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SMALL BISMUTH GERMANATE CRYSTALS

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DYNAMIC POSITRON-EMISSION TOMOGRAPHY IN MAN
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Primary considerations for the design of positron emission tomographs for medical studies in humans are the need for high imaging sensitivity, whole organ coverage, good spatial resolution, high maximum data rates, adequate spatial sampling with minimum mechanical motion, shielding against out of plane activity, pulse height discrimination against scattered photons, and timing discrimination against accidental coincidences. We discuss the choice of detectors, sampling motion, shielding, and electronics to meet these objectives.

1. INTRODUCTION

For the past 50 years, since the pioneering work of Von Hevesy, the radioactive tracer technique has been used with considerable success in the biological sciences to measure fundamental biochemical processes in plants and animals. In this spirit Positron Emission Tomography (PET) is being vigorously developed because it appears to be the best high resolution technique for the quantitative regional measurement of tracer compounds in the human body after a simple injection.

Table 1 lists a few of the positron labeled compounds that have been recently developed and the biochemical processes upon which their biodistribution depends. We believe that many more will be developed in the years to come so that virtually any metabolic process can be measured non-invasively.

2. HISTORY OF PET INSTRUMENTATION

Historically, positron emission tomography for the three-dimensional imaging of positron labeled compounds in the human body has evolved through five stages (Figure 1):

[1] Limited angle tomography using pairs of Anger scintillation cameras,[1-8] parallel planes of scintillation crystals[9-13] or wire chambers with converters[14-25] (Figure 1a). Full angular coverage requires rotation.

[2] A single circular array of closely packed scintillation crystals.[26-44] To obtain multiple transverse sections axial translation is required.

TABLE 1. EXAMPLES OF POSITRON LABELED COMPOUNDS AND THE PROCESSES THAT THEY MEASURE

TRACER	PROCESS MEASURED
Heart:	
ionic ^{82}Rb	muscle perfusion
^{11}C palmitate	fatty acid oxidation
^{18}F deoxyglucose	tissue demand for glucose
^{11}C or ^{13}N amino acids	muscle regeneration and metabolism
Brain:	
^{15}O	blood flow and oxygen utilization
^{11}C bioamines	blood flow and receptor sites
ionic ^{82}Rb	blood brain barrier breakdown
^{18}F deoxyglucose	tissue demand for glucose
^{11}C methionine	blood brain barrier transport
^{11}C, ^{13}N, or ^{18}F psychoactive compounds	receptor sites

[3] Hexagonal or octagonal arrays of scintillation crystals that are both translated and rotated for full linear, angular, and axial coverage (Fig 1c).[45-52]

[4] Multiple layers of configurations [2] and [3] above (Figs 1d and 1e).[53-63]

a) Rotate for Multiple Angles   b) Translate for Multiple Sections

c) Translate-Rotate   d) Translate-Rotate

e) Multiple Circular Arrays   f) Multiple Arrays With Time-of-Flight (T.O.F.)
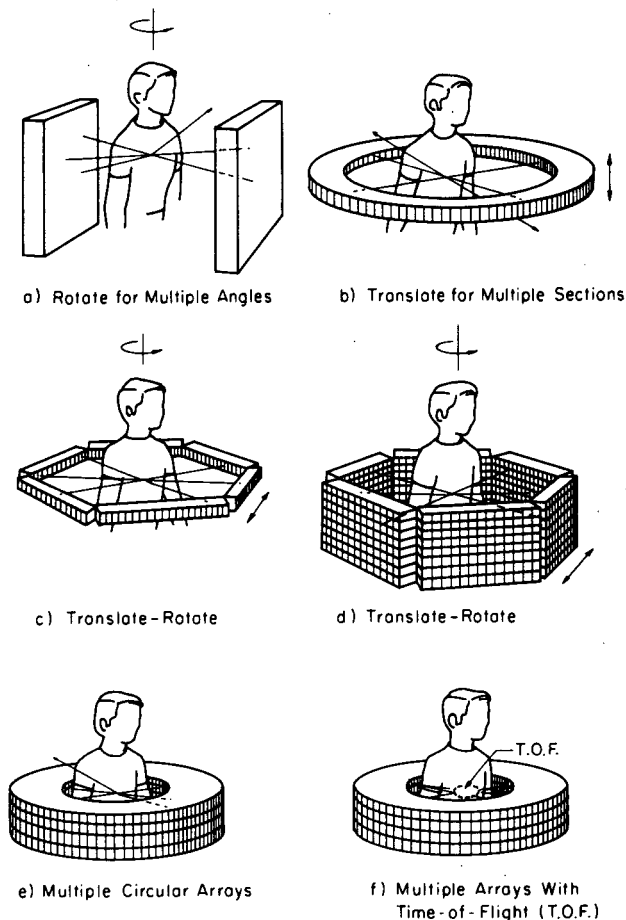
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Figure 1: Evolution of detector geometries for positron emission tomography.

