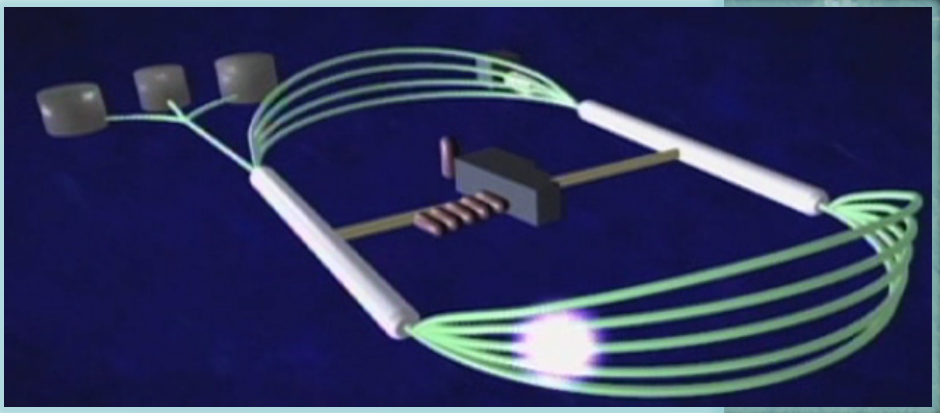
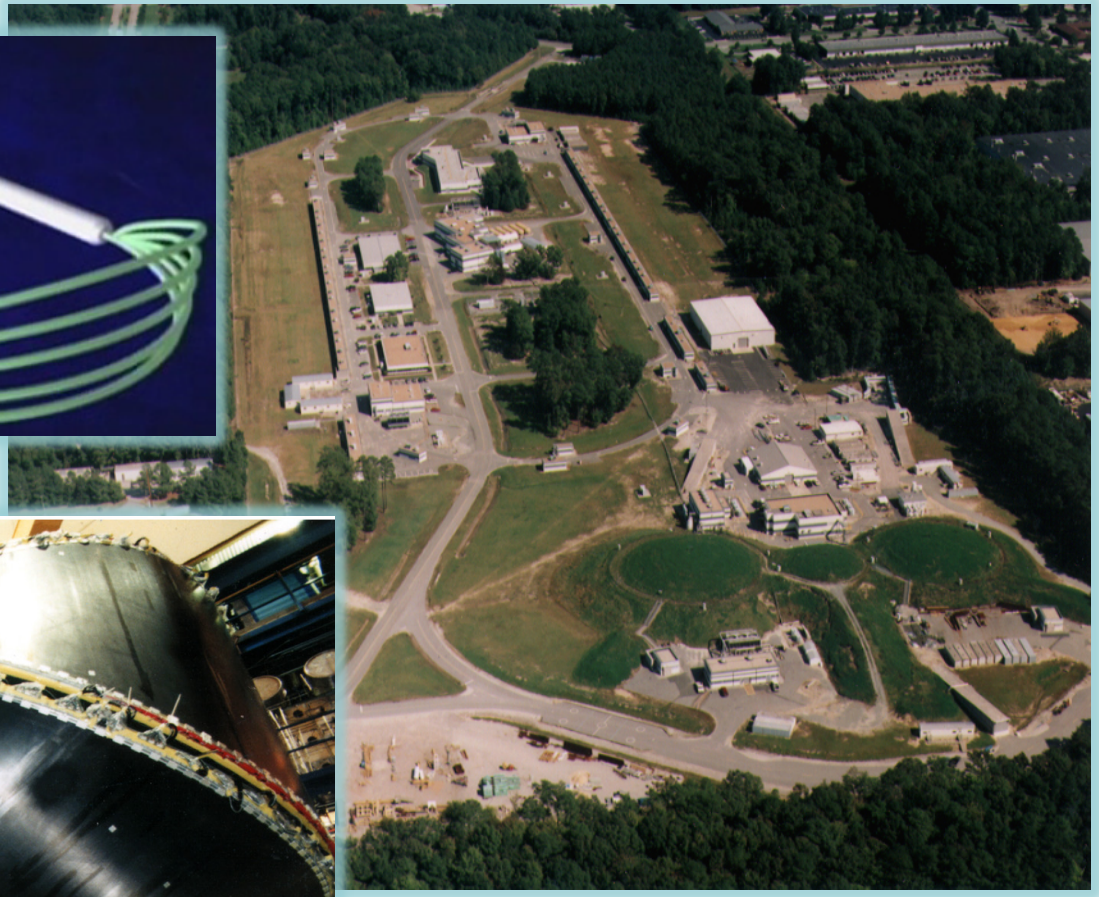
Radiation Detecting & Imaging *Bio/Medical Applications of Jefferson Lab's Nuclear Physics Detector Technology*

Drew Weisenberger
Radiation Detector and Imaging Group
Physics Division
Thomas Jefferson National Accelerator Facility

JLab's Continuous Electron Beam Accelerator Facility





Radiation Detector & Imaging Group

- Support design and construction of new detector systems
- Technical consultants for the lab scientists and users
- Development and use of imaging and non-imaging detector systems
- Expertise in nuclear particle detection

Brian Kross- mechanical engineer
Jack McKisson- electrical engineer
John McKisson- software engineer
Dr. Seung Joon Lee- detector scientist
Dr. Wenze Xi- detector scientist
Dr. Carl Zorn- detector scientist

Bethany Wissman, DOE-SULI intern

Tech Transfer: Leveraging the National Lab Strengths

Technical resources brought together to do basic nuclear physics research:

- advanced radiation detection methods
- state of the art electronics development
- software development for 3D imaging
- high performance data acquisition
- optics

Applying nuclear imaging detector techniques for challenges in other fields:

- **nuclear medicine** for improved patient care
- **bio-medical research** using radioisotopes
- **biological systems research** using radioisotopes

Jefferson Lab is a single purpose lab requiring collaborations →

External Partners

- Oak Ridge National Laboratory
- Triangle Universities Nuclear Laboratory

- West Virginia University
- Hampton University Proton Therapy Institute
- University of Virginia
- University of Maryland
- Johns Hopkins University
- Case Western Reserve University
- College of William and Mary
- Duke University
- Columbia University

- Dilon Technologies, Inc.

Internal Partners

- Fast Elec. Group
- DAQ Group

External Funding
(beyond DOE NP)

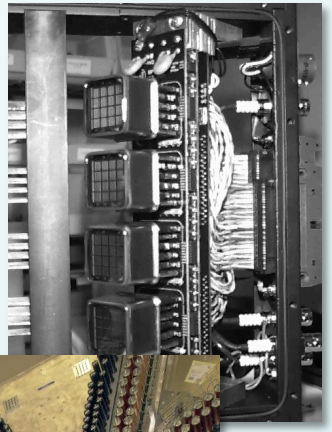
- DOE BER
- NIH (WFO)
- DOD
- JSA

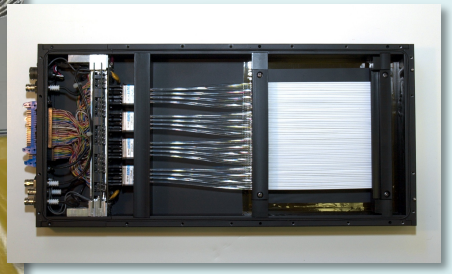
Tech Transfer

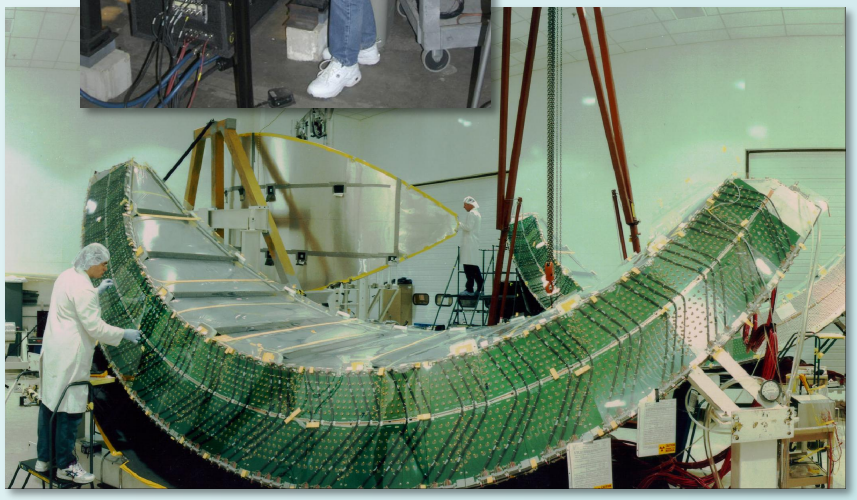
JLab Patents:	1991-present: ~150
Physics Div. Patents:	1995-present: ~40
Detector Grp. Patents:	1995-present: 33

Detector Physics

Detector Components



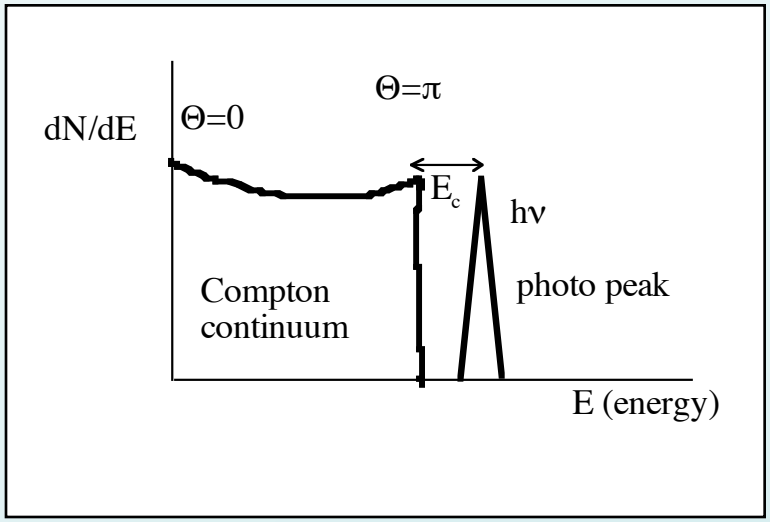


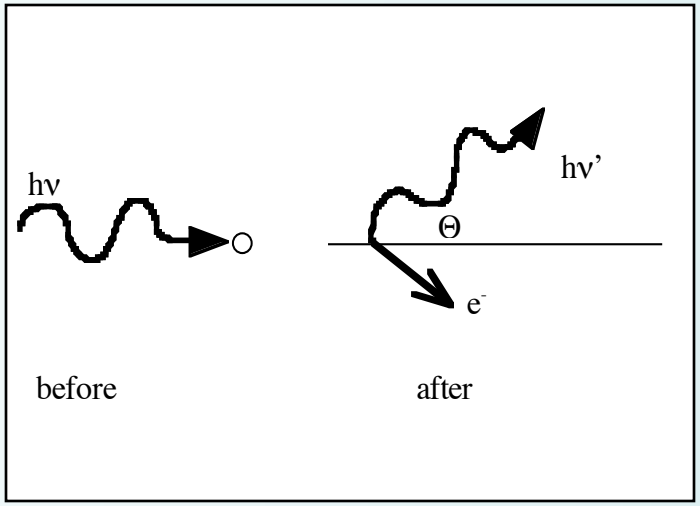


Detecting and Imaging Radioactive Decay (a nuclear process)

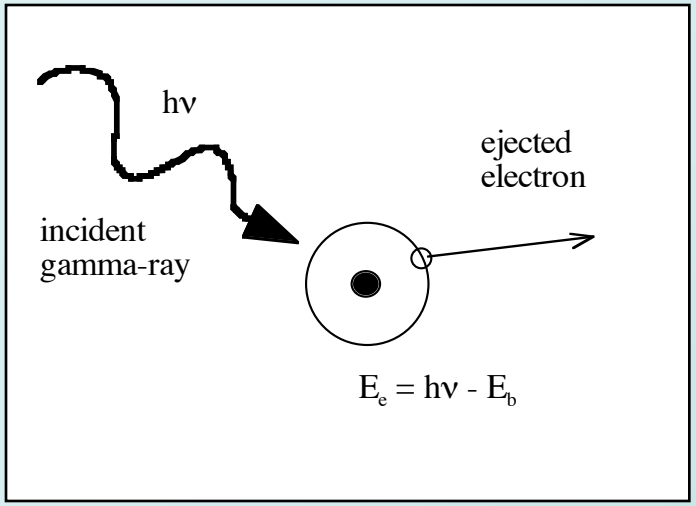
Scintillator: transparent material for detecting high energy photons (i.e. x-rays, gamma-rays)

A high energy photon deposits energy in the atoms of the scintillator resulting in the release of lower energy photons that can then be converted to an electrical signal by devices called photomultiplier tubes (PMTs).



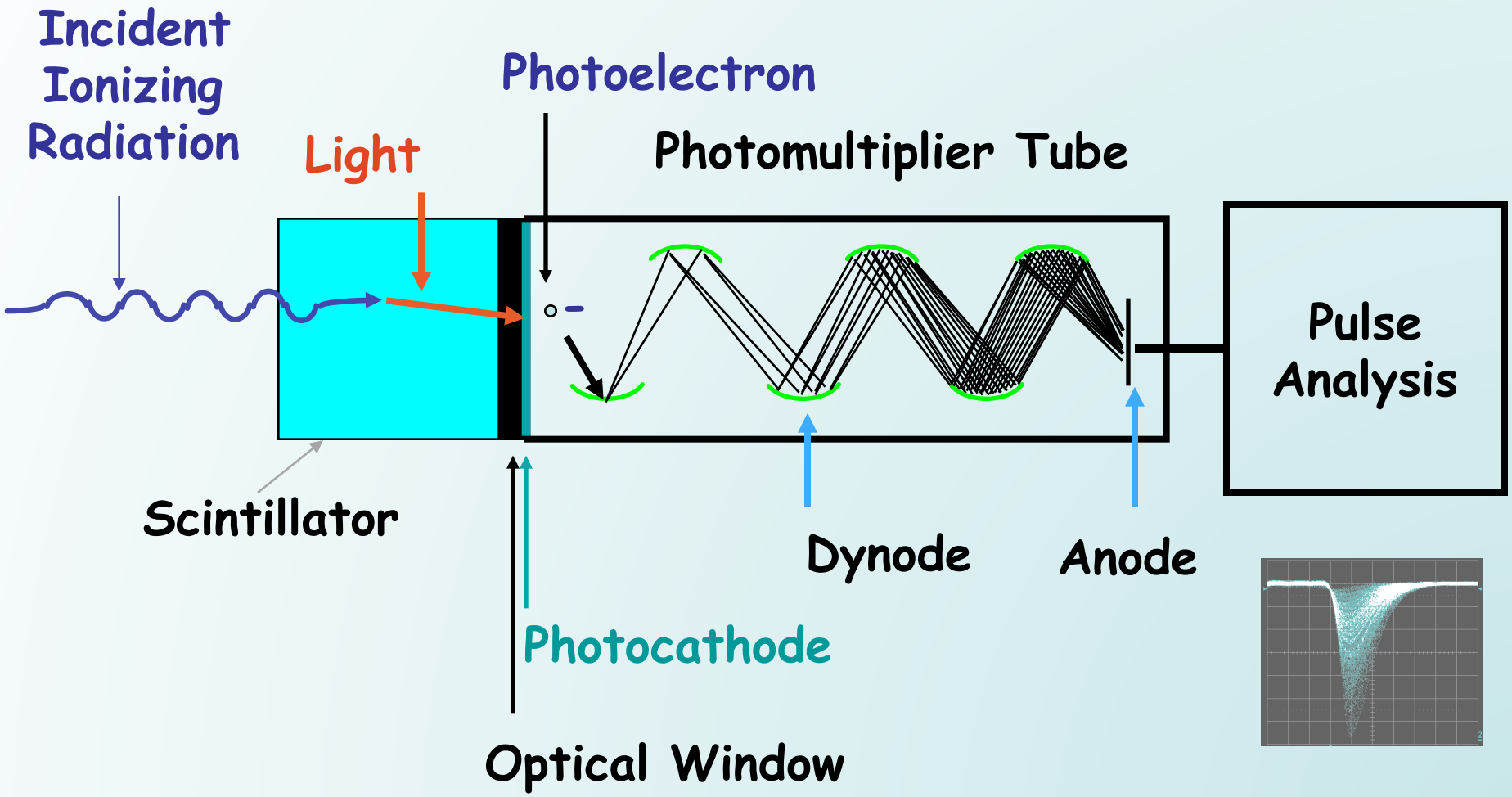


Compton Scattering



Photoelectric Absorption

Scintillation Detection



Radiotracers & Biology

Sensitive

- Tens of Molecules Detected, Tens of Thousands Imaged

Radiation is penetrating

- Image Interior of Object, Not Just Surface

Trace amounts used

- Doesn't Perturb System Measured

Short half-life isotopes

- Object Imaged Not Radioactive for Long
- No Radioactive Waste

Non-destructive

- Object Not Harmed
- Repeat Studies Performed (Including as Own Control)

