Florida Cancer Data System

2018 Updates for Neoplasms of the Thyroid

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2018-2019 FCDS WEBCAST SERIES
12/13/2018
STEVEN PEACE, CTR

CDC & Florida DOH Attribution

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FLccSC LMS – CEU Quiz –FCDS IDEA

FLccSC
Fundamental Learning Collaborative for the Cancer Surveillance Community

- 2017 - Florida Changed How FCDS Awards CEUs for FCDS Webcasts
- Attendees must take and pass a 3-5 question CEU Quiz to get CEUs
- CEU Awards are Restricted to Attendees with a FLccSC LMS Account
- The CEU Quiz will be posted to FLccSC 1-2 hours after the webcast ends

- Only registered FLccSC Users will be given access to the CEU Quiz
- Florida attendees must have a Florida FLccSC Account to take the Quiz
- South Carolina attendees must have a South Carolina FLccSC Account
- New FLccSC States will follow similar instructions for the CEU Quiz

- Attendees can attend any of the live webcasts without receiving CEUs
- Recorded Sessions are also available for non-FLccSC Users – No CEUs

2018 - A Year for Major Changes to Cancer Registry Data Standards

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- New ICD-O-3 Histology Code & Behavior Codes
- New Histology Coding Rules and Tools
- New Reportable Cancers
- 2018 Solid Tumor MP/H Rules
- 2018 Hematopoietic MP/H Rules
- Cancer Staging Updates
  - SS2018
  - Grade Coding
  - Site-Specific Data Items
  - AJCC TNM 8th ed.
  - 2018 SEER EOD
- EDITS v18
- STORE Manual
- 2018 FCDS DAM

Harmonization & Interconnectivity with Lots of Moving Parts

2018 - A Year for Major Changes to Cancer Registry Data Standards

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ICD-O-3 Third Edition - 2007 Updates for Selected Solid Tumors	https://seer.cancer.gov/icd-o-3/
ICD-O-3 Third Edition - 2010 Updates for Hematopoietic and Lymphoid Neoplasms	https://seer.cancer.gov/icd-o-3/
2018 Guidelines for ICD-O-3 Histology Code and Behavior Update	https://seer.cancer.gov/icd-o-3/
2018 Solid Tumor MP/H Coding Rules	https://seer.cancer.gov/tools/solidtumor/
2018 Hematopoietic Database & MPH Rules – web-based version only	http://seer.cancer.gov/seertools/hemelymph/
2018 SEER*Rx – current web version	http://seer.cancer.gov/seertools/seerrx/
2018 Grade Coding Manual, Instructions and Tables	https://apps.naaccr.org/ssdi/list/
2018 Summary Stage Manual	http://seer.cancer.gov/tools/ssm/
AJCC Cancer Staging Manual, 8th ed.	http://www.springer.com/medicine
AJCC Cancer Staging Manual, 8th ed. – errata & breast chapter replacement	https://cancerstaging.org/references-tools/deskreferences/Pages/8EUpdates.aspx#Histology/Topography
AJCC Histology and Topography Code Supplement	https://cancerstaging.org/references-tools/deskreferences/Pages/8EUpdates.aspx#Histology/Topography
2018 Site-Specific Data Items Manual	https://apps.naaccr.org/ssdi/list/
2018 Site/Type Validation Table from SEER	https://seer.cancer.gov/icd-o-3/
CoC STORE Manual - STandards for Oncology Registry Entry	https://www.facs.org/quality-programs/cancer/ncdb/registrymanuals/cocmanuals
SEER*SINQ - Inquiry System	https://seer.cancer.gov/seerinquiry/index.php
Coc Canswer - Inquiry System	http://cancerbulletin.facs.org/forums/
Your State EDITS Metafile – current version	https://fcds.med.miami.edu/inc/downloads.shtml

