Flexible Geometry High Sensitivity SPECT System for Small Animals and Plants

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Sensitivity Motivation

Small animal SPECT sensitivity is typically 0.1% (or lower)
[resolution: typically ~1 mm, though sub-mm achieved in several systems]

With improved sensitivity, *in vivo* radionuclide molecular imaging studies can be performed with:

- Less time per animal (higher throughput for screening)
- Less radiotracer ($ or low-yield chemistry)
- Less dose to investigators and subject
- Better temporal resolution

Applications requiring high sensitivity:

- Imaging of low abundance, easily saturated receptor targets
- Stem cell tracking
- Plant imaging with low uptake

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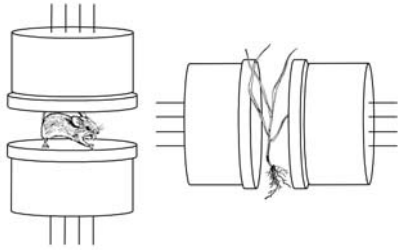
System Concept

Nuclear imaging for thin subjects – small animals and plants



No collimators, compact geometry, large solid angle.
Sensitivity & resolution tradeoff...
Imaging possible with a few μCi? nCi?
Alternative to optical imaging?

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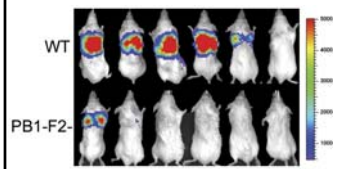
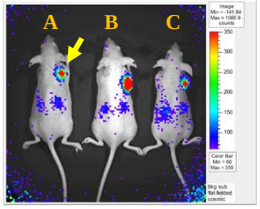
Optical Imaging

For *in vivo* mouse imaging, optical imaging is the predominant modality today-- far more optical imaging studies are performed than PET/SPECT, despite the relatively poor spatial resolution.

Examples:



J. L. McAuley, et al. "Expression of the 1918 Influenza A Virus PB1-F2 Enhances the Pathogenesis of Viral and Secondary Bacterial Pneumonia", *Cell Host and Microbe* **2** (2007) 240-249.



Aweda TA, ***et al.*** "New covalent capture probes for imaging and therapy, based on a combination of binding affinity and disulfide bond formation" Bioconjug Chem. **22** (2011)1479-83.

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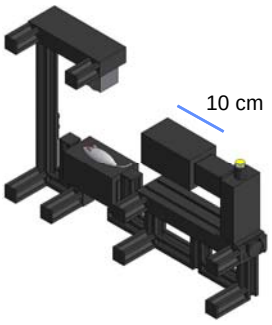
Design for uncollimated detector system

Two detector heads with pixelated scintillator arrays

flexible geometry

interchangeable arrays

based on earlier work:
Phys. Med. Biol. **54** (2009) 1291–1305



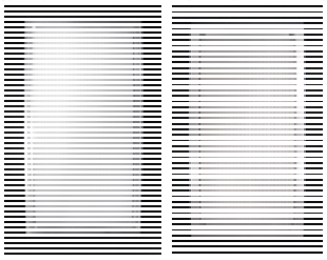
Design for uncollimated detector system

Hamamatsu H8500 (5 cm)
x2 per detector head

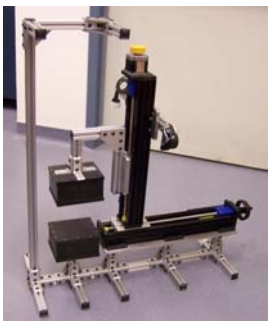
Resistor network readout board (x, y, E)

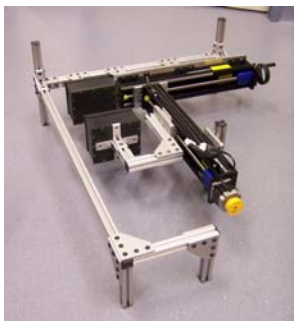
Scintillator arrays

Material	Quantity	Manufacturer	Thickness	Pixel Size	Pitch	Number of Pixels
NaI(Tl)	1	Saint Gobain	3	1.5 x 0.1	1.7 x 0.1	24 x 51
NaI(Tl)	1	Saint Gobain	3	2 x 0.1	2.2 x 0.1	21 x 41
CsI(Na)	2	Hilger	3	1.5 x 0.1	1.6 x 0.1	28 x 56
BGO	2	Proteus	5	1.9225	2	25 x 50

