Core Curriculum: H&N glands
Imaging Thyroid Cancer

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ASHNR 2018 Savanah, GA

Outlines

- Thyroid cancer epidemiology
- Imaging roles – who needs imaging and what we should look for
- Imaging findings of TC
- 2018 AJCC staging – what has changed and why
- New update on management of TC

Epidemic of thyroid cancer DIAGNOSIS

- TC detection increases 4.5% every year – ***fastest rising incidence!***
- Death rate: 0.5 death every 100,000 (2013): unchanged
- 20 year survivals of treated well diff PTC (99%)
- Health benefit of surgery/iodine therapy is unclear
- Potential harm: hypo PTH (hypocalcemia) (2-6%), recurrent laryngeal N palsy (1-2%), dry mouth (2-20%), secondary malignancy, life-time thyroid replacement therapy
- USPSTF recommend AGAINST screening of thyroid cancer in ASYPTOMATIC adult patients

JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

Natural History and Tumor Volume Kinetics of Papillary Thyroid Cancers During Active Surveillance

R. Michael Tuttle, MD; James A. Fagin, MD; Gerald Minkowitz, MD; Richard J. Wong, MD; Benjamin Roman, MD, MSHP; Snehal Patel, MD; Brian Untch, MD; Ian Ganly, MD, PhD; Ashok R. Shaha, MD; Jatin P. Shah, MD; Mark Pace, MBBS, FRACP; Duan Li, MD; Ariadne Bach, MD; Oscar Lin, MD; Adrian Whiting, BS; Ronald Ghossein, MD; Inigo Landa, PhD; Mona Sabra, MD; Laura Boucai, MD; Stephanie Fish, MD; Luc G. T. Morris, MD, MSc

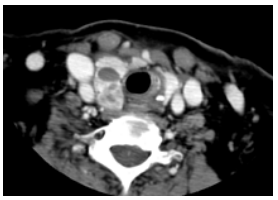
- 291 pts w low-risk PTC <=1.5 cm underwent AS with serial 3D tumor measurement on US at a tertiary care center
- Single arm, single institution study, median AS period of 25M (6-166)
- Growth in 3 mm < was observed in 2.5% in 2 years, 12.1% in 5 years
- No regional LN met during AS
- Independent predictors: Young age at dx (HzR:0.92)
- Highly skilled radiologists are integral part of the AS of PTC

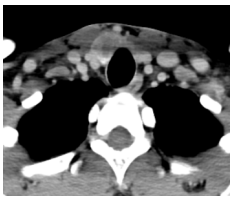
CONCLUSIONS AND RELEVANCE The rates of tumor growth during active surveillance in a US cohort with PTCs measuring 1.5 cm or less were low. Serial measurement of tumor volumes may facilitate early identification of tumors that will continue to grow and thereby inform the timing of surveillance imaging and therapeutic interventions.

Thyroid cancer - roles of CT/MR

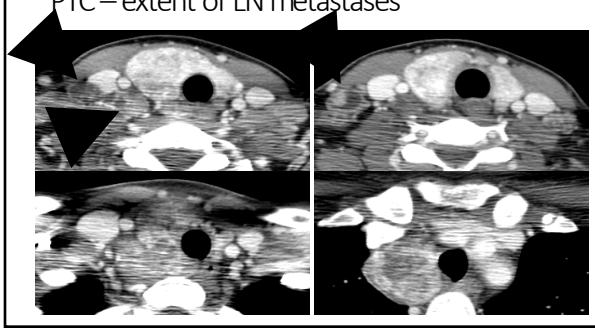
- Early stage cancer: No need for CT/MR/PET:
  - US for nodal screening and biopsy
- What we need to look for
  - Location
  - Capsule invasion
  - Extension to adjacent structures – larynx, trachea, and esophagus
  - Airway compression/VC paralysis
  - Lymph node metastases
  - Distant met – lung and bone

PTC – location matters!





