Sonography of the neck in the patient with thyroid cancer: 
the University of Texas M. D. Anderson Cancer Center Experience

Although nodular thyroid disease is common, the vast majority of thyroid nodules are benign. In fact, thyroid cancer is rare, accounting for less than 1% of all malignant neoplasms. It is estimated that there will be 30,380 new cases diagnosed in 2006 in the USA with only 1,500 deaths expected from it [1].

In the past decade, the use of thyroid sonography (US) at M. D. Anderson Cancer Center has evolved from the diagnosis of palpable and nonpalpable thyroid masses with guided fine-needle aspiration (FNA) biopsy to the preoperative local staging of thyroid cancer and the routine follow-up after thyroidectomy for early detection of recurrent or metastatic disease.

US diagnosis of thyroid cancer

Histologic types

There are four major histopathologic types of thyroid cancer.

✔ Papillary carcinomas (including those with follicular foci) account for about 80% of all thyroid cancers. They typically affect young women, metastasize to the lymph nodes, and have a good prognosis (6% mortality rate at 20 years).

✔ Follicular carcinomas (including so-called Hürthle cell carcinomas) represent about 10% of all thyroid cancers. They spread hematogenously and have a 25% mortality rate at 20 years.

✔ Medullary carcinomas represent 5% of thyroid cancers. They are characterized by the secretion of calcitonin, their association with MEN II syndrome, and their multicentricity.

✔ A papillary or undifferentiated carcinomas are rare, accounting for less than 5% of all thyroid cancers. They are usually found in elderly patients and have the worst prognosis.

Detection of thyroid masses and lymph nodes

While palpable nodules in the thyroid are quite common, US has proved to be highly sensitive in detecting minute (a few mm in size) nonpalpable masses in the thyroid gland and abnormal lymph nodes in the neck. Although the detection rate of focal abnormalities with US is high, the specificity of sonograms is often insufficient to provide a clinically useful characterization of a solid thyroid nodule or to differentiate a malignant from a benign lymph node with certainty. In the differentiation of benign from malignant thyroid nodules, the sensitivity of US ranges from 63% to 94%, its specificity from 61% to 95%, and its overall accuracy from 80% to 94% [2, 3, 4, 5, 6, 7, 8, 9]. Except for invasion through the thyroid capsule, no single US criterion, whether on gray-scale or color Doppler imaging, distinguishes benign thyroid nodules from malignant nodules with complete reliability.

US features

Regardless of their histologic type, thyroid cancers are usually hypoechoic relative to the adjacent normal thyroid parenchyma. However, many benign thyroid nodules are also hypoechoic, and because benign lesions outnumber carcinomas, a hypoechoic nodule is still statistically most likely benign. Papillary thyroid cancers often have a cystic component, which, if important, may mimic a cyst. However, a closer inspection should reveal the presence of papillary projections (with vascularity seen on power Doppler imaging), wall irregularities, or microcalcifications.
The hypoechoic halo, once described as a benign finding, can be found in association with cancer. In that case, it is most likely to be irregular and incomplete.

Malignant lesions tend to have irregular or poorly defined margins. There is a strong association between US-detected calcifications and thyroid malignancy (Fig 1). Patients younger than 40 years with calcified nodules constitute a high-risk group, with a probability of harboring thyroid malignancies four times higher than that in patients of the same age without intranodular calcifications. Similarly, the presence of calcifications within a solitary nodule increases the incidence of malignancy. Therefore, these patients must be further evaluated or followed [10]. Of the various US features of thyroid nodules, microcalcifications show the highest accuracy (76%), specificity (93%), and positive predictive value (70%) for malignancy as a single sign; however, the sensitivity is low (36%) and insufficient to be reliable for detection of malignancy [10, 11].

