Bratisl Lek Listy 2011; 112 (12)
695 – 700

CLINICAL STUDY

From preoperative to intraoperative detection of hyperfunctioning parathyroid glands using tetrofosmin (99mTc) in primary hyperparathyroidism

Balogova S[1], Cambal M[2], Simkova A[3], Kekenak L[3], Stecova A[4], Gregor P[5], Kinova S[3], Labas P[2]

University Hospital of Bratislava, Hospital Stare Mesto, Department of Nuclear Medicine, Bratislava, Slovakia.
sona.balogova@kapor.sk

Abstract: The impact of preoperative scintigraphy on the management of patients with primary hyperparathyroidism has been largely documented for more than two decades. More recently, preoperative scintigraphy has also been used to select patients for intraoperative detection of hyperfunctioning parathyroid glands thanks to a gamma-probe. This procedure is now widely used, with MIBI as the main radiopharmaceutical for both preoperative scintigraphy and intraoperative detection. However MIBI was not available in Slovakia until very recently and tetrofosmin (TF), the alternative 99mTc labelled radiopharmaceutical for myocardial imaging has some advantages over MIBI and a close biological behaviour. Thus we have been using TF also for parathyroid preoperative scintigraphy and for intraoperative detection, a systematic indication which has never been reported by others.
This article aims to demonstrate the feasibility and to present our protocol for TF parathyroid imaging and intraoperative detection, closely associating surgeons, nuclear medicine specialists, pathologists and also biologists as intraoperative assay of intact PTH is necessary.
The results of literature are subsequently reported and discussed *(Tab. 2, Fig. 4, Ref. 35)*. Full Text in free PDF *www.bmj.sk.*
Key words: hyperparathyroidism, adenoma, tetrofosmin, scintigraphy, intraoperative detection, minimally invasive surgery.

Parathyroidectomy is the only curative therapy for primary hyperparathyroidism (HPT) and is both safe and cost-effective. Previously the standard treatment for all patients with primary HPT was the bilateral neck exploration with the goal of identifying and evaluating four parathyroid glands. Visual inspection of the glands, sometimes used in conjunction with intraoperative pathological frozen section assessment, allowed experienced surgeons to identify the pathologic glands and remove them with a success rate of over 90 %. Parathyroid scintigraphy is not meant to diagnose HPT, the diagnosis of which must be assessed on biological criteria, mainly calcium and PTH plasma levels. Parathyroid scintigraphy is useful for the non-invasive localisation of the over-functioning parathyroid glands, with an important impact on patient management.

The major impact of parathyroid scintigraphy with technetium-labelled radiopharmaceuticals has been to modify this scheduled surgical management. In primary HPT, preoperative scintigraphy, in combination with improved ultrasound imaging and intraoperative PTH assay, enables to perform minimally invasive surgery in about 70 % of patients referred for preoperative imaging. This procedure results in a significant reduction in the extent of surgery, the duration of the operation and hospital stay (1).

Radionuclide imaging has been performed in HPT for a very long time, at the beginning with selenomethionine, which had unfavourable physical properties. Its success story started with thallium-201 and the thallium-201 technetium-99m subtraction method. It was originally described in Italy by Ferlin (1983) (2) and its accuracy was rapidly confirmed by various teams in EU e.g. in UK (Young, 1983) (3), Fogelman 1984 (4)) or in the Netherlands (Bolk, 1985) (5). Since thallium-201 is also taken-up by the thyroid gland, the purpose of technetium-99m associated imaging was to obtain a specific image of the thyroid gland and subtract it from the thallium-201 image, to pinpoint the suspicious parathyroid foci and avoid misinterpretation due to thyroid anomalies.

