Development of methods for longitudinal brain PET/CT studies in mice

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Andy Welch

The John Mallard Scottish PET Centre

Aberdeen Biomedical Imaging Centre

Molecular Imaging

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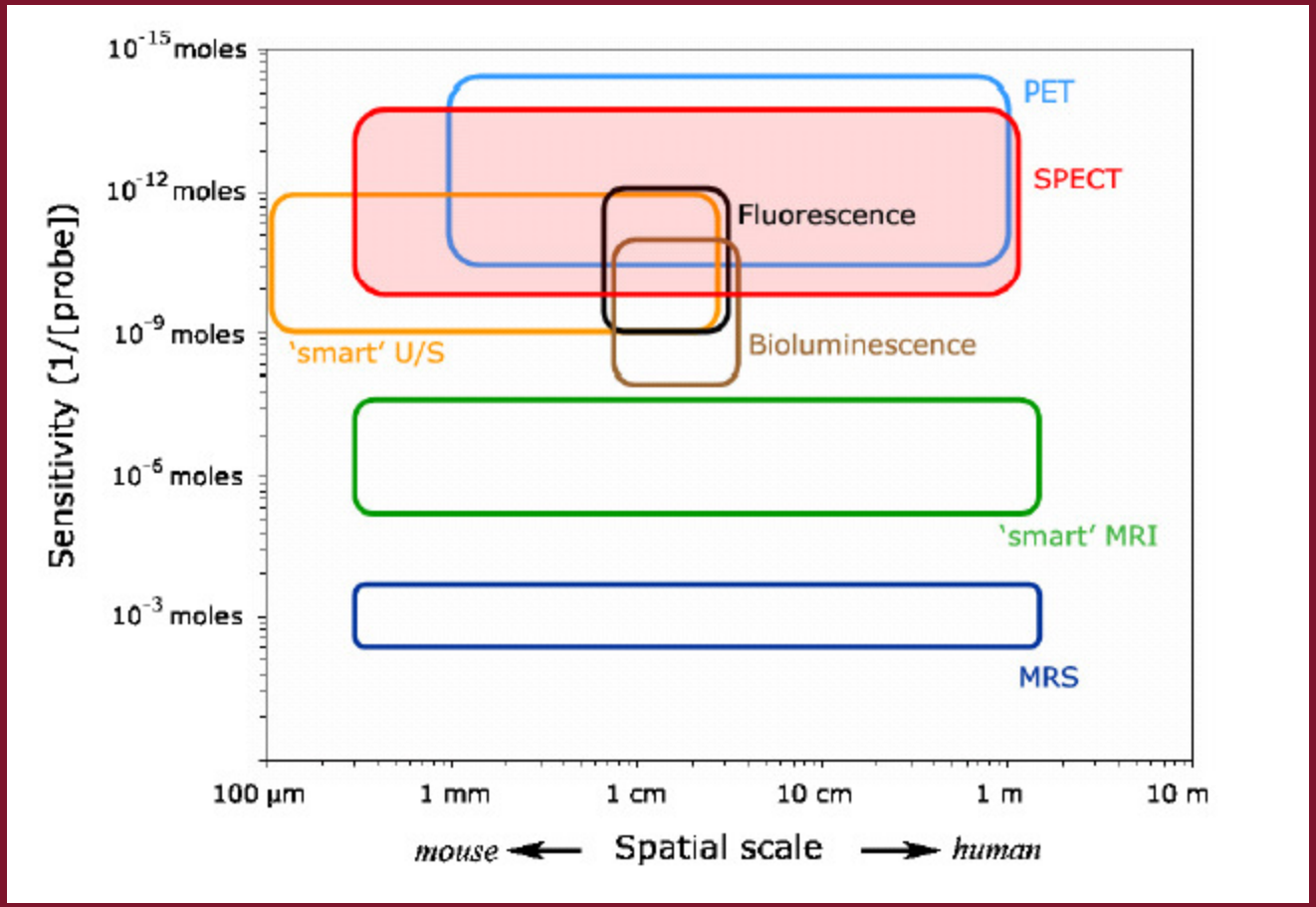

Meikle et al Phys Med Biol vol 50 R45-R61 2005

PET Challenges

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- PET is the most sensitive method for assessing function in-vivo
- PET/SPECT are inherently translational
- Future depends on development of novel imaging biomarkers
- PET is a scarce resource
- Partnerships are key to effective use
- Many skills required