**Color-flow Doppler**

Most well-differentiated thyroid carcinomas are generally hypervascular, with irregular, tortuous vessels and arteriovenous shunting (Fig 2). However, with equipment of high color Doppler sensitivity, most benign thyroid nodules also show some degree of internal or peripheral vascularity. Hyperplastic and adenomatous nodules tend to display peripheral vascularity, whereas carcinomas usually display internal vascularity with or without a peripheral component. Unfortunately, there is significant overlap between the color Doppler appearances of benign and malignant thyroid lesions, which limits the diagnostic role of color Doppler imaging [7]. It is the combination of gray-scale and color Doppler diagnostic criteria that is most helpful in the diagnosis of thyroid cancer.
Elastography

Elastography is a promising imaging technique that may assist in the diagnosis of thyroid cancer. In a recent study, a strain index value greater than 4 on off-line-processed elastograms was the strongest independent predictor of thyroid cancer (p<0.001); this criterion had 96% specificity and 82% sensitivity [12]. Two other elastographic criteria, which were evaluated on real-time elastograms—a margin regularity score higher than 3 (88% specificity, 36% sensitivity) and a tumor area ratio higher than 1 (92% specificity, 46% sensitivity)—also were associated with malignancy (p<0.05). However, the usefulness of these criteria was not considered to be high because of their low sensitivity [12].

Thyroid nodules in children

Thyroid nodules—solitary or multiple—are relatively rare in children, with a prevalence ranging from 0.2% to 1.8% [13]. The US appearances of thyroid cancer in children have recently been reported [14, 15]. In thyroid nodules with a diameter of 15 mm or smaller, the most reliable diagnostic criteria for malignancy are an irregular outline (86.4% specificity, 69.6% sensitivity; p<0.001), subcapsular location (86.4% specificity, 65.2% sensitivity; p<0.001), and increased intranodular vascularization (87.9% specificity, 69.6% sensitivity; p<0.01) [14]. For thyroid nodules larger than 15 mm in diameter, the accuracy of US diagnosis was much lower than that for smaller nodules, and the only reliable criterion for cancer in this group was hypoechogenicity (84.0% specificity, 60.0% sensitivity; p<0.01) [14].

Metastases to the thyroid

Metastases to the thyroid from extrathyroidal malignancies are extremely rare. They usually derive from renal cell, breast, lung, or colon carcinomas or from melanoma. In a patient with a history of cancer, the differential diagnosis of any new mass in the thyroid should include metastasis from the known cancer.

US-guided FNA of thyroid masses and suspicious lymph nodes

Because of the low specificity of US in the diagnosis of cancer, US-guided FNA, which quickly provides a reliable tissue diagnosis, is widely used. At M. D. Anderson, FNA is performed with a 20-gauge, 1.5-inch hypodermic needle. This allows one to obtain an adequate specimen in most cases with a single pass. In the vast majority of cases, local anesthesia is not necessary. Color (power) Doppler is used to map the largest vessels. The direction (medial to lateral or lateral to medial) and angle of the needle are determined on the basis of the location of the target lesion and its relationship with these vessels (Fig 3). Tips include turning the head of the patient to modify the location of the great vessels and provide a better window for the needle’s insertion.

Cytologic diagnosis relies on adherence to strict cyologic criteria and the liberal use of immunostaining techniques involving thyroglobulin, calcitonin, chromogranin, synaptophysin, or parathyroid hormone. Cytologic results should be reported as positive, negative, or indeterminate for malignancy or nondiagnostic. A recent review of 240 patients at M. D. Anderson showed a 5% rate of nondiagnostic specimens and a 4% rate of false-positive and 4% rate of false-negative results of US-guided FNA in the diagnosis of thyroid cancer [16].

A particular situation is the “cystic node without malignant cells.” In this case, a mostly cystic metastatic node is aspirated, and no malignant cells can be identified in the aspirated fluid. If the node has collapsed completely during the aspiration, some of the aspirated fluid should be saved for a thyroglobulin assay, which will reveal a very high concentration, thereby confirming metastatic disease.

The need for large-core needle biopsy is extremely rare and restricted to large tumors for which FNA could not provide a reliable diagnosis for various technical reasons. In this case, an 18-gauge cutting needle is used to minimize the risk of bleeding.
US staging of thyroid cancer

Table 1 shows the TNM classification of thyroid cancer. At M. D. Anderson, we use US to refine the preoperative local and regional staging.

