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# Thallium-201 Scintigraphy of the Suppressed Thyroid: An Alternative for Iodine-123 Scanning After TSH Stimulation

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Thallium-201 scintigraphy of the thyroid gland suppressed by autonomous nodule was compared with  $^{123}\text{I}$  scintigraphy after TSH stimulation. In all patients, similar images were obtained by both methods. In 20 patients, the contralateral lobe was visualized on both scans and in 14 of these, the upper pole of the ipsilateral lobe was also visualized. In one patient, neither  $^{123}\text{I}$  scanning after TSH nor  $^{201}\text{Tl}$  scintigraphy showed any extranodular tissue. This study suggests that  $^{201}\text{Tl}$  scintigraphy is a reliable alternative for scanning after TSH. It is a relatively simple method, not inducing any TSH-related allergic reactions. Iodine uptake in extranodular tissue is not stimulated and therefore,  $^{201}\text{Tl}$  scintigraphy and radioiodine therapy can be combined on one day, without increasing the risk of radiation damage to the normal thyroid tissue with a resultant post-treatment hypothyroidism.

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The solitary autonomous thyroid nodule is "a discrete nodular structure with function both independent of pituitary stimulation and unrelated to that of the remaining thyroid tissue" (1). It is suspected when palpation of the neck reveals a single nodule and preliminary iodine-scintigraphy shows a hot nodule. Other possibilities to differentiate from are thyroïdal anomalies such as thyroïdal hemigenesis. Therefore the diagnosis of a solitary autonomous thyroid nodule depends upon the visualization of suppressed extranodular thyroid tissue.

Stimulation of iodine uptake in the suppressed tissue by thyroid stimulating hormone (TSH) leads to visualization of the suppressed parts on iodine-scan. TSH-stimulation, however, has considerable disadvantages. The bovine proteins may induce allergic reactions either systemic or local (2). It is a time-consuming investigation because of the need of intramuscular TSH injections. On top of this, TSH is no longer available in regular pharmacies in The Netherlands. The production was stopped by the manufacturer because of low demand.

Ultrasonography is another method to visualize thyroid tissue. However, it does not provide any physiological information. A lobe may be present but nonfunctional because of a number of reasons. Ultrasonography can only give additional information provided that it is performed by a radiologist with ample experience and having at his disposal a special transducer for superficial structures.

The use of thallium-201 ( $^{201}\text{Tl}$ ) for diagnosis and follow-up of thyroid carcinoma is well established. In 1979, Fukuchi et al. (3) reported significant thallium uptake in patients with various diseases causing thyroid enlargement. In 1984 Müller-Brand et al. proposed  $^{201}\text{Tl}$  scintigraphy as a new way to visualize suppressed tissue in benign thyroid diseases (4).

In our clinic from October 1985 onward  $^{201}\text{Tl}$  scintigraphy as well as iodine-123 ( $^{123}\text{I}$ ) scintigraphy after TSH were performed in all patients presenting with a hot nodule on  $^{123}\text{I}$  scan. The purpose of the study was to investigate the quality of  $^{201}\text{Tl}$  scintigraphy as an alternative for scanning after TSH.

## MATERIALS AND METHODS

Twenty one patients were studied prospectively.

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### Scintigraphic methods

**Baseline  $^{123}\text{I}$ -scan.** 0.7 mCi (30 MBq) of [ $^{123}\text{I}$ ]sodium iodide (high purity  $^{123}\text{I}$ ) were injected i.v. One hour later the thyroid region was imaged in the anterior and the right and left oblique position using a gamma camera (Picker Dyna camera 4/15) with a pinhole collimator. Antithyroid drugs, if used, were stopped at least 2 days previously.

**Thallium-201 scan.** Carried out 1 to 14 days after base-line  $^{123}\text{I}$  scintigraphy and  $\sim 1$  wk before TSH-stimulation. 2 mCi (74 MBq) of [ $^{201}\text{Tl}$ ]chloride were injected i.v. Fifteen min later scintigraphy of the neck from the anterior view followed. A converging collimator was used because its efficiency compared to that of the pinhole collimator is five times as high.

**Iodine-123 scan after TSH.** On three subsequent days 10 IU of TSH were injected intramuscularly. On the third day, 1 hr after the intravenous administration of 0.7 mCi (30 MBq) of  $^{123}\text{I}$ , an anterior image of the thyroid region was obtained.

