1). Consequently, the most suitable agent to use in the individual patient cannot be predicted from this study.

CONCLUSION

In practice, either ^{99m}Tc-MIBI or ^{99m}Tc-tetrofosmin can be used to depict musculoskeletal sarcomas. The choice of agent may depend on which radiopharmaceutical is used routinely for myocardial studies in the particular laboratory.

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Total-Body Scintigraphy with Thallium-201 and Iodine-131 in the Follow-up of Differentiated Thyroid Cancer

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We analyzed the significance of total body scintigraphy with ^{201}Tl in the follow-up of patients with differentiated thyroid cancer, both in the preablation and ablated stages. **Methods:** Prospective assessment was performed in 116 patients who were involved in 178 studies (115 in preablation and 63 after ablation). For ablation, an absence of uptake in the thyroid bed was required in the total ^{131}I follow-up scan after ^{131}I ablation therapy. Each study consisted of a ^{201}Tl scan performed while the patient was receiving thyroid hormone therapy, an ^{131}I scan performed when endogenous thyroid-stimulating hormone levels were higher than 50 mIU/ml and determination of thyroglobulin (Tg) concentration using the same sample. **Results:** In the 115 scans in the preablation group, the findings for ^{201}Tl and ^{131}I agreed in 26 scans and disagreed in 89 scans. In 59 discordant studies, only ^{131}I detected focal accumulation, and, in 54 of these, Tg levels were undetectable. Of the other 30 discordant studies, ^{201}Tl and ^{131}I detected focal uptake in 27 studies, although they did not reveal the same lesions, and in 3 studies, only ^{201}Tl detected focal accumulation; in these 30 studies, the association of detectable Tg predominated. Of the 63 studies in the ablated group, the results agreed for the two tracers in 49 and disagreed in 14 studies. In 13 of the 14 discordant studies, ^{201}Tl detected focal uptake, and, in 10 of these, Tg was detectable. Thus, 31 of the 116 patients assessed (15 preablation and 16 ablated) had at least one lesion that was detected by ^{201}Tl but not detected by ^{131}I. A definitive diagnosis could be established in 26 patients, and the presence of thyroid cancer was confirmed in 23. The sensitivity and specificity in the ablated group were 94% and 96%, respectively, for ^{201}Tl and 29% and 100%, respectively, for ^{131}I. **Conclusion:** The high sensitivity of ^{201}Tl scintigraphy in detecting tumor tissue indicates that the inclusion of this technique in the follow-up of patients with differentiated thyroid carcinoma should be considered in both the preablation and the ablated stages.

Key Words: differentiated thyroid cancer; thallium-201; iodine-131; thyroglobulin

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Total body scintigraphy with ^{131}I is the established technique for the follow-up of differentiated thyroid cancer (DTC). However, the inherent limitations of the technique are also well known. In recent years, therefore, the introduction of ^{201}Tl total

TABLE 1
Results of 115 Studies in 68 Preablation Patients

Scans	Tg > 1 ng/ml	Tg < 1 ng/ml	Total
Concordant scans (n = 26)			
^{131}I+ ^{201}Tl+	13	7	20
^{131}I− ^{201}Tl−	—	6	6*
Discordant scans (n = 89)			
^{131}I+ ^{201}Tl−	5	54	59
^{131}I+ ^{201}Tl+†	19 (10‡)	8 (5‡)	27 (15‡)
^{131}I− ^{201}Tl+	2	1	3*‡

*Studies in which ablation was confirmed.

†Studies in which ^{201}Tl and ^{131}I scans detected different sites.

‡Studies in which ^{201}Tl scan detected at least one lesion more than did ^{131}I scan.

body scans has been proposed to either replace ^{131}I scintigraphy in some applications (1–3) or complement it, especially in those patients with detectable thyroglobulin levels and negative ^{131}I scans (4–10). Nevertheless, ^{201}Tl scintigraphy has not been generally accepted, and its role has not been clearly established for its use in the routine clinical work. As a result, it has been the center of some controversy, and recent in-depth reviews have suggested the need for deeper studies into the subject so that final conclusions can be reached (11–13).

On the other hand, most of the authors who attempted to evaluate the contribution of ^{201}Tl to the follow-up of DTC in the two post-thyroidectomy clinical situations, that is, with and without residual postsurgical thyroid bed uptake, have classified the population studied into preablation and postablation groups, including in the latter the patients who had received an ^{131}I ablation dose, but without scintigraphic confirmation that the ablation was achieved before being included in the group (2,10).

In the light of this, we performed a prospective assessment of the significance of ^{201}Tl scintigraphy in the follow-up of DTC both in the preablation stage and for scintigraphically confirmed ablation.

