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Papillary Thyroid Carcinoma: MR Diagnosis of Lymph Node Metastasis

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PURPOSE: **The purpose of this study was to ascertain the usefulness of MR imaging in the diagnosis of nodal metastasis of papillary thyroid carcinoma and to establish the most indicative MR criteria of metastasis.**

METHODS: **Pathologic records and MR images in 50 patients with papillary thyroid carcinoma were reviewed. Each neck was divided into four nodal levels, so that 200 nodal levels were assessed in all. The maximum of the minimum transverse diameters of the lymph nodes on each nodal level measured on MR images and the certainty of metastasis as determined by a head and neck radiologist on the basis of morphologic aspects were compared with the pathologic findings by using receiver operating characteristic curves. The presence or absence of cystic nodes on each nodal level was also evaluated.**

RESULTS: **Metastasis was found on 87 (44%) of the nodal levels in 34 (68%) of the patients. A cystic node was identified on 33 (17%) of the nodal levels in 13 (26%) of the patients and was seen only on positive nodal levels. Morphologic diagnosis by the radiologist was better than that obtained by measurement. With the combined criteria of a cystic node or a node of 13 mm or more for the maximum of the minimum transverse diameters, specificity was 100% with an 82% accuracy and always indicated metastasis (100% positive predictive value). However, 41% of the metastatic nodes were missed with this criterion (59% sensitivity).**

CONCLUSION: **MR imaging was useful for diagnosing metastatic nodes; a nodal diameter threshold of 13 mm or the presence of a cystic node strongly indicated metastasis from papillary thyroid carcinoma.**

Papillary thyroid carcinoma is the most common neoplasm in the thyroid gland and accounts for about 70% of all thyroid carcinomas (1). This tumor peaks in the third or fourth decades of life; the female-to-male ratio ranges from 1.6:1 to 3:1 (1–4). The mortality rate for patients in whom the tumor is confined within the thyroid gland is less than 2.5% (5). However, when the tumor has spread beyond the thyroid capsule, mortality increases to 38%. In patients older than 40 years of age, this tumor grows more rapidly and tends to infiltrate adjacent structures (1, 5, 6).

Papillary carcinoma has a marked propensity for lymphatic infiltration (5, 7). When the regional nodes are systematically examined, most patients with papillary carcinoma are found to have microscopic nodal metastases (7). Van den Brekel et al (8) observed that the minimum axial diameter is the most accurate size criterion for lymph node metastasis in patients with head and neck squamous cell carcinoma, and that maximum axial diameter or a ratio of maximum-to-minimum axial diameter is less valid. Although many studies have described the magnetic resonance (MR) imaging appearance of focal and diffuse thyroid disease, little has been written on the role of MR imaging in the diagnosis of nodal metastases from thyroid carcinoma (9–12). This series was designed to study the diagnostic accuracy of MR imaging in detecting lymph node metastasis in patients with papillary thyroid carcinoma and to establish the optimal criteria for nodal metastasis on MR images.

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Methods

Pathologic records and MR images of 50 patients with papillary thyroid carcinoma were reviewed. The subjects comprised 37 women and 13 men, ranging in age from 24 to 81 years (average age, 57 years). Between November 1989 and December 1996, these consecutive patients who had an original (n = 43) or a recurrent thyroid carcinoma (n = 7) underwent MR imaging before surgical intervention to define the extent of the tumor. The seven patients with recurrent disease had had prior neck surgery, including hemithyroidectomy, subtotal thyroidectomy, and total thyroidectomy with neck dissection. The interval between MR imaging and surgery ranged from 1 to 18 days.

