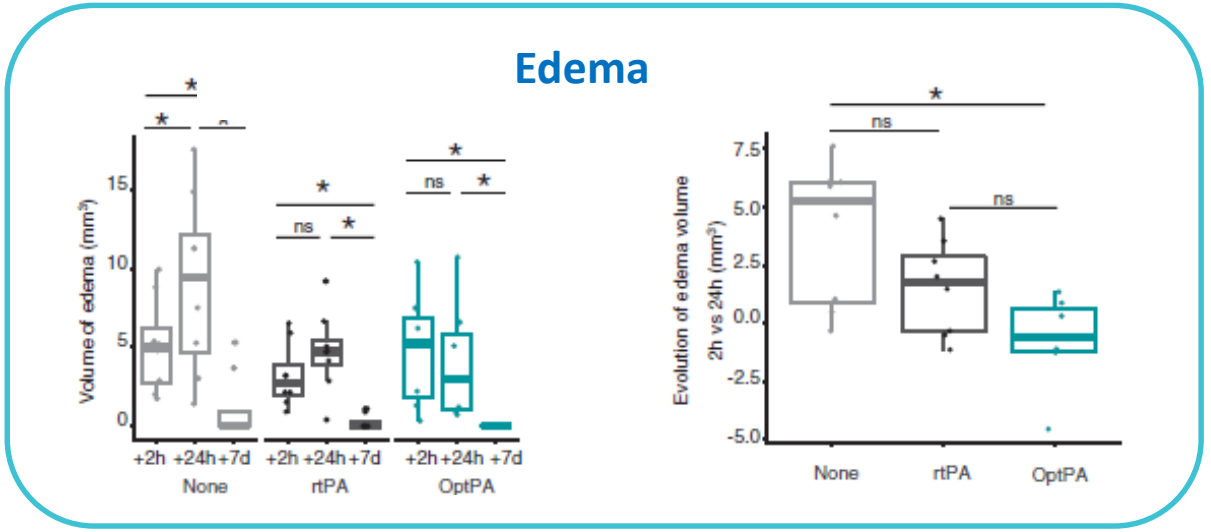
Intracerebral hemorrhages

Optimized tPA: A non-neurotoxic fibrinolytic agent for the drainage of intracerebral hemorrhages





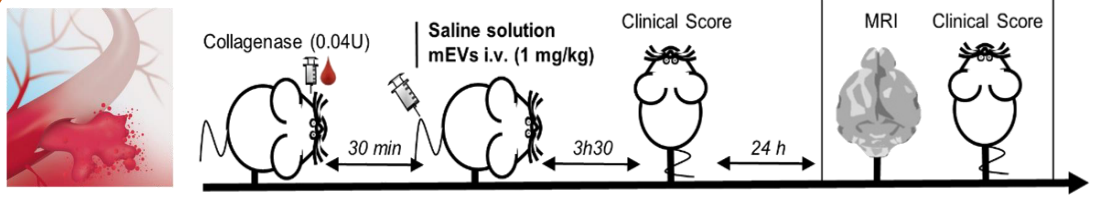


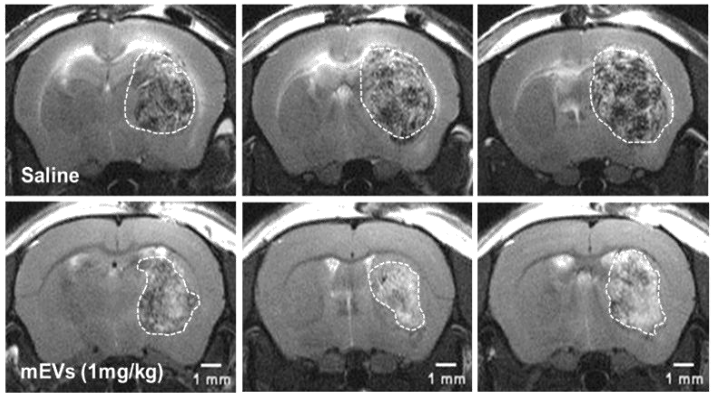


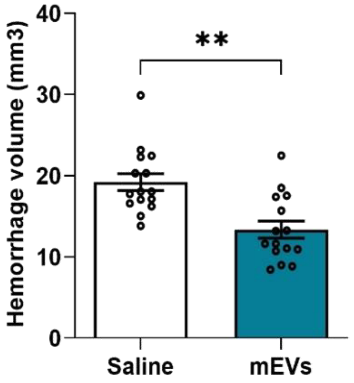
Goulay et al. 2018 JCBFM

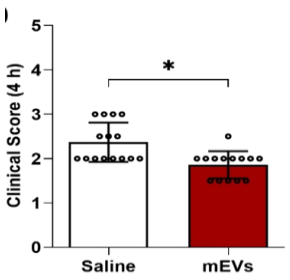
Intracerebral hemorrhages

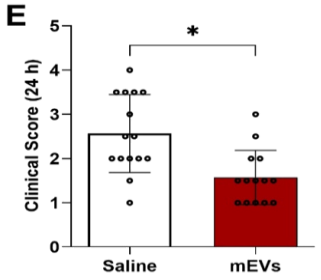
Effect of procoagulant monocytic microparticles on ICH stroke model