METHODS

Assessment was performed in 116 patients (91 women and 25 men) with a diagnosis of DTC (89 papillary and 27 follicular carcinomas). One hundred seventy-eight studies were performed, each consisting of ^{201}Tl and ^{131}I scintigraphy, making a total of 356 scans; each study also included thyroglobulin (Tg) determination. Of the 178 studies, 115 were performed before ablation in 68 patients, and 63 were performed in other 48 patients in whom ablation was confirmed gammagraphically before the study. In the course of assessment, nine patients in the preablation group had their clinical status modified.

TABLE 2
Results of 63 Studies in 48 Ablated Patients

Scans	Tg > 1 ng/ml	Tg < 1 ng/ml	Total
Concordant scans (n = 49)			
^{131}I+ ^{201}Tl+	4	—	4
^{131}I− ^{201}Tl−	1	44	45
Discordant scans (n = 14)			
^{131}I+ ^{201}Tl−	—	1	1
^{131}I− ^{201}Tl+	10	3	13

n = number of scans.
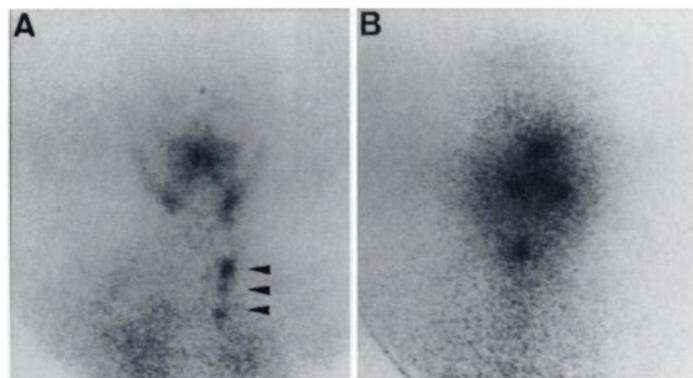
FIGURE 1. A 19-yr-old patient with papillary carcinoma in preablation. In a follow-up study 6 mo after an ablative dose, ^{201}Tl scan (A) shows several foci of uptake in left nodes of the neck (arrowheads). Iodine-131 scan done with TSH levels > 50 mIU/ml shows uptake only in the thyroid bed with absence of uptake in the nodes (B). Tg concentration was 12 ng/ml. Histological analysis confirmed papillary carcinoma.

Thallium-201 scintigraphy was performed while the patients were receiving thyroid hormone therapy. Scanning was initiated 15 min after i.v. administration of 74 MBq of ^{201}Tl-chloride, and images of 5 min per view were acquired with a gamma camera equipped with a high-resolution collimator.

Iodine-131 scintigraphy was performed after discontinuation of hormone therapy to suppress thyroid-stimulating hormone (TSH), and all patients showed levels over 50 mIU/ml. Images were acquired 48 hr after oral administration of 148 MBq of ^{131}I, with each image containing 200,000 counts. Before ^{131}I administration, 10 ml of whole blood was extracted to determine the Tg concentration by means of an IRMA technique with a sensitivity of 1 ng/ml and to check for the presence of antithyroglobulin antibodies; those patients with these antibodies were excluded from the study.

A scan was considered positive when well defined focal accumulation was observed that did not correspond to physiologic uptake. Determinations of Tg were considered detectable when they were higher than 1 ng/ml and undetectable when they were below the detection level for the technique.

TABLE 3
Anatomical Distribution of 135 Lesions Detected in 59 ^{131}I-Positive ^{201}Tl-Negative Studies in Preablation Patients

	Thyroid bed	Neck*	Lung	Others	Total
Tg > 1 ng/ml (n = 5)	9	6	3	1	19
Tg < 1 ng/ml (n = 54)	103	4	4	5	116
Total	112	10	7	6	135

*Outside the thyroid bed.

TABLE 4
Anatomical Distribution of 20 Lesions Detected in 16 ^{131}I-Negative ^{201}Tl-Positive Studies

	Thyroid bed	Neck*	Lung	Others	Total
Tg > 1 ng/ml (n = 12)	3	4	—	8	15
Tg < 1 ng/ml (n = 4)	2	3	—	—	5
Total	5	7	—	8	20

*Outside the thyroid bed.

TABLE 5
Definitive Diagnosis in 13 Preablated Patients with ^{201}Tl-Positive and ^{131}I-Negative Scans

Diagnosis	Tg > 1 ng/ml	Tg < 1 ng/ml	Total
Thyroid carcinoma confirmed			
Histologic analysis	6	1*	7
High-dose ^{131}I uptake	3	—	3
Increase in Tg level	—	1	1
Clinical evidence (previous ^{131}I uptake)	—	1	1
Differentiated thyroid carcinoma ruled out			
Salivary gland disease	—	1	1

*Anaplastic

RESULTS

Comparison of ^{131}I and ^{201}Tl uptake in the 178 studies showed agreement between the two scans in 75 studies and disagreement in 103 studies. Of the 75 concordant results, 26 were in the preablation group and 49 were in the ablated group. Of the 103 discordant studies, 89 were in preablation and 14 were in ablated patients. The most striking finding in the preablation studies was the high incidence of discordant ^{201}Tl and ^{131}I scans. Overall, 115 studies were performed on 68 preablation patients and 63 studies were performed on 48 ablated patients.

