

**Supplementary table 2. Evidence table**

Clinical situation 1.				
Reference	Study design	Patient number	Result	Study quality (KCIG)
25. Brito JP, Gionfriddo MR, Al Nofal A, Boehmer KR, Leppin AL, Reading C, et al. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. <i>J Clin Endocrinol Metab</i> 2014;99:1253-1263	Systematic review & meta-analysis	18288	We included 31 studies between 1985 and 2012 (number of nodules studied 18,288; average size 15 mm). The frequency of thyroid cancer was 20%. The most common type of cancer was papillary thyroid cancer (84%). The US nodule features with the highest diagnostic odds ratio for malignancy was being taller than wider [11.14 (95% confidence interval 6.6-18.9)]. Conversely, the US nodule features with the highest diagnostic odds ratio for benign nodules was spongiform appearance [12 (95% confidence interval 0.61-234.3)]. Heterogeneity across studies was substantial. Estimates of accuracy depended on the experience of the physician interpreting the US, the type of cancer and nodule (indeterminate), and type of reference standard. In a threshold model, spongiform appearance and cystic nodules were the only two features that, if present, could have avoided the use of fine-needle aspiration biopsy.	1
26. Smith-Bindman R, Lebda P, Feldstein VA, Sellami D, Goldstein RB, Brasic N, et al. Risk of thyroid cancer based on thyroid ultrasound imaging characteristics: results of a population-based study. <i>JAMA Intern Med</i> 2013;173:1788-1796	Case-controlled study	8806	A total of 8806 patients underwent 11,618 thyroid ultrasound examinations during the study period, including 105 subsequently diagnosed as having thyroid cancer. Thyroid nodules were common in patients diagnosed as having cancer (96.9%) and patients not diagnosed as having thyroid cancer (56.4%). Three ultrasound nodule characteristics--microcalcifications (odds ratio [OR], 8.1; 95% CI, 3.8-17.3), size greater than 2 cm (OR, 3.6; 95% CI, 1.7-7.6), and an entirely solid composition (OR, 4.0; 95% CI, 1.7-9.2)--were the only findings associated with the risk of thyroid cancer. If 1 characteristic is used as an indication for biopsy, most cases of thyroid cancer would be detected (sensitivity, 0.88; 95% CI, 0.80-0.94), with a high false-positive rate	4

			(0.44; 95% CI, 0.43-0.45) and a low positive likelihood ratio (2.0; 95% CI, 1.8-2.2), and 56 biopsies will be performed per cancer diagnosed. If 2 characteristics were required for biopsy, the sensitivity and false-positive rates would be lower (sensitivity, 0.52; 95% CI, 0.42-0.62; false-positive rate, 0.07; 95% CI, 0.07-0.08), the positive likelihood ratio would be higher (7.1; 95% CI, 6.2-8.2), and only 16 biopsies will be performed per cancer diagnosed. Compared with performing biopsy of all thyroid nodules larger than 5 mm, adoption of this more stringent rule requiring 2 abnormal nodule characteristics to prompt biopsy would reduce unnecessary biopsies by 90% while maintaining a low risk of cancer (5 per 1000 patients for whom biopsy is deferred).	
27. Solbiati L, Osti V, Cova L, Tonolini M. Ultrasound of thyroid, parathyroid glands and neck lymph nodes. Eur Radiol 2001;11:2411-2424	Review	N/A	In the past 15 years high-frequency B-mode sonography and colour-power Doppler have become the most important and most widely employed imaging modalities for the study of the neck, in particular for thyroid gland, parathyroids and lymph nodes. Sonography allows not only the detection but often also the characterization of the diseases of these organs, distinguishing benign from malignant lesions with high sensitivity and specificity, which could be further improved by the employ of ultrasound contrast agents and harmonic imaging. Although no single sonographic criterion is specific for benign or malignant nature of the lesions, the combination of different signs can be markedly helpful to speed up the diagnostic process. Fine-needle aspiration biopsy (FNAB) remains the most accurate modality for the definitive assessment of thyroid gland nodules and of any doubtful case of nodal disease. In association with clinical findings and serum levels of parathormone, FNAB has specificity close to 100% for the characterization of parathyroid adenomas. A combined approach with sonography and FNAB is generally highly	5

			effective.	
28. Chiofalo MG, Signoriello S, Fulciniti F, Avenia N, Ristagno S, Lombardi CP, et al. Predictivity of clinical, laboratory and imaging findings in diagnostic definition of palpable thyroid nodules. A multicenter prospective study. <i>Endocrine</i> 2018;61:43-50	Prospective cohort study	902	Cancer was found in 433/902 (48%) patients. Considering TIR4-5 only as positive cytology, specificity, and PPV were high (94 and 91%) but sensitivity and NPV were low (61 and 72%); conversely, including TIR3 among positive, sensitivity and NPV were higher (88 and 82%) while specificity and PPV decreased (52 and 63%). Ultrasonographic size $\geq 3$ cm was independently associated with benignity among TIR2 cases (OR of malignancy 0.37, 95% CI 0.18-0.78). In TIR3 cases the hard consistency of small nodules was associated with malignancy (OR: 3.51, 95% CI 1.84-6.70, $p < 0.001$ ), while size alone, irrespective of consistency, was not diagnostically informative. No other significant association was found in TIR2 and TIR3. CONCLUSIONS: The combination of cytology with clinical and ultrasonographic parameters may improve diagnostic definition of palpable thyroid nodules. However, the need for innovative diagnostic tools is still high.	2
29. Lee YH, Kim DW, In HS, Park JS, Kim SH, Eom JW, et al. Differentiation between benign and malignant solid thyroid nodules using an US classification system. <i>Korean J Radiol</i> 2011;12:559-567	Case-controlled study	191	Of the 191 solid nodules, 103 were subjected to thyroid surgery. US categories for these 191 nodules were malignant (n = 52), suspicious for malignancy (n = 16), borderline (n = 23), probably benign (n = 18), and benign (n = 82). A receiver-operating characteristic curve analysis revealed that the US diagnosis for solid thyroid nodules using the 5-category US classification system was very good. The sensitivity, specificity, positive and negative predictive values, and accuracy of US diagnosis were 86%, 95%, 91%, 92%, and 92%, respectively, when benign, probably benign, and borderline categories were collectively classified as benign (negative).	1
30. Mandel SJ. Diagnostic use of ultrasonography in	Review	N/A	In two studies that correlated ultrasound findings with physical examination findings in patients with a solitary thyroid nodule	5

patients with nodular thyroid disease. <i>Endocr Pract</i> 2004;10:246-252			detected by palpation, 16% of such patients had no corresponding nodule evident on ultrasonography, and 45% of such patients had an additional nodule detected by ultrasonography. Similarly, approximately 18% of patients with a palpable multinodular thyroid had no nodules larger than 1 cm in diameter on ultrasound studies. Thyroid nodules larger than 1 cm have been found by ultrasonography to be present in from 2 to almost 5% of the population with normal findings on examination of the thyroid. Use of screening ultrasound study of the thyroid has been suggested for patients with a history of childhood irradiation to the head and neck or a family history of thyroid cancer. Numerous investigations that have evaluated ultrasound features of thyroid nodules have suggested five characteristics as suggestive of malignant potential--hypoechoogenicity, microcalcifications, irregular or microlobulated border, absent or irregular thick halo, and increased intranodular vascularity.	
31. Cesur M, Corapcioglu D, Bulut S, Gursoy A, Yilmaz AE, Erdogan N, et al. Comparison of palpation-guided fine-needle aspiration biopsy to ultrasound-guided fine-needle aspiration biopsy in the evaluation of thyroid nodules. <i>Thyroid</i> 2006;16:555-561	Case-controlled study	215	The rates of inadequate material for PGFNAB and UGFNAB were significantly different as 32.3% and 21.4%, respectively ( $p = 0.004$ ). There was significantly higher inadequate material rate in PGFNAB group for small-sized nodules (greatest nodule diameter between 10 and 15 mm) ( $p = 0.009$ ), despite inadequate material rate was not significant for both procedures for larger sized nodules. False-negative results were 15.8% for PGFNAB and 5.6% for UGFNAB. Regarding cost analysis, the difference between the two methods was 20 dollars on average for each patient.	4
32. Hambly NM, Gonen M, Gerst SR, Li D, Jia X, Mironov S, et al. Implementation of evidence-based guidelines for thyroid nodule biopsy: a model for establishment of practice standards. <i>AJR Am J Roentgenol</i> 2011;196:655-660	Case-controlled study	101	The sensitivity and specificity of biopsy recommendation were 96.1% and 52%, respectively. The misclassification rate was 25.7%, and accuracy was 74.3%. Interobserver agreement on biopsy recommendation was fair to substantial ( $\kappa$ , 0.38-0.69). The proportion of agreement was excellent for malignant nodules (0.88-1.0). The risk of malignancy increased with increasing malignancy rating: 4.3% of nodules with a malignancy rating of 1 were malignant versus 93.4% of those assigned a rating of 5.	4

<p>33. Russ G, Bonnema SJ, Erdogan MF, Durante C, Ngu R, Leenhardt L. European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS. <i>European Thyroid Journal</i> 2017;6:225-237</p>	<p>Review</p>	<p>N/A</p>	<p>Thyroid ultrasound (US) is a key examination for the management of thyroid nodules. Thyroid US is easily accessible, noninvasive, and cost-effective, and is a mandatory step in the workup of thyroid nodules. The main disadvantage of the method is that it is operator dependent. Thyroid US assessment of the risk of malignancy is crucial in patients with nodules, in order to select those who should have a fine needle aspiration (FNA) biopsy performed. Due to the pivotal role of thyroid US in the management of patients with nodules, the European Thyroid Association convened a panel of international experts to set up European guidelines on US risk stratification of thyroid nodules. Based on a review of the literature and on the American Association of Clinical Endocrinologists, American Thyroid Association, and Korean guidelines, the panel created the novel European Thyroid Imaging and Reporting Data System, called EU-TIRADS. This comprises a thyroid US lexicon; a standardized report; definitions of benign and low-, intermediate-, and high-risk nodules, with the estimated risks of malignancy in each category; and indications for FNA. Illustrated by numerous US images, the EU-TIRADS aims to serve physicians in their clinical practice, to enhance the interobserver reproducibility of descriptions, and to simplify communication of the results.</p>	<p>5</p>
<p>34. Tessler FN, Middleton WD, Grant EG, Hoang JK, Berland LL, Teefey SA, et al. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee. <i>J Am Coll Radiol</i> 2017;14:587-595</p>	<p>Review</p>	<p>N/A</p>	<p>Thyroid nodules are a frequent finding on neck sonography. Most nodules are benign; therefore, many nodules are biopsied to identify the small number that are malignant or require surgery for a definitive diagnosis. Since 2009, many professional societies and investigators have proposed ultrasound-based risk stratification systems to identify nodules that warrant biopsy or sonographic follow-up. Because some of these systems were founded on the BI-RADS® classification that is widely used in breast imaging, their authors chose to apply the acronym TI-RADS, for Thyroid Imaging, Reporting and Data System. In 2012, the ACR convened committees to (1) provide recommendations for reporting incidental thyroid nodules, (2) develop a set of standard terms (lexicon) for ultrasound reporting, and (3) propose a TI-RADS on the basis of the lexicon. The committees published the results of the first</p>	<p>5</p>