Presentation Outline

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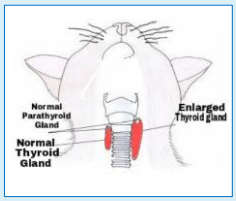
- Introduction to Neoplasms of the Thyroid
- Anatomy and Physiology of the Thyroid Gland
- Signs, Symptoms and Cancer Risk
- Thyroid Cancer Diagnostic Workup
- Biomolecular & Genetic Testing - Thyroid
- Changes to ICD-O-3 Histology Codes - Thyroid
- 2018 Grade Fields and Codes - Thyroid
- 2018 MP/H Rules - Thyroid - Important!!
- Anatomic Staging & Site-Specific Data Items
- Treatment Guidelines - Thyroid
- Text Documentation
- Practice Cases - Pending
- Questions



http://safetyca.info

Introduction – GLOBOCAN 2018

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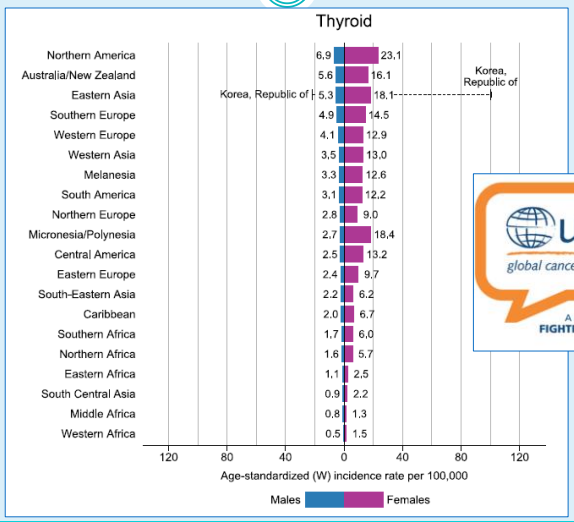

Source: Global Cancer Statistics 2018

Introduction – United States

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Figure 3. Leading Sites of New Cancer Cases and Deaths – 2018 Estimates

Estimated New Cases

Male			Female		
Prostate	164,690	19%	Breast	266,120	30%
Lung & bronchus	121,680	14%	Lung & bronchus	112,350	13%
Colon & rectum	75,610	9%	Colon & rectum	64,640	7%
Urinary bladder	62,380	7%	Uterine corpus	63,230	7%
Melanoma of the skin	55,150	6%	Thyroid	40,900	5%
Kidney & renal pelvis	42,680	5%	Melanoma of the skin	36,120	4%
Non-Hodgkin lymphoma	41,730	5%	Non-Hodgkin lymphoma	32,950	4%
Oral cavity & pharynx	37,160	4%	Pancreas	26,240	3%
Leukemia	35,030	4%	Leukemia	25,270	3%
Liver & intrahepatic bile duct	30,610	4%	Kidney & renal pelvis	22,660	3%
All sites	856,370	100%	All sites	878,980	100%

Estimated Deaths

Male			Female		
Lung & bronchus	83,550	26%	Lung & bronchus	70,500	25%
Prostate	29,430	9%	Breast	40,920	14%
Colon & rectum	27,390	8%	Colon & rectum	23,240	8%
Pancreas	23,020	7%	Pancreas	21,310	7%
Liver & intrahepatic bile duct	20,540	6%	Ovary	14,070	5%
Leukemia	14,270	4%	Uterine corpus	11,350	4%
Esophagus	12,850	4%	Leukemia	10,100	4%
Urinary bladder	12,520	4%	Liver & intrahepatic bile duct	9,660	3%
Non-Hodgkin lymphoma	11,510	4%	Non-Hodgkin lymphoma	8,400	3%
Kidney & renal pelvis	10,010	3%	Brain & other nervous system	7,340	3%
All sites	323,630	100%	All sites	286,010	100%

Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Ranking is based on modeled projections and may differ from the most recent observed data.

American Cancer Society – 2018 Cancer Facts & Figures

Introduction

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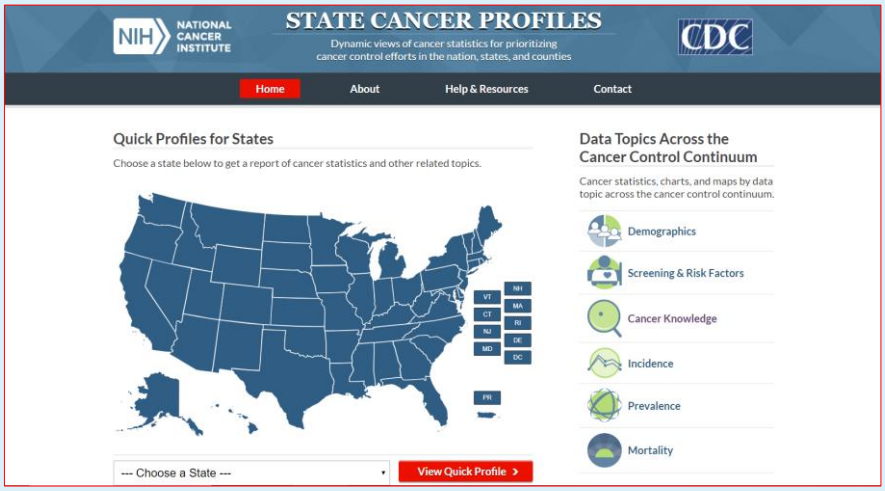

