Technetium-99m-Tetrofosmin for Parathyroid Scintigraphy: A Comparison with Sestamibi

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Parathyroid scintigraphy with the new myocardial perfusion radiopharmaceutical ^{99m}Tc-tetrofosmin was compared with ^{99m}Tc-sestamibi scintigraphy using early and delayed imaging. **Methods:** The two preparations were administered on different days to the same 16 patients suffering from primary hyperparathyroidism. Anterior view gamma camera planar imaging (10-min acquisition) was performed in the period between 5 min and 3 hr after administration of the radiopharmaceutical. For most of the patients, a pertechnetate image of the thyroid was available for eyeball comparison when reading the tetrofosmin and sestamibi images. Imaging results were compared with those from histopathological examination after surgery. **Results:** On early images, all the adenomas visualized with sestamibi were equally well seen with tetrofosmin and vice versa. In 6 of 11 scintigraphically detected neck adenomas, delayed imaging improved the adenoma visualization with sestamibi. In contrast, this differential washout was never seen with tetrofosmin. Histopathological examination of excised tissue specimens after neck exploration (15 patients) or thoracotomy (one patient) revealed a parathyroid adenoma in all 16 patients. Our 12 scintigraphic findings were true-positives, while the remaining four scintigraphies were false-negatives, giving a diagnostic sensitivity of 75% with both preparations. The mediastinal adenoma was detected in a patient with a history of two unsuccessful neck explorations and one unsuccessful thoracotomy. **Conclusion:** Tetrofosmin has the same success rate as sestamibi for detection of parathyroid adenomas on scintigrams acquired immediately after injection. In contrast to sestamibi, delayed imaging has no diagnostic impact. Moreover, the thyroid/parathyroid differential washout of sestamibi failed in 5 of 11 neck adenomas here detected, indicating that delayed sestamibi washout is an unreliable diagnostic criterion. Therefore, whether sestamibi or tetrofosmin is preferred for parathyroid scintigraphy, thyroid scintigraphy seems mandatory.

Key Words: parathyroid scintigraphy; technetium-99m-tetrofosmin; technetium-99m-sestamibi

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Parathyroid imaging with the myocardial perfusion agent ^{99m}Tc-sestamibi was first published in a preliminary report in 1989 (*1*) and in more detail by the same group in 1992 (*2*). With a technetium-labeled preparation available, the commonly used dual radionuclide procedure with ^{201}Tl and $^{99m}TcO_4$ could be replaced by a dual-isotope procedure with ^{123}I and ^{99m}Tc-sestamibi (*3,4*) or a dual radiopharmaceutical procedure with ^{99m}Tc-sestamibi and $^{99m}TcO_4$ (*5*). In 1992, a parathyroid procedure with ^{99m}Tc-sestamibi as the only radiopharmaceutical was introduced by Taillefer et al. (*6*). It was demonstrated that detection of parathyroid adenomas with ^{99m}Tc-sestamibi as the only administered preparation was possible because focal uptake in parathyroid adenomas persisted, with improved visualization on late images 3 hr after the injection, when the thyroid tissue had lost most of its radioactivity. However, other authors conclude that this comparison of early and late images may fail and that accompanying thyroid imaging is, therefore, necessary (*4,7*).

Recently, ^{99m}Tc-tetrofosmin was introduced as a new technetium-labeled pharmaceutical for myocardial perfusion studies (*8,9*). When we changed from sestamibi to tetrofosmin for myocardial scintigraphy, we wondered if tetrofosmin could be used for parathyroid scintigraphy. Tetrofosmin vials then could be shared between patients with hyperparathyroidism and patients with coronary disease.

MATERIALS AND METHODS

Patients

Sixteen consecutive patients routinely referred to our department with the diagnosis primary hyperparathyroidism had parathyroid scintigraphy with ^{99m}Tc-labeled sestamibi and tetrofosmin on separate days. There were 12 women and four men, median age 67 yr (range 35–79 yr). When a patient was excluded from the study, it was because a second parathyroid investigation on a second day was disadvantageous in terms of patient convenience or hospital logistics. On a third day, 14 of the patients underwent thyroid scintigraphy with pertechnetate, but two of these investigations were unsuccessful because the patient had been exposed to high doses of iodine during radiologic procedures. One patient had been previously thyroidectomized with the intention to remove a hidden parathyroid adenoma and was now suspected of having a mediastinal adenoma, while the last one was an out-patient not investigated for practical reasons. The three (or two) investigations on each single patient were completed within a week.