			two efforts in 2015. In this article, the authors present the ACR TI-RADS Committee's recommendations, which provide guidance regarding management of thyroid nodules on the basis of their ultrasound appearance. The authors also describe the committee's future directions.	
35. Hoang JK, Langer JE, Middleton WD, Wu CC, Hammers LW, Cronan JJ, et al. Managing incidental thyroid nodules detected on imaging: white paper of the ACR Incidental Thyroid Findings Committee. J Am Coll Radiol 2015;12:143-150	Review	N/A	The incidental thyroid nodule (ITN) is one of the most common incidental findings on imaging studies that include the neck. An ITN is defined as a nodule not previously detected or suspected clinically, but identified by an imaging study. The workup of ITNs has led to increased costs from additional procedures, and in some cases, to increased risk to the patient because physicians are naturally concerned about the risk of malignancy and a delayed cancer diagnosis. However, the majority of ITNs are benign, and small, incidental thyroid malignancies typically have indolent behavior. The ACR formed the Incidental Thyroid Findings Committee to derive a practical approach to managing ITNs on CT, MRI, nuclear medicine, and ultrasound studies. This white paper describes consensus recommendations representing this committee's review of the literature and their practice experience.	5
36. Shetty SK, Maher MM, Hahn PF, Halpern EF, Aquino SL. Significance of incidental thyroid lesions detected on CT: correlation among CT, sonography, and pathology. AJR Am J Roentgenol 2006;187:1349-1356	Retrospective cohort study	230	CT findings matched the sonographic characterization in 122 patients (53.0%), correctly identified the dominant nodule but missed multinodularity in 69 (30.0%) patients, and underestimated the number of nodules in 24 (10.4%) patients. CT overestimated the number of nodules in 5 (2.2%) patients and was false-positive for lesions in 10 patients (4.3%). Ninetyone patients with a single or dominant nodule on CT had pathologic correlation: 7 nodules were malignant, 17 showed malignant potential, and 67 were benign. Of 27 patients with multinodular or enlarged thyroid glands on CT and histopathologic correlation, 2 lesions were malignant and 25 benign. The presence of punctate calcifications on CT significantly correlated to the presence of microcalcifications on sonography ( $p < 0.02$ ). Benign nodules were significantly smaller (mean, $2.16 \pm 1.01$ cm; range, 0.6–4.5 cm) than malignant and potentially malignant nodules (mean, $2.79 \pm 0.99$ cm; range, 0.7–4.6 cm) ( $p = 0.01$ ). Patients 35 years or younger who had a thyroid lesion on CT were more likely to have malignancy ( $p < 0.01$ ). Overall, among incidentally	2

			detected lesions of the thyroid gland, there was at least a 3.9% rate of malignancy (95% CI: 1.8–7.3%) and 7.4% rate of malignant potential (95% CI: 4.4–11.6%).	
37. Hoang JK, Branstetter BfT, Gafton AR, Lee WK, Glastonbury CM. Imaging of thyroid carcinoma with CT and MRI: approaches to common scenarios. <i>Cancer Imaging</i> 2013;13:128-139	Review	N/A	Computed tomography (CT) and magnetic resonance imaging (MRI) can play an important role in preoperative and post-treatment assessment of thyroid malignancy. The radiologist should be aware of the pathological behavior of thyroid carcinoma, and the characteristic imaging appearance of the primary tumor and metastases. This review describes the approach to imaging thyroid cancer on CT and MRI for four common scenarios: detection of the incidental thyroid nodule, evaluation of thyroid metastases, presurgical imaging for invasive disease, and evaluation for recurrence in the post-treatment neck.	5
Clinical situation 2				
43. Pacini F, Basolo F, Bellantone R, Boni G, Cannizzaro MA, De Palma M, et al. Italian consensus on diagnosis and treatment of differentiated thyroid cancer: joint statements of six Italian societies. <i>J Endocrinol Invest</i> 2018;41:849-876	Review	N/A	The document includes recommendations regarding initial evaluation of thyroid nodules, clinical and ultrasound criteria for fine-needle aspiration biopsy, initial management of thyroid cancer including staging and risk assessment, surgical management, radioiodine remnant ablation, and levothyroxine therapy, short-term and long-term follow-up strategies, and management of recurrent and metastatic disease. The objective of this consensus is to inform clinicians, patients, researchers, and health policy makers about the best strategies (and their limitations) relating to the diagnosis and treatment of differentiated thyroid cancer.	5
44. Eun NL, Son EJ, Kim JA, Gweon HM, Kang JH, Youk JH. Comparison of the diagnostic performances of ultrasonography, CT and fine needle aspiration cytology for the prediction of lymph node metastasis in patients with lymph node dissection of papillary thyroid carcinoma: A retrospective cohort study.	Retrospective cohort study	302	US indication of LN dissection was significantly correlated with malignancy ( $p < .0001$ ). Values of area under the curve of highly suspicious US findings and FNAC+Tg were significantly higher than that of CT (0.786, 0.878, 0.585, $p < .0001$ , respectively). Suspicious US, CT findings and malignant FNAC+Tg were significantly associated with the largest size of metastatic LNs ( $p = .003$ , $p = .0003$ , and $p = .0006$ , respectively) and total number of metastatic LNs ( $p = .007$ , $p = .038$ , and $p = .005$ , respectively).	1

Int J Surg 2018;51:145-150				
45. Jiang HJ, Wu CW, Chiang FY, Chiou HC, Chen IJ, Hsiao PJ. Reliable sonographic features for nodal thyroglobulin to diagnose recurrent lymph node metastasis from papillary thyroid carcinoma. Clin Otolaryngol 2018	Retrospective cohort study	148	Overall, 49 lymph nodes were documented as recurrent nodal metastasis. LN-FNA-Tg greater than serum thyroglobulin and higher than 1 ng/mL achieved 100% of diagnostic rate for recurrent nodal metastasis. The malignant sonographic features that significantly cohered with positive LN-FNA-Tg were cystic and hyperechoic content and lack hilum, in sequence.	1
46. Leboulleux S, Girard E, Rose M, Travagli JP, Sabbah N, Caillou B, et al. Ultrasound criteria of malignancy for cervical lymph nodes in patients followed up for differentiated thyroid cancer. J Clin Endocrinol Metab 2007;92:3590-3594	Prospective cohort study	56	One hundred three LNs were detected on US, 578 LNs were surgically removed, and 56 LNs were analyzed (28 benign and 28 malignant). Sensitivity and specificity were 68 and 75% for the long axis ( 1 cm), 61 and 96% for the short axis ( 5 mm), 46 and 64% for the round shape (long to short axis ratio 2), 100 and 29% for the loss of fatty hyperechoic hilum, 39 and 18% for hypoechogenicity, 11 and 100% for cystic appearance, 46 and 100% for hyperechoic punctuations, and 86 and 82% for peripheral vascularization.	1
47. O'Connell K, Yen TW, Quiroz F, Evans DB, Wang TS. The utility of routine preoperative cervical ultrasonography in patients undergoing thyroidectomy for differentiated thyroid cancer. Surgery 2013;154:697-701; discussion 701-693	Retrospective cohort study	70	Palpable lateral neck adenopathy was thought to be present in 5 (7%) of the 70 patients, but confirmed by US in only 3; 2 patients avoided lateral compartment neck dissection (LCND). Of 65 patients with no palpable lymphadenopathy, 14 (22%) had abnormal lymphadenopathy on preoperative US. All 14 patients underwent total thyroidectomy with central compartment neck dissection (CCND);12 patients with abnormal US findings in the lateral compartment(s) also underwent LCND. Metastatic disease was confirmed in 13 (93%) of the 14 patients: 13 of 14 who underwent CCND and 11 (92%) of 12 who underwent LCND.	1
48. Rosario PW, de Faria S, Bicalho L, Alves MF, Borges MA, Purisch S, et al. Ultrasonographic differentiation between metastatic and benign lymph nodes in patients with papillary thyroid carcinoma. J Ultrasound Med 2005;24:1385-	Retrospective cohort study	112	A total of 198 lymph nodes were metastatic, and 152 were benign (normal or with nonspecific lymphadenitis). Minimum axial diameters of 7 mm for level II (upper internal jugular chain) and 6 mm for the rest of the neck were observed in 93% of metastatic lymph nodes, absence of an echogenic hilum in 88%, hyperechogenicity in relation to the adjacent muscles in 86%, a round shape in 80%, calcifications in 49.5%, and intranodal cystic necrosis in 20%. These ultrasonographic	1



1389			characteristics were observed in 17%, 10%, 4.5%, 29.5%, 0%, and 0% of benign lymph nodes, respectively.	
49. Shimamoto K, Satake H, Sawaki A, Ishigaki T, Funahashi H, Imai T. Preoperative staging of thyroid papillary carcinoma with ultrasonography. <i>Eur J Radiol</i> 1998;29:4-10	Retrospective cohort study	77	In 63 (81.8%) cases, T categories were estimated accurately. The sensitivity in depicting tumor extension into the prethyroidal muscle and/or the sternocleidomastoid muscle was 77.8%, whereas the sensitivity for invasion into the trachea and the esophagus was 42.9 and 28.6%, respectively. In 37 (48.1%) cases, N categories were underestimated, and the sensitivity in the detection of regional lymph node metastasis was 36.7%. Doppler flow imaging was performed in 36 patients, and no correlation was found between flow patterns and the presence of local invasion or regional lymph node metastasis.	1
50. Solorzano CC, Carneiro DM, Ramirez M, Lee TM, Irvin GL, 3rd. Surgeon-performed ultrasound in the management of thyroid malignancy. <i>Am Surg</i> 2004;70:576-580; discussion 580-572	Retrospective cohort study	72	Seventy-two patients underwent operations for thyroid cancer. US influenced the management in 57 per cent (41/72) of patients. US was useful in 1) identification and guidance for the FNA of nonpalpable cancers in 28 per cent (20/72), 2) identification of nonpalpable nodules in the contralateral lobe in 38 per cent (27/72), 3) preoperative diagnosis of nonpalpable metastatic lymph nodes in 24 per cent (17/72), and intraoperative guidance for their excision.	1
51. Stulak JM, Grant CS, Farley DR, Thompson GB, van Heerden JA, Hay ID, et al. Value of preoperative ultrasonography in the surgical management of initial and reoperative papillary thyroid cancer. <i>Arch Surg</i> 2006;141:489-494; discussion 494-486	Retrospective cohort study	770	Ultrasonography identified nonpalpable lateral jugular LNMs in 70 (14.4%) of the patients undergoing initial exploration. Similarly, in reoperative patients, nonpalpable lateral LNMs were detected via US in 106 (64.2%), and 61 (28.2%) had LNMs detected in the central neck. Even when nodes were palpable preoperatively (37 [6.7%] of the initial and 56 [25.6%] of the reoperative patients), US assessment of the extent of LNM involvement altered the operation in 15 (40.5%) of the initial and 24 (42.9%) of the reoperative patients. The sensitivity, specificity, and positive predictive value for US were 83.5%, 97.7%, and 88.8% in initial patients, and 90.4%, 78.9%, and 93.9% in reoperative patients.	1
52. Lee CY, Kim SJ, Ko KR, Chung KW, Lee JH. Predictive factors for extrathyroidal extension of papillary thyroid carcinoma based on preoperative sonography. <i>J Ultrasound Med</i>	Retrospective cohort study	568	Two hundred seventy-five of the 568 patients were proven to have pathologic extrathyroidal extension of papillary thyroid cancer after surgery (75.9% diagnostic accuracy, 83.3% sensitivity, 68.9% specificity, 71.6% positive predictive value, and 81.5% negative predictive value). Of 320 patients with sonographically suspected extrathyroidal extension, a larger	1

