Hand-held gamma probe or hand-held miniature gamma camera for minimally invasive parathyroidectomy: competition, evolution or synergy?

Domenico Rubello[1], Giuliano Mariani[2]

[1] Nuclear Medicine Service and PET Unit, "S. Maria della Misericordia" Hospital, Istituto Oncologico Veneto (IOV), Viale Tre Martiri, 140, 45100 Rovigo, Italy
[2] Regional Center of Nuclear Medicine, University of Pisa Medical School Pisa, Italy

Published online: 11 October 2006

Eur J Nucl Med Mol Imaging (2007) 34:162–164
DOI 10.1007/s00259-006-0250-z

In this issue of the *European Journal of Nuclear Medicine and Molecular Imaging*, Joaquin Ortega and co-workers report their pilot experience with a hand-held miniature gamma camera for performing minimally invasive parathyroidectomy (MIP) in five patients with primary hyperparathyroidism (PHPT) most likely caused by a solitary adenoma [1]. Pre-operative identification of a solitary parathyroid adenoma characterised scintigraphically by clear ^{99m}Tc-sestamibi uptake is widely recognised as the main inclusion criterion for radioguided MIP utilising the "conventional" hand-held intraoperative gamma probe in PHPT patients, based on counting rates (and the corresponding acoustic signal) as the sole guide [2–5]. Despite the small number of patients included in their feasibility study, the data reported by Ortega and colleagues [1] raise several questions that are presently difficult to answer unequivocally, but will presumably be the object of debate in the near future. It should be emphasised that Ortega et al. adopted a high-standard, strict protocol for preoperative scintigraphic localisation of the parathyroid adenoma [1]. In fact, they systematically performed single-photon emission computed tomography (SPECT) to integrate with tomographic information the localisation features of planar ^{99m}Tc-sestamibi dual-phase scintigraphy. Then, intraoperatively they compared the usefulness of a conventional hand-held gamma probe with a new-generation hand-held miniature gamma camera. The authors also performed intraoperative quick assay of parathyroid hormone levels (QPTH) to confirm successful removal of any hyperfunctioning parathyroid tissue.

SPECT can be considered as an essential component of the two scintigraphic procedures that today represent the gold standard for pre-operative imaging of PHPT patients, that is, single-tracer, dual-phase parathyroid scintigraphy with ^{99m}Tc-sestamibi and dual-tracer parathyroid scintigraphy with ^{99m}Tc-sestamibi combined with a thyroid-imaging agent (either ^{123}I-iodide or $^{99m}TcO_4^-$) [2–7]. It should also be emphasised that combining parathyroid scintigraphy with high-resolution ultrasonography of the neck increases the accuracy of the pre-operative imaging work-up, especially in disclosing possible multigland parathyroid disease and in identifying concomitant thyroid nodules. Moreover, ultrasonography provides precise anatomical information about the thyroid/parathyroid regions, such as a possible deep position of the parathyroid adenoma(s), a possible location near to or beyond the jugular vein or carotid artery, and so forth [2–5]. Further improvement of pre-operative imaging can be achieved by using a pinhole collimator during the SPECT acquisition [8] or by employing SPECT/CT and SPECT/MRI image fusion analysis [9].

After imaging of the parathyroid adenoma employing a full diagnostic dose of ^{99m}Tc-sestamibi, Ortega et al. injected 111–185 MBq (3–5 mCi) ^{99m}Tc-sestamibi in the operating suite 10 min before commencing MIP, on a day different from the day on which they performed imaging [1]. Such a "low-dose" protocol for radioguided parathyroid surgery [10–12] represents a relevant modification of the technique originally described by Norman et al. (adopted mainly in the USA), which entails injection of a full ^{99m}Tc-sestamibi imaging dose (740–925 MBq, or 20–25 mCi) 2–3 h before commencing MIP [13, 14]. A first

This editorial commentary refers to the article http://dx.doi.org/10.1007/s00259-006-0239-7.

