Medical Imaging - Spin-off from Particle Physics

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Center for Advanced Imaging,
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Morgantown, WV
Content of the Talk

- Nuclear Medicine – spin off from experimental nuclear physics/high energy physics
- Physics concept of PET and SPECT
- Instrumentation development
- New scintillators
- New photodetectors (new PMTs, Silicon PMTs)
- Multimodality imaging: PET/CT, PET/MRI
- New concepts on improving PET
- TOF PET
- Organ specific PET imagers: breast, prostate, brain, heart
Rationale

-Spin-offs from the “big physics” projects are popular and expected by all the “stakeholders”, even if not part of the main “mission”

-Scientists involved are to a large extent “normal” people sharing the concerns of the society

-Medical imaging was and is a natural spin-off from the particle physics community via:
  - Relevant technical expertise
  - Radiation detection instrumentation
  - Fast readout electronics and data acquisition systems
  - Fast computers
  - Computing algorithms, including simulations (“Monte Carlo”)

-Special opening is in the dedicated organ specific imagers, where the technology advancements (compact, mobile, offer new opportunities to implement what particle physics is using or developed initially for the main mission.
Areas of involvement

- The most obvious field: nuclear medicine: SPECT and PET
- Diagnostic tools (early detection of abnormalities, such as cancer)
- Beam radiation therapy (proton and ion beams, and the latest promise of antiprotons !)
- Monitoring chemo- and radio-therapy
- Organ specific imagers:
  - Breast
  - Prostate
  - Brain
- Small animal SPECT and PET imagers

Special features: MRI compatibility, Time of Flight (TOF) PET
Imaging Modalities

**Ultrasound**
- Structure
- 0.1 mm
- Doppler

**CT**
- Tissue Density, Z
- 20-50 µm

**MRI**
- H Concentration
- 0.1 mm
- BOLD, DCE
- β-galactosidase
- 0.1 µmole H / µmole ³¹P

**PET/SPECT**
- Radiotracer
- ~1-2 mm
- <10⁻¹² mole
- ≠ quantitative

**Optical**
- (Bioluminescence, fluorescence)
- Topography
- µm to mm
- ~10³ cells
- ≠ quantitative

**Center for Advanced Imaging**

AT WEST VIRGINIA UNIVERSITY
Positron Emission Tomography (PET)

- Radionuclide decays by emitting a positron ($\beta^+$).
- $\beta^+$ annihilates with $e^-$ from tissue, forming back-to-back 511 keV photon pair.
- 511 keV photon pairs detected via time coincidence.
- Positron lies on line defined by detector pair.

- Detects Pairs of Back-to-Back 511 keV Photons
- No Collimator Needed $\Rightarrow$ High Efficiency

(Bill Moses, LBL)
Contributions from “Physics”

- Physics concepts: positron range, annihilation, imaging via efficient detection of two 511 keV annihilation gamma rays, two gamma rays colinearity, TOF, etc
- Instrumentation: detectors, electronics
- Radioactive labels (in radiopharmaceuticals)
- Simulations (modeling) of the detection process and electronics
- Reconstruction, filtering algorithms (tomography, including limited angle)
Historically: BGO “Block Detector”

- **Scintillator**: BGO
- **Photodetector**: PMTs
- **511 keV**: (\(^{22}\)Na)
- **1274 keV**

5.3 cm × 5 cm and 3 cm thick
8×4 array, 12.5 mm × 5.25 mm crystal size

(Bill Moses, LBL)
High resolution research tomograph (HRRT)

HRRT brain PET scanner

- 19 mm x 19 mm blocks cut into 8 x 8 crystals per block
- 2.1 mm x 2.1 mm crystals of LSO/GSO (7.5 mm in depth)
- 8 heads per scanner, each head 18 cm x 26 cm
- 140 19 mm PMTs per head
Patient injected with radioactive drug. Drug localizes according to its metabolic properties. Gamma rays, emitted by radioactive decay, that exit the patient are imaged.

1. **Collimator**
   Only gammas that are perpendicular to imaging plane reach the detector.

2. **Scintillator**
   Convert gammas to visible light.

3. **Photomultiplier**
   Convert light to electrical signal.

4. **Readout Electronics**
   Amplify electrical signal and interface to computer.

5. **Computer decoding procedure**
   Elaborate signal and gives image output.
Advances in PET

PET in 1986

- 8 mm Resolution
- 5 cm Axial Extent
- Cardiology / Neurology
- Academic Research

PET in 2006

- 4 mm Resolution
- >15 cm Axial Extent
- Oncology
- Routine Clinical
Applications of PET

-Clinical:
  - Diagnosis: cancer, neurological diseases, trauma
  - Guiding, monitoring therapy: chemotherapy, radiation therapy
-Research in small animal models of human diseases: origins, cure, treatments (stem cells)
-Plant and ecological sciences
-Material sciences
microPET II Imaging in Mice

No gating

32 g mouse
580 μCi, 60 min

0.975 mm LSO
64-ch PMT + F.O.
X-Y Analog decoding
Resolution: 1.2 mm/2.3 μl
Efficiency: 2.26%
Peak NEC: 235 kcps

31 g mouse
1 mCi $^{18}$F-

Yang et al, PMB 2004
& IEEE NSS/MIC 2004
Of Mice and Men ... and Broken Hearts (MRI at UVA)
Structural medical images at its best - reference point

73-year-old man 7 years after an anterior MI.

14-week old C57BL/6N mouse 4 weeks after a reperfused, 2-hour occlusion of the major LAD.

(Courtesy of Dr. Stuart Berr, UVA)
Heart Research in the Mouse

Human – 60 BPM

Mouse Body

Mouse Heart – 500 BPM

(Stuart Berr, UVA)
Spin-off from particle physics?

Simulation of a Higgs event in the CMS detector at the LHC Collider at CERN
Why PET?

Similarities and differences

**Similarities**
- Geometry and granularity
- Detector (Crystals & scintillator)
- Photo Sensor (PM, APD)
- Electronics: Fast and compact
- Event rate & Data volume

**Differences**
- Energy range (10GeV-511keV)
- No synchronisation
  --> free running electronics

6 June 2006
Calor 2006 - P. Le Dû

Producing Images
PET Hardware Development

The HIDAC Camera Project at CERN, 1977-1982

1978

1982
Reconstruction Software

A general method for three-dimensional filter computation

B Schorr, D Townend, and R Clark

Abstract. Application of the Fourier space deconvolution algorithm to three-dimensional (3D) reconstruction problems necessitates the computation of a 3D frequency space filter. This filter is obtained by taking the 3D Fourier transform of the system response function. In this paper, it is shown that for system response functions of a specific form with $\psi / \theta$, with $\psi / \theta$ as an angular function describing the imaging system, the filter computation can always be reduced to a single integration which, in many cases, may be performed analytically. Complete expressions are derived for the general 3D filter, and two examples are given to illustrate the use of such expressions.

