Initial Performance of the RatCAP, a PET Camera for Conscious Rat Brain Imaging

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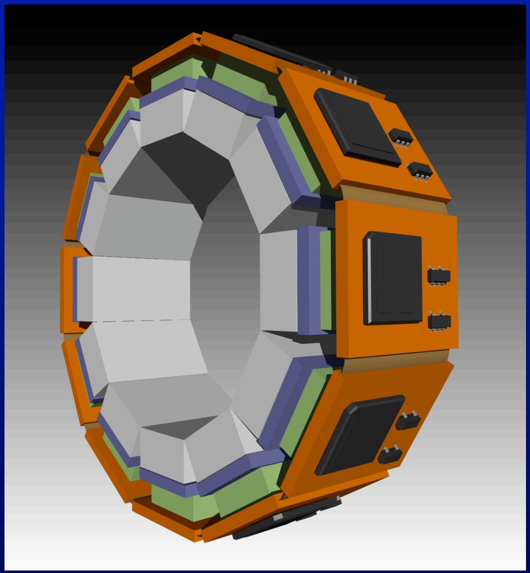


February 8, 2006

Animal Neuroscience with PET

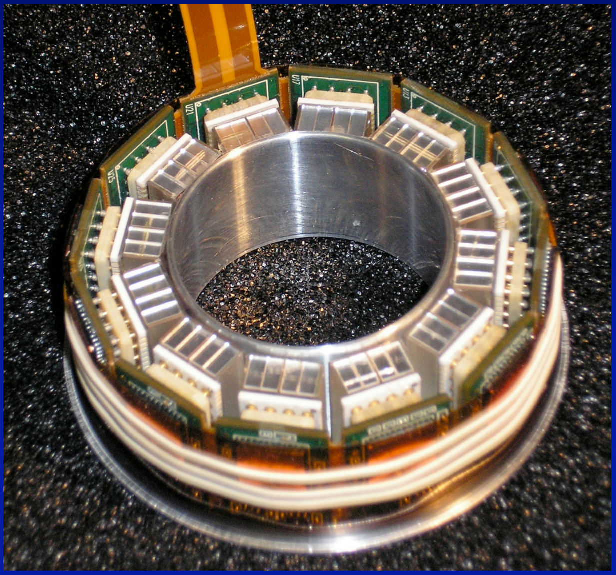
Eliminate anesthesia:

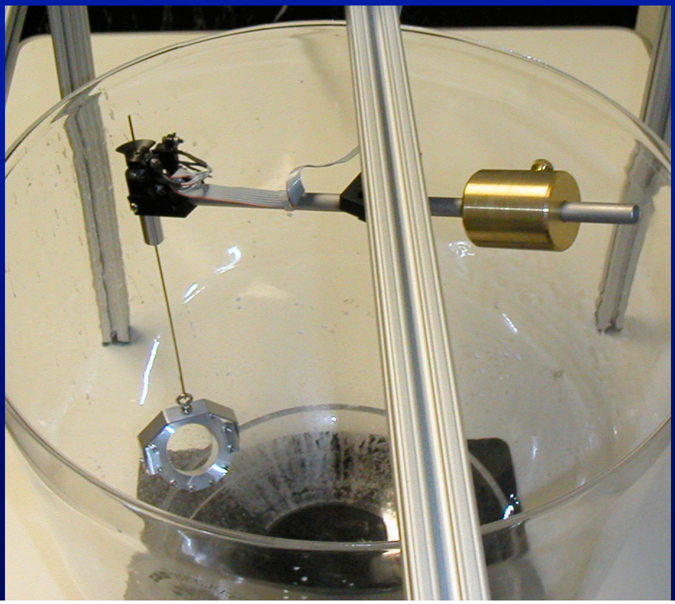
- Why?
  1) removes confounding effects on neurochemistry
  2) enables stimulation during PET scanning and correlation w/ behavior

- How?
  1) miniaturize scanner
  2) attach directly to skull

Rat Conscious Animal PET

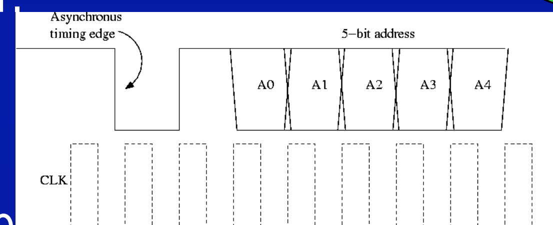
- Mechanical
  - FOV: 38 mm dia. x 18 mm axial
  - OD: 72 mm
  - 194 g counterweighted in rat-turn bowl
- Detectors
  - 12 blocks of 4x8 crystals = 384 crystals
  - LSO: 2.2 mm x 2.2 mm x 5 mm long
  - APD: Hamamatsu S8550
- Electronics
  - rigid-flex circuit board w/ custom ASICs
  - small cable for all interconnections
  - downstream: TSPM, VME daq, PC

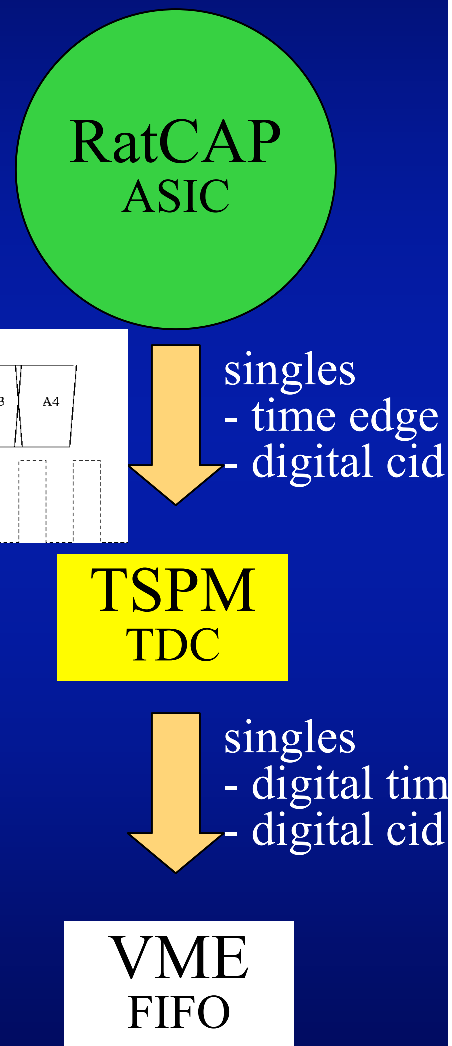




System Features

- Singles mode
- No ADCs
- Custom ASIC CMOS 0.18μm
  - 32 preamps, bipolar shapers, zero-cross discr.
  - ENC <1000 e$^-$ rms, total power ~1 W
  - 32:1 multiplexer to single data line
  - 100 MHz clock: <100 ns deadtime per event per block
- TDC & Signal Processing Module (TSPM)
  - TDC with 1.1 ns time bins
- Data acquisition
  - VME FIFO & pdaq software on linux box
  - > 10 MB/sec w/ no deadtime





System Setup

- Assembly
  - >98% of detectors working
- Gain variations
  - ~ 2:1 max:min within block
  - HV trimmed to reduce variations among blocks >> not optimized!

