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EDITORIAL

Pinhole SPECT: Ultra-High Resolution Imaging for Small Animal Studies

Pinhole SPECT has recently been shown to provide a useful and inexpensive approach to obtaining high and ultra-high resolution images for small animal imaging (*1–5*). The use of small aperture pinhole collimators and short imaging distances for acquiring SPECT projection data can yield a system spatial resolution which is better than the intrinsic spatial resolution of the detector as a result of the large magnification factors (Fig. 1) which can be obtained with large field of view cameras (*6,7*). Since the resolution of pinhole collimators approaches the diameter of the pinhole aperture at small imaging distances, very high or ultra-high spatial resolution can be achieved using collimators with large magnification factors. Unfortunately, these gains in resolution are offset by large decreases in sensitivity; e.g., a 10-fold increase in resolution will result in a 100-fold decrease in sensitivity (Fig. 2). Compromises must be made between demands for spatial resolution and for sensitivity; however, this has not prevented its practical implementation for imaging. The initial reports on pinhole SPECT (*1–5*) were directed towards characterizing this new imaging technique and demonstrating the scope of potential applications for preclinical and research studies, with the potential for limited clinical applications. Of significance, especially in the current climate of increasing competition for a decreasing number of research dollars, is the accessibility of this technique to all institutions that have SPECT camera systems. The technique can be implemented by adding suitable reconstruction software to the conventional image processing software library and using appropriate small diameter pinhole collimator apertures for imaging. Pinhole SPECT, as an add-on to existing equipment, can provide the means for obtaining high-resolution SPECT images at a fraction of the cost of the high-resolution imaging systems which have been designed for small animal imaging studies (*8–10*).

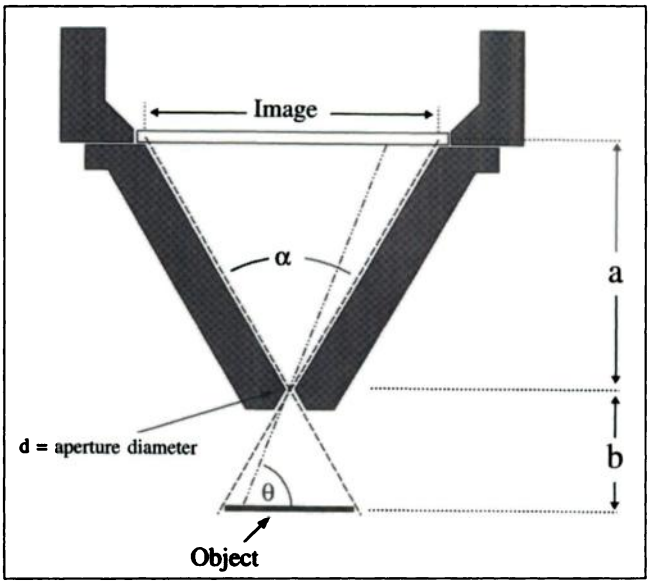

FIGURE 1. Imaging geometry for single pinhole collimator. Magnification of image projected on NaI(Tl) detector of pinhole collimated, scintillation camera is equal to ratio of distance, a, between detector and collimator aperture, to distance, b, between object which is imaged and collimator aperture. The geometric resolution of pinhole collimator, $R_g = [(a + b)\, d_e/a]$ and overall resolution, $R_0 = [R_g^2 + (R_i\, b/a)^2]^{1/2}$, where R_i is intrinsic resolution of detector and d_e is effective diameter of pinhole aperture. The effective diameter of pinhole collimator, d_e, is larger than geometric diameter, d, as a result of penetration of edges of aperture by detected gamma rays, $d_e = [d(d + 2/\mu \tan(\alpha/2))]^{1/2}$, where μ is linear attenuation coefficient of aperture material and α is acceptance angle of collimator. The geometric efficiency of pinhole collimator decreases in radial direction with $\sin^3\theta$ (*6*).

