

## Imaging of the thyroid gland

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### Abstract

Incidental and symptomatic pathology of the thyroid gland is common in the community. Although technological advances have led to the development and improvement of imaging modalities, ultrasound remains the primary diagnostic tool. In this article, the authors examine the role of imaging and its recent advances in the management of thyroid cancer.

Imaging of the head and neck, and in particular the thyroid gland, has improved over recent years. There have been developments enhancing traditional methods of imaging, as well as improved understanding and interpretation of radiological signs. Furthermore, there have been new technologies, which are yet to establish their role in the diagnostic process. Here, we focus on the role of imaging and its recent advances in the management of thyroid cancer.

### The thyroid nodule

The thyroid nodule is a common clinical entity. Palpable nodules are present in approximately 4 to 7% of adults, and up to 50% of adults will have non-palpable nodules discovered at the time of death.<sup>1</sup> With the increasing use of radiology in modern medicine, incidental nodules are reported in up to 27% of the population.<sup>2</sup> Only 1 in 20 palpable thyroid nodules is malignant.<sup>2</sup> Non-palpable nodules have the same risk of malignancy as palpable nodules of the same size.<sup>3</sup> Lack of symptomatology does not exclude malignancy, as 75% of patients with thyroid cancer are asymptomatic.<sup>4</sup>

The incidence of thyroid cancer has almost tripled in the United States in the last 35 years, from 4.85 cases per 100,000 in 1975 to 12.23 cases per 100,000 in 2007.<sup>5</sup> Despite this, it accounts for only 1.5% of all newly diagnosed cancers.<sup>6</sup> Given this combination of a relatively rare malignant disease on the background of a relatively common benign condition, the ability to detect the presence of malignancy is an important challenge in the management of thyroid nodules. Differentiating the malignant from the benign nodule has appeared on the agenda in multiple forums, with decision algorithms involving clinical factors, radiological findings and cytology.

The thyroid nodule has been traditionally evaluated with clinical examination, ultrasound and fine needle aspiration cytology (FNAC). Adjuncts to ultrasound include computed tomography (CT), magnetic resonance imaging (MRI) and more recently, fluorodeoxyglucose positron emission tomography (FDG-PET), ultrasound-based elastography and magnetic resonance spectroscopy (MRS).

Cytological examination of material obtained by fine needle aspiration is the best single test for differentiating malignant from benign thyroid lesions.<sup>7</sup> Compared with

FNAC, ultrasound has the advantage of being a noninvasive procedure and giving immediate information.<sup>8</sup> However, ultrasound is operator dependent. It is used to assess the size and appearance of nodules and is helpful in facilitating FNAC. If the nodule contains a significant cystic component or is located posteriorly, there is a decreased accuracy of FNAC performed with palpation.<sup>9</sup> After an initial non-diagnostic cytology result, repeating the FNAC with ultrasound guidance will yield a diagnostic cytology specimen in 75% of solid nodules and 50% of cystic nodules.<sup>10</sup>

Nodules greater than 10 mm in size in at least two dimensions on ultrasound are deemed clinically significant and should undergo FNAC.<sup>11</sup> Smaller nodules should undergo further evaluation if they are deemed high-risk. High-risk features include aspects of history such as prior head and neck irradiation, the presence of a cancer syndrome, and family history, as well as specific ultrasound findings.<sup>12 13</sup>

Sonographic features suggestive of well-differentiated thyroid cancer include size, irregular infiltrative margins, nodular composition, the absence of a halo, hypoechoogenicity of the nodule and intranodular hypervascularity.<sup>14-16</sup>

Despite the development of high-resolution ultrasound, and abundant studies examining the characteristics of thyroid cancer on modern machines,<sup>17-19</sup> the literature fails to identify a single sonographic feature, or combination of features, which is adequately sensitive or specific to identify all malignant nodules.<sup>20</sup> Previously, malignancy could be predicted with a high level of specificity in only a few patients with ultrasound alone.<sup>21</sup>

