

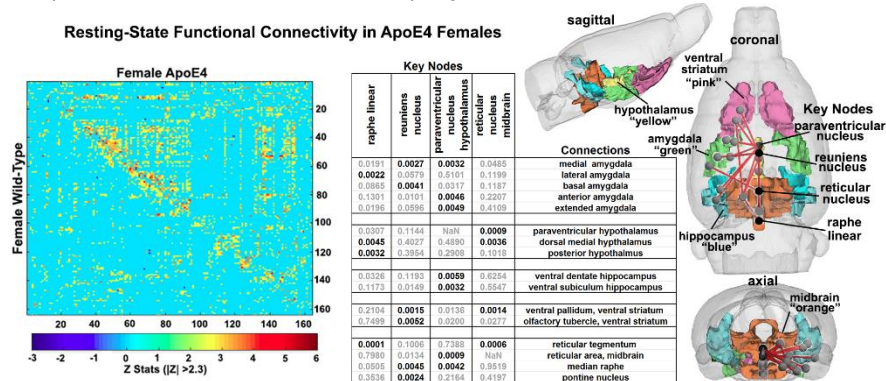
Biomere and Ekam Partnership

Our collaborative relationship with EKAM Imaging provides our clients with access to preclinical Magnetic Resonance Imaging. Ekam is the only CRO performing MRI on conscious subjects—the best possible method for insuring results that will translate to the clinic. Managed by Biomere, Ekam delivers these services with the turnaround times, quality assurance and reporting systems demanded by the world’s leading pharmaceutical and biotechnology firms.

Models of Neurodegenerative Disease

Human APOE 4 knock-in rat for Alzheimer’s Disease

Ekam Imaging uses the human ApoE4 Knock-In rat developed by HorizonDiscovery®. Apolipoprotein E (ApoE) is a critical lipoprotein in brain lipid metabolism. The E4 variant of ApoE (ApoE4) is a major risk factor for Alzheimer’s disease (AD). ApoE4 is found in 40–65% of patients with AD and a patient with 2 ApoE4 alleles has up to 20 times the risk of developing AD.



PINK1 transgenic rat for Parkinson’s Disease

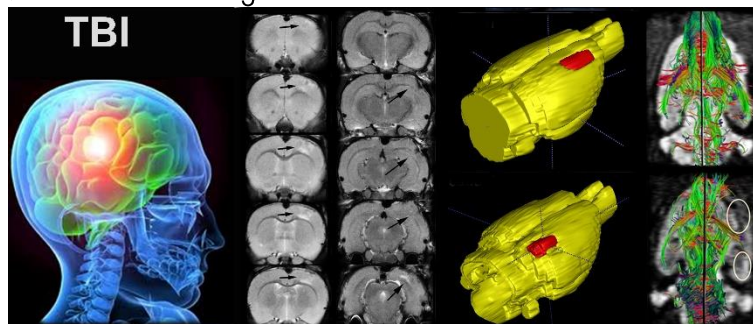
Ekam Imaging uses the PINK1 KO rat developed by HorizonDiscovery® in collaboration with the Michael J Fox Foundation. PTEN-induced kinase 1 (PINK1) is a serine/threonine kinase localized to mitochondria and is the second most frequent cause of autosomal recessive PD.

Human mutant G2019S LRRK2 transgenic rat for Parkinson’s Disease

Ekam Imaging uses the LRRK2 G2019S Rat (BAC Tg) from Taconic Farms. This transgenic (Tg) rat model overexpresses the human mutant G2019S Lrrk2. The G2019S mutation in leucine-rich repeated kinase 2 (LRRK2), is the most common genetic risk factor for PD. PD associated with LRRK2 mutations is clinically and pathologically indistinguishable from sporadic PD

