Ultra-high Resolution Imaging of PET tracers with clustered pinholes

Marlies C. Goorden and Freek J. Beekman

***Abstract*— State-of-the-art small-animal Single Photon Emission Computed Tomography (SPECT) with multi-pinhole collimators (MP-SPECT) can reach sub-half-millimetre image resolutions, which outperforms the reconstructed resolution of high-end small-animal Positron Emission Tomography (PET), that has a resolution just below 1 mm. This naturally raises the question how well positron emitters can be imaged with dedicated pinhole collimators. A SPECT system with an additional collimator to image positron emitters at a high resolution could be extremely cost-effective and has the additional advantage that it can perform simultaneous dual-isotope imaging of PET and SPECT tracers.**

Multi-pinhole collimators for SPECT tracers (typically 30-250keV) are not suitable to image positron emitters, because of the large amount of edge penetration of 511keV annihilation photons. The resulting image blurring can be remedied by using pinholes with smaller acceptance (cone-)angles. However, as a consequence the field-of-view of each pinhole is reduced. Here, we present a completely new collimator geometry, which is based on clusters of pinholes with small acceptance angles. All the pinholes in such a cluster sample about the same field-of-view as a single, traditional pinhole. As a result it is avoided that an undesirable number of bed or detector position has to be used to have complete data of the volume-of-interest (VOI).

To investigate the performance of this new collimator geometry for positron emitters, we compare simulated images of a resolution phantom and a mouse brain striatal phantom with i) a traditional collimator (TMP), ii) a collimator with pinholes with smaller acceptance angles focusing on a smaller central field-of-view (FMP), iii) a collimator with clusters of pinholes (CMP) that samples the same field-of-view as TMP. The smallest rods of the resolution phantom that can be resolved have a diameter of 0.9 mm (TMP), 0.65 mm, (FMP) and 0.65 mm (CMP). Both FMP and CMP enable to visualize uptake in sub-compartments of the mouse brain, which opens up unique possibilities to analyze processes underlying the function of neurotransmitter systems, but FMP needs an undesirably high number of bed movements to sample the entire VOI. We conclude that imaging of positron emitters with CMP collimators is extremely promising, since PET tracers can be imaged with an even better resolution than state-of-the-art co-incidence PET.

***Index Terms*— SPECT, PET, pinholes, fully 3D iterative reconstruction**

M. C. Goorden is with Delft University of Technology, Section Radiation Detection and Matter, Mekelweg 15, 2629 JB Delft, The Netherlands and the Image Sciences Institute, University Medical Centre Utrecht, The Netherlands (e-mail: m.c.goorden@tudelft.nl).

F. J. Beekman is with Delft University of Technology, Section Radiation Detection and Matter, Mekelweg 15, 2629 JB Delft, The Netherlands and Molecular Imaging Laboratories, Utrecht, The Netherlands and the Image Sciences Institute, University Medical Centre Utrecht, The Netherlands

I. Introduction

In recent years, the image resolution of SPECT systems dedicated to imaging small animals has improved dramatically: SPECT with multi-pinhole collimators (MP-SPECT) can now image tracer uptake in structures < 0.35mm [1-4]. These resolutions are much better than those of state-of-the-art small-animal PET (just below 1 mm), despite the much higher sensitivity of PET. This naturally raises the question if cases exist in which PET tracers can be imaged better using special SPECT collimators [5].

Simultaneous imaging of multiple-tracers is of increasing interest. In SPECT, performing simultaneous dual-tracer imaging is possible by setting multiple-energy windows [6-8], whereas this is impractical in PET where all gamma-photons have equal energies. A system performing PET and SPECT scans simultaneously brings many new possibilities of dual-tracer imaging into reach. Compared to separate PET and SPECT devices, a combined PET/SPECT scanner can produce images of different processes that are perfectly aligned, has reduced acquisition time and is potentially much more cost-effective.

The limited resolution in co-incidence PET imaging is caused by i) intrinsic detector resolution, ii) non-collinearity of the annihilation gamma-photons, iii) random co-incidences, and iv) the finite range of positrons. The first three factors are not prominent in pinhole SPECT: the disadvantages of intrinsic detector resolution can be largely overcome by the principle of pinhole magnification, while non-collinearity and random co-incidences do not play a role in single photon imaging. These advantages of pinhole imaging may partly compensate the limited sensitivity of SPECT. As a result, in a subset of imaging situations the extension of MP-SPECT to detect high-energy annihilation photons may yield better resolution for positron emitters than contemporary small-animal PET as will be shown in the next sections.

