Technology Enabling Awake Animal Nuclear Tomographic Imaging

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Motivation for Awake Animal Brain Imaging

1. Anesthesia can profoundly affect radiotracer biodistribution

- Anesthesia perturbs brain function
- Kinetic modeling for dynamic scans beginning with tracer administration may yield unreliable results for reaction rate constants
- Tracer uptake may be affected even if anesthesia is only performed during imaging

2. Desire to image animal behavior in a more natural setting

- Possible stress-induced immobilization

3. Motion-corrected PET brain imaging

- Even under anesthesia there may be involuntary head motion associated with animal respiration

General Strategies for Awake Animal Brain Imaging

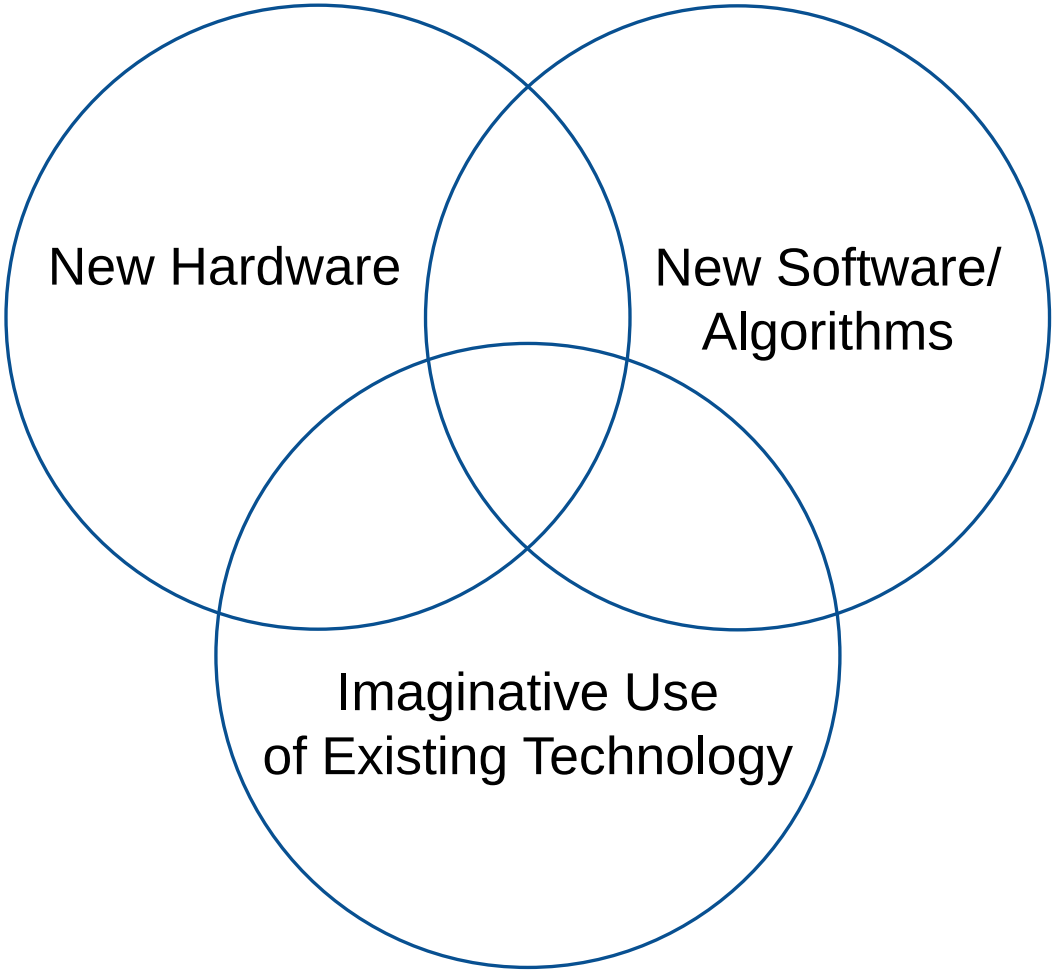
1. Train the animal not to move
- Bite bars for rodent brain imaging
- Training not practical for routine use

2. Attach the animal to the scanner or vice versa
- Fixation device to conventional small animal PET scanner
- Affix a miniature scanner to the animal head