2014;33:231-238			lesion size ( $P < .001$ ) and a higher lymph node stage on sonography ( $P = .004$ ) were the best predictors of extrathyroidal extension among the features that we measured. There were no significant differences in terms of the lesion site or thyroid parenchymal background echogenicity. Thyroid capsular protrusion had a higher predictive value than the abutting ratio ( $P = .001$ ). However, increasing the abutting ratio enabled the prediction of extrathyroidal extension on sonography ( $P = .009$ ).	
53. Kwak JY, Kim EK, Youk JH, Kim MJ, Son EJ, Choi SH, et al. Extrathyroid extension of well-differentiated papillary thyroid microcarcinoma on US. <i>Thyroid</i> 2008;18:609-614	Retrospective cohort study	181	Of the 221 PTMCs, extrathyroidal extension was present in 89 (40.3%) based on pathologic results. The mean size was not significantly different between PTMCs with and without extrathyroidal extension ( $p = 0.527$ ). When the degree of contact was high, extrathyroidal extension of the thyroid cancer was high ( $p < 0.0001$ ). Considering the odds ratio, Az value, and positive predictive value of each US finding, more than 25% contact with the adjacent capsule is the most accurate measurement for predicting extrathyroidal extension.	1
54. Choi JS, Chung WY, Kwak JY, Moon HJ, Kim MJ, Kim E-K. Staging of Papillary Thyroid Carcinoma with Ultrasonography: Performance in a Large Series. <i>Annals of Surgical Oncology</i> 2011;18:3572-3578	Prospective cohort study	722	US predicted 61.7% (142/230) of patients with multifocal PTC and 67.1% (100/149) of patients with bilateral malignancy. Overall accuracy of US for T categorization was 69.7% (503/722) and that of US for N categorization was 59% (426/722). Accuracies of sonographic categorization for N0, N1a, and N1b were 66% (276/418), 33.3% (70/210), and 85.1% (80/94), respectively. Overall US accuracy for prediction of an N category was significantly lower in patients with US-indicated DTD (51.1%, 67/131) than it was in patients without DTD (60.7%, 359/591; $P = 0.043$ ).	1
55. Park JS, Son K-R, Na DG, Kim E, Kim S. Performance of Preoperative Sonographic Staging of Papillary Thyroid Carcinoma Based on the Sixth Edition of the AJCC/UICC TNM Classification System. <i>American Journal of Roentgenology</i> 2009;192:66-72	Prospective cohort study	94	One hundred twenty-seven cancers in the 94 patients were proven after surgery. Sonography accurately identified 75.9% (22/29) of patients with multifocal cancer and 83.3% (15/18) of patients with bilateral cancers. Using a cutoff value of 50% or more of the tumor abutting the thyroid capsule (grade 2), the sensitivity, specificity, and accuracy of sonography in predicting extrathyroidal invasion were 85.3%, 70.0%, and 74.5%, respectively, and the overall accuracy of sonography for T staging was 67.0% (63/94). One hundred forty-seven cervical lymph node levels were dissected. All six sonographic findings were significantly more frequent in metastatic lymph nodes in	1

			the lateral group. However, in the central group, only two criteria-calcification and abnormal Doppler pattern-were found to significantly predict the presence of metastasis. The overall accuracy of sonography for N staging was 71.3% (67/94).	
56. Moon SJ, Kim DW, Kim SJ, Ha TK, Park HK, Jung SJ. Ultrasound assessment of degrees of extrathyroidal extension in papillary thyroid microcarcinoma. <i>Endocr Pract</i> 2014;20:1037-1043	Prospective cohort study	105	Of 105 PTMC cases, the preoperative sonographic diagnoses included intraglandular location (n = 35), subcapsular location (n = 30), mild capsule abutment (n = 7), moderate capsule abutment (n = 19), and perithyroidal invasion without adjacent strap muscle invasion (n = 14). When the sonographic T stages were compared with histopathologic results, all the sonographic categories showed high specificity and low sensitivity. The intraglandular and subcapsular location cases in preoperative US diagnosis showed a low rate of extrathyroidal tumor invasion (6.2%, 4/65). The extrathyroidal tumor invasion cases in preoperative US diagnosis only included 26 extrathyroidal fat invasion cases, and 12 (46.2%, 12/26) true positives. There was a significant correlation between multifocality and histopathologic T stage, but no significant relationship between level VI node metastasis and histopathologic T stage was found.	1
57. Kim SS, Lee BJ, Lee JC, Kim SJ, Lee SH, Jeon YK, et al. Preoperative ultrasonographic tumor characteristics as a predictive factor of tumor stage in papillary thyroid carcinoma. <i>Head Neck</i> 2011;33:1719-1726	Retrospective cohort study	354	Tumor size, echogenicity, and contact with the capsule were predictive for the presence of extrathyroid extension. Size and echogenicity were significantly associated with central lymph node metastasis in the multivariate analysis. Some ultrasonography characteristics such as round shape, well-defined margin, and isoechoic echogenicity were negative predictive factors for extrathyroid extension and central lymph node metastasis.	2
58. Kuo EJ, Thi WJ, Zheng F, Zanoocco KA, Livhits MJ, Yeh MW. Individualizing Surgery in Papillary Thyroid Carcinoma Based on a Detailed Sonographic Assessment of Extrathyroidal Extension. <i>Thyroid</i> 2017;27:1544-1549	Retrospective cohort study	141	Of 141 patients with PTC, 35 (25%) patients were candidates for lobectomy, and 105 (75%) patients were not candidates for lobectomy because of non-tumor (n = 46) or tumor (n = 59) characteristics. Of the 35 patients who were candidates for lobectomy, 27 had sonographic ETE on detailed assessment. Total thyroidectomy was performed in 23 patients, while thyroid lobectomy was performed in 12 patients. Total thyroidectomy was indicated based on final histopathology in 15 patients (ETE, aggressive histology, vascular invasion, or cervical metastasis). Histopathologic ETE was present in 13 of these 15 patients and was the only indication for total	1

			thyroidectomy in the remaining eight patients. Positive and negative predictive values for the prediction of ETE based on detailed sonographic assessment were 52% and 100%, respectively. In comparison to a strategy of routine total thyroidectomy, a detailed sonographic assessment of ETE reduced the rate of potentially avoidable total thyroidectomy from 57% to 31%.	
59. Zhao H, Li H. Meta-analysis of ultrasound for cervical lymph nodes in papillary thyroid cancer: Diagnosis of central and lateral compartment nodal metastases. Eur J Radiol 2019;112:14-21	Systematic review & meta-analysis	4014	Nineteen studies comprising 4014 patients were included in the meta-analysis. The pooled sensitivity, specificity, DOR and area under curve (AUC) of ultrasound in detecting central CLNM were 0.33 (95% confidence interval (95% CI): 0.31-0.35), 0.93 (95% CI: 0.92-0.94), 5.63 (95% CI: 3.50-9.04), and 0.69, respectively; and lateral CLNM were 0.70 (95% CI: 0.68-0.72), 0.84 (95% CI: 0.82-0.85), 18.7 (95% CI: 10.3-33.9) and 0.88, respectively. We found that the rate of central CLNM of PTC was 48.0%, and 36.2% of the dissected lymph nodes were metastatic, meanwhile, the rate of lateral CLNM of PTC was 59.2%, and 46.6% of the dissected lymph nodes were metastatic in the meta-analysis.	1
60. Boi F, Baghino G, Atzeni F, Lai ML, Faa G, Mariotti S. The diagnostic value for differentiated thyroid carcinoma metastases of thyroglobulin (Tg) measurement in washout fluid from fine-needle aspiration biopsy of neck lymph nodes is maintained in the presence of circulating anti-Tg antibodies. J Clin Endocrinol Metab 2006;91:1364-1369	Retrospective cohort study	73	In 51 TgAb-negative patients, Tg-FNAB was positive in 15 (12 with malignant and three with nondiagnostic cytology), all with histologically confirmed DTC metastases. Of the remaining 36 patients with negative Tg-FNAB, 30 had nonsuspicious and six had suspicious cytology. Histology of the latter showed four undifferentiated thyroid cancer metastases and two lymphadenitis. In 22 TgAbpositive patients, Tg-FNAB was positive in 14 (12 with malignant and two with nondiagnostic cytology), all with histologically confirmed DTC metastases.	1
61. Chung J, Kim EK, Lim H, Son EJ, Yoon JH, Youk JH, et al. Optimal indication of thyroglobulin measurement in fine-needle aspiration for detecting lateral metastatic lymph nodes in patients with papillary thyroid carcinoma.	Retrospective cohort study	220	On multivariate analysis, hyperechogenicity, cystic change, presence of calcifications, and peripheral vascularity were independent factors predictive of lymph node metastasis. After adding FNA-Tg, sensitivity and accuracy were significantly increased when the lymph node had 1 or 2 suspicious ultrasound features. However, sensitivity and accuracy were not significantly increased when the lymph node had multiple suspicious ultrasound features.	1