[5] Multiple circular arrays of fast scintillation crystals coupled to moderately large high-speed photomultiplier tubes for localization by differential time-of-flight measurement (Fig 1f).[64-75]

Fundamental considerations in positron emission tomography for medical imaging show the advantages of high density scintillators over wire chambers and converters in terms of detection efficiency, time resolution, sensitivity, and maximum useful event rates.[76] Contemporary designs and the trend for the near future are focussed on the multilayer approaches (Figures 1e and 1f) which provide the highest dose efficiency and useful event rates.

3. MEDICAL OBJECTIVES

We summarize below the primary requirements for the quantitative imaging of flow and metabolism using positron emission tomography. These points have been more fully described in previous papers.[77,78]

[1] The highest possible dose efficiency, which requires both a large solid angle and high detection efficiency. Time-of-flight information can substantially reduce the number of events needed for a given statistical accuracy (especially for large emission regions).

[2] A resolution of 5 mm FWHM or better, capable of quantitative measurements of regions 10 mm in size. The requirement for dynamic, gated imaging means that this resolution must be achieved with little or no mechanical sampling motion.

[3] The ability to measure the arterial input function of the tracer to the organ being imaged and to follow its subsequent accumulation and clearance. This requires the ability to collect sufficient data in typically 10 second time frames and permits very little sampling motion.[77,79]

[4] A sufficient number of transverse sections to cover the volume of interest which is usually more than 5 cm axially.

[5] Discrimination against background events by shielding, and by timing and pulse height discrimination.

[6] Ability to correct data for accidental and prompt scatter backgrounds and for image distortions.

[7] Ability to tilt at least 15°.

[8] A patient port of at least 50 cm for body imaging and 25 cm for head imaging.

4. DESIGN CONSIDERATIONS

Design considerations for positron emission tomographs have been previously described in some detail.[27,47,77,80-83] Primary differences among designs occur in the choice of detector material, the depth of the shielding, and the sampling employed.

4.1 Detector Materials

Table 2 lists the three detector materials used in positron tomographs, NaI(Tl), CsF, and bismuth germanate (BGO). NaI(Tl) leads in photon yield and pulse height resolution, CsF leads in speed, and BGO leads in detection efficiency. An "ideal detector" with the best properties of all three would be very useful.

While solid state detectors have been suggested for positron emission tomography,[84-86] their detection efficiency is relatively low. The development of a semiconductor with the density

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TABLE 2. PROPERTIES OF SCINTILLATION MATERIALS FOR POSITRON EMISSION TOMOGRAPHY				
Material	NaI(Tl)	CsF	BGO	"Ideal Detector"
Density (gm/cm^3)	3.67	4.61	7.13	>6
Atomic numbers	11,53	55,9	83,32,8	>80
Hygroscopic?	YES	VERY	NO	NO
Photoelectron yield (511 keV)	2,500	100	300	>1,000
Scintillation decay time (nsec)	230	3	300	<10
Photoelectrons/nsec	11	35	1	>100
Time resolution (FWHM nsec)	1.5	0.4	7	<0.2
Energy resolution (% FWHM)	7	30	12	<8

and atomic number of bismuth germanate or NaI would provide an attractive alternative to the scintillator detector by the elimination of the photomultiplier coupling problem (discussed in the next section).