Pre-clinical PET/CT

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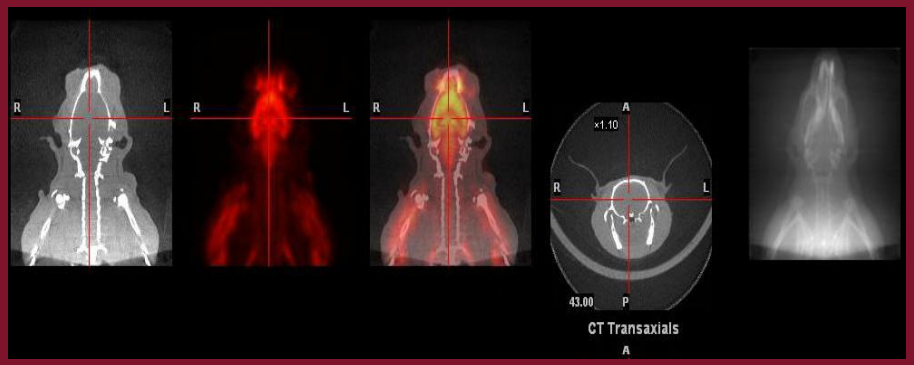
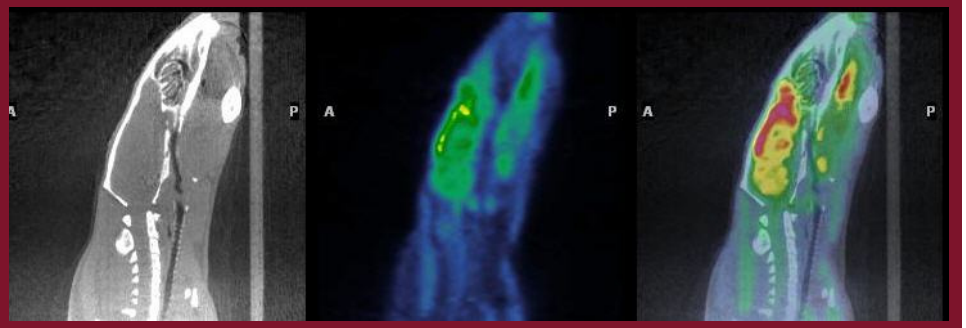
- Bring molecular imaging to preclinical research groups
  - e.g. Transgenic models
- Develop novel PET tracers
- Drug development





Mapping Brain Function in Pre-clinical models of disease

- FDG widely used as a marker of brain function in humans
- Many disease models are based on mice
  - ~3000 times smaller than human brain
  - High degree of accuracy required for registration

MOLECULAR IMAGING AND BIOLOGY

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BRIEF ARTICLE

Limitations of Small Animal PET Imaging with [^{18}F]FDDNP and FDG for Quantitative Studies in a Transgenic Mouse Model of Alzheimer's Disease

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Abstract

Purpose: We evaluated the usefulness of small animal brain positron emission tomography (PET) imaging with the amyloid-beta (Aβ) probe 2-(1-{6-[(2-[^{18}F]fluoroethyl)(methyl)amino]-2-naphthyl}ethylidene)malonitrile ([^{18}F]FDDNP) and with 2-deoxy-2-[F-18]fluoro-D-glucose (FDG) for detection and quantification of pathological changes occurring in a transgenic mouse model of Alzheimer's disease (Tg2576 mice).

Procedures: [^{18}F]FDDNP (n=6) and FDG-PET scans (n=3) were recorded in Tg2576 mice (age 13–15 months) and age-matched wild-type litter mates. Brain volumes of interest were defined by co-registration of PET images with a 3D MOBY digital mouse phantom. Regional [^{18}F]FDDNP retention in mouse brain was quantified in terms of the relative distribution volume (DVR) using Logan's graphical analysis with cerebellum as a reference region.

Results: Except for a lower maximum brain uptake of radioactivity in transgenic animals, the regional brain kinetics as well as DVR values of [^{18}F]FDDNP appeared to be similar in both groups of animals. Also for FDG, regional radioactivity retention was almost identical in the brains of transgenic and control animals.

Conclusions: We could not detect regionally increased [^{18}F]FDDNP binding and regionally decreased FDG binding in the brains of Tg2576 transgenic *versus* wild-type mice. However, small group differences in signal might have been masked by inter-animal variability. In addition, technical limitations of the applied method (partial volume effect, spatial resolution) for measurements in such small organs as mouse brain have to be taken into consideration.

Key words: Alzheimer's disease (AD), PET, [^{18}F]FDDNP, FDG, Transgenic mouse, Amyloid-beta (Aβ)

Registration

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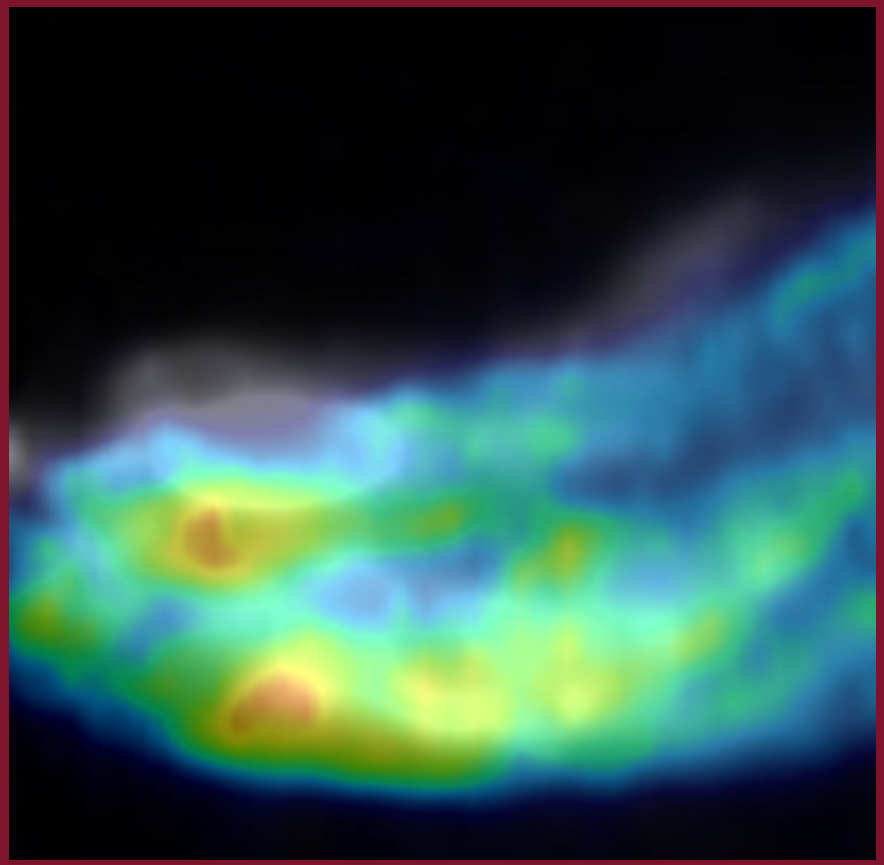