At the same time, thallium-201 was challenged by sestaMIBI (99mTc) or MIBI and by tetrofosmin (99mTc) or TF, for performing myocardium tomoscintigraphy (SPECT). MIBI imaging to localise over-functioning parathyroid glands was proposed in 1989 by Coakley (6), in series of 5 patients. In 1992, the same British team (O'Doherty) (7) published the first comparative

[1]University Hospital of Bratislava, Hospital Stare Mesto, Department of Nuclear Medicine, [2]Comenius University of Bratislava, Faculty of Medicine, Ist Department of Surgery, [3]Comenius University of Bratislava, Faculty of Medicine, Ist Department of Surgery, Faculty of Medicine, Ist Department of Internal Medicine, University Hospital, Bratislava, [4]Medirex laboratory, a.s., and [5]Comenius University of Bratislava, Faculty of Medicine, Institute of Pathological Anatomy, Bratislava, Slovakia

Address for correspondence: S. Balogova, MD, PhD, UNB, Nemocnica Stare mesto, SK-813 69 Bratislava, Slovakia.

study with thallium-201 on 57 patients. This same year, in Canada, Taillefer (1992) (8) described, in series of 23 patients, a "dual phase" MIBI scintigraphy that does not require thyroid uptake subtraction, based on the differential wash out of MIBI from the thyroid gland and the abnormal parathyroid glands: 2 sets of MIBI images were obtained, the initial set at 10–15 min and the second set at 2–3 h after the injection. A positive MIBI study for the presence of a hyperfonctioning parathyroid gland was defined as a focal area of increased uptake of the radiotracer in projection of the thyroid bed and surrounding areas or mediastinum which showed either a relative progressive increase over time or a fixed uptake which persisted on delayed imaging, contrary to the uptake in the surrounding normal thyroid tissue which progressively decreases over time.

Since 1995, the uptake of TF by hyperfunctioning parathyroid glands has also been described (9, 10), opening the way to an alternative technetium-labelled radiopharmaceutical in this indication (11). TF has advantages over MIBI: its labelling with 99mTc is far easier since it does not request heating, and its irradiation of the patient is somewhat lower (effective dose = 7.2 μSv/MBq for TF vs 8.5 μSv/MBq for MIBI).

The intraoperative use of a gamma-probe during parathyroid surgery has been proposed more than a decade ago (12, 13). Radio-guided minimally invasive parathyroidectomy is gaining momentum. It is currently recommended in patients in whom MIBI or TF scintigraphy suggests a high probability of a solitary parathyroid adenoma with a significant tracer uptake, no concomitant thyroid nodules showing MIBI or TF uptake, no history of familial HPT or multiple endocrine neoplasia (MEN) and no history of previous neck irradiation (14). Radio-guided parathyroidectomy is also indicated in case of re-operation for persistent or recurrent HPT and ectopic adenomas. As the gamma probe is much more sensitive than a gamma camera, gamma probe-guided surgery may also be used in patients undergoing bilateral neck exploration with a negative pre-operative scintigraphy because it decreases operation time and gives more guarantee about the pathological parathyroid tissue removal (15).

However no series specifically using TF for this intraoperative detection of hyperfunctioning parathyroid glands have been reported so far. Actually, the only mention in the literature of this possible use of TF appeared in the initial article of Gallowitsch et al published in 1997 (13). This series included 12 patients imaged with either MIBI or TF, but no separate analysis of the two radiopharmaceuticals has been reported.

Our team of nuclear medicine has been using TF and pertechnetate (99mTc) scintigraphy for imaging in HPT; our surgical team has gained experience in the intraoperative use of a gamma probe in this setting. Our aim is thus to report on this first experience of preoperative imaging and intraoperative detection of abnormal parathyroid glands with TF only.

Methods

Patients with HPT and scintigraphic finding in favour of solitary orthotopic parathyroid adenoma were selected for minimally invasive parathyroidectomy. Whole procedure was explained to the patient who gave written informed consent.

