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REFERENCES

1. Silverberg E, Boring CE, Squires TS. Cancer statistics, 1990. *CA* 1990;40:9–26.
2. Pressman D, Korngold D. The in vivo localization of anti-Wagner osteogenic sarcoma antibodies. *Cancer* 1953;6:619–625.
3. Goldenberg DM, Deland F, Kim EE, et al. Use of radiolabeled antibodies to carcino-embryonic antigen for the detection and localization of diverse cancers by external photoscanning. *N Engl J Med* 1978;298:1384–1390.
4. Goldenberg, DM, Larson SM. Radioimmunodetection in cancer identification. *J Nucl Med* 1992;33:803–814.
5. Colcher D, Hand HP, Nuti M, et al. A spectrum of monoclonal antibodies reactive with human mammary tumor cells. *Proc Natl Acad Sci USA* 1981;78:3199–3203.
6. Keenan AM, Colcher D, Larson SM, et al. Radioimmunoscintigraphy of human colon cancer xenografts in mice with radioiodinated monoclonal antibody B72.3. *J Nucl Med* 1984;25:1197–1200.
7. Renda A, Salvatore M, Sava M, et al. Immunoscintigraphy in the follow-up of patients operated on for carcinoma of the sigmoid and rectum. Preliminary report with a new monoclonal antibody B72.3. *Dis Colon Rectum* 1987;30:683–686.
8. Esteban JM, Colcher D, Sugarbaker P, et al. Quantitative and qualitative aspects of radiolocalization in colon cancer patients of intravenously administered MAb B72.3. *Int J Cancer* 1987;39:50–59.
9. Doerr RJ, Abdel-Nabi H, Krag D, et al. Radiolabeled antibody imaging in the management of colorectal cancer. *Ann Surgery* 1991;214:118–124.
10. Abdel-Nabi H, Herrera L, Evans N, et al. Indium-111 CYT-103 MoAb imaging in patients with suspected recurrent colorectal cancer [Abstract]. *J Nucl Med* 1991;32: 1053.
11. Collier BD, Abdel-Nabi H, Doerr RJ, et al. Immunoscintigraphy performed with In-111-labeled CYT-103 in the management of colorectal cancer: comparison with CT. *Radiology* 1992;185:179–186.
12. Loy TS, Nashelsky MB. Reactivity of B72.3 with adenocarcinomas. An immunohistochemical study of 476 cases. *Cancer* 1993;72:2495–2498.
13. Roselli M, Hitchcock CL, Molinolo A, et al. Autoradiographic evaluation of radiolabeled monoclonal antibody B72.3 distribution in tumor and lymph nodes of adenocarcinoma patients. *Anticancer Res* 1995;15:975–984.
14. Virgolini I, Raderer M, Angelberger P, et al. Vasoactive intestinal peptide (VIP) receptor imaging for the localization of intestinal adenocarcinomas and carcinoid tumors. *N Engl J Med* 1994;331:1116–1121.
15. Schwartz CJ, Kimberg DV, Sheerin HE, et al. Vasoactive intestinal peptide stimulation of adenylate cyclase and active electrolyte secretion in intestinal mucosa. *J Clin Invest* 1974;54:536–544.
16. Cohn J. Vasoactive intestinal peptide stimulates protein phosphorylation in a colonic epithelial cell line. *Am J Physiol* 1987;16:420–424.
17. Pincus DW, DiCicco-Bloom EM, Black IB. Vasoactive intestinal polypeptide regulates mitosis, differentiation and survival of cultured sympathetic neuroblasts. *Nature* 1990;343:564–567.
18. Haegerstrand A, Jonzon B, Daalsgard CJ, et al. Vasoactive intestinal polypeptide stimulates cell proliferation and adenylate cyclase activity of cultured human keratinocytes. *Proc Natl Acad Sci USA* 1989;86:5993–5996.
19. Virgolini I, Yang Q, Li SR, et al. Cross-competition between vasoactive intestinal peptide (VIP) and somatostatin for binding to tumor cell receptors. *Cancer Res* 1994;54:690–700.
20. Battari A, Martin JM, Luis J, et al. Solubilization of the active vasoactive intestinal peptide receptor from human colonic adenocarcinoma cells. *J Biochem Res* 1989;263: 17685–17689.
21. Sreedharan SP, Robichon A, Peterson KE, et al. Cloning and expression of the human vasoactive intestinal peptide receptor. *Proc Natl Acad Sci USA* 1991;888:4986–4990.
22. Svoboda M, Neef de P, Tastenoy M, et al. Molecular characteristics and evidence for internalization of vasoactive intestinal peptide receptors in the tumoral rat pancreatic acinar cell line AR 4-2J. *Eur J Biochem* 1988;176:707–713.
23. Virgolini I, Kurtaran A, Raderer M, et al. Vasoactive intestinal peptide receptor scintigraphy. *J Nucl Med* 1995;36:1732–1739.
24. Virgolini I, Muller C, Klepetko W, et al. Human hepatocellular cancers show a decreased prostaglandin E_1 binding capacity. *Br J Cancer* 1990;61:937–941.
25. Virgolini I, Sillaber C, Majdic O, et al. Characterization of prostaglandin binding sites expressed on human blood basophils. Evidence for a prostaglandin E_1, I_2 and D_2 receptor. *J Biol Chem* 1992;267:12700–12708.
26. Scatchard G. The attraction of proteins for small molecules and ions. *Ann NY Acad Sci* 1949;51:660–672.
27. Greiner JW, Guadagni F, Goldstein D, et al. Intraperitoneal administration of interferon gamma to carcinoma patients enhances expression of tumor-associated glycoprotein-72 and carcinoembryonic antigen on malignant ascites cells. *J Clin Oncol* 1992;10:735–746.
28. Becherer A, Raderer M, Scheithauer W, et al. Evaluation of in vivo targeting of adenocarcinomas with ^{111}In-CYT-103 antibody under treatment with interferon gamma [Abstract]. *J Nucl Med* 1994;35:85–86.
29. Vijayakumar V, Blend MJ, Johnson DK, et al. Improved detection of hepatic lesions using MoAb B72.3 and a modified ^{111}In labeling technique in patients with recurrent colon cancer. *Nucl Med Commun* 1993;14:658–666.
30. Lamki LM, Podoloff DA, Singletary SE, et al. Indium-111-labeled B72.3 monoclonal antibody in the detection and staging of breast cancer: a phase I study. *J Nucl Med* 1991;32:1326–1332.
31. Serafini AN, Vargas-Cuba R, Bendetto P, et al. Technetium-99m-labeled Fab fragment of anti-CEA monoclonal antibody for the radioimmunodetection of colorectal adenocarcinoma. *Antibody Immunoconjugates Radiopharm* 1991;4:561–567.
32. Patt YZ, Podoloff DA, Curley S, et al. Technetium-99m-labeled IMMU-4, a monoclonal antibody against carcinoembryonic antigen, for imaging of occult disease in patients with rising serum carcinoembryonic antigen levels. *J Clin Oncol* 1994;12: 489–495.

