

## Emerging Applications of an Experimental Single Photon Emission Computed Tomography: An Analysis of 16 Areas of Interest in the Pig's Model

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### ABSTRACT

*This paper aims to affirm various new applications of single photon emission computed tomography (SPECT) technique by utilizing the pig's models. Evaluation and subsequent analysis of SPECT results was conducted on the jaws of eight experimental pigs with a total of 16 areas of interest. The various reasons for which each experiment was conducted were evaluated and these reasons include: i) validation of a new bone grafting technique for closure of oro-antral communications, ii) comparison of autogenous bone graft with other bone grafts, iii) sequential confirmation of osteoblastic activity of the sandwich bone regeneration technique with another technique, iv) validation of the use of a new membrane for guided tissue regeneration (GTR), v) validation of the fact that osseointegration is better with beaded implants than with threaded implants, and vi) validation of the fact that GTR is essential for immediate implant practice. The outcome of this evaluation is critically analysed against the background of the substantial clinical evidence where applicable, so as to appreciate the position of SPECT. Following the evaluation of 16 areas of interest in eight experimental pigs, it was shown that experimental SPECT was valuable in the validation of the above reasons. It appears to be a modality that can continuously be utilized to validate and compare situations which would display osteoblastic activities. It is concluded that the bone scintigraphy imaging technique accurately reflects osteoblastic activities and can now be used to validate osseointegration of any implant or bone-grafting system. This can be done in conjunction with histological and histomorphometric analysis and such results obtained from SPECT should be correlated with the histological and histomorphometric analysis if available.*

**Keywords:** Guided tissue regeneration, osseointegration, osteoblastic activity, SPECT, validation

## Aplicaciones Emergentes Experimentales de la Tomografía Computarizada por Emisión de Fotones Individuales: un Análisis de 16 Áreas de Interés en el Modelo de Cerdo

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### RESUMEN

*El presente trabajo tiene por objeto dar a conocer varias nuevas aplicaciones de la técnica de la tomografía computarizada por emisión de fotones individuales (inglés SPECT), utilizando modelos de*

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Footnote: This paper was originally presented at the 16<sup>th</sup> Caribbean Academy of Sciences (CAS) Biennial Conference on Science and Technology: Vehicles for Sustainable Economic Development in the Caribbean; 11-13 October 2008, Grenada.

*cerdo. Se llevó a cabo una evaluación y el posterior análisis de los resultados de la SPECT en relación con las mandíbulas de ocho cerdos experimentales con un total de 16 áreas de interés. Se evaluaron las varias razones por las que se llevó a cabo cada experimento. Las razones incluyen: i) validación de una nueva técnica de injerto óseo para el cierre de las comunicaciones oroantrales; ii) comparación del injerto óseo autógeno con otros injertos óseos; iii) confirmación secuencial de la actividad osteoblástica de la técnica de regeneración ósea por "sándwich" o membrana inter-posicional con otra técnica; iv) validación del uso de una nueva membrana para la regeneración tisular guiada (RTG); v) validación del hecho que la osteointegración es mejor con implantes porosos que con implantes roscados; y vi) valoración del hecho de que la RTG es esencial para la práctica del implante inmediato. El resultado de esta evaluación se analiza críticamente contra el trasfondo de la evidencia clínica sustancial donde es aplicable, para apreciar la posición de SPECT. Tras la evaluación de 16 áreas de interés en ocho cerdos experimentales, se vio que la SPECT experimental era valiosa para la validación de las razones anteriores. Parece ser una modalidad que puede utilizarse para validar y comparar situaciones que desplegarían actividades osteoblásticas. Se concluye que la gammagrafía ósea refleja las actividades osteoblásticas con precisión, y puede ahora usarse para validar la osteointegración de cualquier implante o sistema de injerto óseo. Esto puede hacerse junto con análisis histológicos y análisis histomorfométricos. Los resultados obtenidos de la tomografía SPECT deben ponerse en correlación con el análisis histológico e histomorfométrico, si estuviese disponible.*

**Palabras claves:** Regeneración tisular guiada, osteointegración, actividad osteoblástica, tomografía computarizada por emisión de fotones individuales (SPECT), validación

West Indian Med J 2012; 61 (9): 917

## INTRODUCTION

Single photon emission computed tomography (SPECT) is an imaging technique that refines planar imaging and permits a more precise quantization of images acquired by common tomographic techniques by removing the focus from regions not of clinical interest. Single photon emission computed tomography is well established and has found successful clinical application for the study of many organ systems, including the skeletal system (1–11).