Parathyroid scintigraphy-acquisition

Scintigraphic acquisition and processing were performed with a dual-head gamma camera system (MultiSPECT ICON, Siemens) using an all-purpose parallel-hole collimator, with an appropriate electronic zooming. Parathyroid scintigraphy was performed using dual tracer/dual phase technique, thyroid scintigraphy being performed first with 40MBq of 99mTc-pertechnetate, unless a low uptake of pertechnetate could have been suspected from the patient's history (iodine overload in particular due to some therapeutic agents, radiologic contrast media, treatment by thyroid hormones or by lithium...). Six hundred MBq of tetrofosmin-(99mTc) (Myoview; GE Healthcare, United Kingdom) was administered immediately after the completion of pertechnetate-(99mTc) acquisition. A dynamic series of images (one frame per minute) were acquired for the next 30 minutes and a view of the mediastinum was subsequently obtained. One delayed image 150 minutes post injection, was also acquired. Radioactive external markers were used to aid correct repositioning of the patient at the different phases of the study.

Parathyroid scintigraphy-processing

The manufacturer's computer software was used for tetrofosmin-pertechnetate subtraction. A cumulative image of TF generated from the summation of the 11th to the 30th frames of the dynamic series was selected for the subtraction procedure. Manual region of interest (ROI) were drawn over the area of thyroid tissue and of the suspected sites of parathyroid lesions, and subtraction tetrofosmin-technetium image was automatically performed.

Cervical background activity, obtained by means of a rectangular ROI lateral to the thyroid, was previously subtracted.

Parathyroid scintigraphy interpretation

A distinct focus of activity TF, not attributable to functional thyroid tissue in projection of thyroid bed and surrounding areas or in the mediastinum was the criterion for a positive finding of the subtraction study.

Surgery

Minimally invasive surgery was performed on a separate day from TF scintigraphy, which permited to select patients with primary HPT showing a solitary focus with a high TF uptake and a normal thyroid gland: in this case, a lower activity of TF between 30 and 40 MBq administered 15–20 minutes prior surgery was sufficient to perform the intraoperative procedure (16, 17).

To confirm the cutaneous projection of parathyroid adenoma already known from scintigraphy and ultrasonography, the radioactivity of the surface over supposed parathyroid adenoma was measured by gamma probe and a locus with highest radioactivity was identified. At this locus, a small skin incision, revision and carefull resection of parathyroid adenoma were performed using the system Ligasure. After resection of parathy-

roid adenoma, the comparison of ex vivo activity of parathyroid adenoma and in vivo activity over the parathyroid bed was performed, to confirm that no residual adenomatous parathyroid tissue was remaining. As soon as the parathyroid adenoma was removed, the frozen sections of the gland were analysed by pathologist and later a definitive histology was established. Efficiency of surgery was assessed by a decrease of intact PTH plasma levels greater than 50% of its initial value, five minutes after resection of pathologic parathyroid tissue.

Results

Preoperative scintigraphy

As MIBI was not available and registered in Slovakia, we have performed parathyroid scintigraphies with tetrofosmin-(99mTc) and pertechnetate-(99mTc), since 1999. The example of a typical scintigraphic finding in a patient with parathyroid adenoma is illustrated in Figure 1.

Surgery with intraoperative detection

Since 2004, patients with parathyroid adenomas identified on the preoperative scintigraphy, such as illustrated in Figure 1 have been operated using the minimally invasive radioguided approach.

Minimally invasive surgery was performed on a separate day from TF scintigraphy. Activity between 30 and 40 MBq of TF was administered 15–20 minutes prior to surgery (16, 17) to the patient in general anesthesia.

Gamma probe guidance enables the surgeon to perform a rather small skin incision with improved cosmetics effect and also reducing the operating time.

Fifteen to twenty minutes after administration of TF, the patient's neck was scanned with the gamma probe (Fig. 2), to confirm the cutaneous projection of the hyperfunctioning parathyroid gland(s) which was or were already known from preoperative scintigraphy and US results.

After preliminary detection, a revision from a small skin incision was performed (Fig. 3a, b) with careful resection of parathyroid adenoma.