Thallium-201 and Iodine-131 Scintigraphy in Differentiated Thyroid Carcinoma

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The purpose of this study was to determine the concordance and discordance between diagnostic ^{131}I and ^{201}Tl whole-body scintigraphy in patients with differentiated carcinoma of the thyroid. **Methods:** Following thyroidectomy for differentiated thyroid carcinoma, 50 patients underwent whole-body ^{131}I and ^{201}Tl scanning (60 pairs of scans in total). Fifteen pairs of studies were obtained before ablative therapy, 30 pairs after ablative therapy and 15 pairs after ^{131}I therapy for metastatic disease. Serum thyroglobulin levels were concurrently determined by radioimmunoassay. **Results:** Thirty-six ^{131}I whole-body scans (in 34 patients) showed residual uptake in the neck, but only six (17%) of the corresponding whole-body thallium studies had detectable uptake in the neck. Fourteen ^{131}I scans (in nine patients) identified multiple metastatic lesions, whereas the thallium scans were interpreted as either negative, nonspecific or showing fewer lesions. In four study pairs, the thallium scans showed solitary lesions that were not detected by the corresponding radioiodine scans. In 16 scans, the thallium studies gave false-positive results. **Conclusion:** Iodine-131 scintigraphy for differentiated thyroid carcinoma is more sensitive and more specific than ^{201}Tl scintigraphy for detection of distant metastases and residual activity in the neck following thyroidectomy.