4.2 Detector Packing

Figure 2 shows scintillator-phototube coupling schemes presently implemented or planned. Early designs (Figure 2a) were restricted to square or cylindrical crystals larger than 14 mm.[9] Figure 2b shows the coupling of cylindrical phototubes to rectangular crystals half as wide. The light transfer efficiency is approximately 50%.[87] A similar approach as recently been described using several sides of the crystals.[88] Figure 2c

shows the coupling used in the Donner 280-crystal single-layer tomograph which also has a light transfer efficiency of about 50%.[40,29] Figure 2d shows a one-dimensional position-sensitive design using the Anger light ratio principle. This approach can be used for crystals much narrower than the phototubes.[89,90] Figure 2e shows another coding scheme that selectively splits the light among the photo-tubes so that the crystal producing the light may be identified.[91] The device in Figure 2f is based on sense wires as suggested by Charpak and to our knowledge has received only preliminary evaluation thus far.[92-94] Multianode phototubes have been constructed,[95,96] but further development is required for use with small crystals. Microchannel phototubes have high speed but are

a) One-To-One Full Coupling (≥14mm PMT)

b) One-To-One Partial Coupling

c) One-To-One Light Pipe Coupling

d) Light-Proportion Position Logic

e) Coded Coupling

f) Phototube With Crystal Identification by Sense Wires

g) Multi Anode PMT
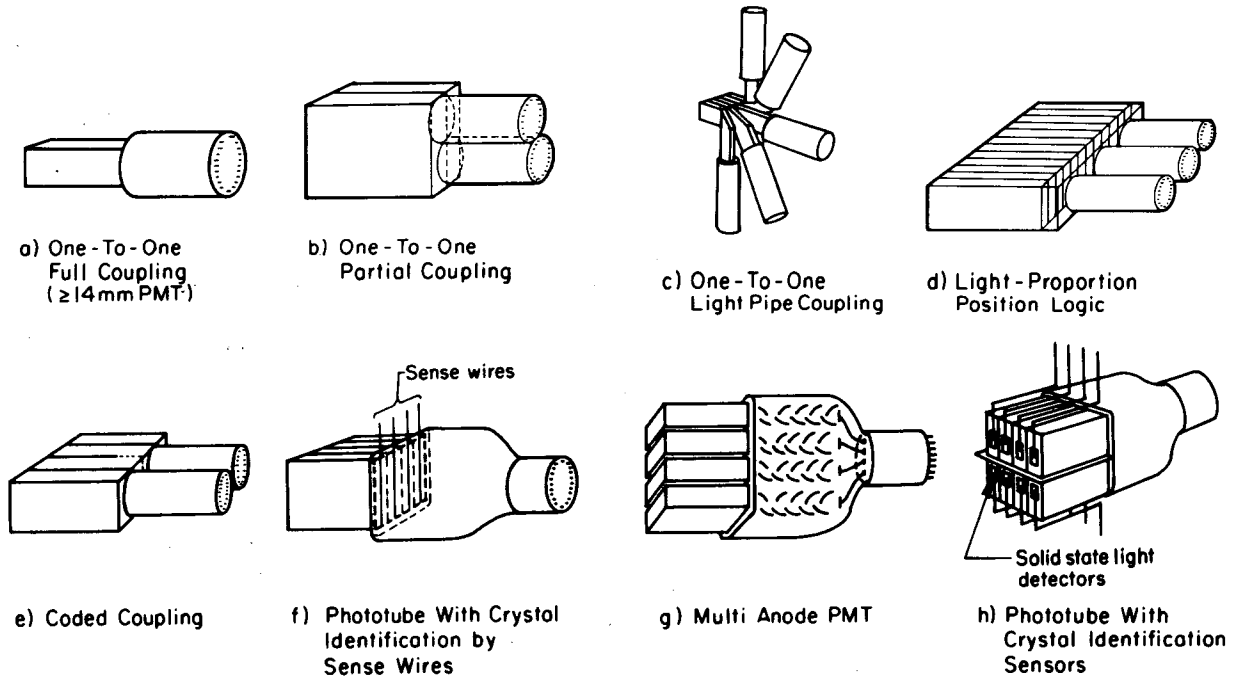
h) Phototube With Crystal Identification Sensors