Bone scintigraphy accurately reflects osteoblastic activity (12) and reveals morphological changes in the developing bone. Consequently, scintigraphy provides a better method than digitized radiography and computed tomography for quantification of bone changes, which fails to detect the dynamics of osteoblastic activity (13–16).

The underlying principles of SPECT are common to most tomographic imaging techniques. The intravenous injection of a radiopharmaceutical agent (such as technetium 99m) which contains a single gamma-photon-emitting radionuclide allows the capture of a 3-dimensional representation of the distribution of radioactivity within an organ or an area of interest in which the radiopharmaceutical's distribution is localized (17). The image is captured with a rotating gamma camera, and the acquired data are then processed by a computer (17). The initial cross-sectional (trans-axial) representation of the distribution of radioactivity can be used to reconstruct sagittal and coronal images. The ability for multiplane image reconstruction confers greater diagnostic accuracy for SPECT, permits accurate volumetric measurements and allows quantitation of the distribution of radioactivity in terms of microcurie per unit volume of tissue (18).

The unique ability of SPECT to quantitate physiological events, such as osteoblastic activity by using a bone-seeking radiopharmaceutical makes SPECT outstanding in comparison with other tomographic techniques which provide excellent morphological details, but not quantitative physiological information. This paper describes the application of SPECT in the evaluation of bone regeneration studies in a pig model, with a view to establishing the various possible uses of this novel technique.

## SUBJECTS AND METHODS

All the files relating to the pigs utilized for experimental SPECT at the School of Veterinary Medicine between 2005 and 2008 (*ie* a period of three years) were reviewed for the indication for the experiment conducted. The objectives of the pigs' studies were evaluated and the outcome of the result critically analysed to ascertain that (experimental) SPECT was utilized successfully to validate the objectives of the studies.

## RESULTS

A total of 16 areas of interest were analysed. Twelve of these areas were rectangular defects of 17 mm x 12 mm which were surgically created and had implantation of the Ogunsalu sandwich unit (or particulate bone (Bio-Oss®)) covered with interceed resorbable material. The remaining areas were immediate extraction sites which received endosseous implants, one of which had autogeneous bone graft in conjunction with guided tissue regeneration (GTR) done with the immediate implant placement in the right side of the mandible of a pig (this was compared with the left side which

had no bone grafting or GTR done) and in another pig, the Entegra implant system (*ie* screw implant) was compared with porous beaded implants (*ie* the Endopore implant system).

The result of the analysis of the SPECT in relation to these 16 areas of interest reveals that SPECT can be authentically utilized for the following:

- \* Validation of a new bone regeneration technique (Fig. 1).
- \* Comparison of autogenous bone graft with any other bone substitutes (Fig. 1, Table 1).

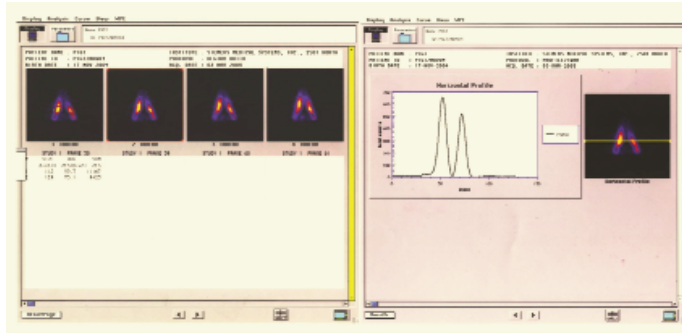


Fig. 1: Osteoblastic activity (a) and activity curve (b) at 14 weeks when the autogenous sandwich is compared with the Bio-Oss® sandwich.

Table 1: Comparison of the osteoblastic activity between the xenograft and autograft sandwich unit

Site	Component of sandwich unit	Size pixel	Avg count	Sum
1. Right mandible	a. Membrane – Bio-Gide®	112	99.7	11167
	b. Bone substitute – autograft			
2. Left mandible	a. Membrane – Bio-Gide®	129	73.1	9425
	b. Bone substitute – xenograft (Bio-Oss®)			

- \* Comparison of any of the bone substitutes (second-hand bones) with each other.
- \* Sequential evaluation of a new bone regeneration technique (Figs. 2–5, Table 2).
- \* Sequential comparative evaluation of a new bone regeneration technique with another technique (Figs. 2–6).

