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Future Trends in Nuclear Medical Imaging

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Abstract. Continuous efforts to integrate recent research findings for the design of different geometries and various detector technologies of single-photon emission computed tomography (SPECT) and positron emission tomography (PET) scanners have become the goal of both the academic community and nuclear medicine industry. As PET has become of more interest for clinical practice, several different design trends seem to have developed. Systems are being designed for "low cost" clinical applications, very high-resolution research applications, and just about everywhere in-between. All of these systems are undergoing revisions in both hardware and software components. The development of dual-modality imaging systems is an emerging research field. One of the major advantages is that SPECT/PET data are intrinsically aligned to anatomical information from the X-ray CT without the use of external markers or internal landmarks. On the other hand, combining PET with Magnetic Resonance Imaging (MRI) technology is scientifically more challenging owing to the strong magnetic fields. Nevertheless, significant progress has been made resulting in the design of a prototype small animal PET scanner coupled to three multi-channel photomultipliers via optical fibers so that the PET detector can be operated within a conventional MR system. Thus, there are many different design paths being pursued - which ones are likely to be the main stream of future commercial systems? It will be interesting, indeed, to see what technologies become the most popular in the future. This paper briefly summarizes state-of-the art developments in nuclear and dual-imaging devices. Future prospects will also be discussed

INTRODUCTION

Radionuclide imaging, including planar projection imaging, single-photon emission computed tomography (SPECT) and positron emission tomography (PET), relies on the tracer principle, in which a minute quantity of a radiopharmaceutical in introduced into the body to monitor the patient's physiological function. In a clinical environment, resulting radionuclide images are interpreted visually to assess the physiological function of tissues, organs, and organ systems, or can be evaluated quantitatively to measure biochemical and physiological processes of importance in both research and clinical applications. Nuclear medicine relies on noninvasive measurements performed with external (rather than internal) radiation detectors in a way that does not allow the radionuclide measurement to be isolated from surrounding body tissues or cross-talk from radionuclide uptake in non-target regions.

An important consequence of the cost- and performance-conscious environments of health care today is the constant pressure to minimize the cost of nuclear medicine imaging devices, while at the same time there is also pressure to provide the most accurate diagnostic answers through the highest performance possible. The dilemma is

that both approaches can lower the cost of health care. Continuous efforts to integrate recent research findings in detector development for the design of different geometries of nuclear medicine imaging instruments have become the goal of both the medical imaging academic community and nuclear medicine industry.

TRENDS IN SPECT INSTRUMENTATION

Most scintillation cameras used for clinical imaging of single-photon emitters are based on the original design proposed by Anger more than 45 years ago [1]. The first nuclear medical imaging systems (single-photon and positron) were designed with NaI(Tl) scintillation detectors. With exception of the recently marketed NeuroFocus (Neurophysics Corporation, Shirley, Massachusetts) multi-conebeam system with a claimed intrinsic spatial resolution of 3 mm, all commercial imaging devices available nowadays employ NaI(Tl) scintillation detectors coupled to photomultiplier tubes (PMT's), likely in the near future, photodiodes or avalanche photodiodes (APDs) to convert the light output into electrical signals.

The system spatial resolution and sensitivity depends to a larger extent on the type of collimator used and the intrinsic performance of the camera. Independent of the collimator, system resolution cannot get any better than intrinsic resolution. There have been several collimator designs in the past fifteen years, which optimized the resolution/sensitivity inverse relation for their particular design. Converging hole collimators, for example fan-beam and cone-beam have been built to improve the trade-off between resolution and sensitivity. More modern collimator designs, such as half-cone beam, astigmatic and rotating slat, have also been conceived. Sensitivity has seen an overall improvement by the introduction of multi-camera SPECT systems. A typical triple-head camera SPECT system equipped with high resolution fan-beam collimators can achieve a resolution of 7-8 mm in typical brain imaging conditions. Other types of collimators with only one or a few channels, called pinhole collimators, have been designed to image small organs and human extremities, such as the wrist and thyroid gland, in addition to research animals such as rats.