https://statecancerprofiles.cancer.gov/

Thyroid Cancer Statistics - CAUTION

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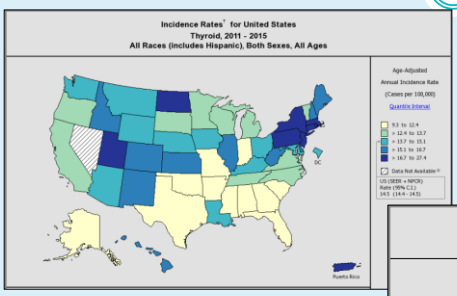

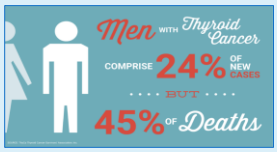

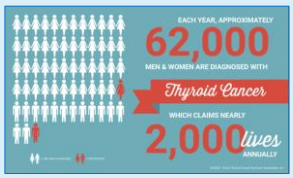

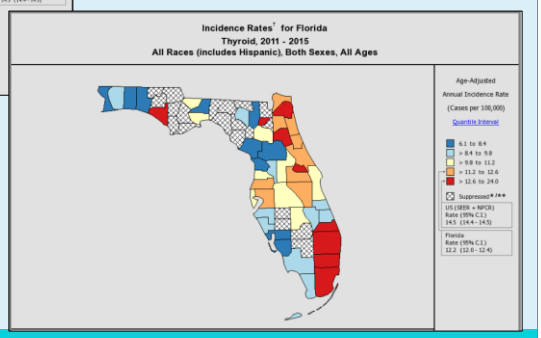

Why Thyroid Cancer and Why Now ???

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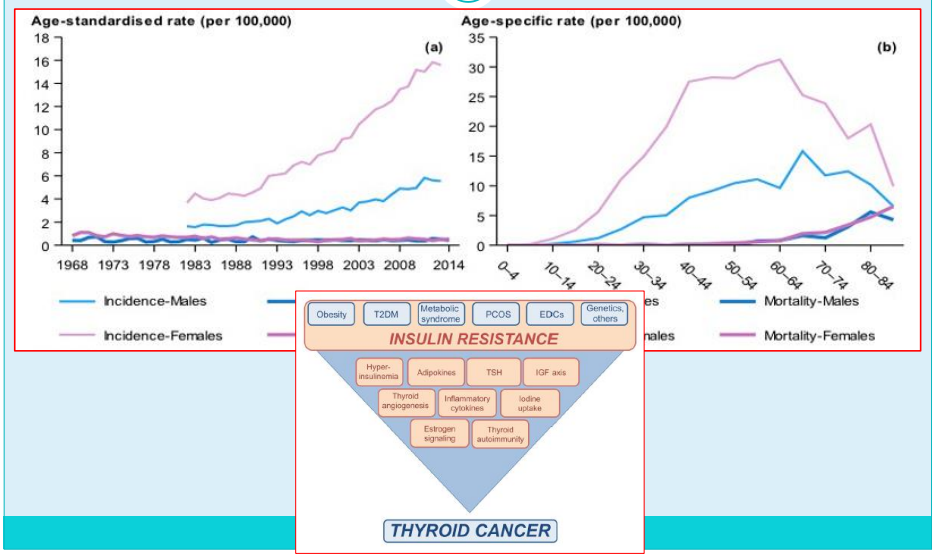