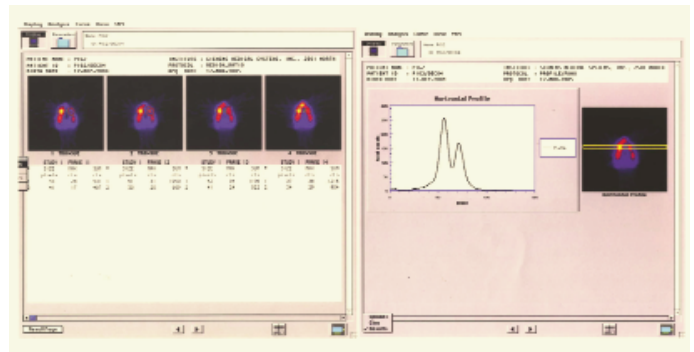


Fig. 2: Osteoblastic activity (a) and activity curve (b) at 8 weeks when the Bio-Oss® sandwich unit is compared with the conventional guided tissue regeneration (GTR) technique.

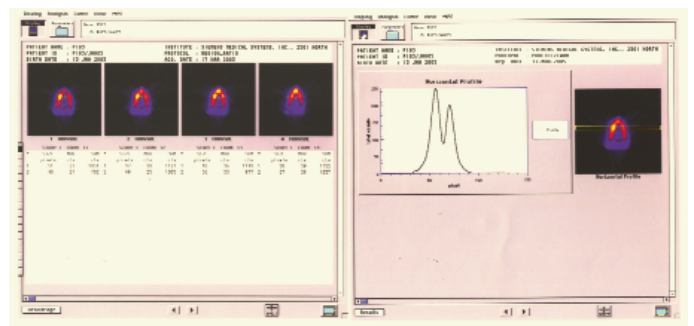
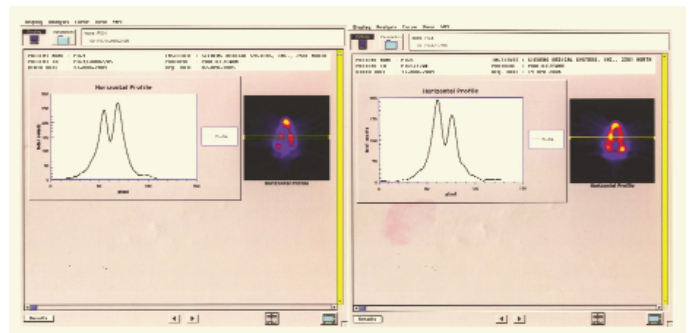


Fig. 3: Sequential osteoblastic activity (a) and activity curve (b) at 11 weeks.



Figs. 4 and 5: Sequential activity curves at 13 weeks and at 17 weeks, respectively

Table 2: Comparative average count and activity ratio

Sides	Pig No. 2		Pig No. 3		Pig No. 4		Pig No. 5		Pig No. 6	
Mandibles	L	R	L	R	L	R	L	R	L	R
Time (weeks)	8		11		13		17		24	
Component of sandwich unit	B	A	B	A	B	A	B	A	B	A
Size of pixel										
Average count	20	25		245	170	260	530	660		200
	0	0								
Activity ratio	1.25		0.89		1.53		1.18		0.77	

A: consists of Bio-Oss® sandwiched between two Bio-Gide® sheaths (the so-called classical sandwich unit); B: the same quantity of Bio-Oss® in A above covered with a sheath of interceed membrane.

- \* Validation of a new type of membrane for GTR in terms of bone formation.
- \* Comparison of the bone formed when two types of GTR membrane are used (Fig. 2).

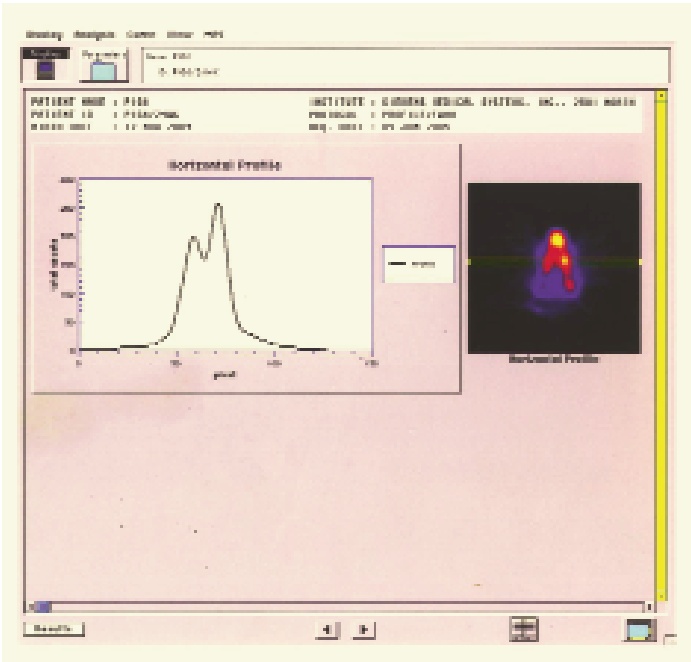


Fig. 6: Sequential activity curve at 24 weeks.