Current pinhole collimators are not suitable for high-resolution imaging of 511 keV annihilation photons, because of the strong pinhole edge penetration at high energies. The resolution loss due to edge penetration can in principle be reduced by using smaller pinhole acceptance angles. This, however, restricts the field-of-view of the collimator. In this paper we investigate a completely new pinhole geometry which uses many pinholes with small acceptance angles, which are grouped in clusters [9]. The pinholes grouped in a single cluster sample a field-of-view that has approximately the same size as the field-of-view of a single traditional pinhole.

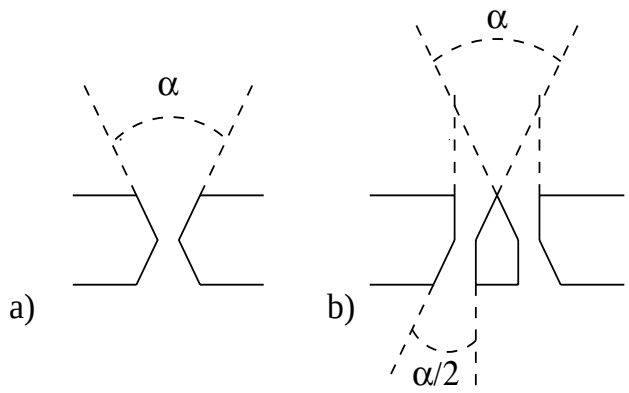


Figure 1: Cross section through a traditional pinhole (a) with opening angle α, that samples the same field-of-view as a cluster of four pinholes (b) with opening angles α/2. This cross section is taken through two of the four pinholes within the cluster.

The application of pinholes to image positron emitters was already investigated in [10]. However, the Uranium collimators used in this study do not give high-resolution images: even for Tc-99m only 1.5 mm reconstructed resolutions were obtained, while in F-18 scans structures with a diameter of 3.9 mm were resolved at best. Other authors have followed the opposite approach of combining PET and SPECT by inserting a collimator in an existing PET system [11]. An attempt to improve resolution of co-incidence PET based on the principles of so-called virtual pinholes, is investigated in [12]

The aim of the present paper is to investigate the performance of the cluster-pinhole collimator geometry by comparing simulated images of a resolution phantom and a mouse brain striatal phantom. Traditional MP-SPECT (TMP), MP-SPECT with small acceptance-angle pinholes and a reduced field-of-view (FMP) and MP-SPECT with clusters of pinholes (CMP) are simulated.

II. METHODS

A. Cluster pinhole design and geometry of collimators

Cluster pinholes. The concept of a cluster of pinholes [9] is illustrated in figure 1, where a cross section through a cluster of four pinholes is shown (cross section through two out of four pinholes). The cluster of pinholes, with acceptance angle $\alpha/2$ each, samples approximately the same field-of-view as a single traditional pinhole with acceptance angle α. A three-dimensional illustration of a ring of clusters containing four pinholes each, is shown in figure 2.

Geometry of collimators. We compare three different geometries which differ only by their collimator design. For the detector geometry, we assume three conventional gamma-detectors placed in a triangular shape [4]. The detectors have an intrinsic resolution of 3.5 mm and 12% of the 511 keV photons that fall onto the detector end up in the photo-peak [14].