Key Words: thyroid carcinoma; thyroidectomy; iodine-131; thallium-201; thyroglobulin

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Thyroid cancer is the most frequently diagnosed malignant endocrine lesion. The incidence in the United States is approximately 15,600 new cases occur annually, with 1200 deaths each year (*1*). Most of these tumors are well-differentiated and

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show slow progression. Survival even in patients with metastatic (*2*). Serial determination of serum thyroglobulin (Tg) levels have been shown to beuseful in detecting recurrence after thyroid ablation (*3*). Prolonged follow-up is necessary and nuclear scintigraphy is often crucial to management decisions in these patients.

Radioiodine undergoes concentration and organification in the thyroid gland and is used extensively to study function and for thyroid imaging (*3*). Although whole-body ^{131}I scintigraphy (WBI) is highly specific for detecting recurrent thyroid cancer, it has certain limitations. For example, it has a need for a prolonged period of thyroid hormone withdrawal, restriction of dietary iodine intake, repeated patient visits and administration of a relatively high radiation dose. Thallium-201, on the other hand, has a relatively low radiation exposure, allowing immediate imaging after injection. Thus, there is no need for preparative thyroid hormone withdrawal. Thallium-201 scintigraphy is increasingly utilized for detection and follow-up of thyroid cancer. The role of ^{201}Tl scintigraphy in the management of patients with thyroid carcinoma is still controversial. Some investigators have suggested that whole-body ^{201}Tl scintigraphy (WBT) is more sensitive than WBI for the detection of recurrent or metastatic differentiated thyroid carcinoma (*4*).

The purpose of this study was to determine the concordance and discordance rates between diagnostic studies with ^{131}I and ^{201}Tl whole-body scintigraphy in patients post-thyroidectomy for differentiated thyroid carcinoma.

MATERIALS AND METHODS

Patients

The study population consisted of 50 patients with differentiated thyroid carcinoma. There were 30 women and 20 men with a mean age of 51 yr (range 24–79 yr). Forty-two patients (84%) had papillary adenocarcinoma of the thyroid and eight (16%) had follicular carcinoma. Forty-four patients underwent total or near total thyroidectomy, three patients underwent subtotal thyroidectomy and three patients had a hemi-thyroidectomy. Lymph node sampling was performed as indicated during surgery. Sixty pairs of ^{131}I and ^{201}Tl scans were performed within 1 wk of each other in these 50 patients. Patients who had only ^{201}Tl or ^{131}I scans or both scans more than 1 wk apart were excluded from the study.

Fifteen pairs of studies were obtained 6 wk after surgical thyroidectomy, 30 pairs of studies were performed after surgery and ^{131}I ablative therapy and 15 pairs of studies were performed after ^{131}I therapy for metastatic thyroid carcinoma. All studies were performed after withdrawal of levothyroxine and adequate endogenous TSH stimulation (>50 mIU/liter). Concurrent radioimmunoassays were performed to measure serum thyroglobulin levels along with screening of serum for anti-thyroglobulin antibodies.

Patient Follow-Up

Patients were followed for a period of 6 mo to 3 yr after surgery. The diagnosis of residual, recurrent or metastatic thyroid cancer was based on clinical examination, serum thyroglobulin measurements, bone scans, CT imaging, fine needle aspiration, cytology and biopsy. Patients with no clinical findings, negative radiological examination, negative ^{201}Tl and ^{131}I scans and low Tg levels (<5 ng/ml) on repeated examinations were considered to be free of disease.

Patients with neck foci greater than 1% uptake on ^{131}I scans were treated by ablation. Patients with foci with less than 1% uptake were also treated if: (a) the patient had additional foci in the neck or distant metastases at the time of surgery; (b) the cancer was reported to have invaded the thyroid capsule; or (c) the patient had a tumor involving the lymph nodes.