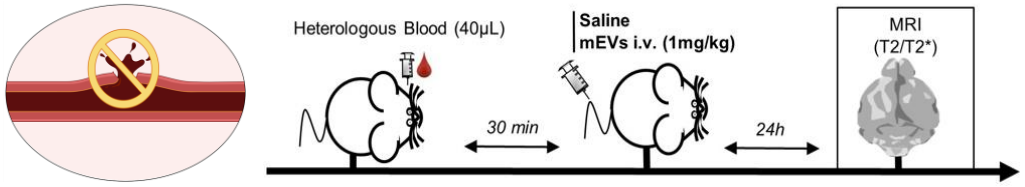


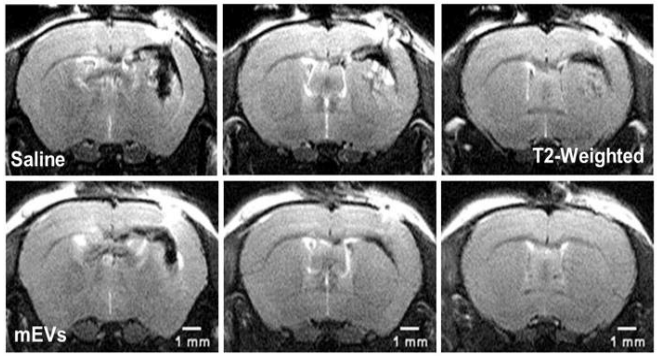


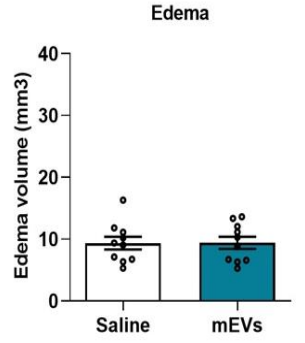


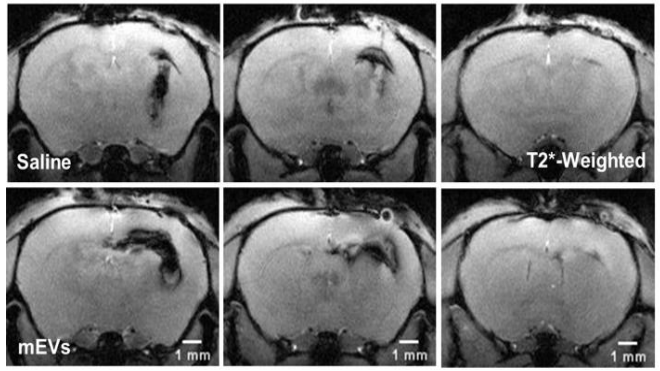


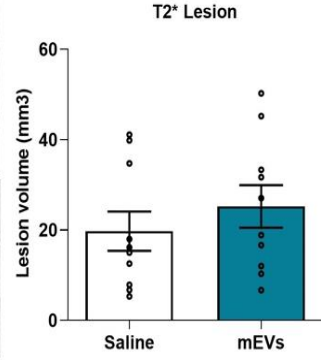








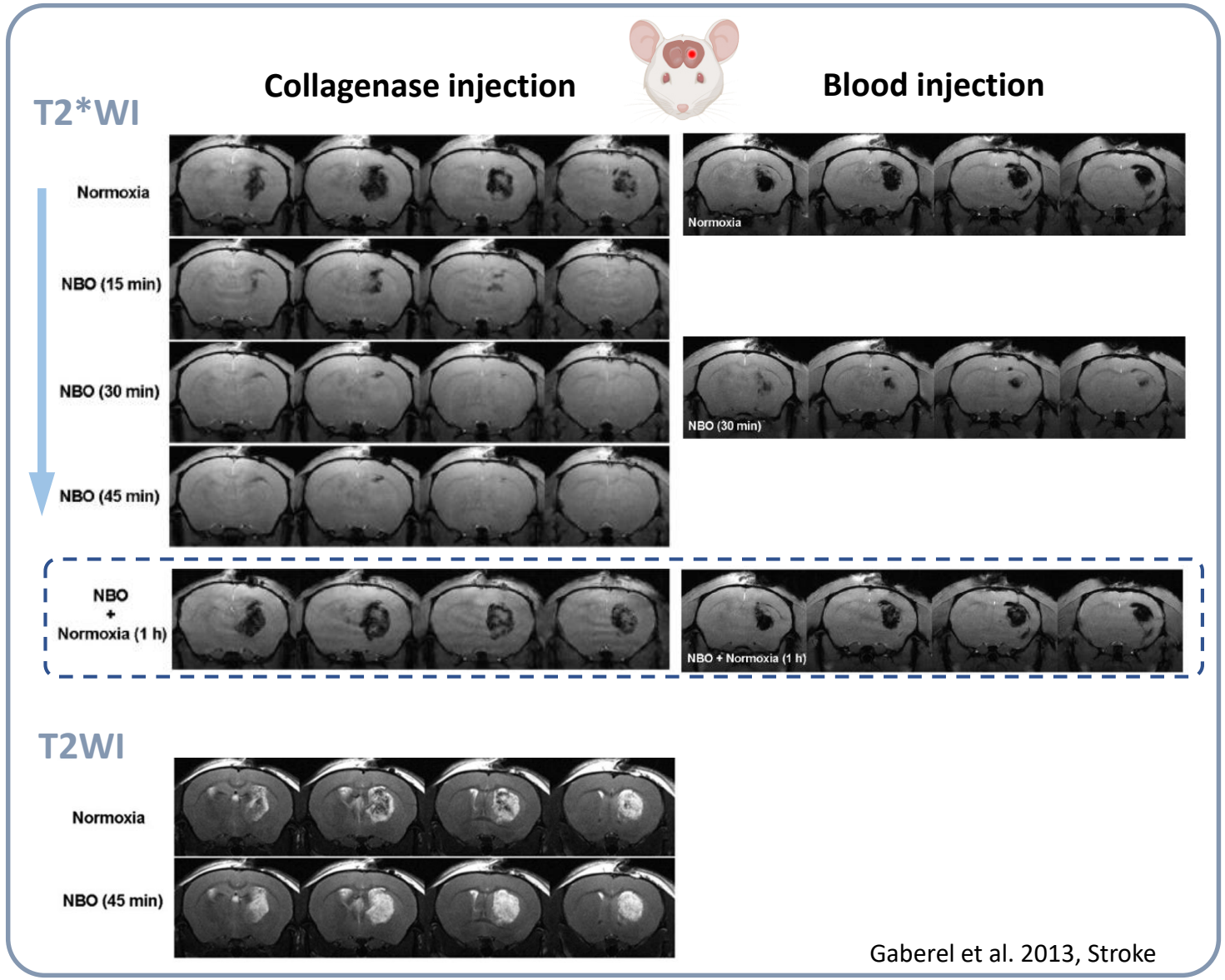




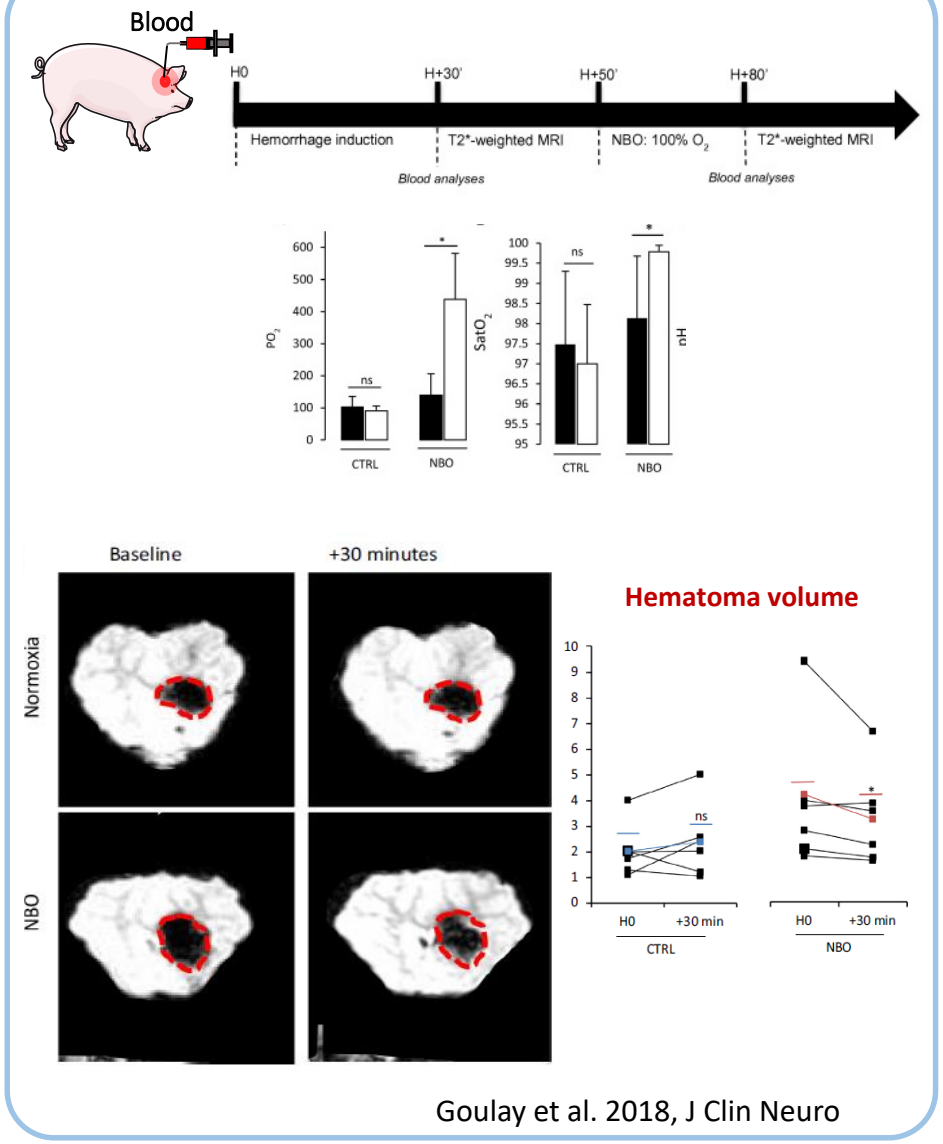
Potzeha F, unpublished results

Intracerebral hemorrhages

Impact of normobaric oxygen therapy on T2* MRI