MR imaging was performed on a Magnetom or a Signa unit with a volume neck coil or a Helmholtz coil. The acquisition matrix was 256 × 192. Conventional unenhanced spin-echo T1-weighted images (700/13/2 or 900/15/2 [repetition time/echo time/excitations]) were obtained in all patients. T2-weighted images were obtained with a conventional spin-echo sequence (2000/70/1) in 38 patients and with a fast spin-echo T2-weighted sequence (3200/91/1) in the 12 most recent patients. Contrast-enhanced T1-weighted images (700/13 or 900/15) were obtained with (n = 10) or without (n = 24) fat suppression immediately after intravenous bolus injection of 0.1 mmol/kg gadopentetate dimeglumine. A total of 18 axial images from the level of the mandibular angle to the sternal notch were obtained with a section thickness of 5 mm and an intersection gap of 1.0 to 2.0 mm using presaturation pulses placed above and below the acquired sections.

The resected nodes were classified according to the nodal classification scheme of the Japanese Society of Thyroid Surgery (prelarynx, pretrachea, paratrachea, thyroid related, upper internal jugular, lower internal jugular, accessory, submandibular, submental) and were submitted for pathologic examination with the names of their nodal class. Pathologic reports documented how many nodes were positive or negative in each nodal class. Although we could not make a node-by-node comparison of MR findings with pathologic findings, we could at least identify the presence or absence of metastasis in each nodal class, even in retrospect.

For our study, we did not use such detailed classifications, because we feared that any errors made in nodal localization might eventually lead to misdiagnosis of the metastatic nodes. Instead, each side of the neck was divided into two parts (upper and lower) at the level of the lower edge of the cricoid cartilage. Thus, the neck was classified into four compartments (right upper, right lower, left upper, and left lower). Without knowledge of the pathologic and surgical findings, two radiologists measured in concert a maximum of the minimum transverse diameters of the lymph nodes in each compartment on MR images. They also evaluated the presence or absence of cystic portions within the nodes and compared the signal intensity of the solid and cystic portions of the nodes with that of surrounding fat tissue. Signal intensity on both T1- and T2-weighted images that was less than that of fat was called *hypointense*; that which was equal to or greater than that of fat was called *hyperintense*. Signal intensity on T2-weighted images that was equal to or greater than that of cerebrospinal fluid was called *markedly hyperintense*.

A precise schema of the surgical findings, including location and size of all the dissected nodes and other relative anatomic landmarks (internal jugular vein, carotid artery, trachea, cricoid cartilage, etc), were documented in surgical records in 15 of the 50 patients. Pathologic results were superimposed on the same schema. Therefore, we could make a node-by-node comparison in these 15 patients (a total of 60 nodal compartments). Of these 60 nodal compartments, 27 contained one or more metastatic nodes. Metastasis was found in the node with the largest minimum diameter in 25 (93%) of 27 positive nodal compartments. For the other two positive nodal compartments (both in the lower part of the neck), we could not reliably identify which node was positive, because they were too small (3 mm and 4 mm, respectively, on MR images) to distinguish from other nodes of similar size. Therefore, the largest node was considered the representative of each nodal compartment and was used for MR and pathologic correlation.

Independently, an experienced head and neck radiologist predicted the probability of lymph node involvement according to the morphologic findings. His judgment was based on the shape (rounded or not), the presence of cystic portions, and the inhomogeneity of the node regardless of size. The MR findings in the 200 largest nodes in 200 nodal compartments of the 50 patients were then compared with the surgical and pathologic records.

TABLE 1: Distribution of the maximum of the minimum transverse diameters of metastatic lymph nodes

Maximum of the Minimum Transverse Diameters, mm	No. (%)
≤3	12 (14)
5–3.1	10 (11)
8–5.1	16 (18)
10–8.1	10 (11)
13–10.1	9 (10)
13<	30 (34)
Total	**87** (98)*

Note.—Total is less than 100% due to rounding off.

The diagnostic performance of the maximum of the minimum transverse diameters and the morphologic criteria for predicting metastasis were compared with the pathologic diagnosis by using receiver operating characteristic (ROC) curves. Next, these two types of readings were compared. ROC curves were calculated by using continuous data with a maximum likelihood method and comparisons between the areas under the two curves (A_z) were calculated, adjusting for the correlation between the data. Finally, we proposed the optimal criteria for lymph node metastasis. In statistical calculation, a *P* value of less than .05 was considered significant.