Tables 1 and 2 give the results obtained for each pair of scans in terms of the patients' clinical status. Table 1 shows in the preablated group that ^{201}Tl and ^{131}I agreed in 26 of 115 studies (23%)—20 positive and 6 negative—and disagreed in 89 (77%).

Of the 20 studies in which ^{131}I and ^{201}Tl detected the same sites, Tg levels were detectable in 13 and the locations were mostly outside the thyroid bed. In the remaining seven studies, Tg was undetectable and uptake was located within the thyroid bed. The six studies with concordant negative ^{201}Tl and ^{131}I scans showed undetectable Tg levels, and all six were the first control studies after treatment with an ablative dose of ^{131}I.
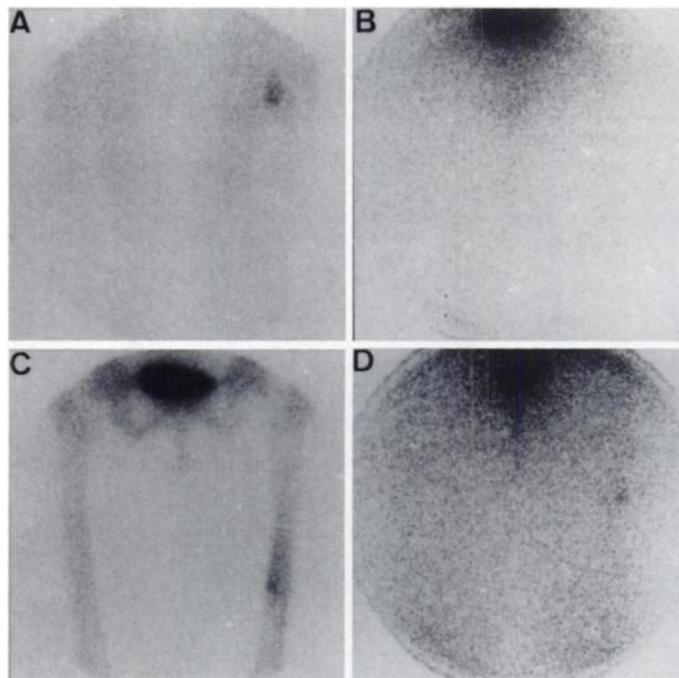
In 59 of the 89 discordant studies, only ^{131}I detected focal accumulation, and 54 of these were associated with undetectable Tg levels. Because of the importance of this finding, the distribution of the sites with these characteristics and the pattern of Tg levels in the patients in this subgroup will be analyzed below.

In 27 studies, both tracers detected focal uptake, but the pattern was different; that is, in the same patient some lesions were ^{201}Tl-positive but ^{131}I-negative, whereas others showed the opposite pattern (Fig. 1). In 19 of these 27 studies, Tg levels were detectable. For ^{131}I, uptake within the thyroid bed predominated, whereas, for ^{201}Tl, uptake was located outside the thyroid bed. There were 15 studies in which ^{201}Tl detected at

FIGURE 2. A 64-yr-old patient ablated for papillary carcinoma. (A) ^{201}Tl scan shows abnormal uptake in left leg. (B) The lesion does not take up ^{131}I and Tg concentration is 68 ng/ml. (C) Four weeks later, the lesion shows uptake in a bone scan. (D) Iodine-131 scan 6 mo later shows lesion uptake by the lesion; Tg concentration is 94 ng/ml.

least one site not detected by ^{131}I. In three studies, only ^{201}Tl-positive accumulation was observed, and in two of these Tg levels were detectable.

Table 2 shows that the two tracers agreed in 49 of the 63 studies. In 45 of these, both scans were negative, Tg levels being undetectable in 44 and detectable in one. In four studies, the ^{201}Tl and ^{131}I scans detected the same lesions. In all four cases, Tg levels were detectable and the sites corresponded to advanced metastases and recurrences. In 14 studies, the results for the two scanning techniques disagreed. In one, ^{131}I detected a site not detected by ^{201}Tl and the Tg level was undetectable. The most striking finding in this group of discordant studies was that in 13 studies, performed in 13 ablated patients, ^{201}Tl was the only tracer that identified focal activity; Tg levels were detectable in 10 studies, although they were in the slightly elevated range (16–180 ng/ml). Given the importance of these findings, they will now be analyzed in more detail.