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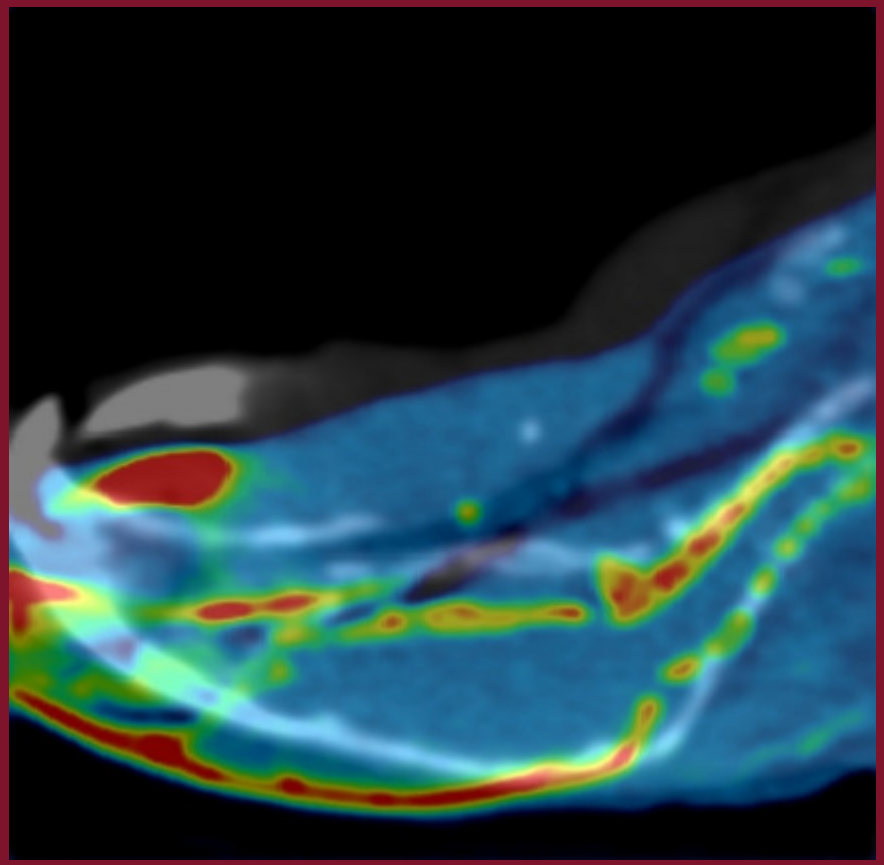

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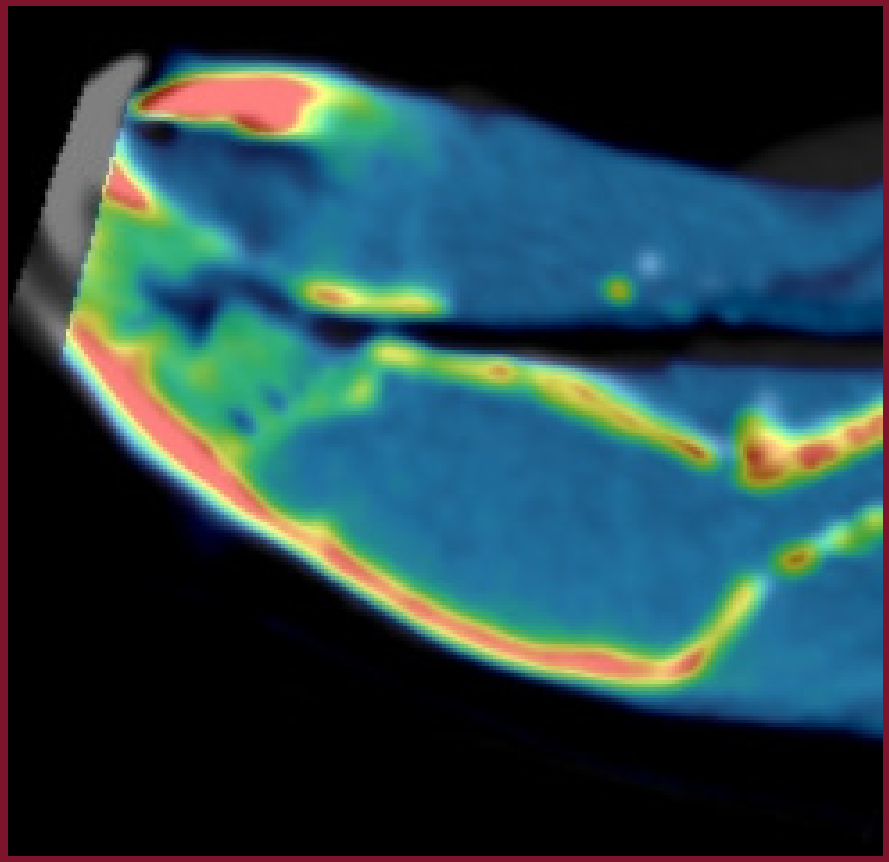

