## Letter to the editor.

## Will high-resolution/high-sensitivity SPECT ensure that PET is not the only survivor in nuclear medicine during the next decade?

In a recent issue of the journal, Abass Alavi and Sandip Basu [1], on the one hand, and Giuliano Mariani, Laura Bruselli and Andriano Duatti [2], on the other, debated the future of planar scintigraphy and single photon emission computed tomography (SPECT) in the face of an ever better performing positron emission tomography (PET). The pros and cons for the use of single photon emitters, positron emitters and the related tracers were thoroughly discussed. It is however our opinion that the discussion relating to the physics and technology of SPECT was biased by the side-stepping of the most recent advances in SPECT, although some points were briefly raised by Mariani et al [2].

From the beginning, PET was developed as a fully tomographic technique [3]. In the pioneer studies, the detectors, although very limited in number in those early times, were already being placed around the patient's body. Breakthroughs in crystal technology, electronics, attenuation correction, scatter correction and tomographic reconstruction (Fourier rebinning, 2D and 3D iterative reconstruction including resolution and/or time-of-flight consideration) have allowed us to benefit from all the information collected by the detectors. This has led to the modern PET scanners with annular detectors and an axial field-of-view of 15-25 cm with full quantitative 3D tomographic capabilities [4-5]. Meanwhile, SPECT continued to be performed with a rotating parallel collimated Anger camera. The only major advances were the dual-head and triple-head cameras, which increased the sensitivity, and the iterative reconstruction algorithms, which improved the overall image quality [6].

Since the beginning of the 1990s, considerable efforts have been focussed on developing high resolution SPECT systems by replacing the traditional parallel hole collimators with converging collimators such as fan-beams, cone-beams, cardio-focals, slit-slat collimators and, last but not least, pinholes [7]. Pinhole SPECT was primarily studied in the context of small animal imaging [8-9]. In the beginning, a single pinhole mounted on a commercial Anger camera was used [8]. Systems with multiple pinhole with or without the multiplexing of the projections were quickly developed and finally non rotating systems with a large number of small pinholes came onto the market [9]. Such systems combined high resolution, high sensitivity and collection of the data needed for tomographic reconstruction, without the need to rotate the detectors. This meant that dynamic studies became as easy in SPECT as they were in PET, and with an even better spatial resolution [9].

Meanwhile, a few studies were being devoted to the application of single pinhole SPECT to humans. They demonstrated the feasibility of pinhole SPECT studies of limited volume of interest (VOI) under not too restrictive conditions: projections could only be collected over 180° around the VOI [10-11]; the distance from the pinhole aperture to the VOI center did not necessarily need to be kept constant [12]; the pinhole could be moderately tilted [10-12] and the detector uniformity requirements were shown to be comparable to those needed for SPECT with conventional parallel hole collimators [13]. Moreover the introduction of resolution recovery in the iterative reconstruction process was shown to be dramatically effective both in improving the resolution and lowering the noise content of the images [14]. The studies were not limited to the technical feasibility of pinhole SPECT in humans and clinically relevant results of the method were reported [15-16].

Combining the results obtained in humans using single pinhole SPECT with progress made in small animal pinhole SPECT would lead to stationary pinhole SPECT cameras for the exploration of limited VOI in humans. These systems would allow a new compromise between overall image quality, acquisition time, patient dose, diagnostic accuracy and diagnostic confidence. It is a matter of public record that active research in this direction has emerged from the recent 2008 IEEE Medical Imaging Conference in Dresden [17-24].

The high intrinsic spatial resolution of solid state detectors that are likely soon to come onto the market [7], should ease the use of multi-pinhole by demanding a smaller geometrical zoom factor. Also their improved energy resolution should help to discriminate and reject scattered photons [25], reducing the need for a powerful scatter correction method. This contrasts with PET where, in 3D-mode, scattered photons can be the majority of the detected coincidence events.

With the use of CT data, attenuation correction is as straightforward in SPECT as in PET, providing that iterative reconstruction is used. This was demonstrated in the first SPECT-CT prototype by Bruce Hasegawa and co-workers [26-27] and has been successfully applied by the first commercial SPECT-CT system [28]. This contradicts Alavi's affirmation [1] that attenuation correction can only be optimal for PET.