Anatomy of Thyroid Gland

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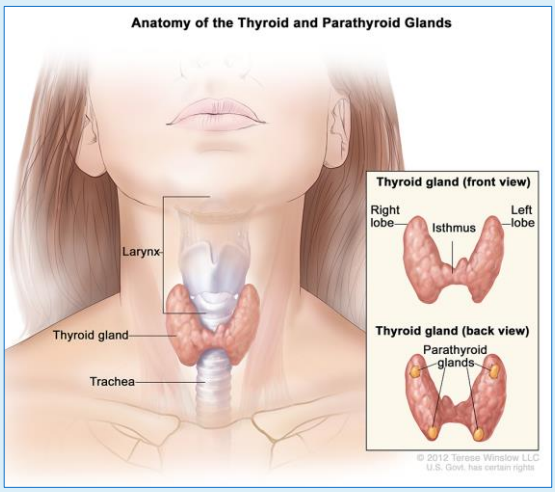

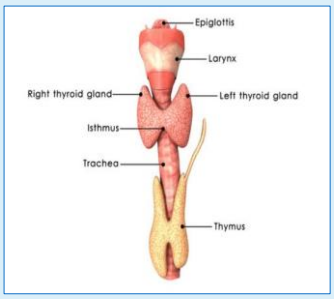

Source: NIH and Terese Windslow LLC, 2012

Anatomy of Thyroid Gland

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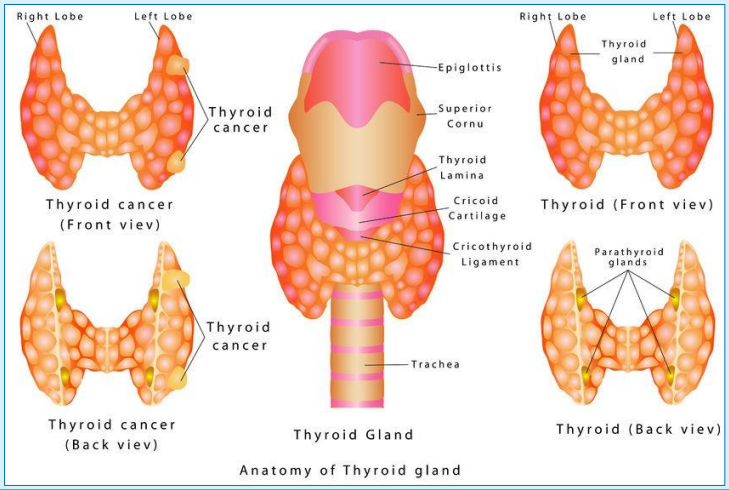

Anatomy of Parathyroid Glands

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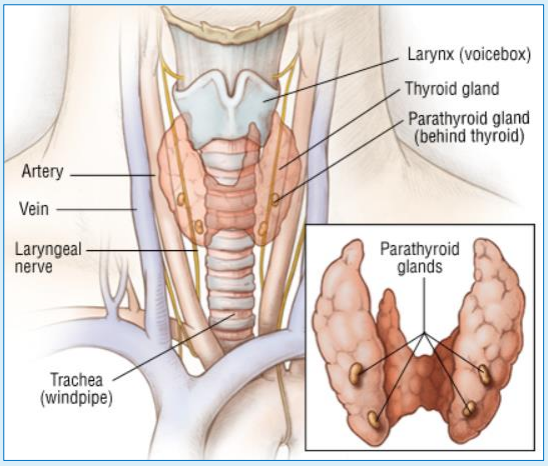
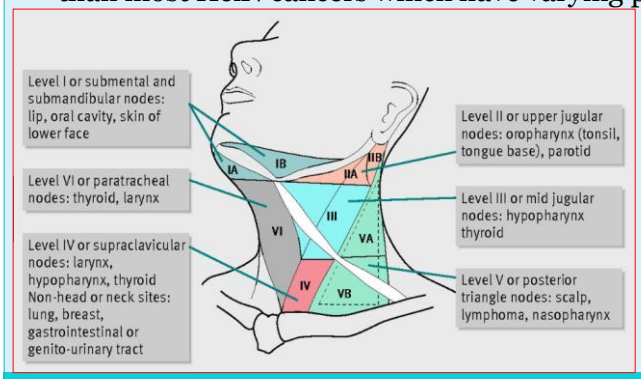
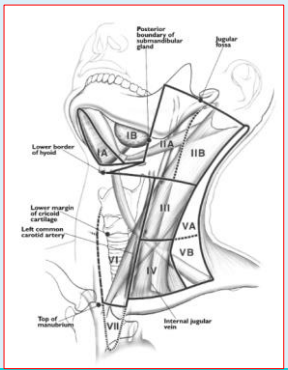