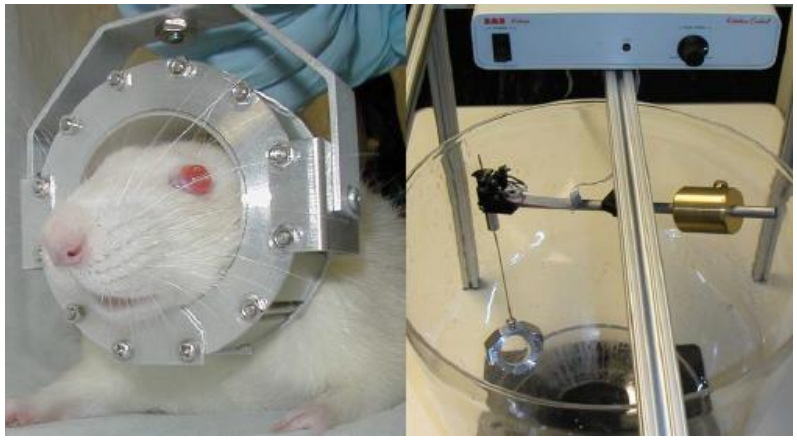
3. Keep the animal in the scanner's FOV
- Confine to a burrow
- Move the animal platform

4. Track the animal head
- Track fiducial markers
- Apply motion correction in image reconstruction

Development of Awake Animal Imaging Methods

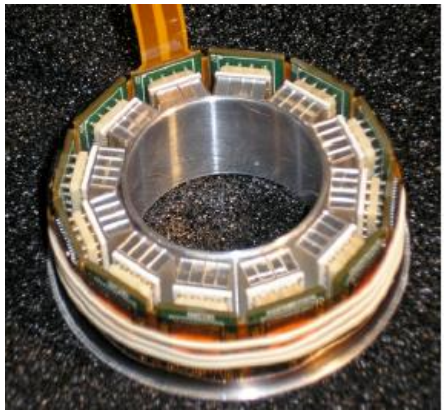


Rat Conscious Animal PET (RatCAP)

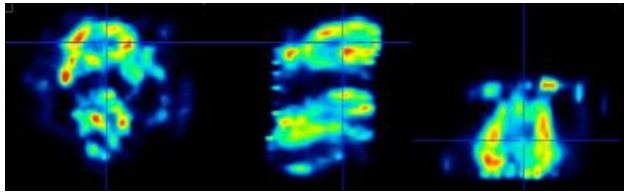


RatCAP Detector Setup

Vaska P et al., IEEE Trans Nucl Sci 2004; 51: 2718-2722
Brookhaven National Lab, NIH, Université de Sherbrooke



Vaska P et al., 2005 IEEE NSS Conference Record, 3040-3044
Brookhaven National Lab, NIH, Université de Sherbrooke