Tables 3 and 4 give the relationship between the location of the lesion, the pattern of tracer uptake (^{131}I and ^{201}Tl) and the Tg in those patients with lesions concentrating only one tracer. Table 3 shows the Tg "pattern" versus location of 135 lesions that only concentrated ^{131}I and were detected in 59 preablation studies. Of the 59 studies, 54 had undetectable Tg levels, and

TABLE 6
Definitive Diagnosis in 13 Ablated Patients with ^{201}Tl-Positive and ^{131}I-Negative Scans

Diagnosis	Tg > 1 ng/ml	Tg < 1 ng/ml	Total
Differentiated thyroid carcinoma confirmed			
Histologic analysis	3	—	3
^{131}I uptake and histology	1	—	1
High-dose ^{131}I uptake	6	—	6
Increase in Tg and ^{131}I uptake	—	1	1
Differentiated thyroid carcinoma ruled out			
Salivary gland disease	—	2	2

TABLE 7
Results of 69 Studies Performed in Ablated Patients with a Definitive Diagnosis

	n	^{201}Tl +	^{201}Tl −	^{131}I +	^{131}I −	Tg (ng/ml) >1	Tg (ng/ml) <1
Metastases and/or recurrence	16	15	1	5	11	14	2
Disease-free	52	2	50	—	52	1	51
Sensitivity (%)		94		29		88	
Specificity (%)		96		100		98	
Positive predictive value (%)		89		100		94	
Negative predictive value (%)		98		81		96	

103 of the 116 detected lesions were within the thyroid bed. The remaining five studies showed detectable Tg levels, and 10 of the 19 detected lesions were outside the thyroid bed.

In Table 4, it can be seen that the 16 ^{131}I-negative and ^{201}Tl-positive studies revealed 20 lesions. In four studies with undetectable Tg levels, five lesions were detected, of which three were in the neck but outside the thyroid bed. In the 12 studies with detectable Tg levels, 15 lesions were identified, 12 being outside the thyroid bed.

It might be of greater interest to present the findings in terms of their clinical impact on the management of the patients. Of the 116 patients included in this assessment, 31 (27%) were shown by the ^{201}Tl scan to have at least one lesion not detected by ^{131}I, and, of these 31, 15 were in the preablation group and 16 in the ablated group. A definitive diagnosis of the nature of the sites showing only ^{201}Tl uptake was established in 26 patients, 13 in preablation (Table 5) and 13 ablated (Table 6).

Of the 13 preablation patients (Table 5), the presence of carcinoma was confirmed in 12. In seven, confirmation was histologic (Fig. 1); Tg levels were detectable in six patients and undetectable in one patient presenting anaplastic cells. Moreover, four of the seven patients did not show ^{131}I uptake, even at doses higher than those used for diagnostic scanning. The presence of DTC was excluded in only 1 of the 13 patients in whom a definitive diagnosis was reached; this patient showed accumulation in the salivary gland and Tg levels were undetectable.

Of the 13 ablated patients (Table 6), the presence of DTC was confirmed in 11. In three, confirmation was histologic and no ^{131}I uptake was observed after administration of a high dose in one of them. In eight patients, diagnosis was confirmed when ^{131}I uptake was observed after administration of a high dose. In one of the eight, diagnosis was also later confirmed histologically and another patient showed a gradual increase in Tg levels (Fig. 2). The presence of DTC was ruled out in only two patients with ^{201}Tl-positive and ^{131}I-negative scans. In both patients, uptake was localized in the salivary glands, associated Tg levels were undetectable, and the clinical picture was compatible with sialoadenitis.

In the group of ablated patients, it was possible to assess sensitivity and specificity, because, as residual thyroid tissue had been removed, the only lesions present were metastases or recurrent disease or both. Seventy-two studies were performed in 57 patients in whom ablation had been achieved and confirmed by gammagraphic techniques. Of these, 48 patients were originally included with this status, and a further nine were added in the course of the study when ablation was confirmed, as mentioned above. Three studies performed in three patients with lesions showing only ^{201}Tl uptake remain in the study, although the presence of disease has been neither confirmed nor excluded. In the other 69 studies in 54 patients, a final diagnosis was reached.

Table 7 shows that, overall, 16 studies revealed the presence of confirmed metastases in 14 patients. Thallium-201 showed uptake in 15 studies (sensitivity 94%) but did not in one study in which a metastasis in the cranial calotte, previously treated with ^{131}I, was associated with undetectable Tg levels. In contrast, ^{131}I showed uptake in only five cases (sensitivity 29%) but did not do so in 11 studies with detectable Tg levels. Overall, Tg levels were detectable in 14 studies (sensitivity 88%) and undetectable in two, one of which showed ^{201}Tl uptake. It can also be seen that 52 studies were performed in patients free of disease and that the specificity was similar for ^{201}Tl, ^{131}I and Tg. In this group, ^{201}Tl did not show uptake in

50 studies and in two accumulation was observed in the salivary glands of patients presenting sialoadenitis. There was no ^{131}I uptake in any of these studies, and Tg levels were undetectable in 51 studies and detectable in one (11 ng/ml), decreasing to undetectable levels 6 mo later.