Three-dimensional filter computation

The 3D filter computation may be written

$$D(\varphi, \theta) = \int_{-\infty}^{\infty} g(x, y, z) e^{i2\pi \varphi x + i2\pi \theta y} dx dy dz$$

where $g(x, y, z)$ is the system response function.

Since

$$\int_{-\infty}^{\infty} g(x, y, z) e^{i2\pi \varphi x + i2\pi \theta y} dx = \left[ \text{sign}(\varphi) - \text{sign}(\theta) \right] f(\varphi)$$

and

$$D(\varphi, \theta) = \int_{-\infty}^{\infty} s(x, z) e^{i2\pi \varphi x + i2\pi \theta z} dx$$

for $0 < \varphi < \pi / 2, 0 < \theta < \pi / 2$ where the functions $s(x, z)$ are given by

$$s(x, z) = \frac{\text{sign}(\varphi) - \text{sign}(\theta)}{2 \pi \varphi} f(\varphi)$$

and

$$g(x, \varphi, \theta) = \frac{\text{sign}(\varphi) - \text{sign}(\theta)}{2 \pi \varphi} f(\varphi)$$

since $d(x, y, z) = d(x, y, -z)$.

Equation (24) is thus reduced to a single integration, equation (35), with the functions $s$ and $g$ given by equations (36) and (37). Computer implementation of equation (35) may be made more efficient by a detailed analysis of equation (36). The function $s(x, \varphi, \theta)$, with a value of $+1$, $-1$, or $0$, has the effect of segmenting Fourier space into at most four regions, as follows:

$$D(\varphi, \theta) = \begin{cases} \pi^2 \tan \varphi \tan \theta & 0 < \varphi < \pi / 2, 0 < \theta < \pi / 2 \\ \pi^2 \tan \varphi \tan \theta & 0 < \varphi < \pi / 2, 0 < \theta < \pi / 2 \\ 0 & \text{otherwise} \end{cases}$$

with

$$a = \max(\Theta - \varphi, 0)$$

and

$$l = \cos^{-1}(\tan \varphi \tan \theta), 0 < l < \pi / 2.$$
Good Publicity

The HIDAC Camera Project at HCUG, 1983-1988

Tribune de Genève, January 1988

Le Courrier, January 1988

Thyroid imaging with $^{124}$I

Scientists Press Plans for New Brain and Heart Research

UN/ News 1988

Financially supported by the Fonds National Suisse
Spin-off from particle physics

The PRT Camera Project 1990 - 1992

PRT-1
Dual rotating arrays
Built at CERN

First FDG brain study on PRT-1,
Geneva Hospital, May 1991

Nouveau Quotidien  July 19, 1992
Financially supported by the CERS
Bio-medical applications of CERN technologies

Some properties of High Energy Physics apparatus

- Highest possible performance
- Lab environment/physicist operated
- Possible complex maintenance
- Possible complex operation
- Single unit production
- Non commercial
- Industry as a manufacturer only

Some properties of biomedical apparatus

- Robustness
- Non-specialist operated
- Minimal maintenance
- Simple to operate
- Small series production
- Commercial distribution
- Industry as a partner

Courtesy of M. Dosanjh/CERN
Using a wire chamber viewed by an image-intensified CCD camera, a CERN/Geneva Cantonal Hospital team obtained a radiograph of a rat kidney a hundred times faster than conventional methods. ‘This rat kidney changed my life,’ says Charpak.

For the future, the quest for ‘Dark Matter’ – the missing material that makes up most of the Universe – will continue to challenge detector builders. ‘The detector research and development work being done for the LHC will also provide valuable spinoffs,’ claims Charpak. ‘When people ask ‘what use is this work’, these are the things to point to’.

Charpak admits to having been surprised by the Nobel news. ‘But CERN wasn’t surprised,’ retorted CERN Director General Carlo Rubbia. ‘It underlines that physics instrumentation is just as important as accelerators. The prize is also a great honour for CERN, and underlines its preeminent position in the forefront of particle physics.’

Born in Poland in 1924, Georges Charpak was educated in France, the country whose nationality he now holds. After an introduction to research at the Collège de France, Paris, he joined CERN in 1959. He passed a formal 65th birthday career milestone in 1969, but is still very active with his driving ambition to apply frontier detection ideas.

While ideas in physics are quickly incorporated into ongoing research, convincing the medical community of the value of new techniques needs a special effort, he says. Charpak has made a considerable personal investment in this research and development work, to the extent of making personal sacrifices. ‘Now I can buy some new shoes,’ he joked after hearing the Nobel news.

Charpak is popular and widely admired at CERN. On hearing the Nobel news on the car radio, a CERN acquaintance was moved to tears. Charpak inspires loyalty – he has worked with three skilled and dedicated specialists – Roger Bouclier, Gilbert Millon and Jean-Claude Santard – for practically the whole of his CERN career. At CERN, he was soon joined by Fabio Sauli, who has continually shared in a long series of new developments, and who now formally heads the unit at CERN. At Charpak’s 65th birthday celebrations at CERN, Sauli declared that the name ‘Charpak Group’ will continue to be used.

Another aspect of Charpak’s personality is his continual concern for less privileged colleagues. He was a driving force in the late 70s and early 80s in the action by physicists that eventually led to the release of Yuri Orlow and Andrei Sakharov.

With his fame previously restricted to physics circles, Charpak became a celebrity overnight after the Nobel announcement. With last year’s physics prize won by Frenchman Pierre-Gilles de Gennes, the news had special impact in France. Charpak’s numerous contributions.

Eight year series – three physics Nobels enjoy the CERN Charpak party entertainment. Left to right CERN Director General Carlo Rubbia (1984), Sam Ting (1976) and Georges Charpak (1992).

(Photo CERN H84.10.92)
40 years with Georges...

Georges Charpak 1924 – 2010
A scientist, humanist, educator, friend

A source of inspiration to many of us:
Fabio Sauli, Francois Pieu, Amos Breskin, Stan Majewski, Vladimir Peskov, Dave Anderson, Nick Solomey, Ariella Cattai, Leszek Ropelewski, WojtekDominik, Paolo Fonte, Joannis Giomataris, Lev Shekhman and may others...
“Groupe Charpak” – Work and Celebrations

David Anderson

Amos Breskin

Roger Bouclier

Vladimir Peskov
Wire Chambers

Gaseous proportional tracking detectors that revolutionized High Energy Physics

Electronic Imaging in 3D

With Fabio Sauli et Jean Claude Santiard
The 1st “Large Wire Chamber”…
CERN-LHC: Enormous wire chambers...