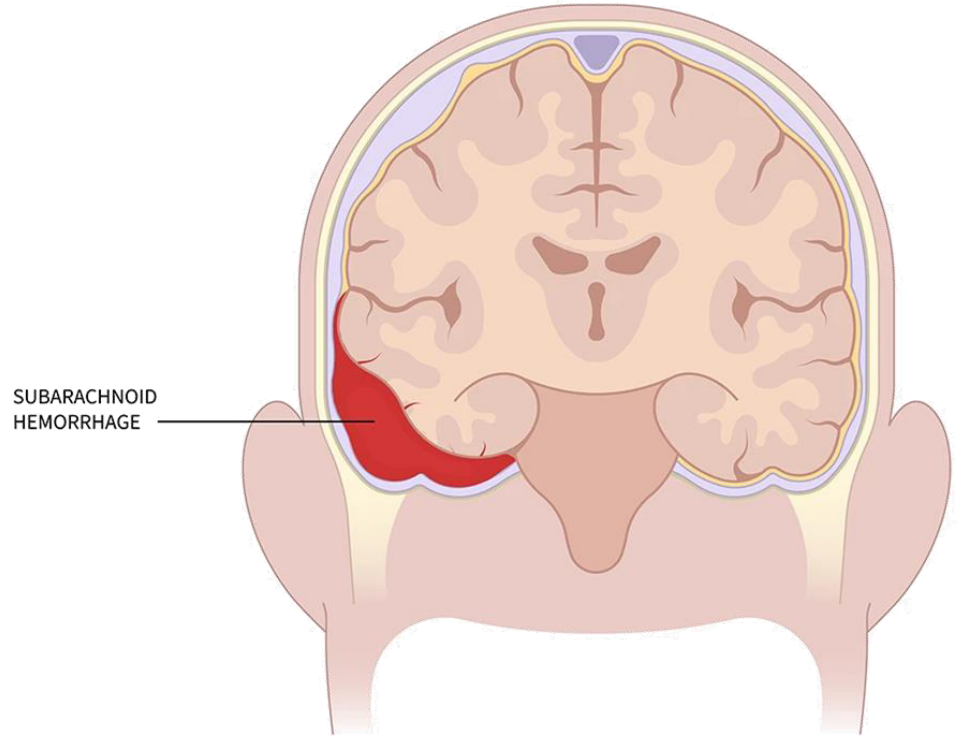
Gaberel et al. 2013, Stroke



Goulay et al. 2018, J Clin Neuro

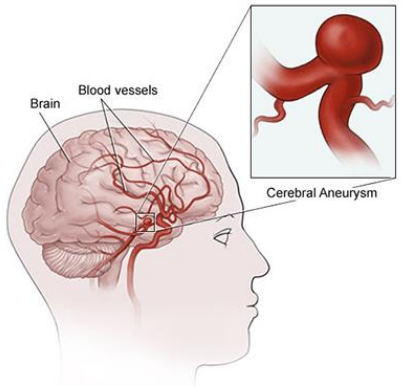
Subarachnoid hemorrhages

Modeling subarachnoid hemorrhages



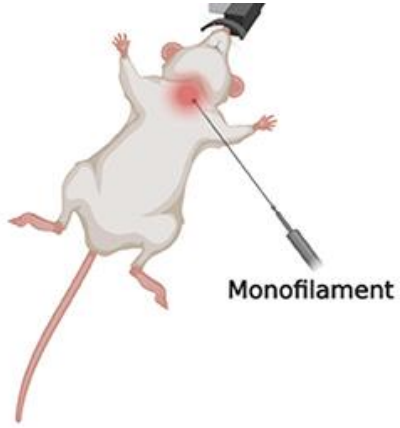
→ **Subarachnoid hemorrhage**

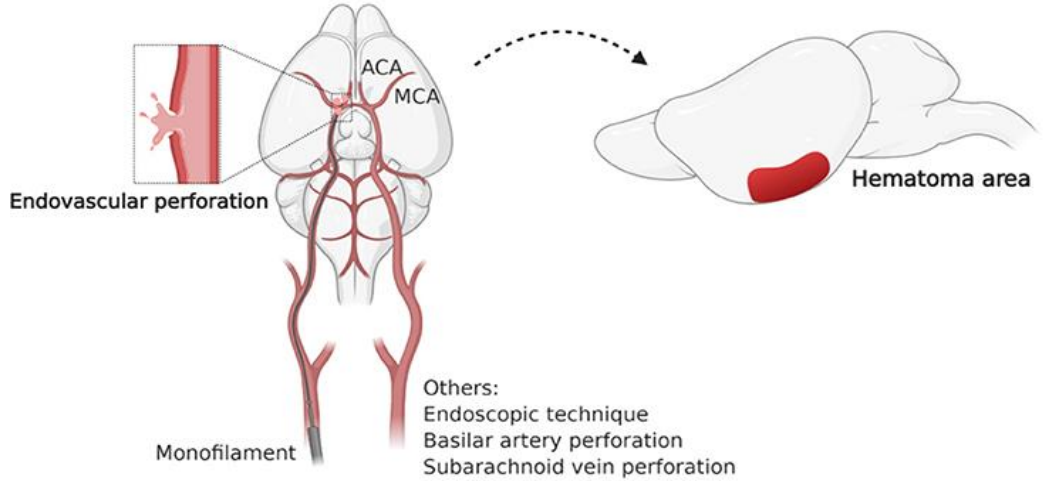
→ **Intracerebral aneurysm**

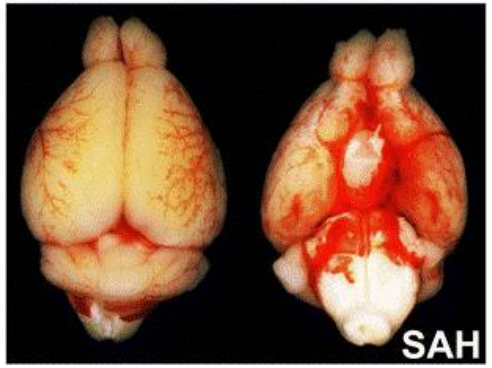


Subarachnoid hemorrhages