Radioiodine Scans

The diagnostic dose of ^{131}I ranged from 1 to 10 mCi (37–370 MBq). Most of the patients (44/50), however, were imaged with a 10-mCi dose. Scintigraphy was performed 48 hr after oral administration of radioiodine. A 16% symmetric window was centered at 364 keV using a wide-range, medium-energy collimator. Anterior and posterior whole-body images were obtained. The ^{131}I uptake in the thyroid bed was measured 24 hr after administration in all patients and the results expressed as the percentage of ingested activity. Pinhole views of the thyroid bed were also obtained in all patients 24 hr after the administration of radioiodine.

Thallium-201 Scintigraphy

WBT scans were performed 10 min following an intravenous dose of 4 mCi (148 MBq) ^{201}Tl-chloride. A 16% symmetric window was centered at 71 keV using a low-energy collimator, and anterior and posterior sequential 5-min images of the whole body were obtained. The WBT scans were performed 1–7 days before the WBI studies.

Scan Interpretation

The ^{201}Tl and ^{131}I scans were interpreted as abnormal if focal increased uptake of the radiopharmaceuticals in pattern and location consistent with metastatic disease was demonstrated. Diffusely increased uptake of ^{201}Tl in the lungs was considered a nonspecific finding, and not diagnostic of metastases. Any focal uptake in the thyroid bed was considered positive for the presence of functioning tissue.

RESULTS

Sixty pairs of ^{131}I and ^{201}Tl scans among the 50 patients were analyzed. Thirty-six scans in 34 patients showed residual uptake in the neck on the WBI studies. Thirty percent (11/36) of scans had >1% uptake in the neck at 24 hr after administration of radioiodine. Only six of the 36 (17%) corresponding WBT scans showed detectable uptake in the neck (Table 1).

In 14 scans (nine patients), the findings on WBI scans were consistent with metastatic thyroid cancer, whereas the WBT scans were either negative (five scans), had nonspecific findings (three scans) or were interpreted as showing fewer lesions compared to the WBI scans (six scans). In the last group, one patient showed multiple bone and pulmonary lesions on the WBI scan and only one skull lesion on the WBT scan (Fig. 1). Another patient had multiple bone lesions on the WBI scan and only two lesions (skull and chest) on the WBT scan.

In four scans (four patients), the thallium studies were more revealing than the radioiodine studies: one patient had a rib lesion on the WBT scan that was detected on a bone scan (Fig. 2) but showed no iodine uptake. Another patient had focal uptake in the left chest on the WBT scan that was not detected with a diagnostic dose of 1 mCi ^{131}I. His postablative WBI scan

TABLE 1
Correlation of Thallium-201 and Iodine-131 Imaging in Patients after Thyroidectomy

	^{201}Tl + (N)*	^{201}Tl − (N)*	^{201}Tl + (M)†	^{201}Tl − (M)†	Total
^{131}I + (N)*	6	30			36
^{131}I − (N)*	1	23			24
^{131}I + (M)†			6	8	14
^{131}I − (M)†			3	43	46
Total	7	53	9	51	

*Neck uptake.
†Metastatic disease outside the neck.