Anatomy of Thyroid - Lymphatics

15

- Patterns of Nodal Mets for Thyroid Cancers begin in the Central Compartment VI then involve the Lateral Compartments III and IV then most commonly to the Contralateral Neck – different than most H&N cancers which have varying patterns of nodal





Signs, Symptoms and Risk Factors

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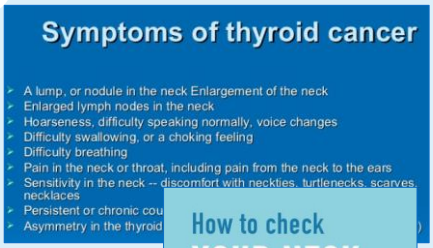
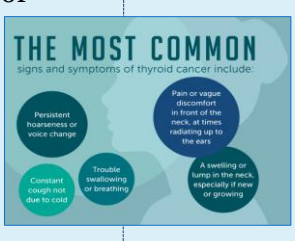
Symptoms – Thyroid

- Lump found in the neck
- Swelling in the neck
- Pain in the front of the neck
- Persistent hoarseness or voice changes
- Swallowing difficulty
- Persistent cough not due to a cold





Benign Nodules and Thyroid Goiter

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- Goiter – An abnormally large thyroid gland – some are diffuse enlarged and some nodular with one or more nodules present.
- Many reasons for development of goiter - most are not cancer.
- Main reason for development of a goiter is hormone imbalance due to nutritional deficit (diet low in iodine) or iodine absorption related disease.
- Most nodules are benign cysts filled with colloid – about 17/18 of every 20, and even most solid nodules are benign.
- Most nodules that overproduce hormones are benign.
- So, most thyroid cancers present with few symptoms other than a lump in the neck or incidental findings in workup for another medical problem – not because of symptoms.

Cold/Warm or Hot Nodule

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- A cold nodule indicates that the cells within the nodule do not produce thyroid hormone resulting in no uptake of the iodine contrast when a thyroid scan is performed.
- About 85% of thyroid nodules are cold nodules.
- About 85% of cold nodules are benign.

- About 10% of thyroid nodules are warm nodules.
- About 90% of warm nodules are benign.

- A hot nodule is a nodular region that takes up large amounts of radioactive iodine relative to the rest of the thyroid gland on thyroid scan, hence it is visualized as a "hot spot" on the scan.
- Hot nodules indicate a over-active thyroid gland.
- Hot nodules are rarely cancerous.
- Hot nodules make up about 5% of findings
- About 95% of hot nodules are benign.

Multiple Endocrine Neoplasia (MEN)

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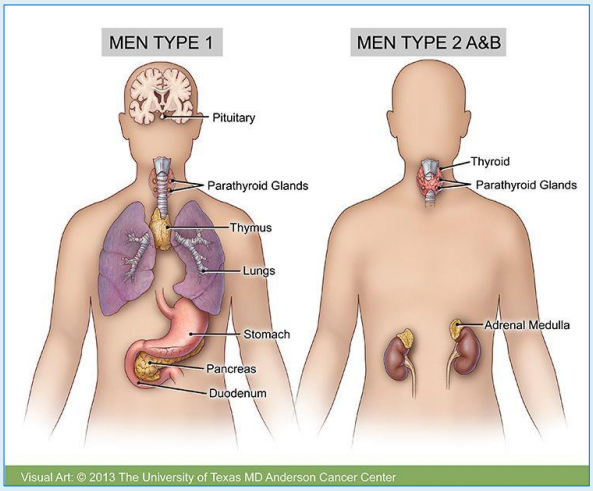

Probably Benign Nodule

20

- Family history of Hashimoto's thyroiditis
- Family history of benign thyroid nodule or goiter
- Symptoms of hyperthyroidism or hypothyroidism
- Pain or tenderness associated with a nodule
- A soft, smooth, mobile nodule
- Multi-nodular goiter without a predominant nodule (lots of nodules, not one main nodule)
- "Warm" nodule on thyroid scan (produces normal amount of hormone)
- Simple cyst on an ultrasound