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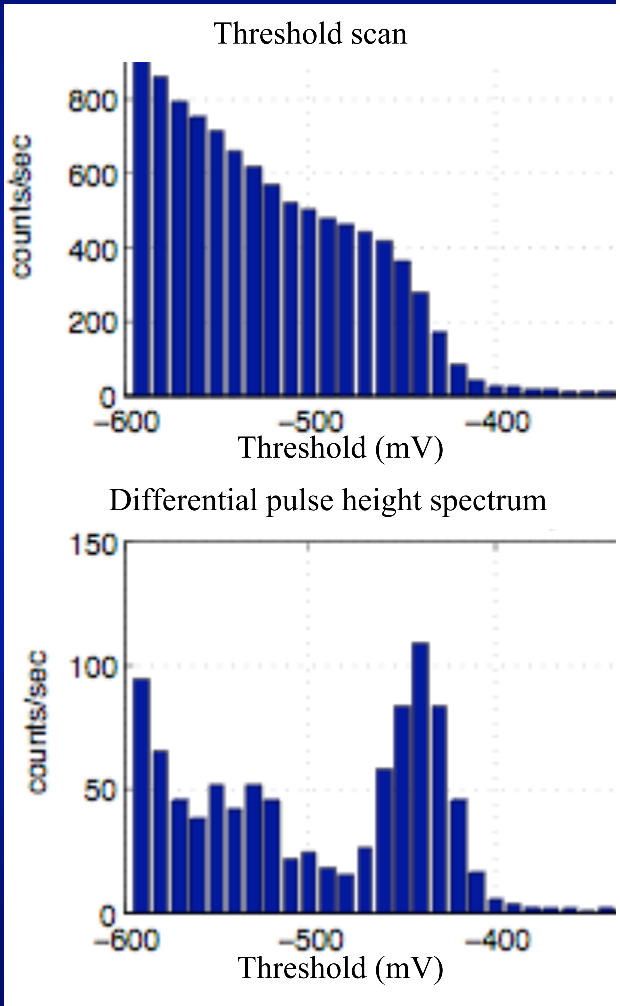
  - energy spectrum via threshold scan
  - HV set to use full dynamic range
  - common LLD voltage



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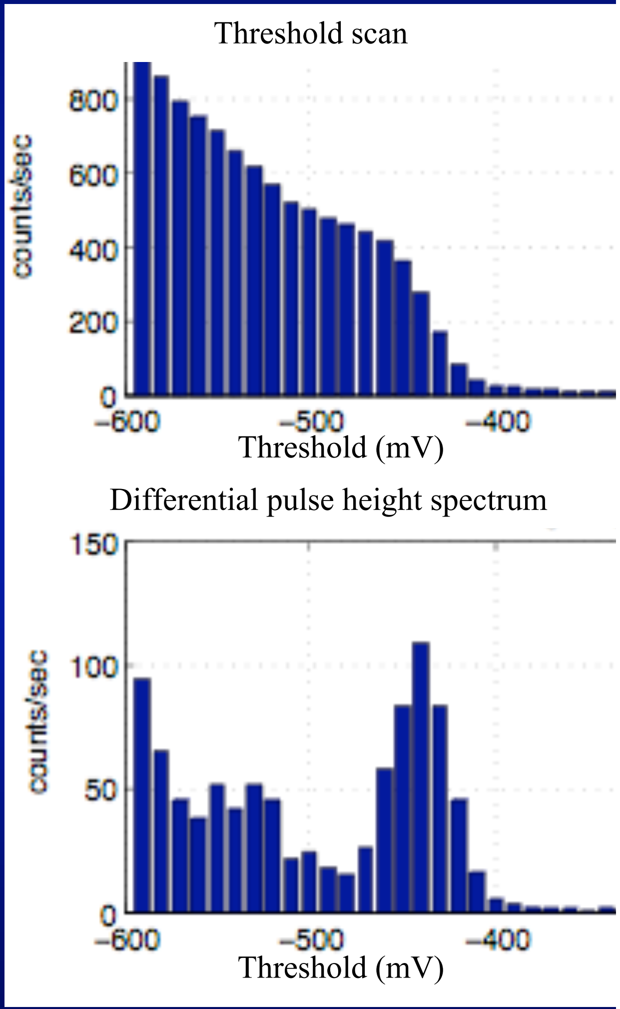
Avg LLD = 146 keV



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- **Time window (offline)**
  - spectrum for each crystal pair
  - 13.9 ns FWHM
  - shifts ~10 ns not yet corrected
  - >> using $2\tau = 40$ ns

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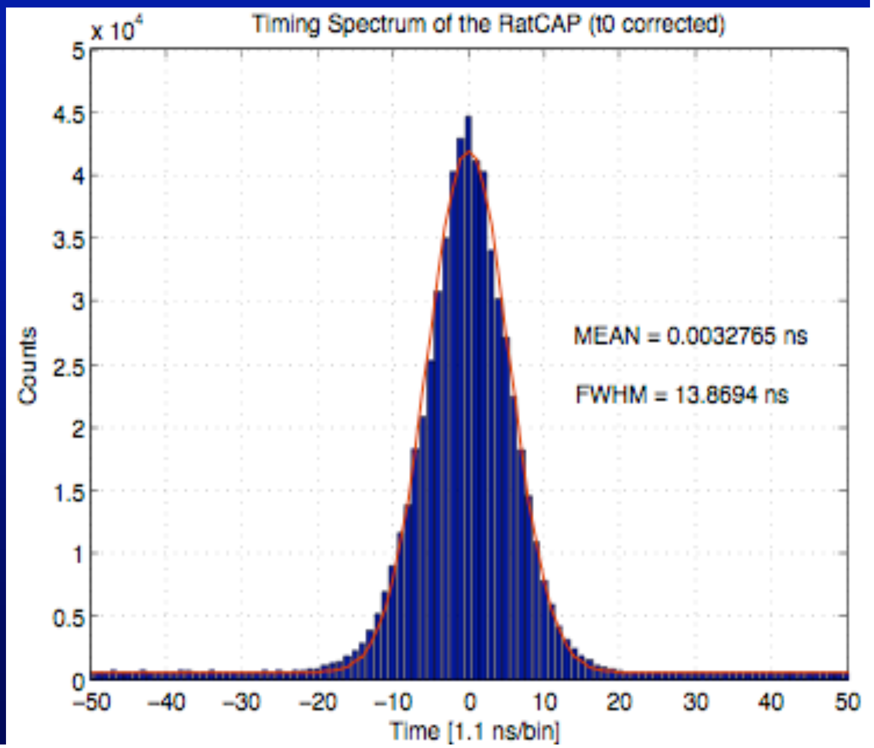

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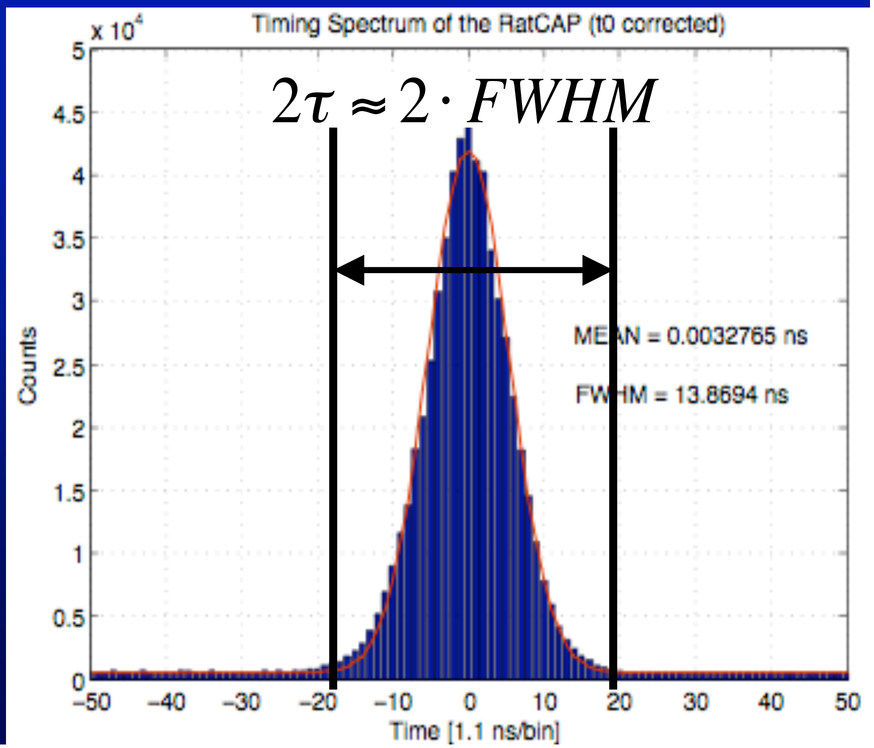
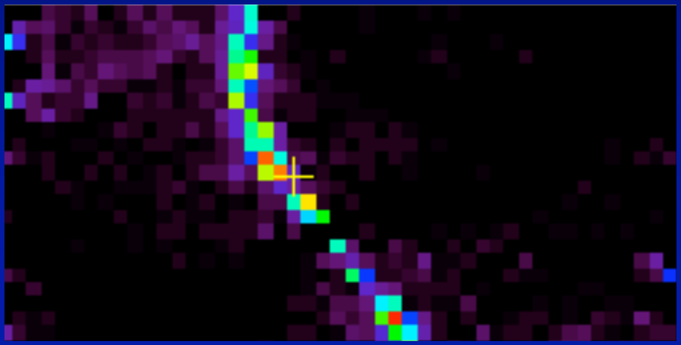
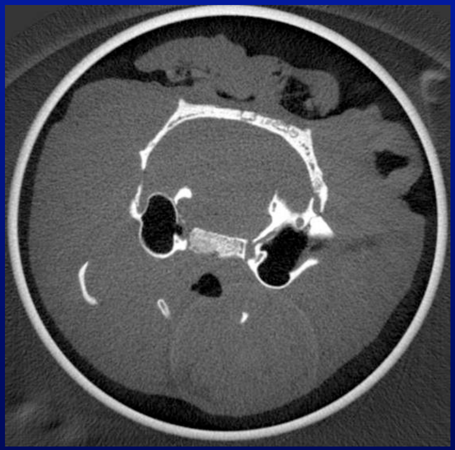