Results

Of the 200 nodal compartments in the 50 patients, metastasis was verified pathologically in 87 nodal compartments (44%) (19 right upper, 25 right lower, 16 left upper, and 27 left lower compartments) of 34 patients (68%). The relationship between the number and the maximum of the minimum transverse diameters of the nodes is summarized in Table 1. Of the 87 largest metastatic nodes, 54% measured 10 mm or less in minimum transverse diameter. Of these 87 nodes, 82 (94%) were detected with MR imaging and five were not detected because of their small size (Figs 1 and 2). All 82 of the largest nodes that were identified with MR imaging appeared hypointense relative to fat on unenhanced T1-weighted images. On T2-weighted images, signal intensity was hypointense relative to fat in 28 nodes (34%), isointense in 37 (45%), and hyperintense in 17 (21%) (Fig 1).

Of the 42 largest metastatic nodes in which contrast-enhanced T1-weighted images were obtained, fat suppression was used in 11 and not used in 31. Of the 31 nodes imaged without fat suppression, 26 (84%) appeared hypointense and five (16%) appeared isointense relative to fat. Of the 11 nodes imaged with fat suppression, five (45%) were hypointense, five (45%) were hyperintense, and one (9%) was isointense. χ^2 tests revealed that signal-intensity patterns of metastases were statistically significantly different between the two groups with and without fat suppression ($P < .001$).

Cystic areas were detected in 31 (38%) of the 82 largest metastatic nodes (Fig 2). Of these 31 positive nodal compartments, 23 (74%) contained an addi-

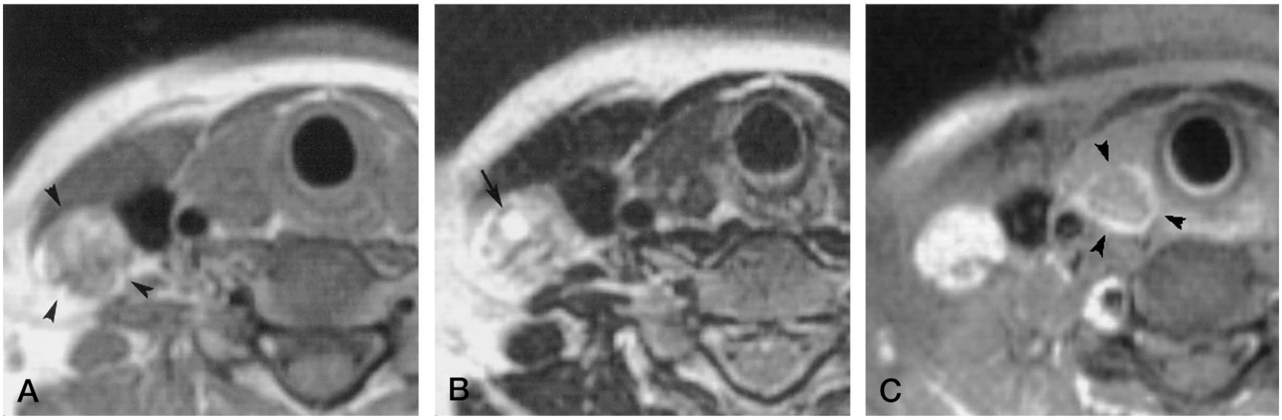

FIG 1. Lymph node metastasis in a 53-year-old woman with primary disease.

A metastatic lymph node 15 mm in minimum transverse diameter (*arrowheads*) is seen in the right lower part of the neck. The node appeared as a hypointense area of inhomogeneous composition relative to surrounding fat on both T1-weighted (900/15/2) (*A*) and T2-weighted (2000/70/1) (*B*) MR images, and as a hyperintense area on a contrast-enhanced fat-suppressed T1-weighted image (900/15/2) (*C*). A small markedly hyperintense area within the node is seen on the T2-weighted image (*arrow, B*). Although this portion was thought to represent hemorrhage and/or thyroid protein, no pathologic verification was obtained. Calcification in the node was confirmed pathologically. The primary tumor in the right lobe of the thyroid gland was not identified on unenhanced T1- and T2-weighted images, but it was depicted as a mass of rim enhancement on a contrast-enhanced fat-suppressed T1-weighted image (*arrows, C*).