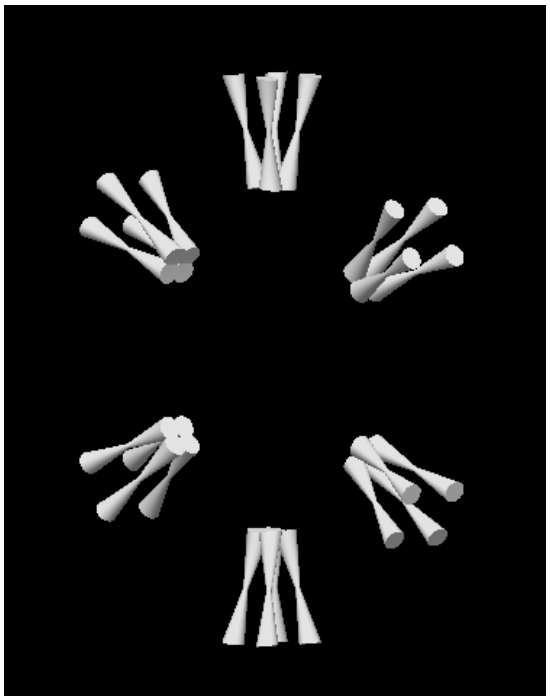


Figure 2: Six clusters of 4 pinholes each placed in a ring

The number of pinholes of each collimator is determined by the requirement that the complete detector area is used but that projections from different pinholes do not overlap. Furthermore, we demand that our collimator is large enough for whole-body mouse imaging and consequently, an inner collimator diameter of 44 mm is required for a central field-of-view (CFOV) with a diameter of 12 mm [15]. We define the CFOV as the area that is seen by all pinholes or pinhole clusters. A reduction of the CFOV diameter requires an equal increase in the inner collimator diameter, because much more mouse translations are necessary. We choose a pinhole diameter d=0.6 mm for all collimators. To prevent direct penetration of the collimator, we assume a collimator wall thickness of 25 mm with pinholes placed symmetrically in the collimator.

TMP. The traditional SPECT geometry we consider has 75 pinholes, placed in 5 rings, with an acceptance angel α=30°. The pinhole centres are at a distance of 34.5 mm from the centre of the collimator. CFOV is about 18 mm in diameter and 12 mm long.

FMP. The second geometry has 270 pinholes with an acceptance angle α=15° and pinholes centres placed at a radius of 37.5 mm. The CFOV is about a factor of two smaller in all directions than that of TMP.

CMP. The cluster-pinhole collimator design has clusters of four pinholes, each pinhole having an acceptance angle of 15°. The CFOV is almost equal to that of TMP and the centres of the

pinholes are at a distance of 34.5 mm from the centre of the collimator.

B. Simulations

Projection simulations representing F-18 are performed with a resolution phantom and a mouse brain striatal phantom. The simulator takes into account effects such as finite positron range, pinhole edge penetration and detector blurring [14]. The resolution phantom consists of six sectors with rods of different diameters (0.6, 0.65, 0.7, 0.75, 0.8 and 0.9 mm), as shown in figure 3.a. An activity concentration in the active areas of the resolution phantom of 250 MBq/ml and a scan duration of 1.5 hours were assumed. The mouse brain striatal phantom is shown in figure 4.a. Our simulations assume that an activity of 40 MBq is injected into the mouse which is scanned during 45 minutes starting 15 minutes post-injection.

Poisson noise was generated in the projection data. The voxel size of both phantoms was 0.125 mm, twice as small as the voxel size during image reconstruction. This was done to emulate the fine resolution properties of real activity distributions.

C. Image reconstruction

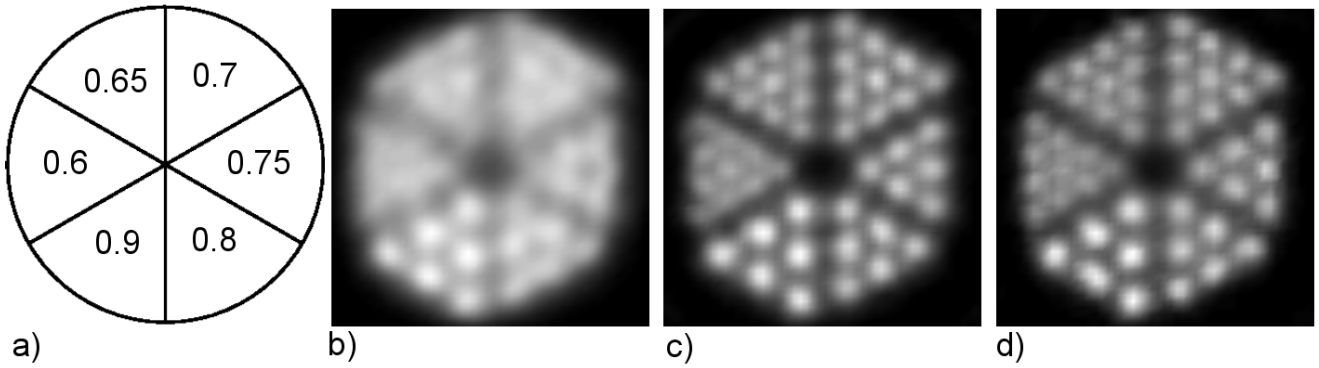
Image reconstruction for all systems was performed using Ordered Subset Estimation Maximization (OSEM[16]) with ten subsets. Relevant non-zero matrix elements were pre-calculated using simulations of point source responses. The voxel size during reconstruction was 0.25 mm.