Many Chemical Compounds can be labeled

- Many different biochemical systems probed

Radiotracer Imaging Properties

Spatial Resolution: 1–10 mm

Field of View: 0.5 meter

Temporal Resolution: 1 second

Sensitivity: nanomolar

Experiment Duration: seconds — hours

Tracer Isotopes: ^{18}F, ^{11}C, ^{13}N, ^{15}O, & many others

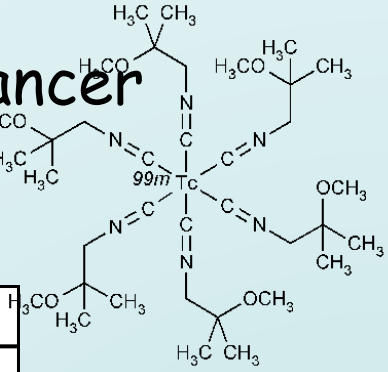
Tracer Compounds: Hundreds…

Most common single photon emitters used in nuclear medicine

Isotope	Half-live	γ energies -keV (photon abundance)
technetium-99m (^{99m}Tc)	6.02 hours	140 (89%)
indium-111 (^{111}I)	2.83 days	170 (94%), 240 (90%)
gallium-67 (^{67}Ga)	3.25 days	93 (37%), 185 (20%), 300 (17%), and 394 (4%)
iodine-123 (^{123}I)	13.3 hours	159 (84%)

^{99m}Tc-sestamibi: $C_{36}H_{66}N_6O_6{}^{99m}Tc$

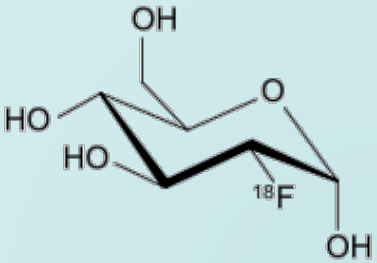
→ targets cells with active mitochondria e.g. cancer



Most common positron emitters used in nuclear medicine

Positron Emitting Isotope	Half-life (minutes)	Positron E_{max} (MeV)
oxygen-15 (^{15}O)	2.07	1.72
nitrogen-13 (^{13}N)	9.96	1.19
carbon-11 (^{11}C)	20.4	0.96
fluorine-18 (^{18}F)	109.7	0.64

^{18}F -fluoro-2- deoxyglucose (FDG): $C_6H_{11}{}^{18}FO_5$



→ targets rapidly growing cells e.g. cancer

Bio-Medical Imaging Modalities

Structural

Functional

Somatostatin receptors (neuroendocrine tumors)

www.radswiki.net

Nuclear Imaging/Molecular Imaging

-the Basics:

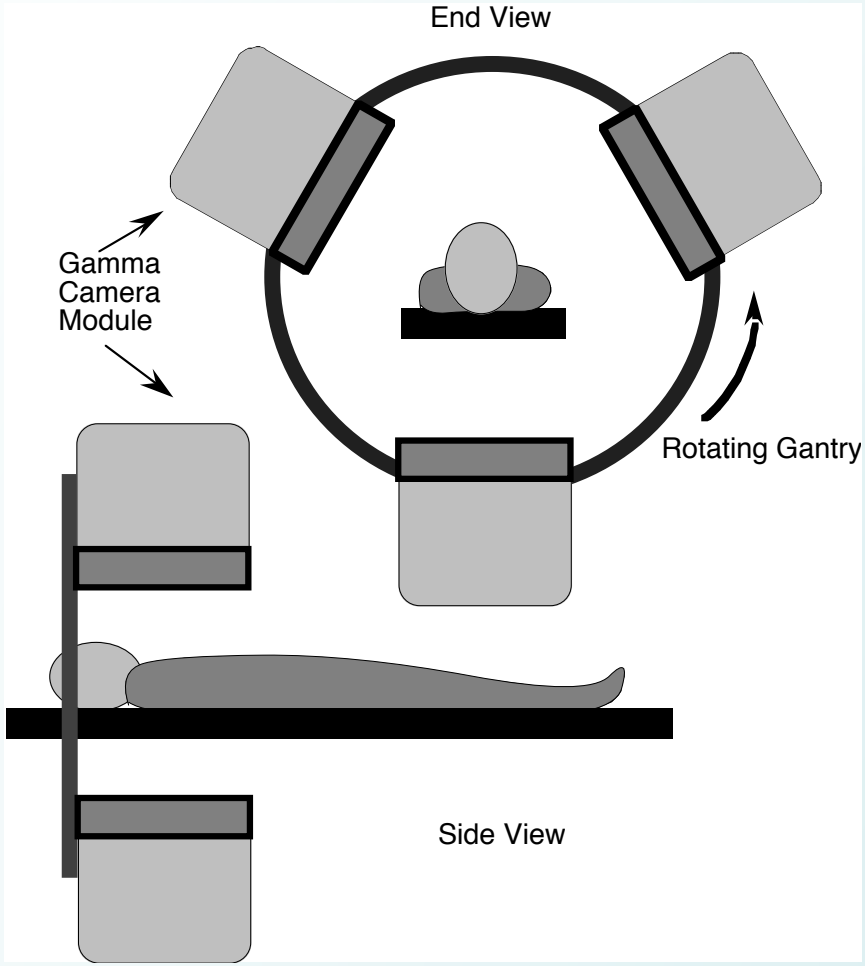
Radioisotopes that emit high energy photons and beta particles are incorporated into molecules that have a biological function of interest. The tagged molecules are then injected or introduced *in vivo* into biological systems:

- people
- animals
- plants
- microbes

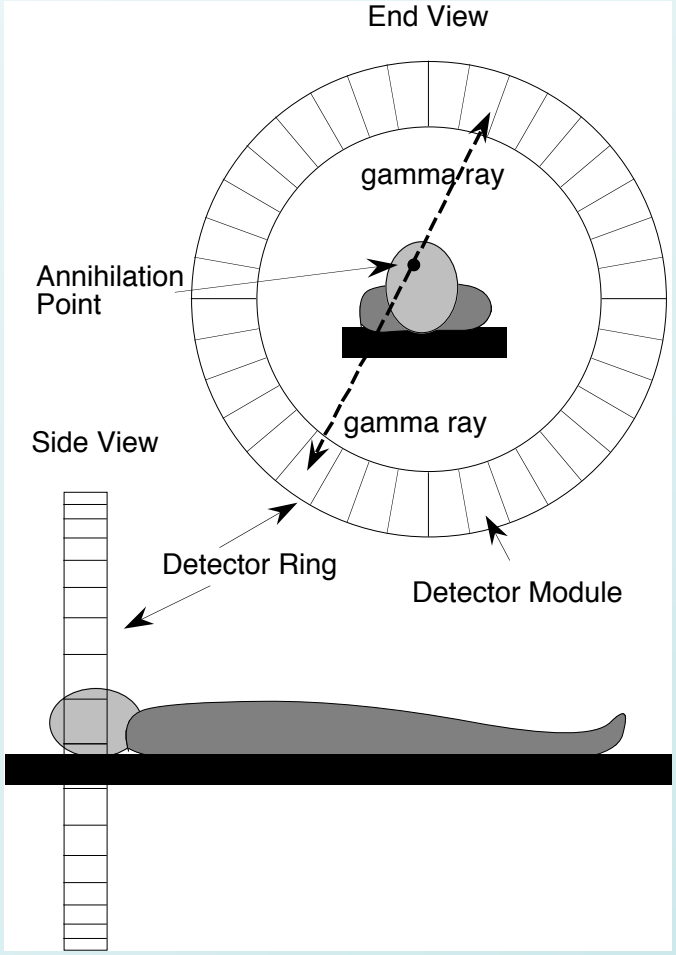
Molecular Imaging: The bio-distribution of tagged molecules is imaged externally by devices capable of detecting the emitted particles. Typically the high energy photons are highly penetrating thus can be detected and imaged externally. Two molecular imaging techniques:

- Single Photon Emission Computed Tomography (SPECT)
- Positron Emission Tomography (PET)

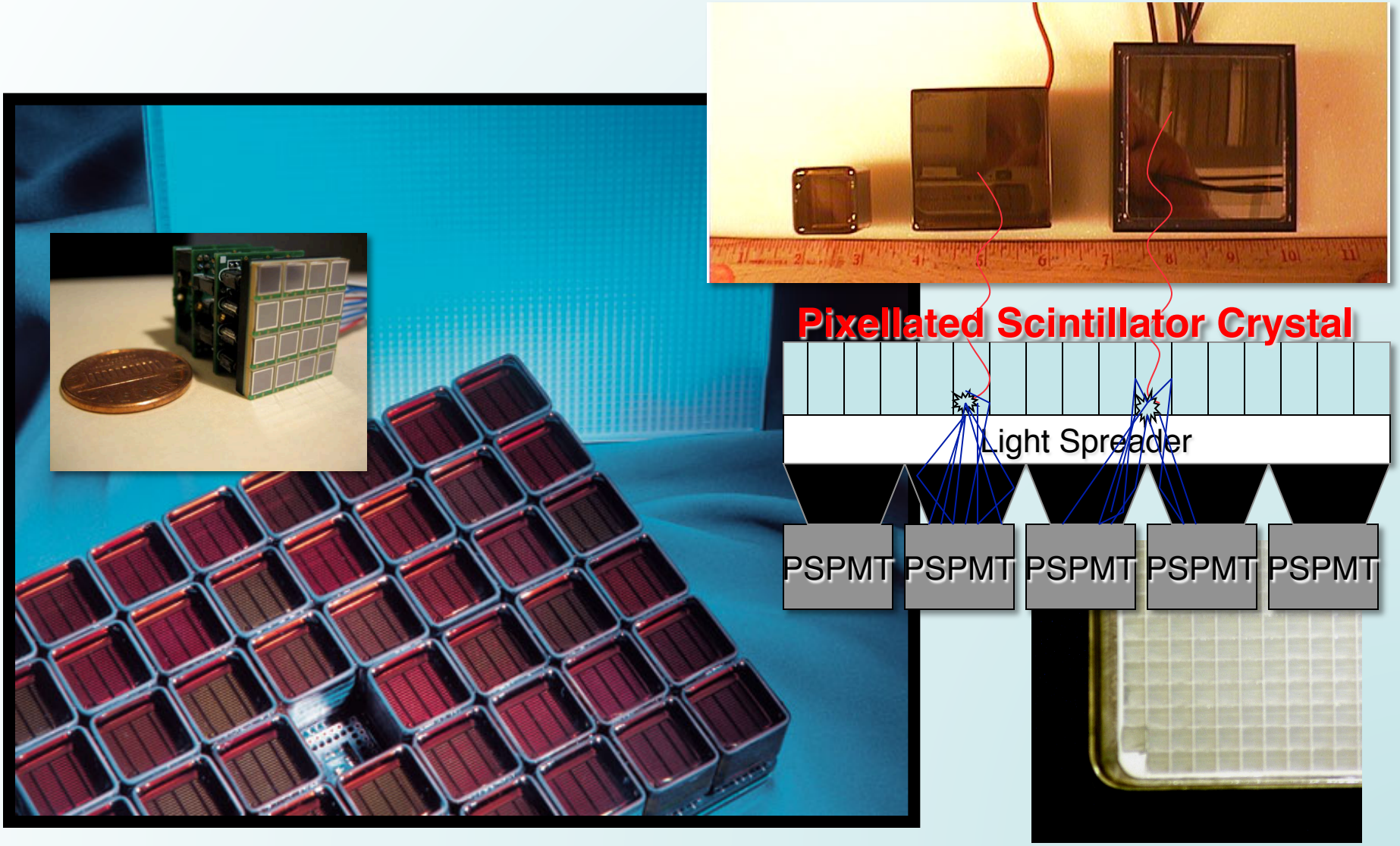
Clinical SPECT System



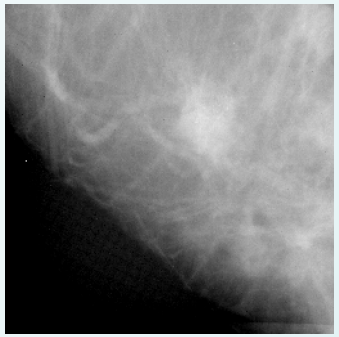
Clinical PET System

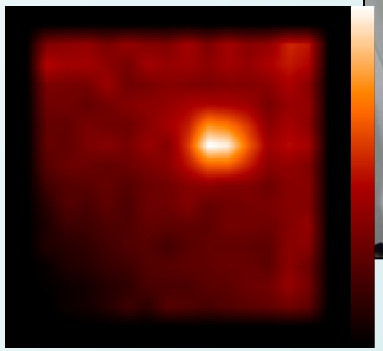


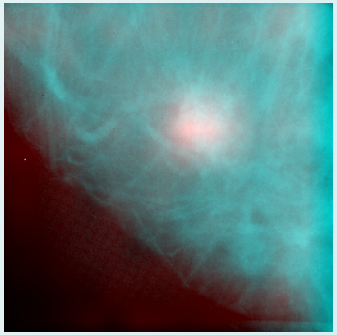
Latest photomultiplier technology allows modular detector construction

