TIPP for Medical Applications

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CERN

Wilhelm Röntgen
First Novel Laureate in Physics (1901)
Discovery of X-Ray: 11/8/1895
First “Medical” Image: 12/23/1895
This Overview

• Only a limited selection of medical applications
• TIPP 2011 papers largely not included
• Emphasis on
  - PP/HEP connections
  - Emerging, forward-looking, next-generation
  - Potentials for routine and wide-spread use (commercialization)
  - Impacts to medicine & health-care

More on Medical Applications:
- TIPP 2011 Tuesday 6/14/2011, 10:30am
  Patrick Le Du: “Application Outside HEP”
- TIPP 2009, Peter Weilhammer: “Particle Physics Instrumentation and Its Impact on Medical Imaging”
Common Ground of PP/HEP & Medicine

- Diagnostic Imaging
- “Radiation” & “Particle” Therapy
- “Thera[g]nostics” (Diagnostics + Therapeutics)

“……Medical Applications serve as ideal ‘prototyping’ test and validation platforms of realistically feasible small-scale for PP/HEP Technology and Instrumentation……”

- In Discussion with Marcel Demarteau
*TruFlight™*: Enhanced Diagnostic Confidence

Data courtesy of J. Karp, University of Pennsylvania

- Improved detectability of small mets in lung
- 67 kg; BMI = 29.0
- 9.8 mCi; 1 hr post-inj. (2min/bed)
**TruFlight™**: Enhanced Diagnostic Confidence

Lymphoma within right iliopsoas muscle with central area of necrosis

116 kg; BMI = 31.2
14 mCi; 2 hr post-inj

Data courtesy of J. Karp, University of Pennsylvania
What Timing Can An LSO Module Achieve?

Crystal Geometry

Light Sharing

PMT Quality

Multiple PMTs

Predicted Limit

Measured Value

550 ps

575 ps

Already Near LSO Block Detector Theoretical Limit
Side-Coupled Design

Conventional Geometry
(End-Coupled Crystal)

LBNL Geometry
(Side-Coupled Crystal)

Shorter Optical Path Length & Fewer Reflections

543 ps (coincidence)

309 ps (coincidence)
Optimization: LSO Composition

Ca-Doping Gives High Light Output & Short Decay Time

- Normal LSO
- High Light Output
- Short $\tau$
- The Good Stuff!

0.3%, 0.4%, 0.2%, 0.1% Ca-doped

$\star$ = Ca-doped

Ca-Doping Provides a Balance between High Light Output and Short Decay Time.
• Ca-Doping Gives Good Timing Resolution
• ~15% Improvement Over Normal LSO
Measured Results: High QE PMTs

- Increased QE Improves Timing Resolution by 7%
- Expect 10% Improvement with 35% SBA PMT

Normal ("28% QE") PMTs

Scaled by $1/\sqrt{\text{Blue Index}}$

= "32% QE" PMTs

Time Resolution (ps fwhm)

Blue Sensitivity Index
### Additional Improvements

- TOF PET with *Significantly* Better Timing is Possible
- To Achieve, We Must “Think Outside the Block Detector"

<table>
<thead>
<tr>
<th>Hardware</th>
<th>Coinc. (ps fwhm)</th>
<th>TOF Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>End-Coupled Crystal</td>
<td>543</td>
<td>4.3</td>
</tr>
<tr>
<td>Side-Coupled Crystal</td>
<td>309</td>
<td>7.6</td>
</tr>
<tr>
<td>Co-Doped LSO</td>
<td>258</td>
<td>9.1</td>
</tr>
<tr>
<td>32% QE PMT</td>
<td>219</td>
<td>10.6</td>
</tr>
</tbody>
</table>
Detector Module Design

Two LSO Crystals
(each 6.15 x 6.15 x 25 mm³)

Reflector
(on all five faces of each crystal, including the face between the two crystals)

Optical Glue
(between lower crystal faces and PMT)

PMT
(Hamamatsu R-9800)

Hole in Reflector On Top Face Crystals

Two Side-Coupled Scintillator Crystals per PMT
How Far Can TOF PET Go?