Data Processing

- Sinogram binning (offline)
  - fully uncompressed, 3D, span=1 sinograms
  - prompt & delayed

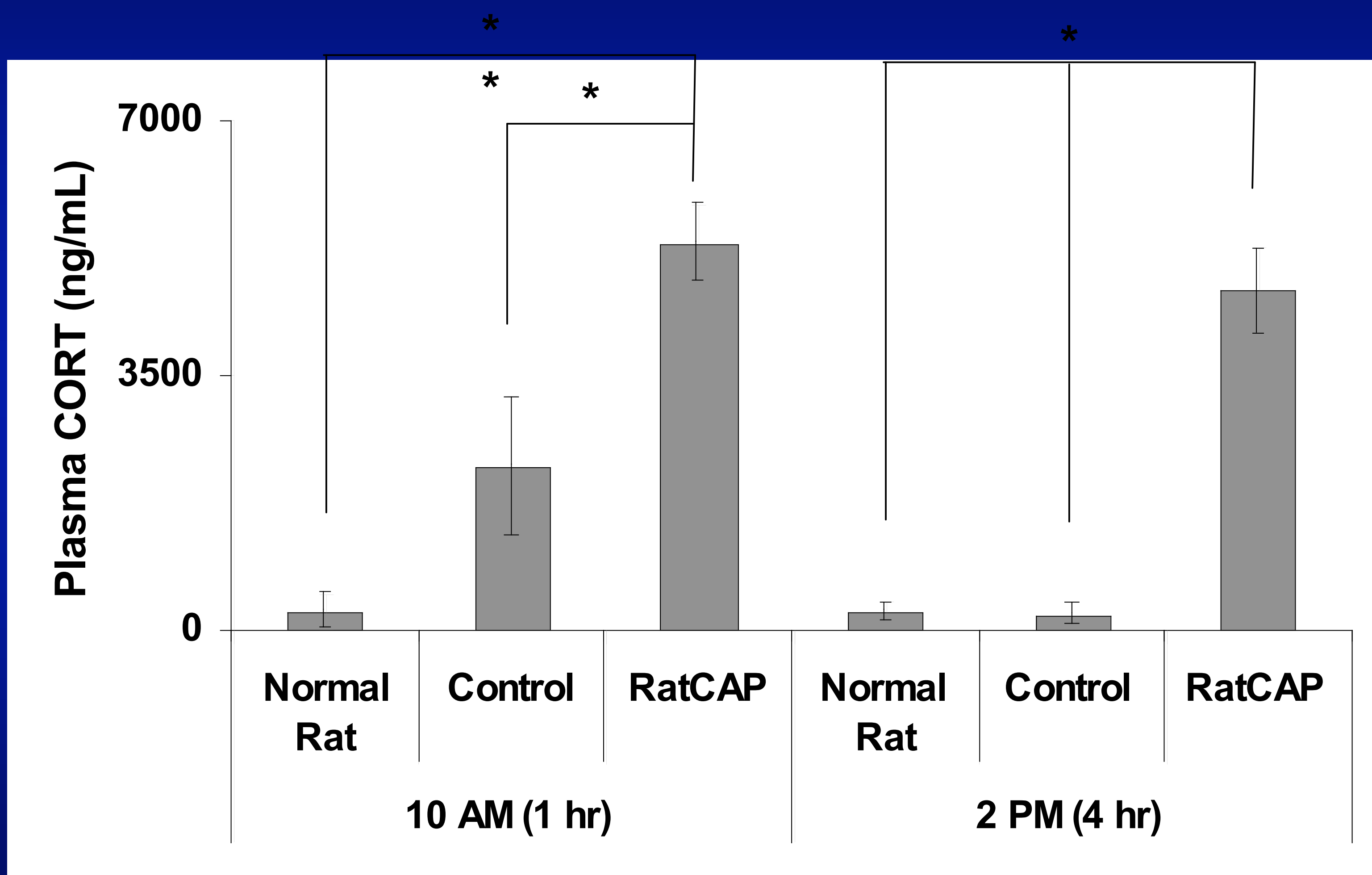


- Image reconstruction: MLEM
  - Monte Carlo precalculated system matrix p_{ij} (SimSET)
  - 1 mm^3 voxels
  - decays per voxel >10x expected in animal study
  - ~20 sec/iteration

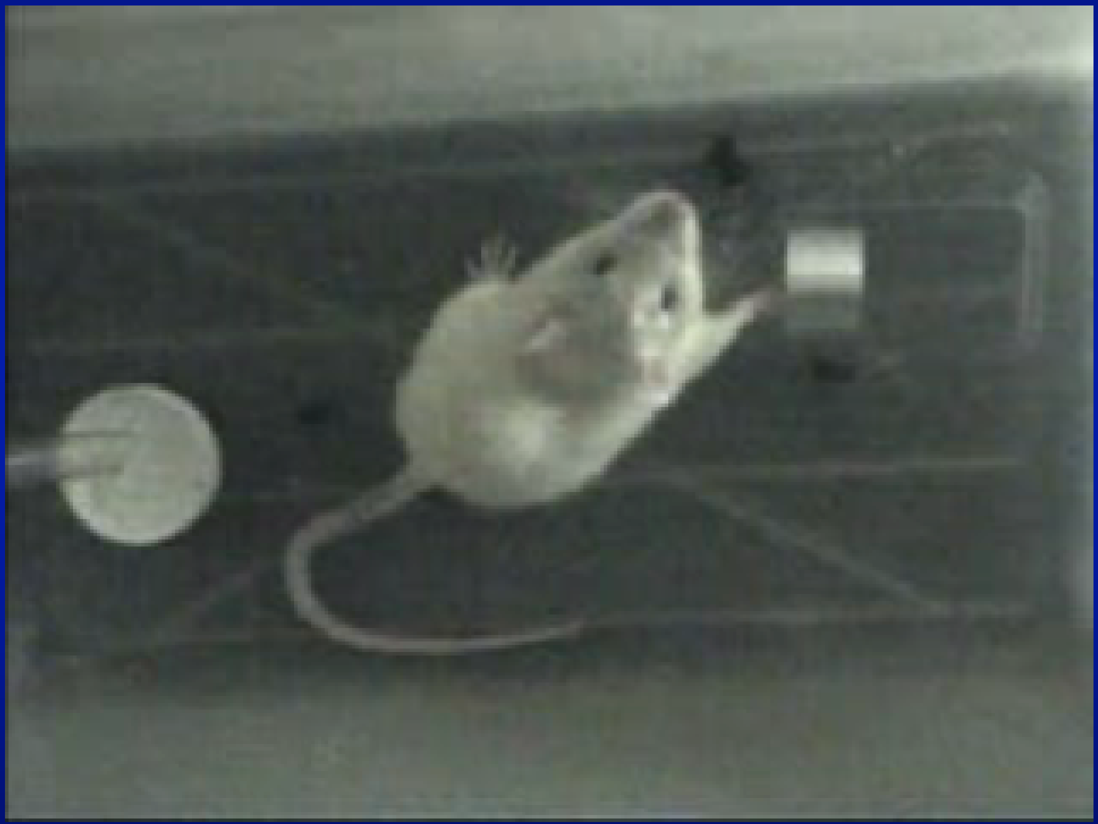


- Quantitative corrections
  - scatter, attenuation - fixed, from microCT
  - detector-pair efficiencies ε_i
    - "direct inversion" = ratio of measured to simulated sinograms of uniform phantom
  - randoms R_i from delayed sino