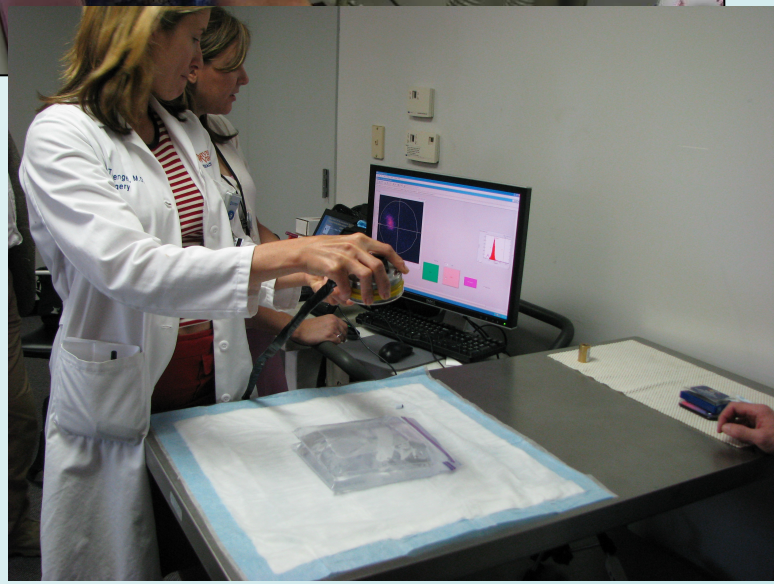


Clinical Nuclear Medicine Imaging

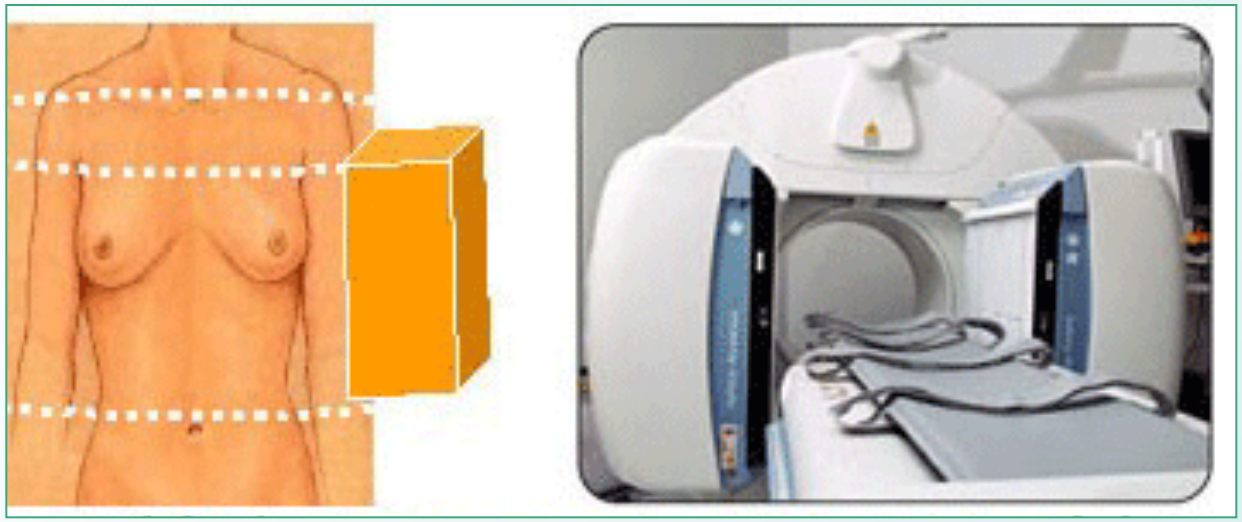




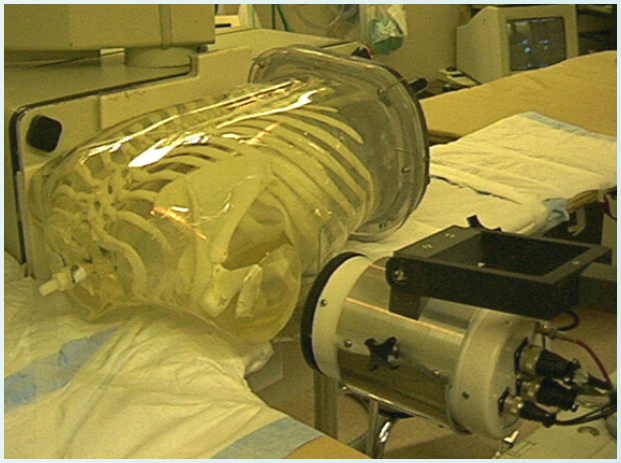




Detect Cancer: Breast-Specific Gamma Imaging



Need for a Detector Built for the Task



Dilon 6800 Gamma Camera

Smart Shield™ immobilizes the breast and prevents shine-through

Compact detector allows imaging close to the chest wall

Several patents licensed from JLab

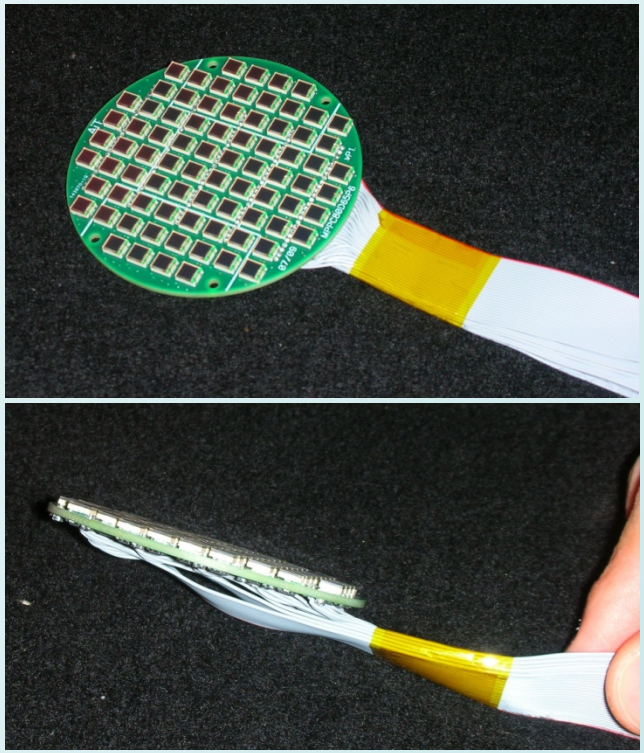
www.dilon.com

Clinical Application- Cancer Surgery

Problem: Need for compact handheld imaging gamma-ray detector to do lymphoscintigraphy for use in cancer surgery

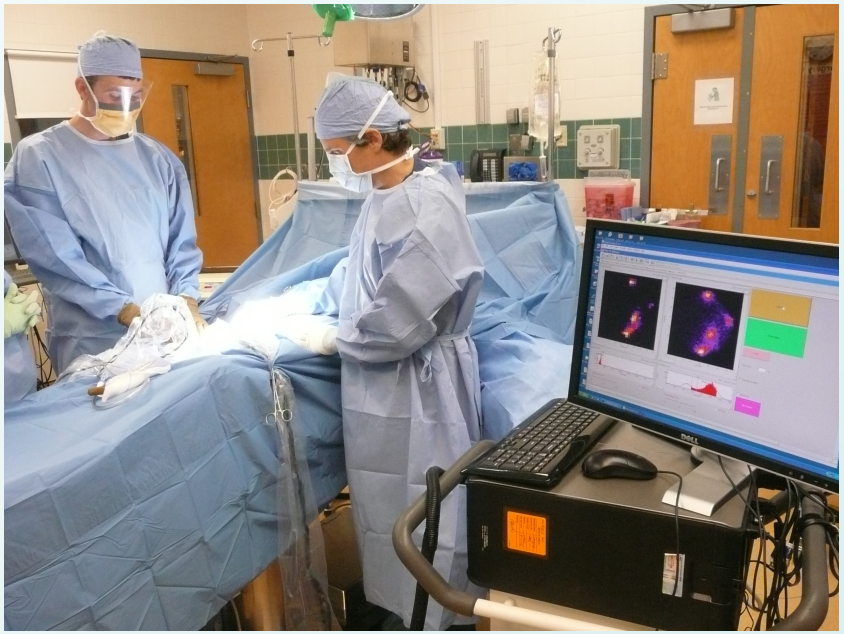
Solution: Use array of 80 SiPMs to develop a compact detector with $LaBr_3$ (5 cm diam, 6 mm thick) scintillator and custom tungsten-polymer composite two-part collimator

"Gamma Puck": Handheld detector with tungsten shell and tungsten collimators

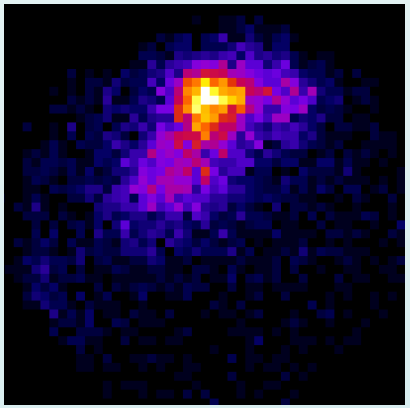


SiPMs mounted to PCB

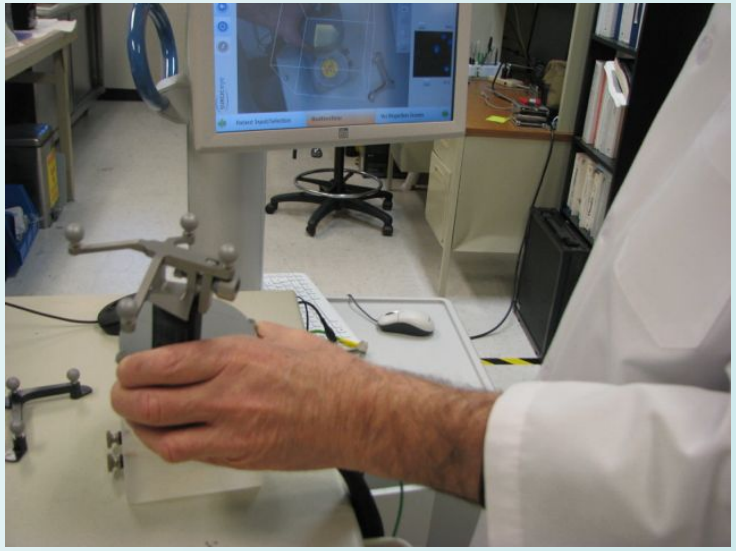
Gamma Puck Project
University of Virginia Medical Center/Dilon Diagnostics



radiopharmaceutical used to identify sentinel lymph nodes with cancer involvement during breast cancer surgery

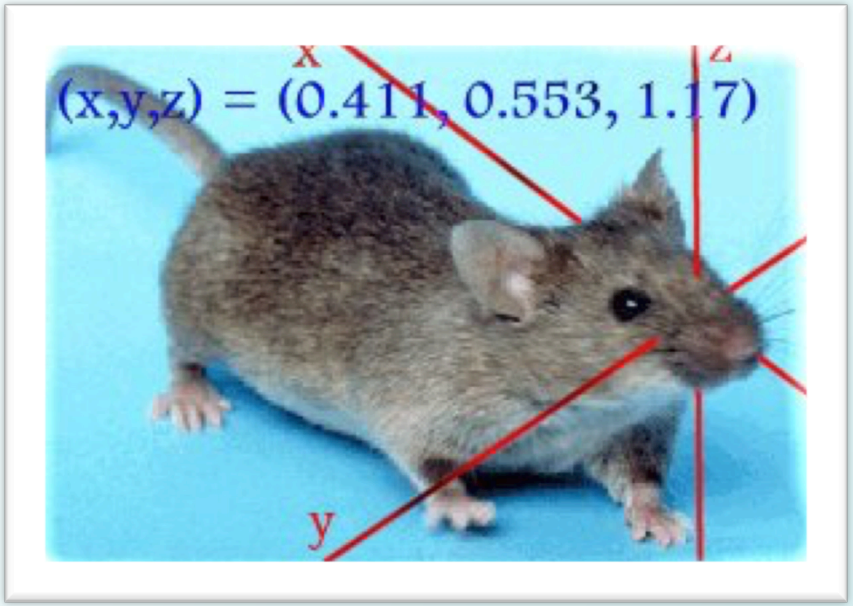


~ 3cm lymph node



Real-time tracking: Free hand SPECT

Awake Small Animal Imaging

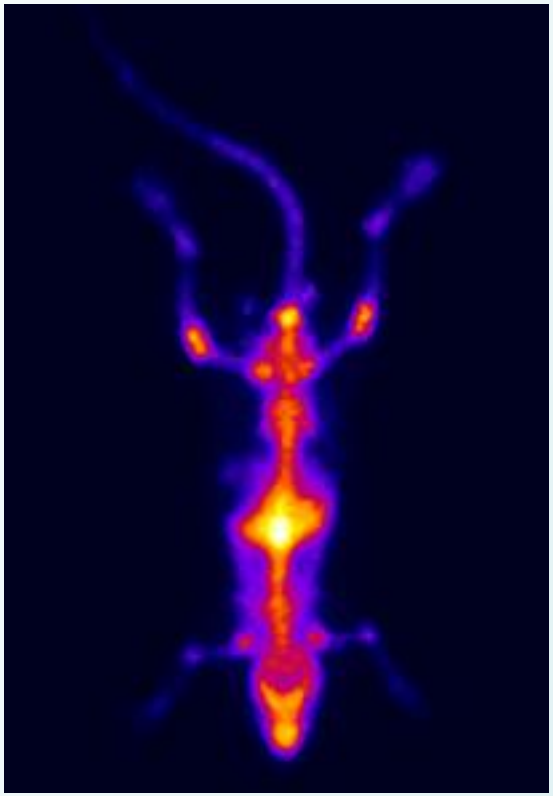


A new tool for biological research under development:

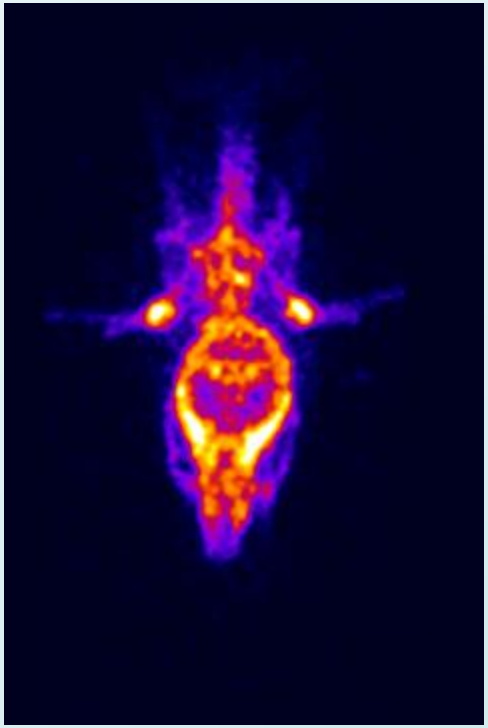
JLab, ORNL and JHU

Several patents awarded and pending

Image of mouse injected with bone marker MDP-Tc99m



Using high resolution parallel hole collimator



Using 1mm pinhole ~2x magnification

Indications for awake animal SPECT imaging

Addiction research

Neuro-degeneration:

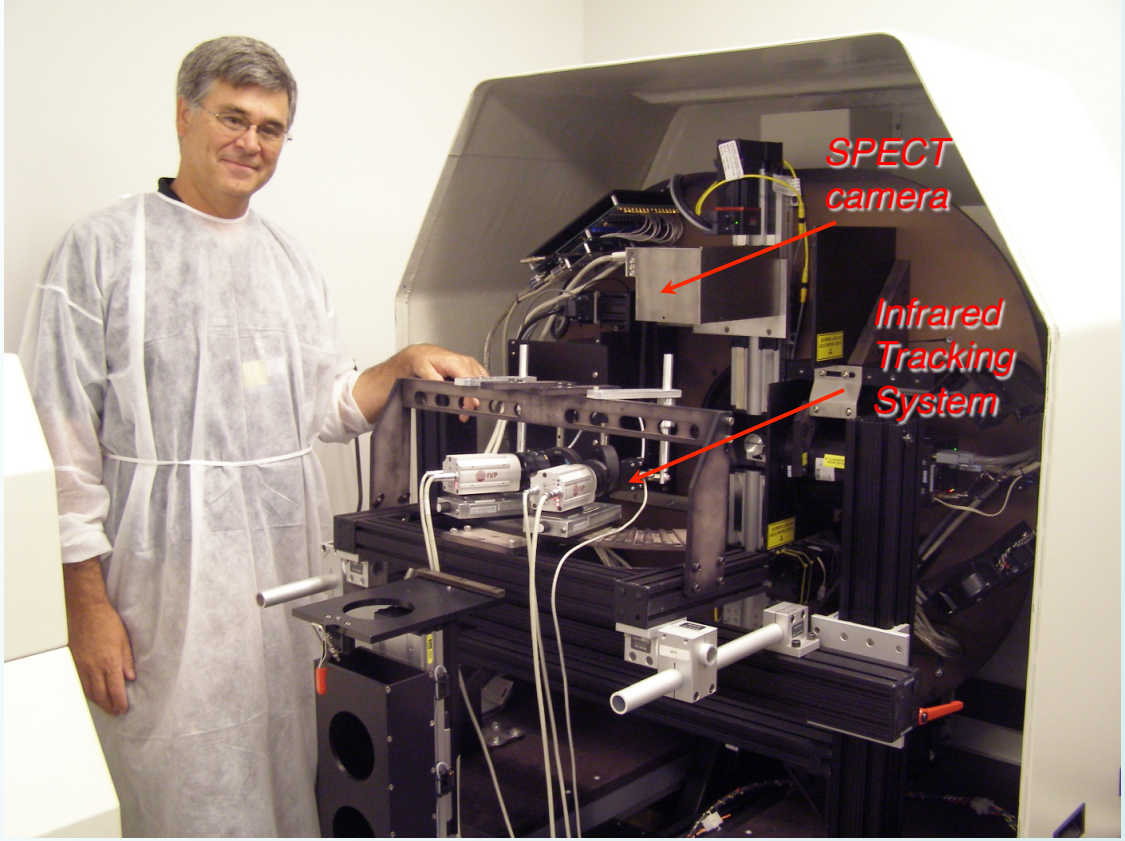
- Alzheimer's Disease
- Parkinson's Disease

Brain inflammation (i.e. HIV, MS).

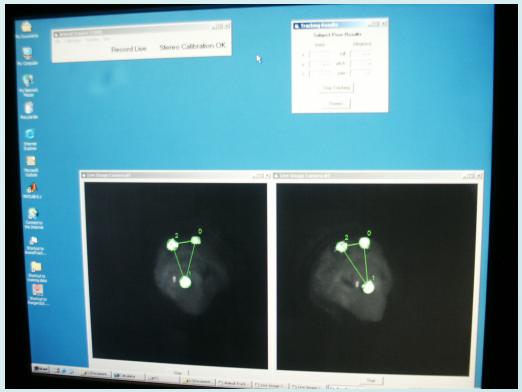
Stem cell trafficking

- ❑ avoid influence of anesthesia on: blood flow, metabolism, neural-vascular coupling
- ❑ elucidate disease pathophysiology
- ❑ drug/radiopharmaceutical development
- ❑ mimic the human state

Awake Animal SPECT-CT Imaging System

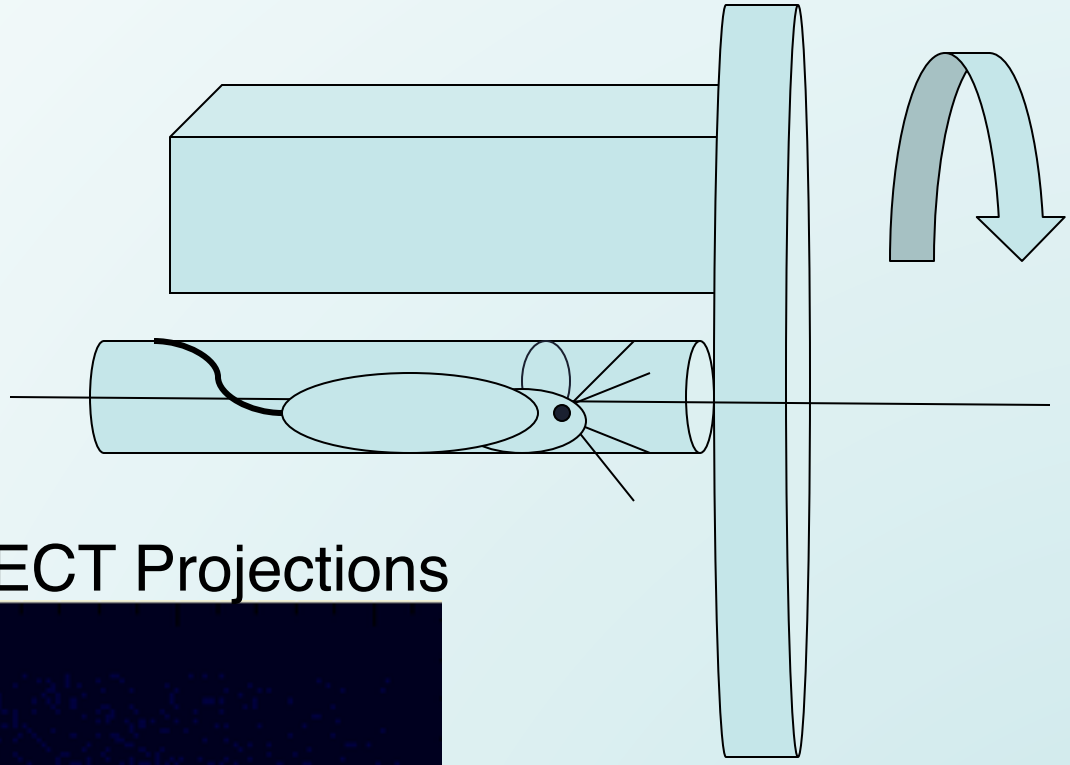


An awake mouse with infrared reflectors for head tracking shown in imaging burrow.

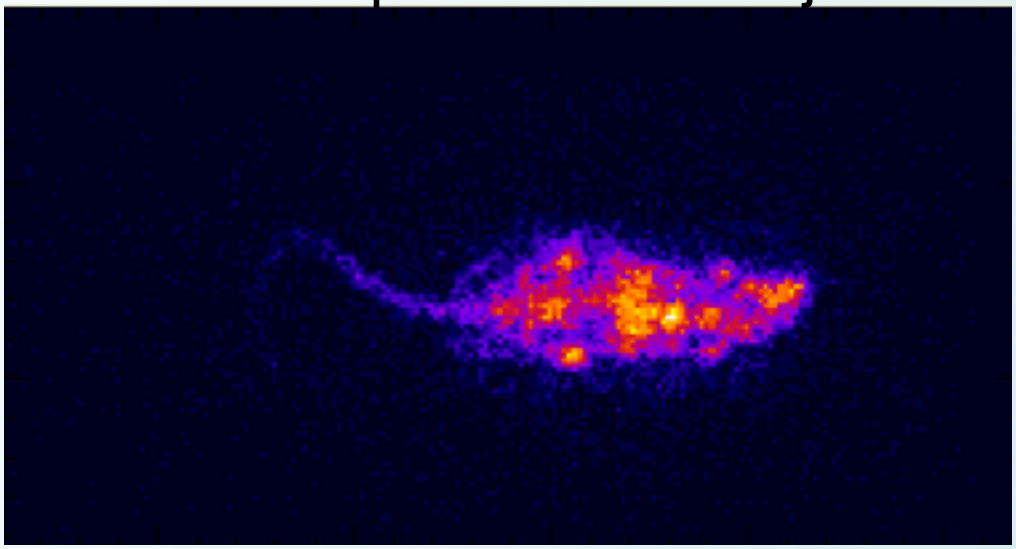


Computer display illustrating real-time pose tracking via the stereo infrared CCD cameras.

SPECT Scan of Awake Mouse

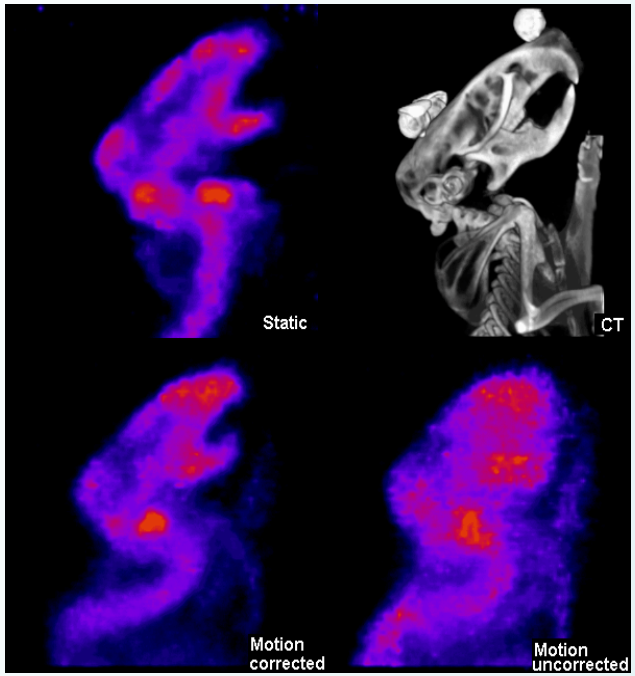


Movie of Multiple SPECT Projections



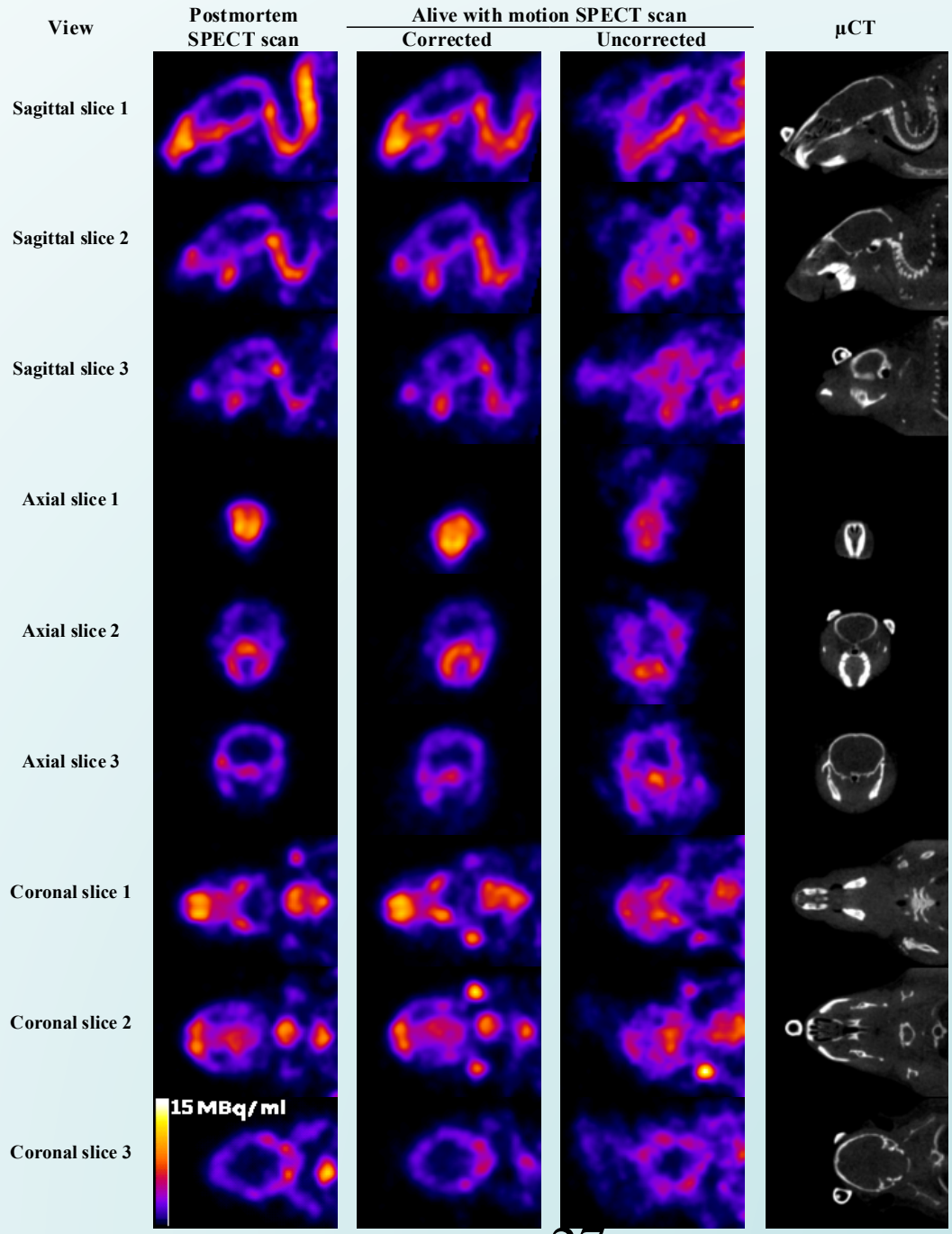
Tc99m-MDP

Motion Correction Applied to Moving Mice: 99mTc-methylene diphosphonate bone imaging



pinhole diameter: 1.5 mm
focal length (pinhole to detector): 111.1 mm pinhole to AOR distance: 49.3 mm magnification: 2.25

MLEM recon algorithm with 40 iterations, a 0.5 mm voxel size and post-filtering with a 3-D, 0.6 mm FWHM Gaussian function.