40 years later...

ATLAS 2009

ALICE 11 2010

The Time Projection Chamber (TPC)

Thin-Gap Wire Chambers (TGC)
A THIN MULTIWIRE CHAMBER OPERATING IN SATURATED AND LIMITED STREAMER MODES -- PRELIMINARY RESULTS

S. Majewski and G. Charpak

Fig. 1 Test chamber structure. Gap L = 1 mm; step of 50 μm diameter, stainless-steel anode wires: s = 2 mm. Field wires: gold-plated molybdenum, 100 μm diameter. External cathodes made of 50 μm thick aluminium foil.

Fig. 2 Geometry of electrostatic field distribution in the structure of Fig. 1. External cathodes are at the ground potential. Two extreme cases were analysed: a) Sense wires at -1.00 kV; field wires at -1.00 kV. Note that majority of the lines of force are collected on field wires (computer simulation). b) Anode sense wires at +2.00 kV, field wires at 0 kV (resistive paper simulation).
Thin Wire Chamber

S. Majewski, G. Charpak, A. Bluskin, and G. Mikenberg

A THIN MULTIWIRE CHAMBER OPERATING IN THE HIGH MULITPLICATION MODE

1. Introduction

At present there exist many different structures of multiwire chambers that operate in the limited streamer or saturated modes. Some of the applications are in the domain of sampling counters in calorimeters. The advantage of such a sampling counter in comparison with the standard multiwire proportional chamber (MWPC) lies in the very high, saturated amplitude response for each particle in a shower.

But the disadvantage of most of the limited streamer counters operational at present is in the size of their active cells, which is of the order of 1 cm x 1 cm (see refs. 2 and 3). Such large sizes are dictated by the range of photon fluxes produced in an avalanche. Photons limit the attainable amplitudes by the photo-feedback mechanism acting at places where secondary photons are produced and secondary avalanche, thus deteriorating both the amplitude and the position resolutions of a detector. The second effect can be cured by introducing walls between cells which simply absorb photons. But there still remains a problem of photons propagating along gas. Here the idea of a resistive cathode coating was found helpful, locally desensitizing the detector around an original streamer avalanche. However, this solution probably cannot be accepted for electromagnetic calorimeters at higher energies where the density of shower particles becomes high. The best and simplest solution could be to use a gas that absorbs its own photons well enough. For example, avoiding air by using the argon or neon in a gas mixture should give a good result.

The other limit on the chamber distances comes from practical reasons related to the necessity of keeping a sufficient level of electrode parallelism compatible with the assumed energy (amplitude) resolution of the counter over its surface. The minimum practically attainable thickness is very much dependent on the active surface of the detector. With this restriction, voltages necessary to operate the counter filled with strongly self-quenching gas in the limited streamer or saturated modes could be prohibitively high.

This sampling counters have the advantage of limiting the longitudinal size of a calorimeter and hence the lateral extension of showers and permits the construction of calorimeters with a large number of sampling layers without increasing the overall longitudinal size of a calorimeter. Moreover, they should also lower the relative importance of delta ray. This was the reason why we decided to develop thin gas counters. We concentrated our work on multiwire detectors, aiming at a thin thickness of 2-3 mm only.

2. Chambre structure

The sampling test-chamber structure is presented in Fig. 1. The chamber has 50 μm diameter, sense (anode) wires and aluminium or graphite-coated mylar foils as cathodes. Originally we started with a 1 mm gap chamber having thin field wires of 100 μm diameter. Then we tried a similar simpler version of a detector without field wires and a gap of 1 and 1.5 mm. We found that the operation of this detector quite satisfactorily as shown in Fig. 1. The use of a detector with field wires the usual idea was that by having a large fraction of the positive charges on the 50 μm sense wires (SW)
Further Results in Nuclear Scattering Radiography

G. CHARPAK, S. MAJEWSKI, Y. PERRIN, J. SAUDINOS, F. SAULI, D. TOWNSEND and J. VINCIARELLI
CERN, 1211 Geneva 23, Switzerland

Received 15 April 1976

Abstract. A further investigation of the nuclear scattering of 500–1000 MeV protons is described. Three-dimensional information on the density distribution within carbon, CH and H₂O phantoms is obtained with a volume resolution of 2 mm³. The separation of scattering on hydrogen from that on heavier nuclei, such as carbon and oxygen, is demonstrated, providing the statistics are sufficient. Some preliminary measurements on animals are reported, but with a volume resolution limited by statistics to 45 mm³.

Fig. 1. Experimental set-up (vertical cut). The drift chambers DC₁, DC₂, DC₃ and DC₄ measure the trajectories of the incident and scattered protons.

Fig. 6. Positions of the animals relative to the beam: (a) rabbit; (b) mouse with an abdominal tumour. The dashed lines give the limits in X of the useful area.

Fig. 7. Density distribution: (a) Rabbit, vertical direction Y/Z of 3.5 mm, perpendicular to the beam direction; (b) mouse with tumour, horizontal plane (plane Z/Z) of 3.5 mm. The skin corresponds to the horizontal beam axis. The scale of colours is given at the bottom of the figure. Colour 23 (maroon) is changed to black in the figure in order to increase the contrast.

RABBIT SLICES IN 3.5 MM

G. Charpak et al.
An Efficient, Gaseous Detector with Good Low-energy Resolution for (≤50 keV) Imaging

Nguyen Ngoc Hoan, S. Majewski, G. Charpak, and A.J.P.L. Polcarpo

Institut National de Physique Nucléaire et de Physique des Particules, Orsay, France, University of Warsaw, Warsaw, Poland, and University of Coimbra, Coimbra, Portugal

An imaging detector with good energy resolution and reasonable spatial accuracy has been designed for biomedical applications. It is based on a scintillating proportional gas chamber. The energy resolution is typically 5.4% (FWHM) at 27 keV and the spatial resolution is 2.7 mm (FWHM) for 22-kV x-rays. The physical processes involved in this detector are discussed along with its main limitations and merits.


FIG. 4. (A) Energy resolution and linearity of detector observed with radioactive sources and fluorescence spectra induced by 60-keV radiation from Am-241. (B) Energy resolution of camera. Spectrum of x-rays emitted at 130° relative to 60-keV beam emitted by Am-241, impinging on a 3% solution of KI in water. Shown are Kα and Kβ lines of iodine (27.5 and 31.0 keV) with a resolution of 5.4%. Lower-energy peaks are Kα, xenon escape peaks from the Compton radiation scattered at 130°.