Extending the approach reported earlier for pinhole collimated, single-detector gamma camera SPECT systems (*1–5*), the article by Ishizu et al. in this issue of the *Journal* (*11*) shows that high-resolution tomographic slices can be obtained with a significant gain in sensitivity using a multicamera SPECT sys-

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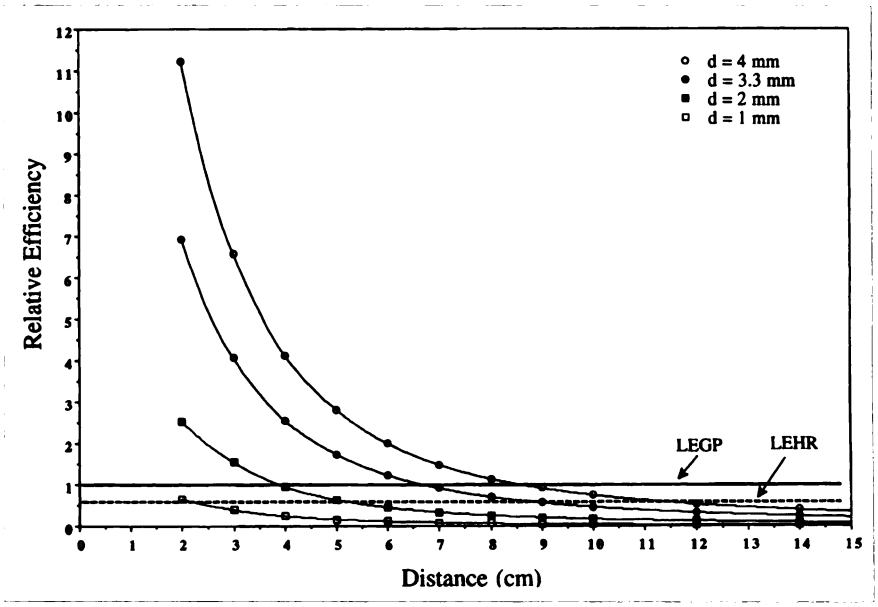

FIGURE 2. Relative sensitivity of pinhole collimator plotted as function of distance between collimator and 2.2-cm diameter disk source of ^{99m}Tc compared with sensitivity of LEHR and LEGP collimators (2). Sensitivity falls rapidly as the distance between collimator aperture and object increases.

tem. The findings are not unexpected, since the advantages gained from using pinhole collimators on the four-detector SPECT system would be expected to closely resemble those gains made in planar and SPECT imaging when switching from single to multiple detector systems (*12,13*). The move to a multidetector SPECT system is an appropriate and logical step forward to improve the sensitivity of the pinhole SPECT technique to accommodate lower activity doses and to facilitate improved image quality. The reported work presents performance measurements and images for a pinhole collimated, four gamma camera detector SPECT system which employs a pinhole collimator on each detector (*11*). Here, the investigators show that the multidetector SPECT system provides adequate sensitivity to allow slow dynamic SPECT imaging of some radiopharmaceuticals. These findings of improved sensitivity and the additional capability of providing for serial imaging of live animals make pinhole SPECT an attractive alternative to well-cup counting of activity in excised tissues or to autoradiography for imaging regional distribution properties of administered radiopharmaceuticals. The spatial resolution of pinhole SPECT cannot compete with high-resolution microautoradiography obtained using nuclear emulsions; however, it can provide a useful alternative to macroautoradiography in which tissue specimens are placed in direct contact with high speed x-ray films or scintillation detectors to record regional radiopharmaceutical uptake in organs and tissues (*14,15*).

In our initial studies of the pinhole SPECT system using a single gamma camera as the detector, we were impressed with the image quality that could be obtained for in vivo radiopharmaceutical imaging (*2*). We saw this approach as being suitable "... to perform serial and repeat imaging studies in the same living animal at multiple times to investigate tumor growth, tissue pathology, effects of therapy, intervention and activation..." and useful for providing "... an accurate mapping of regional localization with and without activation in vivo." Similarly, we saw its potential for imaging selected anatomic regions in human subjects where an acceptable balance among the diameter of the collimator aperture, imaging distance, and localized activity can be achieved. The improved sensitivity and similar spatial resolution potential demonstrated with the multiple gamma camera detector system makes pinhole SPECT an even more practical approach to high-resolution, small animal imaging.