Global Climate Change and Plant Productivity

DOE-Biological and Environmental Research

➢Funding basic ecological research to understand the direct impacts of enhanced atmospheric CO_2

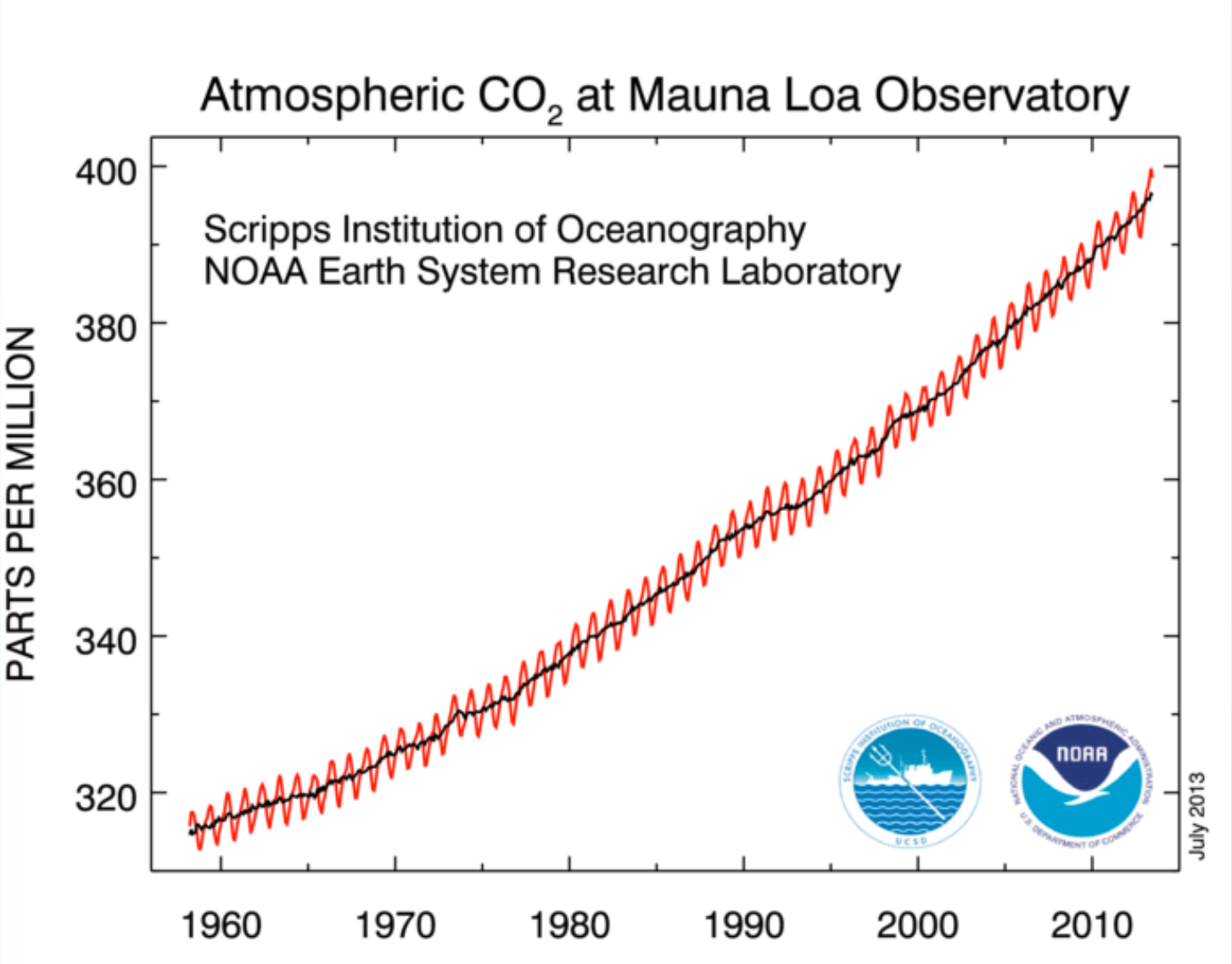
1980s-1990's: Findings of enhanced plant productivity with enhanced CO_2 in greenhouse and open top chamber experiments were only partially confirmed suggesting nutrient limitations to plant productivity in natural ecological settings.

Some remaining questions include:

- How can the initial enhanced plant productivity with increased CO_2 be maintained?

- What is the role of enhanced plant photosynthate production to the short-term microbial activity that could stimulate nutrient turnover?

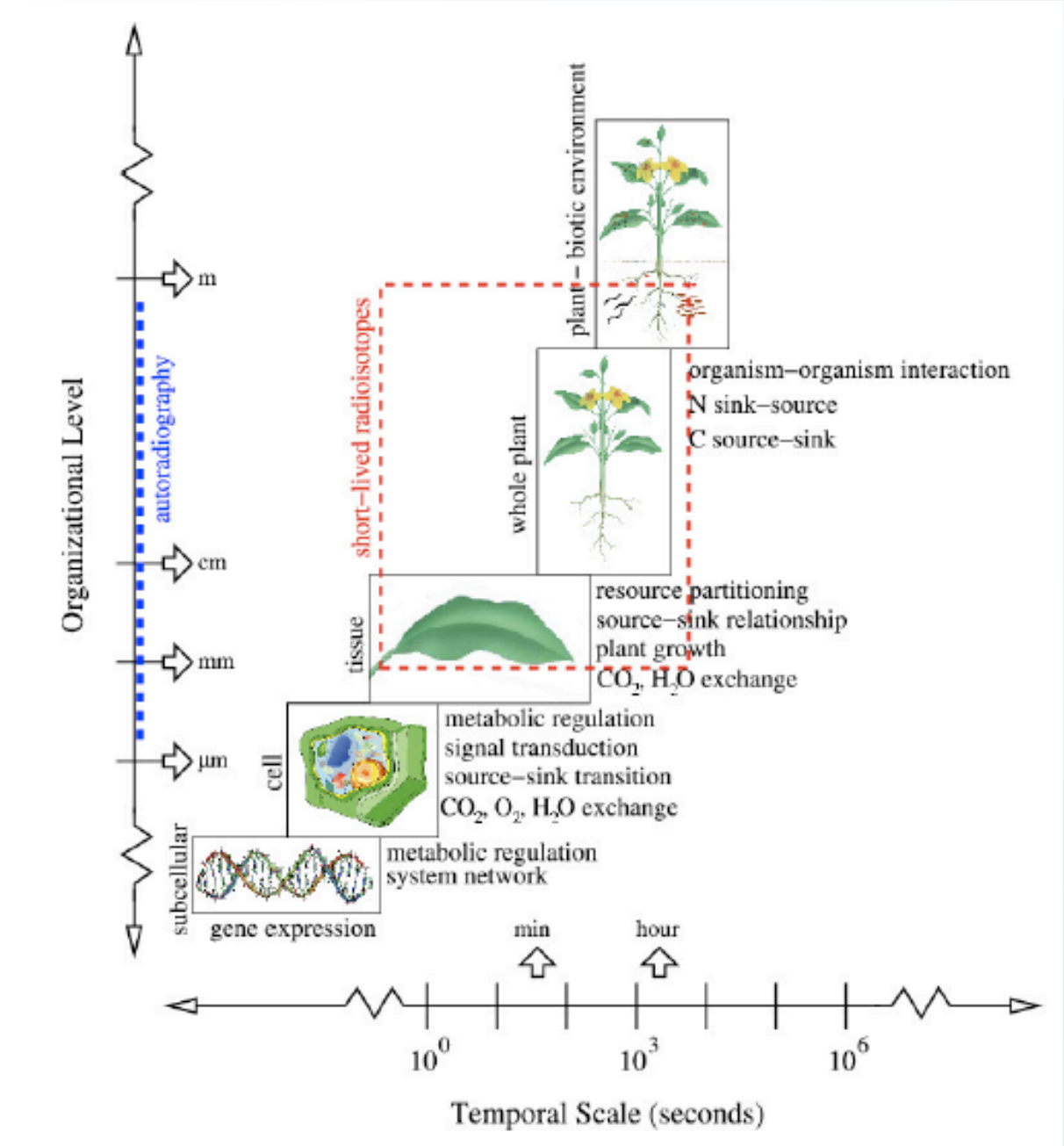
- Are there ways to stimulate plants to sequester more CO_2?



prior ~1880 280 ppm

May 2014 401 ppm

C-14/C-12 ratio decreasing (C-14: cosmogenic isotope-^{14}N (n, p) ^{14}C)



Hierarchical temporal and spatial processes of plant growth and development

(based on Osmond, CB "Photosynthesis from the molecule to the biosphere: a challenge for Integration". In Photosynthesis, Briggs, WR (ed.) pp 5-17. Alan R. Liss Inc., New York,

Radiotracers

Positron Emitters

Carbon-11	20 min
Nitrogen-13	10 min
Oxygen-15	2 min
Fluorine-18	110 min
Manganese-52	5.7 hours
Iron-52	8.3 hours
Zinc-62	9 hours
Copper-62*	9.7 min
Copper-64	12.7 hours
Gallium-68*	68 min
Arsenic-74	17.8 days
Rubidium-82*	1.2 min
Cadmium-107	6.5 hours
Iodine-122	3.6 min
Iodine-124	4.3 days

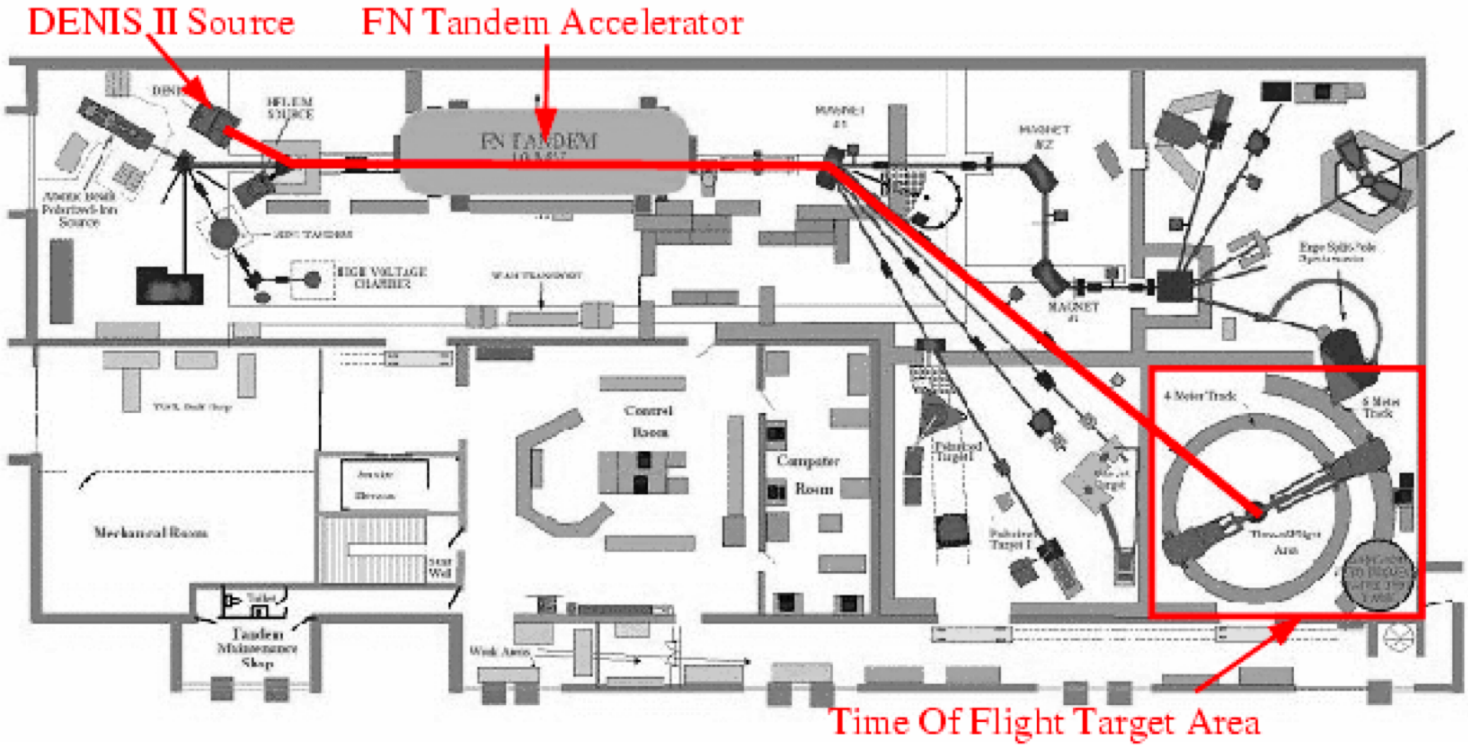
Single Photon Emitters

Chromium-51	26.6 days
Gallium-67	78 hour
Technetium-99m*	6 hour
Iodine-123	13 hour
Potassium-43	22.3 hours
Iodine-131	8 days
Iodine-125	60.1 days
Thallium-201	72.5 hour

Autoradiography

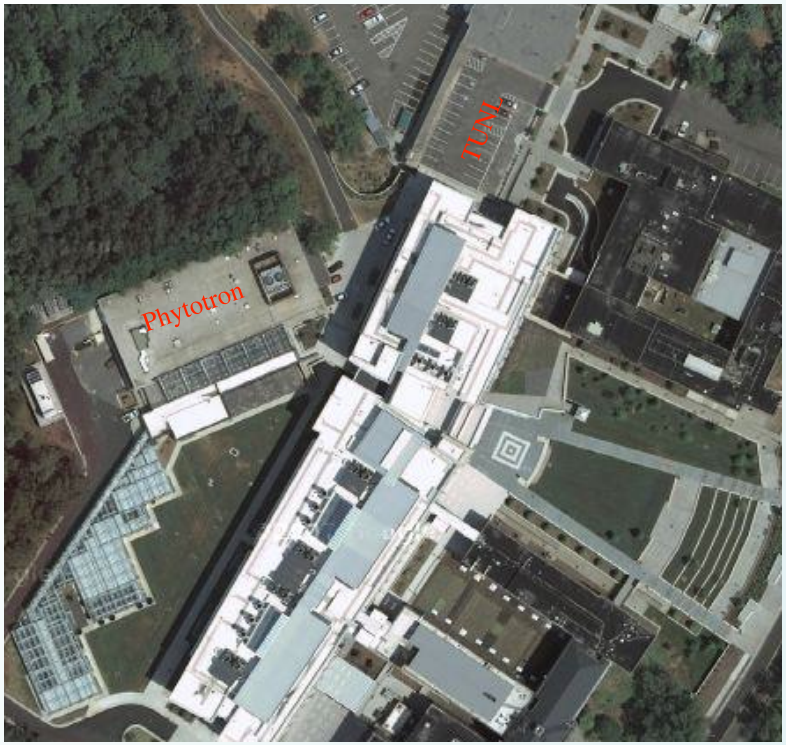
Tritium	12.3 years
Carbon-14	5730 years
Phosphorous-32	14.3 days
Phosphorous-33	25 days
Sulfur-35	86.7 days