❖ SAH model : endovascular perforation

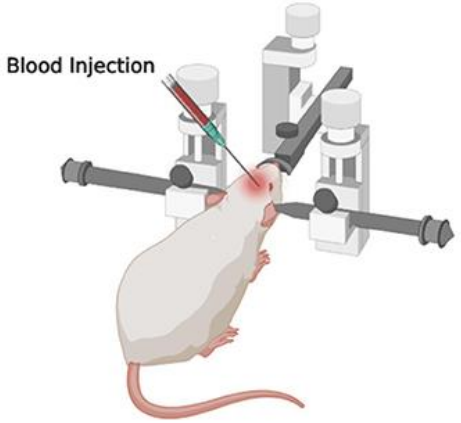


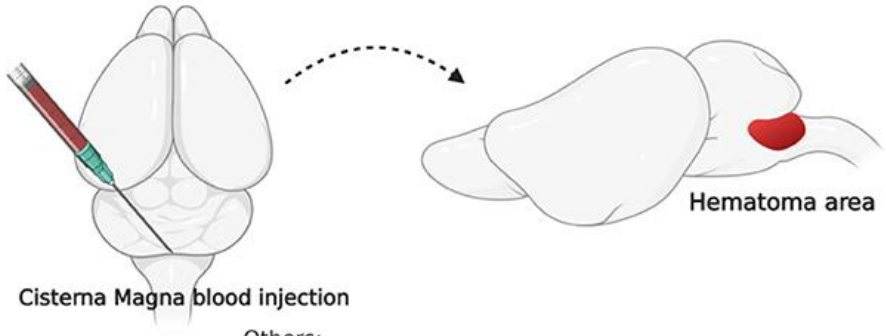




Goursaud et al. 2021

❖ SAH model : cisterna magna blood injection



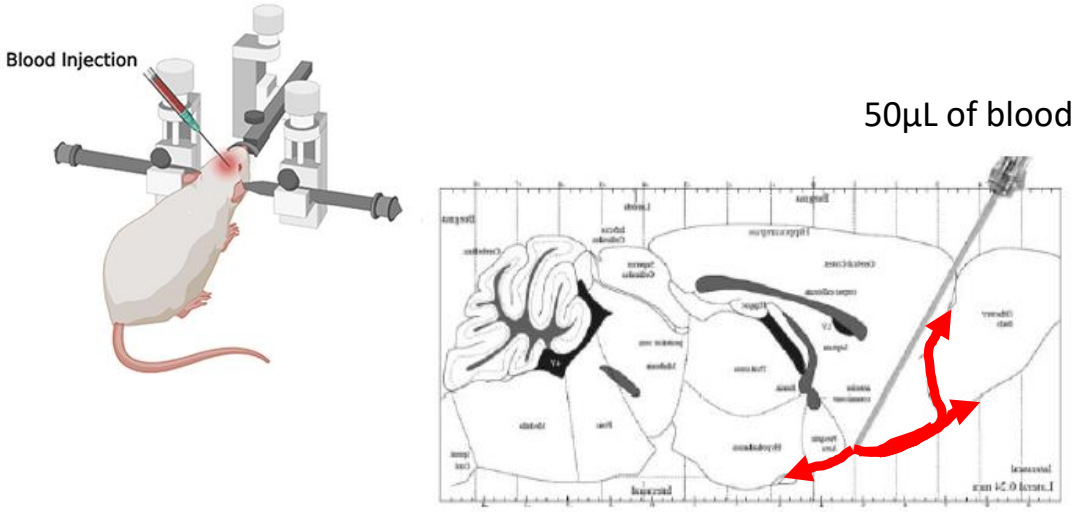


Goursaud et al. 2021

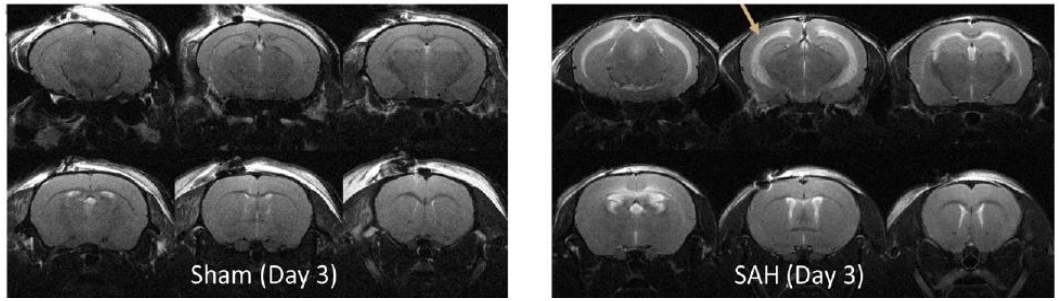
Subarachnoid hemorrhages

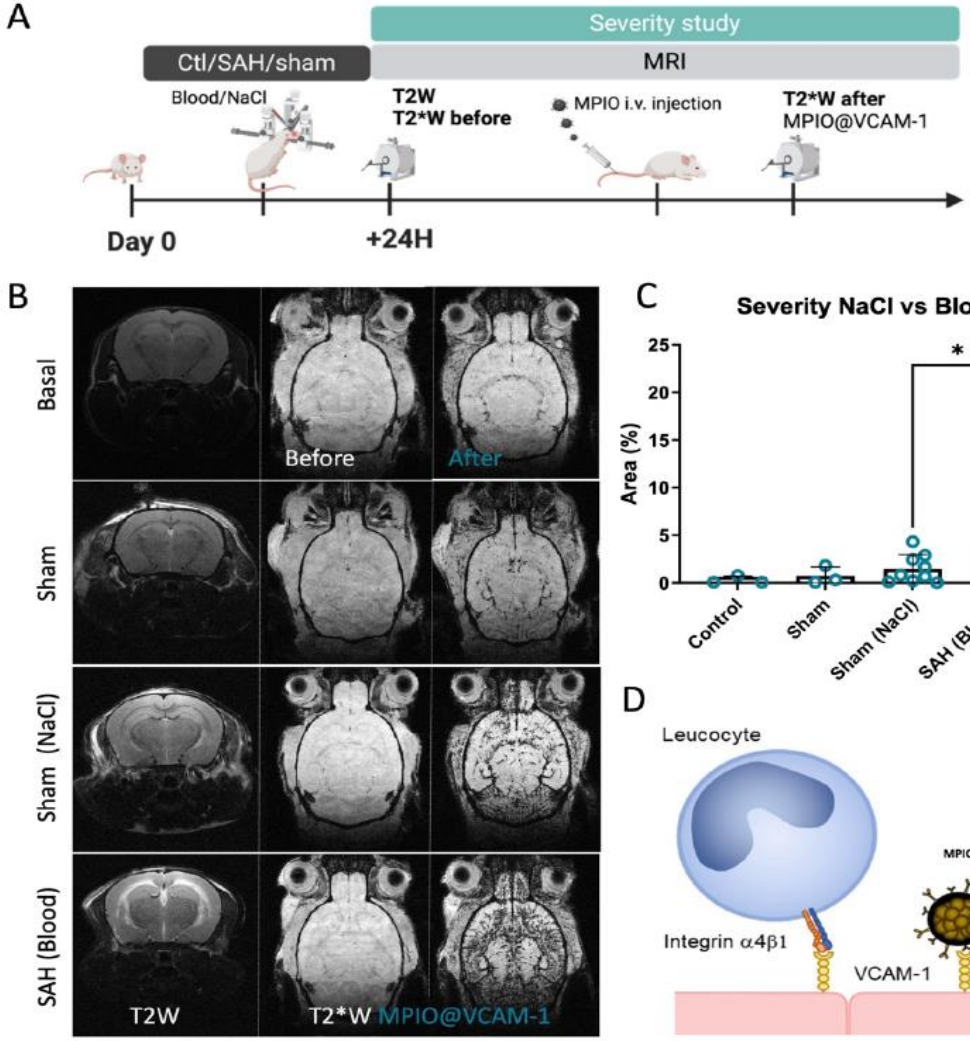
Molecular imaging of early brain injury in subarachnoid hemorrhage