DISCUSSION

After thyroidectomy, there are two possible clinical situations, preablation and ablated, with different therapeutic requirements. For preablation patients, ^{131}I is established as irreplaceable, since the postoperative existence of thyroid remnants showing ^{131}I uptake requires the application of metabolic radiotherapy at least for ablative purposes in order to achieve longer survival (14). In this situation, the role of ^{201}Tl, should it prove useful, would be complementary to that of [131]I.

After ablation, ^{131}I continues to be used for diagnostic purposes despite certain limitations: hypothyroidism associated with withdrawal of replacement therapy, delay before the scan can be performed and negative uptake by some Tg-producing lesions (15–20).

Several studies have been performed to evaluate the contribution of ^{201}Tl scintigraphy in both pre- and postablation (2,10,21). However, a detailed analysis of these studies shows that the situations considered were before ablation and after ablative treatment; that is, ablated patients are not defined as those patients in whom ablation has been confirmed gammagraphically before assessment by ^{201}Tl scintigraphy, but as patients evaluated after an ablative dose of ^{131}I, which may or may not have been successful. In fact, only those in whom the dose was successful should have been considered ablated, whereas the others, despite receiving an ablative dose, should have been regarded as preablation patients, since the ^{131}I scan will continue to detect the original uptake in the thyroid bed.

Thus, in contrast to previous reports, our patient population has been divided into preablation patients and ablated patients, the latter including only those patients in whom ablation was confirmed scintigraphically. This has allowed a clearer observation of the patterns for ^{201}Tl and ^{131}I accumulation in the different lesions found in the follow-up of DTC patients after thyroidectomy.

In preablation patients, sites showing only ^{131}I uptake were also seen to be predominantly associated with undetectable Tg levels and localization within the thyroid bed (Table 3). In our population, all patients evaluated immediately after thyroidectomy presented these sites, which are not observed after ablation (22). In the absence of histological confirmation, we can assume such sites hypothetically corresponding to tumor-free thyroid remnants, as has been reported previously (23,24). These findings suggest that the avidity of residual thyroid tissue for ^{131}I uptake is greater than its ability to secrete hormones and to produce detectable Tg levels.

We also noted that among preablation patients with detectable Tg levels there were more studies showing focal ^{201}Tl accumulation. These sites were usually localized outside the thyroid bed; in 15 of the 68 patients in preablation (22%) sites showing only ^{201}Tl uptake were detected whereas in the others ^{131}I uptake was observed (Table 1). In 12 of the 15 (80%) (Table 5), the presence of thyroid cancer was confirmed (11 DTC and 1 anaplastic).

Coexistence of lesions with different behavior for the two tracers in the same patient has been reported by other authors (1,9,10,21), but the clinical significance was not dealt with. The importance of this finding is that in these patients treatment with metabolic radiotherapy is unavoidable because of the presence of the ^{131}I-positive lesion. However, the finding of
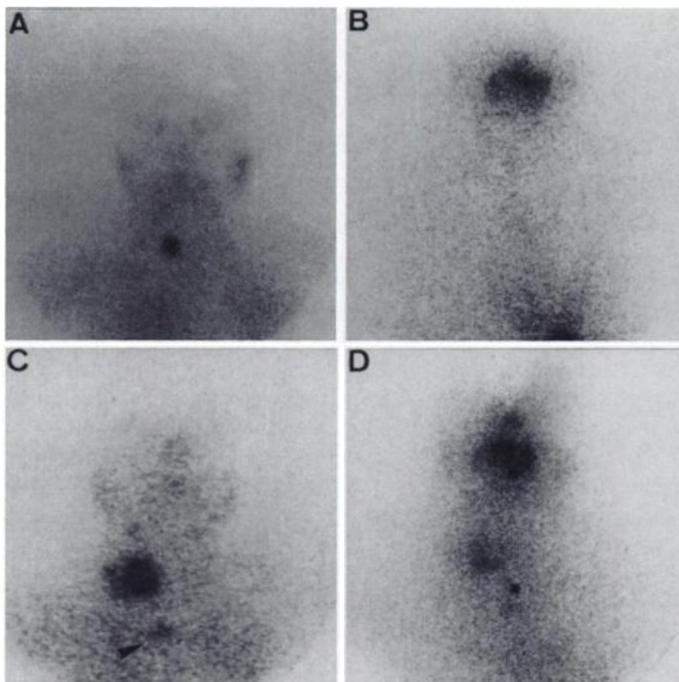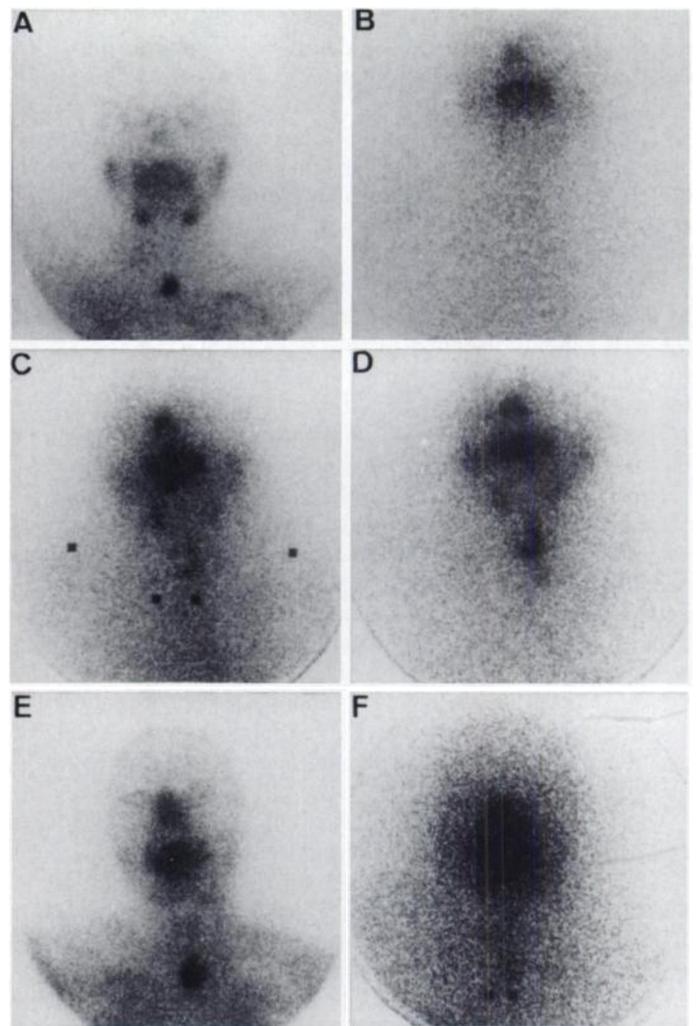
FIGURE 3. A 72-yr-old patient ablated for papillary carcinoma. (A) Thallium-201 scan shows abnormal uptake in right supraclavicular region. (B) Iodine-131 scan was negative, with TSH > 50 mIU/ml and TG 85 ng/ml. (C) A ^{201}Tl scan 1 yr later revealed an important increase in size of the known lesion and a new uptake focus (arrowhead). (D) The corresponding ^{131}I scan showed uptake in both lesions, although smaller in size and lower in intensity. Tg concentration was 1700 ng/ml. Histological analysis confirmed papillary carcinoma.