FIG. 6. Image of thyroid phantom (Picker No. 3802) filled with 30 μCi of I-125. Collimator has 1-mm holes, septa 0.1 mm, length 20 mm, transmission 1.24 × 10^{-4}. Acquisition time 5 min.

FIG. 7. Thyroid image from unanesthetized rabbit with 100 μCi of I-125 injected 24 hr before observation. Acquisition time 5 min.
High Pressure Xenon Cardiac Camera invented by Georges Charpak

- Limited to Tl201 imaging
- Complicated mechanics and electronics
- Difficult to operate
- Response uniformity issues

Fig. 19: Immagine digitalizzata del phantom del cuore.
History

The 1992 Nobel Prize for Physics was awarded to a revolutionary invention: a high energy particle detector.

This detector design gave birth to EOS; it enabled X-ray imaging to be performed at a much lower dose, with an expanded dynamic range and without the vertical distortion inherent in today’s long length film and digital imaging systems. A collaboration with a team of world-class physicists, engineers and most importantly orthopedic surgeons and radiologists brought EOS from proof of concept to a fully operational machine. All thanks to a radically new vision of what imaging could and should bring to orthopedics.

- 2005: Clinical testing in Paris and Brussels hospitals completed with first EOS prototype
- 2006: biospace med is created and has received its first venture capital round
- 2007: EOS has received market approval in Europe and North America
- 2010: EOS equips hospitals and private clinics in the USA, Canada and 5 European countries
- 2012: The company changes its corporate name to EOS imaging

EOS imaging development and production facilities are located in central Paris. The company has subsidiaries in Cambridge, USA and Montreal, Canada.
Many were inspired by Georges, and his direct and indirect contributions to science and technology, including medical technology, will continue for a long time...

Georges was not only a passionate genius, but his very positive attitude and acceptance, as well as his broad interests, were unusual.
Spin-offs from particle physics

- new dense and fast scintillating crystals or direct conversion materials
- finely segmented and compact photodetectors
- low noise and highly integrated electronics
- data acquisition systems based on highly parallelized architecture with efficient data recording and storage
- filtering algorithms
- modern and modular simulation software based on universally recognized standards
- high performance image reconstruction and analysis algorithms

(Paul Lecoq, CERN)
<table>
<thead>
<tr>
<th></th>
<th>BGO</th>
<th>LSO</th>
<th>Ce/LaBr$_3$</th>
<th>LuI$_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminosity (ph/MeV)</td>
<td>8,200</td>
<td>25,000</td>
<td>60,000</td>
<td>100,000</td>
</tr>
<tr>
<td>Energy Resol. (@ 511 keV)</td>
<td>12%</td>
<td>10%</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Decay Time (ns)</td>
<td>300</td>
<td>40</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>Density (g/cc)</td>
<td>7.1</td>
<td>7.4</td>
<td>5.0</td>
<td>5.6</td>
</tr>
<tr>
<td>Atten. Length (mm, 511 keV)</td>
<td>11</td>
<td>12</td>
<td>24</td>
<td>18</td>
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<tr>
<td>Photofraction (@ 511 keV)</td>
<td>43%</td>
<td>34%</td>
<td>14%</td>
<td>29%</td>
</tr>
<tr>
<td>Wavelength (nm)</td>
<td>480</td>
<td>420</td>
<td>370</td>
<td>470</td>
</tr>
<tr>
<td>Natural Radioactivity?</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Hygroscopic?</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

(Bill Moses, Berkeley)
Hybrid (multi-modality) imaging

- **Morphology**
  - CT
  - Dynamic, Perfusion

- **Physiology**
  - US
  - Dynamic, Flow, Perfusion

- **Metabolism**
  - MRI, MRS
  - Dynamic, Flow, Perfusion, Diffusion, Molecules

- **Molecules**
  - NM
  - Perfusion, Molecules

- **Hybrid (multi-modality) imaging**
  - Fluorescence-Optical
  - Several molecules/cell
  - Molecules

1 molecule/cell

$10^6$ - $10^8$ molecules/cell
PET/CT Dual Modality Imaging

Whole-Body PET/CT

Image courtesy of UCLA
Fused image accurately localizes uptake into a lymph node and thus demonstrates spread of disease.

**Why combine form and function?**

- to image different aspects of disease
- to identify tracer uptake
- to simplify the image interpretation
- to give added value to CT and PET

**Form + function**

CT (anatomy)  PET/CT  PET (function)

Courtesy of David Townsend, Ph.D. University of Tennessee Medical Center
Combine PET & CT

CT Image  PET Image  Fused Image  Post-Therapy

Images courtesy of Stig Larsson, Karolinska Institute

• Anatomy from X-Ray CT, Function from PET
• Current “Standard of Care”
Lung cancer: response to therapy

Responder: Patient alive 20 months after end of chemotherapy

Non-responder: Patient survived 2 months after end of chemotherapy

Courtesy of David Townsend, Ph.D.
University of Tennessee Medical Center
What are the benefits of PET/CT?

- Accurate spatial localization of abnormalities detected on PET—which can be VERY difficult to locate on PET alone
- Accurate determination of location of questionable abnormalities on PET—are they normal tissues with FDG uptake or tumor?
- More rapid scans, less motion of patient
- Higher quality transmission counts/precision
- Consolidation of visits to imaging specialist

- Goal: Better Diagnostic Accuracy
One view of the history of PET

Some milestones in medical imaging:

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1976*</td>
<td>first dual HIDAC detectors developed</td>
</tr>
<tr>
<td>1977*</td>
<td>first (^{18})F mouse image with HIDAC</td>
</tr>
<tr>
<td>1980*</td>
<td>3D reconstruction algorithms for PET</td>
</tr>
<tr>
<td>1982</td>
<td>HIDAC camera in Cantononal Hospital</td>
</tr>
<tr>
<td>1984</td>
<td>BGO block detector invented</td>
</tr>
<tr>
<td>1986</td>
<td>first multi-ring BGO scanner (ECAT 931)</td>
</tr>
<tr>
<td>1991*</td>
<td>partial ring tomograph PRT-1 developed</td>
</tr>
<tr>
<td>1991</td>
<td>PET/CT concept envisaged</td>
</tr>
<tr>
<td>1993</td>
<td>partial ring tomograph PRT-2 developed</td>
</tr>
<tr>
<td>1994</td>
<td>ECAT ART announced</td>
</tr>
<tr>
<td>1995</td>
<td>PET/CT project receives NIH funding</td>
</tr>
<tr>
<td>1998</td>
<td>First PET/CT images acquired on patients</td>
</tr>
<tr>
<td>2001</td>
<td>First commercial PET/CT scanner installed</td>
</tr>
</tbody>
</table>