Recent studies with high-resolution ultrasound report a sensitivity and specificity in the order of 80%, and have a positive predictive value of only 40%.<sup>22</sup> Some features useful in the accurate identification of thyroid cancer subtypes have been identified in the literature. Microcalcifications, resulting from superimposed psammoma bodies, have a specificity as high as 95% for the presence of papillary thyroid carcinoma.<sup>16</sup> Papillary thyroid carcinoma has been identified in 87% of solid nodules.<sup>17</sup> A spongiform appearance is 99.7% specific for benign thyroid nodules.<sup>23-25</sup> Despite a growing body of research on sonography, management algorithms for the thyroid nodule continue to rely on the role of FNAC. The primary contribution of ultrasound lies in the determination of nodule size and guidance for FNAC.

Radiological adjuncts in the assessment of the thyroid nodule are used on a case-by-case basis. Although MRI has a more established role in the assessment of locally advanced disease, it has been used in the diagnostic process of thyroid nodules. Most malignant thyroid tumours demonstrate iso-intense signal to normal thyroid tissue on T1 weighted images and hyperintense signal on T2 weighted images, though malignancy is often indistinguishable from benign thyroid nodules.<sup>26 27</sup>

FDG-PET scanning has been used to help distinguish benign from malignant nodules based on the increased glucose metabolism of malignant cells. 1-2% of people undergoing FDG-PET imaging for other reasons have incidental thyroid nodules, and the risk of malignancy in these nodules can be as high as 33%.<sup>24 28 29</sup> PET scans appear to have relatively high sensitivity for malignancy but low specificity, though results vary among studies.<sup>30</sup> There may be little advantage to routine PET-CT over modern high-resolution ultrasound scanners.<sup>22</sup>

Another imaging technology, MRS, allows biochemical characterisation of scanned tissue, and has been investigated as a feasible means of identifying malignant nodules.<sup>31</sup> Thyroid nodule proton spectroscopy ex vivo has been able to distinguish purely benign follicular neoplasms from follicular tumours that have an atypical follicular pattern on cytology.<sup>32</sup> A study correlated choline peaks with the presence of malignancy with a sensitivity of 100% and specificity of 89%.<sup>33</sup>

Elastography is an emerging new technique that uses ultrasound to provide an estimation of tissue stiffness by measuring the degree of distortion under the application of an external force.<sup>34</sup> Ultrasound elastography has been estimated to predict malignancy with up to 96% specificity and 85% sensitivity.<sup>35 36</sup> Although promising developments, these radiological adjuncts to ultrasound are not routinely used in the characterisation of thyroid nodules.

## **Imaging of thyroid cancer—pre- and post-treatment**

Once diagnosed, the staging of thyroid cancer is determined by lymph node involvement, the presence of metastatic disease, the anatomical extent of the tumour, and, unlike other malignancies, the patient's age and tumour histology.<sup>6</sup>

Ultrasound is the primary imaging modality for T staging. For T3 and T4 tumours, CT and MRI provide additional information. They have a role in the assessment of large, rapidly growing or retrosternal tumours, and cancers complicated by vocal cord paralysis, fixation to adjacent tissues and symptoms suggestive of compression or invasion of surrounding structures.<sup>11</sup>

Compared with ultrasound, tumour invasion into posterior paratracheal tissues and the substernal area is better visualised on MRI,<sup>37</sup> though CT is more sensitive for the detection of calcifications.<sup>38</sup> MRI and CT are also helpful in the anatomical localisation of an abnormal focus on radioiodide or FDG-PET scan.<sup>39</sup>

The American Thyroid Association recommends the use of preoperative neck ultrasound for assessing the contralateral thyroid and cervical lymph nodes in patients with malignant cytological findings.<sup>40</sup> Although ultrasound is operator dependent, it has a higher sensitivity for the detection of cervical lymph node metastases than CT, MRI or PET.<sup>41</sup> Preoperative ultrasound identifies suspicious cervical lymphadenopathy in 20-31% of cases,<sup>42 43</sup> potentially altering the surgical approach in as many as 20% of patients.<sup>44 45</sup>