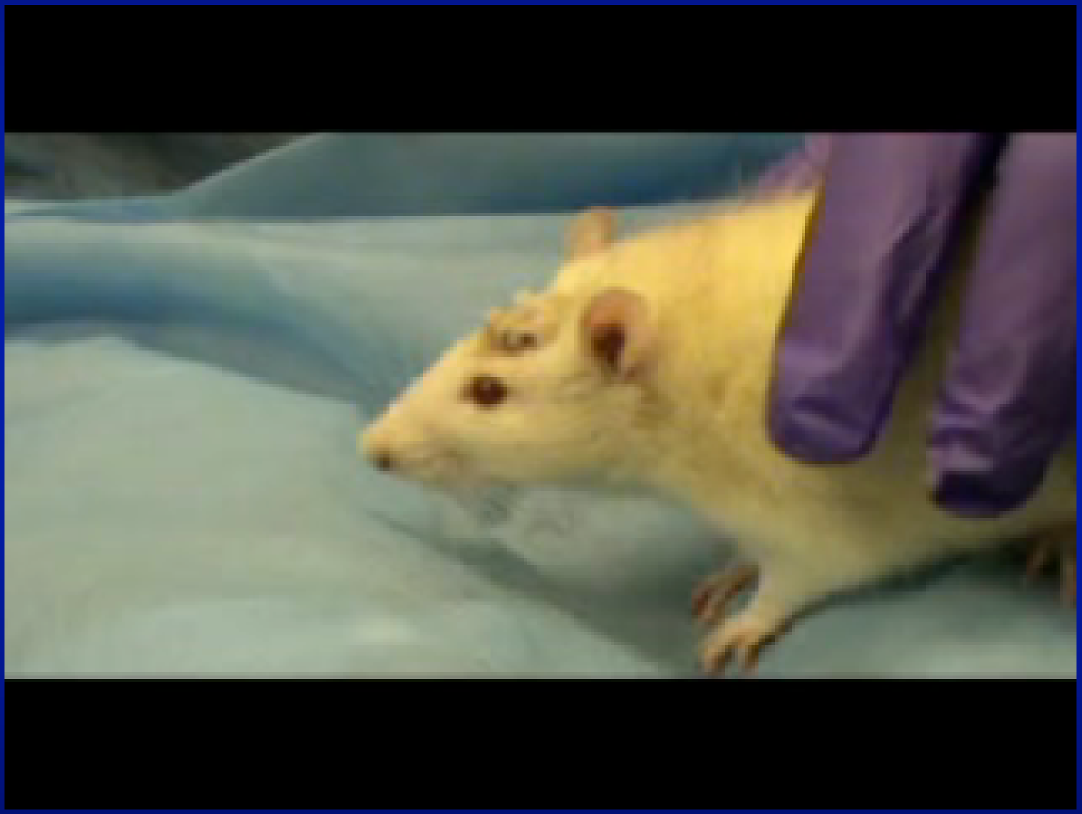
Animal Conditioning - Why?



Animal Conditioning



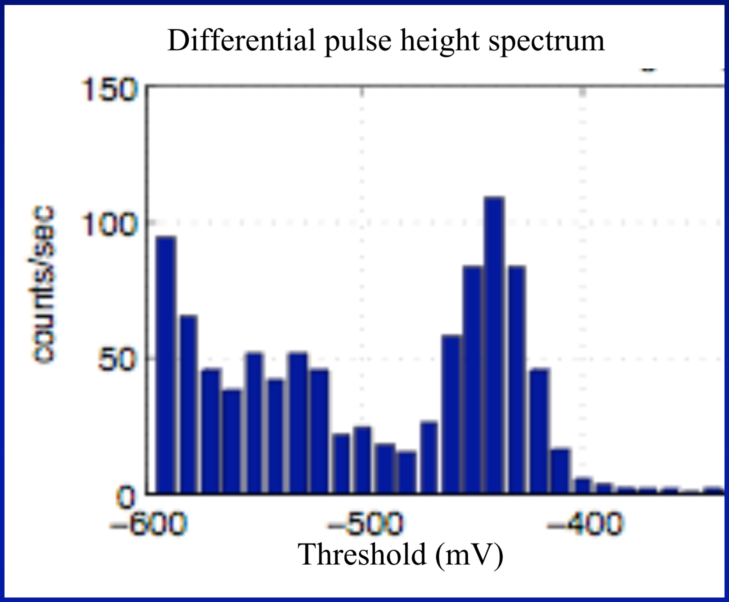
Mounting on Conditioned Animal



Wearing Full System

Preliminary Performance

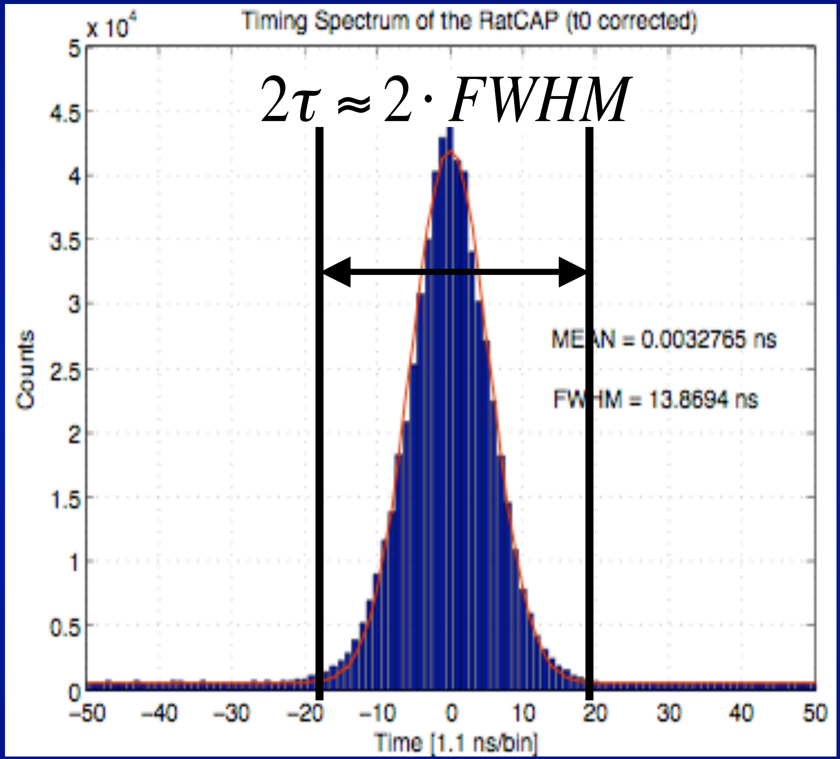
- Energy resolution - scatter rejection
  - avg 23% FWHM



Preliminary Performance

- Energy resolution - scatter rejection
  - avg 23% FWHM

- Time resolution - randoms rejection
  - avg 14 ns FWHM



$$R = 2\tau s_1 s_2$$

Preliminary Performance

- Energy resolution - scatter rejection
  - avg 23% FWHM
- Time resolution - randoms rejection
  - avg 14 ns FWHM
- Point source sensitivity - trues only
  - 0.7% @ 150 keV (0.4% @ 400 keV)

small-animal PET sensitivities
(@ LLD = 250 keV)

orig microPET (Cherry)	0.56%
ATLAS	1.8%
microPET R4	4.4%
microPET P4	2.3%
microPET II (Cherry proto)	2.3%
microPET Focus 220	3.4%
microPET Focus 120	7.7%