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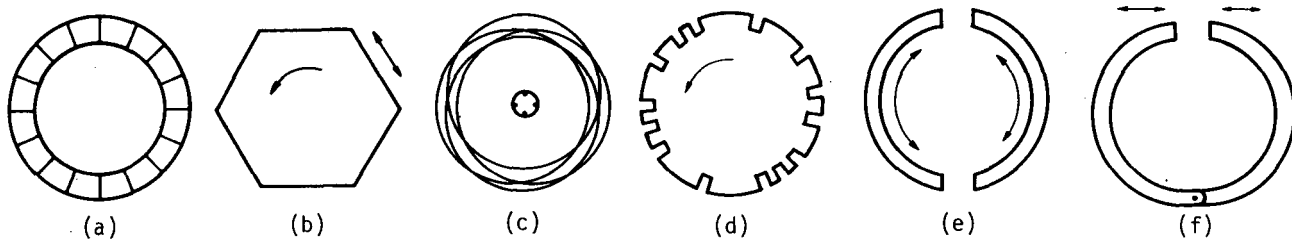Figure 2: Various scintillator-phototube coupling schemes.

Figure 3: Various sampling schemes: (a) Stationary ring[26-44] (b) Scan-rotate[45-52] (c) wobble[32,83,103-106] (d) positology[39,107] (e) dichotomic[108,109] (f) clamshell[110,111]

limited by low packing density, high price, and a relatively short useful lifetime.[97-100] The concept shown in Figure 2h uses a high quality single-anode square phototube for timing and pulse height selection. Separate light sensors are used to determine which crystal produced the light. The use of photodiode sensors to identify crystals has been suggested by others as well.[101] The requirement for this design is that the crystal identifier must reliably detect some of the scintillation photons available from the 511 keV photon interaction in the scintillator.

4.3 Spatial Resolution

A system with a resolution similar to or coarser than one-half the dimension of the quantitation volume will necessarily give erroneous quantitative information.[80,102] Below we list the factors that determine the spatial resolution in the reconstructed tomographic images:

[1] Sampling Density

Rapid or, ideally, instantaneous complete spatial sampling is needed for those studies requiring rapid imaging. Stationary circular positron emission tomographic systems using closely packed detectors give optimum sensitivity but the spatial resolution is limited by the linear sampling to approximately the distance between the detector centers and is not uniform throughout the image space.[35,40,81] Systems that employ large crystals have both limited linear and angular sampling, so that motion of the detector array is required for good spatial resolution. The use of lead apertures to improve spatial resolution results in a significant loss in sensitivity and an increased number of sampling positions. Several approaches employed to overcome these limitations are shown in Figure 3. The most commonly employed method is the circular wobble motion which has been shown to be quite effective.[32,55,83,103-106] A pure rotation of a nonuniformly spaced array ("positology") has been proposed,[39,107] as well as the oscillation of half-rings about the axis of the system ("dichotomic").[108,109]