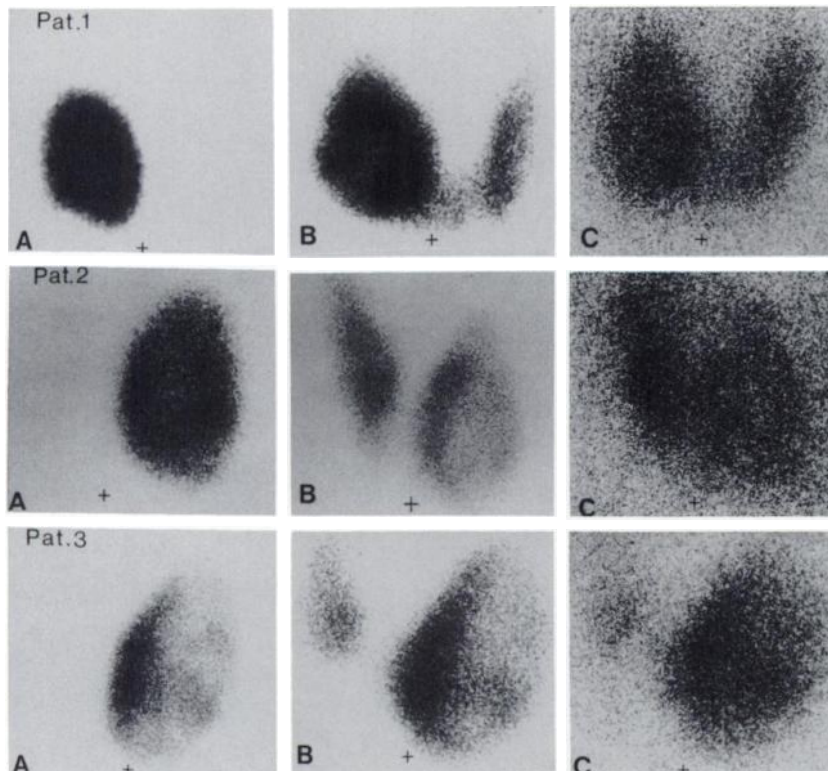
### RESULTS

In all patients the base-line  $^{123}\text{I}$  scan showed a hot nodule with suppression of supposedly remaining thyroid tissue. Mean size of the nodules was  $16 \pm 5 \text{ cm}^2$ . The nodules did not necessarily have a homogeneous uptake. In twenty of the patients the  $^{123}\text{I}$  scan after TSH-stimulation visualized suppressed tissue. These patients were considered to have a solitary autonomous thyroid nodule. The remaining patient is discussed separately.

Seventeen out of 20 patients with a solitary autonomous thyroid nodule were female. This female preponderance has often been observed (1,4). Biochemical

manifestations of hyperthyroidism were present in every patient: thyroxine  $178 \pm 19 \text{ nmol/l}$ , free thyroxine  $38 \pm 24 \text{ pmol/l}$ , triiodothyronine  $3.9 \pm 0.6 \text{ nmol/l}$ , TSH  $< 0.2 \text{ mU/l}$ , 3 hr  $^{131}\text{I}$  uptake  $32 \pm 14\%$ . This explains the high mean age of the patients ( $59.5 \pm 12.8 \text{ yr}$ ) and the relatively big size of the nodules, since hyperthyroidism in patients with solitary autonomous thyroid nodule is seen more often in elderly people with bigger nodules (1,5).

Examples of the scans in three patients are shown in Figure 1. On visual interpretation of the scans the sizes of the lobes both on  $^{201}\text{Tl}$  scan and on  $^{123}\text{I}$  scan after TSH were similar. Estimation of the exact sizes of the lobes on both scans was not possible because of the use of two different collimators, which render the factor of diminution unreliable. For that reason, only the presence of a contralateral lobe and the visibility of the upper pole of the ipsilateral lobe (not shown on the basal  $^{123}\text{I}$  scan) were accounted for as evidence of the visualization of suppressed thyroid tissue. In all 20 patients a contralateral lobe was visible on  $^{201}\text{Tl}$  scan as well as on  $^{123}\text{I}$  scan after TSH-stimulation. The upper pole of the ipsilateral lobe was visualized on both scans in 14 patients. In 17 patients uptakes in the nodule and in the surrounding thyroid tissue were equal on thallium-scan and on iodine-scan after TSH. In three patients the uptake in the nodule was significantly higher than in the extranodular tissue. Photopenic zones in the nodules, already visible on base-line  $^{123}\text{I}$  scan, were seen on both scans in 12 patients.



**FIGURE 1**

Visualization of the thyroid (anterior view) in three patients with a solitary autonomous thyroid nodule with  $^{123}\text{I}$  (A), with  $^{123}\text{I}$  after 3 days of 10 IU of TSH i.m. (B) and with  $^{201}\text{Tl}$  (C). Pat. 1 (upper row): Equal uptake in nodule and extranodular tissue. Pat. 2 (middle row): Higher uptake in extranodular tissue compared to nodule. Pat. 3 (lower row): Nonuniform uptake in the nodule and lower uptake in extranodular tissue compared to nodule. + represents sternal notch.