2001: First commercial PET/CT installed
2011: over 5000 PET/CT scanners installed worldwide
(data from: Institute for Clinical PET)
2. Clinical implementation and results for carbon ion therapy

- Control of the carbon ion range
- Verification of field position
- Detection and quantification of deviations between real and planned dose (misalignments, local changes of anatomy), allowing intervention prior to next fraction (W. Enghardt et al. Radiother. Oncol. 73, 2004)

For every treatment fraction (typically 20 days)
3. The prediction of proton induced $\beta^+$-activity

Necessary for clinical implementation of in-beam PET

Calculation of $\beta^+$-emitter density $P(r)$
1) $\phi_p(r,E)$ given by Monte Carlo code FLUKA
2) Experimental cross sections $\sigma(E)$
3) $P(r)$ convolved with Gaussian kernel of 7 mm FWHM (spatial resolution of imaging system)

Comparison with measured $\beta^+$-activity
Good agreement
- Spatial distribution
- Time dependence due to different $\beta^+$-emitters
($^{11}$C: $T_{1/2}$=1222.8 s, $^{15}$O: $T_{1/2}$ = 121.8 s)
How to Detect Smaller Lesions with PET

- Improve spatial resolution
- Improve sensitivity (SNR)
- Improve reconstruction algorithms
- Synergistic use of PET and CT information
- New radiotracers for specific targets

(slide provided by Dr Simon Cherry, UC Davis)
The clinical importance of spatial resolution

Low-REZ; 8.6 mCi; 60 min uptake

HI-REZ; 11.2 mCi; 90 min uptake
<table>
<thead>
<tr>
<th>Isotope</th>
<th>Max. Positron Energy (keV)</th>
<th>Levin and Hoffman</th>
<th>Sanchez, Andreo, Larsson</th>
<th>Our Results (EGS4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>FWHM (mm)</td>
<td>FWTM (mm)</td>
<td>FWHM (mm)</td>
</tr>
<tr>
<td>$^{18}$F</td>
<td>635</td>
<td>0.10</td>
<td>1.03</td>
<td>0.19</td>
</tr>
<tr>
<td>$^{11}$C</td>
<td>970</td>
<td>0.19</td>
<td>1.86</td>
<td>0.28</td>
</tr>
<tr>
<td>$^{13}$N</td>
<td>1190</td>
<td>0.28</td>
<td>2.53</td>
<td>0.33</td>
</tr>
<tr>
<td>$^{15}$O</td>
<td>1720</td>
<td>0.50</td>
<td>4.14</td>
<td>0.41</td>
</tr>
<tr>
<td>$^{68}$Ga</td>
<td>1899</td>
<td>$0.6^z$</td>
<td>$4.6^x$</td>
<td>0.49</td>
</tr>
<tr>
<td>$^{94m}$Tc</td>
<td>2438</td>
<td>$0.8^z$</td>
<td>$8.2^x$</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Table I. Positron range for various positron emitters from three separate simulations. The Levin and Hoffman results with an asterisk were found using a linear approximation to scale the data taking into account the maximum positron energy.
Penetration Blurs Image

Low Density $\Rightarrow$ Radial Elongation

Resolution vs. Position

Some Degradation with $\text{LuI}_3$, More with $\text{LaBr}_3$
Achieving High Resolution at Good Efficiency

- Must have high spatial resolution
- Must (generally) have good DOI resolution
- Must (sometimes) have good energy resolution
- Must have solution for using events that scatter first
“Conventional” Approach to High Resolution
Build ring of high resolution detectors

Large Diameter Ring

\[ \varepsilon = \frac{R_1 R_2}{R_1 + R_2} \times \delta \]

Reduces DOI effects
Increases acolinearity
Expensive

Small Diameter Ring

Reduces acolinearity
Increases DOI problem

(Neal Clinthorne, U. Michigan)
Other Geometries Allowing High Resolution in a Region-of-Focus

- Position and orientation of detectors known with time
- Reconstruction straightforward but limited angle tomography issues

Full ring, partial inner detector

Partial-Partial

High resolution inner detector

(Neal Clinthorne, U. Michigan)
Axial Position Determined Accurately w/ TOF

- Can Assign Chord to Correct Axial Plane
- Reduces Axial Blur in Reconstructed Image
- Reconstruction Algorithm Converges Faster

500 ps Time-of-Flight Localizes Source Position to ~7.5 cm fwhm Along Direction of Travel

Because Chord is Nearly Vertical, Source Position Localization is 6x – 200x Finer in Axial Direction
How does TOF help?

$\Delta t = \text{uncertainty in measurement of } t_1 - t_2$

$\Delta x = \text{uncertainty in position along LOR}$

$= c \cdot \Delta t / 2$

$D/\Delta x \sim \text{reduction in variance or gain in sensitivity}$

(Joel Karp, U. Penn)
Time-of-Flight and SNR

\[ \Delta x = \frac{\Delta t}{2} c \]

\[ SNR_{TOF} \approx \sqrt{\frac{D}{\Delta x}} \cdot SNR_{conv} \]

<table>
<thead>
<tr>
<th>Time Resolution (ns)</th>
<th>( \Delta x ) (cm)</th>
<th>SNR improvement (20 cm object)</th>
<th>SNR improvement (40 cm object)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>1.5</td>
<td>3.7</td>
<td>5.2</td>
</tr>
<tr>
<td>0.3</td>
<td>4.5</td>
<td>2.1</td>
<td>3.0</td>
</tr>
<tr>
<td>0.5</td>
<td>7.5</td>
<td>1.6</td>
<td>2.3</td>
</tr>
<tr>
<td>1.2</td>
<td>18.0</td>
<td>1.1</td>
<td>1.5</td>
</tr>
</tbody>
</table>

( Joel Karp, U. Penn)
non-Hodgkin’s lymphoma 136 kg (45 BMI)

TOF tumor contrast superior (x1.8) for 10 min and 30 min scan

(Philips PET/CT, Joel Karp, U. Penn)
Improvement in lesion detectability with TOF

Colon cancer  119 kg (BMI = 46.5)  3 min/bed; 27 min tot

(Philips PET/CT, Joel Karp, U. Penn)
Scintillators

TOF PET systems in 1980’s with BaF$_2$ achieved system TOF of 500-700 ps, but low light output led to poor energy and spatial resolution. Did not match overall performance of BGO systems with higher sensitivity.