PTC – extent of LN metastases



57 F with PTC invading Larynx

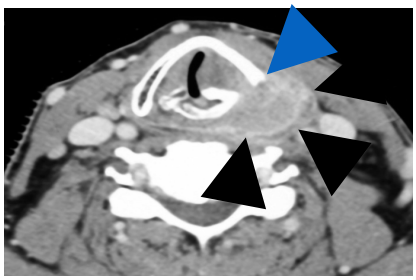


Table 2: Comparison of the AJCC 7th and 8th edition staging system.

	Stage	7th Edition Description	7th Edition 10 yr DSS	8th Edition Description	8th Edition Expected 10 yr DSS
Younger patients	I	< 45 years old All patients without distant metastases regardless of tumor size, lymph node status or extrathyroidal extension	97-100%	< 55 years old All patients without distant metastases regardless of tumor size, lymph node status or extrathyroidal extension	98-100%
	II	< 45 years old Distant metastases	95-99%	< 55 years old Distant metastases	85-95%
Older patients	I	≥ 45 years old ≤ 2 cm tumor Confined to the thyroid	97-100%	≥ 55 years old ≤ 4 cm tumor Confined to the thyroid	98-100%
	II	≥ 45 years old 2-4 cm tumor Confined to the thyroid	97-100%	≥ 55 years old Tumors > 4cm, Or tumors of any size with central or lateral neck lymph nodes, Or gross extrathyroidal extension into strap muscles	85-95%
	III	≥ 45 years old >4 cm tumor, Or minimal extrathyroidal extension, Or central neck lymph node metastasis	88-95%	≥ 55 years old Tumors of any size with gross extrathyroidal extension into subcutaneous tissue, larynx, trachea, esophagus, recurrent laryngeal nerve	60-70%
	IV	≥ 45 years old Gross extrathyroidal extension, Or lateral neck lymph node metastasis, Or distant metastasis	50-75%	≥ 55 years old Tumors of any size or lymph node status with gross extrathyroidal extension into prevertebral fascia, encasing major vessels Or distant metastasis	< 50%

Changes from the AJCC 7th to 8th edition of TC staging

Age cut off (younger vs older)

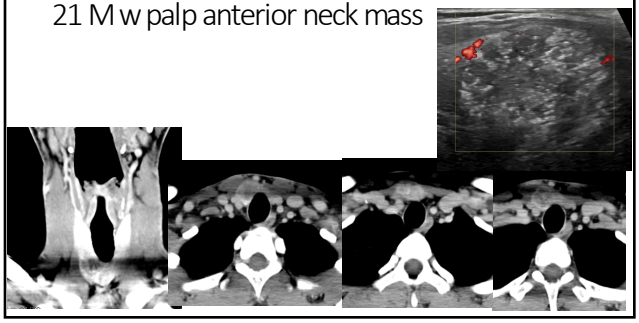
For Older patients;
Size cut off (2cm to 4 cm)
Central LN met – Stage III to Stage II
Lateral LN met – Stage IV to Stage II

Extrathyroidal extension to strap M – stage II to stage III
Gross extrathyroidal extension (except for PVF, Carotid encase) – Stage IV to Stage III

Table 3: A clinically based approach to staging in differentiated thyroid cancer using the 8th edition AJCC/TNM update.