Head Neck 2014;36:795-801				
62. Frasoldati A, Toschi E, Zini M, Flora M, Caroggio A, Dotti C, et al. Role of thyroglobulin measurement in fine-needle aspiration biopsies of cervical lymph nodes in patients with differentiated thyroid cancer. <i>Thyroid</i> 1999;9:105-111	Retrospective cohort study	130	The identification of metastatic neck lymph nodes in patients awaiting surgery for differentiated thyroid tumor permits their excision during thyroidectomy. In order to detect thyroid cancer lymphatic metastasis before surgery, we measured thyroglobulin (Tg) in the needle wash-out of fine-needle aspiration biopsy (FNAB). Ultrasound-guided FNAB on enlarged neck nodes was performed in 23 patients awaiting surgery for differentiated thyroid tumor (n = 33 lymph nodes), 47 patients previously thyroidectomized for thyroid tumor (n = 89 lymph nodes), and 60 patients without thyroid disease (n = 94 lymph nodes). Immediately after aspiration biopsy, the needle was rinsed with 1 mL of normal saline solution and Tg levels were measured on the needle wash-out (FNAB-Tg). FNAB-Tg levels were markedly elevated in metastatic lymph nodes both in patients awaiting thyroidectomy (metastatic vs. negative lymph nodes, mean +/- SEM, 16,593 +/- 7,050 ng/mL vs. 4.91 +/- 1.61 ng/mL; p < 0.001) and in thyroidectomized patients (11,541 +/- 7,283 ng/mL vs. 0.45 +/- 0.07 ng/mL; p < 0.001). FNAB-Tg sensitivity, evaluated through histological examination in 69 lymph nodes, was 84.0%. The combination of cytology plus FNAB-Tg increased FNAB sensitivity from 76% to 92.0%. In conclusion, FNAB-Tg measurement is a useful technique for early diagnosis of lymph node metastasis originating from differentiated thyroid cancer.	2
63. Grani G, Fumarola A. Thyroglobulin in lymph node fine-needle aspiration washout: a systematic review and meta-analysis of diagnostic accuracy. <i>J Clin Endocrinol Metab</i> 2014;99:1970-1982	Systematic review & meta-analysis	2865	Including all the selected studies (24 studies, 2865 LNs) in the pooled analysis, overall sensitivity was 95.0% (95% confidence interval [CI], 93.7–96.0%), specificity was 94.5% (95% CI, 93.2–95.7%), and diagnostic odds ratio (DOR) was 338.91 (95% CI, 164.82–696.88) with significant heterogeneity (inconsistency [I <sup>2</sup> ] 65.7%; heterogeneity, P .001). Stratifying different populations and including only patients with thyroid gland (410 LNs), pooled sensitivity was 86.2% (95% CI, 80.9–90.5%), specificity was 90.2% (85.1–94.0%), and DOR was 56.621 (22.535–142.26; I <sup>2</sup> 37.3%; heterogeneity, P .121). Including only patients after thyroidectomy (1007 LNs), pooled sensitivity was 96.9% (95% CI, 94.9–98.2%), specificity was 94.1% (91.7–96.0%), and DOR was 407.65 (198.67–836.46; I <sup>2</sup> 0.0%; heterogeneity,	1

			P .673).	
64. Moon JH, Kim YI, Lim JA, Choi HS, Cho SW, Kim KW, et al. Thyroglobulin in washout fluid from lymph node fine-needle aspiration biopsy in papillary thyroid cancer: large-scale validation of the cutoff value to determine malignancy and evaluation of discrepant results. <i>J Clin Endocrinol Metab</i> 2013;98:1061-1068	Retrospective cohort study	419	In the final diagnosis, 190 LNs were malignant, and 338 LNs were benign. The median FNA-Tg was 521.2 (3676.8) ng/mL in malignant LNs, and 0.1 (0.2) ng/mL in benign LNs. The optimal cutoff value of FNA-Tg in distinguishing malignant LNs from benign LNs was 1.0 ng/mL (sensitivity, 93.2%; specificity, 95.9%) in all cases. Combining FNA-Tg and FNA cytology showed superior diagnostic power (sensitivity, 98.4%; specificity, 94.4%) when compared with diagnostic strategy using either FNA cytology or FNA-Tg alone. FNA-Tg, serum TSH, and serum Tg were higher in nonthyroidectomized patients than in thyroidectomized patients (P .001, respectively). FNA-Tg was correlated with serum TSH and Tg levels (P .001, respectively), and binary logistic regression analysis showed that serum TSH suppression and serum Tg presence independently affected the diagnosis made by FNA-Tg.	2
65. Pacini F, Fugazzola L, Lippi F, Ceccarelli C, Centoni R, Miccoli P, et al. Detection of thyroglobulin in fine needle aspirates of nonthyroidal neck masses: a clue to the diagnosis of metastatic differentiated thyroid cancer. <i>J Clin Endocrinol Metab</i> 1992;74:1401-1404	Retrospective cohort study	35	FNA-Tg was always detectable in 14 patients with thyroid cancer metastases demonstrated by histology, with a mean (+/- SD) of 27,087 +/- 37,622 ng/FNA (P less than 0.002) compared to patients without thyroid cancer metastases (mean +/- SD, 12.1 +/- 4.8 ng/FNA in 7 cases; undetectable in 14 cases). Assuming 21.7 ng/FNA (the mean +/- 2 SD of the negative patients) as the cut-off value, all patients with metastases from DTC were detected by FNA-Tg. FNA-Tg had better negative predictive value than cytology, since this last technique gave 10 inconclusive results, comprising 2 false negative results in patients with metastases from DTC. Our results indicate that elevated concentrations of FNA-Tg in nonthyroidal neck nodes strongly suggest the diagnosis of metastases from DTC.	4
66. Pak K, Suh S, Hong H, Cheon GJ, Hahn SK, Kang KW, et al. Diagnostic values of thyroglobulin measurement in fine-needle aspiration of lymph nodes in patients with thyroid cancer. <i>Endocrine</i> 2015;49:70-77	Systematic review & meta-analysis	843	Eight studies including 843 lymph nodes (LNs) were eligible for this study. The pooled sensitivity and specificity of preoperative studies are 0.89 [95 % CI 0.82–0.95], 0.60 [0.49–0.70], and those of postoperative studies are 1.0 [0.83–1.0], 1.0 [0.92–1.0]. To determine best cutoffs from each preoperative and postoperative study, the distance between the point (0, 1) and each observed cutoff values (1-specificity, sensitivity) was calculated, and the distance is minimal when the cutoff value of 32.04 for preoperative studies and of 0.9 for postoperative one	1

			are selected. FNA-Tg can be used for both preoperative and postoperative evaluation of LN metastasis. Although the cutoff values for the FNA-Tg has not been standardized, preoperative values of 32.04 ng/ml and postoperative values of 0.9 ng/ml are recommended for identifying neck LN metastasis	
67. Snozek CL, Chambers EP, Reading CC, Sebo TJ, Sistrunk JW, Singh RJ, et al. Serum thyroglobulin, high-resolution ultrasound, and lymph node thyroglobulin in diagnosis of differentiated thyroid carcinoma nodal metastases. J Clin Endocrinol Metab 2007;92:4278-4281	Retrospective cohort study	88	Fifty of 52 nonmalignant FNAB samples (96.2%) had Tg 1 ng/ml or less. All 70 malignant FNAB had Tg greater than 1 ng/ml. Of 103 specimens with diagnostic cytology, five (4.9%) had discordant Tg results; in four of these FNAB Tg was concordant with the final diagnosis. Eighteen of 19 (94.7%) FNAB with nondiagnostic (n = 16) or absent (n = 3) cytology were correctly classified by FNAB needlewash Tg. Undetectable (0.1 ng/ml) serum Tg was associated with a negative diagnosis in 21 of 23 biopsies (91.7%); the two cancer-positive samples were both serum Tg autoantibody positive and classified as suspicious by ultrasonography.	2
68. Lee Y, Kim JH, Baek JH, Jung SL, Park SW, Kim J, et al. Value of CT added to ultrasonography for the diagnosis of lymph node metastasis in patients with thyroid cancer. Head Neck 2018;40:2137-2148	Prospective cohort study	351	Of 801 pathologically proven neck levels, ultrasound/CT showed higher sensitivities in both central and lateral compartments and improved accuracy in the lateral compartment compared to ultrasound alone. In the retropharyngeal/superior mediastinal compartment, although CT could detect lymph node metastasis an ultrasound could not. Patient-based benefit was demonstrated in 13.1% of patients (46/351), and was higher in patients with cancers >1 cm than cancers ≤1 cm.	1
69. Suh CH, Baek JH, Choi YJ, Lee JH. Performance of CT in the Preoperative Diagnosis of Cervical Lymph Node Metastasis in Patients with Papillary Thyroid Cancer: A Systematic Review and Meta-Analysis. AJNR Am J Neuroradiol 2017;38:154-161	Systematic review & meta-analysis	1691	Nine eligible studies, including a total sample size of 1691 patients, were included. CT showed a summary sensitivity of 62% (95% CI, 52%-70%) and specificity of 87% (95% CI, 80%-92%) for diagnosing cervical lymph node metastasis when using level-by-level analysis. There was a positive correlation between the sensitivity and the false-positive rate (correlation coefficient, 0.807) because of the threshold effect. The summary sensitivity of combined CT/ultrasound (69%; 95% CI, 61%-77%) was significantly higher than ultrasound (51%; 95% CI, 42%-60%), though the summary specificity did not differ.	1
71. Hoang JK, Vanka J, Ludwig BJ, Glastonbury CM. Evaluation	Review	N/A	The presence and extent of nodal metastases in head and neck cancer has a great impact on treatment and prognosis.	5

of cervical lymph nodes in head and neck cancer with CT and MRI: tips, traps, and a systematic approach. <i>AJR Am J Roentgenol</i> 2013;200:W17-25			Pretreatment CT and MRI of the neck are commonly performed to evaluate for nodal metastases.	
72. Cho SJ, Suh CH, Baek JH, Chung SR, Choi YJ, Lee JH. Diagnostic performance of CT in detection of metastatic cervical lymph nodes in patients with thyroid cancer: a systematic review and meta-analysis. <i>Eur Radiol</i> 2019	Systematic review & meta-analysis	6378	Seventeen (6378 patients, 11,590 lymph nodes) studies were included. The pooled sensitivity was 55% (95% CI, 47–63%), and the pooled specificity was 87% (95% CI, 90–95%). Higgins I2 statistic demonstrated substantial heterogeneity in the sensitivity (I2 = 96.3%) and specificity (I2 = 93.8%). In a per-neck level subgroup analysis, the Higgins I2 statistic demonstrated reduced heterogeneity in both sensitivity and specificity. In the meta-regression analysis, variation in the CT protocols, such as contrast amount, scan phase, and reconstruction slice thickness, was a statistically significant factor causing heterogeneity.	1
73. Cho SJ, Suh CH, Baek JH, Chung SR, Choi YJ, Lee JH. Diagnostic performance of MRI to detect metastatic cervical lymph nodes in patients with thyroid cancer: a systematic review and meta-analysis. <i>Clin Radiol</i> 2020	Systematic review & meta-analysis	504	The pooled sensitivity and specificity in the diagnosis of metastatic cervical lymph nodes were 80% (95% confidence interval [CI]: 68e88%) and 85% (95% CI: 63e95%), respectively. The sensitivity and false-positive rate (correlation coefficient, 0.655) showed a positive correlation due to a threshold effect, which was responsible for heterogeneity across the studies, as indicated by a Q-test (p<0.01) and Higgins I2 statistic (sensitivity, I2¼490.11%; specificity, I2¼492.49%). In the meta-regression analysis, fat-suppressed imaging, and the analysis method were significant factors influencing the heterogeneity in diagnostic performance.	1
74. Choi JY, Choi YS, Park YH, Kim JH. Experience and analysis of level VII cervical lymph node metastases in patients with papillary thyroid carcinoma. <i>J Korean Surg Soc</i> 2011;80:307-312	Retrospective cohort study	195	Nine (4.6%) of 195 patients with papillary thyroid carcinoma had level VII metastasis. Clinicopathologic factors that were related to level VII metastasis included lateral neck metastasis (P < 0.01), tumor size (P < 0.01) and lymphovascular invasion (P < 0.05).	2
75. Seo YL, Yoon DY, Lim KJ, Cha JH, Yun EJ, Choi CS, et al. Locally advanced thyroid cancer: can CT help in	Retrospective cohort study	84	The mean sensitivity, specificity, and accuracy of CT were as follows: 59.1%, 91.4%, and 83.2% for tracheal invasion; 28.6%, 96.2%, and 90.7% for esophageal invasion; 75.0%, 99.4%, and 98.8% for invasion of the common carotid artery;	1