Surgery

Fifteen of the patients had surgical neck exploration, and one was thoracotomized. The excised tissue specimens were examined histopathologically. When a presumed neck adenoma was verified preoperatively by examination of frozen sections, and no preoperative indications for an adenoma on the contralateral side of the neck had been found, surgery was stopped without exploration of the contralateral side.

Radiopharmaceuticals

Technetium-99m-pertechnetate was eluted from an IFETEC ^{99m}Tc-generator (Institutt for energiteknikk, Kjeller, Norway). For thyroid scintigraphy, 180 MBq [^{99m}Tc]pertechnetate were injected intravenously. For parathyroid scintigraphy, the eluate was used to label tetrofosmin (Myoview, Amersham International, Amersham, UK) or sestamibi (Cardiolite, DuPont Pharmaceuticals Ltd., Hertfordshire, UK) as described by the manufacturers. After labeling, 900 MBq were injected.

Gamma Camera

Parathyroid and thyroid scintigraphy were performed with a General Electric MaxiCamera 300 Autotune ZS (Milwaukee, WI) with a general-purpose, parallel-hole, low-energy collimator. The

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TABLE 1
Parathyroid Adenoma Patients with Positive Scintigraphs

Patient no.	Age (yr)	Sex	Visual analysis: Sestamibi E	Sestamibi D	Tetrofosmin E	Tetrofosmin D	Thyroid scintigraphy with pertechnetate on a second day	Adenoma location	Adenoma weight (g)
1	79	F	2	2	2	2	Normal	Right lower neck	0.82
2	50	F	3	4	3	3	Focal defect in upper right lobe	Right upper neck (two adenomas)	1.87 0.37
3	53	M	2	3	2	2	Focal defect in lower right iobe	Right lower neck	14.74
4	35	F	3	4	3	3	Not done	Right lower neck	1.00
5	75	F	1	1	1	1	Normal	Left lower neck	0.43
6	50	F	3	4	3	3	Normal	Left upper neck	Size 1.5 × 0.5 cm (not weighed)
7	50	M	3	3	3	3	Normal	Right lower neck	2.28
8	78	M	3	4	3	3	Normal	Left upper neck	1.60
9	75	F	2	2	2	2	Exposed to iodine contrast during CT	Left lower neck	2.08
10	69	F	2	2	2	2	Nodular goiter	Left lower neck	1.12
11	72	F	2	3	2	2	Normal	Left lower neck	0.55
12*	37	M	—	—	—	—	Thyroidectomized	Mediastinum	0.96

E = Early (5-min image); D = Delayed (3-hr) image.

Visual analysis: a four-point scale was applied when evaluating areas with focal uptake relative to the thyroid, indicating parathyroid adenomas: 1 = possible adenoma, slightly higher intensity than the thyroid; 2 = definite, but with moderate intensity relative to the thyroid; 3 = definite, with high intensity relative to the thyroid; 4 = definite, with very low remaining tetrofosmin or sestamibi activity in the thyroid (i.e., barely visible thyroid gland after 3 hr).

*Low intensity in ectopic adenoma but no thyroid gland for comparison (thyroidectomy in 1979).

camera was connected to an Elscint Apex SP-1 (Haifa, Israel) computer.

Parathyroid Imaging

After administration of either ^{99m}Tc-labeled sestamibi or tetrofosmin, planar anterior view scintigraphy of the neck and thorax was performed with the patient in a supine position. The camera was positioned to obtain an image with the submandibular glands close to the upper edge of the scintigram and most of the heart above the lower edge. Multiple 10-min scintigrams were acquired during a 3-hr period after the injection. Acquisition of the first image was started after 5 min, followed by images at 15, 30, 60, 90, 120 and 180 min after the injection. With the camera in preset-time mode (600 sec) and an administered dose of 900 MBq, images (256 × 256 matrix) with an image count of 5–7 megacounts were acquired in the early period 5–15 min postinjection, decreasing to 2–3 megacounts after 3 hr.

Thyroid Imaging

Anterior view planar imaging of the neck (preset-count mode, 600 kilocounts, 256 × 256 matrix) was performed about 20 min after administration of pertechnetate with the same collimator used for the parathyroid imaging.