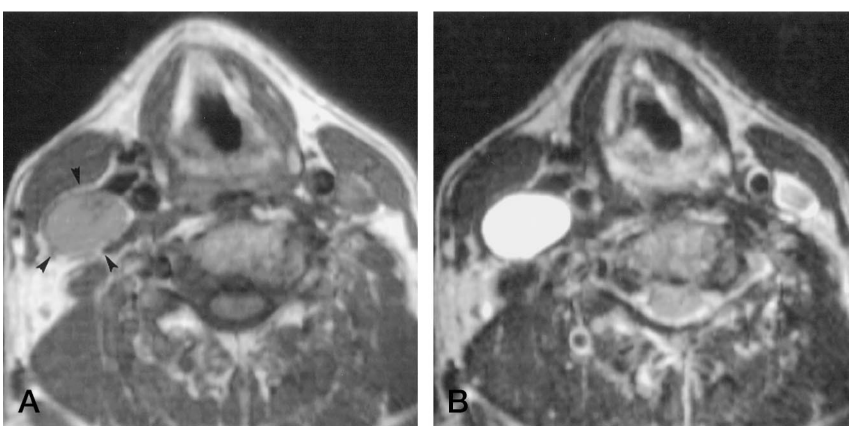

FIG 2. Lymph node metastasis in a 67-year-old man with primary disease.

A metastatic lymph node 14 mm in minimum transverse diameter with extensive cystic change (*arrowheads*) is seen in the right upper part of the neck. The node appeared hypointense relative to fat on a T1-weighted image (700/13/2) (*A*) and as a markedly hyperintense area of homogeneous composition on a fast spin-echo T2-weighted image (3200/91/2) (*B*). Aspirated fluids obtained via sonographically guided biopsy contained high levels of thyroglobulin.

tional one or more smaller nodes with cystic changes. Another two positive nodal compartments in which the largest nodes had no cystic changes contained smaller nodes with cystic portions on MR images. Thus, cystic nodes were identified in a total of 33 nodal compartments in 13 patients. Of the 31 largest nodes with cystic changes, pathologic proof of cystic changes was obtained in 22. Of these 22 nodes, five underwent sonographically guided fine-needle aspiration biopsy before surgery; markedly elevated thyroglobulin levels of the aspirated fluid were verified in all. On unenhanced T1-weighted images, the cystic portions appeared hypointense relative to fat in 23 (73%) of the 31 largest nodes and hyperintense in eight (27%), whereas on T2-weighted images, all were markedly hyperintense.

Lymph nodes were identifiable on MR images in 189 (95%) of the 200 nodal compartments (107 nonmetastatic nodes and 82 metastatic nodes). The maximum of the minimum transverse diameters measured on MR images ranged from 2 to 12 mm (mean, 4 mm ± 2 SD) in nodes without metastasis and ranged from 2 to 37 mm (mean, 12 mm ± 8) in nodes with metastasis. Morphologic diagnosis by the experienced head and neck radiologist (A_z = 0.88 ± 0.03) was better than that obtained by measurement (A_z = 0.85 ± 0.03) (Fig 3); however, the difference was not statistically significant (P = .23).

By using a threshold of 8 mm or more for the maximum of the minimum transverse diameter, we attained 81% accuracy with 61% sensitivity, 96% specificity, 93% positive predictive value (PPV), and 76% negative predictive value (NPV) (Table 2). Increasing the threshold to 13 mm produced no false-positive diagnoses (100% specificity), and gave a 37% sensitivity, 72% accuracy, 100% PPV, and 67% NPV. When the combined criteria of a cystic node or an 8-mm threshold was used, we obtained the highest accuracy of 84%, with 96% specificity and 93% PPV; however, sensitivity (67%) was not adequate. Using the criterion of a cystic node regardless of its size, we attained 100% PPV and 100% specificity, with 40% sensitivity and 74% accuracy. With the combined criteria of a cystic node or a 13-mm threshold, sensitivity (59%) and accuracy (82%) were improved while maintaining the 100% PPV.