prediction of extrathyroidal invasion to adjacent structures? AJR Am J Roentgenol 2010;195:W240-244			33.3%, 98.8%, and 97.1% for invasion of the internal jugular vein; and 78.2%, 89.8%, and 85.5% for invasion to the recurrent laryngeal nerve. Interobserver agreement was moderate to good in the five categories of extrathyroidal invasion with a mean kappa value of 0.65 (range, 0.49-0.77).	
76. Takashima S, Takayama F, Wang J, Kobayashi S, Kadoya M. Using MR imaging to predict invasion of the recurrent laryngeal nerve by thyroid carcinoma. AJR Am J Roentgenol 2003;180:837-842	Retrospective cohort study	66	Thirty-two (48%) of the 66 patients had surgically or pathologically verified recurrent laryngeal nerve invasion. Logistic modeling revealed that the amount of effaced fatty tissue ( $p < 0.001$ ) and the lesion size ( $p = 0.033$ ) were the significant factors. Using the threshold values for the lesion size to predict invasion, we found that a threshold of more than 2.9 cm showed the highest accuracy, 76%, with 78% sensitivity and 74% specificity. For the amount of effaced fatty tissue, a grade of 3 or more had the highest accuracy, 88%, with 94% sensitivity and 82% specificity. Addition of the lesion size to this criterion did not improve the diagnostic accuracy of using the amount of effaced fatty tissue alone.	1
77. Wang J, Takashima S, Matsushita T, Takayama F, Kobayashi T, Kadoya M. Esophageal invasion by thyroid carcinomas: prediction using magnetic resonance imaging. J Comput Assist Tomogr 2003;27:18-25	Retrospective cohort study	67	Seventeen (34%) of the 67 patients had pathologically or surgically verified esophageal invasion. The logistic modeling revealed that outer layer invasion ( $P < 0.001$ ) and poorly defined margins ( $P = 0.001$ ) were the significant factors. The outer layer invasion showed the highest accuracy of 91%, with 82% sensitivity and 94% specificity. The addition of poorly defined margins to this criterion did not improve its accuracy.	1
78. Wang JC, Takashima S, Takayama F, Kawakami S, Saito A, Matsushita T, et al. Tracheal invasion by thyroid carcinoma: prediction using MR imaging. AJR Am J Roentgenol 2001;177:929-936	Retrospective cohort study	67	Twenty-three (34%) of the 67 patients had tracheal invasion. Logistic regression model analysis revealed that significant MR characteristics for determining tracheal invasion included soft-tissue signal in the tracheal cartilage ( $p < 0.001$ ), intraluminal mass ( $p < 0.001$ ), and degree of tumor circumference around the trachea ( $p = 0.001$ ). The highest accuracy (90%) for determining tracheal invasion was achieved using a combination of	1

			findings. A case was considered positive for tracheal invasion if there was soft-tissue signal in the cartilage, an intraluminal mass, or a tumor that abutted a circumference of the trachea of 180 degrees or greater. Using these factors resulted in seven false-positive diagnoses because soft-tissue signal in the cartilage was sometimes seen in healthy trachea. Although intraluminal mass invariably reflected deep tracheal invasion, soft-tissue signal in the cartilage rarely indicated actual cartilage invasion but rather indicated tumor extension between the cartilaginous rings.	
79. Lee YS, Son EJ, Chang HS, Chung WY, Nam KH, Park CS. Computed tomography is useful for preoperative identification of nonrecurrent laryngeal nerve in thyroid cancer patients. <i>Otolaryngol Head Neck Surg</i> 2011;145:204-207	Retrospective cohort study	6546	All 20 cases were right-sided NRLN, and no clinical symptoms were observed preoperatively in any patient. Two patients had type I NRLN and 18 had type II NRLN. NRLN injury occurred in 1 patient at a point where the nerve was close to the superior thyroid artery. Prior to surgery, surgeons identified only 5 suspected NRLN cases based on identification of vascular anomalies on CT scans. However, this review of CT scans revealed that vascular anomalies could be identified on the scans of all patients.	2
80. Haq M, Harmer C. Differentiated thyroid carcinoma with distant metastases at presentation: prognostic factors and outcome. <i>Clin Endocrinol (Oxf)</i> 2005;63:87-93	Retrospective cohort study	111	The median follow-up of living patients was 3.9 years (0.3-48) with a 10-year cause-specific survival rate of 31%. Histology identified 46 papillary, 60 follicular and five Hürthle cell cancers. Sites of metastases comprised 54 lung (49%), 27 bone (24%), 21 multiple sites (19%) and nine with other single sites affected (8%). Near-total, total or completion thyroidectomy was performed in 56% of patients, radioiodine ablation in 76% and radioiodine therapy in 67%. External beam radiotherapy was given to 12 patients and the same number received chemotherapy. Univariate analysis was performed with cause-specific survival as the main outcome measure. Age over 70,	2

			<p>poorly differentiated tumours and Hürthle cell cancers were associated with worse outcomes (<math>P &lt; 0.01</math>). Patients with multiple organ metastases had a worse survival (<math>P = 0.02</math>). Radical surgery did not significantly improve outcome compared to more conservative forms of surgery (subtotal thyroidectomy, hemi-thyroidectomy or lobectomy) but patients receiving radioiodine ablation and therapy had improved survival (<math>P &lt; 0.01</math>). Multivariate analysis identified age over 70, poorly differentiated tumours and Hürthle cell variant to be the only independent factors associated with worse outcome (<math>P &lt; 0.01</math>). Treatment in the 1991-2002 era was associated with an improved survival compared to all previous decades (<math>P = 0.009</math>).</p>	
<p>81. Leite AK, Kulcsar MA, de Godoi Cavalheiro B, de Mello ES, Alves VA, Cernea CR, et al. DEATH RELATED TO PULMONARY METASTASIS IN PATIENTS WITH DIFFERENTIATED THYROID CANCER. <i>Endocr Pract</i> 2017;23:72-78</p>	Retrospective cohort study	54	<p>Tumor dedifferentiation marked by cellular aberrations and radioiodine (RAI) therapy resistance occurred in 5 (9.3%) patients. Four of them died due to pulmonary progression (80.0%), and the median survival of this group was 30 months compared to 279 months in the patients without dedifferentiation. The cumulative disease-specific survival was 20.0% in the patients with dedifferentiation during the follow-up versus 46.1% among the cases without this condition (<math>P = .003</math>, log-rank test). Moreover, dedifferentiation was independently associated with shorter disease-specific survival (hazard ratio [HR] = 31.607; 95% confidence interval [CI]: 4.815-207.478; <math>P &lt; .0001</math>, Cox regression model) as were age over 45 years (HR = 10.904; 95% CI: 1.145-103.853; <math>P = .038</math>) and male sex (HR = 4.210; 95% CI: 1.056-16.783; <math>P = .042</math>).</p>	2
<p>82. Vuong HG, Duong UNP, Pham TQ, Tran HM, Oishi N, Mochizuki K, et al.</p>	Systematic review & meta-analysis	73219	<p>Thirty-four articles with 73,219 patients were included for meta-analyses. In DTCs, male gender, age <math>\geq 45</math> years, tumor size <math>\geq 4</math> cm, multifocality, vascular invasion (VI),</p>	1

<p>Clinicopathological Risk Factors for Distant Metastasis in Differentiated Thyroid Carcinoma: A Meta-analysis. World Journal of Surgery 2018;42:1005-1017</p>			<p>extrathyroidal extension (ETE), lymph node metastasis (LNM), and lateral LNM were demonstrated to be associated with significant risks for DM. In addition, several clinicopathological factors such as age <math>\geq 45</math> years, VI, ETE, and LNM were shown to be significant risk factors for DM in both PTC and FTC subgroups.</p>	
<p>83. Lee YS, Lim YS, Lee JC, Wang SG, Kim IJ, Son SM, et al. Clinical implications of bilateral lateral cervical lymph node metastasis in papillary thyroid cancer: a risk factor for lung metastasis. Ann Surg Oncol 2011;18:3486-3492</p>	<p>Retrospective cohort study</p>	<p>949</p>	<p>In total, 949 patients were enrolled. The median age was 49 years (<math>\pm 13</math> years) with 829 women. Lung metastasis was found in 20 patients (2.1%). Patients were divided into three groups by tumor size (<math>\leq 1</math> cm, 1-2 cm, <math>&gt; 2</math> cm); the groups comprised 47.3%, 28.5%, and 24.1% of the patients, respectively. BLNM was identified in 4.4% (n=43). In a univariate analysis, male gender, old age, large tumor, extrathyroidal extension, lymph node metastasis, lateral lymph node metastasis, and BLNM were significantly related to lung metastasis (<math>P &lt; 0.05</math>). In a multivariate analysis, BLNM appeared to be the only significant risk factor for lung metastasis (<math>P = 0.026</math>; odds ratio=10.219).</p>	<p>2</p>
<p>95. Spate VL, Morris JS, Nichols TA, Baskett CK, Mason MM, Horsman TL, et al. Longitudinal study of iodine in toenails following IV administration of an iodine-containing contrast agent. Journal of Radioanalytical and Nuclear Chemistry 1998;236:71-77</p>	<p>Case-controlled study</p>	<p>1212</p>	<p>The literature on the relationship between diet and thyroid cancer (TC) risk and the higher incidence of TC among Asian immigrants to the US compared to second and third generation subgroups has prompted epidemiologists to hypothesize that increased levels of iodine consumption may be associated with TC risk, particularly among persons with a history of clinical or subclinical thyroid dysfunction. At the University of Missouri Research Reactor (MURR), we have applied epiboron neutron activation analysis to investigate human nails as a dietary monitor for iodine. Preliminary studies have indicated a positive correlation between dietary iodine intake and the concentration of iodine in toenails. However, these studies are confounded by high iodine</p>	<p>4</p>