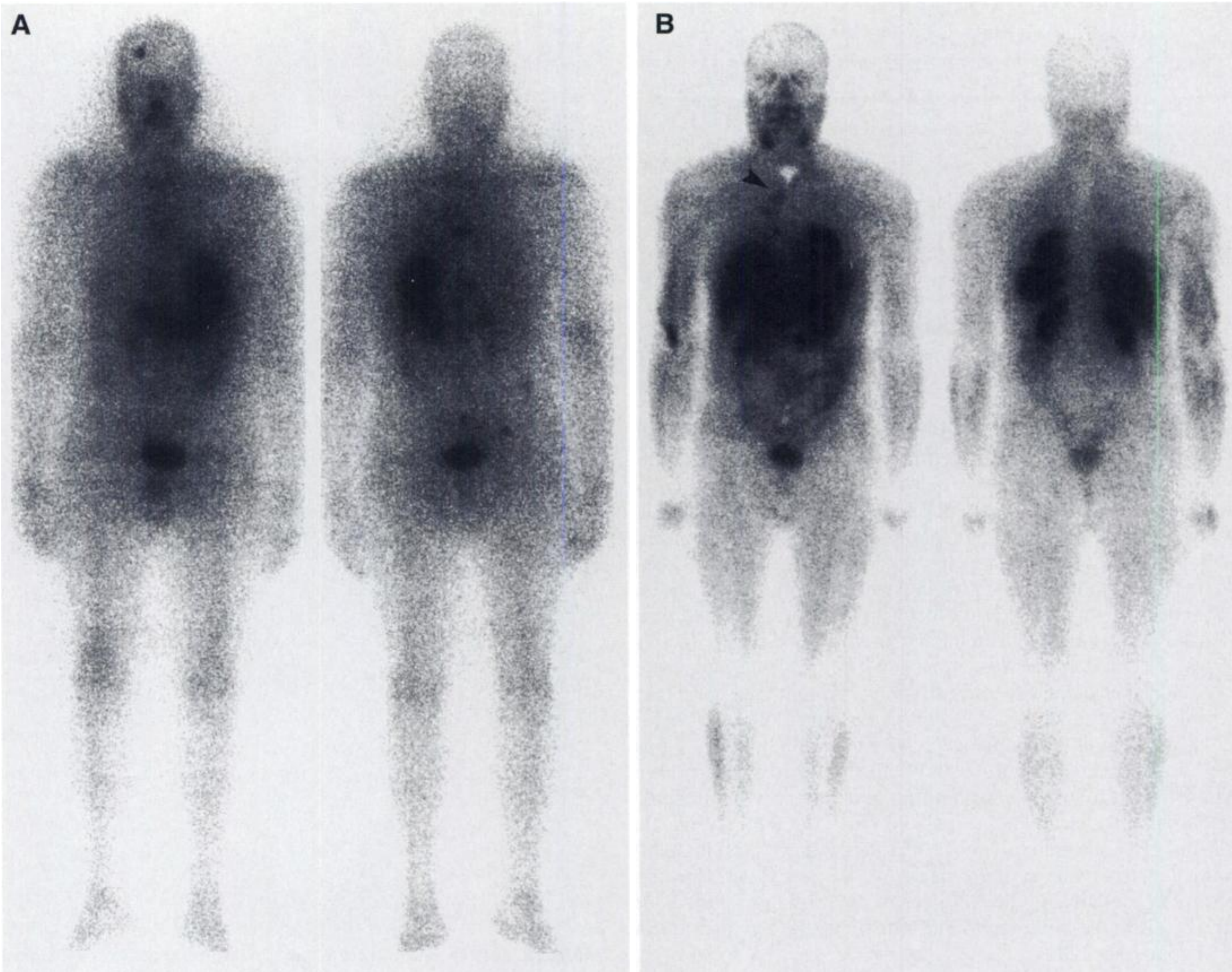

FIGURE 1. A 51-yr-old man with mixed papillary thyroid carcinoma. Iodine-131 whole-body images (A) show multiple metastases in the spine, pelvis and right skull. The whole-body thallium scan (B) shows less intense uptake in the right skull lesion but no detectable lesions in the spine or pelvis. A focus in the right chest (arrow) is not visualized on the ^{131}I scan.

performed after the oral administration of 75 mCi ^{131}I confirmed the findings of the WBT scan and demonstrated pulmonary parenchymal uptake. The third patient had a lymph node metastasis in the neck that was not detected on the WBI scan.

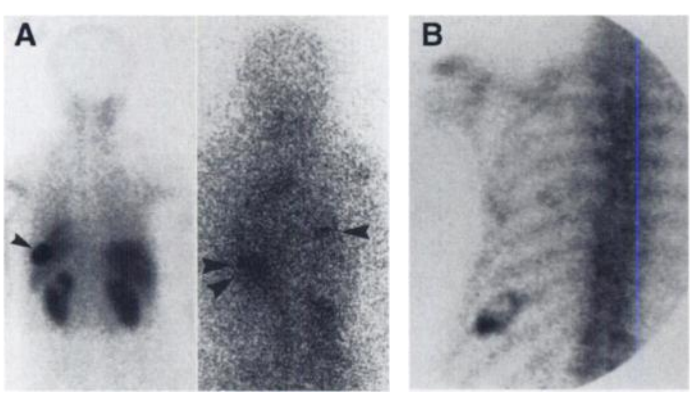

FIGURE 2. A 79-yr-old woman with papillary thyroid carcinoma. The posterior view of the thallium scan (A, left) demonstrates an intense focus of activity in the left lower posterior chest (arrow). Corresponding iodine scan (A, right) shows no detectable lesion at this site but another rib lesion in the right posterior chest (small arrow). Stomach activity is marked with double arrows. Spot view from a ^{99m}Tc-methylene diphosphonate scan (C) shows a lytic lesion in the left posterior 9th rib.