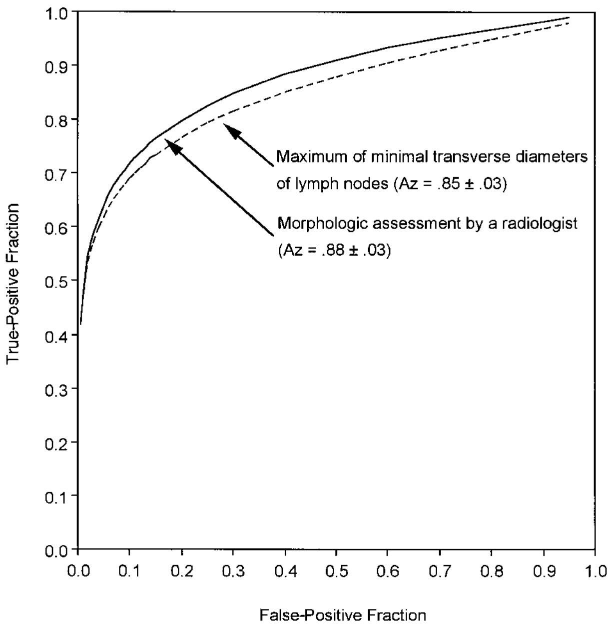

FIG 3. ROC curves for the diagnosis of lymph node metastasis by morphologic assessment by a head and neck radiologist and by measurement of the maximum of the minimum transverse diameters of the lymph nodes.

Discussion

There is some debate as to the clinical significance of regional lymph node metastasis (1, 3–5, 13–15). Many investigators insist that nodal metastases have an adverse effect on the rate of survival or recurrence (1, 3, 13, 14). Mazzaferri and Young (3) found recurrence rates to be increased approximately fivefold in patients over age 40 who were found to have regional nodal metastases at initial surgery. Harwood et al (14) reported that death resulting from papillary carcinoma occurs more frequently in patients with nodal involvement than in those without nodal metastasis. Others have found that differentiated thyroid carcinomas, including primary-site tumors and nodal metastasis, have the potential to develop into anaplastic carcinoma (1, 5, 6, 15, 16). Although this is an uncommon event, when such transformation does occur, the outcome for patients is invariably death within a year from the time of diagnosis (15, 16). Thus, although the most important prognostic indicator for patients with papillary thyroid carcinoma is whether the tumor is confined to the thyroid gland or has spread beyond the glandular capsule (1, 5, 6), we think it is worthwhile clinically to define the useful criteria for nodal metastasis.

The frequency of regional node metastasis in patients with papillary carcinoma is reported to vary from 39% to 90% (2–4, 7, 14), depending on the surgical method undertaken and the population studied. More radical surgery yields a greater number of metastatic nodes; and young patients with differentiated thyroid carcinoma are reported to have a higher prevalence of nodal metastases than older patients (14). Therefore, the greater the proportion of young patients in a studied population, the higher the frequency of nodal metastases. Carcangiu et al (4) found that 54% of 241 patients with papillary thyroid carcinoma had nodal metastasis. They also noted that 75% of these had cystic foci, with 25% of these being marked.

We found nodal metastasis in 68% of the 50 patients studied. Cystic lymph nodes were detected in 13 (38%) of the 34 patients with nodal metastasis and were specific to metastasis from papillary carcinoma. Therefore, we suggest that if the largest node has a normal signal intensity and a smaller node appears to have a cystic component, the smaller node would be more important in diagnosing metastasis. In our retrospective study, we evaluated only the maximum of the minimum transverse diameters in each nodal compartment, because studies have shown that the largest node has the highest possibility of metastasis (8), and because our node-by-node comparison in 15 patients revealed that the largest node almost always contained metastasis in the corresponding positive nodal compartment.