FIGURE 4. A 65-yr-old patient ablated for follicular carcinoma. In a follow-up study, ^{201}Tl scan (A) revealed uptake in a negative ^{131}I-lesion (B); Tg concentration was 40 ng/ml. One year later, a ^{131}I scan in the same region (C) showed region circular uptake with a central defect that appears to correspond to the previous ^{201}Tl uptake. (D) A 30-mCi ^{131}I scan did not revealed additional findings and Tg concentration was 89 ng/ml. (E) Six months later, ^{201}Tl scan showed an important growth of the lesion. (F) Positive ^{131}I scan; Tg concentration was 270 ng/ml. Histologic analysis revealed Hurthle cells and DTC.

sites showing only ^{201}Tl uptake may modify the clinical approach and lead to other specific therapeutic decisions besides ^{131}I treatment. In our study, the finding of only ^{201}Tl uptake justified sending seven patients for further surgical treatment (Fig. 1). More significantly, in six of the seven patients, histologic examination confirmed the presence of DTC and, in the other, of anaplastic thyroid cancer. Moreover, five of these patients did not show ^{131}I uptake at high doses (30 mCi).

These results favor the use of ^{201}Tl to diagnose spread in the presence of thyroid remnants postoperatively (1,2,4,5,25) and provide an answer to the question raised by Boyd (26) in 1990 concerning the usefulness of ^{201}Tl when ^{131}I uptake is present.

In the group of preablation patients, the better detection rate of ^{201}Tl compared with ^{131}I for lesions with DTC, in contrast to what occurred when the uptake foci were located within the thyroid bed, might be explained by the increased metabolism of the tumor, which would enhance ^{201}Tl uptake (27). Moreover, the absence of uptake of ^{131}I would be explained hypothetically by the dedifferentiation that DTC is reported to undergo in its natural history (28-31). However, in contrast, these patients showed raised Tg (12-392 ng/ml). Therefore, it could be suggested that there is not enough differentiation for the lesions to take up ^{131}I but enough for producing Tg.

The lower affinity reported by other authors (2,24) of tumor-free residual thyroid tissue for ^{201}Tl as compared with tissue with DTC may be due to the lower metabolic rate of the cells and/or to the small amount of tissue, which does not allow concentration of enough ^{201}Tl for detection, since attenuation of ^{201}Tl due to organic tissues is greater than that of ^{131}I. Thus, tumor-free remnants of some size can be detected, and several solutions have been proposed to optimize the methodology, including use of SPECT (1,25). The nonspecificity of ^{201}Tl with regard to residual thyroid tissue has occasionally been reported in the literature. Thus, Tonami and Hisada (4) noted that a large

amount of residual thyroid tissue can show ^{201}Tl accumulation, as observed after hemithyroidectomy. Support for this theory comes not only from our observations but also from the finding by Ramanna et al. (2) that some patients assessed months after receiving a dose of 100 mCi of ^{131}I presented focal ^{201}Tl and ^{131}I uptake associated with undetectable Tg levels. Such findings, as well as those of others (21) and those of this study, can be explained by the amount of residual tissue.

