

Evidence Discussion (ONC 6)

Thyroid Cancer

Suspected/Diagnosis (ONC-6.1): See Neck-8.1 (thyroid nodule). Presentation is most commonly neck swelling and hoarseness. Initial work-up is typically with neck ultrasound for a palpable thyroid nodule/mass/asymmetry/goiter to include those incidentally found on CT, MRI or PET and to assess regional lymph nodes. Ultrasound guided fine needle aspiration when indicated is the diagnostic procedure of choice to confirm malignancy that can be classified as papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC), Hurthle cell carcinoma (HCC), medullary thyroid carcinoma (MTC) and anaplastic thyroid carcinoma (ATC). 1

Initial Work-up/Staging (ONC-6.2): For Follicular, Papillary and Hurthle Cell carcinomas, focused imaging of the neck using contrast enhanced CT or MRI is recommended to assess extent of local disease and guide pre-surgical planning. CT chest with contrast may be indicated based on these results to include substernal extension of the thyroid mass. There are no established guidelines regarding the minimum gap between contrast enhanced CT with iodinated contrast agents and iodine-131/123 for whole body scintigraphy (WBS) in the treatment of residual disease and distant metastases, with majority recommendation of a gap of 4 weeks and 2 months. 1, 2 In the post-thyroidectomy setting, WBS is recommended to assess for either extent of thyroid remnant, when results may alter the decision to treat and prior to administration of radioactive iodine (RAI) therapy. In the presence of skeletal pain, whole body bone scan or WBS to assess for osseous metastases. Medullary thyroid carcinoma is frequently aggressive with 48% of patients having localized disease, 35% with tumors extending beyond the thyroid into surrounding tissues or regional nodes and 13% with distant metastases typically to the lung, liver or bones. 4 Due to these concerns, more extensive staging is indicated that includes contrast enhanced CT of neck, chest and abdomen as well as bone scan if there are elevated CEA levels, calcitonin level > 400 pg/nL or positive lymph nodes. Skeletal pain can be imaged with bone scan. 2, 5 Gallium-68 labelled Dotatate PET/CT or if not available Indium-111-pentetreotide (Octreoscan) is useful due to high expression of somatostatin receptors in MTC and is indicated if conventional imaging is inconclusive due to its high sensitivity compared to other imaging modalities especially if calcitonin levels are > 500. 6 Anaplastic thyroid carcinoma is the most aggressive variant of thyroid cancer with distant metastases in over 50% of cases at presentation most commonly involving the lung, bone and brain with 5 year survival < 10%. 7 Complete staging with CT neck, chest, abdomen and pelvis or FDG PET/CT is indicated at diagnosis as well as MRI of the brain.

Restaging/Recurrence (ONC 6.3): For Follicular, Papillary and Hurthle Cell carcinomas, CT or MRI neck can be performed if gross residual disease is found in the neck post-thyroidectomy. RAI therapy is administered after thyroidectomy for several reasons to include remnant ablation, treat presumed foci of neoplastic cells and/or treat persistent or recurrent disease. Within 2 weeks of treatment, WBS is indicated to stage the disease and document the I-131 avidity of any structural lesion. 8 Follow-up is usually a combination of exam, laboratories (thyroglobulin and anti-thyroglobulin antibody levels) and ultrasound. If there is concern for recurrence, CT of the neck/chest as well as any symptomatic body

area along with WBS should be performed to complete restaging. In the setting of rising thyroglobulin level with negative conventional imaging, inconclusive conventional imaging or known RAI-refractory disease with negative/inconclusive CT scans, FDG PET/CT can be performed due to its high sensitivity (94%) and specificity (80-84%) compared to conventional imaging. FDG uptake is associated with a worse prognosis and refractoriness to RAI therapy. 8 Initial imaging for MTC recurrence based on elevated CEA levels, calcitonin level ≥ 150 pg/mL or signs/symptoms of recurrence should undergo CT neck/chest/abdomen and bone scan. If this imaging is inconclusive and calcitonin is ≥ 150 , Gallium-68 labeled Dotatate PET/CT or if not available Indium-111-pentetreotide (Octreoscan) is indicated as outlined in the initial work-up/staging section. Initial imaging for ATC recurrence includes either CT neck, chest, abdomen and pelvis or FDG PET/CT as well as MRI brain due to its aggressive and widespread behavior. For individuals on systemic therapy, CT of neck/CAP with any additional involved/symptomatic sites can be done every 2 cycles.

Surveillance/Follow-up (ONC 6.4): For Follicular, Papillary and Hurthle Cell carcinomas, all individuals are monitored with ultrasound either every 6 months for 2 years then annually (active surveillance) or once at 6-12 months then annually (post-treatment). 1 For node positive disease or RAI-avid metastases, WBS annually. MTC is monitored with CEA and calcitonin levels with no routine imaging indicated. 9 ATC requires close monitoring with CT neck/CAP and MRI brain every 3 months for 2 years as the vast majority of relapses occur within this timeframe.

1. Chakrabarty N, Mahajan A, Basu S and D'Cruz, A. Comprehensive Review of the Imaging Recommendations for Diagnosis, Staging, and Management of Thyroid Carcinoma. *Journal of Clinical Medicine* 2024, 13(10): 2904.
2. Haugen, B.R.; Alexander, E.K.; Bible, K.C.; Doherty, G.M.; Mandel, S.J.; Nikiforov, Y.E.; Pacini, F.; Randolph, G.W.; Sawka, A.M.; Schlumberger, M.; et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2016, 26, 1–133.
3. Hoang, J.K.; Branstetter, B.F.; Gafton, A.R.; Lee, W.K.; Glastonbury, C.M. Imaging of thyroid carcinoma with CT and MRI: Approaches to common scenarios. *Cancer Imaging* 2013, 13, 128–139
4. Kushchayev S, Kushchayeva Y, Tella A et al. Medullary Thyroid Carcinoma: An Update on Imaging. *Journal of Thyroid Research* 2019, doi: <https://doi.org/10.1155%2F2019%2F1893047>.
5. Wells SA Jr, Asa SL, Dralle H, et al. American Thyroid Association guidelines for the management of medullary thyroid carcinoma. *Thyroid*. 2015;25(6):567-610. doi:10.1089/thy.2014.0335.
6. Tran K, Khan S, Taghizadehasl M, et al. Gallium-68 Dotatate PET/CT is superior to other imaging modalities in the detection of medullary carcinoma of the thyroid in the presence of high calcitonin. *Hell J Nucl Med* 2025; 18(1) 19-24.
7. Medscape, Anaplastic Thyroid Carcinoma, updated 4/22/2024.
8. Filetti S, Durante C, Hartl D, et al. Thyroid Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology* 2019; 30: 1856-1883.
9. NCCN Guidelines Version 2.2024, Thyroid Carcinoma (MS-34)