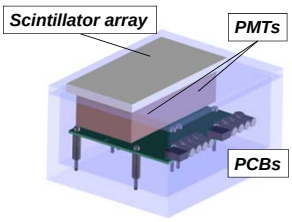


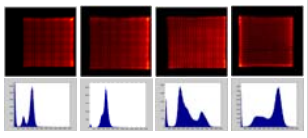
Design for uncollimated detector system





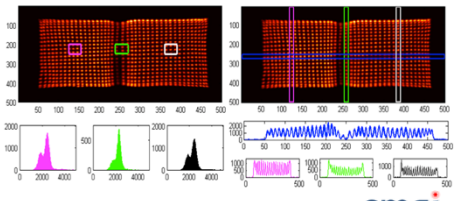
Design for uncollimated detector system





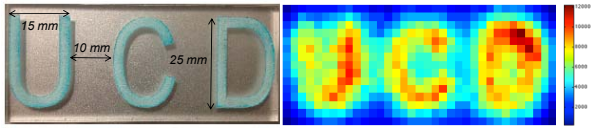
NaI(Tl): Co-57 source
(122 and 136 keV)

Energy resolution:
14% (22% in gap)



Simple phantom image (1 µCi ^{99m}Tc per letter)

Phantom (photo) *Image (one detector)*



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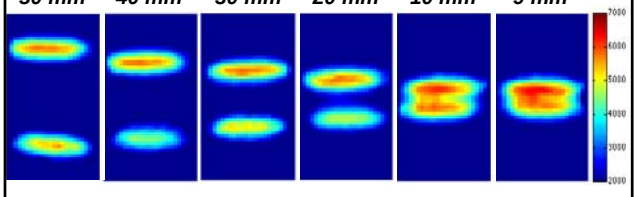
Spatial Resolution

- Two 1 mm diameter capillary tubes (each with 1 µCi Tc-99m)
- 3 mm from detector face, image from lower detector only
- Spatial resolution ~1 cm

50 mm *40 mm* *30 mm* *20 mm* *10 mm* *9 mm*



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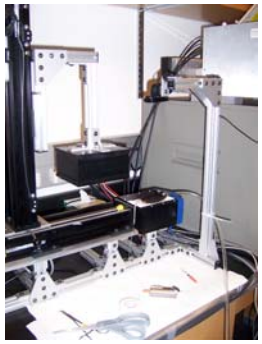
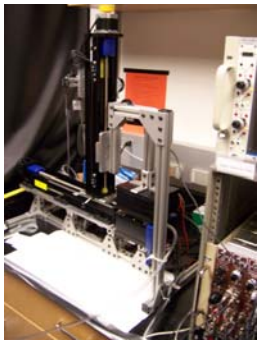
Small Animal Imaging





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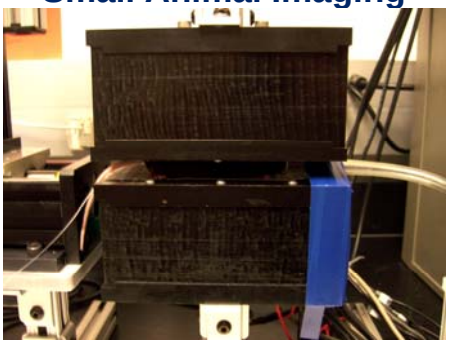
Small Animal Imaging



dynamic scan: injection with 5 µCi (185 kBq) of Tc-99m MAG-3 (mercaptoacetyltriglycine), a renal function imaging probe

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In vivo Dynamic Imaging

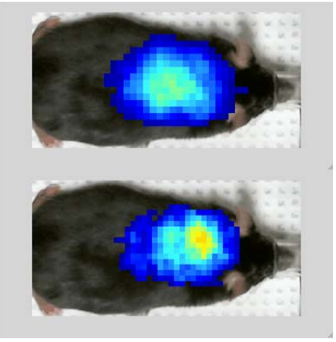
5 µCi Tc-99m MAG-3

Event rate 66 kcps

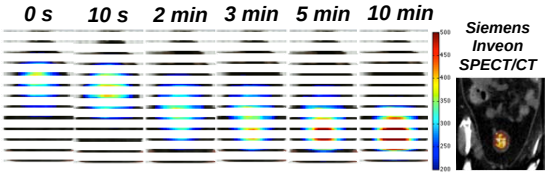
Each frame 6 s of data
Total movie ~14 minutes