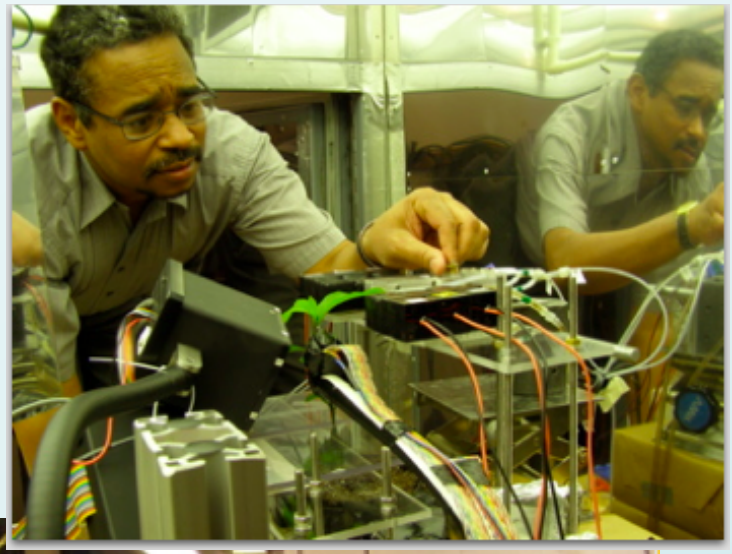
Triangle Universities Nuclear Laboratory



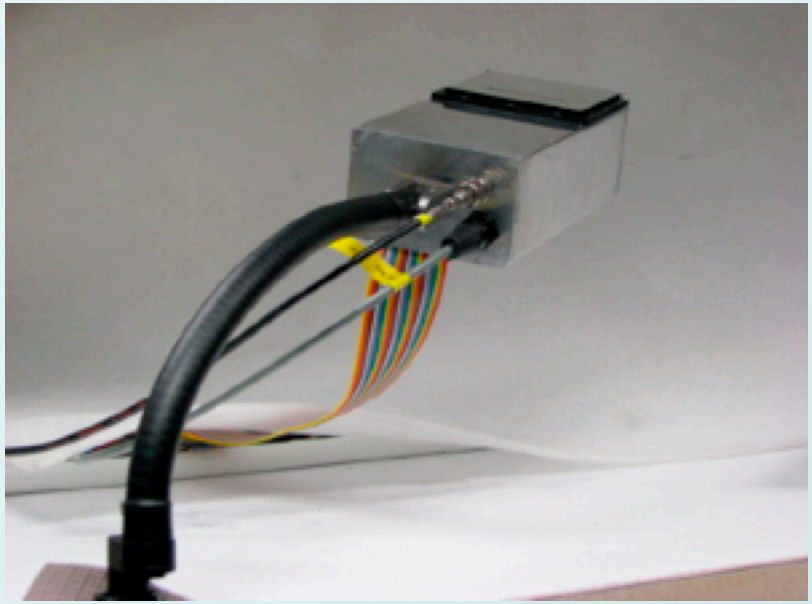
1. $^{11}CO_2$ (half life = 20 min.) $^{14}N + p \rightarrow {}^{11}C + \alpha$ Target: gas	3. $^{18}F^-$ (half life = 109 min.) $^{18}O + p \rightarrow {}^{18}F + n$ Target: ^{18}O enriched water
2. $^{13}NO_3^-$ (half live = 10 min.) $^{16}O + p \rightarrow {}^{13}N + \alpha$ Target: ^{18}O depleted water	4. $H_2{}^{18}O$ (half life = 2 min.) $^{16}O + p \rightarrow {}^{15}O + d$ Target: water

The Duke University Phytotron Facility



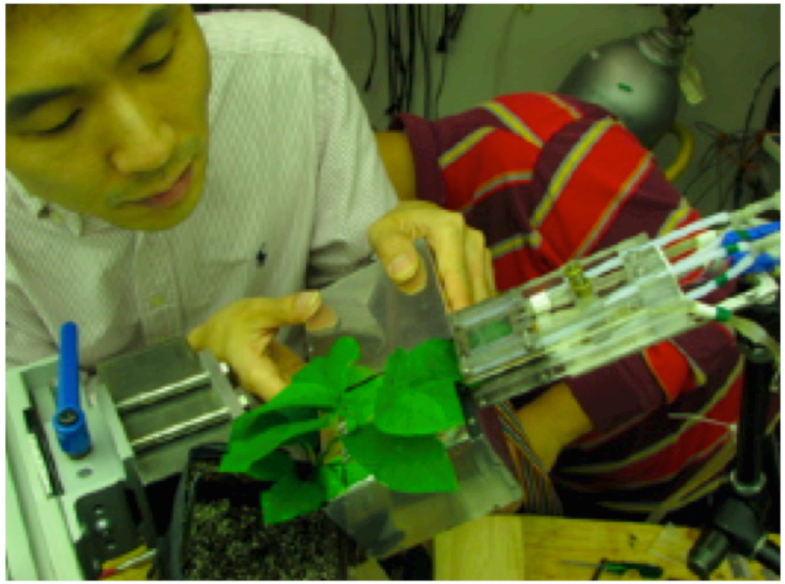


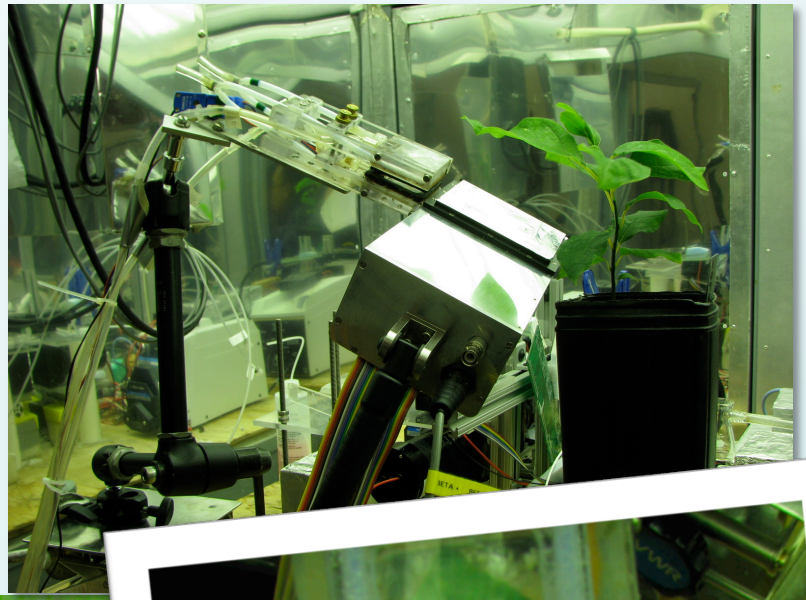
Spicebush (*Lindera benzoin*) a native shrub used to compare with invasive species by measuring $^{11}CO_2$ to carbohydrate utilization



- Bulky
- Leaf positioning problems
- Too much dead space
- Blocked too much light
- Electronics in EGC

- Flatter enclosure
- 5 cm x 5 cm
- Less dead space
- Reflective surfaces
- Electronics external to EGC

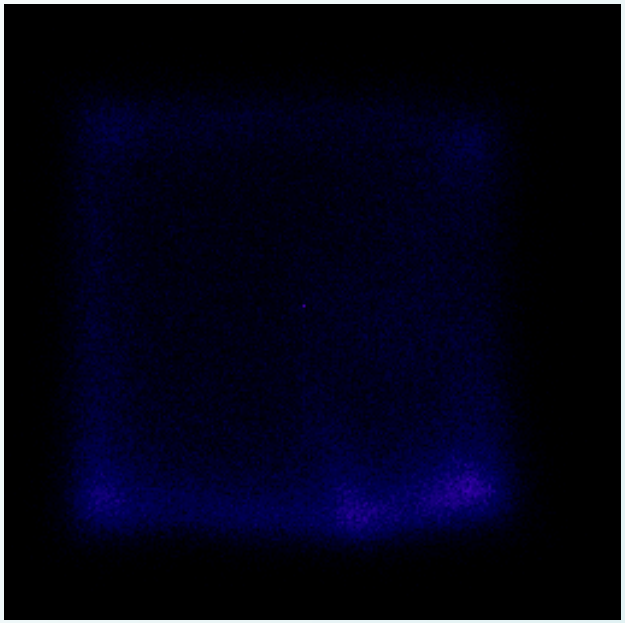




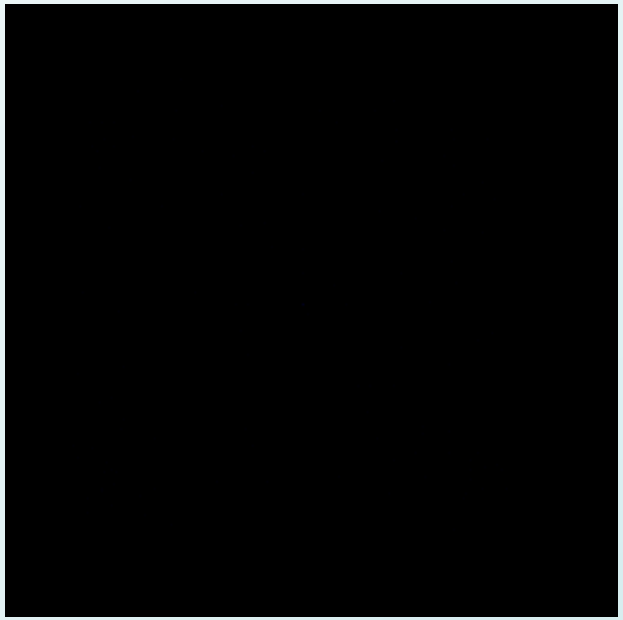
Spicebush (*Lindera benzoin*)

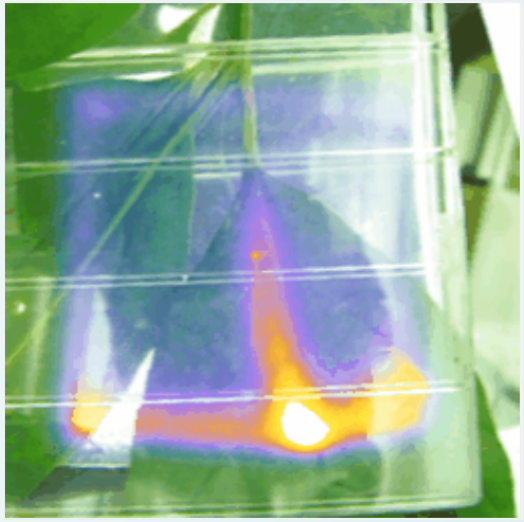
Spicebush $^{11}CO_2$ Study

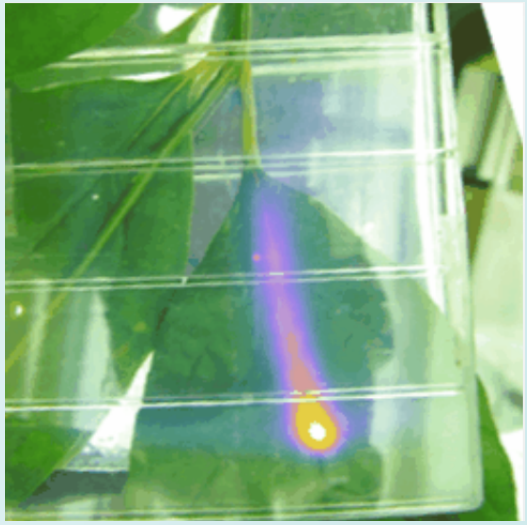
Shaded



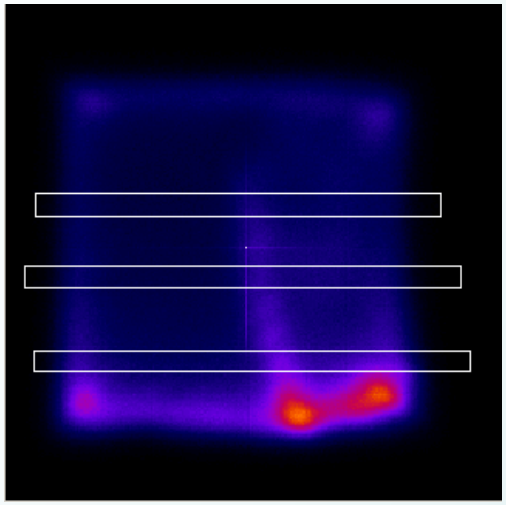
Un-Shaded







Dynamic Profiles

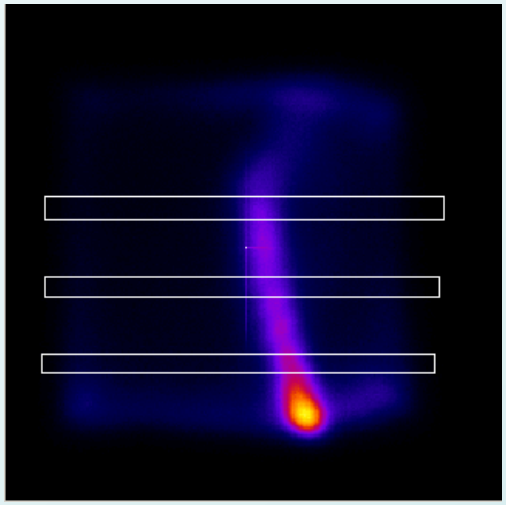


Shaded

red

green

blue



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red

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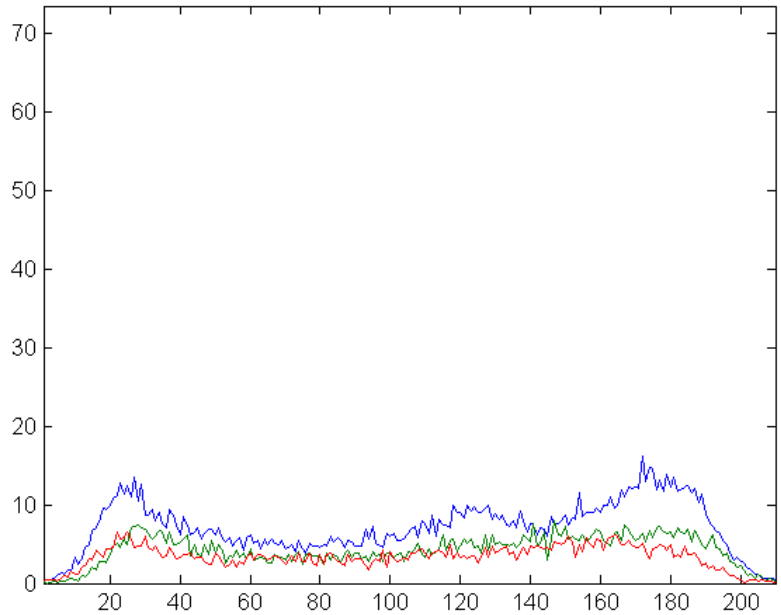
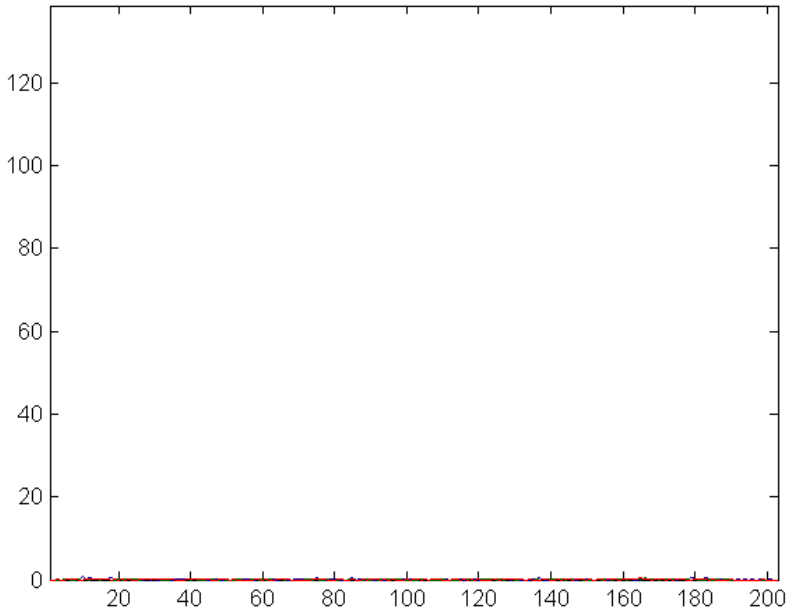
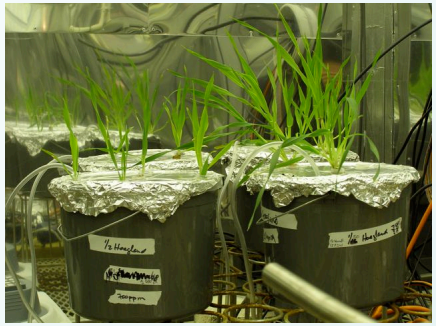