III. RESULTS

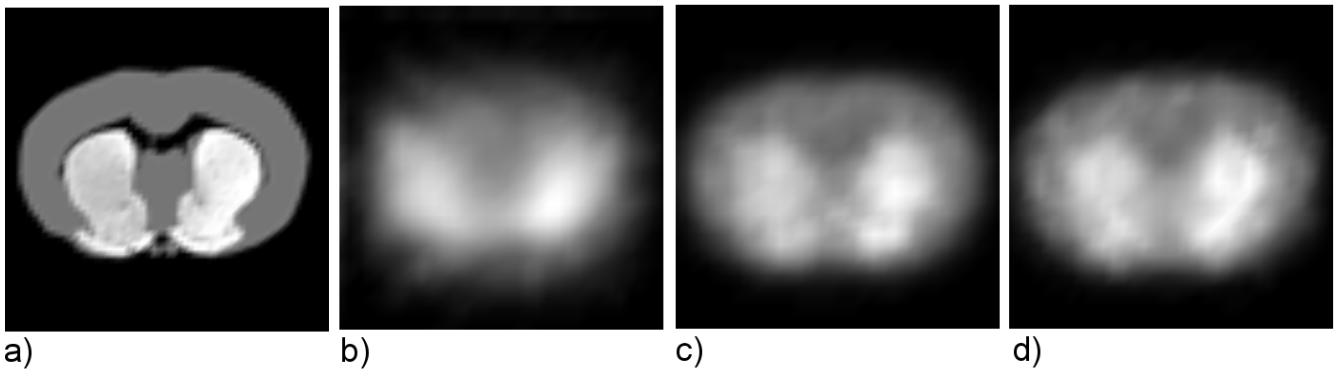
In figure 3 we show images of the hot rod resolution phantom for TMP, FMP, and CMP. The smallest rods that can be resolved have a diameter of 0.9 mm (TMP), 0.65 mm (FMP), and 0.65 mm (CMP). In figure 4, images of the mouse brain striatal phantom are shown. FMP and CMP show much more details than TMP and it is even possible to partly distinguish sub-striatal structures.

IV. DISCUSSION

It is clear from the simulated images of figure 3, that



a) Hot rod phantom with cappilary diameters of 0.6, 0.65, 0.7, 0.75, 0.8 and 0.9 mm simulated with b) TMP, c) FMP, d) CMP. Slice thickness is 1.5 mm.



a) A trans-axial slice through a mouse brain striatal phantom simulated with b) TMP, c) FMP, d) CMP. Slice thickness is 1.5 mm.

decreasing the pinhole acceptance angle is a good remedy against the strong blurring due to pinhole edge penetration of 511 keV gamma-rays. However, the improved resolution is traded for a smaller CFOV and as a consequence, an increase in the number of steps with a factor of 8 is necessary to sample the same VOI with FMP compared to TMP. The resolution of the cluster-pinhole geometry is equal to that of FMP, while it has the same CFOV as traditional pinhole SPECT.

While the resolution of CMP is distinctively improved compared to high-end small-animal co-incidence PET, the sensitivity of this newly proposed device cannot reach the level of co-incidence PET devices. We believe that for applications where only small parts of a mouse are imaged, such as sub-compartments of the mouse brain (see figure 4), the limited sensitivity does not necessarily pose a large problem and that in many cases our cluster-pinhole collimator could allow imaging of structures that are not resolvable by any traditional PET device. For whole body imaging, the limited sensitivity may have more consequences. Although it has been shown that MP-SPECT with SPECT tracers is able to achieve sub-mm image resolutions [15], further investigations are needed to find our in which cases this also holds for CMP. A detailed comparison of CMP and ring-PET will be performed in the future to investigate all these issues for a wide range of imaging situations.