Image pixels are detector crystals

Images thresholded & smoothed



In vivo Dynamic Imaging



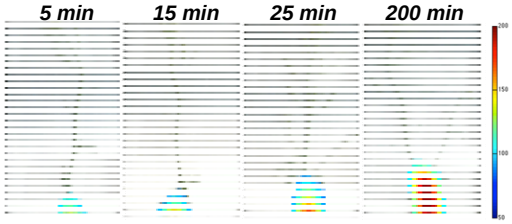
Six frames of a ^{99m}Tc MAG-3 dynamic scan. Color scale units are counts per crystal per 2 s.

Reconstructed coronal slice of mouse from Siemens Inveon SPECT/CT scan 45 min post injection.

Plant Imaging

- Arabidopsis thaliana cuttings incubated in 100µL/30 µCi Tc-99m pertechnetate solution for different durations.

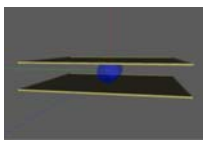
→Shows migration of the isotope in the xylem.

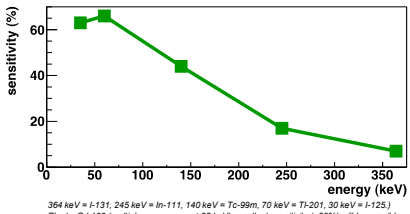


[Images thresholded and Gaussian smoothed. Rightmost image: 1500 cps = 100 nCi in plant.]

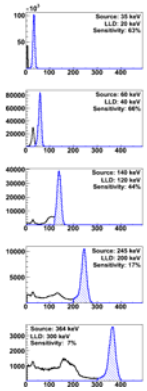
Sensitivity: GATE simulation

- two 3x130x130 mm^3 NaI detectors
- separation 22 mm
- 2 cm dia. x 6 cm long water cylinder
- monoenergetic point source at CFOV
- 20% energy resolution

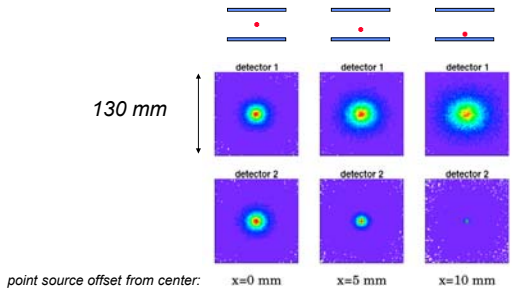




364 keV = I-131, 245 keV = In-111, 140 keV = Tc-99m, 70 keV = Tl-201, 30 keV = I-125.)
Plants: Cd-109 (multiple gamma rays ≤ 88 keV) excellent sensitivity (~50%) will be possible; Zn-65 (1.116 MeV gamma ray) ~2% with 3 mm thick BGO



2D response of detectors vs. depth



The difference in p.s.f. with depth provides a (limited) ability to resolve in the z direction (normal to the detector faces)

Sensitivity (*in vivo*)

- 185 kBq (5 μCi) injected activity
- Tc-99m b.r. 89% -->140 keV gamma

- 66 kcps recorded events, accept 95% on energy and position cuts
- Background < 400 cps

(66 x 0.95)/(185 x 0.89) =
38% sensitivity for emitted gammas

Summary

The prototype system has:

- Average energy resolution of 17% at 140 keV.
- Effective spatial resolution of ~1 cm. [Sufficient to distinguish major organs in the mouse.]
- Sensitivity of 38% at 140 keV (Tc-99m) in an *in vivo* study.

Summary

- We have built a prototype high-sensitivity single photon imaging system.
- With extremely compact geometry and no collimators, images are formed by solid angle effects alone.
- We are working to calibrate and characterize our system, and (currently with Monte Carlo data) to study ideas for tomographic reconstruction, using geometrical sparsity constraint.

Planned studies:

- In-111 oxine stem cell trafficking (mouse)
- I-125 labeled antibody against xenograft tumor in mouse (anti-CD20, Raji cell line)
- Zn-65 & Cd-109 imaging of heavy metal hyperaccumulation (Arabidopsis halleri vs. Arabidopsis thaliana)

- There are many applications for radionuclide imaging which do not require good spatial resolution.

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