	Distant Metastasis	Gross ETE present?	Structures involved with gross ETE	T category	N Category	Stage
< 55 yrs	No	Yes or No	Any or None	Any	Any	I
	Yes	Yes or No	Any or None	Any	Any	II
≥ 55 yrs	No	No	None	≤4 cm (T1-2)	N0/Nx N1a/N1b	I II
				> 4 cm (T3a)	N0/Nx/N1a/N1b	II
		Yes	Only strap muscle (T3b)	Any	Any	II
			Subcutaneous, larynx, trachea, esophagus, recurrent laryngeal nerve (T4a)	Any	Any	III
			Prevertebral fascia, encasing major vessels (T4b)	Any	Any	IVA
	Yes	Yes or No	Any or None	Any	Any	IVB

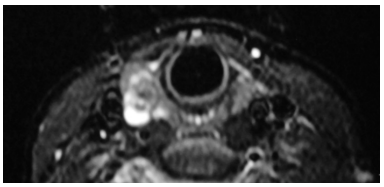
21 M w palp anterior neck mass



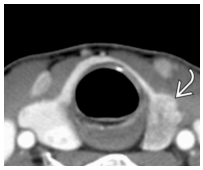
52F with right thyroid nodule

1.7 cm mass
Thyroid capsule invasion

T3, N0 => Stage III



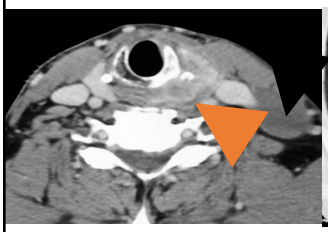
65 F with left lateral neck mass

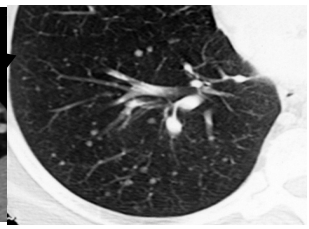


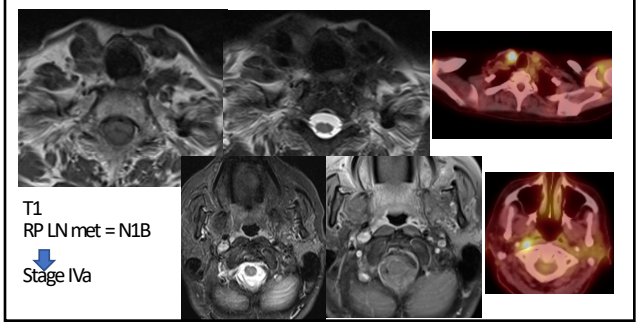
Lateral compartment LN metastasis- N1b
TN =2.5 cm

T2N1B => Stage IVa

Pap ca w cystic LN & diffuse lung mets







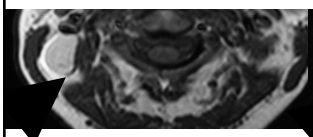
T1
RP LN met = N1B

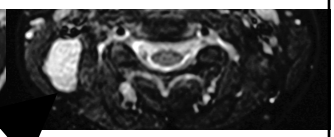
Stage IVa

Papillary ca w High T1 LN met

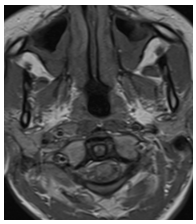
T1 non Gd

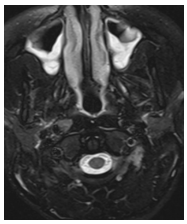
T2

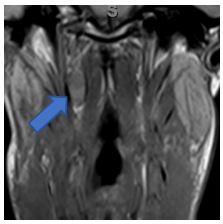




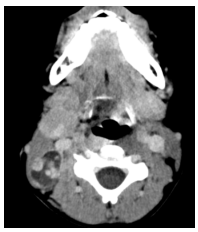
17 F s/p total thyroidectomy, rising TG, recurrent RP LN