The fourth patient had more lesions on the WBI scan. One lesion in the right chest seen on the WBT scan, however, failed to accumulate radioiodine (Fig. 1). Serum thyroglobulin levels were significantly elevated in these patients.

In 16 patients, the thallium scans showed areas of abnormal uptake that were proven to be false-positive for disease by clinical follow-up, repeat WBI and WBT studies and low serum Tg levels. Table 2 lists the sites of false-positive uptake on WBT scans. The most common site of false-positive uptake was in the right lower mediastinum (Fig. 3). Seven additional patients had diffusely increased lung uptake which was not considered positive for disease.

DISCUSSION

The advantages of ^{201}Tl scintigraphy include low radiation exposure relative to ^{131}I scintigraphy, immediate imaging after injection, the convenience of a complete study in a single visit, no restriction of dietary iodine intake and no need for thyroid hormone withdrawal that may result in symptomatic hypothyroidism. Thyroid cancer metastases accumulate radioiodine less avidly than normal thyroid tissues and high levels of circulating thyroid stimulating hormone (TSH) are necessary to enhance radioiodine uptake before scanning. Elevated TSH levels may potentially stimulate the growth of thyroid carcinoma (*5*).

TABLE 2
False-Positive Findings on Thallium-201 Scans

Location	No. of patients
Right axilla	2
Chest	9
Right shoulder	1
Right gluteal	1
Right pelvis	1
Muscles of right hand	1
Right sacroiliac joint	1

Although radioiodine scintigraphy is more specific for thyroid carcinoma, it cannot differentiate locally recurrent tumor from normal residual thyroid tissue after thyroidectomy, adding to the difficulty in interpretation.

Lida et al. (*6*) reported a diagnostic accuracy of 86.9% for ^{201}Tl scintigraphy. Seven of ten patients, however, with negative ^{201}Tl scans and elevated Tg levels were subsequently diagnosed with recurrent or metastatic lesions. Ramanna et al. (*4*) reported that 29% of patients in their series had localized neck and chest abnormalities on ^{201}Tl scans that were not seen on the ^{131}I studies subsequently proven to represent tumor. Consequently, they suggested that ^{201}Tl is more sensitive than ^{131}I for detection of differentiated thyroid carcinoma. In this series, the ^{201}Tl scans were done 6 wk prior to the diagnostic ^{131}I studies, using an exceptionally long imaging time of 15 min per view. Hoefnagel et al. (*7*) reported a sensitivity of 94% for ^{201}Tl scintigraphy but only 48% sensitivity for ^{131}I scintigraphy. The respective specificity of both studies was comparably high (97% versus 99%). No information was provided regarding the time interval between ^{201}Tl and ^{131}I scans. Similarly, Tonami (*8*) reported a higher sensitivity for ^{201}Tl imaging compared to ^{131}I after thyroidectomy. He postulated that the poor results obtained with ^{131}I may be due to shorter periods of thyroid hormone withdrawal and insufficiently elevated levels of endogenous TSH.

In contrast to these reports, the present study shows that ^{131}I is more sensitive in detecting distant metastases as well as normal residual thyroid tissue postoperatively. Similarly, Dadparvar et al. (*9*) found only a 36% concordance rate between ^{131}I and ^{201}Tl scan findings in the presence of disease, with ^{131}I imaging being more sensitive and specific compared to ^{201}Tl. Brendel et al. (*10*) reported a low detection rate of 45% for thallium compared to 84% for imaging with ^{131}I administered in therapeutic doses. Underestimation of the extent of disease by ^{201}Tl may affect patient management, e.g., external beam radiation for a single bony lesion versus ^{131}I therapy for multiple lesions, or by altering therapeutic doses of ^{131}I for different extent or location of lesions.