Stationary systems based on multi-pinhole and eventually new  $\gamma$ -detectors would make SPECT of limited VOI in humans faster, better and eventually dynamic. These VOI could be large enough [9] to allow exploration of the brain, the heart, the parathyroid, the thyroid, and some bone regions, such as the ankle, cervical spine, knee, shoulder and wrist, where high resolution and sensitivity are needed. These stationary systems would also allow, to the greater benefit of the patient, the use of the tracers now available and give radiochemists the opportunity to pursue research on both single-photon and positron emitting tracers. In the light of events of the last few years in America and Europe, a possible shift from single-photon to positron emission imaging cannot possibly come from the instrumentation (where progress is actually much more rapid in SPECT than in PET), but from the supply of the emitters.

It is a common experience that the future is hard to predict. This is probably even more true in the case of research outcomes and how these will affect daily life or, in this context, how they will change the clinical use of the various imaging modalities. We merely suggest that we should believe in the very active and productive research in the field of nuclear medicine and trust in the power of the industry to translate some of the research advances into commercial products with an acceptable level of patient cost-effectiveness, as it was demonstrated in the last decade for PET-CT and SPECT-CT. Clearly dynamism is still present in SPECT and in PET and at the heart of nuclear medicine as it has been for so many years.

Is it possible that the next months could represent a wonderful tribute to the memory of Bruce Hasegawa [29], who nearly started his research in the field by studying a multipinhole system for the heart [30] (and reinvestigated these systems recently [20, 31]) and who invented SPECT-CT [26], through the launch of a commercial multi-pinhole SPECT or SPECT-CT system? We will see, but, whatever happens, thank you and good bye Mister Hasegawa.

Prof. Alain SERET

Experimental Medical Imaging Department of Physics Université de Liège Liège, Belgium.

## References.

- 1. Alavi A, Basu S. Planar and SPECT imaging in the era of PET and PET–CT: can it survive the test of time? Eur J Nucl Med Mol Imaging 2008;35:1554-1559.
- 2. Mariani G, Bruselli L, Duatti A. Is PET always an advantage versus planar and SPECT? Eur J Nucl Med Mol Imaging 2008; 35:1560-1565.
- 3. Graham LS, Perez-Mendez V. Special imaging devices. In: Rollo F D, editor. Nuclear medicine physics, instrumentation and agents. Saint Louis: Mosby; 1977. pp 271-321.
- 4. Cherry SR. The 2006 Henry N. Wagner lecture: of mice and men (and positrons)-advances in PET imaging technology. J Nucl Med 2006;47:1735-1745.
- 5. Cherry SR, Dahlbom M. PET: physics, instrumentation, and scanners. In: Phelps ME, editor. PET: physics, instrumentation, and scanners. New York: Springer; 2006. pp 1-130.
- 6. Bruyant PP. Analytic and iterative reconstruction algorithms in SPECT. J Nucl Med 2002; 43:1343–1358.
- 7. Zaidi H, Hasegawa BH. Overview of nuclear medicine imaging. In: Zaidi H, editor. Quantitative analysis in nuclear medicine imaging. New York: Springer Science+Business Media; 2006. pp 1-34.
- 8. Weber DA, Ivanovic M. Ultra-high-resolution imaging of small animals: implications for preclinical and research studies. J Nucl Cardiol 1999;6:332-344 and references therein.
- 9. Beekman F, van der Have F. The pinhole: gateway to ultra-high-resolution three-dimensional radionuclide imaging. Eur J Nucl Med Mol Imaging 2007;34:151-161 and references therein.
- 10. Wanet P, Sand A, Abramovici J. Physical and clinical evaluation of high-resolution thyroid pinhole tomography. J Nucl Med 1996;37:2017-20.
- 11. Seret A, Defrise M, Blocket D. 180° pinhole SPET with a tilted detector and OS-EM reconstruction: phantom studies and potential clinical applications. Eur J Nucl Med 2001:28:1836-1841.
- 12. Seret A, Flérès D, Firket O, Defrise M. Body contour 180° pinhole SPET with or without tilted detector: a phantom study. Eur J Nucl Med Mol Imaging 2003;30:1205-1210.
- 13. Seret A, Bleeser F. Intrinsic uniformity requirements for pinhole SPECT. J Nucl Med Technol 2006;34:43-47.
- 14. Seret A, Andreyev A, Vanhove C, Defrise M. Resolution recovery iterative reconstruction for human pinhole SPECT: a phantom study. Eur J Nucl Med Mol Imaging 2007;34:S236.
- 15. Seret A, Hustinx R. Clinical applications of pinhole single photon emission tomography. Current Medical Imaging Reviews 2006;2:347-52 and references therein.
- 16. Carlier T, Oudoux A, Mirallié E, Seret A, Daumy I, Leux C, Bodet-Milin C, Kraeber-Bodéré F et Ansquer C. 99mTc-MIBI pinhole SPECT in primary hyperparathyroidism: comparison with conventional SPECT, planar scintigraphy and ultrasonography. Eur J Nucl Med Mol Imaging 2008;35:637-43.
- 17. Asma E, Manjehwar R. Evaluation of the impact of resolution-sensitivity tradeoffs on detection performance for SPECT imaging. Abstract book of the 2008 IEEE Medical Imaging Conference Dresden; 2008. p 353.
- 18. Blevis IM, Volokh L, Tsukerman L, Hugg JW, Jansen FP, Bouhnik JP. CZT gamma camera with pinhole collimator: detector efficiency. Abstract book of the 2008 IEEE Medical Imaging Conference Dresden; 2008. p 377.