Subsequently the comparison of ex vivo activity of parathyroid adenoma (Fig. 3c) and in vivo activity of parathyroid bed

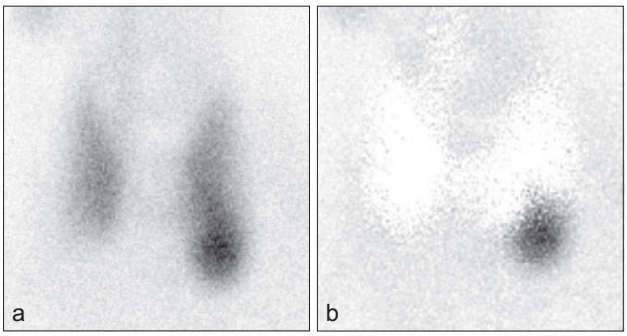

Fig. 1 a, b. Scintigraphy: Focal uptake of TF in favour of left inferior parathyroid adenoma: 99mTc-tetrofosmin scintigraphy (a) and thyroid subtraction image (b).

Fig. 2. The gamma probe.

was performed to make sure that no residual pathologic parathyroid tissue was remaining.

In the same time, the frozen sections of the gland were analysed by pathologist and later a definitive histology was performed (Fig. 4).

All parathyroid adenomas detected and resected according to this procedure were histologically confirmed. When those criteria have been fulfilled, a blood sample was sent to the laboratory for a rapid assay of serum intact PTH levels. A decrease of intact PTH serum levels greather than 50 % was the final criterion for a successful resection of all hyperfunctionning parathyroid tissue, and the minimally invasive cervical operation was completed. If this objective would not have been achieved, the

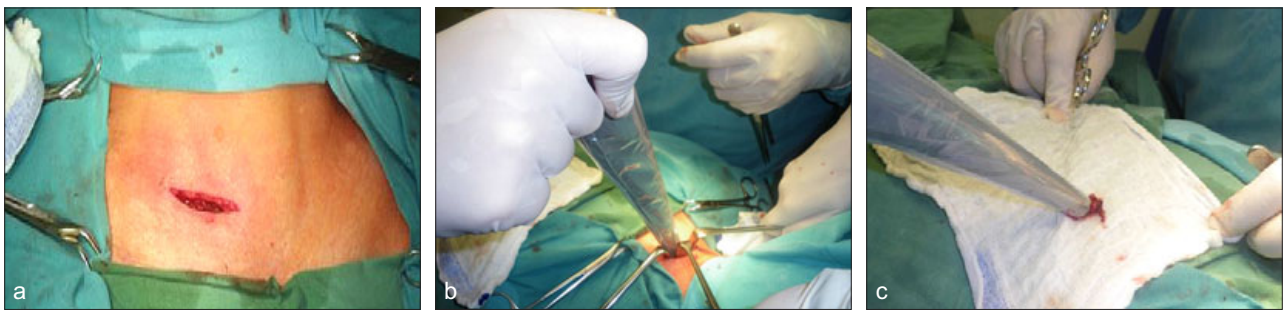

Fig. 3 a, b, c. Surgery: preliminary detection and revision from a small skin incision (a, b) with careful resection of parathyroid adenoma, measurement of ex vivo activity of parathyroid adenoma (c).

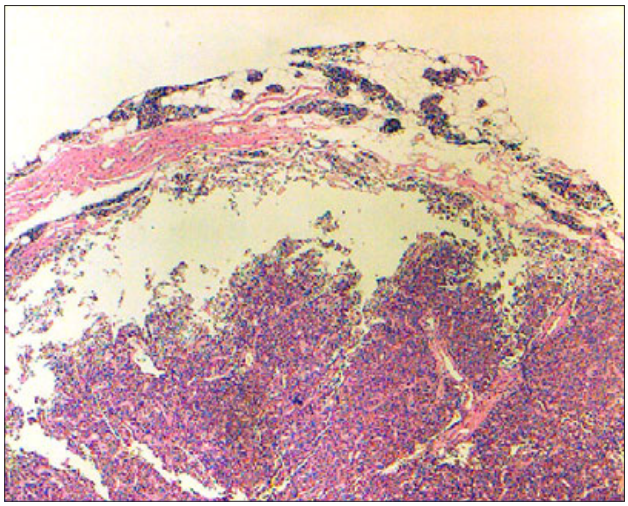

Fig. 4. Parathyroid adenoma – histology: the parathyroid adenoma is composed of hypercellular parathyroid tissue without atypical nuclear or architectural features. The adenoma is lined by a capsule and a thin rim of „normal“ parathyroid tissue is compressed along one side of the mass (upper portion of the picture).

exploration with the gamma probe would be resumed, another blood sample would be sent to laboratory and if still high PTH, exploration of the 4 glands would have been performed.