Both  $^{201}\text{Tl}$  scans and  $^{123}\text{I}$  scans after TSH-stimulation provided sufficient visualization of the thyroid gland, including the previously suppressed tissue. Delineation of the thyroid gland was slightly better on  $^{123}\text{I}$  scan after TSH in ten patients, in nine patients the images were equal and in one case the  $^{201}\text{Tl}$  scan proved to be superior.

## DISCUSSION

This study emphasizes that suppressed thyroid tissue in patients with a solitary autonomous nodule can be visualized by  $^{201}\text{Tl}$  scintigraphy equally well as by  $^{123}\text{I}$  scintigraphy after TSH-stimulation. In this series an upper pole and a contralateral lobe were seen on both scans with the same frequency and always in the same patients. In 17 out of 20 patients the nodule was clearly localized in the lower pole of the lobe. In three patients no differentiation between lower and upper pole was possible. We could not find a convincing explanation for the observed preferential localization of hot nodules in the lower part of the thyroid.

The target to non-target ratio was unequivocally better in iodine-scintigraphy after TSH-stimulation. Nevertheless there was a good delineation of the thyroid tissue on  $^{201}\text{Tl}$  scans too. In one patient with a hot nodule on base-line  $^{123}\text{I}$  scan the  $^{201}\text{Tl}$  scintigraphy showed no extranodular tissue.  $^{123}\text{I}$  scintigraphy after TSH-stimulation was in complete agreement with this finding, as was ultrasonography. This patient in all probability has agenesis of one thyroid lobe.

Thallium uptake in the thyroid has been assumed to depend upon a factor other than mere blood flow. Thallium forms a gradient in thyroid tissue which is similar to the gradient of potassium and which probably is mediated by  $\text{Na}^+\text{-K}^+$  ATPase, since it can be inhibited by ouabain and potassium (6). Uptake is not inhibited by perchlorate, indicating that the anionic side of the iodide pump is not used on concentrating thallium (7). Our study is in accordance with these findings, for in 17 scans uptakes in the nodule and in the surrounding thyroid tissue in which the iodide trapping mechanism was suppressed were equal. In only three out of 20  $^{201}\text{Tl}$  scans the extranodular tissue showed less activity than the nodule. Photopenic zones in the nodules can probably be accounted for by cystic degeneration of the nodules (1,8). Some authors (6,9) concluded that the entry not only of anions such as iodide, but also of cations, for example thallium, is controlled by TSH. Others could not prove a statistically significant correlation between TSH stimulation and thallium uptake (3,7). In our study  $^{201}\text{Tl}$  scans were performed in patients with low serum concentrations of TSH ( $<0.2$  mU/l) and prior to TSH administration. Therefore the clear imaging of thyroid tissue resulting from sufficient

$^{201}\text{Tl}$  uptake suggests that TSH control is not a major determinant of thallium uptake.

Every method has its pitfalls. The rare occurrence of the unilateral thyroiditis in our area might mimic a solitary autonomous thyroid nodule on  $^{201}\text{Tl}$  scan. Therefore additional information like radioactive iodine uptake, search for thyroid antibodies and erythrocyte sedimentation rate are still not superfluous.

On the basis of this study we conclude that  $^{201}\text{Tl}$  scintigraphy can be used to visualize suppressed thyroid tissue in patients with a "hot" nodule on preliminary  $^{123}\text{I}$  scan. A disadvantage of this technique, compared to ultrasonography, is the radiation burden. However, most of these patients will subsequently be treated with a high dose of radioactive iodine. The effective dose equivalent from 74 MBq of  $^{201}\text{Tl}$  is 7 mSv, compared to 5 mSv from 30 MBq of  $^{123}\text{I}$  (10).

There are some considerable advantages of  $^{201}\text{Tl}$  scintigraphy over  $^{123}\text{I}$  scanning after TSH. It does not induce systemic or local allergic reactions from the TSH, and it can be performed without discontinuation of antithyroid drug therapy. Furthermore, a therapeutic dose of radioiodine ( $^{123}\text{I}$ ) can be administered immediately after  $^{201}\text{Tl}$  scintigraphy since iodine uptake in the extranodular tissue has not been stimulated. After TSH-stimulation radioiodine treatment should be postponed for several weeks in order to reduce the chances of post-treatment hypothyroidism due to TSH-stimulation of the extranodular tissue. In fact, suppression of the extranodular tissue has to be ascertained again immediately before the administration of the therapeutic  $^{123}\text{I}$  dose. The use of  $^{201}\text{Tl}$  scintigraphy enables one physician in one department of nuclear medicine to combine reliable diagnostics and therapy with  $^{123}\text{I}$  in a short space of time. Thallium-201 scintigraphy can be performed in approximately one-half hour by a laboratory assistant. This makes it a relatively simple investigation, whereas ultrasonography can only be performed in a hospital having a specialist with experience in thyroid imaging at its disposal. Most departments of nuclear medicine doing cardiac examinations with radio-thallium have  $^{201}\text{Tl}$  readily available.

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