- 100 ps Timing Resolution
- 23x Effective Efficiency Increase
- Very Fast Reconstruction

Acquire & Reconstruct Image in <1 Minute
Conclusions

Benefits of TOF are **HUGE**:
- 5x effective efficiency gain w/ 500 ps timing
- Greatest improvement in large patients
- Faster reconstruction algorithm convergence

Rebirth of TOF PET Due To New Scintillators:
- 575 ps for LSO, 350 ps for LaBr$_3$

Still **LOTS** To Do:
- Electronics
- Module Design
- Reconstruction
- Photodetectors
- Scintillators
- Evaluation

*Much More Improvement To Come!*
Large-Area Picosecond Photo-Detector (LAPPD) Project

Next-Generation MCP-PMT

Project with 4 primary goals:
1. Low-Cost LAPPD with good timing and spatial resolution (~$10/sq-in area cost)
2. Large-Area TOF particle/photon detectors with picosecond time resolution
3. Understanding photo-cathodes so that high QE cathodes can be reliably made with tailored spectral response, and new materials & geometries can be developed
4. Produce commercializable modules within 3 years & transfer technology to industry
Panel-Based DOI-Coded TOF PET

Micro-Channel Micro-PET (MCMP)

Potential Applications:

(DOI+TOF)-PET/CT
Reconfigurable, Integrative, Modular “Super-Modules”
[a] High-Resolution “Cube”
[b] High-Sensitivity “Multi-Layer”
[c] High-Throughput “Multi-Object”
[d] Whole-Body

UC, ANL, FNAL, etc.
High-Sensitivity Dual-Panel DOI-PET

- Sensitivity 25-30% (3-10 folds increase)
- High-throughput, multi-object
- Novel reconstruction/no rotation
- Super-resolution recovery
- Uniform resolution within large FOV
- Pre-clinical drug development
- Clinical or research brain imaging

Q-Sharing PMT (HRRT)

New CNS Drug Development For Stroke

Reaching task involving the left forelimb

FDG imaging of a rat’s brain shows increased FDG uptake in the right brain due to the motor task performed by the left forelimb of the subject.

(UChicago)
Modular, Re-Configurable, Integrative PET/SPECT/CT
For Flexible Application-Specific Imaging

Semiconductor Detectors (CdTe/CZT)
Energy Resolved Photon Counting (ERPC)

Integrative: Assemble & dis-assemble based on application-specific needs.
Flex-Configure: Novel Recon for flexible scanning trajectories
Multi-Modality: PET/SPECT/CT

UIUC, WashU, UC
On-Board, In-Beam, In-Room CT, PET or SPECT for Radiation & Particle Therapy (Theranostics)

UC US Patent 7,265,356

Target organ: spinal cord  

MGH, El Fakhri

MGH, IJROBP, 58:727, 2004

Dose distribution from treatment plan

In room short (5 min)
In room long (30 min)
Offline (30 min)
Sum (45 min)

In room short
In room long
Offline
Fast Electronics and All Digital PET

32-Channel Transmission Line Board

Prototype MCP PMT & TL Module

DRS4 Evaluation Board

14.1 % FWHM Energy

~310 ps FWHM Timing

0.26 mm FWHM Resolution across TL

~41 ps FWHM Timing along TL

2.8 mm FWHM position accuracy

UC, ANL, etc.
OpenPET Front End

PMTs

A

Gain Adjust, Anti-Alias

Discriminator

B

Gain Adjust, Anti-Alias

Discriminator

C

Gain Adjust, Anti-Alias

Discriminator

D

Gain Adjust, Anti-Alias

Discriminator

Free-Running (80 MHz)

+5V \rightarrow V_{\text{in}}\rightarrow \textbf{ADC} \rightarrow \textbf{TDC}

Crystal Lookup (X & Y \Rightarrow ID)

Energy Validation (E & ID \Rightarrow 511?)