Processing

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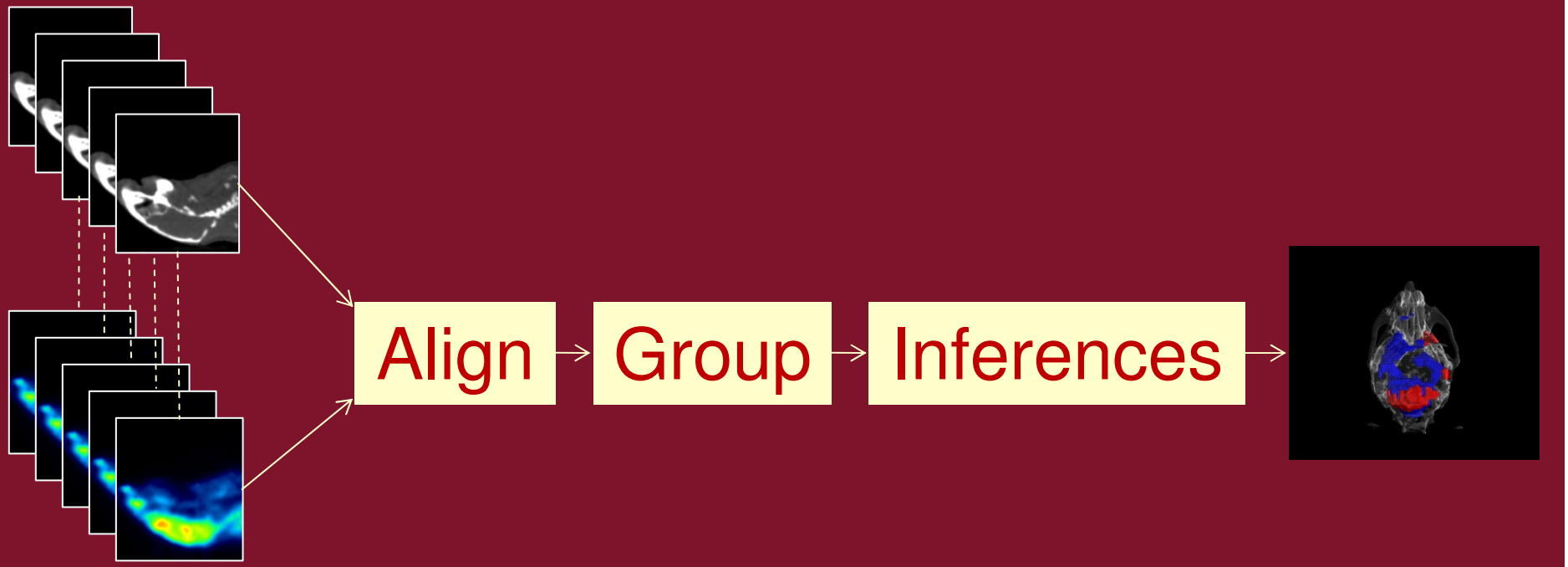

Changes in Metabolism with Age in Black 6 Mice

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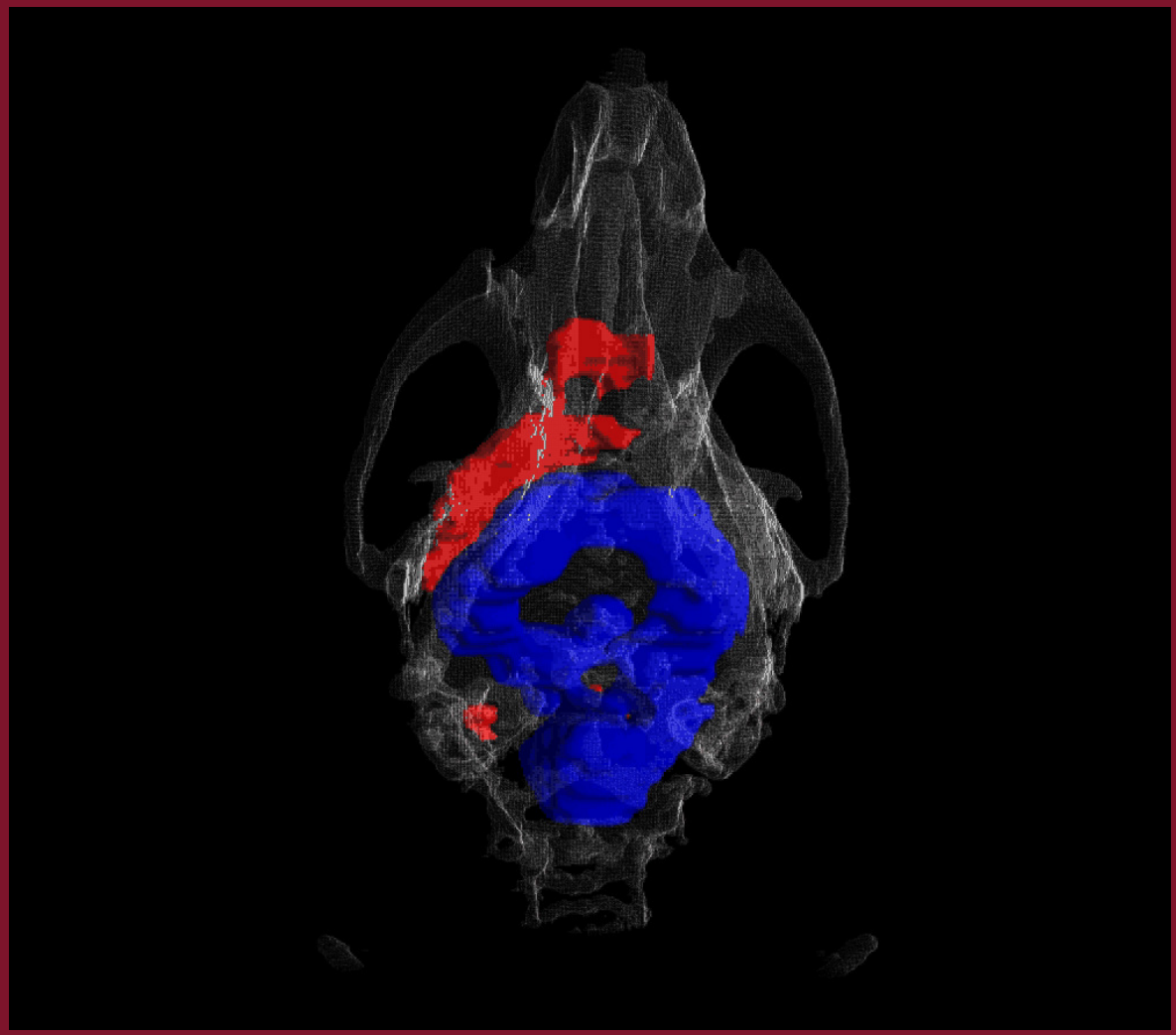