The only method we know that can improve the sampling at all angles with only two mechanical positions is the "clamshell" motion (Figure 4).[110,111] Figure 4a shows a circular array with lines connecting opposing groups of crystals.
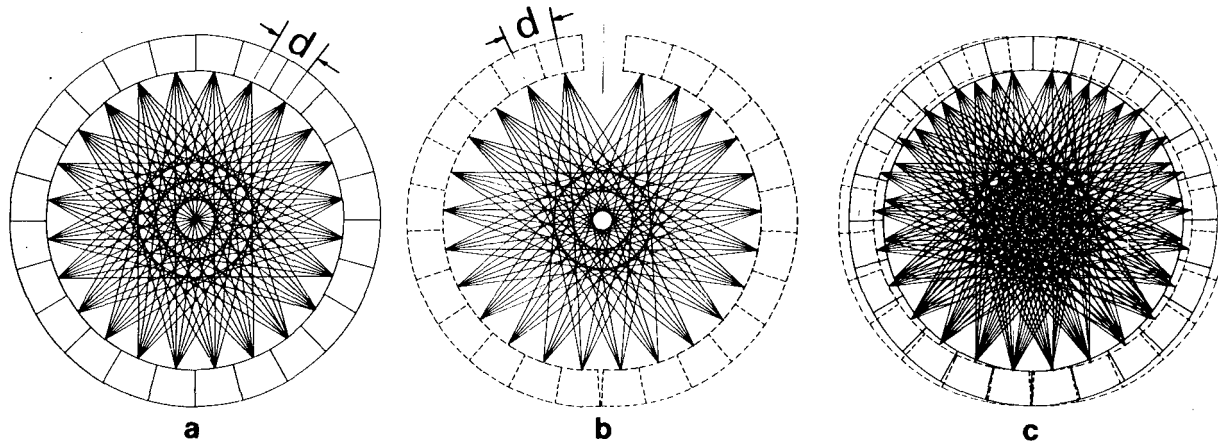
XBL802-3113

Figure 4: Clamshell method for improving linear sampling with only two mechanical positions. Position (a) is a circular array with sampling rings d/2 apart, where d is the distance between detector centers. In position (b) the halves of the detector ring are hinged open to produce a gap of width d and the sampling rings have been shifted by d/4. The combination (c) provides concentric sampling rings of spacing d/4.

TABLE 3. POSITRON RANGE DISTRIBUTIONS IN WATER

Isotope	^{18}F	^{11}C	^{68}Ga	^{82}Rb
Half-Life	110 min	20.4 min	68.3 min	76 sec
Max Energy (MeV) [Abundance]	0.64[97%]	0.96[99%]	1.90[90%] 0.82[1%]	3.35[83%] 2.57[12%]
Projected point spread function in water:				
FWHM (mm)	0.13	0.13	0.31	0.42
FW(0.1)M (mm)	0.38	0.39	1.6	1.9
rms (mm)	0.23	0.39	1.2	2.6
radius(mm) for 50%*	0.31	0.60	1.6	3.8
radius(mm) for 75%	0.58	1.06	2.7	6.2
radius(mm) for 90%	0.88	1.6	3.7	8.8
Line spread function in water:				
FWHM (mm)	0.22	0.28	1.35	2.6
FW(0.1)M (mm)	1.09	1.86	5.92	13.2
rms (mm)	0.38	0.69	1.60	3.8

*table entry gives the radius of the circle within which the stated percentage of anni-
hilation points projects

The pattern of lines forms "sampling rings" in the imaging field that are d/2 apart, where d is the distance between detector centers. Figure 4b shows the two halves of the detector array hinged open to produce a gap of width d. The sampling rings have been shifted by d/4. Figure 4c shows the combination of the two positions which provides concentric sampling rings of spacing d/4.

[2] Positron Range

By using the Donner 280-Crystal positron tomograph, we have imaged thin positron sources in polyurethane foam (density 0.02 to 0.05 gm/cm^3) and performed a precision measurement of the positron end point distribution for ^{18}F, ^{11}C, ^{68}Ga, and ^{82}Rb which have maximum positron energies of 0.64 MeV, 0.96 MeV, 1.90 MeV, and 3.35 MeV, respectively.[112] The results are summarized in Table 3.