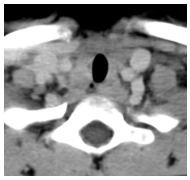






11 boy with h/o PTC, s/p total thyroidectomy

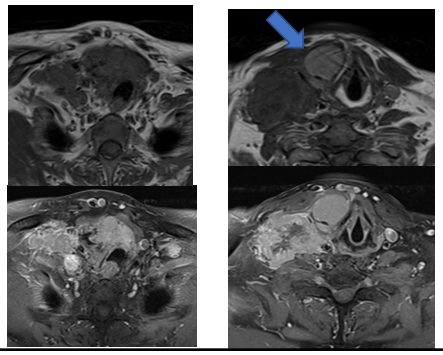




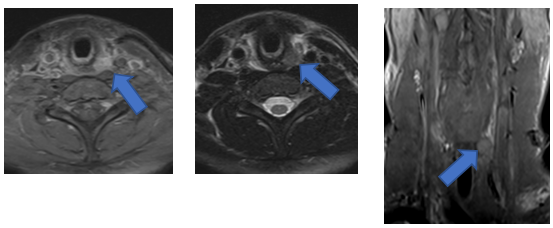
44 F noticed neck mass 7 years ago, treated with holistic medicine, increased in size, & breathing and swallowing difficulty

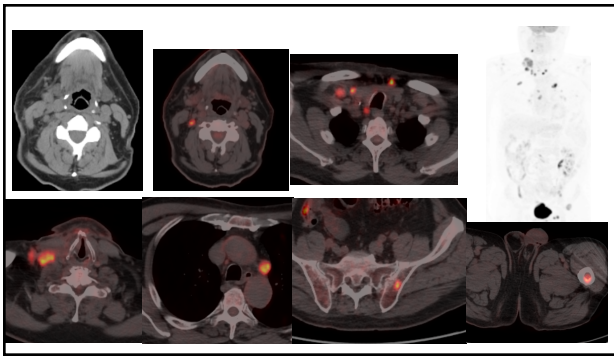
79 M w PTC

Not all PTC are indolent



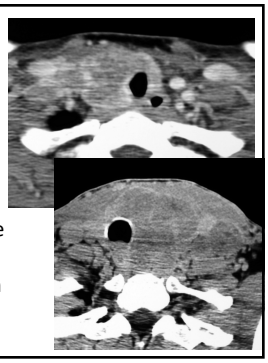
S/p "total thyroidectomy" @OSH, high TG post op & Left recurrent laryngeal nerve palsy



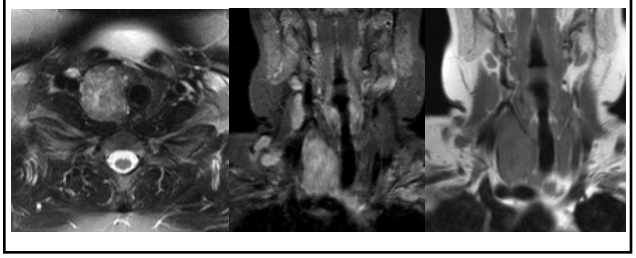


MEDULLARY THYROID CA

- 5 % thyroid cancer, 25% familial
- Parafollicular C-cell: ↑ calcitonin
- No Iodine uptake or Rx
- Somatostatin receptor, ^{111}In-Octreotide: sens: 34-57%
- Multiple Endocrine Neoplasia Syndrome (MEN type II)
- Diffuse or focal mass w capsule invasion
- Mets: Bone, Lung, Liver



53F with metastatic MTC



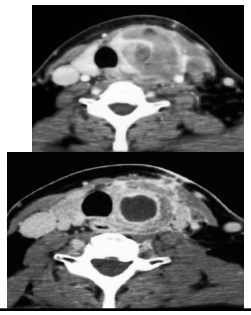
New PET-CT tracer for MTC

- Gallioun -68 Dotatate PET/CT – a new somatostatin receptor imaging for detection of NET approved by FDA
- Gallium-68 Dotatate PET/CT far superior to Indium-111 octreotide SPECT-CT (sens/spec: 100/93 versus 46/53)
- Superior detection of metastasis in bone and liver
- 177-Lu Dotatate – remarkable response for neuroendrine tumors – Phase III NETTER I trial
- Progression free survival benefit (65.2% vs 10.8% at 20 months, p<0.001)