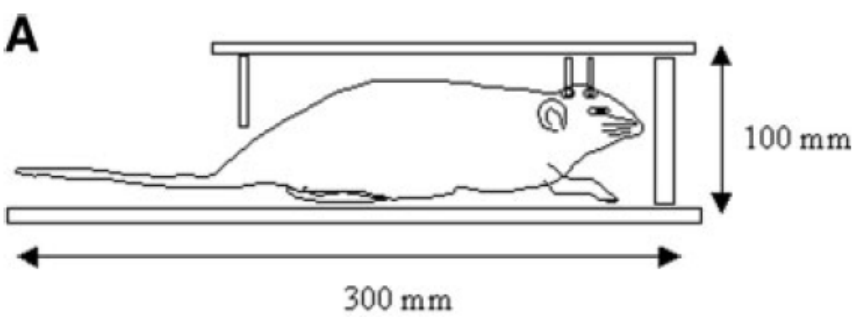


Transverse **Sagittal** **Coronal**

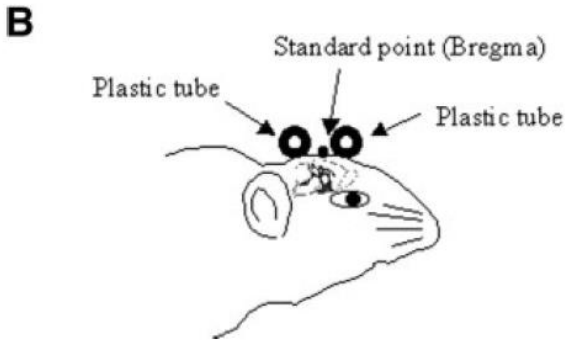
F-18 FDG

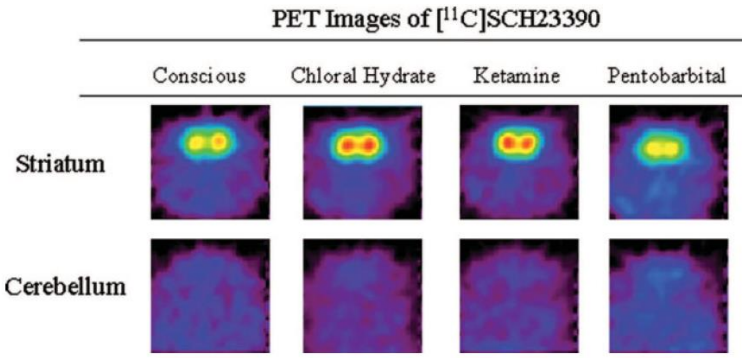
- PET imaging of conscious rats
- Technology
  - Ring of small detector blocks, pixelated LSO (Proteus), Hamamatsu S8550 APD array
  - DAQ: CMOS ASIC, CAMAC-based, NIM hardware for coincidence, KMaxNT control software
  - Scanner attached to rat head with a counterbalancing arm

Conscious Rat PET



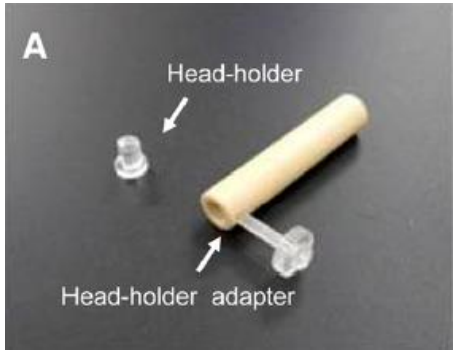
Momosaki S et al., Synapse 54: 207-213 (2004)
National Institute for Longevity Sciences and Osaka University, Japan

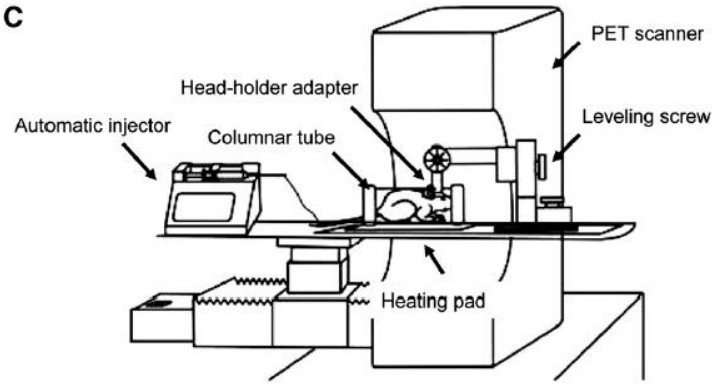




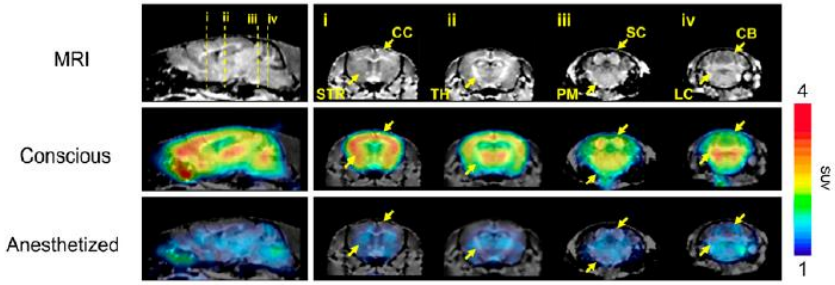
- PET imaging of conscious rats
- Technology
  - SHR-2000 animal PET camera (Hamamatsu)
  - Plastic tubes affixed by dental cement, head fixed to wooden box using the tubes
  - Training to acclimate the rat to the apparatus

Conscious Mouse PET





Mizuma H et al., J Nucl Med 2010; 51: 1068-1075
RIKEN Center for Molecular Imaging Science, Kobe, Japan