With the exception of coded aperture techniques, all collimators exhibit a limiting detection sensitivity that is inversely proportional to the spatial resolution. This motivated the development of Compton cameras, which provide information about the incoming photon direction electronically without any restriction with respect to the solid detection angle [2]. The development of pixelated detectors allowed improving the spatial resolution at the expense of deteriorating the energy resolution as a result of light losses in the crystals compared to that of a single crystal [3].

An interesting design, which if successful in a clinical environment, will revolutionize the practice of nuclear medicine and result in a quantum jump in the history of nuclear medicine instrumentation, is the SOLid STate Imager with Compact Electronics (SOLSTICE). This system combines the direct gamma ray conversion through solid-state detectors with the better compromise offered by rotating slat collimators (Figure 1) to break the limitations of conventional scintillation cameras-based design [4]. Some promising results have been presented during the last few years but the instrument is still in a development phase and appears to be well suited

for high resolution small-animal imaging. The viability and cost-effectiveness of the product still needs to be demonstrated.

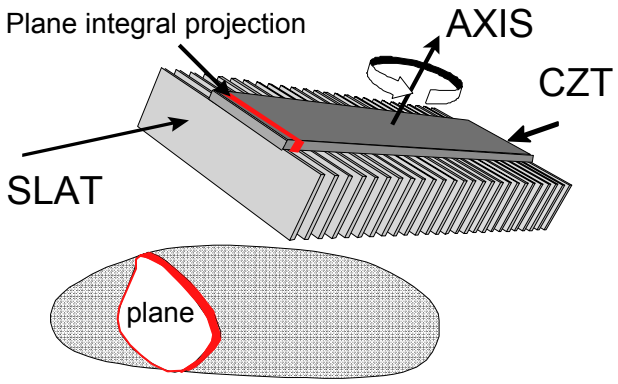

FIGURE 1. Schematic illustration of the SOLSTICE prototype system. Plane integrals are measured by the SOLSTICE imaging system for each projection angle in contrast to line integrals measured in the conventional approach. A specially designed reconstruction algorithm which handles this acquisition geometry has been developed for this purpose.

TRENDS IN PET INSTRUMENTATION

There has been a significant evolution in PET instrumentation from a single ring of bismuth germanate (BGO) detectors with a spatial resolution of 15 mm, to multiple rings of small BGO crystals resulting in a spatial resolution of about 4-6 mm. Improvements in spatial resolution have been achieved by the use of smaller crystals and the efficient use of photomultiplier tubes (PMT's) and Anger logic-based position readout.

Dedicated full-ring PET tomographs have evolved through at least 4 generations since the design of the first PET scanner in the mid 1970s and are still considered the high-end devices. The better performance of full-ring systems compared to camera-based dual or triple-headed systems is due to higher overall system efficiency and count rate capability which provides the statistical realization of the physical detector resolution and not a higher intrinsic physical detector resolution. Obviously, this has some important design consequences since even if both scanner designs provide the same physical spatial resolution as estimated by a point spread function, the full-ring system will produce higher resolution images in patients as a result of the higher statistics per unit imaging time. Figure 2 illustrates possible geometric designs of positron imaging systems used so far. The most important aspect related to the outcome of research performed in the field is the improvement of the cost/performance optimization of clinical PET systems.

The geometric camera design actually affects to a greater extent the solid angle coverage, which has direct consequences on the resulting sensitivity. On the other hand, the reconstruction algorithm used significantly affects the achieved spatial resolution. It has been shown that iterative algorithms outperform conventional analytic methods [5, 6].

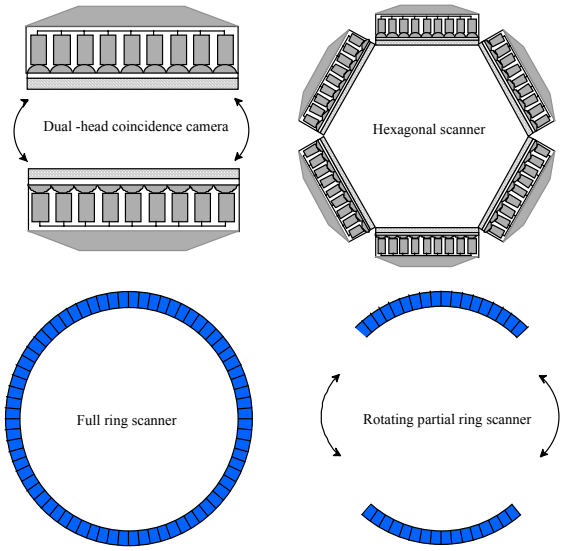

FIGURE 2. Illustration of the range of different geometries of positron volume imaging systems. The dual-head coincidence camera and partial ring tomographs require the rotation of the detectors to collect a full 180° set of projection data.