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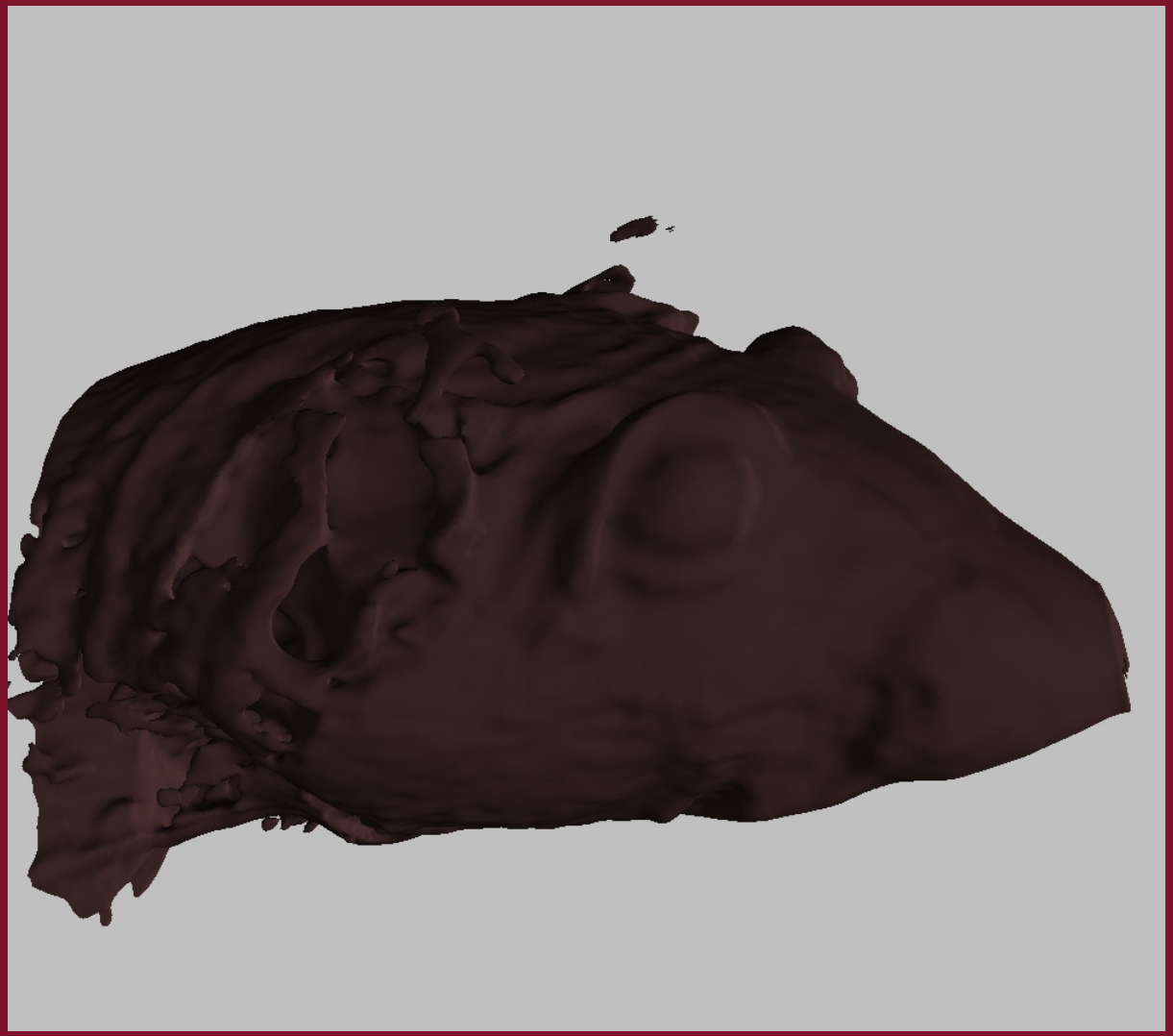