In our series, solid portions of the metastatic nodes appeared hypointense on unenhanced T1-weighted images and hypointense (34%), isointense (45%), or hyperintense (21%) on T2-weighted images obtained without fat suppression. On contrast-enhanced T1-weighted images without fat suppression, most nodes were hypointense relative to fat, whereas with fat suppression, approximately half the nodes were hyperintense. Our results support the usefulness of contrast-enhanced fat-suppressed T1-weighted imaging for detecting metastatic nodes. The MR features seen in this study were indistinguishable from those of benign or other malignant conditions (17). Som et al (11) reported that a thin-walled cystic mass that appeared hyperintense on both T1- and T2-weighted images might be suggestive of nodal metastasis from papillary thyroid carcinoma. As for the signal intensity of cystic portions within the node, hyperintensity relative to fat was seen in 27% of the subjects in our study on both T1- and T2-weighted images; the rest of these cystic components were hypointense on T1-weighted images and markedly hyperintense on T2-weighted images. Although our pathologic and chemical studies were limited, we think that cystic portions of metastatic nodes represent thyroid protein of various concentrations, hemorrhagic fluid, or tumor necrosis.

Despite the fact that the head and neck radiologist in our study judged the nodal metastasis from various viewpoints, his diagnostic accuracy was not statistically different from that obtained via measurement of the maximum of the minimum transverse diameters of the nodes. Our optimal size criterion (8 mm or more of the minimum transverse diameter) was slightly smaller than that (10 mm) for metastasis from squamous cell carcinoma (8). The diagnostic accuracy in this series (81%) was slightly inferior to that (84% or 85%) obtained in a series of patients with metastatic neck disease from squamous cell carcinoma (18, 19). When the finding of cystic areas within a node was added to this size criterion, accuracy increased to 84%. A threshold of 13 mm or a cystic node of any

TABLE 2: Diagnostic statistics for lymph node metastasis with MR findings

MR Findings	Sensitivity	Specificity	Accuracy	Positive Predictive Value	Negative Predictive Value
Lymph node diameter, mm*					
3≤	96	24	56	49	90
4≤	87	53	68	59	84
5≤	80	70	75	67	82
6≤	73	85	80	79	81
7≤	63	93	80	88	77
8≤	61	96	81	93	76
9≤	56	98	80	96	74
10≤	50	98	77	95	72
11≤	43	98	74	95	69
12≤	40	99	74	97	68
13≤	37	100	72	100	67
Cystic node	40	100	74	100	69
Cystic node 8 mm ≤	67	96	84	93	79
Cystic node 13 mm ≤	59	100	82	100	76

Note.—Data are given as percentages.

* Maximum of minimum transverse diameters of lymph nodes on MR images.

size was specific and strongly suggestive of metastasis from papillary thyroid carcinoma (100% PPV).

Even with our most accurate criterion, one third of the metastatic nodes were missed with MR imaging (67% sensitivity). With the most indicative criterion, 41% of the neck metastases were not identified. According to the literature, more than half the metastatic nodes from papillary carcinoma are less than 3 mm in diameter (7). Despite this fact, metastatic nodes develop clinically in fewer than 10% of patients (14). The prognosis or the rate of recurrence in patients with papillary thyroid carcinoma depends on the presence of clinically overt nodal metastasis but not on the microscopic nodal disease (13). Furthermore, relatively large metastatic nodes are frequently missed with palpation because of large thyroid tumors (20).

Conclusion

A cystic node or a node of 13 mm or more in the minimum transverse diameter strongly indicates metastasis from papillary thyroid carcinoma on MR images. These criteria should contribute to the ability to plan appropriate surgery and to predict the prognosis for patients with this disorder.