Prechiasmatic injection of blood to induce SAH



Hydrocephalus induced after SAH



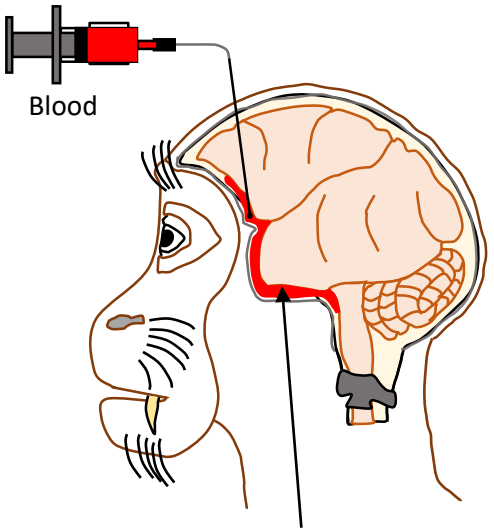


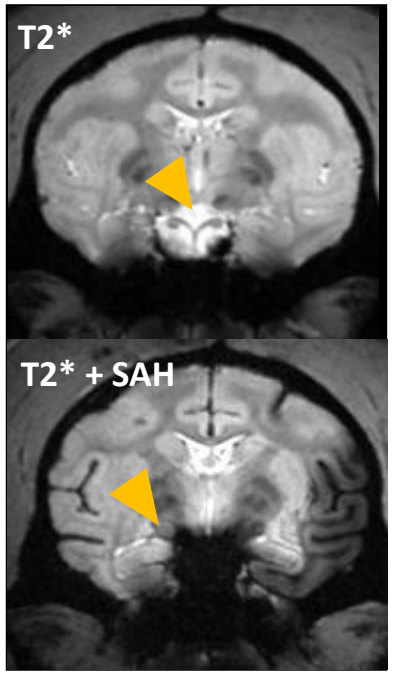
Goursaud S, unpublished data

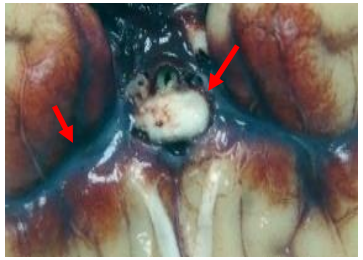
Subarachnoid hemorrhages

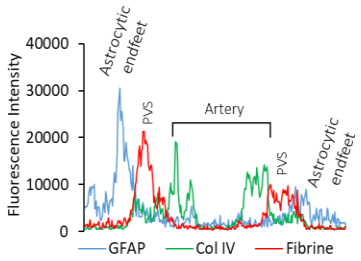
SAH impairs cerebrospinal fluid circulation in NHP