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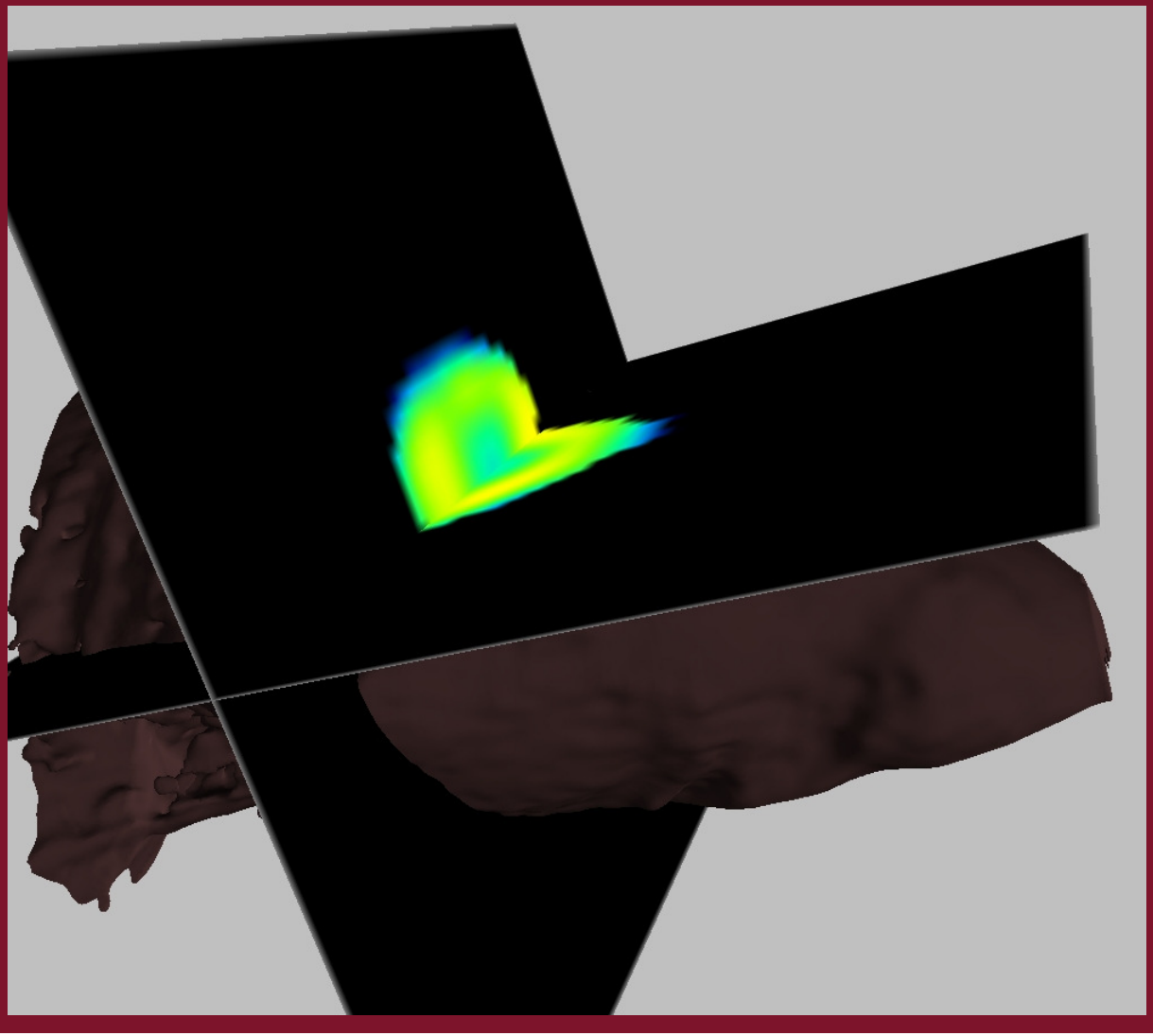