Traumatic Brain Injury in rat

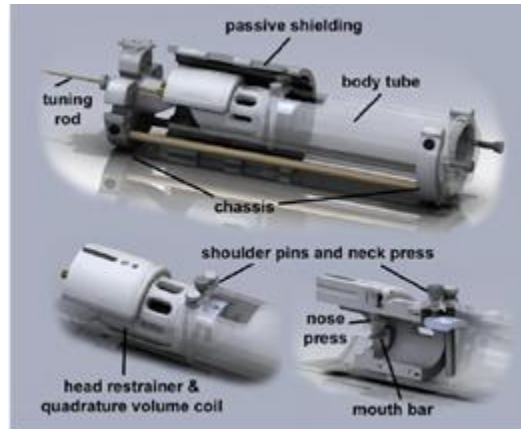
Ekam Imaging uses the closed head, momentum exchange model published by Viano¹ to study mild to severe head injury. This momentum exchange method was developed to provide biomechanical measures related to impact velocity, head acceleration, change in head velocity, and energy transfer that scale and translate to head injuries in the National Football League².



Why are there so many failed clinical trials? Clinical researchers make the argument that we lack “informative preclinical models and biomarkers” and what we do in the lab does not translate to the clinic³.

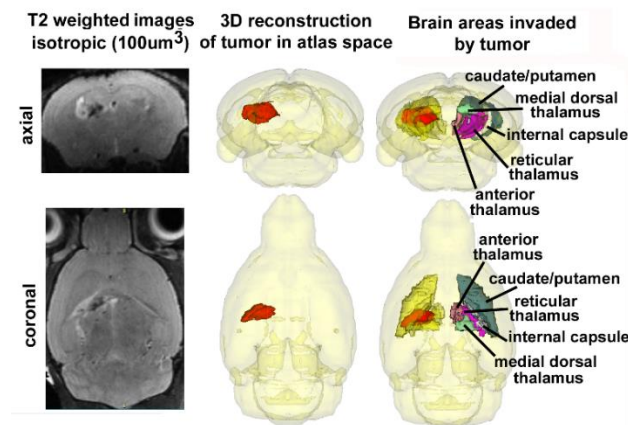
What is Ekam’s solution to the problem? Ekam uses clinically relevant rat models that reflect the human condition. Ekam uses the same technology to study these animals that clinical researches use to diagnose and follow disease progression and treatment efficacy in patients.

What technology is used in the clinic? Magnetic Resonance Imaging: 1) Diffusion tensor imaging with quantitative anisotropy (DTI-QA) is used to assess white and gray matter damage, 2) magnetic resonance spectroscopy (MRS) is used to assess brain chemistry, 3) resting state functional connectivity (rsFC) is used to assess organization and function of brain neural circuits, and 4) Quantitative Ultra-Short Time-to-Echo Contrast Enhanced (QUTE-CE) is used to quantitate blood volume, small vessel health and capillary density.



Ekam uses these noninvasive imaging modalities in awake rats, to provide clinically relevant neuroradiological evidence of brain injury and treatment efficacy over the life of the animal. All these MRI measures are correlated with behavioral measures of cognition, motor coordination, and emotion and neuropathology confirmed at autopsy.

Why rats instead of mice? Ekam prefers to the use rats instead of mice in early drug discovery for three important reasons: 1) the rat is physiologically, genetically and morphologically closer to humans than mice⁴, 2) as a model for human diseases the rat has many advantages over the mouse as reported by the National Institutes of Health⁵ and, 3) given their size, rats have a huge advantage over mice in magnetic resonance imaging



REFERENCES

1. Viano DC, et al., Neurosurgery 2009, 64:1162-1173.
2. Viano DC, et al. Annals of biomedical engineering 2012, 40:213-226.
3. Schwamm LH The New England journal of medicine 2014, 371:2522-2523
4. Gibbs RA et al., Nature 2004, 428:493-521.
5. Iannaccone P.M & Jacob, HJ, Disease Models and Mechanisms 2009, 2:206-210