

Magnetic Resonance Imaging and Functional Analysis of a Novel Middle Cerebral Artery Ischemic Stroke Pig Model

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Introduction: Stroke is the leading cause of long-term disability among adults in the United States. Despite hundreds of drugs going to clinical trials, only one has been approved by the Food and Drug Administration. One likely major cause of failed translation is limited clinical testing in large animal models more similar to humans. Our objective was to develop a pig middle cerebral artery occlusion (MCAO) ischemic stroke model to address this need. Pigs are more similar to humans than rodents with respect to brain gray-white matter composition, architecture, and size. We hypothesized that cauterization of the MCA in pigs would lead to ischemic infarction and functional deficits.

Methods: The MCA was permanently occluded on 8 male Yucatan miniature pigs. Magnetic resonance imaging (MRI) was performed 1 and 90 days post-MCAO surgery. A computational video capture system was used to assess changes in motor function pre- and post-stroke. Histological analysis was performed 90 days following MCAO surgery.

Results: MRI images confirmed stroke damage 1 day post-MCAO. T1-FLAIR MRI analysis showed a loss of 59.17 ± 10.06 cc of tissue from day 1 to day 90. Histological examination of the brain demonstrated severe atrophy of the affected right hemisphere. The white matter in the affected cortex could not be defined due to loss of normal elements, glial proliferation, and infiltration of gitter cells. Motor function analysis showed loss of gait symmetry and changes in stride length and hoof maximum hoof height.

Conclusion: MRI, histological, and gait analysis demonstrated consistent severe brain infarction and loss of motor function indicative of a stroke.

Translational Impact: The development of a pig MCAO model will allow stringent assessment of efficacy and safety of novel stroke therapies in a large animal model that shares important anatomical and physiological features with humans.