The Road to Time-of-Flight PET

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Outline:

• Time-of-Flight PET
• History
• Future

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Time-of-Flight in PET

- Can localize source along line of flight.
- Time of flight information reduces noise in images.
- Variance reduction given by $2D/c\Delta t$.
- 500 ps timing resolution $\Rightarrow$ 5x reduction in variance!

$c = 30 \text{ cm/ns}$

500 ps timing resolution $\Rightarrow 7.5 \text{ cm localization}$

Time of Flight Provides a Huge Performance Increase!
Statistical Noise in PET

Signals from Different Voxels are Coupled
⇒ Statistical Noise Does Not Obey Counting Statistics

If there are $N$ counts in the image,

$$\text{SNR} = \frac{N}{\sqrt{N}}$$
Whole-Body TOF Simulations

2x10^6 Trues, 1x10^6 Randoms, Attenuation Included
OP-OSEM w/ TOF Extensions, 2 Iterations, 14 Subsets

Phantom
(1:2:3 body:liver:tumor)

Conventional

1.2 ns

700 ps

500 ps

300 ps

Clear Improvement Visually

*Data courtesy of Mike Casey, CPS Innovations
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
The Road to Time-of-Flight PET
In the 80’s…

- Work on TOF PET was begun.
- CsF scintillator used.
- Good (500 ps) timing resolution, but…
  - Low density & atomic number (poor spatial resolution, low efficiency)
  - Low light output (poor energy resolution, one crystal per PMT)
  - *Extremely* hygroscopic

The Journey Begins…
Fast Component of BaF$_2$ Discovered

- Better PET properties than CsF
  - Higher density & atomic number (better spatial resolution & efficiency)
  - Higher light output (better energy resolution, 2 crystals per PMT)
- Not hygroscopic
- Similar (500 ps) timing resolution

BaF$_2$ Replaces CsF in TOF PET
TOF PET Cameras Built in the 80’s

- ~One dozen TOF cameras constructed
- Some were commercial cameras
- 500 ps timing resolution
- CsF and/or BaF$_2$ scintillator
- ~1 cm spatial resolution
- 1–4 layers
- Advantages of TOF were experimentally verified
Problems With TOF in the 1980’s

- BaF$_2$ has drawbacks (compared to BGO)
  - Lower density & atomic number (worse spatial resolution & efficiency)
  - “Fast” emission is in UV (quartz PMTs, no transparent glues)
- Few “fast” PMTs (most 2” diameter, all expensive)
- GHz electronics was “beyond state-of-the-art”
  - Time alignment and stability problems

Non-TOF PET with BGO Dominates
Work on TOF PET Stops
PET Changes a LOT During the 1990’s

- Larger axial extent
  \(1–2 \text{ cm} \Rightarrow 12–15 \text{ cm}\)
- Whole body imaging
- Different medical applications
  (cardiology & neurology \(\Rightarrow\) oncology)
- Reconstruction algorithms
  (filtered backprojection \(\Rightarrow\) iterative)

PET Enters “Routine” Clinical Use
Technology Changes in the 1990’s

• GHz electronics becomes routine
• Fast, inexpensive, 1” diameter PMTs developed
• LSO scintillator developed. Compared to BGO, LSO has:
  • Similar density & atomic number (good spatial resolution & efficiency)
  • Similar energy resolution
  • Better timing resolution & dead time

TOF Bottlenecks Removed
People Realize That TOF Is Possible Again
LSO in the 2000’s

- 220 ps timing resolution demonstrated with small crystals
- 350 ps timing resolution demonstrated with PET-shaped crystal
- 500 ps timing resolution demonstrated for PET detector module
- Camera not designed for TOF run in TOF mode with 1.2 ns timing resolution (electronics limited)

Rapid Progress With LSO
LaBr$_3$ in the 2000’s

- LaBr$_3$ discovered
- <100 ps timing resolution demonstrated with small crystals
- 300 ps timing resolution demonstrated for PET detector module
- Camera **designed for TOF** run in TOF mode with 500 ps timing resolution (electronics limited)

Rapid Progress With LaBr$_3$
Commercial TOF PET Recently Announced

Can time of flight change PET/CT imaging?