Complications

No local complications of surgery occured. Only slight hypocalcaemia was often observed early after surgery and treated by orally administered calcium. No definitive hypoparathyroidism or recurrent nerve palsy was induced thanks to the minimally invasive character of the intervention which avoids the necessity to localise and possibly damage the four parathyroid glands.

The mean time of hospitalisation was 3 days, all patients left the hospital with normal calcium blood levels.

Discussion

The use of TF instead of MIBI in the management of HPT shall be discussed according to the two different applications: preoperative imaging and intraoperative detection.

TF vs MIBI for preoperative imaging in HPT

Several studies have compared the performance of MIBI and TF in case of HPT. As soon as in the second case reported with both radiopharmaceuticals (10), it has been noticed that “thyroid wash-out was observed with MIBI but not with TF”. This fact has been confirmed in further studies (18, 19). TF is thus less suited than MIBI for the “dual phase” technique (20, 21). But in fact, a large fraction of the parathyroid adenomas does not present with this uptake pattern, showing a significant wash out of MIBI from the over-functioning parathyroid tissue, without significant activity on the late images which leads to false negative results. This rapid wash out can occur as frequently as in 16/41 = 39% of cases (22). Furthermore, some thyroid nodules can concentrate MIBI intensely and persistently on the late images, leading to false positive results, since it is difficult to identify their origin without a scintigraphic image of the thyroid.

Thus most teams perform a “dual tracer” MIBI scintigraphy, similarly to parathyroid scintigraphy with thallium-201 and pertechnetate (99mTc), as it was proposed originally by Coakley in 1989 (6). This is actually the method that we used.

With TF as well as with MIBI, the “dual tracer” subtraction technique can be coupled with the “dual phase” technique (23). The early images subtraction is used to detect parathyroid adenomas with potentially rapid wash out of TF and improves sensitivity; the late images bring further evidence in case of persistent uptake and help to recognise TF uptake by thyroid nodules, increasing specificity.

By using the “dual tracer” technique as we did similar diagnostic performances for TF and MIBI have been reported by several teams (Tabs1, 2).

TF vs MIBI for intraoperative detection

According to the very recent guidelines of the European Association of Nuclear Medicine (EANM) (29), advantages of the gamma probe-guided surgery of HPT are:

Tab. 1. Non-comparative studies: sensitivity of tetrofosmin-(99mTc) scintigraphy to detect hyperfunctioning parathyroid glands.

Authors	No of patients	TF detection rate
Gallowitsch et al. 2000 (24)	33	Planar 87% SPECT 96%
Dugonjic 2009 (23)	46	93%

Tab. 2. Comparative studies: sensitivity of tetrofosmin-(99mTc) scintigraphy and of comparator to detect parathyroid adenoma.

Authors	No of patients	TF Se, Sp	Comparator	Comparator Se, Sp
Apostolopoulos (25) 1998	27	Se=76% Sp=92%	201Tl/99mTc	Se=52% Sp=85%
Hiromatsu 2000 (26):	20	Se=95% Sp=95%	US	Se=85% Sp=94%
Wakamatsu 2001 (27)	25	Se=63%(single-gland disease) Se=42% (multi-gland disease)	MIBI	Se=68%%(single gland disease) Se=42% (multi-gland disease)
Alexandrides 2006 (28)	59	Se=100%	MIBITl	Se=96%Se=78%

1) An easier surgical approach and shorter operation time since the gamma probe guides the surgeon to the pathologic tissue

2) Verification of the correct excision of the pathological tissue and success of surgery since the gamma probe measures counts of the removed specimen ex vivo.