<table>
<thead>
<tr>
<th>Scintillator</th>
<th>NaI(Tl)</th>
<th>BGO</th>
<th>BaF$_2$</th>
<th>GSO</th>
<th>LSO/LYSO</th>
<th>LaBr$_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\tau$ (ns)</td>
<td>230</td>
<td>300</td>
<td>2</td>
<td>60</td>
<td>40</td>
<td>27</td>
</tr>
<tr>
<td>$\mu$ (cm$^{-1}$)</td>
<td>0.35</td>
<td>0.95</td>
<td>0.45</td>
<td>0.70</td>
<td>0.86</td>
<td>0.47</td>
</tr>
<tr>
<td>Photons (per MeV)</td>
<td>41,000</td>
<td>7000</td>
<td>2000</td>
<td>10,000</td>
<td>26,000</td>
<td>60,000</td>
</tr>
</tbody>
</table>

- high stopping -> better sensitivity & better spatial resolution
- high light output -> better energy resolution & better spatial resolution
- fast decay & high light -> better timing resolution (TOF) & lower deadtime

(Joel Karp, U. Penn)
Measured Coincidence Time Resolution

**Two LaBr\(_3\) crystals (4x4x30 mm\(^3\))**
- FWHM = 280 ps

**Measured Coincidence Time Resolution

**Two LYSO crystals (4x4x20 mm\(^3\))**
- FWHM = 380 ps

Crystal array: Light sharing with 7 PMTs

**Two LYSO arrays (4x4x20 mm\(^3\))**
- FWHM = 640 ps

**Two LaBr\(_3\) arrays (4x4x30 mm\(^3\))**
- FWHM = 315 ps

( Joel Karp, U. Penn)
Large-Area Picosecond Photo-Detector (LAPPPD) Project

Next-Generation MCP-PMT

Project with 4 primary goals:
1. Low-Cost LAPPPD with good timing and spatial resolution ($\sim$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

(Chin-Tu Chen, University of Chicago)
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

(Chin-Tu Chen, University of Chicago)
openPET Vision

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

(Chin-Tu Chen, University of Chicago)
OpenPET Front End

PMTs

Gain Adjust, Anti-Alias
Discriminator

Gain Adjust, Anti-Alias
Discriminator

Gain Adjust, Anti-Alias
Discriminator

Gain Adjust, Anti-Alias
Discriminator

Free-Running (80 MHz)

$V_{in}$
$V_{ref}$

$+5V$

FPGA & Memory

TDC

A

Crystal Lookup
(X & Y $\Rightarrow$ ID)

Energy Validation
(E & ID $\Rightarrow$ 511?)

Time Stamp
(T & ID $\Rightarrow$ T Stamp)

Event Formatting

Analog Done w/ Discrete, Digital Done w/ FPGA

(Chin-Tu Chen, University of Chicago)
Improvements In Electronics

- Excellent TDC ASICs available
- Need High Performance CFD ASICs
  - Delay line difficult in ASICs
- Need integrated PET-specific ASICs
  - High-precision timing (CFD & TDC)
  - Energy measurement
  - Crystal identification
  - Calibration & testing

ASIC & Non-ASIC Solutions Underway Today
Needed Improvements in Photodetectors

- High Quantum Efficiency
  - 4x Larger Signal $\Rightarrow$ 2x Better Timing

- GHz Bandwidth

- Reasonable Gain

- Individual Small Pixels
  - High Light Collection Efficiency
  - Crystal by Crystal Time Correction

- Practical (compact, reliable, inexpensive...)

Geiger Mode APDs (SiPMs) Show Promise...

(Bill Moses, Berkeley)
Improvements in Photodetectors

Avalanche Photodiode Array

• High Quantum Efficiency
• GHz Bandwidth w/ Reasonable Gain
• Individual Small Pixels
• Practical (compact, reliable, inexpensive...)

Position-Sensitive APD

LSO Array

Hamamatsu Photonics

RMD, Inc.
Silicon Photo Multiplier:

- Immune to magnetic fields
- Gain = \((10^5-10^6)\) at low voltage (<100V)
  (typical APD gain: ~100)
- High photon detection efficiency (up to 50%)
- Dark count (0.1 to 1 MHz)
- Micro APDs in Geiger mode (>breakdown voltage)
Hall D Detector at Jlab (12 GeV energy regime)

$B_z$ (gauss)

Planacon Pair

Fiber Bundles

Acrylic Light Guides

BCAL [390 cm]

CDC [200 cm]
New Hybrid imaging: MR-PET

Benefits

• Isocentric & simultaneous measurements
  • Perfect anatomical matching
  • Important for attenuation correction and motion correction
• Good soft tissue contrast
  • Neuro
  • Abdomen
• No additional ionizing radiation through MR
  • Enables follow-up studies
• Gating and Motion Correction MR → PET
  • Prospective and retrospective
• Functional MR data adds further information
  • Spectroscopy, fMRI, CE dynamics
• (Resolution enhancement due to reduced positron range at UHF)
MR-PET Concepts

Analogous to PET-CT

- No simultaneous measurement, no isocentric measurement
- Reduced MRI compatibility demand (only main field)

PET-Insert

- Upgrade of existing MRI scanners possible
- Reduced FOV for PET

Integrated System

- Integrated development necessary
Oh, YES! SiPM

(Chin-Tu Chen, University of Chicago)
Dedicated organ imagers
example: PET breast imagers

• **Advantages**
  - Higher spatial resolution
  - Higher sensitivity
  - Should translate to better image quality
    • Detection of smaller lesions?

• **Disadvantages**
  - Limited to imaging breast
  - Difficulty visualizing chest wall region
Predicting the survival of patients with breast carcinoma using tumor size, JS Michaelson, M Silverstein, J Wyatt, et. al. *Cancer* 2002; 95: 713-723

(slite provided by Dr Simon Cherry, UC Davis)
Camera Comparison: Patient Positioning

Large field-of-view gamma camera - not designed to image the breast

Dilon 6800 small field-of-view gamma camera (anatomically specific)
JLab Imaging Detector Technology

- Pixellated scintillator
- Array of position-sensitive PMTs
Removable Smart Shield™ modified to accommodate biopsy hardware.

Removable sliding slant-hole collimator system for stereo viewing.
The Dilon 6800 Gamma Camera can replicate any mammographic view.
Mammogram: right breast shows area of microcalcifications (see arrow). Previous needle biopsy of this area was negative.