Suspect Malignant Disease

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- Age less than 20
- Age greater than 70
- Male gender
- New onset of swallowing difficulties
- New onset of hoarseness
- History of external neck irradiation during childhood
- Firm, irregular, and fixed nodule
- Presence of cervical lymphadenopathy (swollen, hard lymph nodes in the neck)
- Previous history of thyroid cancer
- Nodule that is "cold" on scan (shown in picture above, meaning the nodule does not make hormone)
- Solid or complex on an ultrasound

Cancer Screening - Thyroid

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- November 2016 AHRQ Recommendations to USPSTF: "Although ultrasonography of the neck using high-risk sonographic characteristics plus follow-up cytology from fine needle aspiration can reasonably identify thyroid cancers, it is unclear if population-based or targeted screening can decrease mortality or improve important patient health outcomes."
- "More importantly, screening results in the identification indolent thyroid cancers, and treatment of these over-diagnosed cancers can pose real patient harms."

Over-Diagnosis of Thyroid Cancer

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- Over-diagnosis of thyroid cancers contributes to increased incidence of thyroid cancers worldwide, which is already a serious public health problem.
- A great number of medical tests, helping to detect thyroid cancer, may result in an epidemic of diagnosis.
- A dramatic increase in the number of detected cases of thyroid cancer may be associated with a great number of neck ultrasounds, fine- needle aspirations and incidental findings during examination.
- Over-diagnosis can lead to overtreatment.
- Many patients undergoing surgery and receiving radioactive iodine as part of their therapy may never have developed clinical disease.
- Mortality due to this pathology remains relatively stable.
- It is important to differentiate stationary cancers from potentially aggressive diseases.

Source: WHO Press and the World Scientific News 101 (2018) 120-131

Diagnostic Workup - Thyroid

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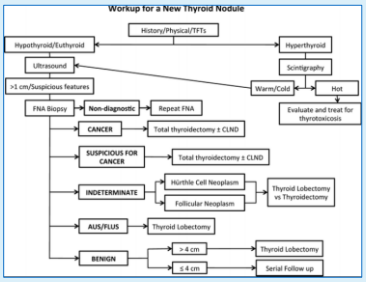
- Physical exam and history
- Laryngoscopy
- Blood hormone studies
- Blood chemistry studies
- Ultrasound exam
- Computed tomography scan
- Fine-needle aspiration biopsy of the thyroid
- Surgical excision
- Gene Panel



Source: Textbook – Surgical Oncology – Thyroid Cancer, pp 539-561

Most Common Types of Thyroid Cancer

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- **Papillary Thyroid Cancer**
  - 75% to 85% of all thyroid cancers
  - Histology often miscoded by registrars who don't know the rules to code for papillary thyroid cancers
  - Women in the 20-55-year age group are more likely to get thyroid cancer than men.
  - Children with previous history of thyroid cancer children suffering from thyroid cancer
  - Patients who have undergone previous radiation to thyroid. These tumors are still often still well-differentiated and slow-growing.
- **Follicular Thyroid Cancer**
  - 15% of thyroid cancer cases.
  - Women over 50 are more likely to get thyroid cancer than men.
  - Thyroglobulin, a tumor marker, for 50% of all the proteins of the thyroid gland.
  - Thyroglobulin can be used as a tumor marker for well-differentiated follicular thyroid cancer.

Less Common Types of Thyroid Cancer

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- **Medullary Thyroid Cancer**
  - 3% of all thyroid cancer cases.
  - **Familial MTC** - RET proto-ongogene positive cancers a familial form of medullary thyroid cancer.
  - **Sporadic MTC** is not a familial cancer but can be paraneoplastic syndrome in people with MEN2
- **Anaplastic Thyroid Cancer** is a very aggressive form of thyroid cancer with a very poor prognosis
  - 2% of all thyroid cancers
  - They all exhibit aggressive behavior with less than 1 year survival not uncommon

Clinical Features - Epithelial Thyroid Malignancy

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Table 1: Clinical Features of Epithelial Thyroid Malignancies