As mentioned in the introduction, no report of the intraoperative use of TF specifically has yet been published, and only one early series associated TF and MIBI in this setting (13). Our present experience showed that the intraoperative use of TF is effective, apparently as effective as that of MIBI, which as been much more widely reported, as it will be summarized below.

The advent of preoperative detection of over-functioning parathyroid glands with MIBI impacted deeply on the management of HPT, opening the way to minimally invasive surgery. Consequently, intraoperative detection by means of nuclear probe has been proposed to further shorten and make more effective parathyroid surgery. In large series o f 345 patients, Murphy (30) showed, in patients with primary HPT who had a positive MIBI scintigraphy, that removed glands, which contains more than 20 % of the radioactivity that is measurable in the operative basin, were parathyroid adenomas. However, Friedman (2007) (31) concluded from performing this procedure in 46 patients that "ex vivo radioactivity percentages can differentiate hyperactive parathyroid tissue from any other tissue, but they cannot differentiate adenoma from hyperplasia and thus are not helpful in ruling out multiglandular disease. Interpretation of ex vivo radioactivity percentages should take into consideration the size of the specimen". Ortega (32) proposed in 2007 to use a mini portable gamma camera in replacement of the radioactive probe.

This procedure of intraoperative detection enhanced the performance of MIBI as compared to preoperative imaging, the detection rate increasing over 90%, even with a reduced injected activity: Rubello (33) reported that the procedure was successfully performed in 321 of 344 patients (93.3 %). Chen (34) performed radioguided parathyroidectomy on 769 patients with primary HPT who had a MIBI scintigraphy, irrespectively of the positivity of the MIBI scintigraphy. All enlarged parathyroid glands were localised with the gamma probe in patients with a negative or with a positive MIBI scintigraphy, with similar sensitivities. This occurred despite the fact that smaller parathyroid glands were present, on average, in patients with negative MIBI scintigraphy (428 mg vs 828 mg, p=0.001). Equivalent high postoperative eucalcemia rates (>98 %) and low complication rates (0.5 %) were achieved with radioguided techniques in both patient populations. These data suggest that the gamma probe has an important role for localisation of parathyroid glands, even in patients with negative preoperative MIBI scintigraphy.

Conclusion

In conclusion, the use of parathyroid scintigraphy in HPT is widely accepted by the clinicians and the surgeons. According to our experience, TF, which is easier to label and is registered in Slovakia, can be used in an effective way for both preoperative imaging and intraoperative detection of the hyperfunctioning parathyroid glands. The success of this procedure, even though TF is not registered at this moment for this indication, over six years favours a further step which will be to practice minimally invasive surgery under local anesthesia only (35).

References

1. Carty SE, Worsey MJ, Virji MA, Brown ML, Watson CG. Concise parathyroidectomy: The impact of preoperative SPECT ^{99m}Tc sestamibi scanning and intraoperative quick parathormone assay. Surgery 1997; 122: 1107-16.

2. Ferlin G, Borsato N, Camerani M, Conte N, Zotti D. New perspectives in localizing enlarged parathyroids by technetium-thallium subtraction scan. J Nucl Med 1983; 24: 438–41.

3. Young AE, Gaunt JI, Croft DN, Collins RE, Wells CP, Coakley AJ. Location of parathyroid adenomas by thallium-201 and technetium-99m subtraction scanning. Br Med J (Clin Res Ed). 1983 ; 286 (6375): 1384-6.

4. Fogelman I, McKillop JH, Bessent RG, Boyle IT, Gray HW, Gunn I, Hutchison JS. Successful localisation of parathyroid adenomata by thallium-201 and technetium-99m subtraction scintigraphy: description of an improved technique. Eur J Nucl Med. 1984; 9 (12): 545-7.