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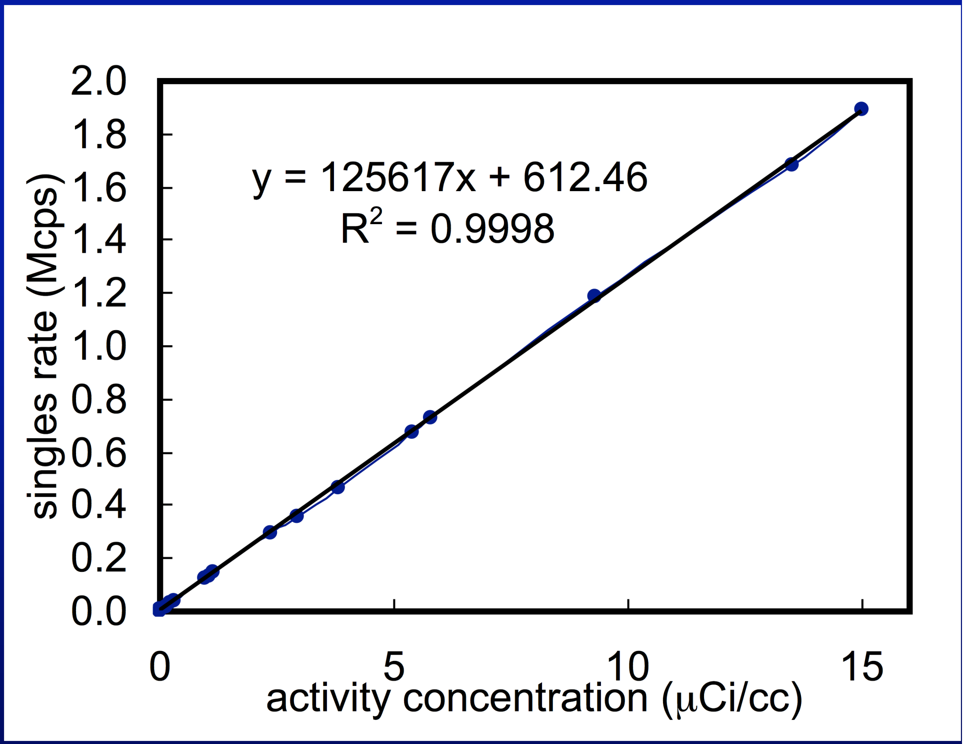

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- Point source sensitivity - trues only
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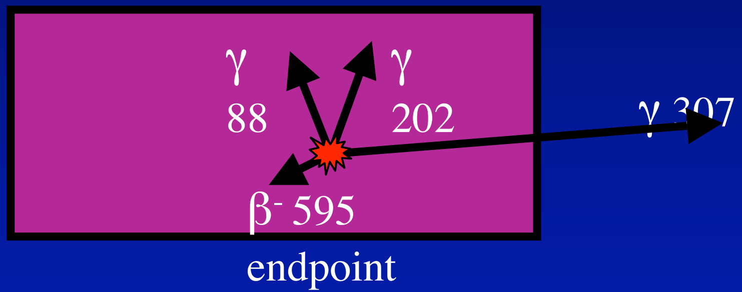
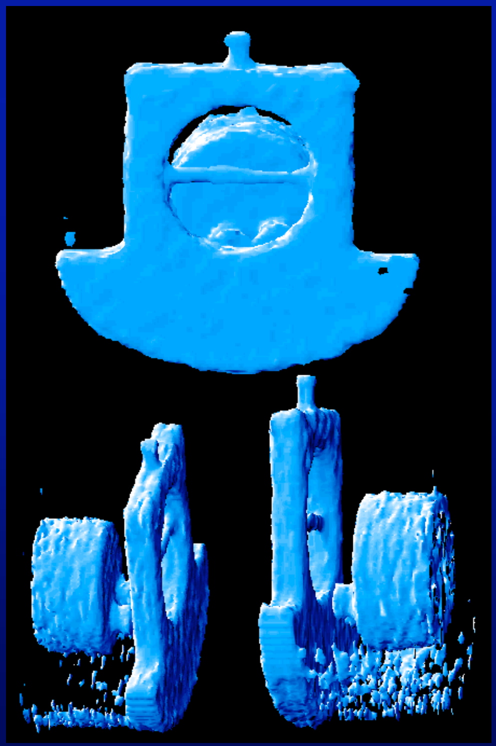
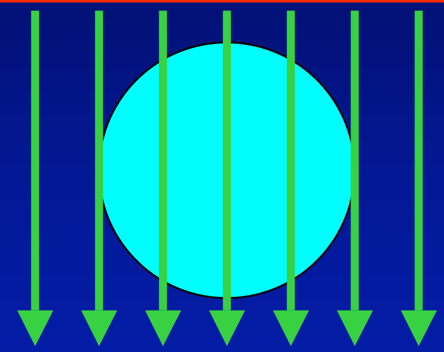
- Deadtime - bias
- Natural background from ^{176}Lu decay
  - calculate 2600 dps for whole system
  - true coincidence rate = 80 cps

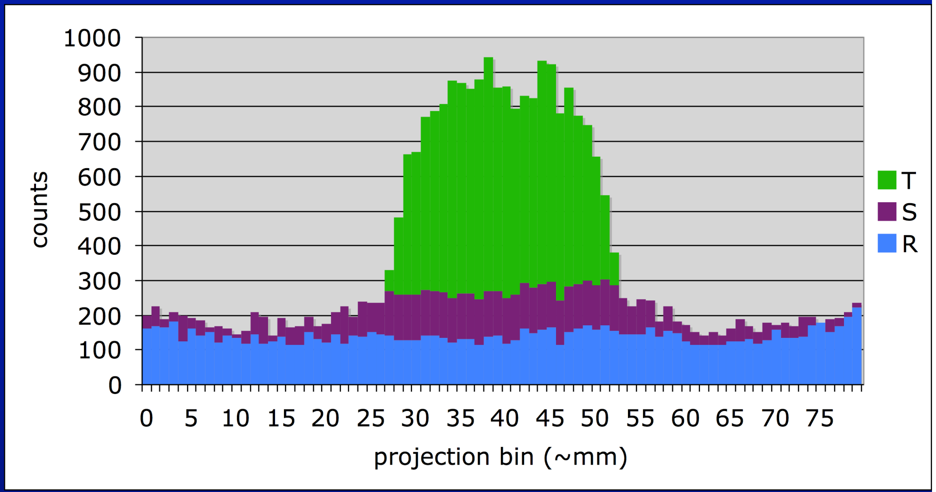




Noise Equivalent Countrate

- Trues rate alone not useful for estimating SNR
- Must account for added noise from background
- NEC = effective counting efficiency
- Counting statistics >> Poisson





$$N = T + S + R$$

$$T = N - S - R$$

$$\sigma_T = \sqrt{\sigma_N^2 + \sigma_R^2} = \sqrt{N + kR} = \sqrt{T + S + (1+k)R}$$

$$\frac{\sigma_{NEC}}{NEC} = \frac{1}{\sqrt{NEC}} \equiv \frac{\sigma_T}{T} = \frac{\sqrt{T + S + (1+k)R}}{T}$$