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References

1. Mazzaferri EL. **Treatment of carcinoma of follicular epithelium.** In: Braverman LE, Utiger RD, eds. *The Thyroid.* 6th ed. Philadelphia, Pa: Lippincott; 1991:1329–1348
2. Woolner LB, Beahrs OH, Black BM, McConahey WM, Keating FR Jr. **Classification and prognosis of thyroid carcinoma: a study of 885 cases observed in a thirty year period.** *Am J Surg* 1961;102: 354–387
3. Mazzaferri EL, **Young RL. Papillary thyroid carcinoma: a 10 year follow-up report of the impact of therapy in 576 patients.** *Am J Med* 1981;70:511–518
4. Carcangiu ML, Zampi G, Pupi A, Castagnoli A, Rosai J. **Papillary carcinoma of the thyroid: a clinicopathologic study of 241 cases treated at the University of Florence, Italy.** *Cancer* 1985;55:805–828
5. Greenfield LD, Luk KH. **Thyroid.** In: Perez CA, Brady LW, eds. *Principles and Practice of Radiation Oncology.* 2nd ed. Philadelphia, Pa: Lippincott; 1992:1356–1380
6. Tollefsen HR, DeCosse JJ, Hutter RVP. **Papillary carcinoma of the thyroid: a clinical and pathologic study of 70 fatal cases.** *Cancer* 1964;17:1035–1044
7. Noguchi S, Noguchi A, Murakami N. **Papillary carcinoma of the thyroid, I: developing pattern of metastasis.** *Cancer* 1970;26:1053–1060
8. van den Brekel MWM, Stel HV, Castelijns JA, et al. **Cervical lymph node metastasis: assessment of radiologic criteria.** *Radiology* 1990; 177:379–384
9. Higgins CB, McNamara MT, Fisher MR, Clark OH. **MR imaging of the thyroid.** *AJR Am J Roentgenol* 1986;147:1255–1261
10. Gefter WB, Spritzer CE, Eisenberg B, et al. **Thyroid imaging with high-field-strength surface-coil MR.** *Radiology* 1987;164:483–490
11. Som PM, Brandwein M, Lidov M, Lawson W, Biller HF. **The varied presentation of papillary thyroid carcinoma cervical nodal disease: CT and MR findings.** *AJNR Am J Neuroradiol* 1994;15:1123–1128
12. Takashima S, Nomura N, Noguchi Y, Matsuzuka F, Inoue T. **Primary thyroid lymphoma: evaluation with US, CT, and MRI.** *J Comput Assist Tomogr* 1995;19:282–288
13. Seller M, Beenken S, Blankenship A, et al. **Prognostic significance of cervical lymph node metastases in differentiated thyroid cancer.** *Am J Surg* 1992;164:578–581
14. Haywood J, Clark OH, Dunphy JE. **Significance of lymph node metastasis in differentiated thyroid cancer.** *Am J Surg* 1978;136: 107–112
15. Rossi RL, Cody B. **Surgery of thyroid gland.** In: Wickland ED, ed. *Surgery of the Thyroid and Parathyroid Glands.* 3rd ed. Philadelphia, Pa: Saunders; 1991:187–214
16. Rossi R, Cady B, Meissner WA, Sedgwick CE, Weber J. **Prognosis of undifferentiated carcinoma and lymphoma of the thyroid.** *Am J Surg* 1978;135:589–596
17. Som PM. **Detection of metastasis in cervical lymph nodes: CT and MR criteria and differential diagnosis.** *AJR Am J Roentgenol* 1992; 158:961–969
18. Friedman MF, Mafee MF, Pacella BL Jr, Storigl TL, Dew LL, Toriumi DM. **Rationale for elective neck dissection in 1990.** *Laryngoscope* 1990;100:54–59
19. van den Brekel MWM, Castelijns JA, Croll GA, et al. **Magnetic resonance imaging vs palpation of cervical lymph node metastasis.** *Arch Otolaryngol Head Neck Surg* 1991;117:666–673
20. Takashima S, Morimoto S, Ikezoe J, et al. **CT evaluation of anaplastic thyroid carcinoma.** *AJNR Am J Neuroradiol* 1990;11:361–367