Domenico Rubello (✉)
Nuclear Medicine Service and PET Unit,
"S. Maria della Misericordia" Hospital,
Istituto Oncologico Veneto (IOV),
Viale Tre Martiri, 140,
45100 Rovigo, Italy
e-mail: domenico.rubello@libero.it
Tel.: +39-425-394427-31, Fax: +39-425-394434

important consequence of the low-dose protocol is that radiation exposure to surgical staff in the operating suite is minimised (it is approximately 10- to 15-fold lower than in Norman's protocol). Furthermore, injection of ^{99m}Tc-sestamibi just a few minutes before commencing surgery allows intraoperative detection also of parathyroid adenomas characterised by fast washout of the radiopharmaceutical, which account for approximately 20–30% of PHPT patients [15].

One of the most intriguing issues raised by Ortega's article [1] is whether the use of the conventional counting and acoustic hand-held gamma probe for parathyroid MIP could be substituted by a hand-held miniature gamma camera. In this regard, the first hand-held miniature gamma camera was patented by Soluri et al. in 1997 [16] and subsequently validated by Scopinaro et al. for sentinel lymph node biopsy in patients with breast cancer [17]. This device was based on a CsI(Tl) crystal coupled with a position-sensitive photomultiplier tube (PSPMT). Other subsequent miniature gamma cameras utilised either scintillation crystals or semiconductor materials such as CdTe and CdZnTe [18, 19]. In the clinical setting, use of these cameras was explored mostly for sentinel lymph node biopsy or radioguided occult lesion localisation (ROLL) in breast cancer patients [17, 19], radioguided biopsy of equivocal breast lesions trapping ^{99m}Tc-sestamibi or ^{99m}Tc-bombesin [19], and radioguided identification for excision/biopsy of bone lesions such as osteoid osteoma (with ^{99m}Tc-diphosphonates) or in the diabetic foot (with ^{99m}Tc-HMPAO-labelled autologous leucocytes) [19]. Independent preliminary experiences also concerned the detection by external imaging of small thyroid nodules not visualised by a conventional Anger gamma camera [20] and radioguided parathyroid surgery [21].

One of the major problems encountered with the use of those first-generation miniature gamma cameras, such as that described by Kitagawa et al. [21], was that they were quite bulky and cumbersome to handle, thus requiring systematic support with a mechanical arm. This reduced the surgeon's ability to handle the miniature gamma camera properly in the operating suite, and therefore increased the overall operating time. In contrast, the more recent hand-held miniature gamma cameras, such as the one employed by Ortega et al. [1], weigh only 1 kg or less, and are significantly easier to handle and suitable for use in the operating suite. Furthermore, they are characterised by high sensitivity and a high spatial resolution, with values approaching that of the conventional counting and acoustic gamma probes. Moreover, it is possible to perform dynamic real-time imaging (e.g. of the thyroid and parathyroid glands) in the operating suite, including lateral views of the neck and exploration of the mediastinal space. This combination provides the surgeon with important information on the operating basin, and can further help to localise the parathyroid adenoma(s).

Although the conventional gamma probe has proven to be of high value for the intra-operative detection of parathyroid adenomas, especially when they are located ectopically or deeply [2–5], it can now be speculated that the gamma probe and the hand-held miniature gamma camera could perform synergistically when operating on some parathyroid adenomas that are difficult to localise intra-operatively. On the other hand, the advantage of the miniature gamma cameras in providing imaging information in addition to the counting rates and acoustic signal is somewhat counterbalanced by their cost, which is at present approximately 10–15 times that of a conventional gamma probe [19, 22]. Therefore, the purchase of a miniature gamma camera seems to be justified only in specialised medical centres where radioguided surgery is routinely performed for a wide range of applications (sentinel lymph node biopsy, ROLL etc.) [23].

Two additional issues raised by the report of Ortega et al. [1] concern the possibility of substituting pre-operative scintigraphic localisation of parathyroid adenoma(s) with intra-operative real-time dynamic acquisition with the hand-held miniature gamma camera, and avoidance of the intra-operative QPTH assay by using the hand-held miniature gamma camera.