Interpretation of the Scintigrams

The sestamibi and tetrofosmin scintigrams were investigated for focal areas indicating parathyroid adenomas. All the interpretations were performed by the same consultant in nuclear medicine and consecutively reported to the referring physician according to our standard reporting routine. For some of the patients ultrasound or CT findings were known to the interpreter, for other patients the results from these alternative imaging modalities were unknown. When a thyroid image was available, this was used for eyeball comparison with the tetrofosmin and sestamibi images.

RESULTS

Our reported imaging results (10-min acquisition period) are from 5 min (early) and 3 hr (delayed) after injection. Additional scintigrams were acquired between 5 min and 3 hr to explore if these alternative imaging intervals would improve the diagnostics. This was not the case, and these results are therefore not presented in detail.

There was complete agreement between the scintigraphic diagnostic conclusions with the two preparations (Tables 1, 2). Histopathological examination showed that all 12 patients with scintigraphically detectable lesions (Table 1), as well as the four with negative scintigraphy (Table 2), had parathyroid adeno-

TABLE 2
Parathyroid Adenoma Patients with Negative Scintigraphs

Patient no.	Age (yr)	Sex	Thyroid scintigraphy with pertechnetate on a second day	Adenoma location	Adenoma weight (g)
1	65	F	Normal	Right upper neck	0.23
2	69	F	Exposed to iodine contrast during CT	Left lower neck	0.89
3	67	F	Nodular goiter	Right lower neck	0.16
4	76	F	Nodular goiter	Right upper neck	1.37

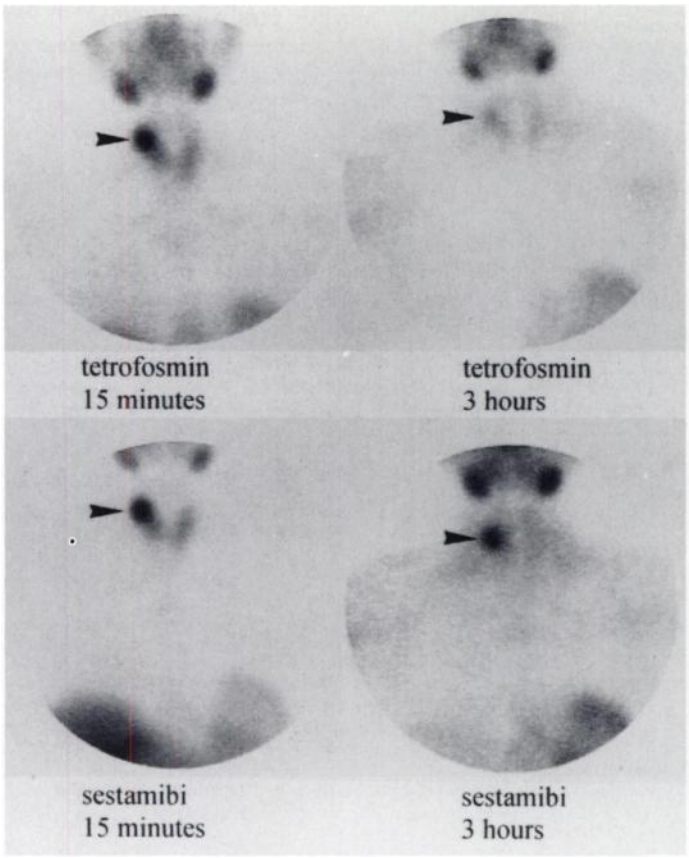

FIGURE 1. Early and delayed ^{99m}Tc-tetrofosmin and ^{99m}Tc-sestamibi planar anterior view scintigraphy from a 50-yr-old woman with two parathyroid adenomas, 1.87 and 0.37 g, in the right upper neck. They were interpreted as a single adenoma, probably because they were situated close to each other. Note the difference in adenoma activity washout rate between the two agents.