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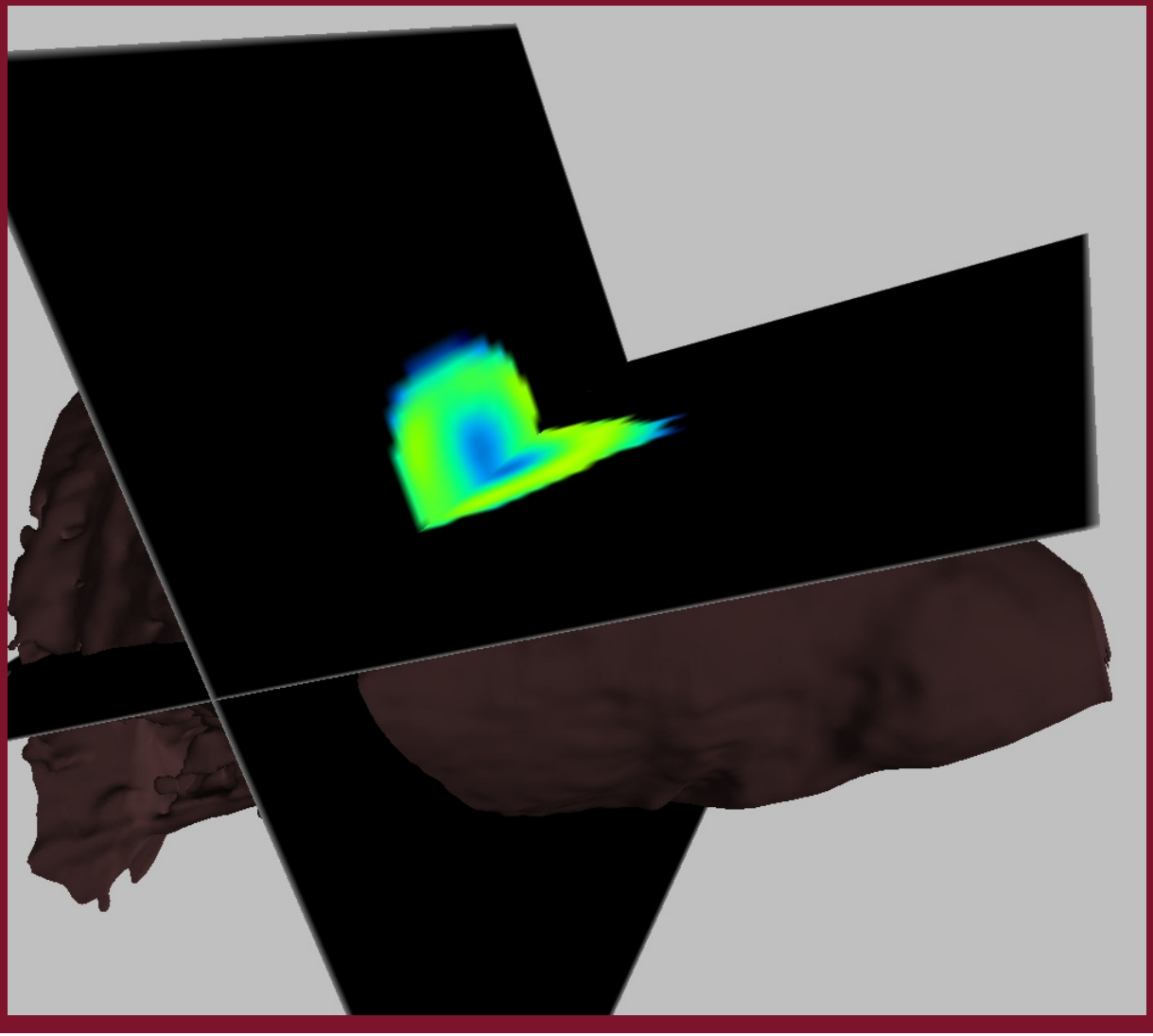

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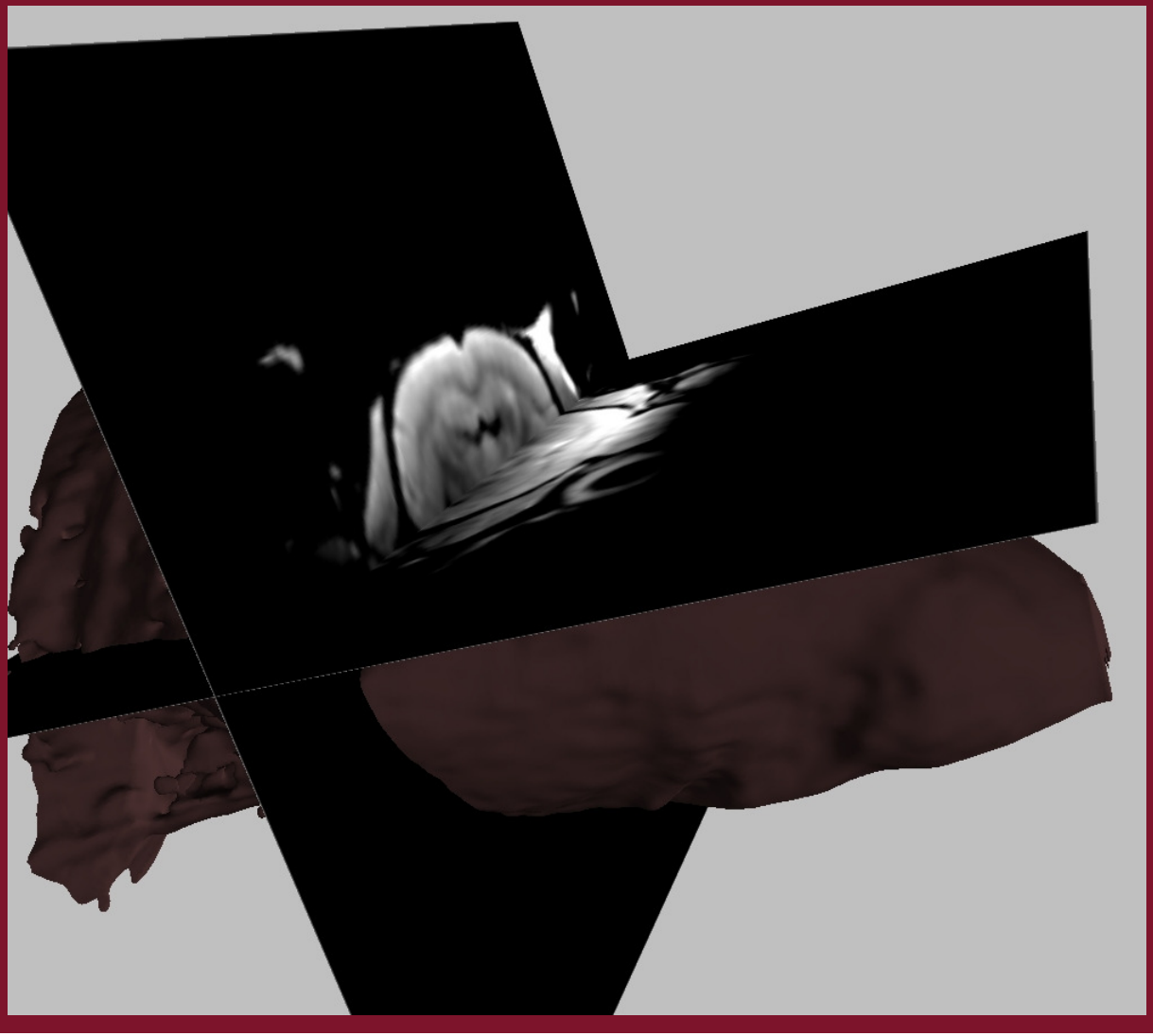