The critical component of PET tomographs is the scintillation detector. New detection technologies that are emerging include the use of new Cerium doped crystals (LSO:Ce, GSO:Ce and $LaBr_3$:Ce) as alternatives to conventional BGO crystals, the use of layered crystals and other schemes for depth-of-interaction (DOI) determination. In particular phoswich detectors received considerable attention for the design of high resolution scanners dedicated for brain, positron emission mammography (PEM) and small animal imaging. This may be implemented with solid-state photodiode readouts, which also allows electronically collimated coincidence counting. Such a design has been implemented on the ECAT high resolution research tomograph (HRRT) with LSO crystals [7]. Figure 3 illustrates the principle of the conventional detector block and the phoswich approach where two detectors are assembled in a sandwich-like design, the difference in decay time of the light is used to estimate the crystal where the interaction occurred.

The intrinsic physical performance of conventional designs (even with DOI capability) seem to have been reached encouraging the development of innovative approaches capable of providing improved performance at a reduced or comparable cost. This motivated the proposal of a novel design concept which provides full 3D reconstruction with high resolution over the total detector volume, free of parallax errors. The key components are a matrix of long scintillator crystals and Hybrid Photon Detectors (HPDs) with matched segmentation and integrated readout electronics [8]. The HPDs read out the two ends of the scintillator package. Both excellent spatial (x,y,z) and energy resolution is obtained. The concept allows enhancing the detection efficiency by reconstructing a significant fraction of events which underwent Compton scattering in the crystals.

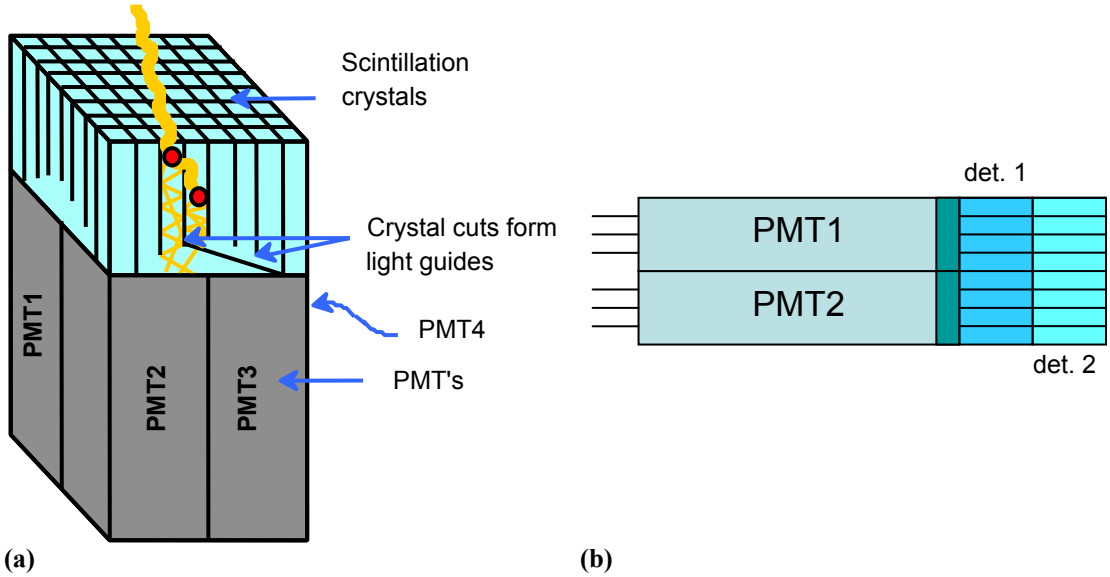

FIGURE 3. (a) Conventional block detector consisting of a set of crystals having cuts of different depths acting as light guides and segmenting the block into 64 (8x8) detection elements in this example. The block is optically coupled to four photomultiplier tubes at the back, and the crystal in which photoabsorption occurs is identified by comparing the outputs of the four photomultiplier tubes (Anger logic). (b) Detector block consisting of a phoswich (detector 1 and 2) with depth-of-interaction measurement capability.