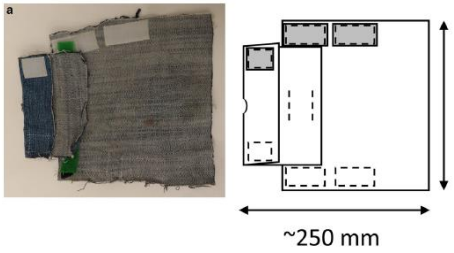


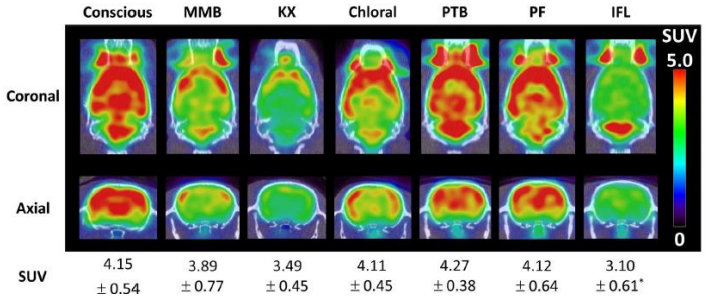
F-18 FDG

- PET imaging of conscious mice
- Technology
  - MicroPET Focus-220 (Siemens)
  - Attach acrylic head-holder with adhesive cement (Super-Bond C&B) adapter attached to fixed positioning system

Conscious Rat PET with Soft Immobilization

Suzuki C et al., EJNMMI (2021) 11: 46
Hamamatsu University School of Medicine, Japan

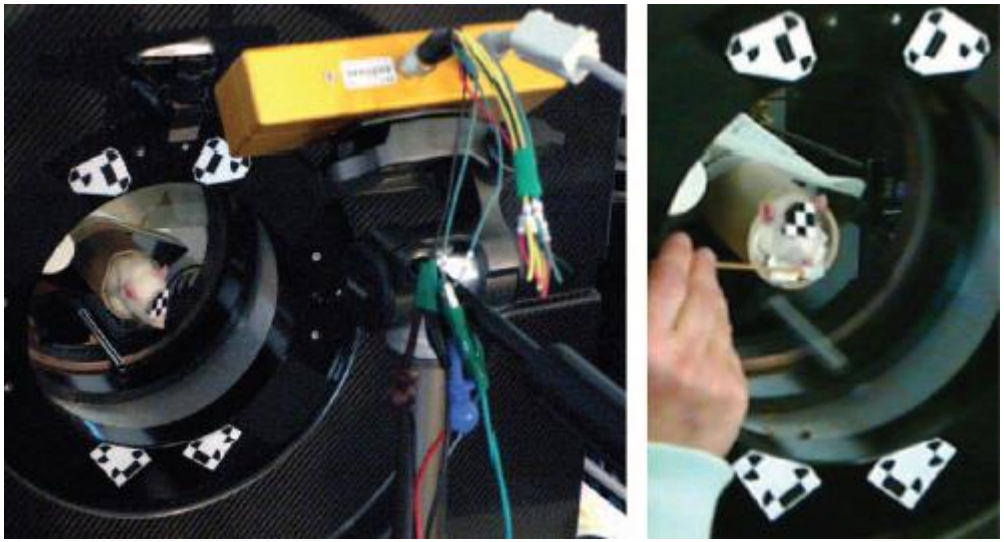




F-18 FDG

- PET imaging of conscious rats
- Technology
  - FLEX small animal PET/SPECT/CT (Gamma Medica)
  - Handmade restrainer from denim fabric, with hook and loop fasteners
  - Scissors, sewing machine, needle, thread
  - Rats trained to acclimate to the restraint