We also observed a significant number of nonspecific and false-positive thallium studies which may lower the specificity of this imaging modality. Thallium is normally taken up by the lungs and is slowly cleared. Incomplete clearance may explain the mild diffuse uptake noted in seven of our patients. Although in patients without evident metastatic disease this finding is nonspecific, diffuse lung uptake in patients with pulmonary metastases may obscure mild focal activity. Focal uptake in the chest was also observed in nine patients, localizing to the right lower mediastinum. This characteristic pattern of uptake in the chest is apparently a normal variant. Increased uptake in the axilla and shoulder was noted in three patients with subcutaneous infiltration of the thallium dose and may reflect lymphatic drainage of the radioisotope. Pelvic uptake of thallium may be secondary to normal concentration of activity in the bowel. Foci in the abdomen that are usually attributed to bowel activity may also cause confusion. These potential false-positive results should be recognized as normal variants by careful review of the scans and evaluation of injection sites.

FIGURE 3. Anterior view of whole-body thallium scan delineates a typical focus of increased activity in the right lower mediastinum, just to the right of the midline (arrow).

Four patients in our study showed solitary lesions on the WBT studies that were not detected by the WBI scans. Failure of known residual thyroid cancer or metastases to concentrate a significant amount of radioiodine may be caused by inadequate TSH stimulation, high concentrations of inorganic iodine in the serum, or may also be due to the inherent biologic characteristics of the cancer. Radiation therapy in some patients with metastatic papillary thyroid carcinoma may result in anaplastic conversion and loss of the ability to concentrate radioiodine (*11*). It has also been suggested that therapeutic doses of ^{131}I may preferentially destroy more differentiated subpopulations of thyroid cancer that have the capacity to accumulate ^{131}I (*12*).

CONCLUSION

Our data indicate that WBI imaging with ^{131}I is more accurate than ^{201}Tl imaging in patients with differentiated thyroid cancer. The specificity of the WBT scans can be significantly improved by recognition of normal variants and careful reading of other abnormalities. Nevertheless, WBT scanning cannot be used as the primary diagnostic test because of its poor sensitivity for detection of metastases and thyroid remnants. Although some isolated lesions may accumulate thallium but not iodine, the yield of using both imaging modalities in all patients is low. Thallium-201 scintigraphy should be reserved for circumstances in which ^{131}I scintigraphy is negative and when thyroglobulin levels are elevated or recurrent or widespread differentiated thyroid cancer is suspected on a clinical basis.

REFERENCES

1. Parker SL, Tong T, Bolden S, Wingo PA. Cancer statistics, 1996. *CA Cancer J Clin* 1996;46:5–28.
2. Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med* 1994;97:418–428.
3. Hurley JR, Becker DV. The use of radioiodine in the management of thyroid cancer. In: *Nuclear medicine annual.* Freeman LM, Weissman HS, eds. New York: Raven, 1983:329–384.
4. Ramanna L, Waxman A, Braunstein G. Thallium-201 scintigraphy in differentiated thyroid cancer: comparison with radioiodine scintigraphy and serum thyroglobulin determinations. *J Nucl Med* 1991;32:441–446.
5. Robbins J. Thyroid suppression therapy for prevention of thyroid tumors after radiation exposure. In: *Radiation-associated thyroid carcinoma.* Degroot LJ, Frohman LA, Kaplan EL, Refetoff S, eds. New York: Grune & Stratton Inc.; 1977:419–431.
6. Lida Y, Hidaka A, Hatabu H, Kasagi K, Konishi J. Follow-up study of postoperative patients with thyroid cancer by ^{201}Tl scintigraphy and serum thyroglobulin measurement. *J Nucl Med* 1991;32:2098–2100.
7. Hoefnagel CA, Delprat CC, Marcuse HR, de Vijlder JJM. Role of ^{201}Tl total-body scintigraphy in follow-up of thyroid carcinoma. *J Nucl Med* 1986;27:1854–1857.
8. Tonami N, Hisada K. Thallium-201 scintigraphy in postoperative detection of thyroid cancer: A comparative study with ^{131}I. *Radiology* 1980;136:461–464.
9. Dadparvar S, Krishna L, Brady LW, Slizofski WJ, Brown SJ, Chevres A, Micaily B. The role of iodine-131 and thallium-201 imaging and serum thyroglobulin in the management of differentiated thyroid carcinoma. *Cancer* 1993;71:3767–3773.
10. Brendel AJ, Guyot M, Jeandot R, Lefort G, Manciet G. Thallium-201 imaging in the follow-up of differentiated thyroid carcinoma. *J Nucl Med* 1988;29:1515–1520.
11. Leeper RD. The effect of ^{131}I therapy on survival of patients with metastatic papillary or follicular thyroid carcinoma. *J Clin Endocrinol Metab* 1973;36:1143–1152.
12. Krishna L, Dadparvar S, Brady LW, et al. Paradoxical changes in iodine-131 scintigraphic findings in advanced follicular thyroid cancer. *J Nucl Med* 1993;34: 1574–1576.