- 19. Spilker ME, Bal G, Uribe J, Thurfjell L, Tan Hehir C, Tao X, Can A, Sarachan B, Jansen F. Evaluation of different multi-pinhole geometries for SPECT imaging of parkinsonian disorders. Abstract book of the 2008 IEEE Medical Imaging Conference Dresden; 2008. pp 393-394.
- 20. Huang Q, Boutchko R, Hasagawa BH, Budinger TF, Gulberg GT. Computer evaluation of novel multipinhole SPECT system for myocardial perfusion imaging. Abstract book of the 2008 IEEE Medical Imaging Conference Dresden; 2008. p 394.
- 21.De Smet J, Van Holen R, Staelens S, Vandenberghe S, Lemahieu I. Slat collimated multipinhole human brain SPECT. Abstract book of the 2008 IEEE Medical Imaging Conference Dresden; 2008. pp 396-397.
- 22. Goorden MC, Rentmeester MCM, Beekman FJ. Theoretical analysis of multi-pinhole brain SPECT. Abstract book of the 2008 IEEE Medical Imaging Conference Dresden; 2008. p 397.
- 23. Zeniya T, Watabe H, Kudo H, Hirano Y, Minato H, Iida H. Clinical usability of a compact high resolution detector for high resolution and quantitative SPECT imaging in a selected small ROI. Abstract book of the 2008 IEEE Medical Imaging Conference Dresden; 2008. p 418.
- 24. Blevis IM, Volokh L, Tsukerman L, Hugg JW, Jansen FP, Bouhnik JP. CZT gamma camera with pinhole collimator: spectra measurements. Abstract book of the 2008 IEEE Medical Imaging Conference Dresden; 2008. pp 488-489.
- 25. Volokh L, Hugg JW, Blevis I, Asma E, Jansen FP, Manjehwar R. Effect of detector energy response on image quality of myocardial perfusion SPECT. Abstract book of the 2008 IEEE Medical Imaging Conference Dresden; 2008. p 398.
- 26. Lang TF, Hasegawa BH, Liew SC, Brown JK, Blankespoor SC, Reilly SM, Gingold EL, and Cann CE. Description of a prototype emission transmission computed tomography imaging system. J Nucl Med 1992;33:1881-188.
- 27. Hasegawa BH, Brown JK, Lang TF, Reilly SM, Liew SC, Gingold EL. Object-specific attenuation correction of SPECT with simultaneous x-ray CT. IEEE Trans Nucl Sci 1993:40:1242-1252.
- 28. Bocher M, Balan A, Krausz Y, Shrem Y, Lonn A, Wilk M, Chisin R. Gamma cameramounted anatomical X-ray tomography: technology, system characteristics and first images. Eur J Nucl Med 2000;27:619–627.
- 29. Jones EF, Gould RG, VanBrocklin HF. In memoriam Bruce H Hasegawa, PhD, 1951-2008. J Nucl Med 2008;49:37N-38N.
- 30. Hasegawa B, Kirch D, Sternt D, Adams M, Skier J, Johnson T, Steele P. Single photon emission tomography with a 12-pinhole collimator. J Nucl Med 1982;23:606-612.
- 31. Funk T, Kirch D, Koss J E, Botvinick E, Hasegawa B. A novel approach to multipinhole SPECT for myocardial perfusion imaging. J Nucl Med 2006;47:595–602.