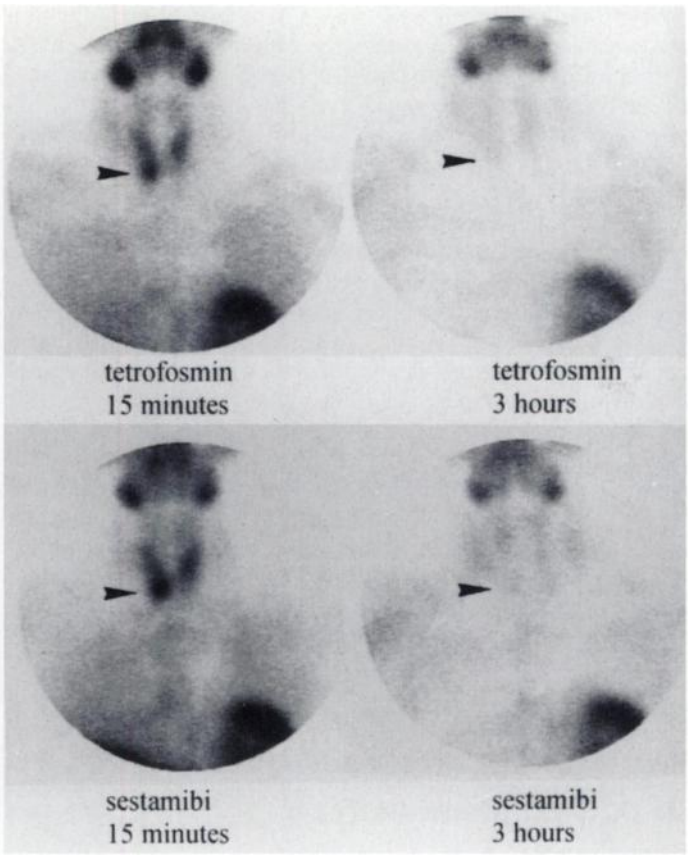

FIGURE 2. Early and delayed ^{99m}Tc-tetrofosmin and ^{99m}Tc-sestamibi planar anterior view scintigraphy from a 50-yr-old woman with a 2.28-g parathyroid adenoma in the right lower neck. In this case, the two radiopharmaceuticals had similar washout rates.

mas, giving a diagnostic sensitivity of 75% with both preparations.

A different washout rate for parathyroid and thyroid tissues, and thereby improved adenoma vizualization on the delayed images, was only observed with sestamibi and never with tetrofosmin (Table 1). Hence, when interpreting late images, parathyroid adenomas were often better visualized with sestamibi than with tetrofosmin (Fig. 1), and this phenomenon is of diagnostic value in distinguishing between parathyroid and thyroid adenomas (*6*). However, differential sestamibi washout was frequently not obtained (Fig. 2): 5 of 11 verified neck adenomas had a sestamibi washout rate similar to the thyroid (Table 1).

On the early images, the parathyroid adenomas were always equally well visualized with sestamibi and tetrofosmin. Because the differential washout diagnostic criterion could not be used with tetrofosmin, and frequently failed with sestamibi, an accompanying thyroid image seems obligatory, irrespective of which of the two preparations are preferred.

In a 37-yr-old man with a 16-yr history of persisting hyperparathyroidism after one unsuccessful neck exploration in 1978 and a second unsuccessful operation in 1979, exploring the neck and thorax simultaneously, an ectopic adenoma was located in the mediastinum with both preparations. He had been thyroidectomized during the second operation in 1979, suspecting a hidden parathyroid adenoma within the thyroid.

DISCUSSION

This study demonstrates that tetrofosmin can be used for parathyroid scintigraphy. Every adenoma visualized with sestamibi also was visible with tetrofosmin. And when the adenoma was not scintigraphically detected preoperatively, this was the case with both preparations. There were no false-positives or true-negatives in this study.

In spite of the fact that corresponding diagnostic conclusions were obtained with the two preparations, their relative washout rate from the thyroid and parathyroid tissue were different. Delayed parathyroid adenoma washout relative to the thyroid was only observed with sestamibi and never with tetrofosmin. This contrasts with a published result from parathyroid scintigraphy with tetrofosmin in a single patient, where improved focal adenoma visualization on the delayed image was reported (*10*). Moreover, our study demonstrated that sestamibi differential washout was not a constant observation. Several parathyroid adenomas had a sestamibi washout rate similar to the thyroid, which corresponds with the experience of other authors (*7*). Such adenomas were not invisible on the delayed images, but delayed imaging was of no benefit because it did not improve the adenoma visualization.

This study was planned as a comparative study between sestamibi and tetrofosmin. The sestamibi differential washout phenomenon was published by Taillefer et al. (*6*) as an important diagnostic criterion. The main objectives of our study were to explore if tetrofosmin could be used for parathyroid imaging and if it had the same differential washout quality as sestamibi. Our answer is yes to the first question and no to the second.