BSGI: demonstrated a high-uptake region highly suspicious and the patient was sent for open biopsy. Ductal Carcinoma.
Dense Breast - Negative BSGI

The slightly heterogeneous pattern seen in the BSGI image closely correlates with the bilateral dense parenchyma tissue seen in the mammogram. Negative.

Courtesy of West Valley Imaging
Mayo Clinic - Molecular Breast Imaging

- **CZT gamma camera technology**
  - Energy resolution < 5%
  - Intrinsic resolution 1.6 mm
- **Dual-detector design optimized for breast imaging**
- **Requires only light pain-free breast compression**
- **Utilizes radiotracer for tumor localization**
- **Prototype developed at Mayo Clinic**
Comparative Sensitivity of Scintimammography, single-head MBI and dual-head MBI

(Michael O’Connor, Mayo)
Positron Emission Mammography

FDG - glucose labeled with F-18

Positron annihilation: $e^+e^- \rightarrow \gamma\gamma$

Two 511 keV photons in opposite directions

Photon detection
Signal processing
Data acquisition
Image reconstruction

(ClearPEM collaboration)
Historically: BGO “Block Detector”

5.3 cm × 5 cm and 3 cm thick
8×4 array, 12.5 mm × 5.25 mm crystal size

511 keV (22Na)
1274 keV

(Bill Moses, LBL)
Advances in PSPMT Photodetector Technology

Compact position sensitive PMTs:
Hamamatsu’s R8520, H8500, and Burle’s 85002.
Naviscan PEM Imager
ClearPEM Concept

- **ClearPEM design parameters:**
  - High detection sensitivity (5% at 10 cm plate separation)
  - DoI resolution 2mm
  - Spatial resolution (1.4 mm FWHM)
  - Time resolution 1.3 ns r.m.s.

- **Scanner concept:**
  - Two planar heads
  - Mammary gland and axilla region exams
  - Exam with the patient in prone position
  - Adjustable distance between heads and rotation angle
LYSO Scintillating Crystals

<table>
<thead>
<tr>
<th>Density (g.cm⁻³)</th>
<th>Light Yield (photons/MeV)</th>
<th>Emission peak (nm)</th>
<th>Time constant (ns)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.4</td>
<td>27000</td>
<td>420</td>
<td>40</td>
</tr>
</tbody>
</table>

Avalanche Photodiodes

- Operating voltage $V_R$: 350-450 V
- Gain uniformity within a sub-array: ±15%
- Dark current $I_d$ per APD pixel at $V_R$: ≤ 10 nA
- Quantum efficiency at $\lambda$=420 nm: ≥ 70%
- Excess noise factor at $V_R$: ≤ 2.3 @ $\lambda$=420 nm
Frontend Electronics Integration

Compact system in the Detector

Head:

- 6144 APD channels
- 384 HV lines
- 128 high speed (600 MHz) output lines

High-voltage board

Detector Supermodule

Detector Plate

Modules (12x32 crystals, 24 APDs)

Frontend Board

ASICs (2x192 channels)

4.5 cm
Detector Heads

Data Acquisition Electronics (L1 hardware trigger)

Detector Heads

Cooling system: water cooled plates 18.0±0.1 °C
Nitrogen atmosphere inside detector head
Data Acquisition System

L1 Trigger/DAQ system is housed in a single crate with two dedicated buses

Sophisticated coincidence trigger (36k calibration constants)

Frontend to L1 bandwidth up to 156 Gb/s

Level 2 DAQ: high-end computer server

Level 2 bandwidth: up to 300 MB/s
ClearPEM scanner

Robotized gantry: 6 movement axis

Detector Heads

Operation, Monitoring, Reconstruction and Visualization Software

http://www.youtube.com/watch?v=90cJUHOMzVk&NR=1
- Two acquisitions with orthogonal plate orientations for each source location (400-600 keV)
- Simultaneous reconstruction of 16 source positions

**Na-22 source 30 uCi**

**Grid with 5 mm pitch**

**1 mm Na-22 source**

**ClearPEM Images**

- OSEM-3D
- OSEM-2D

FWHM_HOR = 1.5 mm
FWHM_VER = 1.2 mm
Clinical Trials

Scanner installed at IPO Hospital, Porto

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

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

IHEP

PEMi

Rat imaging

(Chin-Tu Chen, University of Chicago)
PEM is in clinical trial stage for SFDA registration
Drawbacks of the Standard PET Camera for Prostate Imaging

- Detectors are too far away from prostate
  ---> poor spatial resolution (6-12mm)
  ---> poor photon detection efficiency (<1%)
- Accepts activity from outside organs
  ---> poor contrast resolution
- Relative high cost per study
Prostate-Specific PET Scanner

- “Focused” on the Prostate
- Higher Efficiency & Resolution than Conventional PET
- Uses 4x Fewer Detector Modules than Conventional PET

Images courtesy of Jennifer Huber, LBNL
Dual-Modality PET / Ultrasound Imaging

PET

Trans-Rectal Ultrasound (TRUS)

Merged PET / TRUS Image?
Rationale for small PET camera dedicated to prostate imaging

- Close-proximity imaging $\rightarrow$ improved spatial resolution
  $\rightarrow$ improved photon detection efficiency
- Reduce background from active organs outside FOV
- Mobile--can be taken into different clinical environments
- Design favoring high spatial resolution at a reasonable cost
- Lower cost device $\rightarrow$ lower cost studies?

$\rightarrow$ Increase PET’s role in prostate cancer management?
Transrectal PET Camera

- Close to Prostate ⇒ High Spatial Resolution & Efficiency
- No Collimators or Shielding Needed ⇒ More Compact
- Fewer Detectors than Conventional PET ⇒ Low Cost
- Rectal Detector Must Be Very High Performance

(Bill Moses, Berkeley)
PET Prostate Probe - Simulation

Top view of the LSO crystals

2 layer of LSO modules
1 LSO module measures 10mm×40mm×3mm and consists of 400 LSOs

The LSO modules

Detection efficiency w.r.t. # rings

Projection images of a source in the prostate 0.5mm-by-0.5mm/pixel

Neal Clinthorne, U. Michigan)
Several approaches under study for high resolution PET imaging of the prostate. Top: the PET probe with single PET panel, and probe with two panels in a stereotactic geometry. Bottom: four-panel rotating PET + probe system, and the prostate PET probe operating with the ring PET (for example from a standard PET/CT scanner).
Optimal Probe Option
Tests of the monolithic MPPC module

No active electronics inside the MRI coil

0.7mm step x 10mm thick DOI LYSO array with double sided output, from Proteus. S10943-3344MF-050 MPPC array from Hamamatsu. Amplifier board, interface module, cable adaptor, and DAQ box all from AiT Instruments.
Example of $^{18}$F-Fluorocholine (FCH) use in a PET/CT scan

Tumor SUV = 5.7

Some other compounds:
- $^{11}$C-choline
- $^{11}$C-acetate
- $^{18}$F-fluorodihydrotestosterone
- $^{18}$F-fluoroethylcholine
- $^{18}$F-fluorothymidine

Tumor SUV = 2.2

(Tim Turkington, Duke)
Prostate Radiopharmaceuticals

- \([^{11}\text{C}]\text{choline}\) is an attractive PET tracer for imaging primary and metastatic tumors of the prostate.
- Several \(^{18}\text{F}\) radiopharmaceuticals are also under investigation.

