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

\[ E_e = h\nu - E_b \]
Scintillation Detection

- Incident Ionizing Radiation
- Scintillator
- Photoelectron
- Photomultiplier Tube
- Dynode
- Anode
- Pulse Analysis
- Photocathode
- Optical Window
- Light
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

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Half-life</th>
<th>( \gamma ) energies -keV (photon abundance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>technetium-99m ( ^{99m}\text{Tc} )</td>
<td>6.02 hours</td>
<td>140 (89%)</td>
</tr>
<tr>
<td>indium-111 ( ^{111}\text{I} )</td>
<td>2.83 days</td>
<td>170 (94%), 240 (90%)</td>
</tr>
<tr>
<td>gallium-67 ( ^{67}\text{Ga} )</td>
<td>3.25 days</td>
<td>93 (37%), 185 (20%), 300 (17%), and 394 (4%)</td>
</tr>
<tr>
<td>iodine-123 ( ^{123}\text{I} )</td>
<td>13.3 hours</td>
<td>159 (84%)</td>
</tr>
</tbody>
</table>

\( ^{99m}\text{Tc} \)-sestamibi: \( \text{C}_{36}\text{H}_{66}\text{N}_{6}\text{O}_{6}\space^{99m}\text{Tc} \)

\( \rightarrow \) targets cells with active mitochondria e.g. cancer

Most common positron emitters used in nuclear medicine

<table>
<thead>
<tr>
<th>Positron Emitting Isotope</th>
<th>Half-life (minutes)</th>
<th>Positron ( E_{\text{max}} ) (MeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>oxygen-15 ( ^{15}\text{O} )</td>
<td>2.07</td>
<td>1.72</td>
</tr>
<tr>
<td>nitrogen-13 ( ^{13}\text{N} )</td>
<td>9.96</td>
<td>1.19</td>
</tr>
<tr>
<td>carbon-11 ( ^{11}\text{C} )</td>
<td>20.4</td>
<td>0.96</td>
</tr>
<tr>
<td>fluorine-18 ( ^{18}\text{F} )</td>
<td>109.7</td>
<td>0.64</td>
</tr>
</tbody>
</table>

\( ^{18}\text{F} \)-fluoro-2- deoxyglucose (FDG): \( \text{C}_{6}\text{H}_{11}\text{F}^{18}\text{O}_{5} \)

\( \rightarrow \) targets rapidly growing cells e.g. cancer
Bio-Medical Imaging Modalities

Structural

Functional

Somatostatin receptors (neuroendocrine tumors)
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 LaBr₃ (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\textsubscript{2}.

1980s-1990’s: Findings of enhanced plant productivity with enhanced CO\textsubscript{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\textsubscript{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\textsubscript{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

<table>
<thead>
<tr>
<th>Positron Emitters</th>
<th>Single Photon Emitters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon-11 20 min</td>
<td>Chromium-51 26.6 days</td>
</tr>
<tr>
<td>Nitrogen-13 10 min</td>
<td>Gallium-67 78 hour</td>
</tr>
<tr>
<td>Oxygen-15 2 min</td>
<td>Technetium-99m* 6 hour</td>
</tr>
<tr>
<td>Fluorine-18 110 min</td>
<td>Iodine-123 13 hour</td>
</tr>
<tr>
<td>Manganese-52 5.7 hours</td>
<td>Potassium-43 22.3 hours</td>
</tr>
<tr>
<td>Iron-52 8.3 hours</td>
<td>Iodine-131 8 days</td>
</tr>
<tr>
<td>Zinc-62 9 hours</td>
<td>Iodine-125 60.1 days</td>
</tr>
<tr>
<td>Copper-62* 9.7 min</td>
<td>Thallium-201 72.5 hour</td>
</tr>
<tr>
<td>Copper-64 12.7 hours</td>
<td></td>
</tr>
<tr>
<td>Gallium-68* 68 min</td>
<td></td>
</tr>
<tr>
<td>Arsenic-74 17.8 days</td>
<td></td>
</tr>
<tr>
<td>Rubidium-82* 1.2 min</td>
<td></td>
</tr>
<tr>
<td>Cadmium-107 6.5 hours</td>
<td></td>
</tr>
<tr>
<td>Iodine-122 3.6 min</td>
<td></td>
</tr>
<tr>
<td>Iodine-124 4.3 days</td>
<td></td>
</tr>
<tr>
<td><strong>Autoradiography</strong></td>
<td></td>
</tr>
<tr>
<td>Tritium 12.3 years</td>
<td>Carbon-14 5730 years</td>
</tr>
<tr>
<td>Phosphorous-32 14.3 days</td>
<td>Phosphorous-33 25 days</td>
</tr>
<tr>
<td>Phosphorous-33 25 days</td>
<td>Sulfur-35 86.7 days</td>
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</tr>
<tr>
<td>1.</td>
<td>$^{11}\text{CO}_2$ (half life = 20 min.)</td>
</tr>
<tr>
<td></td>
<td>$^{14}\text{N} + \text{p} \rightarrow ^{11}\text{C} + \alpha$</td>
</tr>
<tr>
<td></td>
<td>Target: gas</td>
</tr>
<tr>
<td>2.</td>
<td>$^{13}\text{NO}_3^-$ (half life = 10 min.)</td>
</tr>
<tr>
<td></td>
<td>$^{16}\text{O} + \text{p} \rightarrow ^{13}\text{N} + \alpha$</td>
</tr>
<tr>
<td></td>
<td>Target: $^{18}\text{O}$ depleted water</td>
</tr>
</tbody>
</table>
The Duke University Phytotron Facility
Spicebush (*Lindera benzoin*) a native shrub used to compare with invasive species by measuring $^{11}\text{CO}_2$ 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 $^{11}\text{CO}_2$ Study

Shaded

Un-Shaded
Dynamic Profiles

Shaded
- red
- green
- blue

Un-shaded
- red
- green
- blue
Plant Biology Specific PET Detector Development

**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

**Hordeum distichum L**

**Duke Forest FACE**

**Reach in EGC**

**Silicon Photomultiplier (SiPM)**
- Compact
- MRI compatible
The model plant used for the experiment was **barley (Hordeum distichum L.)** in which $^{11}\text{CO}_2$ introduce to leaf (A) of plant grown in hydroponic fluid (B).
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 with LYSO scintillator based detector modules to allow flexible geometries for plant imaging.

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
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.
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

Partners:

• Oak Ridge National Laboratory (ORNL)
• Triangle Universities Nuclear Laboratory (TUNL)
• Los Alamos National Laboratory (LANL)
• West Virginia University
• Hampton University Proton Therapy Institute
• University of Virginia
• Johns Hopkins University
• Case Western Reserve University
• College of William and Mary
• Duke University
• Columbia University
• Dilon Technologies, Inc.