- \* Comparison of the osteoblastic activity and osseointegration between two implant systems (Fig. 7).

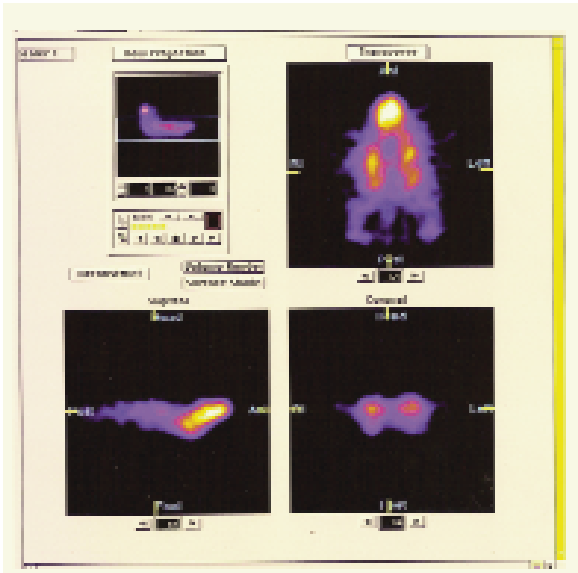


Fig. 7: Dynamic osteoblastic activity (a) and activity curve (b) when Endopore implant is utilized *versus* when Entegra implant is utilized for guided tissue regeneration.

- \* Comparison of the osteoblastic activity and osseointegration of immediate implant when autogenous bone

graft with GTR is utilized *versus* when no GTR is done (Fig. 8).

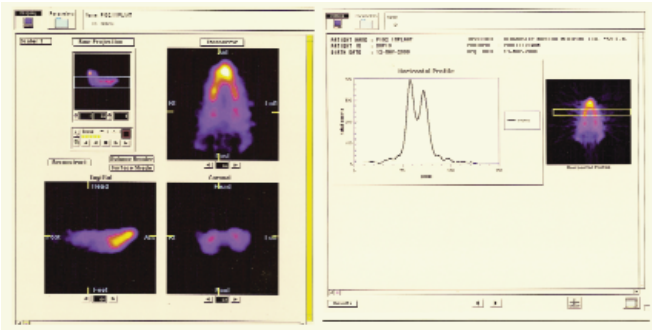


Fig. 8: Osteoblastic activity (a) and activity curve (b) when immediate implant is done with bone grafting and guided tissue regeneration *versus* when no bone grafting is done.

DISCUSSION

The technique of SPECT which has found successful clinical application for the study of many organ systems including the skeletal system (19, 20) recently gained attention in the field of dental implantology when Khan *et al* (17) demonstrated its role in the osseous integration process of dental implant. They utilized SPECT as a simple, reproducible, objective and physiologic approach to study the osseous integration process that occurs after endosseous dental implants are placed. They concluded that this method of SPECT also has the capability of quantitating bone activity in absolute terms of uCi/gram (microcurie per gram) and can be useful when bone grafting and other surgical procedures are involved and investigated.

It is for this reason that further applications for this novel technique were investigated by Ogunsalu and co-workers (21). The result of our analysis showed that by using SPECT in a single experiment we can validate a new bone regeneration technique and compare autogenous bone graft with any other bone substitute in terms of osteoblastic activity (Fig. 1). Because of the above-mentioned validation utilizing SPECT, one can deduce that it can also be utilized to compare any of the bone substitutes (second-hand bones) in the market with each other.

Also, sequential evaluation of activities that occur over a period of up to 24 weeks or more when a new bone regeneration technique is utilized can be a new or additional application for SPECT (Figs. 2–5, Table 2). As such, SPECT can also be used for the validation and comparison of any two-bone regeneration technique.

In our review, SPECT has also been found useful in the comparative evaluation of GTR when two different resorbable membranes are utilized and as such can be used similarly to compare GTR when resorbable *versus* non-resorbable membrane is used (Figs. 2–5, Table 2).

Finally, the technique of SPECT has found application in the comparison of the osteoblastic activity and osseo-



integration between two implant systems and between a clinical situation in which immediate implant was done in conjunction with bone grafting and GTR *versus* without bone grafting and GTR.

## CONCLUSION

Single photon emission computed tomography is a unique imaging modality for assessment of osteoblastic activity and osseointegration in any experimental or clinical situation; as such, various applications for SPECT have been introduced recently and it would seem that more applications would still emerge in the near future.