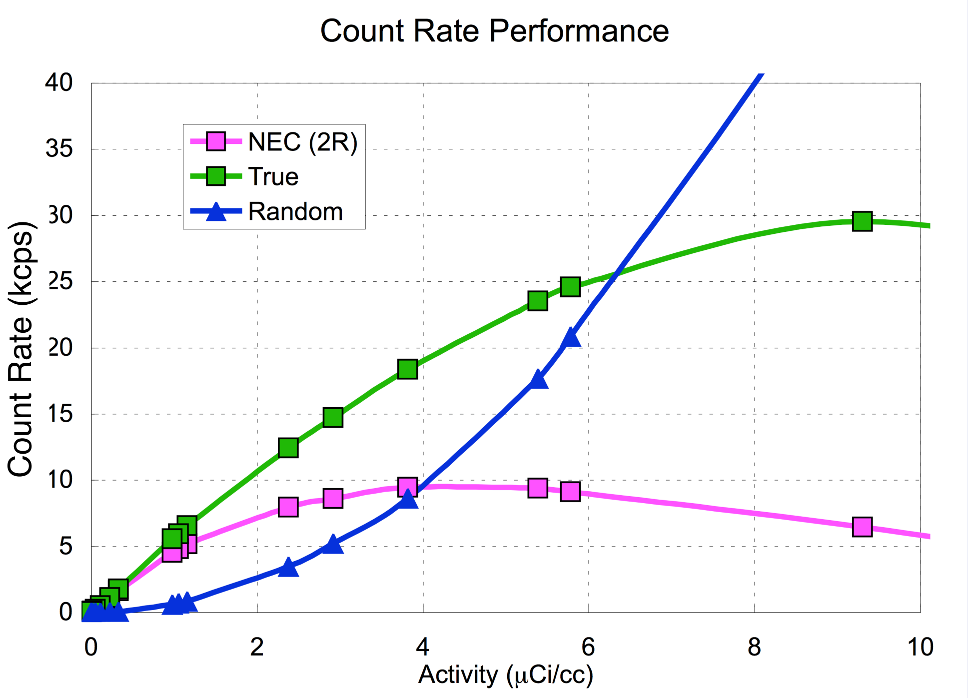
$$NEC = \frac{T^2}{T + S + (1+k)R}, \quad k = 0,1$$

if $S << T$ and $S << R$,

$$NEC \approx \frac{T}{1 + (2)(R/T)}$$

Preliminary Performance

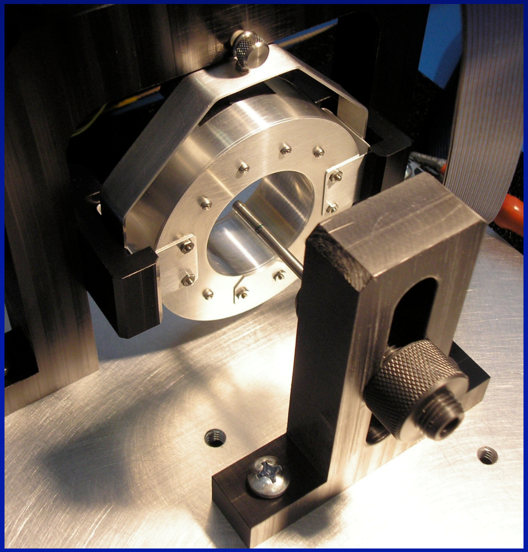
- NEC Results
  - phantom fills FOV, 19 cc
  - peak NEC 10 kcps @ 4 μCi/cc
  - 20 ns window: NEC to 14 kcps
  - microPET proto: 4 kcps @ 8 μCi/cc
  - microPET R4: 45 kcps @ 6 μCi/cc

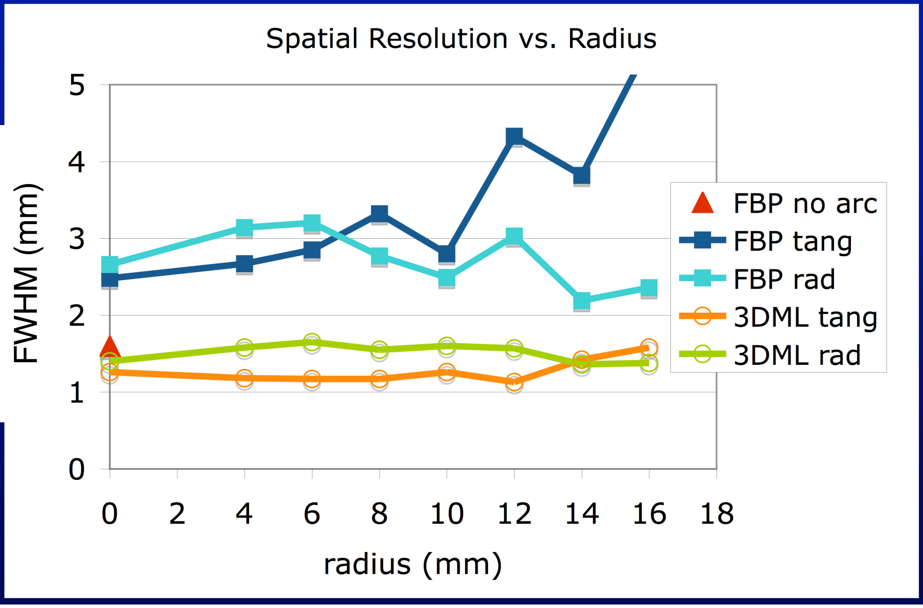


- Limitations
  - Difficult to estimate where real data falls
  - Phantom only within FOV: no OOFOV background randoms!
  - NEC ignores non-statistical aspects of image quality

Spatial Resolution

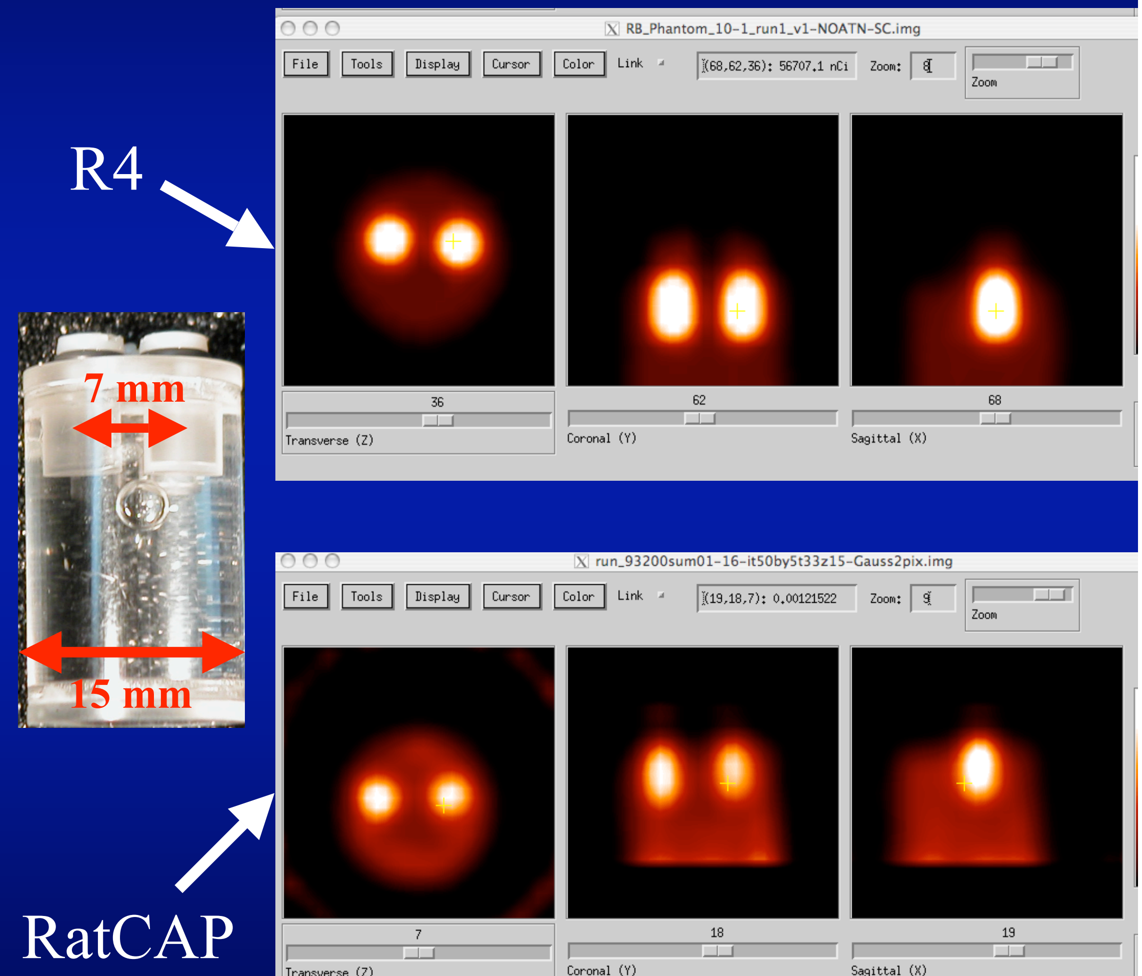
- ^{68}Ge point source
  - ~1 mm dia.
  - r = 0-16 mm
- 2D FBP
  - sinogram arc correction by linear resampling
  - ramp filter
- 3D Monte Carlo MLEM
  - 50 iterations
- Note:
  - arc correction parameters to be optimized
  - point source size NOT deconvolved