The methods used in this study are similar to those previously reported for use in single rotating, gamma camera SPECT (*1–5,16*). There are, however, a couple of important and major differences in the approach to image reconstruction and in the observed levels of sensitivity reported by Ishizu et al. (*11*) that deserve comment. Throughout their article, Ishizu et al. state that a filtered backprojection algorithm (FBP) is used to reconstruct SPECT images from data that has undergone a "... fanbeam to parallel beam data conversion." The authors also make the same statement in an earlier description of their work (*17*). This presents a problem since the pinhole imaging geometry is a conebeam geometry. If the authors used a fanbeam geometry data conversion, this would not give an accurate translation of the projection data for image reconstruction. Either a true three-dimensional pinhole reconstruction algorithm or a three-dimensional tilted fanbeam or conebeam data conversion algorithm needs to be used (*2–5,18*). The distortions in the axial direction (in the planes outside the central plane) that are common to three-dimensional FBP reconstruction algorithms can be minimized if a three-dimensional maximum-likelihood-expectation-maximum (ML-EMI) algorithm is used (*3,5*). A very good discussion of this and other possible approaches to minimize axial blurring can be found in an article by Jaszczak et al. (*3*).

TABLE 1
Comparison of Pinhole Collimator Sensitivities Normalized to Imaging Distance b of 4 cm

Weber et al. (2)*			Jaszczak et al. (3)*			Ishizu et al. (11)†		
d (mm)	d_e (mm)	Sensitivity (cps/μCi)	d (mm)	d_e (mm)	Sensitivity (cps/μCi)	d (mm)	d_e (mm)	Sensitivity (cps/μCi/ml)
—	—	—	—	—	—	4.0	4.2	6703.1
3.3	3.5	10.9	—	—	—	—	—	—
2.0	2.2	4.0	2.0	2.4	5.7	2.0	2.2	1859.4
1.0	1.2	1.1	1.2	1.6	2.6	1.0	1.2	609.4
—	—	—	0.6	1.0	0.9	—	—	—

*Sensitivity for single gamma camera SPECT system.
†Sensitivity for four gamma camera SPECT system.
d = pinhole aperture diameter; d_e = effective pinhole aperture diameter.

A second area of concern that we have with the Ishizu article is how the sensitivity and resolution were reported and how the sensitivity was calculated. In the abstract, the authors state that "The system provided a reconstructed spatial resolution of 1.65 mm (FWHM) and a sensitivity of 4.3 kcps/mCi/ml with the best type of pinholes." We believe that this statement may mislead some readers, since the spatial resolution reported as 1.65 mm (FWHM) is for a 1.0-mm aperture pinhole collimator at an imaging distance or "rotation radius" of 40 mm, whereas the sensitivity of 4.29 kcps/mCi/ml is for a 4-mm aperture pinhole collimator at an imaging distance of 50 mm. As shown in their Table 1, a sensitivity of 4.29 kcps/mCi/ml with the 40-mm aperture collimator is accompanied by much poorer spatial resolution. Spatial resolution for this size aperture is 4.15 mm (FWHM) at an imaging distance of 50 mm.

In addition, Ishizu et al. report their comparative levels of sensitivity in terms of cps/mCi/ml. Although this allows them to compare the different collimators they tested, the lack of an explanation as to how the units for sensitivity were derived prevents comparison with other work. Weber et al. (2) and Jaszczak et al. (3) report similar sensitivities for their independent measurements made with single gamma camera pinhole SPECT systems. Ishizu et al. report sensitivities that are more than two orders of magnitude greater (Table 1). Normalizing the sensitivity to a source distance of 4.0 cm for a 2-mm aperture collimator, Weber and Jaszczak report a sensitivity of 4.0–5.7 cps/μCi, whereas Ishizu et al. report a value of 1859 cps/μCi/ml. We would expect the gain in sensitivity to be, at most, a factor of four.

In conclusion, the article by Ishizu et al. provides a logical step forward in improving the sensitivity of pinhole SPECT for high spatial resolution imaging. Although clarification is needed on how the pinhole projection data were converted for image reconstruction and how sensitivity was determined in their study, the correct implementation of the pinhole technique on higher sensitivity multicamera SPECT systems will help make pinhole SPECT a more practical and efficacious approach to small animal imaging and may lead to new clinical imaging methods.

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