In our group of ablated patients, the peculiarity of the study design (i.e., prior gammagraphic confirmation of ablation) allowed evaluation of ^{201}Tl and ^{131}I in the two possible situations: patients free of disease and patients presenting tumor tissue. Unlike the approach used in other studies (2,10), our approach meant that any uptake observed within the thyroid bed could be considered as recurrent disease, since the possibility of incomplete ablation had been excluded. This approach also allowed us to assess the figures for sensitivity and specificity obtained for our population (Table 7), which for ^{201}Tl at 94% and 96%, respectively, are among the highest reported (1,3,13). In contrast, despite the maximum specificity, 100%, of the ^{131}I

scan, the sensitivity is, together with that of Tonami and Hisada (4), extremely low compared with that of ^{201}Tl.

Although very high ^{201}Tl sensitivity and specificity have been reported by other authors (1,3,13), differences in the approaches adopted in the studies makes comparison difficult because of the different criteria used. Also, the different criterion for separating preablation and ablated patients in some studies (2,10) will make the sensitivity for ^{131}I higher, since uptake by the incompletely ablated thyroid tissue will be detected. In other studies (8), ^{131}I scans performed with therapeutic doses of up to 100 mCi were included, whereas we used diagnostic doses of 4 mCi. Finally, some studies were performed on a very small number of cases (23) or on highly selected populations (5,6).

In the group of ablated patients, of great interest is the relationship that ^{201}Tl and ^{131}I uptake show with Tg levels. There was a clear association between positive ^{201}Tl scans and Tg levels; in fact, in the only case of a tumor lesion in which a positive ^{201}Tl scan was associated with an undetectable Tg level initially, there was a subsequent gradual rise in Tg. In contrast, there was considerable discrepancy between Tg levels and ^{131}I scans, the latter being negative in 10 cases showing detectable Tg levels. These 10 patients with confirmed DTC showed slightly elevated Tg levels, ranging from 16 to 180 ng/ml, which might be explained by the their lower functional ability to take up ^{131}I. Therefore, it should be tempting to assume that the differentiation underwent by those lesions was enough to account for the absence of ^{131}I uptake, at diagnostic dosis, but not to prevent the Tg production.

· However, it is significant that of the four patients who initially had detectable Tg levels with positive ^{201}Tl and negative ^{131}I scans and who later showed a gradual increase in Tg with a positive ^{131}I scan at diagnostic doses, in two patients the histologic analysis of the lesions ruled out the presence of dedifferentiated tissue and confirmed the diagnosis of DTC (Fig. 3). This seems to contradict the previous explanations claiming that dedifferentiation is the only mechanism leading to accumulation of ^{201}Tl but not of ^{131}I (28–31). In this sense, it is also possible that different parts, even of small lesions, with different degrees of dedifferentiation could show different avidity for the two tracers. This would be supported by the example shown in Figure 4, and it agrees with recently published reports (31).

The problem of the nonspecificity of ^{201}Tl scintigraphy has been addressed previously (1,25). We would recommend that these patients have a more exhaustive follow-up centered on the course shown by tracer uptake and Tg levels. As a result, in our population, there were only three false-positives for the ^{201}Tl scan, all with uptake localized in the salivary glands and undetectable Tg levels throughout the follow-up. Moreover, in all three cases, the localization and characteristics of focal uptake leave little or no doubt that it is the salivary glands that are involved.

The clinical significance of the inclusion of ^{201}Tl scintigraphy in the follow-up of our patients with DTC is reflected in the detection of sites showing only ^{201}Tl uptake in 27% of the population (31/116), 26% (18/68) of preablation patients and 27% (13/48) of ablated patients. The most significant aspects of these results are not only that DTC was confirmed in 23 of the 26 patients for whom a definitive histologic diagnosis was established but also that detection of ^{201}Tl uptake led to a change in the clinical treatment of these patients.

The therapeutic strategy was modified in 12 patients who were sent for further surgery and/or external radiotherapy, as most of them did not show ^{131}I uptake even after administration of higher doses (30 mCi). In the other 11 patients, administration of high doses (up to 30 mCi) of ^{131}I showed positive activity and the strategy of metabolic treatment was maintained. Thus, the contribution of ^{201}Tl was an intensification or change in ^{131}I scintigraphy reflected in the administration of higher doses.