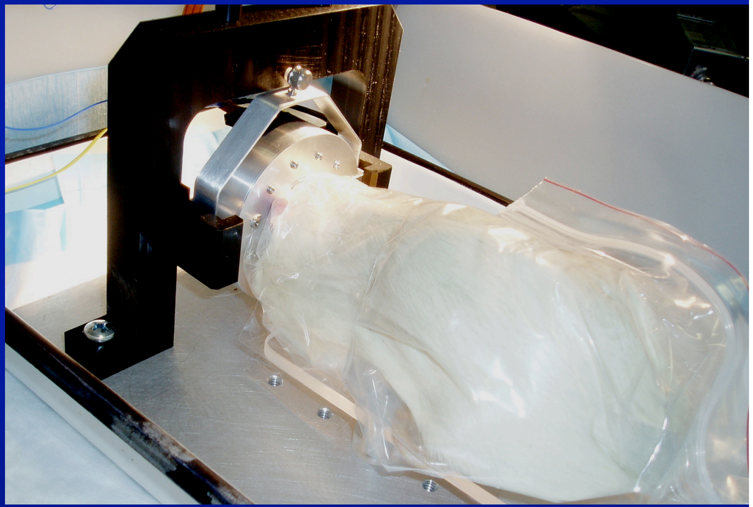
First Phantom Data

- Rat striatum phantom
  - 3.4:1 ratio
  - microPET R4
    - FBP (ramp)
  - RatCAP
    - MLEM
    - 25 iterations
    - post-smoothing with 2 mm FWHM Gaussian



First Rat Image

- Rat data
  - 517 g, 802 μCi ^{18}F-FDG i.p.
  - 45 min awake uptake, then chloral hydrate euthanasia
- microPET R4 scan
  - 10 min, LLD = 250 keV, 2τ = 10 ns
  - 3D MLEM (MAP w/ β=0, 20 iterations)
- RatCAP scan
  - 33 minutes livetime over 150 min scan
    - equivalent to 1.9 X decays of R4 scan
  - Monte Carlo-based 3D MLEM
    - 200 iterations
    - randoms correction
    - no efficiency correction (yet)

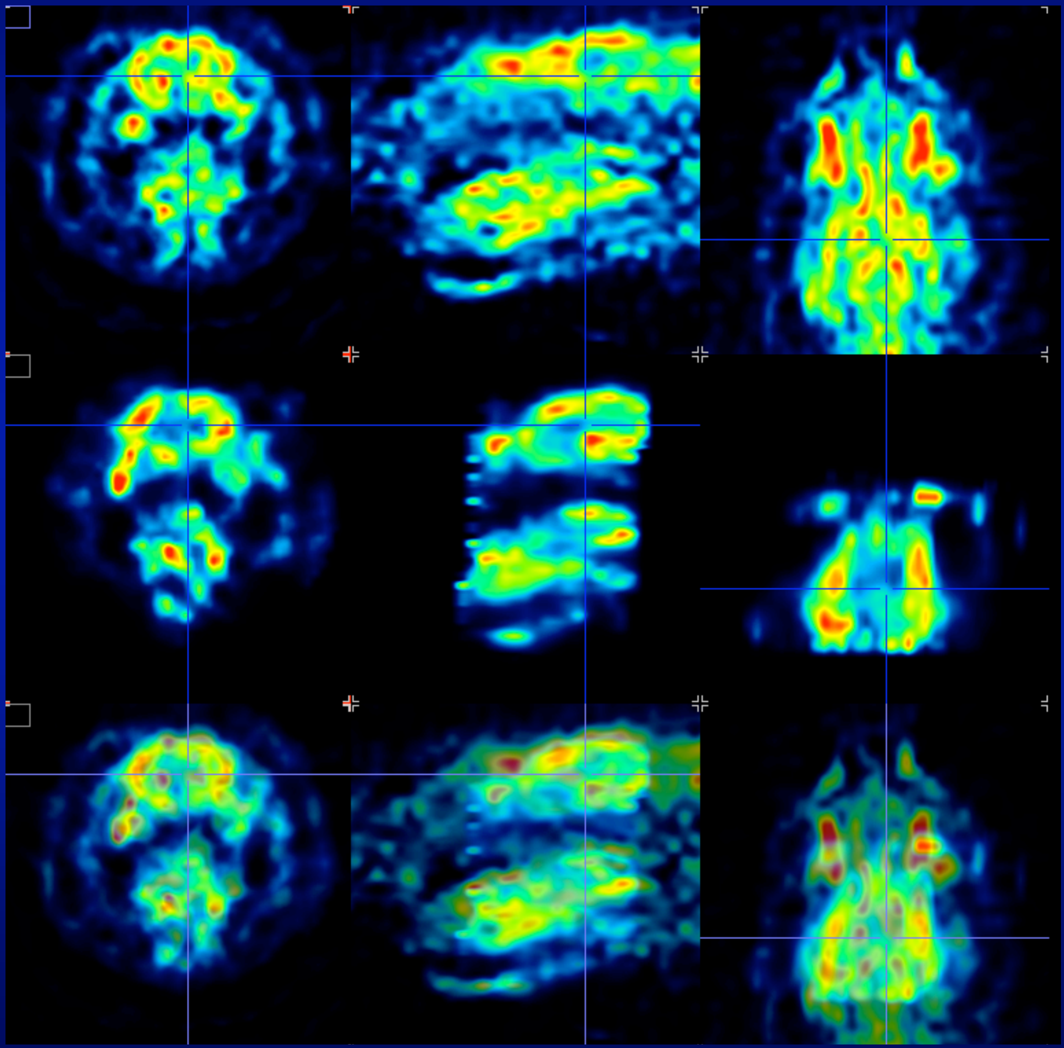


First Rat Image

microPET R4

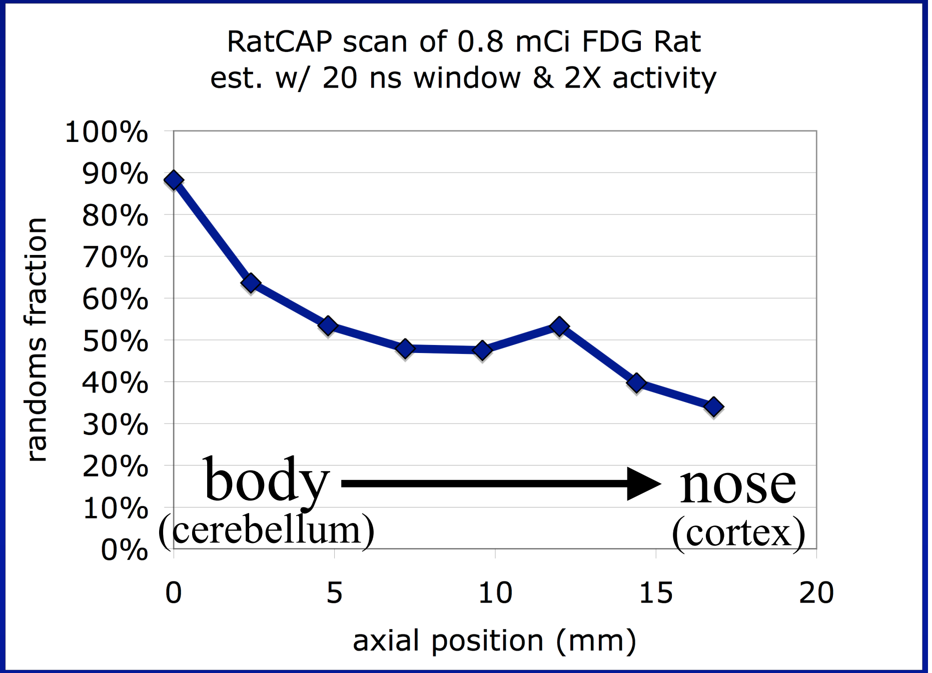
RatCAP
(coreg using pmod)