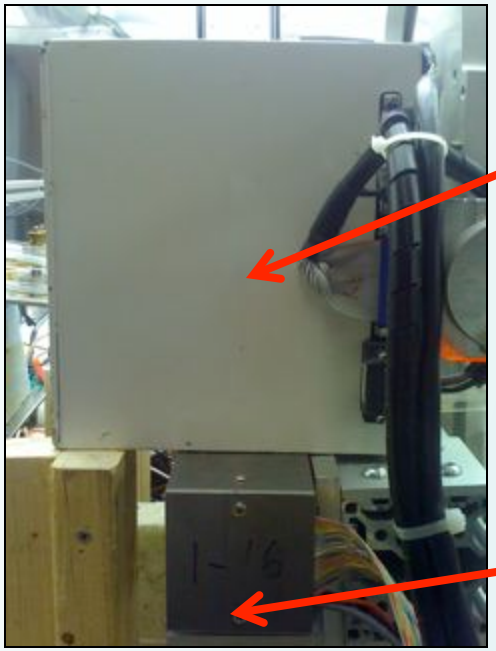
Plant Biology Specific PET Detector Development



Hordeum distichum L

Duke Forest FACE

Reach in EGC



Dual 15 cm x 20 cm Planar PET system

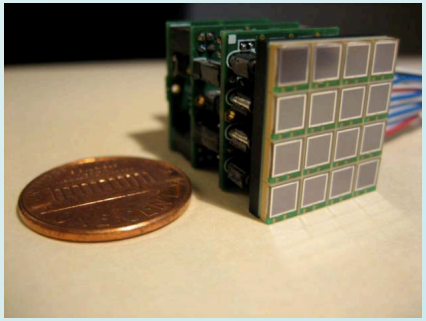
◆3.03 mm step pixellated, 10 mm thick LGSO (90% LSO, 10% GSO) array

◆ 6x8 array of Hamamatsu R7600-00-C8 PSPMTs

Dual 5 cm x 5 cm Planar PET system

◆1.5 mm step pixellated, 10 mm thick, LYSO array using 4ch PEM readout

◆Single Hamamatsu H8500 PSPMT



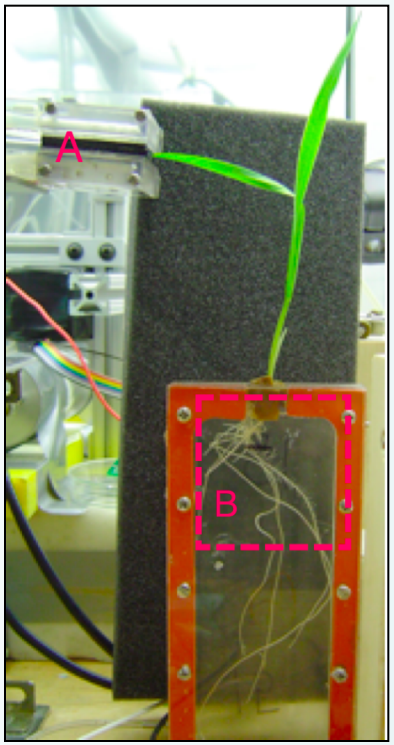
Silicon Photomultplier (SiPM)

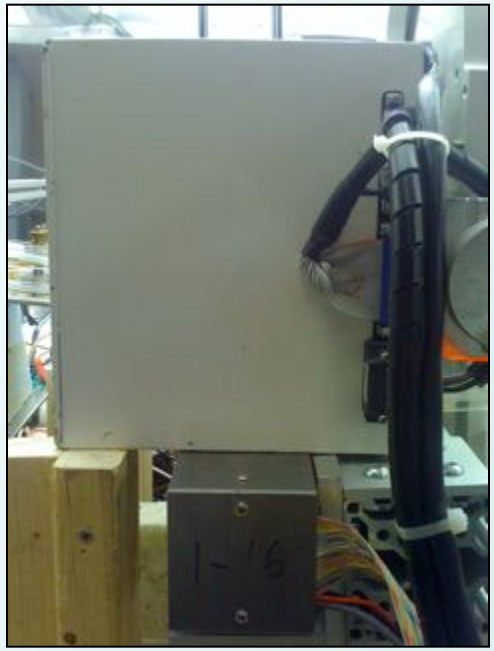
◆Compact

◆MRI compatible

Plant Biology PET Prototypes: dual detector plane based limited angle tomography for carbon-11 imaging using coincident detection of positron annihilation 511 keV photons to facilitate photosynthesis studies

Prototype studies

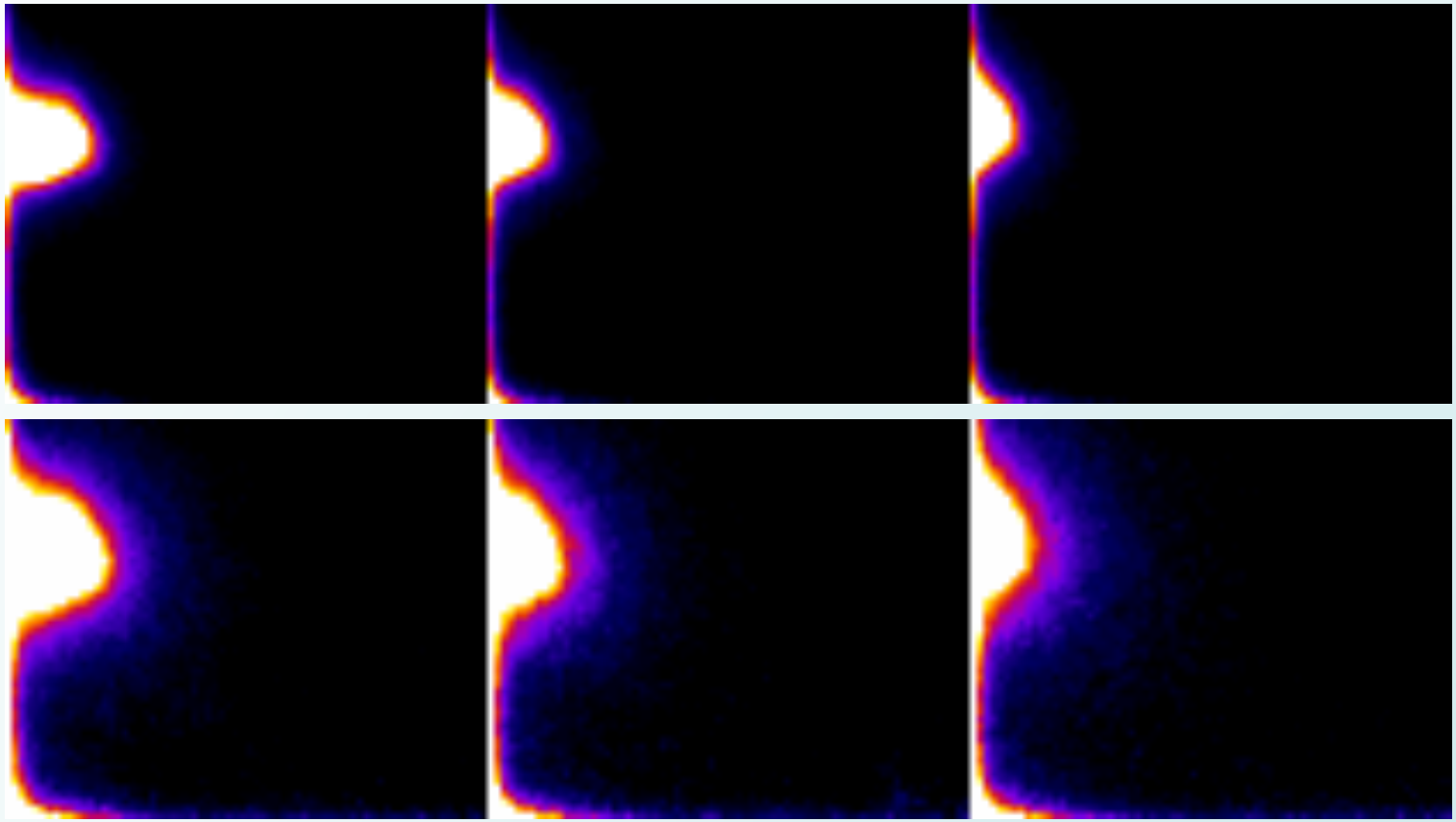




The model plant used for the experiment was barley (*Hordeum distichum L.*) in which $^{11}CO_2$ introduce to leaf (A) of plant grown in hydroponic fluid (B)

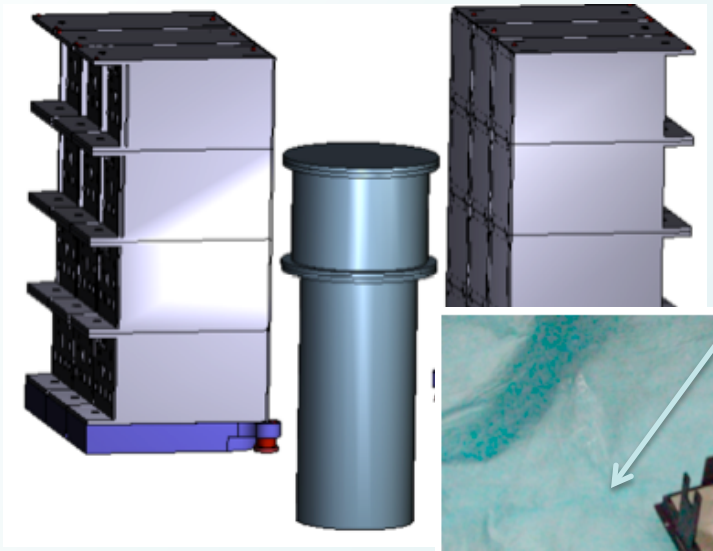
Overlay movie of carbon translocation in barley plant, 5 min x 12 frames = 1 hour

Carbon translocation during photosynthesis

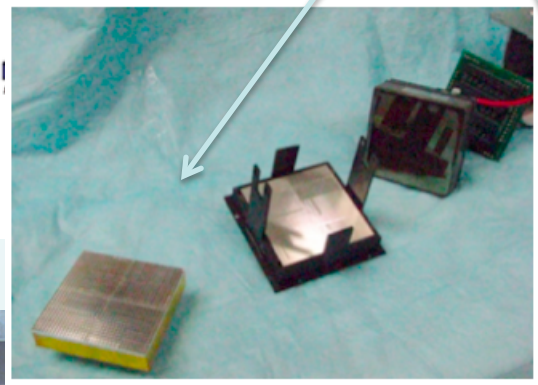


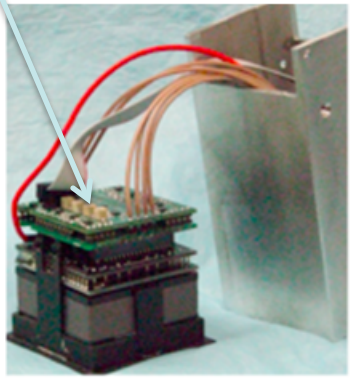
Bottom images are re-scaled to visualize better dynamics
24 frames of animation: each frame is reconstruction from 5 min. (total 2 hrs)
No C-11 decay compensation

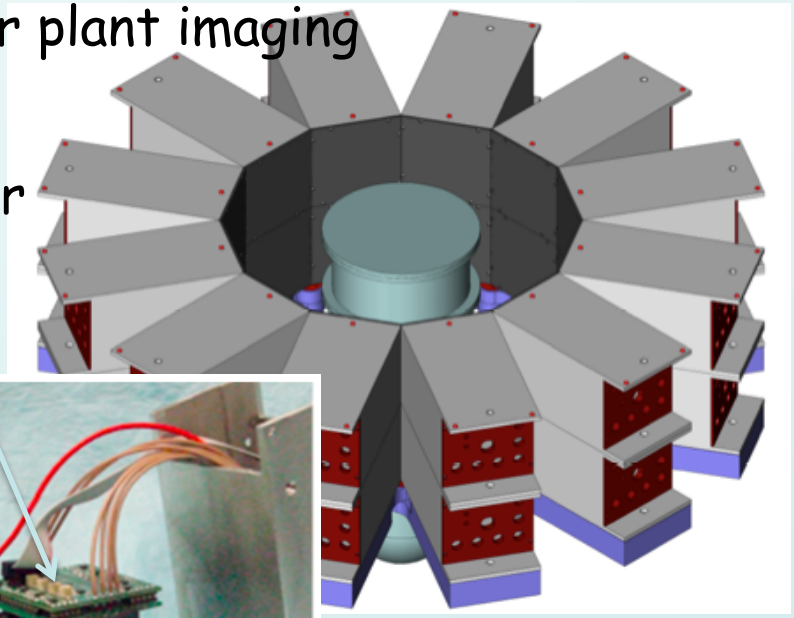
Development of Position-Sensitive (PS)PMT Based PhytoPET: arrays of PSPMTs w/ LYSO scintillator based detector modules to allow flexible geometries for plant imaging