Time Stamp (T & ID \Rightarrow T Stamp)

Event Formatting

FPGA & Memory

Analog Done w/ Discrete, Digital Done w/ FPGA
Detector 1: Conventional Block Detector

12x12 array of 4x4x22 mm³ LSO crystals
4 Hamamatsu R-9800 PMTs

- Pre-Prototype Circuit Boards
- Excellent Flood Map and Energy Resolution
Detector 2: SiPM Array

16x16 array
3x3 mm² SiPMs

Adapter Board
16x16 array
to
16 Row &
16 Column
Analog Sums

Natural LSO Activity

3x3x20 mm³ &
3x3x30 mm³ LSO

Pixel Intensity $\propto$
Energy x Count Rate

Same Electronics with Very Different Type of Detector
Timing Resolution

Test Pulse

TOF Module Pair

HPTDC (CERN)

FPGA

- 16 Channel TDC in Cyclone II FPGA
- Performance Good Enough for Time-of-Flight PET
Open Source
- Hardware, Firmware, and Software
- Schematics, Gerbers, BOM, ...

Active User Community
- Share Software and Expertise
- Module, Calibration, DAQ, Display, ...

Fall, 2011
- Detector & Support Boards Available
- Work on Coincidence Board Begins

http://OpenPET.LBL.gov
RatCAP for PET Imaging of Awake Animals
LSO + APD
Simultaneous PET/MRI Based on RatCAP in Small Animals & for Breast Imaging

Flex circuit board covered with Copper case
Large-FOV Positron Emission Mammography

- A large field-of-view (15 cm x 20 cm) PEM
- Two-Panel pixelated LGSO/LYSO
- Coupled to an array of PSPMTs

DOD & NIH Funded large-scale clinical trials
Conducted at Duke Univ.

Jefferson Lab
Molecular Breast Imaging (BMI)

Dilon 6800 Acella
Expanded FOV
20 cm X 25 cm

Dilon 6800 Gamma Camera
15 cm X 20 cm

Successful Technology Transfer to and commercialization by Dilon Diagnostics

Jefferson Lab

BMI
High resolution & high counting-rate animal PET scanner

CFOV resolution: 1.67 mm
Scanners for Molecular Imaging

\( \mu \text{PET} \),

\( \mu \text{PET/CT} \)

\( \mu \text{SPECT/CT} \)
Scanners for Molecular Imaging

Optical $\mu$PET

$\mu$CT
High Resolution whole-body PET Scanner (currently detector research)

Designed Feathers:

- Gantry aperture: >650 mm
- Axial FOV: >150mm
- Spacial Resolution: ~3.5mm
- Crystal material: LYSO
- Crystal number: 30976
- Detector number: 256
- Dia. of detector ring: 810mm

**LYSO**: an patent-free Cerium-doped Lutetium Yttrium Oxyorthosilicate ($\text{Lu}_{2(1-x)}\text{Y}_x\text{SiO}_5:\text{Ce}$)
Performance of detector and electronics

Detectors and flood-histogram for 11×11 crystal array

Front-end electronics (ASIC) and 32-Chanel digital board
Mammography is a morphological technique

A PEM system is a PET device dedicated to breast cancer detection, and has higher gain and lower noise.

Sensitivity to small tumors (1-2 mm)

Morphological
Sensitive to tissue density

Functional
Sensitive to metabolism

The PEM system we designed is prone-style, with annular detector structure.
Design and production of PEM system have been completed. Performance testing is under way.

Detector ring of our PEM

Reconstruction algorithm & user interface

A/D & Coincidence system

Initial imaging results

Rat imaging
IHEP in Beijing

PEM is in clinical trial stage for SFDA registration
Radiotracer More Readily Available
Mobile & Compact Biomarker Generator

Micro Accelerator

Microchemistry & Microfluidics

Courtesy of ABT
Oh, YES!

SiPM

Siemens

LBL