TRENDS IN IN SMALL ANIMAL IMAGING INSTRUMENTATION

The advent of molecular imaging attracted the interest of biomedical researchers in the small animal imaging technology. The use of animal models has been motivated to a great extent by the availability of modern transgenic and knockout techniques. This interest motivated the development of high resolution research prototype systems dedicated for imaging small animals including projection imaging, SPECT and PET (or both), the latter being the most appealing approach for molecular imaging research owing to ease of incorporation into a wide range of molecules and more advanced tracer development activities using this imaging modality [9].

An important conclusion drawn from simulation studies is that unlike human imaging where both sensitivity and spatial resolution limitations significantly effect the quantitative imaging performance of a tomograph, the imaging performance of dedicated animal tomographs is almost solely based upon its spatial resolution limitations. Thus, different PET designs have been suggested encompassing conventional small ring radius cylindrical block-detector based design with DOI capability and APDs readout, a renewed interest in the 3D high density avalanche chamber (HIDAC) camera that achieves sub-millimeter resolution along with many other designs. Nowadays, high-resolution animal scanner designs are plentiful and are being developed in both academic and corporate settings, with more than three such devices (both SPECT and PET) being offered commercially (Fig. 4). More recently, advanced versions of these same technologies have begun to be used across the

breadth of modern biomedical research to study non-invasively small laboratory animals in a myriad of experimental settings. In addition, combined imaging devices such as SPECT/CT, PET/CT and PET/MRI are under development by different research groups and scanner manufacturers, leading the biomedical imaging community to forecast a promising progress during the next few years.

(a) **(b)** **(c)**

FIGURE 4. Photographs of small animal PET scanners showing (a) the Hamamatsu SHR-7700 PET scanner based on BGO detector blocks designed for non-human primate imaging, (b) the multiwire proportional chamber technology-based HIDAC system, and (c) the microPET P4 scanner using LSO scintillation crystals. (Photographs courtesy of Hamamatsu Photonics KK, Japan, Oxford Positron Systems, UK and Concorde Microsystems, USA, respectively).

TRENDS IN DUAL-MODALITY IMAGING INSTRUMENTATION

The principle of dual-modality imaging technology is to combine a functional imaging device (SPECT or PET) with an anatomical imaging instrument (CT or MRI) to acquire coregistered images with a single integrated system. This is a hardware approach to image fusion as opposed to the software approach where manual or automated image registration techniques are used to realign intra-modality images acquired separately on two different imaging systems [10]. This development is an emerging research field driven particularly by whole-body imaging in clinical oncology. One of the major advantages is that SPECT/PET data are intrinsically aligned to anatomical information from the X-ray CT without the use of external markers or internal landmarks. Figure 5 shows a clinical study illustrating the principle of PET/CT image fusion and highlights the value of this technology for better anatomic localization of abnormal tissue metabolism (tumors). Different designs of combined SPECT/CT and PET/CT tomographs were developed for diagnostic purposes in clinical oncology and three such systems are now commercially available from the major vendors. Quantification is also improved by using the low noise CT transmission information during the correction of the PET data for self-attenuation, contamination from scattered photons and for partial volume effects.

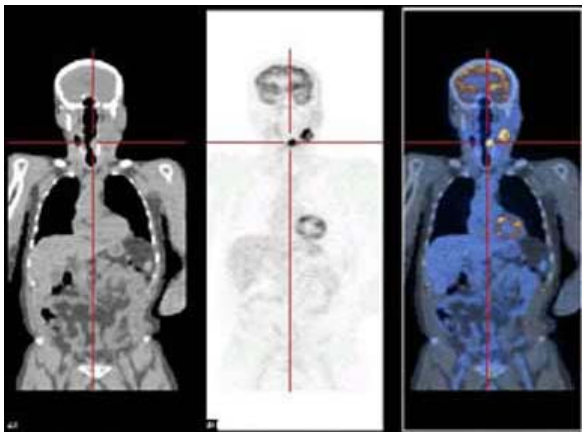

FIGURE 5. Clinical study of a patient with head and neck cancer illustrating the anatomical CT images (left), PET image (center), and the fused PET/CT image (right) allowing better localization of the tumor.