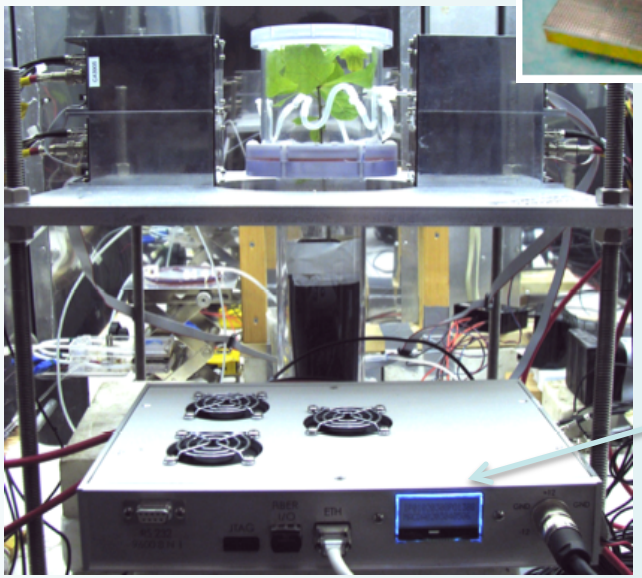


PSPMT-scintillator detector modules

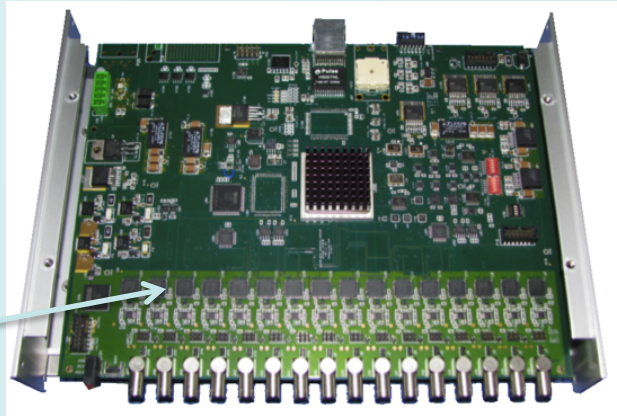




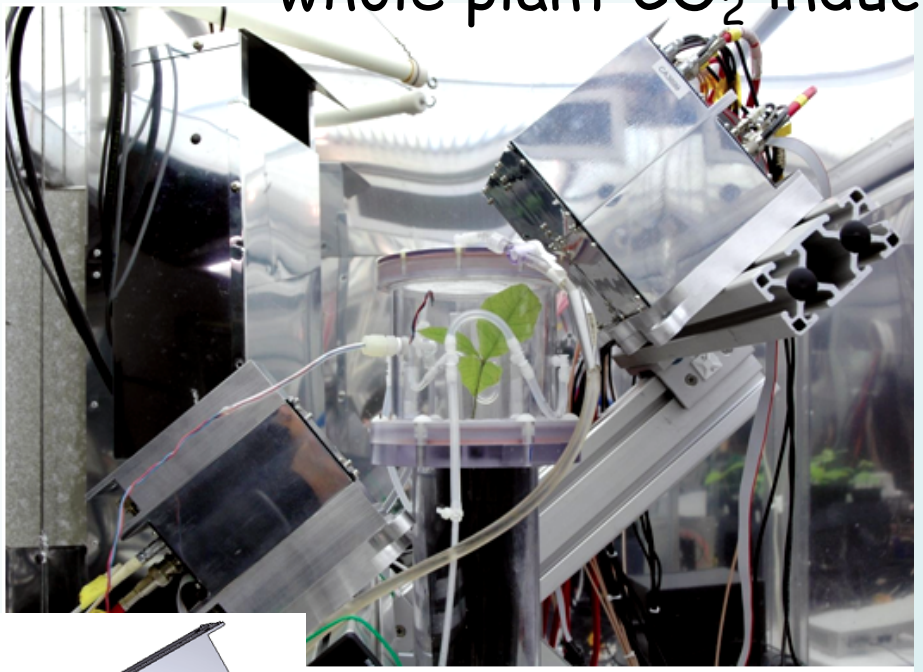


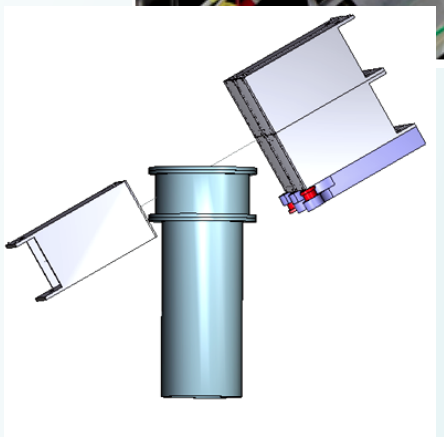


JLab 16 channel FPGA base flash ADC developed by JLab Fast Electronics Group

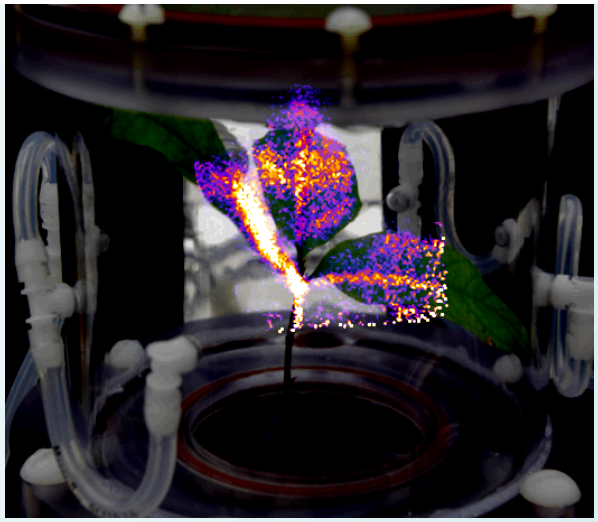


CO_2 Studies w/five PhytoPET modules: oak seedling in whole plant CO_2 induction chamber





detector arrangement

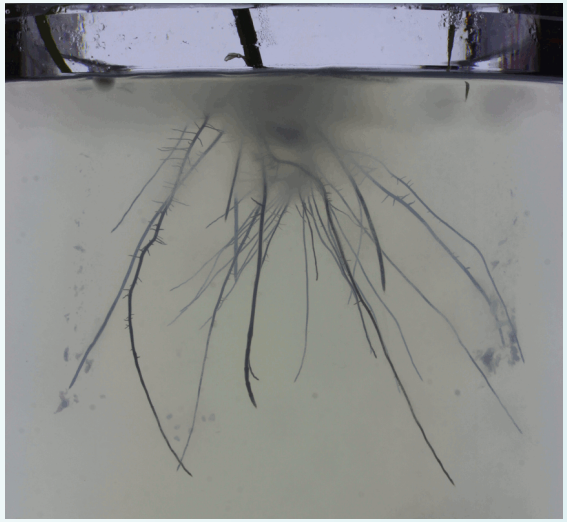


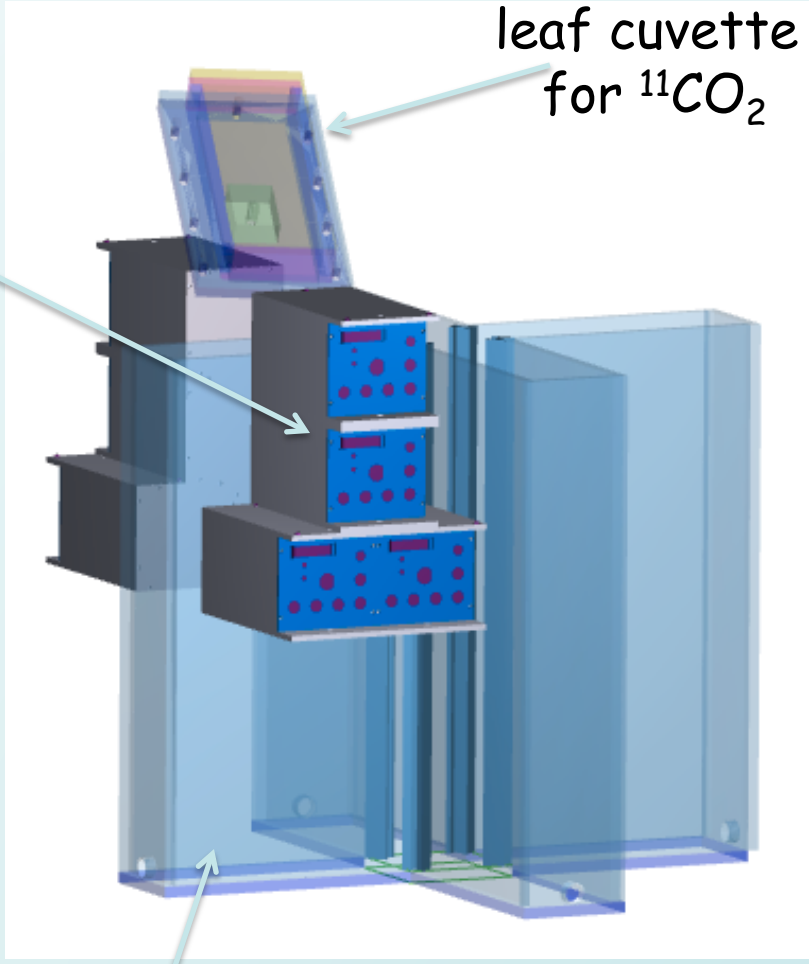
Carbon translocation in oak seedling using whole plant CO_2 induction chamber

PhytoPET detector modules

leaf cuvette for $^{11}CO_2$

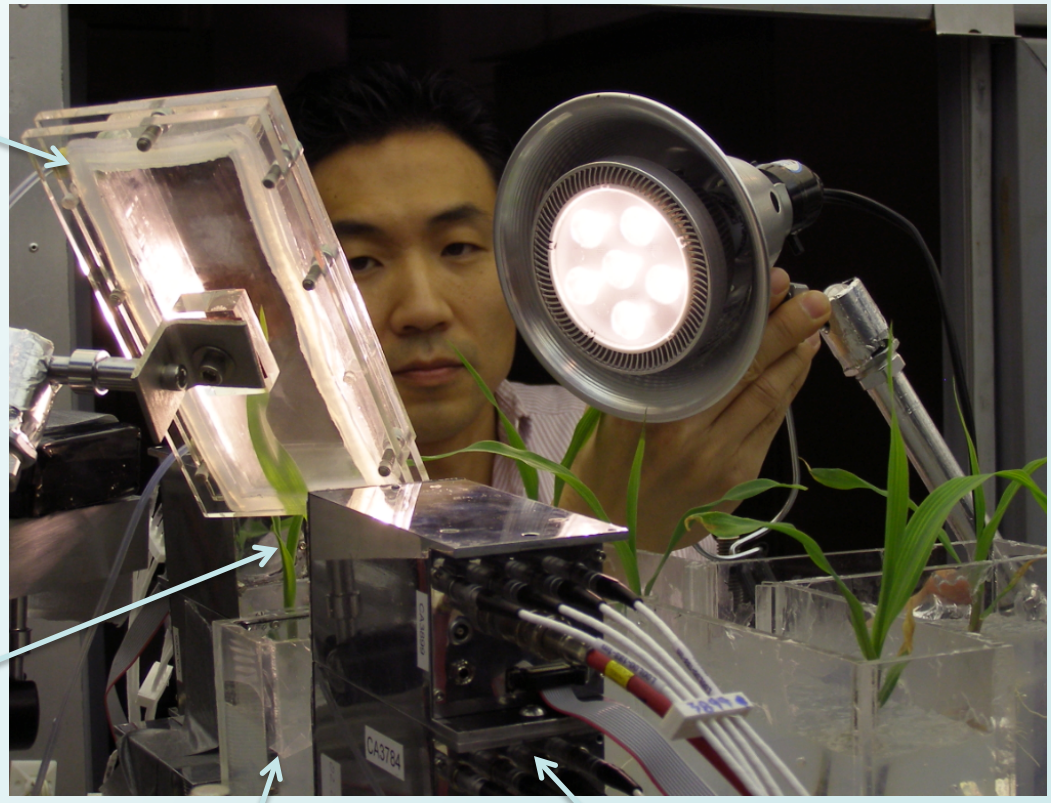
Corn root/microbe study in which carbon dioxide gas in which the carbon PET radioisotope C-11 is used. A corn seedling is grown in a cross shaped root cuvette filled with transparent nutrient gel





root cuvette

Positioning the PhytoPET detectors and plant in preparation for PET imaging.

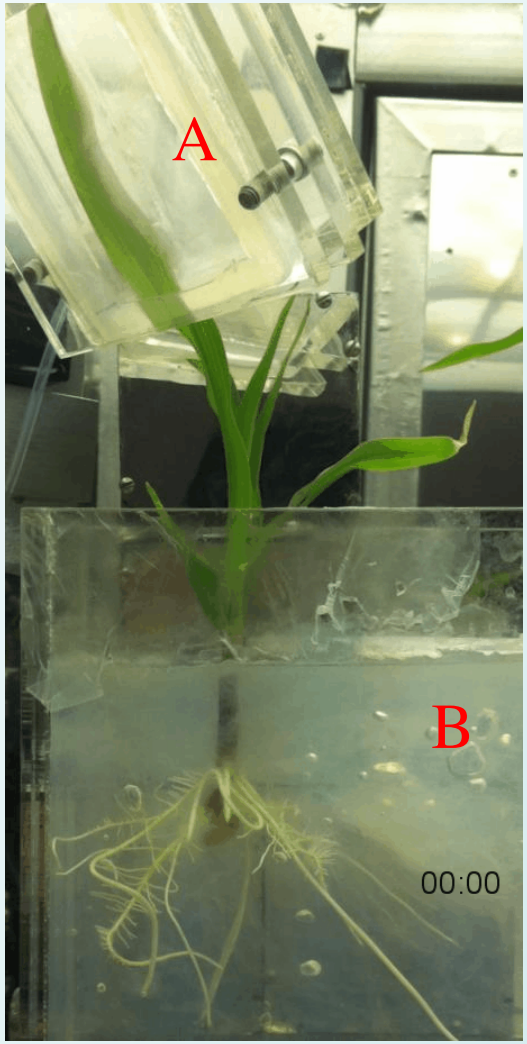


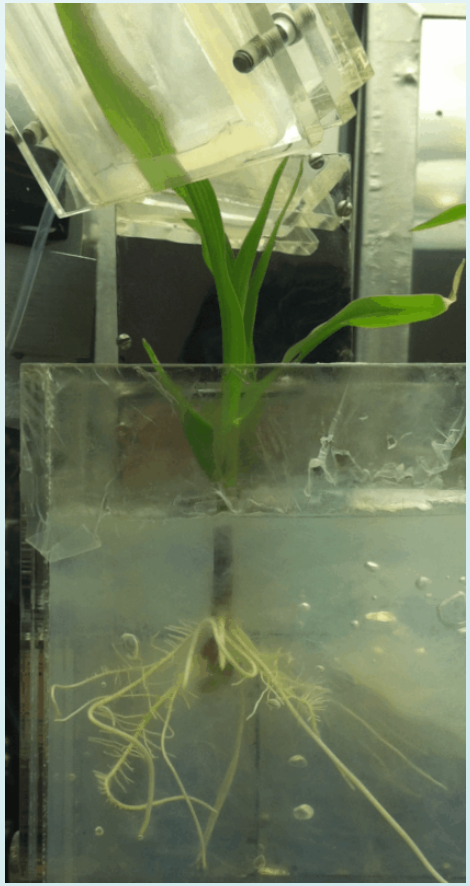
Corn root/microbe study in which $^{11}CO_2$ introduce to leaf (A) of a corn seedling grown in a transparent nutrient gel (B)

Image showing uptake of $^{11}CO_2$ and co-registered with a photograph of the corn seedling.

Total imaging session lasting ~6 hour with three separate bursts of $^{11}CO_2$ gas loading.

The translocation of ^{11}C labeled sugars from the upper part of the plant to the roots is apparent.





Gamma-ray Imaging for Biological Systems

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