## REFERENCES

1. Santos MM, Pantoja Mda R, Cwajg E. Prognostic value of Tc-99m tetrofosmin myocardial perfusion gated SPECT in patients with diabetes mellitus and suspected coronary artery disease. *Arq Bras Cardiol* 2008; **90**: 2–10.
2. Van der Wall H, Fogelman I. Scintigraphy of benign bone disease. *Semin Musculoskelet Radiol* 2007; **11**: 231–300.
3. Horger M, Bares R. The role of single-photon emission computed tomography/computed tomography in benign and malignant bone disease. *Semin Nucl Med* 2006; **36**: 286–94.
4. Schafers KP, Stegger L. Combined imaging of molecular function and morphology with PET/CT and SPECT/CT: image fusion and motion correction. *Basic Res Cardiol* 2008; **103**: 191–9.
5. Dasgeb B, Mulligan MH, Kim CK. The current status of bone scintigraphy in malignant diseases. *Semin Musculoskelet Radiol* 2007; **11**: 301–11.
6. Sarikaya I, Sarikaya A, Holder LE. The role of single photon emission computed tomography in bone imaging. *Semin Nucl Med* 2001; **31**: 3–16.
7. Ozyurt G, Kaya FN, Kahveci F, Alper E. Comparison of SPECT findings and neuropsychological sequelae in carbon monoxide and organophosphate poisoning. *Clin Toxicol (Phila)* 2008; **46**: 218–21.
8. Kalita J, Misra UK, Ranjan P, Pradhan PK. Pattern of cerebellar perfusion on single photon emission computed tomography in subcortical hematoma: a clinical and computed tomography correlation. *Neurol India* 2008; **56**: 17–21.
9. Crespo C, Gallego J, Cot A, Falcon C, Bullich S, Pareto D et al. Quantification of dopaminergic neurotransmission SPECT studies with 123I-labelled radioligands. A comparison between different imaging systems and data acquisition protocols using Monte Carlo simulation. *Eur J Nucl Med Mol Imaging* 2008; **35**: 1334–42.
10. Massardo T, Lavados H, Jaimovich R, Herrera E, Quevedo L, Alfaro L et al. Interobserver correlation in the interpretation of 99mTc-sestamibi SPECT in reperfused acute myocardial infarction. *Rev Esp Med Nucl* 2008; **27**: 83–9.
11. Ellis RJ, Zhou EH, Fu P, Kaminsky DA, Sodee DB, Faulhaber PF et al. Single photon emission computerized tomography with capromab pentetide plus computerized tomography image set co-registration independently predicts biochemical failure. *J Urol* 2008; **179**: 1768–73; discussion 1773–4.
12. Galasko CS. Proceedings: The pathological basis for skeletal scintigraphy. *Br J Radiology* 1975; **48**: 72–3.
13. Mayfield L, Skoglund A, Nobreus N, Attstrom R. Clinical and radiographic evaluation, following delivery of fixed reconstructions, at GBR treated titanium fixtures. *Clin Oral Implants Res* 1998; **9**: 292–302.
14. Van der Stelt PF. Computed-assisted interpretation in radiographic diagnosis. *Dent Clin North Am* 1993; **37**: 683–96.
15. Bragger U, Burgin W, Lang NP, Buser D. Digital subtraction radiography for the assessment of changes in peri-implant bone density. *Int J Oral Maxillofac Implants* 1991; **6**: 160–6.
16. Alberto PL. Implant reconstruction of the jaws and craniofacial skeleton. *Mt Sinai J Med* 1998; **65**: 316–21.
17. Khan O, Archibald A, Thomson E, Maharaj P. The role of quantitative single photon emission computerized tomography (SPECT) in the osseous integration process of dental implants. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000; **90**: 228–32.
18. Ell PJ, Khan O, Jarritt PH, Callum ID. Radionuclide section scanning: an atlas of clinical cases. London: Chapman and Hall; 1982: 46–60.
19. Khan O, Ell PJ, Jarritt PJ, Callum ID. Emission and transmission computed tomography in the detection of space occupying diseases of the liver. *Br Med J* 1981; **283**: 1212–4.
20. Ell PJ, Khan O. Radioisotope section scanning. *Cancer Res* 1980; **40**: 3059–64.
21. Ogunsalu CO, Rohrer M, Prasad H, Archibald A, Watkins J, Daisley H et al. Single photon emission computerized tomography and histological evaluation in the validation of a new technique for closure of oro-antral communication: an experimental study in pigs. *West Indian Med J* 2008; **57**: 166–72.