[3] Deviations from 180°

The measurements of Colombino[113] for positron annililation in water at 20°C show that the deviations from 180° emission have a distribution that is nearly Gaussian with FWHM= 5.7 mrad. Note that for a detector ring of diameter D, the positional deviation Δ at the center of the ring corresponding to an angular deviation θ is given by Δ= (D/4) · θ.

[4] Detector scattering and detector penetration for angles ≠ 0°

Compton scattering and a subsequent second interaction in another detector can be a source of position error for any detector material, but is least with bismuth germanate.[114] The use of a

pulse height threshold on each detector is effective in reducing these errors but cannot be employed for the coupling schemes shown in Figures 2d and 2e.

Detector penetration for off-axis sources causes a radial elongation of the reconstructed point spread function. This is a much smaller effect for bismuth germanate than for NaI(Tl).[40]

[5] Reconstruction filter

The process of reconstructing the projection data taken by the detector array will generally smooth the resulting image to an extent determined by the reconstruction filter.[115] Our philosophy has been to use a filter such as that described by Shepp and Logan[116] that achieves nearly the resolution of the tomograph. Other workers have advocated smoothing the statistical fluctuations of the data during the reconstruction with the intention of improving the appearance of the image, but this causes a smearing of data from one region to the next. We prefer to sum over regions of interest which provides a more accurate estimate of the activity in the regions of interest and also averages over the statistical fluctuations. Use of a sharper filter such as that described by Ramachandran and Lakshminarayanan[117] will provide slightly better resolution but also can cause ringing (aliasing) artifacts.

4.4 Shielding and Backgrounds

The primary backgrounds in positron emission tomography are accidental coincidences of unrelated annihilation photons[118,119] and true coincidences of photon pairs where one or both have scattered.[27,29,120]

Extensive shielding is used both to define the transverse sections being imaged and to shield the detectors from activity outside those sections. Increasing the depth of the shielding decreases the sensitivity for good coincident events but also decreases the fraction of accidental and prompt scatter events. Proper tomograph design requires a choice of shielding that maximizes the signal to noise ratio in the reconstructed images.[76,121,122]

4.5 Quantitation

Ideally, the reconstructed images should provide a quantitative measurement of the amount of positron emitter in each volume element. This ideal can be closely approached if: [1] the system resolution is at least a factor of two finer than the quantitation volume,[80,102] [2] the tissue attenuation has been corrected,[123] [3] scatter and accidental backgrounds have been subtracted, [4] deadtime losses have been corrected, and [5] a sufficient number of events have been collected such that the statistical uncertainties are acceptably small.[124-126]

4.6 Electronics

All portions of the electronics, the detector preamplifiers, the coincidence and address circuits, the data storage and reconstruction must be designed for low deadtime and high speed.[127]

Electronics for time-of-flight data acquisition and storage are presently under development and add another level of complexity to the overall problem.[71,75,126,128,129]

The display of three-dimensional data accumulated from multilayer positron emission tomographs is an important issue with no clear solution as yet.[130]

5. CONCLUSIONS

The trend in the design of positron emission tomographs designs for medical imaging is toward multilayer circular detector arrays with high dose efficiency, good spatial resolution, high imaging rates, and very little mechanical motion. The major instrumentation challenge is centered about the development of small, efficient detectors that can be closely packed to achieve a resolution in the reconstructed image of 5mm FWHM or finer. Solutions include multianode phototubes, supplementary light sensors for crystal identification, and a semiconductor with high detection efficiency for 511 keV photons. Achieving a resolution much below 2 mm FWHM will be difficult due to other factors such as positron range and deviations from 180° emission.

The realization of the great potential of time-of-flight imaging will require the development of a very fast scintillator with good detection efficiency, and a very fast phototube that can couple to small crystals for high resolution imaging.

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