Concerning the first issue, it actually appears hard today to think of parathyroid surgery, especially MIP, without accurate planning based on pre-operative localisation imaging. This enables the surgeon to expect certain anatomical conditions at operation and therefore to plan the most feasible surgical approach: (i) MIP via a middle neck access; (ii) MIP via a lateral neck access; (iii) unilateral neck exploration (skin incision greater than MIP) to treat a concomitant uninodular goitre associated with an ipsilateral parathyroid adenoma; or (iv) bilateral neck exploration in the case of multigland parathyroid disease or concomitant multinodular goitre. In this regard, accurate pre-operative localisation imaging (especially when SPECT is performed) most likely represents a more objective examination than intra-operative real-time dynamic acquisition with a hand-held miniature gamma camera, which is expected to be more operator dependent. Furthermore, pre-operative SPECT examination with semi-quantitative assessment of ^{99m}Tc-sestamibi uptake by the parathyroid adenoma is useful for better selection of PHPT patients for MIP [24].

Concerning, finally, the issue of whether or not to systematically employ QPTH measurements intra-operatively, it is worth noting that in the experience of Murphy and Norman (who adopted a high-dose ^{99m}Tc-sestamibi protocol, commencing surgery 2–3 h post injection), the so-called 20% rule enables avoidance of the QPTH procedure without increasing the failure rate of radioguided parathyroid surgery [25]. Unfortunately, the 20% rule does not perform as well with the low-dose protocol (^{99m}Tc-sestamibi injected a few minutes before commencing surgery) [10, 26]. This difference is probably due to different kinetics of ^{99m}Tc-sestamibi washout from parathyroid adenomas in the early phase and in the later phase post injection [10, 26].

In conclusion, it is reasonable to speculate that hand-held miniature gamma cameras will play a relevant role for MIP in PHPT patients affected by a solitary parathyroid adenoma. Availability of low-weight gamma cameras will certainly favour the diffusion of this approach. Nevertheless, very close cooperation in the operating suite between the surgeon and the nuclear medicine physician will be crucial for the development of the intra-operative hand-held miniature gamma camera.