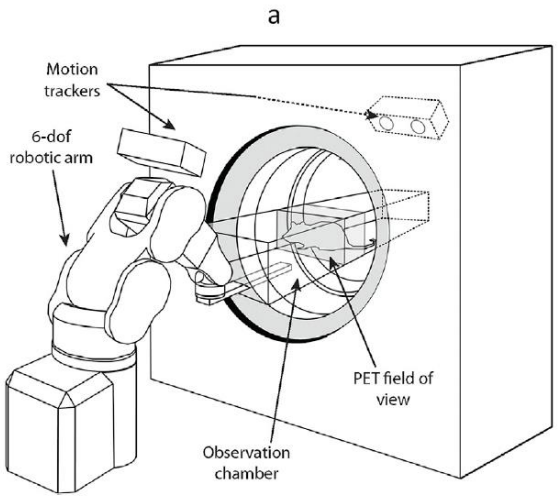
Fully Conscious Small Animal PET

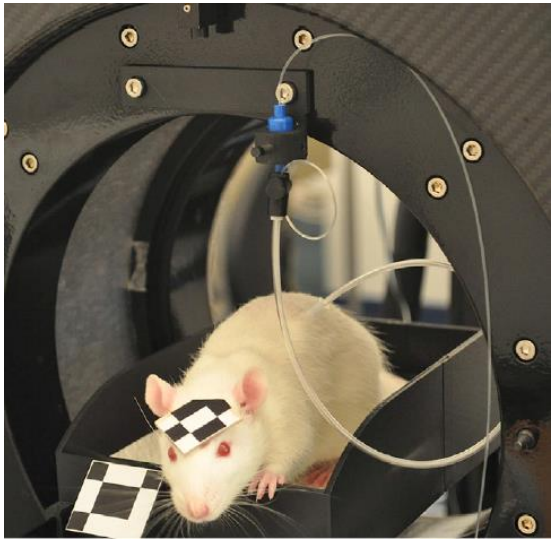


Kyme AZ et al., 2009 IEEE NSS Conference Record
University of Sydney

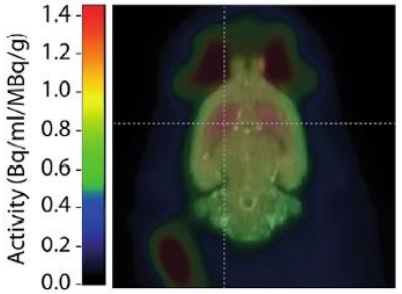
- PET imaging of conscious rats in a burrow
- Technology
  - microPET Focus 220 (Siemens)
  - MicronTracker Sx60 binocular tracking system, 30 fps (ClaroNav)
  - PVC pipe burrow, free head motion at end of tube
  - List-mode image reconstruction with event-by-event motion correction

Open-Field PET





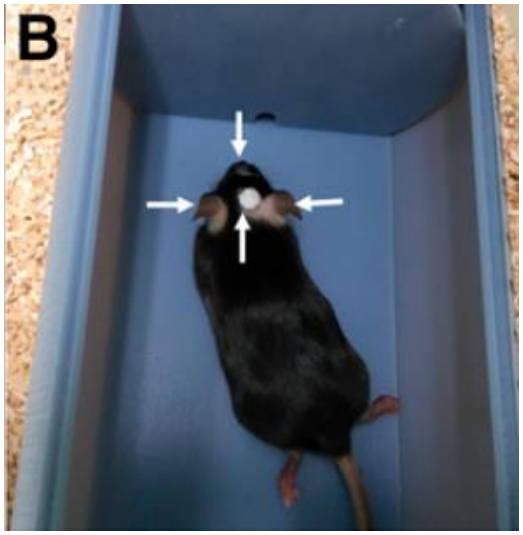
Kyme AZ et al., NeuroImage 188 (2019) 92-101
University of Sydney



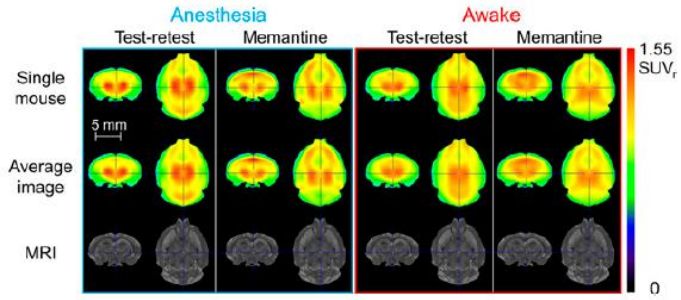
C-11 raclopride

- PET imaging of freely moving rats (conscious, unrestrained)
- Technology
  - microPET Focus 220 (Siemens)
  - MicronTracker Sx60 binocular tracking system, 30 fps (ClaroNav)
  - 3D printed animal enclosure
  - Tethered catheter for drug infusion, swivel mount on gantry
  - 6-axis DOF robot (Epson C3-A601S) to keep head near the center of the FOV
  - Control software
  - List-mode image reconstruction with event-by-event motion correction