			levels (up to 30 ppm) in approximately 5% of the nails studied. We hypothesize that, in the subjects we have studied, the high iodine levels may be due to iodine-containing medications, in particular contrast-agents containing iopamidol. This paper will report on longitudinal studies using contrast agent subjects who were followed-up for almost two years compared to a longitudinal control and a population mean. Based on this study, we suggest that iodine-containing contrast agents contaminate nail samples via non-specific binding in the short term followed by incorporation in the nail as a result of absorption.	
96. Sohn SY, Choi JH, Kim NK, Joung JY, Cho YY, Park SM, et al. The impact of iodinated contrast agent administered during preoperative computed tomography scan on body iodine pool in patients with differentiated thyroid cancer preparing for radioactive iodine treatment. <i>Thyroid</i> 2014;24:872-877	Retrospective cohort study	1023	The median (interquartile range) of UIE ( $\mu\text{g/gCr}$ ) in each group was 44.4 (27.7-73.2) in group A, 33.3 (22.8-64.7) in group B, 32.7 (20.8-63.0) in group C, 32.0 (20.6-67.0) in group D, and 30.4 (19.6-70.8) in group E. There was no significant difference between group A and the remaining groups ( $p>0.05$ ) Also, the proportion of patients who achieved the appropriate UIE for RAIT according to our hospital's cutoff ( $\leq 66.2 \mu\text{g/gCr}$ ) was not different between groups (A, 72.4%; B, 76.1%; C, 77.5%; D, 74.8%; E, 74.6%) ( $p=0.78$ ).	2
97. Mishra A, Pradhan PK, Gambhir S, Sabaretnam M, Gupta A, Babu S. Preoperative contrast-enhanced computerized tomography should not delay radioiodine ablation in differentiated thyroid carcinoma patients. <i>J Surg</i>	Prospective cohort study	128	The median basal UIC levels were not significantly different between the four groups (232.2 versus 263.9 versus 268.2 versus 178.2 $\mu\text{g/L}$ , respectively, $P = 0.443$ ). In contrast, groups having preoperative CECT had significantly higher UIC levels at discharge (924 versus 329 versus 776 versus 661 $\mu\text{g/L}$ , respectively, $P = 0.001$ ). These differences became insignificant at follow-up (225 versus 252 versus 310 versus 275 $\mu\text{g/L}$ , respectively, $P = 0.505$ ). Patients having follow-up UIC values above the	2

Res 2015;193:731-737			conventional cut-off of clinically relevant iodine excess (>200 µg/L) also had significantly higher basal values than those having lower follow-up values (283.0 versus 181.7 µg/L; P = 0.037).	
98. Tala Jury HP, Castagna MG, Fioravanti C, Cipri C, Brianzoni E, Pacini F. Lack of association between urinary iodine excretion and successful thyroid ablation in thyroid cancer patients. J Clin Endocrinol Metab 2010;95:230-237	Retrospective cohort study	201	According to the criterion of no visible uptake, 84.6% of the patients were successfully ablated, with no significant difference between THW and rhTSH groups. Mean UIE at the time of ablation was 132 +/- 160 microg/liter, not significantly different between patients of the THW and rhTSH groups. There was no significant difference in UIE between ablated or nonablated patients both in the whole group and the rhTSH or THW groups. According to the criterion of no visible uptake plus undetectable stimulated serum Tg (in anti-Tg negative patients) at control WBS 8-12 months after ablation, UIE was not significantly different in ablated and nonablated patients.	2
Clinical scenario 3				
43. Pacini F, Basolo F, Bellantone R, Boni G, Cannizzaro MA, De Palma M, et al. Italian consensus on diagnosis and treatment of differentiated thyroid cancer: joint statements of six Italian societies. J Endocrinol Invest 2018;41:849-876	Review	N/A	The document includes recommendations regarding initial evaluation of thyroid nodules, clinical and ultrasound criteria for fine-needle aspiration biopsy, initial management of thyroid cancer including staging and risk assessment, surgical management, radioiodine remnant ablation, and levothyroxine therapy, short-term and long-term follow-up strategies, and management of recurrent and metastatic disease. The objective of this consensus is to inform clinicians, patients, researchers, and health policy makers about the best strategies (and their limitations) relating to the diagnosis and treatment of differentiated thyroid cancer.	5
45. Jiang HJ, Wu CW, Chiang FY, Chiou HC, Chen IJ, Hsiao PJ. Reliable	Retrospective cohort study	148	Overall, 49 lymph nodes were documented as recurrent nodal metastasis. LN-FNA-Tg greater than serum thyroglobulin and higher than 1 ng/mL achieved 100% of diagnostic rate for recurrent nodal metastasis. The malignant sonographic features	1

sonographic features for nodal thyroglobulin to diagnose recurrent lymph node metastasis from papillary thyroid carcinoma. Clin Otolaryngol 2018			that significantly cohered with positive LN-FNA-Tg were cystic and hyperechoic content and lack hilum, in sequence.	
46. Leboulleux S, Girard E, Rose M, Travagli JP, Sabbah N, Caillou B, et al. Ultrasound criteria of malignancy for cervical lymph nodes in patients followed up for differentiated thyroid cancer. J Clin Endocrinol Metab 2007;92:3590-3594	Prospective cohort study	19	One hundred three LNs were detected on US, 578 LNs were surgically removed, and 56 LNs were analyzed (28 benign and 28 malignant). Sensitivity and specificity were 68 and 75% for the long axis ( 1 cm), 61 and 96% for the short axis ( 5 mm), 46 and 64% for the round shape (long to short axis ratio 2), 100 and 29% for the loss of fatty hyperechoic hilum, 39 and 18% for hypoechogenicity, 11 and 100% for cystic appearance, 46 and 100% for hyperechoic punctuations, and 86 and 82% for peripheral vascularization.	1
85. Pacini F, Molinaro E, Castagna MG, Agate L, Elisei R, Ceccarelli C, et al. Recombinant human thyrotropin-stimulated serum thyroglobulin combined with neck ultrasonography has the highest sensitivity in monitoring differentiated thyroid carcinoma. J Clin Endocrinol Metab 2003;88:3668-3673	Retrospective cohort study	340	We studied 340 consecutive patients with differentiated thyroid carcinoma, previously treated with near-total thyroidectomy and 131I thyroid ablation, scheduled for routine diagnostic tests. At baseline on L-T4-suppressive therapy, 294 patients had undetectable (<1 ng/ml) serum Tg and negative anti-Tg autoantibodies (TgAb), 25 patients had undetectable serum Tg and positive TgAb, and 21 patients had detectable serum Tg and negative TgAb. These patients were tested for the presence of active disease by rhTSH stimulation. The results of our study showed that rhTSH-stimulated Tg alone had a diagnostic sensitivity of 85% for detecting active disease and a negative predictive value (NPV) of 98.2%. After adding the results of neck ultrasound, sensitivity increased to 96.3%, and the NPV to 99.5%. rhTSH-stimulated WBS had a sensitivity of only 21% and a NPV of 89%. The combination of rhTSH-stimulated Tg and WBS had a sensitivity of 92.7% and a NPV of 99%.	1
86. Torlontano M, Crocetti U,	Prospective	80	rhTSH-Tg was 1 ng/ml or less in 45 (Tg ) and more than 1 n 35	2

Augello G, D'Aloiso L, Bonfitto N, Varraso A, et al. Comparative evaluation of recombinant human thyrotropin-stimulated thyroglobulin levels, 131I whole-body scintigraphy, and neck ultrasonography in the follow-up of patients with papillary thyroid microcarcinoma who have not undergone radioiodine therapy. J Clin Endocrinol Metab 2006;91:60-63	cohort study		(Tg ) patients. WBS showed no pathological uptake in any patient. US identified node metastases in two Tg ( ) and one Tg ( ) patients. rhTSH-Tg levels positively correlated with thyroid bed iodine uptake (r 0.40, P 0.0001). To date (32 13 months aftersurgery), all node-negative patients have undetectable Tg levels on T4 treatment and negative US.	
87. Lee JI, Chung YJ, Cho BY, Chong S, Seok JW, Park SJ. Postoperative-stimulated serum thyroglobulin measured at the time of 131I ablation is useful for the prediction of disease status in patients with differentiated thyroid carcinoma. Surgery 2013;153:828-835	Prospective cohort study	218	The relevant cutoff value of postoperative stimulated Tg for the prediction of disease-free status was 2 ng/mL. A total of 138 patients (63.3%) showed values of <2 ng/mL. Postoperative-stimulated Tg < 2 ng/mL had a negative predictive value of 94.9%, which increased to 97.7% when low Tg was combined with negative neck US findings.	3
88. Lepoutre-Lussey C, Maddah D, Golmard JL, Russ G, Tissier F, Tresallet C, et al. Post-operative neck ultrasound and risk stratification in differentiated thyroid cancer patients with initial lymph node involvement. Eur J Endocrinol 2014;170:837-846	Retrospective cohort study	638	After a median follow-up of 41.6 months, local recurrence occurred in 138 patients (21.6%), of which 121 were considered to have PD. Sensitivity, specificity, NPV, and PPV of POCUS for the detection of the 121 PD were 82.6, 87.4 95.6, and 60.6% respectively. Cumulative incidence of recurrence at 5 years was estimated at 26% in ETA HR patients, 17% in ATA intermediate-risk patients, and 35% in ATA HR patients respectively. This risk fell to 9, 8, and 11% in the above three groups when the POCUS result was normal and to !6% when it was combined with thyroglobulin results at ablation.	1
89. Leenhardt L, Erdogan MF, Hegedus L, Mandel SJ, Paschke R, Rago T, et al. 2013 European	Review	N/A	Cervical ultrasound scanning (US) is considered a key examination, by all major thyroid and endocrine specialist societies for the postoperative follow-up of thyroid cancer	5