SAH induction

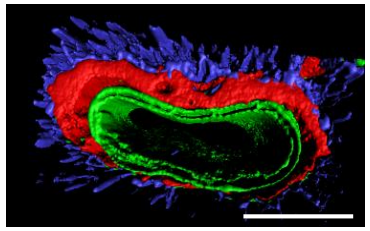






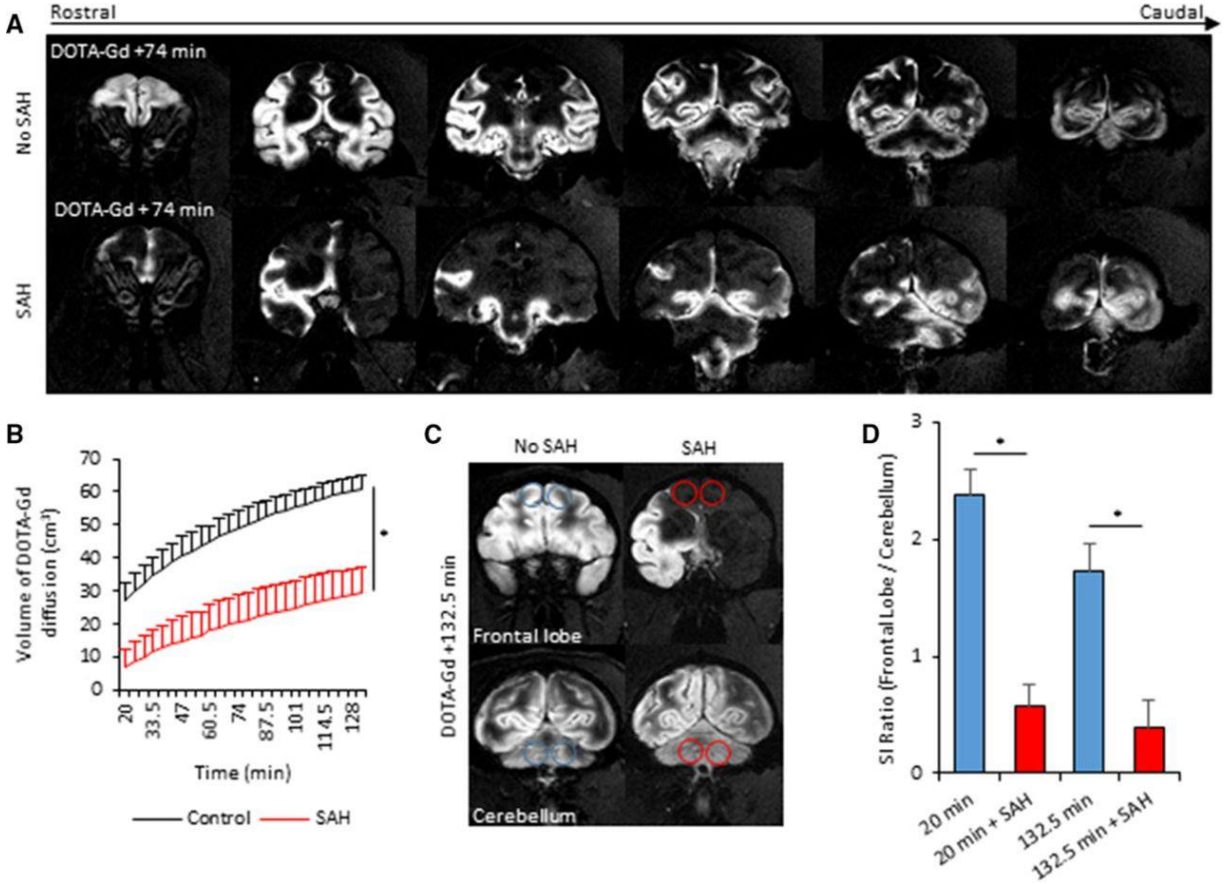


GFAP Col IV Fibrin



Scale bar = 20µm

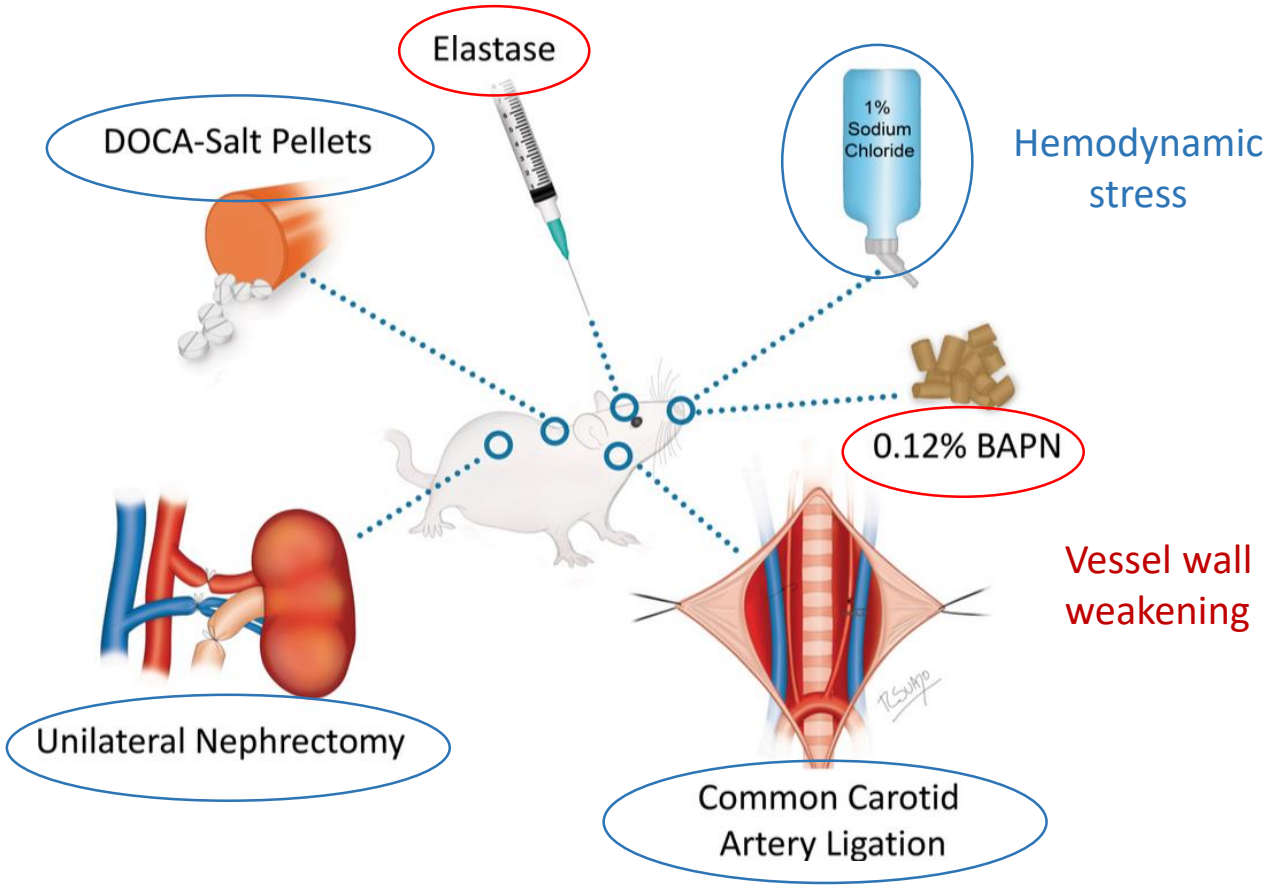
Brain parenchymal cerebrospinal fluid circulation