On the other hand, combining PET with MRI technology is scientifically more challenging owing to the strong magnetic fields. Nevertheless, significant progress has been made resulting in the design of a prototype small animal PET scanner with LSO:Ce detector blocks of 3.8 cm ring diameter coupled to three multi-channel photomultipliers via optical fibers [11] so that the PET detector can be operated within a conventional MR system. The authors reported no appreciable artifacts caused by the scintillators in the MR images. A second larger (11.2 cm) prototype is being developed for simultaneous PET/MR imaging of mice and rats at different magnetic field strengths [12]. While the advantages of combined PET/CT could in principle be replicated by combined PET/MRI, the usefulness of MRI for attenuation correction in radionuclide imaging has not been established until recently in brain scanning [13]. Potential applications of the technique in whole-body imaging still need to be demonstrated.

The availability of dual-modality instruments is likely to influence the approaches to image correction and reconstruction, with algorithms that combine anatomical information likely to increase in popularity. These approaches have previously relied on accurate registration and ready access to anatomical data. The advent of dual modality instruments makes this much more practical. In particular, the development of dual-modality imaging systems stimulated the interest in Bayesian-type maximum a posteriori (MAP) reconstruction algorithms. This approach uses the anatomical information from a registered MRI or CT image to guide and tune the noise suppressing prior in a MAP-algorithm, by limiting smoothing to within organ boundaries revealed by the anatomical data.

SUMMARY

In many respects, the field of nuclear medicine has been ahead of other areas of image science in objective assessment and optimization of image quality. Nuclear medicine has poor spatial resolution compared to other imaging modalities in radiology, although its ability to measure physiological processes is unsurpassed.

While the potential for PET in this field is undisputed, the challenges must also be recognized.

A brief overview of current state-of-the art developments in nuclear medicine instrumentation was presented. It has been emphasized that there are many different design paths being pursued in both academic and corporate settings - which ones are likely to be the main stream of future commercial systems? It will be interesting, indeed, to see what technologies become the most popular in the future.

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REFERENCES

1. Anger H. *Rev. Sci. Instr.* **29**, 27-33 (1958).
2. Meier D, Czermak A, Jalocha P, et al. *IEEE Trans. Nucl. Sci.* **49**, 812-816 (2002).
3. Loudos GK, Nikita KS, Giokaris ND, et al. *Appl. Radiat. Isot.* **58**, 501-508 (2003).
4. Gagnon D, Zeng GL, Links JM, et al. *Proc.* IEEE Nuclear Science Symposium and Medical Imaging Conference, Oct. 4-10, San Diego, CA, 2002, pp. 1156-1160.
5. Qi J and Leahy RM. *IEEE Trans. Med. Imaging* **19**, 493-506 (2000).
6. Moses WW and Qi *J. Nucl. Instr. Meth. Phys. Res.* A **497**, 82-89 (2003).
7. Wienhard K, Schmand M, Casey ME, et al. IEEE Trans. Nucl. Sci. **49**, 104 -110 (2002).
8. Braem A, Chesi E, Joram C, et al. *Conf. Proc.*of the First International meeting on Applied Physics, 13-18th October 2003, Badajoz, Spain. 2003, pp. 86-67.
9. Green MV, Seidel J, Vaquero JJ, et al. *Comput Med Imaging Graph* **25**, 79-86 (2001).
10. Hasegawa BH, Iwata K, Wong KH, et al. *Acad. Radiol.* **9**, 1305-1321 (2002).
11. Shao Y, Cherry SR, Farahani K, et al. *Phys. Med. Biol.* **10**, 1965-1970 (1997).
12. Slates RB, Farahani K, Shao Y, et al. *Phys. Med. Biol.* **44**, 2015-2027 (1999).
13. Zaidi H, Montandon M-L, Slosman DO. Med. Phys. **30**, 937-948 (2003).