<p>thyroid association guidelines for cervical ultrasound scan and ultrasound-guided techniques in the postoperative management of patients with thyroid cancer. Eur Thyroid J 2013;2:147-159</p>			<p>patients to assess the risk of recurrence. Neck US imaging is readily available, non-invasive, relatively easy to perform, cost-effective, and can guide diagnostic and therapeutic procedures with low complication rates. Its main shortcoming is its operator-dependency. Because of the pivotal role of US in the care of thyroid cancer patients, the European Thyroid Association convened a panel of international experts to review technical aspects, indications, results, and limitations of cervical US in the initial staging and follow-up of thyroid cancer patients. The main aim is to establish guidelines for both a cervical US scanning protocol and US-guided diagnostic and therapeutic procedures in patients with thyroid cancer. This report presents (1) standardization of the US scanning procedure, techniques of US-guided fine-needle aspiration, and reporting of findings; (2) definition of criteria for classification of malignancy risk based on cervical US imaging characteristics of neck masses and lymph nodes; (3) indications for US-guided fine-needle aspiration and for biological in situ assessments; (4) proposal of an algorithm for the follow-up of thyroid cancer patients based on risk stratification following histopathological and cervical US findings, and (5) discussion of the potential use of US-guided localization and ablation techniques for locoregional thyroid metastases.</p>	
<p>90. Nascimento C, Borget I, Al Ghuzlan A, Deandreis D, Chami L, Travagli JP, et al. Persistent disease and recurrence in differentiated thyroid cancer patients with undetectable postoperative stimulated thyroglobulin level. Endocr Relat Cancer 2011;18:R29-40</p>	<p>Retrospective cohort study</p>	<p>242</p>	<p>Among 1031 patients ablated, 242 (23%) consecutive patients were included. Persistent disease occurred in eight cases (3%) (seven abnormal WBS and one abnormal n-US), all with initial neck lymph node metastases (N1). N1 was a major risk factor for persistent disease. Among 203 patients with normal WBS and a follow-up over 6 months, TSH-Tg 6-18 months after ablation was undetectable in the absence of TgAb in 173 patients, undetectable with TgAb in 1 patient and equal to 1.2 ng/ml in 1 patient. n-US was normal in 152 patients and falsely positive in 3 patients. After a mean follow-up of 4 years, recurrence occurred in two cases (1%), both with aggressive histological variants. The only risk factor for recurrence was an aggressive histological variant (P = 0.03). In conclusion, undetectable postoperative TSH-Tg in the absence of TgAb at the time of ablation is frequent. In these patients, repeating TSH-Tg 6-18 months after ablation is not useful. (131)I</p>	<p>3</p>

			ablation could be avoided in the absence of N1 and aggressive histological variant.	
91. Schlumberger M, Pacini F, Wiersinga WM, Toft A, Smit JW, Sanchez Franco F, et al. Follow-up and management of differentiated thyroid carcinoma: a European perspective in clinical practice. Eur J Endocrinol 2004;151:539-548	Review	N/A	As differentiated (follicular and papillary) thyroid cancer (DTC) may recur years after initial treatment, follow-up of patients with DTC is long term. However, this population has changed, with more individuals being discovered at an earlier stage of disease, so that previous follow-up protocols based mostly on data from high-risk patients no longer apply. We have proposed, in a previous issue of this Journal, an improved protocol for the follow-up of low-risk patients with DTC based on the findings of recent studies. We report here the case of a paradigmatic patient with papillary thyroid carcinoma, with the goal of illustrating the benefits of applying this algorithm in routine clinical practice. We also offer expanded and additional comments on various issues in the management of DTC.	5
92. Grani G, Ramundo V, Falcone R, Lamartina L, Montesano T, Biffoni M, et al. Thyroid Cancer Patients With No Evidence of Disease: The Need for Repeat Neck Ultrasound. J Clin Endocrinol Metab 2019;104:4981-4989	Retrospective cohort study	226	In patients with an undetectable Tg level at the 1-year evaluation, sonographically suspicious neck lymph nodes were found in 1.2% of patients at 3 years and in 1.8% at the last visit [negative predictive values (NPVs) of 1-year Tg < 0.2 ng/mL: 98.8% (95% CI 95.8% to 99.9%) and 98.2% (95% to 99.6%), respectively]. Similar NPVs emerged for low detectable 1-year Tg levels [98.2% (90.3% to 99.9%) and 94.5% (84.9% to 98.9%) at the 3-year and last visits, respectively]. Seventy-five percent of the nodal lesions were likely false positive; none required treatment.	3
Clinical situation 4.				
45. Jiang HJ, Wu CW, Chiang FY, Chiou HC, Chen IJ, Hsiao PJ. Reliable sonographic features for nodal thyroglobulin to diagnose recurrent lymph node metastasis from papillary thyroid carcinoma. Clin Otolaryngol 2018	Retrospective cohort study	148	Overall, 49 lymph nodes were documented as recurrent nodal metastasis. LN-FNA-Tg greater than serum thyroglobulin and higher than 1 ng/mL achieved 100% of diagnostic rate for recurrent nodal metastasis. The malignant sonographic features that significantly cohered with positive LN-FNA-Tg were cystic and hyperechoic content and lack hilum, in sequence.	1
46. Leboulleux S, Girard E, Rose M, Travagli JP, Sabbah N, Caillou B, et al. Ultrasound criteria of malignancy for	Prospective cohort study	56	One hundred three LNs were detected on US, 578 LNs were surgically removed, and 56 LNs were analyzed (28 benign and 28 malignant). Sensitivity and specificity were 68 and 75% for the long axis ( > 1 cm), 61 and 96% for the short axis ( > 5 mm), 46	1

cervical lymph nodes in patients followed up for differentiated thyroid cancer. J Clin Endocrinol Metab 2007;92:3590-3594			and 64% for the round shape (long to short axis ratio 2), 100 and 29% for the loss of fatty hyperechoic hilum, 39 and 18% for hypoechogenicity, 11 and 100% for cystic appearance, 46 and 100% for hyperechoic punctuations, and 86 and 82% for peripheral vascularization.	
60. Boi F, Baghino G, Atzeni F, Lai ML, Faa G, Mariotti S. The diagnostic value for differentiated thyroid carcinoma metastases of thyroglobulin (Tg) measurement in washout fluid from fine-needle aspiration biopsy of neck lymph nodes is maintained in the presence of circulating anti-Tg antibodies. J Clin Endocrinol Metab 2006;91:1364-1369	Retrospective cohort study	73	In 51 TgAb-negative patients, Tg-FNAB was positive in 15 (12 with malignant and three with nondiagnostic cytology), all with histologically confirmed DTC metastases. Of the remaining 36 patients with negative Tg-FNAB, 30 had nonsuspicious and six had suspicious cytology. Histology of the latter showed four undifferentiated thyroid cancer metastases and two lymphadenitis. In 22 TgAbpositive patients, Tg-FNAB was positive in 14 (12 with malignant and two with nondiagnostic cytology), all with histologically confirmed DTC metastases.	1
61. Chung J, Kim EK, Lim H, Son EJ, Yoon JH, Youk JH, et al. Optimal indication of thyroglobulin measurement in fine-needle aspiration for detecting lateral metastatic lymph nodes in patients with papillary thyroid carcinoma. Head Neck 2014;36:795-801	Retrospective cohort study	220	On multivariate analysis, hyperechogenicity, cystic change, presence of calcifications, and peripheral vascularity were independent factors predictive of lymph node metastasis. After adding FNA-Tg, sensitivity and accuracy were significantly increased when the lymph node had 1 or 2 suspicious ultrasound features. However, sensitivity and accuracy were not significantly increased when the lymph node had multiple suspicious ultrasound features.	1
62. Frasoldati A, Toschi E, Zini M, Flora M, Caroggio A, Dotti C, et al. Role of thyroglobulin measurement in fine-needle aspiration biopsies of cervical lymph nodes in patients with differentiated thyroid cancer.	Retrospective cohort study	130	Ultrasound-guided FNAB on enlarged neck nodes was performed in 23 patients awaiting surgery for differentiated thyroid tumor (n = 33 lymph nodes), 47 patients previously thyroidectomized for thyroid tumor (n = 89 lymph nodes), and 60 patients without thyroid disease (n = 94 lymph nodes). Immediately after aspiration biopsy, the needle was rinsed with 1 mL of normal saline solution and Tg levels were measured on	2

Thyroid 1999;9:105-111			the needle wash-out (FNAB-Tg). FNAB-Tg levels were markedly elevated in metastatic lymph nodes both in patients awaiting thyroidectomy (metastatic vs. negative lymph nodes, mean +/- SEM, 16,593 +/- 7,050 ng/mL vs. 4.91 +/- 1.61 ng/mL; p < 0.001) and in thyroidectomized patients (11,541 +/- 7,283 ng/mL vs. 0.45 +/- 0.07 ng/mL; p < 0.001). FNAB-Tg sensitivity, evaluated through histological examination in 69 lymph nodes, was 84.0%. The combination of cytology plus FNAB-Tg increased FNAB sensitivity from 76% to 92.0%. In conclusion, FNAB-Tg measurement is a useful technique for early diagnosis of lymph node metastasis originating from differentiated thyroid cancer.	
63. Grani G, Fumarola A. Thyroglobulin in lymph node fine-needle aspiration washout: a systematic review and meta-analysis of diagnostic accuracy. J Clin Endocrinol Metab 2014;99:1970-1982	Systematic review & meta-analysis	2865	Including all the selected studies (24 studies, 2865 LNs) in the pooled analysis, overall sensitivity was 95.0% (95% confidence interval [CI], 93.7–96.0%), specificity was 94.5% (95% CI, 93.2–95.7%), and diagnostic odds ratio (DOR) was 338.91 (95% CI, 164.82–696.88) with significant heterogeneity (inconsistency [I2] 65.7%; heterogeneity, P .001). Stratifying different populations and including only patients with thyroid gland (410 LNs), pooled sensitivity was 86.2% (95% CI, 80.9–90.5%), specificity was 90.2% (85.1–94.0%), and DOR was 56.621 (22.535–142.26; I2 37.3%; heterogeneity, P .121). Including only patients after thyroidectomy (1007 LNs), pooled sensitivity was 96.9% (95% CI, 94.9–98.2%), specificity was 94.1% (91.7–96.0%), and DOR was 407.65 (198.67–836.46; I2 0.0%; heterogeneity, P .673).	1
64. Moon JH, Kim YI, Lim JA, Choi HS, Cho SW, Kim KW, et al. Thyroglobulin in washout fluid from lymph node fine-needle aspiration biopsy in papillary thyroid cancer: large-scale validation of the cutoff value to determine malignancy and evaluation of discrepant	Retrospective cohort study	419	In the final diagnosis, 190 LNs were malignant, and 338 LNs were benign. The median FNA-Tg was 521.2 (3676.8) ng/mL in malignant LNs, and 0.1 (0.2) ng/mL in benign LNs. The optimal cutoff value of FNA-Tg in distinguishing malignant LNs from benign LNs was 1.0 ng/mL (sensitivity, 93.2%; specificity, 95.9%) in all cases. Combining FNA-Tg and FNA cytology showed superior diagnostic power (sensitivity, 98.4%; specificity, 94.4%) when compared with diagnostic strategy using either FNA cytology or FNA-Tg alone. FNA-Tg, serum TSH, and serum Tg were higher in nonthyroidectomized patients than in thyroidectomized patients (P .001, respectively). FNA-Tg was correlated with serum TSH	2