Freely Moving Awake Animal PET



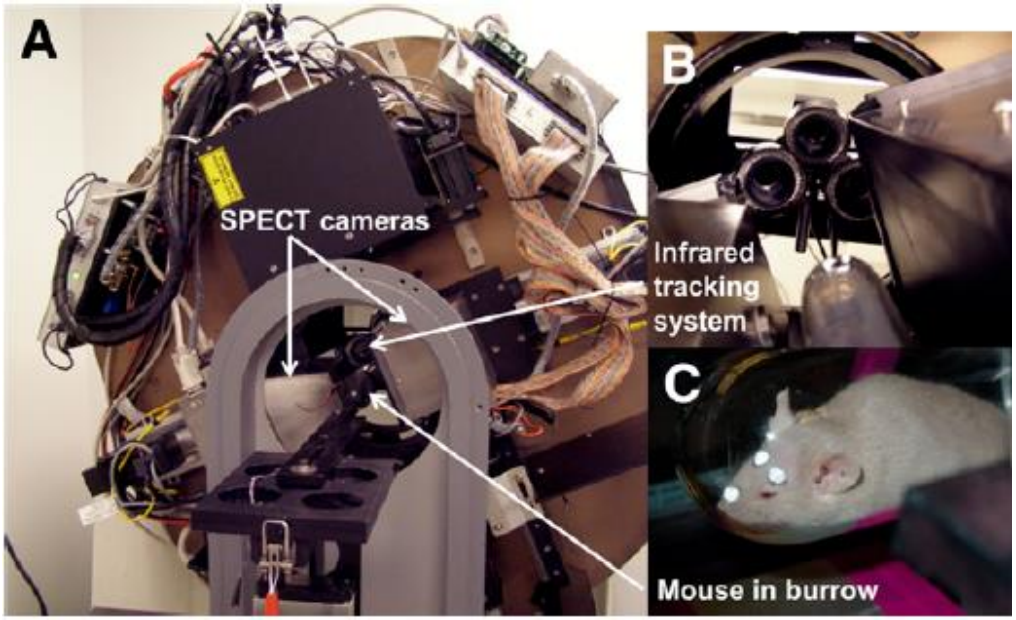
Miranda A et al., J Nucl Med 2019; 60: 844-850
University of Antwerp

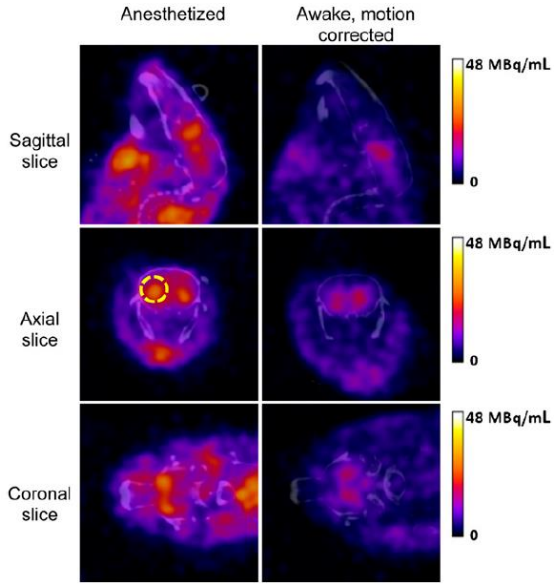


F-18 FDG

- PET imaging of freely moving mice (conscious, unrestrained)
- Technology
  - Inveon microPET (Siemens)
  - Custom-built cylindrical animal holder
  - Radioactive point sources attached to head
  - List-mode OSEM image reconstruction with event-by-event motion correction

Awake Animal SPECT





I-123 ioflupane

Baba JS et al., J Nucl Med 2013; 54: 1-8

ORNL, Jefferson Lab, Univ. of Maryland, Baltimore, West Virginia Univ., Johns Hopkins Medical Inst.

- SPECT imaging of awake mice in a confinement tube (conscious, unrestrained)
- Technology
  - Custom detectors (pinhole, parallel hole collimation), pixelated NaI(Tl) with PSPMTs
  - Custom-built FPGA readout
  - Custom-modified Siemens MicroCAT II rotation gantry
  - Custom-built confinement NIR transparent tube
  - Retroreflective point sources attached to head, NIR tracking with 3 cameras at 10 fps
  - List-mode acquisition, motion-dependent histogramming, reconstruction with motion correction

Concluding Comments

How might awake animal imaging be advanced?

1. Improved detectors
- Component miniaturization, faster readout/electronics
- Better localization of gamma ray interaction points in detector elements -> improved resolution

2. Head motion determination
- Can a data-driven method win out? Problematic at early times with few events in FOV.
- Routine robust markerless head tracking

3. Data Analysis
- Directly estimate kinetic rate constants from list-mode data without the intermediate steps of sinograms, projection data or images

4. Artificial Intelligence
- Can it be reliably used for head motion determination from video images?
- Can it enable motion correction fast enough for possibly real-time image reconstruction?

5. Whole body freely moving awake animal imaging
- Feasible using existing technologies if they are integrated appropriately
- Would need 4π optical camera coverage (or 3D navigators in a PET/MR), non-rigid deformations
- Sufficient agency funding support