5. Bolk JH, Heslinga JM, Blokland JA, Ruiter DJ, Goslings BM, van de Velde CJ, Pauwels EK. Initial results of preoperative localization of parathyroid adenomas using subtraction scintigraphy with technetium-99m and thallium-201. Ned Tijdschr Geneeskd. 1985; 129 (5): 216-20.

6. Coakley AJ, Kettle AG, Wells CP, O'Doherty MJ, Collins RE. 99Tcm sestamibi -a new agent for parathyroid imaging. Nucl Med Commun. 1989; 10 (11) : 791-4.

7. O'Doherty MJ, Kettle AG, Wells P, Collins RE, Coakley AJ. Parathyroid imaging with technetium-99m-sestamibi: preoperative localization and tissue uptake studies. J Nucl Med. 1992; 33(3): 313-8.

8. Taillefer R, Boucher Y, Potvin C, Lambert R. Detection and localization of parathyroid adenomas in patients with HPT using a single radionuclide imaging procedure with technetium-99m-sestamibi (double-phase study). J Nucl Med 1992; 33 (10): 1801-7.

9. Ishibashi M, Nishida H, Kumabe T, Morita S, Matoba F, Nomura G, Hayabuchi N. Tc-99m tetrofosmin. A new diagnostic tracer for parathyroid imaging. Clin Nucl Med. 1995; 20(10): 902-5.

10. Mansi L, Rambaldi PF, Marino G, Pecori B, Del Vecchio E. Kinetics of Tc-99m sestamibi and Tc-99m tetrofosmin in a case of parathyroid adenoma. Clin Nucl Med. 1996; 21(9): 700-3.

11. Giordano A, Meduri G, Marozzi P. Parathyroid imaging with 99Tcm-tetrofosmin. Nucl Med Commun. 1996; 17(8): 706-10.

12. Perkins AC, Hardy JG. Intra-operative nuclear medicine in surgical practice. Nucl Med Commun. 1996; 17 (12): 1006-15.

13. Gallowitsch HJ, Fellinger J, Kresnik E, Mikosch P, Pipam W, Lind P. Preoperative scintigraphic and intraoperative scintimetric localization of parathyroid adenoma with cationic Tc-99m complexes and a hand-held gamma-probe. Nuklearmedizin. 1997; 36 (1): 13-8.

14. Mariani G, Gulec SA, Rubello D, Boni G, Puccini M, Pelizzo MR, Manca G, Casara D, Sotti G, Erba P, Volterrani D, Giuliano AE. Preoperative localization and radioguided parathyroid surgery. J Nucl Med 2003; 44(9): 1443-58.

15. Bozkurt MF, Uđur O, Hamalođlu E, Sayek I, Gulec SA. Optimization of the gamma probe-guided parathyroidectomy. Am Surg 2003; 69: 720–5.

16. Rubello D, Casara D, Pelizzo MR. Optimization of preoperative procedures. Nucl Med Commun 2003; 24: 133–40.

17. Rubello D, Al-Nahhas A, Mariani G, Gross MD, Rampin L, Pelizzo MR. Feasibility and long-term results of focused radioguided parathyroidectomy using a „low“ 37 MBq (1 mCi) 99mTc-sestamibi protocol. Int Semin Surg Oncol. 2006; 3: 30.

18. Aigner RM, Fueger GF, Nicoletti R. Parathyroid scintigraphy: comparison of technetium-99m methoxyisobutylisonitrile and technetium-99m tetrofosmin studies. Eur J Nucl Med. 1996; 23(6): 693-6.

19. Vallejos V, Martin-Comin J, Gonzalez MT, Rafecas R, Muńoz A, Fernăndez A, Mora J, Ramos M. The usefulness of Tc-99m tetrofosmin scintigraphy in the diagnosis and localization of hyperfunctioning parathyroid glands. Clin Nucl Med. 1999; 24(12): 959-64.

20. Fröberg AC, Valkema R, Bonjer HJ, Krenning EP. 99mTc-tetrofosmin or 99mTc-sestamibi for double-phase parathyroid scintigraphy? Eur J Nucl Med Mol Imaging. 2003; 30(2): 193-6.

