Using the minimally invasive subcortical parafascicular transsulcal access for clot evacuation (MiSPACE) concept in a swine model for eloquent white matter tracts monitoring and regeneration.

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Disclosure

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Introduction

Intracerebral hemorrhage is a major cause of morbidity and mortality. Currently, no effective intervention exists for ICH. Importantly, most pre-clinical animal models use rodents, which have very little myelin and poor brain homology to humans. We propose a novel way of modeling ICH which focuses on white matter pathology by utilizing Gottingen mini-pigs, aged 6-7 months.
Methods

On the morning of MRI planning, fiducial markers are placed on the pig’s head. Conventional T1 and DTI are obtained according to a Synaptive protocol (Synaptive Medical, Toronto, ON) to establish tractography that will allow for intra-operative neuro-navigation. Pre-operatively, a target and entry point is planned on the Synaptive planning station based on the conventional MRI and DTI. The internal capsule is targeted on the right. Autologous blood injected into pig skull based on this predetermined trajectory. Additionally, AAV-pCMV-GFP (serotype 9) virus was injected by micro pipette into motor strip for corticospinal tract labeling. Immediate post-operative conventional MRI T1 was obtained to confirm hematoma creation. The pig was then perfused and the brain harvested for immunohistochemistry.
Figure 1. The injection is placed with frameless stereotactic guidance. Tractography allows for placement of the hematoma in close proximity to the corticospinal tract.
Results

Our preliminary data demonstrates that the injection of blood using preoperative MRI and image-guided placement within the internal capsule, creates a graded injury of white matter fibers that includes axonal loss, demyelination with axon sparing and micro-gliosis. CST were successfully labeled 1 week post injection. There was significant gliosis within the hematoma but also spreading to the internal capsule. There was deflection of the internal capsule, creating axonal damage and gliosis. There was decreased myelin basic protein localization in internal capsule fibers compared to the contralateral control brain.
Figure 2. Post operative T2 weighted MRI demonstrates placement of hematoma adjacent to the internal capsule
Figure 3. Pathology at 10x demonstrates descending corticospinal tract with adjacent hematoma.
Conclusions

We describe a novel way of modeling ICH which focuses on white matter pathology. This model will assist in understanding ICH pathophysiology and may become a testing ground for future therapeutics.
Summary Points

- Intracerebral hemorrhage is a major source of morbidity and mortality
- Previous animal models of ICH have been in rodents which have little white matter and limited brain homology to humans
- We describe a method to model ICH which focuses on white matter tract damage and may be used in the future to test therapeutics