PET/CT Satellite Lunch Symposium
Saturday, March 4th, Vienna, Austria

Uses LYSO
Much More TOF PET Development Needed!

Timing Resolution is Currently ~500 ps
Improvements In Electronics

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

Non-ASIC Solutions Underway Today
Module Design Limits PET Timing Resolution

- Scintillator Crystal Geometry
  - Short & squat vs. Long & thin
- Photomultiplier Tube
  - Expensive, high-performance vs. Economical
- Light Loss
  - Well-coupled vs. Light sharing
- Time Alignment of PMTs
  - Single PMT vs. Multiple PMTs

Present Systems Not Optimized for TOF
Improvements In PMTs

Good Timing w/ Uniform Transit Time

Time Resolution
Transit Time
Improvements In Scintillators

Combine Best Properties of:
- LaBr$_3$:30% Ce
  - Timing resolution <100 ps
  - Energy resolution <4%
- LuI$_3$:Ce
  - Light output >100,000 ph/MeV
- PbWO$_4$
  - Density >8 g/cc
  - High atomic number
  - Inexpensive

PET Performance Determined by Scintillator
Algorithm Improvements Also Needed

- TOF reconstruction in 1980’s used 2-D filtered backprojection
- Modern non-TOF reconstruction uses 3-D iterative reconstruction
- 3-D iterative TOF reconstruction well-understood, but:
  - Data organization must be changed
    - More data bins than events
      (25,000 crystals ⇒ 100 M chords
       x20 TOF bins / chord ⇒ 2 G data bins)
    - List mode data, list-mode ML reconstruction
  - Reconstruction time must be reduced
    - Currently >1 hour on Beowulf-type cluster

Practical Implementation Needed
How Do We Measure Improvement?

How Can Clinical Improvement Be Measured?

Non-TOF

35 cm dia. w/ 1 cm dia. 6:1 hot spot
300k events, T:S:R = 1:1:1, 500 ps fwhm

TOF
How Far Does the TOF Road Go?

- 100 ps Timing Resolution
- 23x Variance Reduction
- Very Fast Reconstruction

Acquire & Reconstruct Image in <1 Minute
Include Time-of-Flight in Reconstruction ⇒ Reduced Noise Variance

**Conventional:**
Detected event projected to *all* voxels between detector pairs
Statistical noise from activity in one voxel adds noise to *all* voxels
⇒ Large Noise Amplification

**Time-of-Flight:**
Detected event projected *only* to voxels consistent w/ measured time
Statistical noise from one voxel adds noise to *only a few nearby* voxels
⇒ Small Noise Amplification

Height represents weight assigned to each voxel by reconstruction algorithm
Narrow Coincidence Timing Window ⇒ Reduced Random Event Rate

- Randoms Rate is Proportional to Coincidence Window Width
- Narrow Width Increases Peak Noise Equivalent Count Rate (NECR)
- Fewer Randoms Decreases Coincidence Processor Load
- Cannot Use Coincidence Window Width < 4 ns
  (Limited by Time-of-Flight Across Detector Ring)
What Are the Contributions in the Module?

CPS Accel V1 Block
8x8 Array
6.75 x 6.75 x 25 mm³ LSO

CPS PMT Assembly
Hamamatsu PMTs

Baseline
221 ps

Crystal
326 ps

Light Sharing
454 ps

PMT
422 ps

PMT Array
274 ps

Quadrature Sum of Components
784 ps

Measured Value
789 ps
Scintillator “Block Effects”

CPS Accel V1 Block
8x8 Array
6.75 x 6.75 x 25 mm³ LSO

Hamamatsu Fast 2” PMT
250 ps TTJ
1500 ps Rise Time
Prototype On Loan

Configuration | Resolution
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Single Crystal Block | 355 ps
Block | 577 ps

⇒ Block Contribution 454 ps