V. Conclusion

In this paper we have shown that pinhole geometries based on cluster of pinholes are extremely promising for imaging PET tracers and possibly combined imaging of PET and SPECT tracers. Our simulations indicate that the resolution that can be obtained with clustered pinholes surpasses that of state-of-the-art small-animal PET devices in case of imaging objects with the size of mouse organs. The high image resolution, the possibility to perform simultaneous dual-tracer imaging as well as the enormous costs saved by the fact that only a single scanner is needed for PET and SPECT can have a large impact on several future research applications.

References

[1] R.J. Jaszczak, J. Li, H. Wang, M.R. Zalutsky, and R.E. Coleman, “Pinhole collimation for ultra-high-resolution small-field-of-view SPECT”, *Phys. Med. Biol.*, Vol. 39, pp. 425-37, 1994.

[2] F.J. Beekman *et al*, “U-SPECT-I: A novel system for submillimeter-resolution tomography with radiolabeled molecules in mice”, *J. Nucl. Med.*, vol. 46 (7), pp. 1194–1200, 2005.

[3] F.J. Beekman and F. van der Have, “The pinhole: gateway to ultra-high-resolution three-dimensional radionuclide imaging”, *Eur. J. Nucl. Med. Mol. Im.*, vol. 34 (2), pp. 151–161, 2007.

[4] F. van der Have *et al*, “U-SPECT-II: an ultra-high resolution device for molecular small-animal Imaging”, J. Nucl. Med, vol. 50, pp. 599-605, 2009.

[5] F.J. Beekman and F. van der Have, “High resolution tomography of positron emitters using highly focussed pinhole collimation”, *J. Nucl. Med. Meeting Abstracts*, vol. 48, 92P-b, 2007.

[6] H.W.A. M. de Jong, F. J. Beekman, M. A. Viergever and P. P. van Rijk, “Simultaneous Tc-99m/ Tl-201 dual-isotope SPET with Monte Carlo-based down-scatter correction”, *Eur. J. Nucl. Med.*, vol. 29 (8), pp. 1063-1071, 2002.

[7] Y. Du. B. M. W. Tsui, and E.C. Frey, “Model-based crosstalk compensation for simulaneous Tc-99m/ I-123 dual-isotope brain SPECT imaging”, *Med. Phys.*, vol. 34 (9), pp. 3530-3543, 2007.

[8] D. J. Kadrmas, E.C. Frey, and B. M. W. Tsui, “Simultaneous technetium-99m/ thallim-201 SPECT imaging with model-based compensation for cross-contaminating effects”, *Phys. Med. Biol.*, vol. 44 (7), pp. 1843-60, 1999.

[9] F. J. Beekman, Collimator with pinhole clusters, European Patent Application No. 07076118.4

[10] C. R. Tenney, M. P. Tornai, M. F. Smith, T.G. Turkington, and R. J. Jaszczak, “Uranium pinhole collimators for 511-keV photon SPECT imaging of small volumes”, *IEEE Trans. Nucl. Sci.*, vol. 48 (4), pp. 1483-1489, 2001.

[11] C. A. Cardi, Z. Cao, M. L. Thakur, J. S. Karp, P. D. Acton, “Pinhole PET (pPET): A Multi-Pinhole Collimator Insert for Small Animal SPECT Imaging on PET cameras”, 2005 IEEE Nuclear Science Symposium Conference Record, pp. 1973-1976.

[12] Y.-C. Tai, H. Wu. D. Pal, and J. A. O’Sullivan, “Virtual-Pinhole PET”, J. Nucl. Med., Vol. 49 (3), pp.471-479, 2008.

[13] B. Vastenhouw *et al*, “Movies of dopamine transporter occupancy with ultra-high resolution focusing pinhole SPECT”, *mol. psych.*, vol.12, pp. 984-987, 2007.

[14] M. C. Goorden, F. van der Have, and F. J. Beekman, “Efficient simulator of multi-pinhole SPECT with PET isotopes”, submitted.

[15] B. Vastenhouw and F. J. Beekman, ”Submillimeter total-body murine imaging with U-SPECT-I”, *J. Nucl. Med.*, vol. 48, pp. 487-493, 2007.

[16] H. M. Hudson and R. S. Larkin, “Accelerated image-reconstruction using ordered subsets of projection data”, *IEEE Trans. Med. Im.*, vol. 13 (4), pp. 601-609, 1994.