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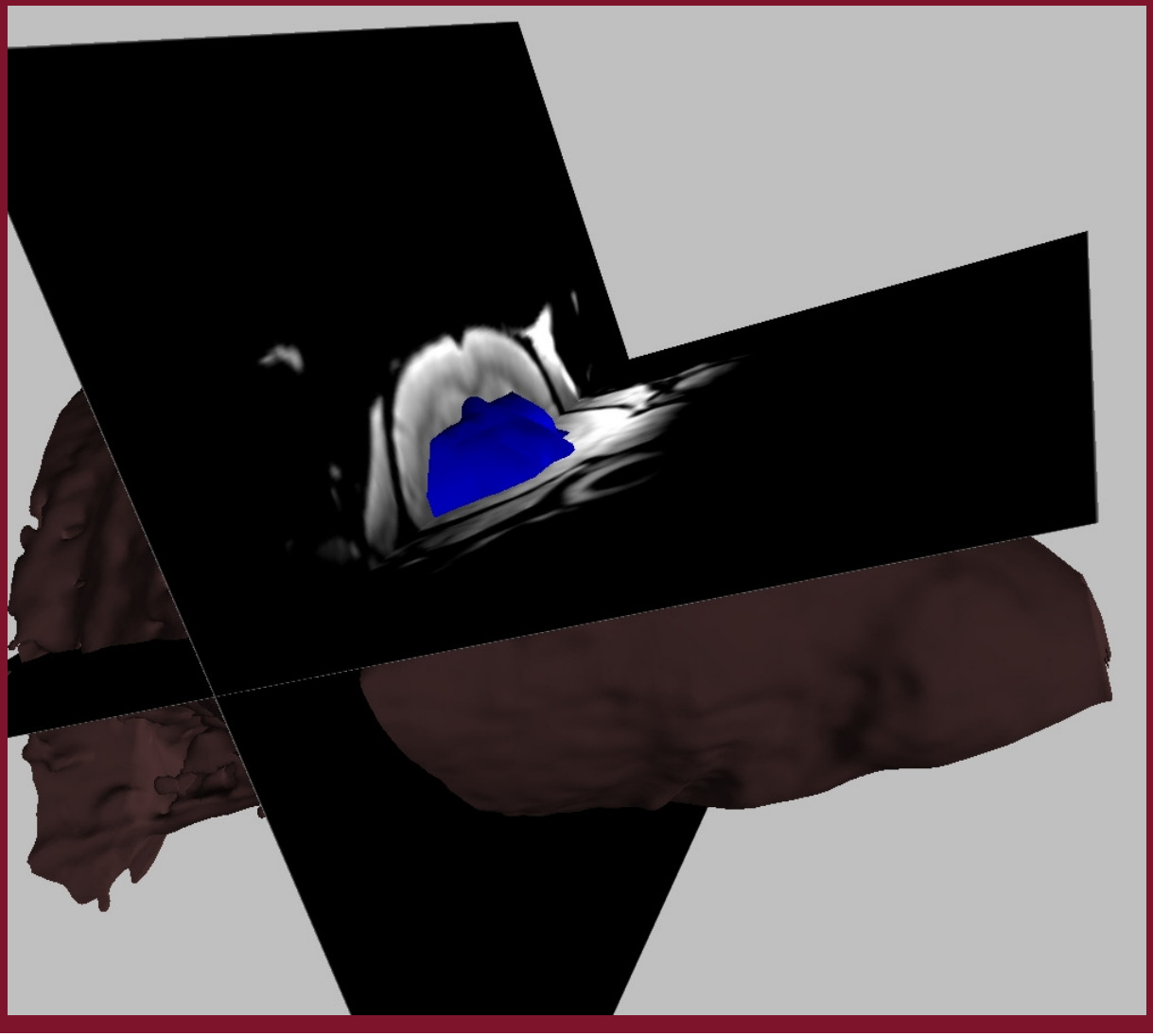

Conclusions

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- Generic tool for assessing brain function in mice is being developed
  - Use CT to aid registration
- Registration with MRI appears possible
- Applying to transgenic models of AD
- Provides benchmark for novel biomarkers