overlay



RatCAP v. microPET

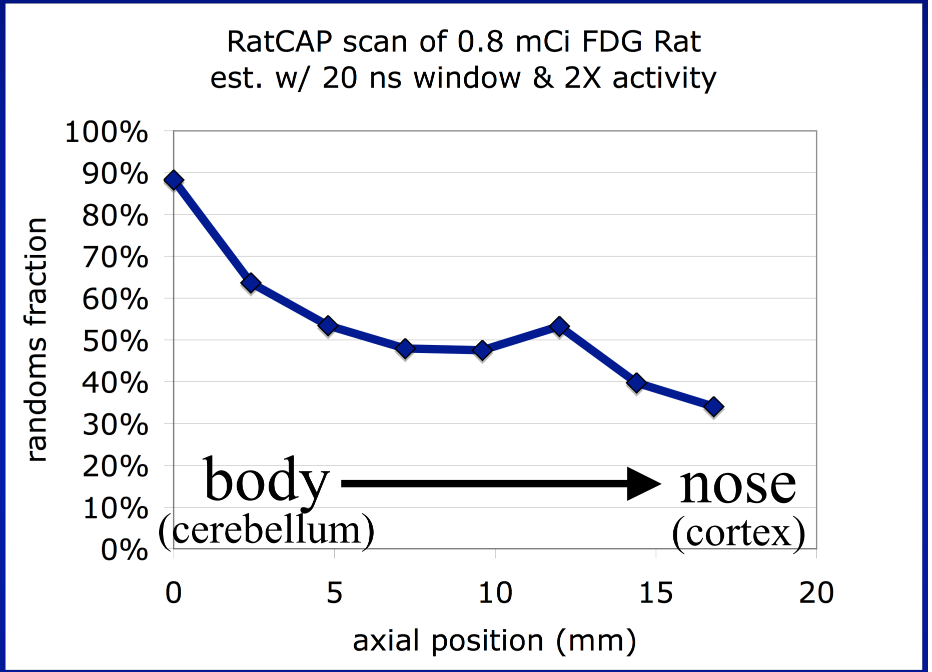
- Sensitivity lower but not easily improved
- Randoms fractions:
  - Realistic rates?
    - large rat, but FDG ~0.8 mCi >> high end of expected count rates for neuroreceptor studies
    - average activity ~1/2 of mPET activity (scanned later and for 3X longer)
    - cancels w/ 20 ns window
  - microPET data:
    - ~5 % randoms fraction within subject



$$NEC \approx \frac{T}{1+(2)(R/T)}$$

Goals for Timing

- Effects of planned improvements:
  - individualized, higher LLDs
    - T ~ same, S lower, R lower due to lower singles rates
  - variance reduction in randoms should give factor of 2!
  - to 1st order, thicker crystals do NOT change fraction (2x length gives 2x singles = 4x randoms but also 4x trues)



- Goal
  - Reduce R/T at FDG brain rates to ~10%
  - Now, estimate ~ 50% average, or 25% w/ randoms variance reduction
  - >> ~2X better timing = 5 ns FWHM to allow 10 ns window

$$NEC \approx \frac{T}{1 + (2)(R/T)}$$

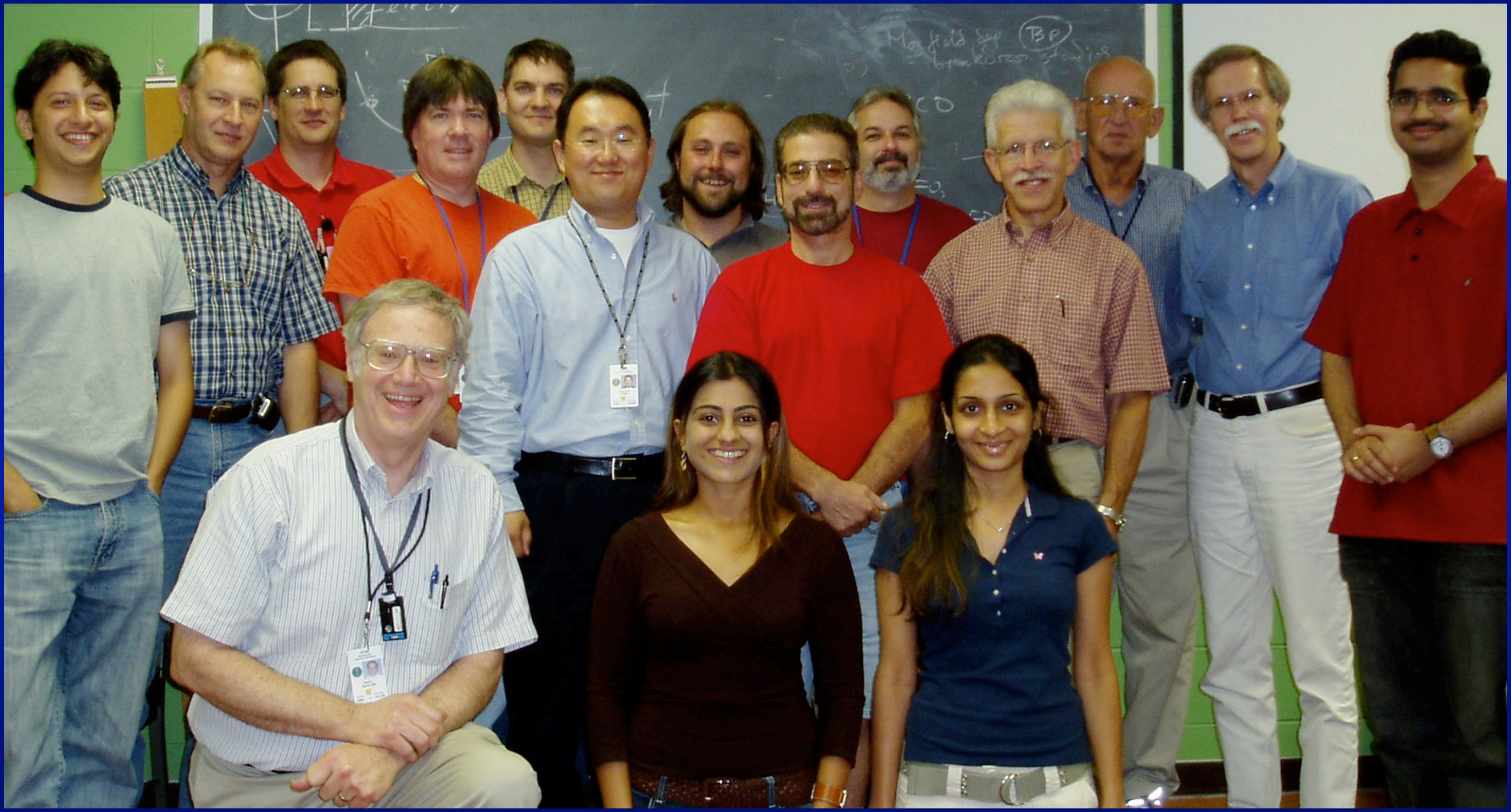
Developments Underway

- Hardware:
  - ASIC
    - Add individually adjustable thresholds and/or VGA
    - Add ESD pad protection
    - Future: improved timing & some energy info (time-over-threshold?)
  - Improve sensitivity w/ longer crystals: parallax/weight tradeoff
  - MRI-compatible version & testing

- Software
  - Correct for timing offsets & narrow coincidence window
  - Validate quantitative corrections, including scatter from outside the FOV
  - Reduce variance caused by randoms correction by calculating from singles rates (no coinc proc deadtime)

- Animal studies
  - Quantify stress levels w/ corticosterone & behavior measures
  - Full neuroreceptor study
  - F-18 fluoride bone scan

Thanks!



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