<table>
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<th>Primary tumor (T)</th>
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<td>TX: Primary tumor cannot be assessed.</td>
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<td>T0: No evidence of primary tumor.</td>
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<td>T1: Tumor ≤2 cm in greatest dimension, limited to the thyroid.</td>
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<td>T2: Tumor &gt;2 cm but ≤4 cm in greatest dimension, limited to the thyroid.</td>
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<td>T3: Tumor &gt;4 cm in greatest dimension, limited to the thyroid or any tumor with minimal extrathyroidal extension (e.g., extension to sternothyroid muscle or parathyroid soft tissues).</td>
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<td>T4a: Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve.</td>
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<tr>
<td>T4b: Tumor invades prevertebral fascia, mediastinal vessels, or encases carotid artery.</td>
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<td>All anaplastic carcinomas are considered T4 tumors.</td>
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<tr>
<td>T4a: Intrathyroidal anaplastic carcinoma: surgically resectable.</td>
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<tr>
<td>T4b: Extrathyroidal anaplastic carcinoma: surgically unresectable.</td>
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<td>Multifocal tumors of all histologic types are designated (m); the largest lesion determines the classification.</td>
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Regional lymph nodes (N)

Regional lymph nodes are the central compartment, lateral cervical, and upper mediastinal lymph nodes.

- N0: No regional lymph node metastasis.
- N1: Regional lymph node metastasis.
- N1a: Metastasis to level VI (pretracheal and paratracheal, including prelaryngeal and Delphian lymph nodes).
- N1b: Metastasis to other unilateral, bilateral, or contralateral cervical or upper mediastinal lymph nodes.

Distant metastases (M)

- M0: No distant metastasis.
- M1: Distant metastasis cannot be assessed.
- MX: Distant metastasis.

US with Doppler is effective in demonstrating encasement of the carotid artery or tumor thrombus in the internal jugular vein.

### Regional staging

The American Joint Committee on Cancer Staging classifies the lymph nodes as level I through level VII (Table 2).

<table>
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<th>Level</th>
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<td>Ia: Submental.</td>
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<td>Ib: Submandibular.</td>
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<td>IIa: Nodes anterior, medial, or lateral to the internal jugular vein.</td>
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<td>IIIb: Nodes posterior to the internal jugular vein with a fat plane between the node and the vessel.</td>
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<td>III: Nodes along the internal jugular chain between the hyoid bone and the cricoid cartilage.</td>
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<td>IVa: Nodes along the spinal accessory chain, posterior to the sternocleidomastoid muscle.</td>
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<td>Va: Level V nodes from the skull base to lower border of cricoid cartilage.</td>
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<td>V: Level V nodes from lower border of cricoid cartilage to the clavicle.</td>
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<td>VI: Nodes in the visceral compartment from the hyoid bone superiorly to the suprasternal notch inferiorly. On each side, the lateral border is formed by the medial border of the carotid sheath.</td>
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<td>VII: Nodes in the superior mediastinum.</td>
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- Level VI is the central thyroid compartment.
- Level VII nodes are those in the superior mediastinum.
- Levels III, IV, and V contain the cervical lymph nodes in the lower jugular chain and posterior triangle that are at risk of containing metastatic disease.
- Level II nodes occupy the jugular chain above the level of the hyoid bone.

The most common locations for nodal metastases in thyroid cancer are the paratracheal and level IV nodes. Lymph node metastases in differentiated thyroid cancer are often multiple and of various sizes. The spread of disease is usually ipsilateral and typically involves progression in an orderly manner from level VI, either laterally to levels III and IV, or inferiorly into the mediastinum (level VII). Involvement of level II occurs either from the superior pole of the thyroid or directly from levels III and IV.

The US examination of the nodal basins should include not only level VI but also the “at-risk levels” in both lateral compartments (i.e., levels III, IV, and V).

In the diagnosis of metastatic nodes, suspicious US findings include large size, rounded shape, increased number of nodes, a cystic component (highly specific for papillary thyroid cancer), absence of echogenic center/hilum, extra-
capsular extension, markedly decreased echogenicity (or diffusely and mildly increased echogenicity similar to that of the thyroid), presence of (micro) calcifications, and disorganized hypervascularity on color (power) Doppler imaging (Fig 4, 5).