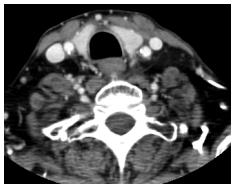
ging
September 2017, Volume 44, Issue 10, pp 1695–1701

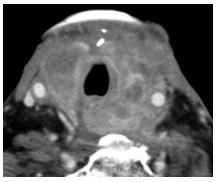
Anaplastic cancer

- 2-3% thyroid cancer
- 40% of death from TC
- Aggressive & rapidly progressive
- 50% non-resectable or met at initial dx
- 1 y survival: 18%
- Diffuse infiltrative mass
- No Iodine uptake
- Tx: Surgery, RT, and CT

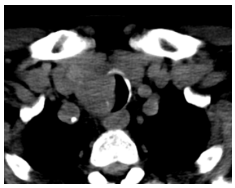


h/o OP SCC surveillance CT & pt present with neck swelling 3M later

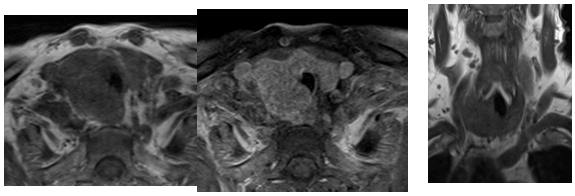




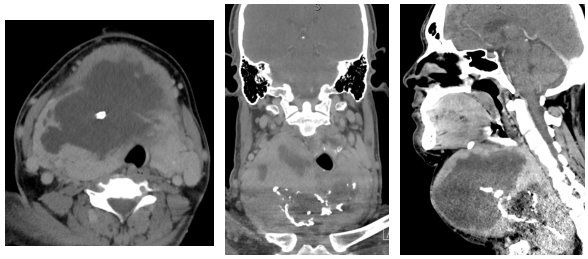
81M p/w wheezing, mass invading trachea, FNA shows pap TC, surgical path revealed anaplastic transformation of PTC



86M with increasing neck mass, Underwent total thyroidectomy and total laryngectomy, Final Path shows anaplastic ca, BRAF positive, later develop lung met, diseased in 8 months from initial dx



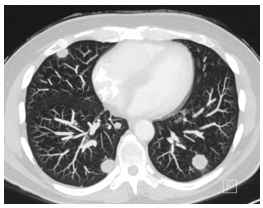
41 M Difficulty in breathing and growing neck mass



Final path, anaplastic carcinoma with squamous differentiation arising in association with a follicular variant papillary thyroid carcinoma

Post OP

3 M later



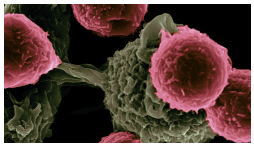
Cell therapy provides shot at a cure for fatal thyroid cancer

Sunday, April 2, 2017

Patients with a rare, fatal form of thyroid cancer may finally have a chance at a cure thanks to cutting-edge cell therapy at Weill Cornell Medicine.

In the first demonstration of the potential for CAR-T therapy for previously untreatable advanced thyroid cancers, researchers from the Sandra and Edward Meyer Cancer Center were able to eliminate cancerous cells in cultures and mice.

Investigators are now hoping to validate their findings in human trials within a year.



In her studies of the disease, Irene M. Min, Ph.D, Assistant Professor of Molecular Biology Research in Surgery, found ATC tumors had an increased expression of intercellular adhesion molecule-1 (ICAM-1). So she decided to investigate whether she could target ICAM-1 to attack the cancer. Her weapon of choice: CAR-T immunotherapy.

The Oncologist

Precision Medicine Clinic: Molecular Tumor Board

Exceptional Response with Immunotherapy in a Patient with Anaplastic Thyroid Cancer

Revathi Kollipara,[a] Bryan Schneider,[a,b,c] Milan Radovich,[a,b,c] Sunil Babu,[d] Patrick J. Kiel [a,b,c]
[a]Indiana University School of Medicine, [b]Indiana University Health, and [c]IU Simon Cancer Center, Indiana University, Indianapolis, Indiana, USA; [d]Fort Wayne Medical Oncology/Hematology, Fort Wayne, Indiana, USA

Disclosures of potential conflicts of interest may be found at the end of this article.