21. Harrell RM, Mackman DM, Bimston DN. Nonequivalent results of tetrofosmin and sestamibi imaging of parathyroid tumors. Endocr Pract. 2006; 12(2): 179-82.

22. Lorberboym M, Ezri T, Schachter PP. Preoperative technetium Tc 99m sestamibi SPECT imaging in the management of primary HPT in patients with concomitant multinodular goiter. Arch Surg. 2005; 140 (7): 656-60.

23. Dugonjić S, Ajdinović B, Cerović S, Janković Z. Validity of dual tracer 99mTc-tetrofosmin and 99mTc-pertechnetate subtraction parathyroid scintigraphy in patients with primary and secondary hyperparathyroidism. Vojnosanit Pregl. 2009; 66(12): 949-53.

24. Gallowitsch HJ, Mikosch P, Kresnik E, Unterweger O, Lind P. Comparison between 99mTc-tetrofosmin/pertechnetate subtraction scintigraphy and 99mTc-tetrofosmin SPECT for preoperative localization of parathyroid adenoma in an endemic goiter area. Invest Radiol. 2000; 35(8): 453-9.

25. Apostolopoulos DJ, Houstoulaki E, Giannakenas C, Alexandrides T, Spiliotis J, Nikiforidis G, Vlachojannis JG, Vassilakos PJ. Technetium-99m-tetrofosmin for parathyroid scintigraphy: comparison to thallium-technetium scanning. J Nucl Med. 1998; 39(8): 1433-41.

26. Hiromatsu Y, Ishibashi M, Nishida H, Okuda S, Miyake I. Technetium-99m tetrofosmin parathyroid imaging in patients with primary hyperparathyroidism. Intern Med. 2000; 39(2): 101-6.

27. Wakamatsu H, Noguchi S, Yamashita H, Yamashita H, Tamura S, Jinnouchi S, Nagamachi S, Futami S. Technetium-99m tetrofosmin for parathyroid scintigraphy: a direct comparison with (99m)Tc-MIBI, (201)Tl, MRI and US. Eur J Nucl Med. 2001; 28(12): 1817-27.

28. Alexandrides TK, Kouloubi K, Vagenakis AG, Yarmenitis S, Spyridonidis T, Vassilakos P, Apostolopoulos D. The value of scintigraphy and ultrasonography in the preoperative localization of parathyroid glands in patients with primary hyperparathyroidism and concomitant thyroid disease. Hormones (Athens). 2006; 5(1): 42-51.

29. Hindié E, Ugur O, Fuster D, O'Doherty M, Grassetto G, Ureña P, Kettle A, Gulec SA, Pons F, Rubello D; Parathyroid Task Group of the EANM. 2009 EANM parathyroid guidelines. Eur J Nucl Med Mol Imaging. 2009; 36 (7): 1201-16.

30. 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 (6): 1023-8.

31. Friedman M, Gurpinar B, Schalch P, Joseph NJ. Guidelines for radioguided parathyroid surgery. Arch Otolaryngol Head Neck Surg. 2007; 133 (12): 1235-9.

32. 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. 2007; 34(2): 165-9.

33. Rubello D, Mariani G, Pelizzo MR; Italian Study Group of Radioguided Surgery and ImmunoScintigraphy. Minimally invasive radio-guided parathyroidectomy on a group of 452 primary hyperparathyroid patients: refinement of preoperative imaging and intraoperative procedure. Nuklearmedizin. 2007; 46(3): 85-92.

34. Chen H, Sippel RS, Schaefer S. The effectiveness of radioguided parathyroidectomy in patients with negative technetium Tc 99m-sestamibi scans. Arch Surg. 2009; 144(7): 643-8.

35. Shindo ML, Rosenthal JM, Lee T. Minimally invasive parathyroidectomy using local anesthesia with intravenous sedation and targeted approaches. Otolaryngol Head Neck Surg. 2008; 138(3): 381-7.

Received April 8, 2010.
Accepted August 18, 2011.