Goulay et al. 2017, Stroke

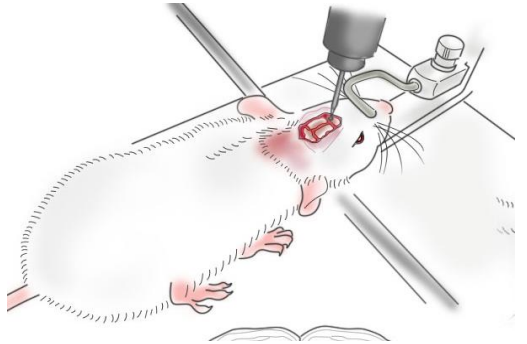
Subarachnoid hemorrhages

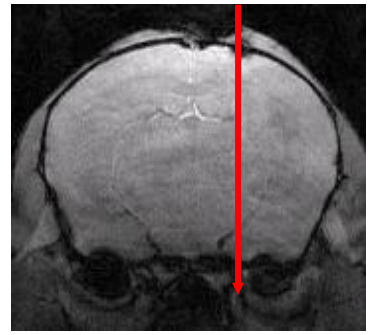
❖ SAH model : brain aneurysm



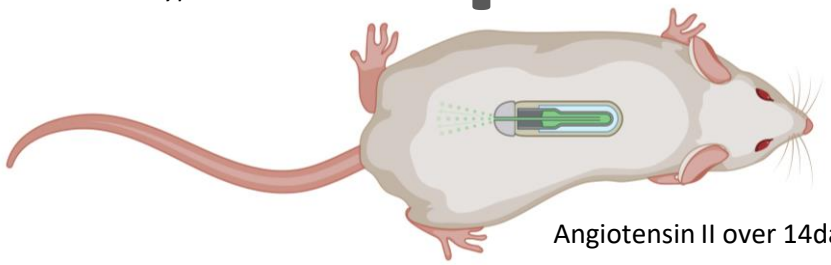
Thompson et al. 2019, Neurosurg. Focus

Elastase injection in the basal cisterna

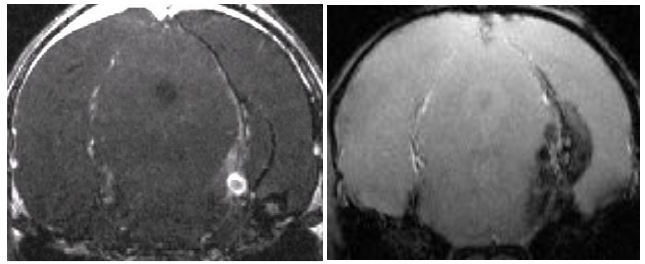




Nuki et al. 2009, Hypertension



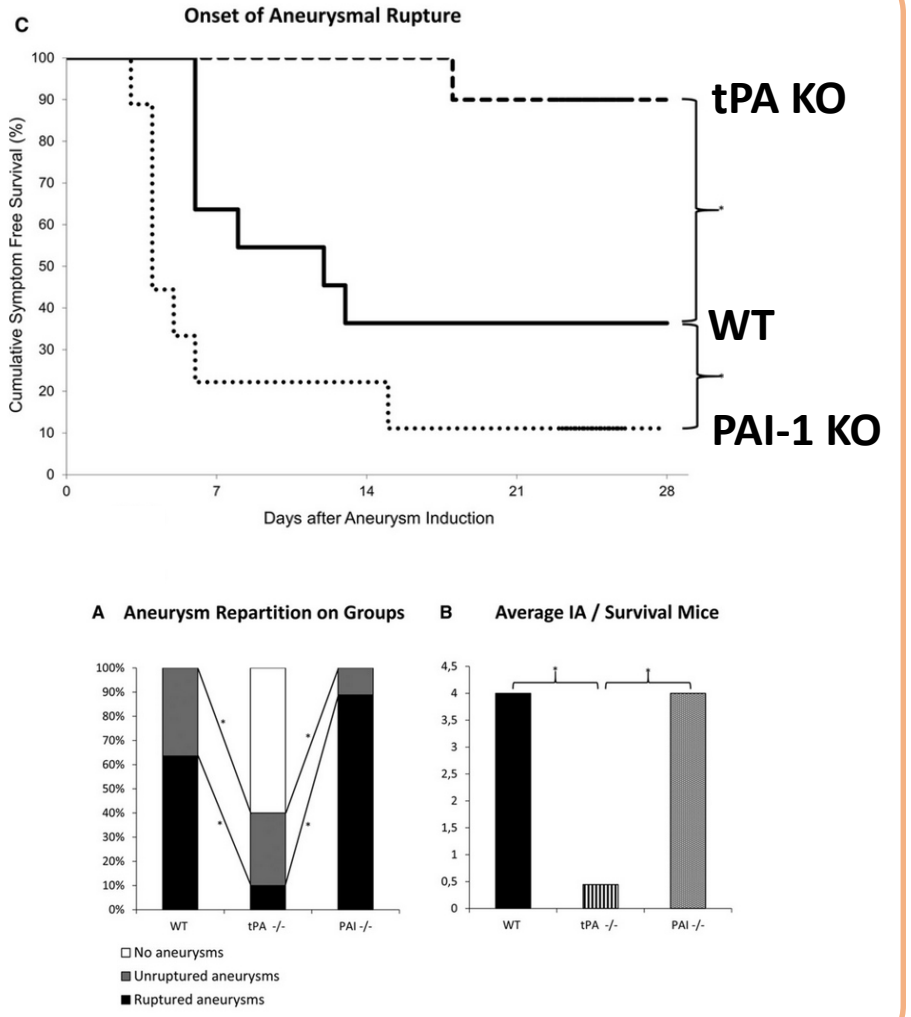
Angiotensin II over 14days

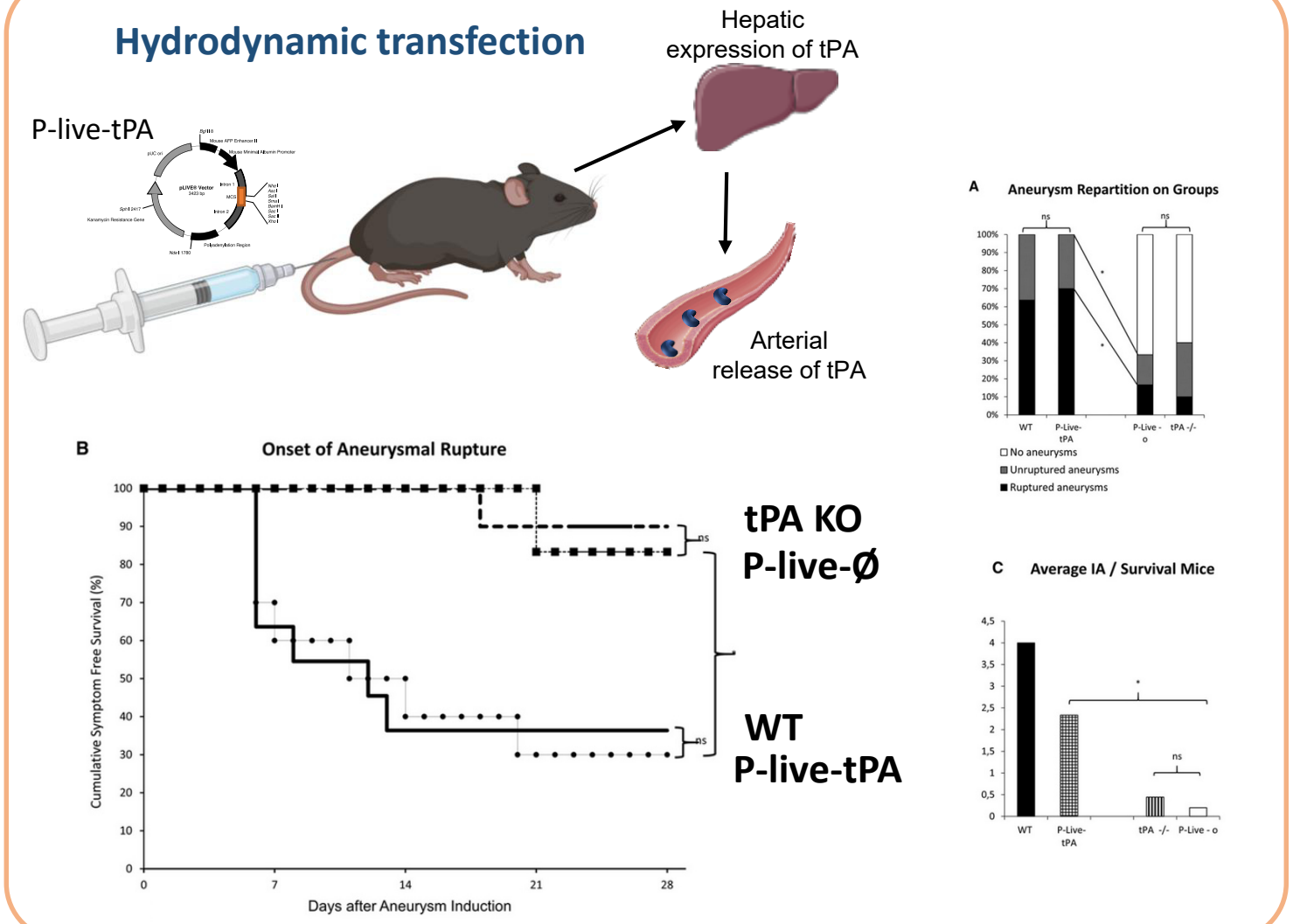


Labeyrie et al. 2017, Stroke

Subarachnoid hemorrhages

Vascular tPA promotes intracranial aneurysm formation

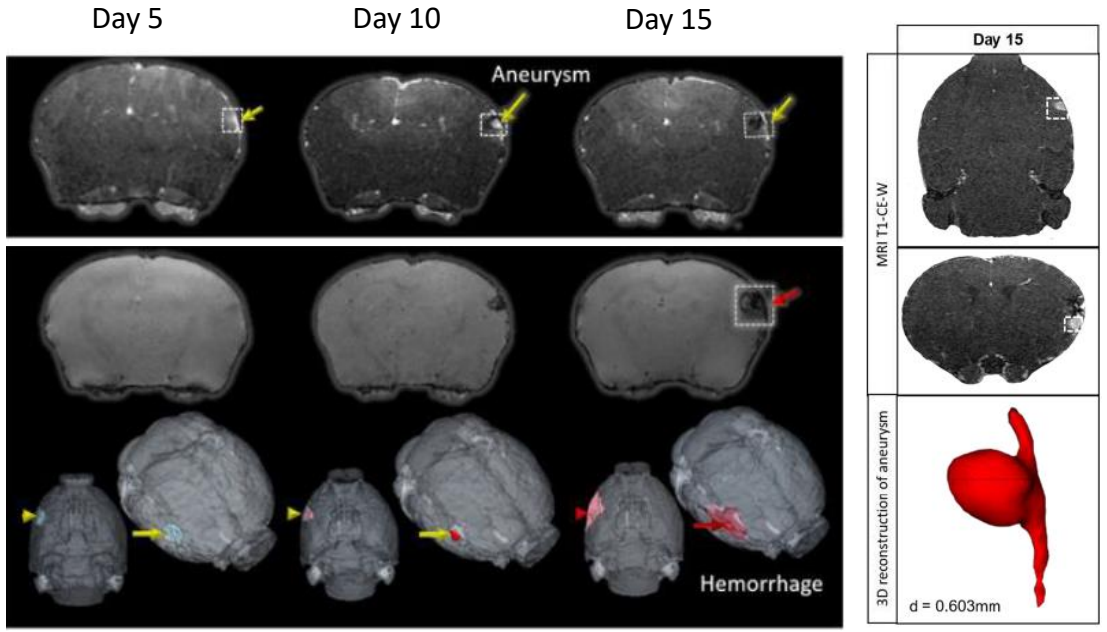


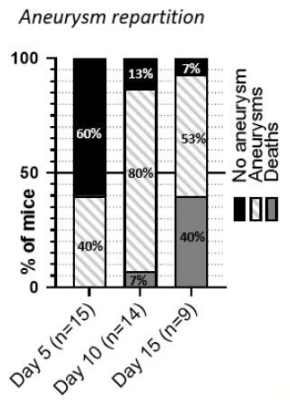


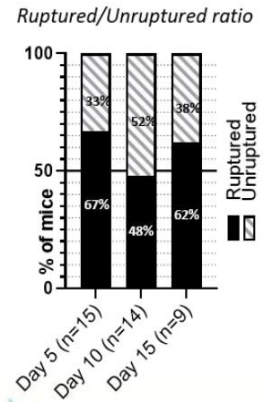
Labeyrie et al. 2017, Stroke

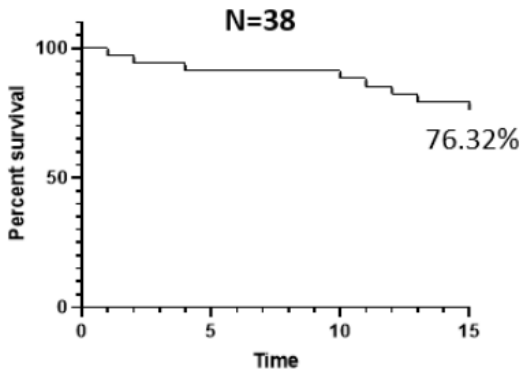
Subarachnoid hemorrhages

A new mouse model of IAs at the MCA to study inflammation

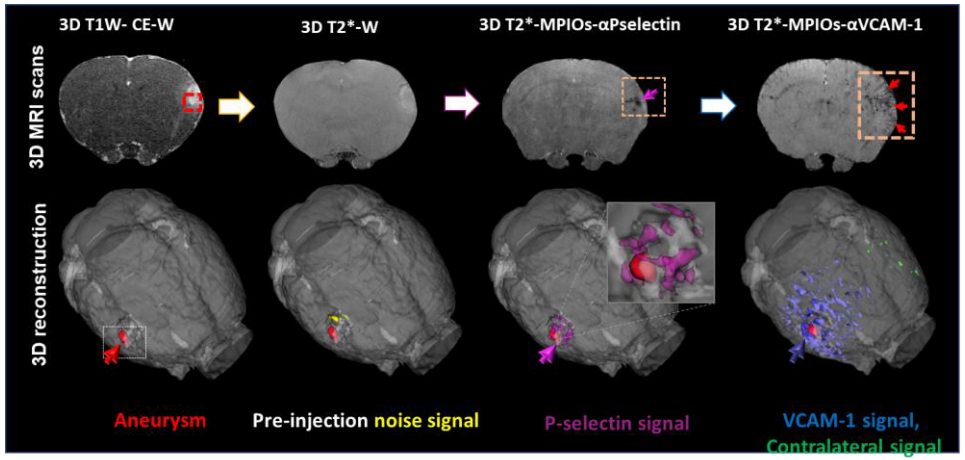