In conclusion, our study indicates that ^{201}Tl scintigraphy should be included in the follow-up of DTC both in preablation and ablated patients. In preablation patients, it can be used in addition to the ^{131}I scan in the first post-thyroidectomy control study to detect the presence of sites showing only ^{201}Tl uptake because of its ability to detect ^{201}Tl-positive DTC lesions, which will usually be located outside the thyroid bed. In ablated patients, a disease-free situation means that follow-up could be based only on ^{201}Tl scintigraphy and Tg determinations. After ablation, detection of a ^{201}Tl-positive lesion should be followed by a high-dose ^{131}I scan, especially if Tg is detectable.

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Standardized Uptake Value and Quantification of Metabolism for Breast Cancer Imaging with FDG and L-[1-^{11}C]Tyrosine PET

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The aims of the study were to compare the value of L-[1-^{11}C]tyrosine (TYR) and [^{18}F]fluoro-2-deoxy-D-glucose (FDG) as tumor tracers in patients with breast cancer, to investigate the correlation between quantitative values and standardized uptake values (SUVs) and to estimate the value of SUVs for the evaluation of therapy. **Methods:** Eleven patients with one or more malignant breast lesions and two patients with one or more benign breast tumors were studied with TYR and FDG. Doses of 300 MBq of TYR and 230 MBq of FDG were given intravenously. All PET sessions were performed using a Siemens ECAT 951/31 camera. Of 10 malignant tumors and the 3 benign lesions, glucose consumption and protein synthesis rate were quantified. All lesions were studied using SUVs based on body weight, body surface area and lean body mass, with and without correction for plasma glucose or tyrosine levels. **Results:** All malignant tumors were visualized with both FDG and TYR, but the visual contrast was better with FDG. Increased uptake of the tracers was seen in patients with fibrocystic tissue and complicated the visual assessment and the outlining of tumor tissue. Uptake in fibrocystic disease was more prominent with FDG than with TYR. No difference in tumor/nontumor ratio between the two tracers could be established. FDG showed a false-positive result in one benign lesion. No major differences between the SUVs as defined above were found, although the best correlation between glucose consumption and the SUV was observed when the SUV was based on body surface area and corrected for plasma glucose level (r = 0.85–0.87). The SUV based on lean body mass was found to correlate best with protein synthesis rate (r = 0.83–0.94). **Conclusion:** In this group of patients, TYR appears to be a better tracer than FDG for breast cancer imaging, because of lower uptake in fibrocystic disease. SUVs correlate well with quantitative values, but future studies must determine whether treatment evaluation is also reliable with SUVs.

Key Words: PET; standardized uptake value; fluorine-18-FDG; carbon-11-tyrosine; breast cancer

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Glucose metabolism of many malignant tumors is high compared to normal tissues. This fact is used in PET with the glucose analog [^{18}F]fluoro-2-deoxy-D-glucose (FDG) to visualize tumors and to analyze and quantify their metabolism. PET with FDG has proven to be a sensitive method with a high negative predictive value for the visualization of primary breast tumors and the detection of metastases, at least if a correction for attenuation has been made (*1–6*). However, with FDG, one cannot differentiate between viable tumor tissue and inflammatory tissue, which may cause problems in sequential imaging for treatment evaluation (*7,8*). Therefore, it would be better to apply tracers such as amino acids that are less avidly metabolized by inflammatory cells. In animal studies, carboxyl-labeled amino acids appeared to be the best amino acids for quantitative PET (*9,10*). At our institution, L-[1-^{11}C]tyrosine (TYR) is used. Breast cancer can be visualized with this tracer (*11,12*). The uptake of TYR is increased due to a high protein synthesis rate (PSR) (*13*), and the PSR can be quantified using the method described by Willemsen et al. (*14*). Whereas absolute quantification may have its advantages, e.g., in treatment evaluation, quantifying metabolism with PET requires a prolonged study time to calculate a time–activity curve and also requires arterial cannulation or arterialized venous cannulation with repeated blood sampling to obtain the plasma input function. Therefore, a PET study seems to be cumbersome for most patients. In a strive for "unbloody PET," many centers have adopted standardized uptake values (SUVs). This value gives a measure of uptake in the region of interest relative to a uniform distribution over the body. (*15*) With the application of SUVs, PET is less constraining, due to a shorter acquisition time and the omission of repeat blood sampling. The use of SUVs is widespread, despite reports of considerable drawbacks in their application (*16,17*). The SUV of many tissues shows a strong positive correlation with weight, because fat has a much lower uptake of both FDG and TYR (Fig. 1). Consequently, results may not be comparable if patients do not have the same weight and habits. When a patient is losing weight during cancer treatment, the PET results using SUVs after therapy should also be interpreted with caution. SUVs based on body surface area (BSA) or lean body mass (LBM) may therefore be preferable to body weight (BW). A quantitative approach would avoid this problem.

In this study, TYR and FDG were compared for their usefulness as a tumor tracer in a group of patients clinically and mammographically suspect for breast cancer. Moreover, the