Intraperitoneal Radioimmunotherapy of Ovarian Cancer with Lutetium-177-CC49

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Twelve ovarian cancer patients who failed chemotherapy entered a Phase I trial of intraperitoneal ^{177}Lu-CC49 antibody. **Methods:** Patients had disease confined to the abdominal cavity ± retroperitoneal lymph nodes, adequate organ function and no previous radiation. **Results:** Side effects included mild discomfort with administration (1/12), delayed transient arthralgia (2/12), and mild marrow suppression (calculated marrow doses of 11–54 cGy). The maximum tolerated dose has not been reached with levels of 10, 18, 25 and 30 mCi/m^2. Radioimmunoscintigraphy revealed localization consistent with tumor in 11 of 12 patients. One of eight patients with gross disease had >50% tumor reduction after therapy, while six progressed and one went off study with stable disease. Of patients with microscopic or occult disease, one relapsed at 10 mo and three remain without evidence of disease after 18 mo. **Conclusion:** Intraperitoneal radioimmunotherapy with ^{177}Lu-CC49 is well tolerated and appears to have antitumor activity against chemotherapy-resistant ovarian cancer in the peritoneal cavity.

Key Words: ovarian cancer; radioimmunotherapy; lutetium-177-CC49

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Eradication of ovarian cancer implants in the peritoneal cavity has been the major obstacle to disease control in most patients. Although the introduction of platinum-based chemotherapy has increased the response rates of ovarian cancer, there has been only a modest improvement in survival rates (*1*) and half of the patients who have laparotomy-confirmed complete response will relapse. Since most relapses are confined to the abdominal cavity, improved therapy should be possible with intensification of treatment directed to this area. Some abdominal failures have been successfully treated with external radiation, intraperitoneal or systemic administration of chemotherapy, or a form of radionuclide therapy (*2–11*).

Positive results have been reported for intraperitoneal delivery of radiolabeled tumor-reactive antibodies to selected patients, but this technology has not yet been fully exploited. Early results from imaging (*12*) and dosimetry (*13*) studies of intraperitoneal administration of radiolabeled antibodies have demonstrated selective tumor localization and slow absorption into the bloodstream (*14–16*). These studies have also shown that the intraperitoneal route is superior to intravenous administration for intraperitoneal implants, while the reverse is true for solid tumor metastases to lymph nodes and areas of hematogenous metastasis (*14–16*). An early therapeutic trial of intraperitoneal radiolabeled antibody for ovarian cancer, in which patients received >140 mCi ^{131}I-antibody, showed beneficial effects in 9/16 patients with a tumor mass of <2 cm (*2*). Eight patients in that study with larger tumor masses died of progressive disease within nine months. Similar results are reported for several antibodies using at least three radionuclides (^{131}I, ^{186}Re, ^{90}Y) (*4–5,8,10–11*). That is, antitumor effects, and in many cases prolonged survival, have been noted when disease volume is small. There is decreasing efficacy, however, with increasing size of tumor nodules (*4*).

We are conducting a dose-escalating trial of intraperitoneal radioimmunotherapy in ovarian cancer patients with persistent disease using a new agent, ^{177}Lu-CC49, which is linked by the chelator PA-DOTA (*17*). Lutetium-177 is a rare earth material with a physical half-life of 6.7 days and with beta emissions (E_{avg} = 133 KeV) that penetrate 0.2 to 0.3 mm in soft tissue. Lutetium-177 also emits two relatively low-abundance, low-energy gamma rays (113 and 208 keV) that allow imaging with a gamma camera, but pose less radiation hazard to health care personnel as compared to ^{131}I.

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