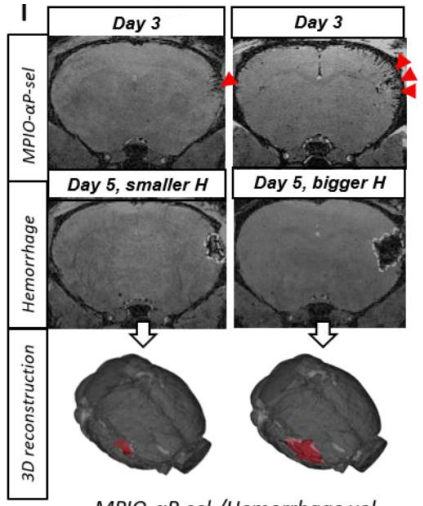






MRI molecular imaging as a predictive marker



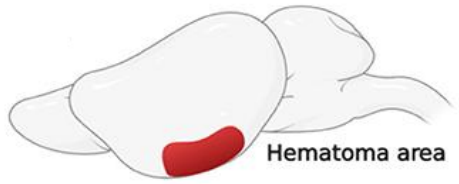


MPIO-αP-sel./Hemorrhage vol. correlation:

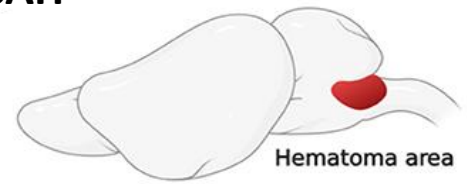
Glavan et al. 2024, Acta Neuropathol Com

Conclusion

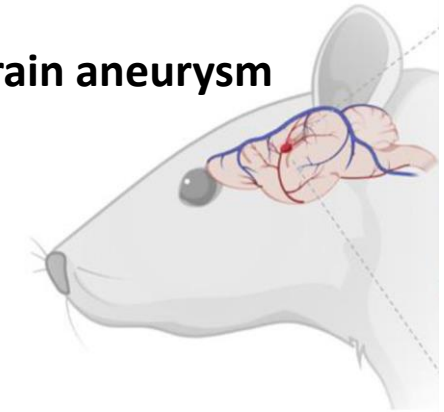
Subarachnoid hemorrhages

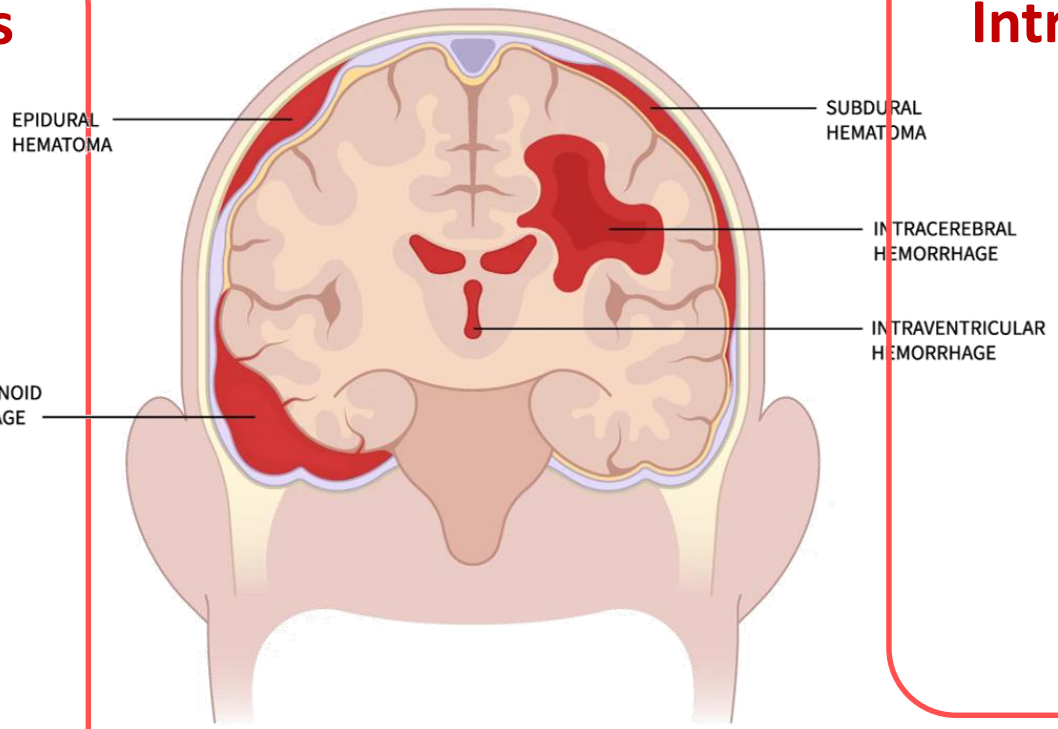


SAH

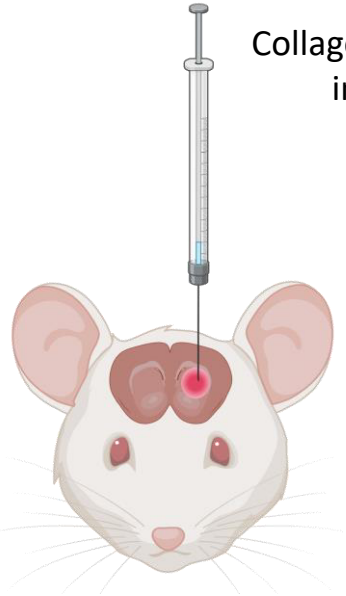


Brain aneurysm





Intracerebral hemorrhages



Collagenase/Blood injection

- **Consider the moratlity rate**
- **Some models were adapted in different animal species**
- **Customize the model to adress the scientific question**

PhIND

PHYSIOPATHOLOGY & IMAGING OF NEUROLOGICAL DISORDERS

UMR-S U1237 "Physiopathology and Imaging of Neurological Disorders"

Experimental Stroke Research/Ressources/Recovery Platform

Thank you

INSERM U1237, ESRP, Bd Henri Becquerel, 14000 CAEN, France