(\([^{11}\text{C}]\text{choline}\) images provided by T. Hara and co-workers)

(Bill Moses, Berkeley)
Brain diseases are wide-spread

- Brain disease is becoming more prevalent in the aging population because of increased life span
  - Alzheimer’s disease will increase as US and European populations continue to age. The US is expected to have 16 million cases by 2050.
  - An estimated 1.5 million people in the US have Parkinson’s. It affects 1% of Americans over 60 and each year there are 100,000 new cases.
- Many new PET radiopharmaceuticals for brain function imaging are under development
- PET+CT and MRI+PET are insufficient due to poor PET resolution and poor CT/MRI/fMRI specificity
- 4-5mm resolution provided by current clinical PET scanners is insufficient in many situations
- Current clinical PET scanners are large, expensive, and not optimized for brain imaging, and usually are available only in a package with CT
- Siemens produced recently dedicated brain imager, but due to servicing problems (readout issues) discontinued after selling less than 20 units
Awake Animal Project

DOE funded research on imaging of the awake rat

For the first time we can watch the brain in action during behavior in small animals
The key to making the RatCAP possible was the development of a minaturized, novel electronics device which allows the signals from the RatCAP to be collected, amplified and analyzed.
RatCAP Methamphetamine Images from the Rat

RatCAP

MicroPET

The resolution of the scanner is slightly better that the state of the art commercial MicroPET scanner.
Small Animal (Rat) PET / MRI Camera

Standard Non-Magnetic Components

- LSO crystals
- Aluminum housing
- Fiberglass, kapton, plastic, silicon

Special Non-Magnetic Components

- APDs (special pins)
- APD sockets
- Non-magnetic flex circuit board (substrate)
- Non magnetic electronic components (solder leads)

Shielding from RF

- Aluminum housing
- Kapton cable carrying signals

Non-Magnetic Version of RATCAP

- Planned to Use for Neurology
Simultaneous PET/MRI Based on RatCAP in Small Animals & for Breast Imaging

Flex circuit board covered with Copper case

(Chin-Tu Chen, University of Chicago)
Limitations of current scanners for brain scans

-MRI is a large machine that requires a large space and heavily shielded room
- Patients need to lie down and be still (with very few exceptions)
- MRI may not be able to differentiate between malignant and benign tumors
- Poor detection of Alzheimer’s plaques
- Some individuals cannot be placed in high magnetic fields

-PET is able to distinguish abnormal biology such as malignant tumors, plaque, etc
- High radioactive dosage (~25 mSv for standard PET/CT compared to 6-8 mSv for X-ray)
- Patient must lie down, enter tube, be very still - difficult for many who are elderly, have movement disorders, back pain, claustrophobia, etc.
- Also a large machine requiring a shielded room

- 19 mm x 19 mm blocks cut into 8 x 8 crystals per block
- 2.1 mm x 2.1 mm crystals of LSO/GSO (7.5 mm in depth)
- 8 heads per scanner, each head 18 cm x 26 cm
- 140 19 mm PMTs per head
18FDG brain imaging with the HRRT

40 min FDG frame fused with the corresponding MRI-T1 (courtesy K. Wienhard - Koln)
• Upright compatible
• High efficiency
• Low dose
• Pediatric compatible
• Screening compatible
• Mobile
• Head movement compatible (co-registered to head/brain)
• High resolution
• MRI compatible - potential (as insert)

Examples of some possible situations with patients wearing the imager helmet: sitting in a chair (left), exercising (center), and laying down on a bed (right). Another option with a (helium) balloon supporting the weight of the helmet, allowing for even more movement freedom during imaging session, is not shown here. Except for the case of a patient on a bed, the helmet is suspended by a flexible harness/suspension attached to a hook on the helmet.
Photograph of a novel PET Hat ring imager, permitting imaging a 4.5 cm brain section of a sitting person. The detector modules are built on the basis of the H8500 PMTs. (Yamamoto, Kobe).

The prototype brain PET consisting of 72 compact detector modules built with SensL SiPMs. This imager covers a narrow 12mm slice of the brain but can operate in an MRI magnet (Korea).
Short History of IP for the Wearable PET Brain Imagers: From RatCap to HelmetPET

Left: RatCap PET (non-compliant animal); Center: PET Hat and compliant sitting patient; Right: Helmet for a compliant standing, moving etc patient.
Examples of use: Left: balancing tests using the computer controlled platform system. Brain imager will be installed on the patient’s head. Center and right: F18-PIB and F18-FDG PET images in Alzheimer’s (obtained with the standard PET/CT scanner). The marked region in the center bottom image demonstrates that even a 5cm vertical region covered by the wearable PET prototype can provide valid information about the presence and distribution of brain plaque.
Left: Assembly of one ~5cm square compact module of the first Helmet_PET prototype. Four Hamamatsu 25 MPPC arrays assembled on one resistive readout base from AiT Instruments. Four 1.5mm step 10mm thick LYSO arrays from Proteus coupled to form one compact module. There are no amplifiers or other active components on board the detector module, but in the distant (at the other end of the 2m cable) electronics board. There are 4 output channels per module.
Interesting Activity = Meeting Important People
Summary

- Physicists have played and still play a substantial role in medical imaging: basic concepts, detectors, electronics, simulations, reconstructions
- PET invented many years ago but only now gets full recognition for its unique clinical role combined with CT
- PET imaging is providing critical assistance with patient diagnosis and treatment, as well as with work on understanding disease origin and cures (in small animal studies)
- PET improvements are under way to reach the physical limits of the technique (role for physicists)
- Rebirth of TOF PET
- New technologies: scintillators, photodetectors, solid state materials - spin-offs from particle physics
- Organ-specific PET imagers are becoming available with better performances and at a lower cost
- MRI - compatibility is becoming an important necessary feature