In a situation when comparison of early and late scintigraphy is useless (tetrofosmin) or unreliable (sestamibi), thyroid scintigraphy was found useful. When a tetrofosmin or sestamibi image indicated parathyroid adenoma in the neck, a completely

normal thyroid pertechnetate image or a thyroid image with a cold area corresponding to the area with increased focal uptake with tetrofosmin and sestamibi supported the parathyroid adenoma conclusion. Moreover, most parathyroid adenoma patients are elderly women, among whom irregular structure in the thyroid gland is a frequent phenomenon. Therefore, though not experienced in this study, thyroid scintigraphy may also eliminate false-positives caused by misinterpretation of tetrofosmin or sestamibi uptake in thyroid adenomas. In accordance with the recommendations from Hindie et al. (*4*) and Rossitch et al. (*7*), knowledge of the thyroid anatomy should improve the scintigraphic interpretation. Hence, irrespective of which of the two parathyroid preparations that is preferred, we strongly recommend that thyroid scintigraphy be included in the procedure.

Two of the 4 false-negative scintigraphic results were from investigations on patients with relatively small parathyroid adenomas: 0.16 and 0.23 g (Table 2). The patient with the 0.16-g adenoma had a thyroid scintigram indicating moderate multinodular goiter, while the other had a completely normal thyroid gland. A third patient with negative scintigraphy had a large adenoma of 1.37 g situated behind a multinodular goiter. When the scintigrams of this patient were revised postoperatively, we realized that the adenoma actually was visible.

Further investigations are in progress in our laboratory, with the intention to improve the image resolution and to find a simple and reliable same-day procedure for parathyroid scintigraphy with ^{99m}Tc-labeled tetrofosmin and thyroid scintigraphy with ^{99m}Tc-pertechnetate.

CONCLUSION

Tetrofosmin is an alternative to sestamibi for parathyroid scintigraphy. However, among the 16 patients in this study, the thyroid-parathyroid differential washout of sestamibi previously reported by other authors was never observed with tetrofosmin. Moreover, differential washout of sestamibi was not seen in 5 of 11 scintigraphically positive adenomas in the neck, and is, therefore, not a reliable diagnostic criterion. Irrespective of the preparation preferred for parathyroid visualization–sestamibi or tetrofosmin–combination with thyroid scintigraphy seems mandatory. Further studies are necessary to optimize the procedure for scintigraphic detection of parathyroid lesions.

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Comparison of Parathyroid Imaging with Technetium-99m-Pertechnetate/Sestamibi Subtraction, Double-Phase Technetium-99m-Sestamibi and Technetium-99m-Sestamibi SPECT

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The ability of ^{99m}Tc-pertechnetate/sestamibi subtraction, double-phase ^{99m}Tc-sestamibi and ^{99m}Tc-sestamibi SPECT imaging to localize abnormal parathyroid tissue was compared. **Methods:** Fifty-five consecutive patients had parathyroid imaging before surgery for hyperparathyroidism. Imaging consisted of ^{99m}Tc-pertechnetate pinhole images of the neck followed by ^{99m}Tc-sestamibi pinhole images of the neck and parallel-hole images of the neck and chest (early images). Within 2.5–4.0 hr later pinhole images of the neck, parallel-hole and SPECT images of the neck and chest were obtained (late images). Nodular foci of increased sestamibi activity were considered abnormal. **Results:** The sensitivity for abnormal parathyroid glands by visual comparison of early images and pertechnetate images was 72%–75%, late images and pertechnetate images was 73%–78% and double-phase (early and late) sestamibi images was 62%–65%; computer subtraction of pertechnetate from early images was 71%–74%; and SPECT imaging was 79%. The sensitivity for parathyroid adenomas was 89%–98%, while the sensitivity for hyperplastic parathyroid glands was only 47%–58%. **Conclusion:** Late imaging, computer subtraction and SPECT may not be necessary since they provided only marginal improvements on visual comparison of early sestamibi with pertechnetate images. Double-phase sestamibi imaging was less sensitive, so baseline thyroid imaging with pertechnetate is recommended.

Key Words: parathyroid; hyperparathyroidism; technetium-99m-sestamibi; technetium-99m-MIBI

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