References

1. Ortega J, Ferrer-Rebolleda J, Cassinello N, Lledo S. Potential role of a new hand-held miniature gamma camera in performing minimally invasive parathyroidectomy. Eur J Nucl Med Mol Imaging 2006 (in press). DOI 10.1007/s00259-006-0239-7.
2. Casara D, Rubello D, Pelizzo MR, Shapiro B. Clinical role of $^{99m}TcO_4^-$/MIBI scan, ultrasound and intra-operative gamma probe in the performance of unilateral and minimally invasive surgery in primary hyperparathyroidism. Eur J Nucl Med 2001;28:1351–9.
3. Rubello D, Pelizzo MR, Casara D. Nuclear medicine and minimally invasive surgery of parathyroid adenomas: a fair marriage [editorial]. Eur J Nucl Med Mol Imaging 2002;29:189–92.
4. Rubello D, Casara D, Pelizzo MR. Symposium on parathyroid localising imaging. Optimization of preoperative procedures. Nucl Med Commun 2003;24:133–40.
5. Mariani G, Gulec SA, Rubello D, Boni G, Puccini M, Pelizzo MR, et al. Preoperative localization and radioguided parathyroid surgery. J Nucl Med 2003;44:1443–58.
6. Moka D, Voth E, Dietlein M, Larena-Avellaneda A, Schica H. Technetium 99m-MIBI-SPECT: a highly sensitive diagnostic tool for localization of parathyroid adenomas. Surgery 2000;128:29–35.
7. Giordano A, Rubello D, Casara D. New trends in parathyroid scintigraphy. Eur J Nucl Med 2001;28:1409–20.
8. Spanu A, Falchi A, Manca A, Marongiu M, Cossu A, Pisu N, et al. The usefulness of neck pinhole SPECT as a complementary tool to planar scintigraphy in primary and secondary hyperparathyroidism. J Nucl Med 2004;45:40–8.
9. Gayed IW, Kim EE, Broussard WF, Evans D, Lee J, Broemeling LD, et al. The value of ^{99m}Tc-sestamibi SPECT/CT over conventional SPECT in the evaluation of parathyroid adenomas or hyperplasia. J Nucl Med 2005;46:248–52.
10. Rubello D, Piotto A, Medi F, Gross MD, Shapiro B, Erba P, et al. "Low dose" ^{99m}Tc-sestamibi for radioguided surgery of primary hyperparathyroidism. Eur J Surg Oncol 2005;31:191–6.
11. Rubello D, Fig LM, Casara D, Piotto A, Boni G, Pelizzo MR, et al. Radioguided surgery of parathyroid adenomas and recurrent thyroid cancer using the "low sestamibi dose" protocol. Cancer Biother Radiopharmacol 2006;3:194–205.
12. Rubello D, Pelizzo MR, Boni G, Schiavo R, Vaggelli L, Villa G, et al. Radioguided surgery of primary hyperparathyroidism using the low-dose ^{99m}Tc-sestamibi protocol: multiinstitutional experience from the Italian Study Group on Radioguided Surgery and Immunoscintigraphy (GISCRIS). J Nucl Med 2005;46:220–6.
13. Norman J, Chheda H. Minimally invasive parathyroidectomy facilitated by intraoperative nuclear mapping. Surgery 1997;122:998–1004.
14. Norman J, Rubello D, Giuliano AE, Mariani G. Minimally invasive radioguided parathyroidectomy in parimary hyperparathyroidism. In: Mariani G, Giuliano AE, Strauss HW (eds) Radioguided surgery—a comprehensive team approach. Berlin Heidelberg New York: Springer; 2006; p. 239–58.
15. Rubello D, Piotto A, Casara D, Muzzio PC, Shapiro B, Pelizzo MR. Role of gamma probes in performing minimally invasive parathyroidectomy in patients with primary hyperparathyroidism: optimization of preoperative and intraoperative procedures. Eur J Endocrinol 2003;149:7–15.
16. Soluri A et al, inventors. Miniaturized gamma camera with very high spatial resolution. Italian patent RM97A000233, April 23, 1997; US patent 6 242 744 B1, June 5, 2001.
17. Scopinaro F, Di Luzio E, Pani R. Sentinel lymph node biopsy in breast cancer: use of an imaging probe. In: Limouris GS, Shukla SK, Biersack HJ, eds. Radionuclides for lymph nodes. Athens: Mediterranea Publishers; 1999; p. 60–5.
18. Mori I, Takayama T, Motomura N. The CdTe detector and its imaging performing. Ann Nucl Med 2001;15:487–94.
19. Scopinaro F, Soluri A. Gamma ray imaging probes for radioguided surgery and site-direct biopsy. In: Mariani G, Giuliano AE, Strauss HW (eds) Radioguided surgery—a comprehensive team approach. Berlin Heidelberg New York: Springer; 2006; p. 29–36.
20. Spanu A, Soluri A, Scopinaro F, Falchi A, Mangano M, Marongiu P, et al. A new radioisotopic procedure in small-size thyroid nodule detection: a preliminary study [abstract]. Eur J Nucl Med Mol Imaging 2003;30:S358.
21. Kitagawa W, Shimizu K, Kumita S. Radioguided parathyroidectomy for primary hyperparathyroidism combined with video-assisted surgery using the solid state multicrystal gamma camera. J Surg Oncol 2002;80:173–5.
22. Goldstein RE, Blevins L, Delbeke D, Martin WH. Effect of minimally invasive radioguided parathyroidectomy on efficacy, length of stay, and costs in the management of primary hyperparathyroidism. Ann Surg 2000;231:732–42.
23. Mariani G, Giuliano AE, Strauss HW (eds) Radioguided surgery—a comprehensive team approach. Berlin Heidelberg New York: Springer; 2006.
24. Rubello D, Massaro A, Cittadin S, Rampin L, Al-Nahhas A, Boni G, et al. Role of ^{99m}Tc-sestamibi SPECT in accurate selection of primary hyperparathyroid patients for minimally invasive radio-guided surgery. Eur J Nucl Med Mol Imaging 2006;33:1091–4.
25. Murphy C, Norman J. The 20% rule: a simple, instantaneous radioactivity measurement defines cure and allows elimination of frozen sections and hormone assays during parathyroidectomy. Surgery 1999;126:1023–8 [discussion 1028–9].
26. Rubello D, Casara D, Giannini S, Piotto A, De Carlo E, Muzzio PC, et al. Importance of radio-guided minimally invasive parathyroidectomy using hand-held gamma probe and low ^{99m}Tc-MIBI dose: technical considerations and long-term clinical results. Q J Nucl Med 2003;47:129–38.