The major contribution of US in the staging of thyroid cancer is the detection of a clinically occult nodal metastasis in a neck compartment that would not have been included in the surgical dissection, thus altering the surgical treatment plan. A typical example is the detection of contralateral disease when a unilateral dissection has been planned based on physical examination. We retrospectively compared preoperative US and physical examination results in the detection of locoregional metastases in patients with thyroid cancer [18]. Patients were divided into three groups: group 1, those undergoing primary thyroid or neck surgery; group 2, those undergoing reoperation for persistent disease; and group 3, those undergoing reoperation for recurrent thyroid carcinoma. For each group, the frequency with which US detected disease in a neck compartment (central or lateral) that was normal on physical examination was recorded. In total, 212 patients underwent surgery for primary, persistent, or recurrent papillary (n = 130), medullary (n = 61), or follicular or Hürthle cell (n = 21) carcinoma. US detected additional sites of metastatic disease not appreciated on physical examination in 21 (20%) of 107 patients in group 1; 9 (32%) of 28 patients in group 2; and 52 (68%) of 77 patients in group 3. US findings altered the operative procedure in these patients, facilitating complete resection of disease and potentially minimizing locoregional recurrence. In fact, of the 107 group 1 patients, cervical recurrence has been detected in only 6 (6%) at a median follow-up time of 36 months, in spite of 67 (63%) having tumors larger than 2 cm or lymph node metastases.

Intraoperative localization of nonpalpable lesions

At M. D. Anderson, we perform a limited US examination of the neck in the operating room in selected cases to map the disease in the thyroid bed and/or the nodal basins and thereby help the neck surgeon determine the most appropriate surgical technique. If needed, US can be performed through the open wound to identify a lesion that would not be found during surgery.

Follow-up of patients with thyroid cancer

At M. D. Anderson, patients are followed up with periodic US in addition to regular physical examinations, chest
Fig 6 • Early recurrence in the thyroid bed. Transverse gray-scale sonogram of the right thyroid bed shows a minute irregular hypoechoic mass (arrows) suspicious for recurrent disease. C, common carotid artery; T, trachea.

Fig 7 • Recurrent papillary thyroid cancer in the thyroid bed. Transverse power Doppler sonogram shows a small, elongated, but irregular hypoechoic mass (arrows) with focally increased vascularity highly suspicious for recurrent disease. C, common carotid artery; T, trachea.

Fig 8 • Early local recurrence from a medullary thyroid cancer. A: Transverse gray-scale sonogram shows a nonspecific – albeit new – 0.4-cm, slightly irregular, hypoechoic, solid nodule in the left thyroid bed (arrow and calipers). T, trachea. B: Transverse power Doppler sonogram shows vascularity associated with the recurrence (arrow) despite its minute size, which raises the suspicion for malignancy. T, trachea. C: Transverse sonogram obtained during the FNA shows the tip of the needle (arrowheads) within the recurrence (arrows). One pass was sufficient to confirm malignancy. Note that the scan direction has been reversed and that the needle is inserted from the midline in a medial to lateral direction for a safer approach, avoiding the carotid artery. C, common carotid artery.
radiographs, periodic whole-body iodine scintigraphy, and laboratory work, mainly serum thyroglobulin for papillary and follicular carcinoma and calcitonin and CEA for medullary thyroid carcinoma.

Cervical recurrence has been reported in up to 30% of patients with differentiated thyroid carcinoma and up to 65% of patients with medullary thyroid carcinoma [18]. This is largely due to regional lymph node metastases. Men younger than 40 years, women younger than 50 years, and children and adolescents are considered at low risk for recurrence regardless of histologic type. An intermediate risk group includes men older than 40 years and women older than 50 years who have papillary carcinoma; men older than 40 years and women older than 50 years who have follicular carcinoma are at a higher risk for recurrence.

US is highly sensitive in detecting nonpalpable thyroid bed masses and abnormal cervical nodes. A “new”-even slow-growing-solid, hypoechoic mass in the thyroid bed with irregular margins and increased vascularity on color Doppler, especially if (micro) calciifications and/or a cystic component are present, is considered a recurrence until proven otherwise (Fig 6, 7, 8). However, not every solid hypoechoic mass in the thyroid bed is a recurrent thyroid cancer. Benign masses that can develop or be found in the thyroid bed include postoperative changes (pseudonodules), residual normal thyroid tissue, small reactive nodes, suture granulomas, posttraumatic neuromas, and minimally enlarged parathyroid glands.

New emerging US-guided therapeutic approaches

New US-guided therapeutic options, including US-guided percutaneous ethanol injection, radiofrequency ablation, or cryotherapy of recurrent or metastatic diseases have been reported or are being considered in the management of the patient with thyroid cancer [19, 20].

Conclusion

In 2006, real-time US examination with US-guided FNA of the thyroid bed and regional nodal basins is the best imaging modality for preoperative locoregional staging of thyroid cancer and routine follow-up of thyroid cancer patients after thyroidectomy.