Sonographic features suggestive of abnormal metastatic lymph nodes include loss of the fatty hilum, short axis, hypoechoogenicity, cystic change, calcifications, and peripheral vascularity.<sup>46 47</sup> Lymph nodes greater than 9 mm in diameter, those with a longitudinal-transverse ratio less than 2.0, and those with a round configuration rather than oval shape are more likely to contain metastatic disease.<sup>14</sup> Malignant lymph nodes are more likely to occur in levels III, IV and VI.<sup>47 48</sup>

Preoperative ultrasound identifies only half of the lymph nodes found at surgery, due to anatomical structures obscuring the sonographic view.<sup>48</sup> In this context, CT and MRI have a role in the evaluation of metastatic nodal disease. However, intravenous contrast used for a CT scan may compromise the use of postoperative radioactive iodine and non-contrast studies may prove difficult to interpret. Unlike iodine contrast, MRI with gadolinium does not affect thyroidal iodine uptake.<sup>49</sup>

After total thyroidectomy and radioactive iodine (RAI) remnant ablation, surveillance cervical ultrasound is performed to evaluate the thyroid bed and cervical nodal compartments. Serum thyroglobulin should be undetectable and is followed as a reliable indicator for persistent or recurrent disease.<sup>50</sup> When thyroglobulin levels rise, the patient may be assessed with ultrasound, CT, RAI whole body scan, and FDG-PET for the presence of recurrent local or metastatic disease. Any suspicious lymph nodes or thyroid bed nodules are biopsied.

Cervical ultrasonography is highly sensitive in the detection of local recurrence and cervical lymph node metastases in patients with well-differentiated thyroid cancer,<sup>16 44 50 51</sup> even when TSH-stimulated serum thyroglobulin levels remain undetectable.<sup>52 53</sup>

Cervical ultrasonography combined with recombinant human TSH has been shown to have a sensitivity of 96% and a negative predictive value of 99% in the detection of active disease.<sup>54</sup> However, CT and MRI are better for the evaluation of retropharyngeal, parapharyngeal and retrotracheal nodes, which are obscured by airway or bony structures on ultrasound.<sup>48</sup>

Diagnostic RAI whole body scans are useful when there is little or no remaining thyroid tissue. Disease not visualised on the RAI whole body scan, regardless of the activity of <sup>131</sup>I employed, may occasionally be visualised on the treatment whole body scan images after larger therapeutic doses of <sup>131</sup>I.<sup>55</sup>

FDG-PET is used to localise disease in thyroglobulin-positive, RAI scan-negative patients. In poorly differentiated cancers, which are unlikely to concentrate RAI, FDG-PET helps to identify sites of disease that may be missed with conventional RAI scanning. FDG-PET also has a role in the staging and surveillance of invasive or metastatic Hurthle cell carcinoma. It is also used to monitor the clinical response of recurrent disease following surgical resection, embolisation, external beam irradiation or systemic therapy.<sup>56</sup>

## Summary

Radiology and nuclear medicine play an important role in the management of the thyroid nodule and thyroid cancer. However, decision-making algorithms on the clinical management of thyroid nodules continue to hinge on the findings of FNAC. The traditional modality of ultrasound, now with enhanced high-resolution, is important in facilitating FNAC, as well as the staging and surveillance of thyroid cancer.

With the increasing detection of thyroid nodules as incidental findings on imaging, there has been attention on alternate imaging in the attempt to distinguish benign from malignant disease, and to reduce the rate of invasive interventions such as diagnostic hemithyroidectomy. These remain largely experimental, confined to the realm of research, and are not easily accessible.

In the investigation of recurrent thyroid cancer, imaging methods such as CT and MRI may have a role. The modalities of MRS, RAI scanning and FDG-PET are yet to establish their position in the clinical management of thyroid disease.

**Competing interests:** None.

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