- PD-L1 positive tumors promote autoimmunity against the tumor; therefore, PD-1/PD-L1 blockade may be beneficial.
- Molecular profiling could possibly result in improved targeted therapy for certain malignancies.

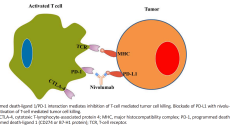


Figure 1. Programmed death-ligand 1/PD-1 interaction mediates inhibition of T cell–mediated tumor cell killing. Blockade of PD-L1 with nivolumab results in reactivation of T cell–mediated tumor cell killing.
Abbreviations: CTLA-4, cytotoxic T lymphocyte–associated protein 4; MHC, major histocompatibility complex; PD-1, programmed death 1; PD-L1, programmed death-ligand 1 (CD274 or B7-H1 protein); TCR, T-cell receptor.

PD-1 and PD-L1 expression is associated with worse PFS and OS

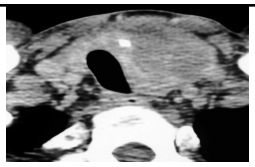
Molecular testing for TC

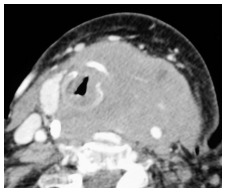
- DNA break and fused in a wrong way – creating new chromosomes –
  - RAS mutation – follicular ca
  - RET/PTC – PTC
  - RET gene – MTC
  - BRAF mutation in PTC - worse prognosis
  - BRAF V600E – 45.7% of PTC are positive (low PPV), 5.5% of BRAF mutation died, c/w 1.1% without mutation (mainly stage 4 disease)
  - Routine testing for TN yet to be proven due to higher costs and high FP

Xing M et.al. Association between BRAF v600e mutation and mortality in patients with papillary thyroid cancer. JAMA 2013; Vol. 309: pp.1493-1501.

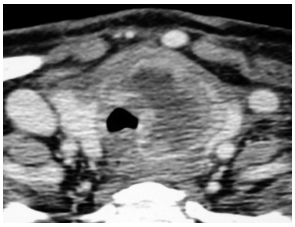
Thyroid Lymphoma

- 1-3% thyroid tumors
- Non-Hodgkin
- Exclude lymphoma invading thyroid
- Long Hx of goiter or Hashimoto thyroiditis
- Curable by RT and/or Chemo



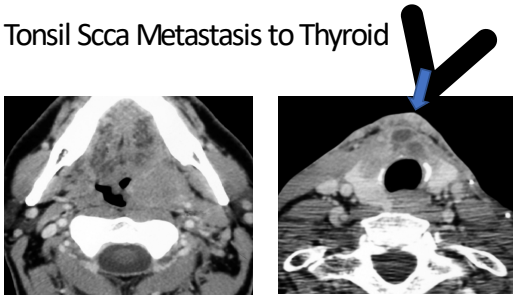


Lung cancer Metastasis to Thyroid



Lung and RCC: common primary sites that mets to thyroid

Tonsil Scca Metastasis to Thyroid



In summary..

- Not all TC are indolent – 7 -10 % of TC are non-papillary/follicular
- Cervical LN + => requires neck dissection => Bigger scar in neck
- Vascular Invasion => possible iodine therapy – adverse effects
- TC in the posterior TG – near TEJ – increased risk of RLN invasion
- AS study shows 12% of PTC < 1.5 cm grows more than 3 mm in 5 years – anxiety and cost
- Genetic tests for biologically aggressive PTC
- Molecular imaging Ga-dotatate for MTC