results. J Clin Endocrinol Metab 2013;98:1061-1068				
65. Pacini F, Fugazzola L, Lippi F, Ceccarelli C, Centoni R, Miccoli P, et al. Detection of thyroglobulin in fine needle aspirates of nonthyroidal neck masses: a clue to the diagnosis of metastatic differentiated thyroid cancer. J Clin Endocrinol Metab 1992;74:1401-1404	Retrospective cohort study	35	FNA-Tg was always detectable in 14 patients with thyroid cancer metastases demonstrated by histology, with a mean (+/- SD) of 27,087 +/- 37,622 ng/FNA (P less than 0.002) compared to patients without thyroid cancer metastases (mean +/- SD, 12.1 +/- 4.8 ng/FNA in 7 cases; undetectable in 14 cases). Assuming 21.7 ng/FNA (the mean +/- 2 SD of the negative patients) as the cut-off value, all patients with metastases from DTC were detected by FNA-Tg. FNA-Tg had better negative predictive value than cytology, since this last technique gave 10 inconclusive results, comprising 2 false negative results in patients with metastases from DTC.	4
85. Pacini F, Molinaro E, Castagna MG, Agate L, Elisei R, Ceccarelli C, et al. Recombinant human thyrotropin-stimulated serum thyroglobulin combined with neck ultrasonography has the highest sensitivity in monitoring differentiated thyroid carcinoma. J Clin Endocrinol Metab 2003;88:3668-3673	Retrospective cohort study	340	At baseline on L-T4-suppressive therapy, 294 patients had undetectable (<1 ng/ml) serum Tg and negative anti-Tg autoantibodies (TgAb), 25 patients had undetectable serum Tg and positive TgAb, and 21 patients had detectable serum Tg and negative TgAb. These patients were tested for the presence of active disease by rhTSH stimulation. The results of our study showed that rhTSH-stimulated Tg alone had a diagnostic sensitivity of 85% for detecting active disease and a negative predictive value (NPV) of 98.2%. After adding the results of neck ultrasound, sensitivity increased to 96.3%, and the NPV to 99.5%. rhTSH-stimulated WBS had a sensitivity of only 21% and a NPV of 89%. The combination of rhTSH-stimulated Tg and WBS had a sensitivity of 92.7% and a NPV of 99%. We conclude that the rhTSH-stimulated Tg test combined with neck ultrasonography has the highest diagnostic accuracy in detecting persistent disease in the follow-up of differentiated thyroid carcinoma.	1
86. Torlontano M, Crocetti U, Augello G, D'Aloiso L, Bonfitto N, Varraso A, et al. Comparative evaluation of recombinant human thyrotropin-stimulated thyroglobulin levels, 131I	Prospective cohort study	80	rhTSH-Tg was 1 ng/ml or less in 45 (Tg ) and more than 1 n 35 (Tg ) patients. WBS showed no pathological uptake in any patient. US identified node metastases in two Tg ( ) and one Tg ( ) patients. rhTSH-Tg levels positively correlated with thyroid bed iodine uptake (r 0.40, P 0.0001). To date (32 13 months after surgery), all node-negative patients have undetectable Tg levels on T4 treatment and negative US.	2

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87. Lee JI, Chung YJ, Cho BY, Chong S, Seok JW, Park SJ. Postoperative-stimulated serum thyroglobulin measured at the time of 131I ablation is useful for the prediction of disease status in patients with differentiated thyroid carcinoma. Surgery 2013;153:828-835	Prospective cohort study	218	The relevant cutoff value of postoperative stimulated Tg for the prediction of disease-free status was 2 ng/mL. A total of 138 patients (63.3%) showed values of <2 ng/mL. Postoperative-stimulated Tg < 2 ng/mL had a negative predictive value of 94.9%, which increased to 97.7% when low Tg was combined with negative neck US findings.	3
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89. Leenhardt L, Erdogan MF, Hegedus L, Mandel SJ, Paschke R, Rago T, et al. 2013 European thyroid association guidelines for cervical ultrasound scan and ultrasound-guided techniques in the postoperative management of patients with thyroid cancer.	Review	N/A	Cervical ultrasound scanning (US) is considered a key examination, by all major thyroid and endocrine specialist societies for the postoperative follow-up of thyroid cancer patients to assess the risk of recurrence. Neck US imaging is readily available, non-invasive, relatively easy to perform, cost-effective, and can guide diagnostic and therapeutic procedures with low complication rates. Its main shortcoming is its operator-dependency. Because of the pivotal role of US in	5

Eur Thyroid J 2013;2:147-159			the care of thyroid cancer patients, the European Thyroid Association convened a panel of international experts to review technical aspects, indications, results, and limitations of cervical US in the initial staging and follow-up of thyroid cancer patients. The main aim is to establish guidelines for both a cervical US scanning protocol and US-guided diagnostic and therapeutic procedures in patients with thyroid cancer. This report presents (1) standardization of the US scanning procedure, techniques of US-guided fine-needle aspiration, and reporting of findings; (2) definition of criteria for classification of malignancy risk based on cervical US imaging characteristics of neck masses and lymph nodes; (3) indications for US-guided fine-needle aspiration and for biological in situ assessments; (4) proposal of an algorithm for the follow-up of thyroid cancer patients based on risk stratification following histopathological and cervical US findings, and (5) discussion of the potential use of US-guided localization and ablation techniques for locoregional thyroid metastases.	
93. Ahn JE, Lee JH, Yi JS, Shong YK, Hong SJ, Lee DH, et al. Diagnostic accuracy of CT and ultrasonography for evaluating metastatic cervical lymph nodes in patients with thyroid cancer. World J Surg 2008;32:1552-1558	Retrospective cohort study	37	By "per level" analysis, the sensitivities, specificities, and diagnostic accuracies were 77%, 70%, 74% for CT and 62%, 79%, 68% for USG, respectively, with a significant difference in the sensitivities ( $p = 0.002$ ). When the lymph node levels were grouped into central and lateral compartments, all of the values for the lateral compartment tended to be higher than those for the central compartment for both CT (78%, 78%, 78% versus 74%, 44%, 64%) and USG (65%, 82%, 71 versus 55%, 69%, 60%). By per patient analysis, the sensitivities, specificities, and diagnostic accuracies of CT and USG were 100%, 90%, 97% and 100%, 80%, 95%, respectively.	2
94. Choi JS, Kim J, Kwak JY, Kim MJ, Chang HS, Kim E-K. Preoperative Staging of Papillary Thyroid Carcinoma: Comparison of Ultrasound Imaging and CT. American Journal of Roentgenology 2009;193:871-878	Prospective cohort study	722	US predicted 61.7% (142/230) of patients with multifocal PTC and 67.1% (100/149) of patients with bilateral malignancy. Overall accuracy of US for T categorization was 69.7% (503/722) and that of US for N categorization was 59% (426/722). Accuracies of sonographic categorization for N0, N1a, and N1b were 66% (276/418), 33.3% (70/210), and 85.1% (80/94), respectively. Overall US accuracy for prediction of an N category was significantly lower in patients with US-indicated DTD (51.1%, 67/131) than it was in patients without DTD (60.7%, 359/591; $P = 0.043$ ).	1

<p>95. Spate VL, Morris JS, Nichols TA, Baskett CK, Mason MM, Horsman TL, et al. Longitudinal study of iodine in toenails following IV administration of an iodine-containing contrast agent. Journal of Radioanalytical and Nuclear Chemistry 1998;236:71-77</p>	<p>Case-controlled study</p>	<p>1212</p>	<p>The literature on the relationship between diet and thyroid cancer (TC) risk and the higher incidence of TC among Asian immigrants to the US compared to second and third generation subgroups has prompted epidemiologists to hypothesize that increased levels of iodine consumption may be associated with TC risk, particularly among persons with a history of clinical or subclinical thyroid dysfunction. At the University of Missouri Research Reactor (MURR), we have applied epiboron neutron activation analysis to investigate human nails as a dietary monitor for iodine. Preliminary studies have indicated a positive correlation between dietary iodine intake and the concentration of iodine in toenails. However, these studies are confounded by high iodine levels (up to 30 ppm) in approximately 5% of the nails studied. We hypothesize that, in the subjects we have studied, the high iodine levels may be due to iodine-containing medications, in particular contrast-agents containing iopamidol. This paper will report on longitudinal studies using contrast agent subjects who were followed-up for almost two years compared to a longitudinal control and a population mean. Based on this study, we suggest that iodine-containing contrast agents contaminate nail samples via non-specific binding in the short term followed by incorporation in the nail as a result of absorption.</p>	<p>4</p>
<p>96. Sohn SY, Choi JH, Kim NK, Joung JY, Cho YY, Park SM, et al. The impact of iodinated contrast agent administered during preoperative computed tomography scan on body iodine pool in patients with</p>	<p>Retrospective cohort study</p>	<p>1023</p>	<p>The median (interquartile range) of UIE (<math>\mu\text{g/gCr}</math>) in each group was 44.4 (27.7-73.2) in group A, 33.3 (22.8-64.7) in group B, 32.7 (20.8-63.0) in group C, 32.0 (20.6-67.0) in group D, and 30.4 (19.6-70.8) in group E. There was no significant difference between group A and the remaining groups (<math>p&gt;0.05</math>) Also, the proportion of patients who achieved the appropriate UIE for RAIT according to our hospital's cutoff (<math>\leq 66.2 \mu\text{g/gCr}</math>) was not</p>	<p>2</p>



differentiated thyroid cancer preparing for radioactive iodine treatment. <i>Thyroid</i> 2014;24:872-877			different between groups (A, 72.4%; B, 76.1%; C, 77.5%; D, 74.8%; E, 74.6%) (p=0.78).	
97. Mishra A, Pradhan PK, Gambhir S, Sabaretnam M, Gupta A, Babu S. Preoperative contrast-enhanced computerized tomography should not delay radioiodine ablation in differentiated thyroid carcinoma patients. <i>J Surg Res</i> 2015;193:731-737	Prospective cohort study	128	The median basal UIC levels were not significantly different between the four groups (232.2 versus 263.9 versus 268.2 versus 178.2 µg/L, respectively, P = 0.443). In contrast, groups having preoperative CECT had significantly higher UIC levels at discharge (924 versus 329 versus 776 versus 661 µg/L, respectively, P = 0.001). These differences became insignificant at follow-up (225 versus 252 versus 310 versus 275 µg/L, respectively, P = 0.505). Patients having follow-up UIC values above the conventional cut-off of clinically relevant iodine excess (>200 µg/L) also had significantly higher basal values than those having lower follow-up values (283.0 versus 181.7 µg/L; P = 0.037).	2
98. Tala Jury HP, Castagna MG, Fioravanti C, Cipri C, Brianzoni E, Pacini F. Lack of association between urinary iodine excretion and successful thyroid ablation in thyroid cancer patients. <i>J Clin Endocrinol Metab</i> 2010;95:230-237	Retrospective cohort study	201	According to the criterion of no visible uptake, 84.6% of the patients were successfully ablated, with no significant difference between THW and rhTSH groups. Mean UIE at the time of ablation was 132 +/- 160 microg/liter, not significantly different between patients of the THW and rhTSH groups. There was no significant difference in UIE between ablated or nonablated patients both in the whole group and the rhTSH or THW groups. According to the criterion of no visible uptake plus undetectable stimulated serum Tg (in anti-Tg negative patients) at control WBS 8-12 months after ablation, UIE was not significantly different in ablated and nonablated patients.	2