Feature and Cell of Origin	PTC	FTC	MTC	ATC
Cell of origin	Follicular	Follicular	Parafollicular (C cell)	Follicular
Percentage of all thyroid cancers	80%–85%	10%–15%	3%–5%	1%–2%
Most common age group	Third to fourth decade	Fourth to sixth decade	Fourth to sixth decade	>65 years
Gender predilection (female-to-male ratio)	2.5:1	3:1	3:2	3:1
Familial inheritance	5%	5%	25%	...
Common sites of metastasis	Lymph nodes	Lungs and bone	Liver	Lungs
Prognosis (10-year survival)	95%–98%	90%–95%	60%–80%	<10%

Source: RadioGraphics 2016; 36:1478–1493

Revised Classifications

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- Papillary Neoplasms of Thyroid – remove the word 'carcinoma' from the diagnosis – entirely
- EFVPTC – encapsulated follicular variant of papillary thyroid carcinoma – now 10-20% of dx
- NIFTP – noninvasive follicular thyroid neoplasm with papillary-like nuclear features
- Will affect care and treatment of more than 45,000 patients every year – worldwide
- NCI and CDC will be monitoring changes to new terminology and treatment guidelines very closely

Biomolecular & Genetic Tumor Markers

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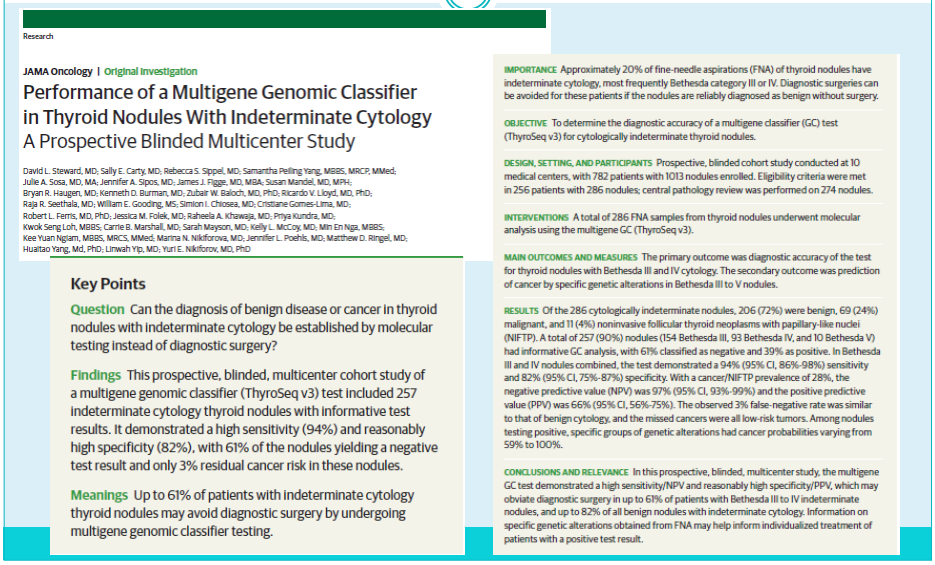

Research

JAMA Oncology | Original Investigation

Performance of a Multigene Genomic Classifier in Thyroid Nodules With Indeterminate Cytology
A Prospective Blinded Multicenter Study

David L. Steward, MD; Sally E. Carty, MD; Rebecca S. Sippel, MD; Samantha Pelling Yang, MBBS, MRCP, MMed; Julie A. Sosa, MD, MA; Jennifer A. Sipos, MD; James J. Figge, MD, MBA; Susan Mandel, MD, MPH; Bryan R. Haugen, MD; Kenneth D. Burman, MD; Zubair W. Baloch, MD, PhD; Ricardo V. Lloyd, MD, PhD; Raja R. Seethala, MD; William E. Gooding, MS; Simion I. Chiosea, MD; Cristiane Gomes-Lima, MD; Robert L. Ferris, MD, PhD; Jessica M. Folek, MD; Raheela A. Khawaja, MD; Priya Kundra, MD; Kwok Seng Loh, MBBS; Carrie B. Marshall, MD; Sarah Mayson, MD; Kelly L. McCoy, MD; Min En Nga, MBBS; Kee Yuan Ngiam, MBBS, MRCS, MMed; Marina N. Nikiforova, MD; Jennifer L. Poehls, MD; Matthew D. Ringel, MD; Hualtao Yang, Md, PhD; Linwah Yip, MD; Yuri E. Nikiforov, MD, PhD

Key Points

Question Can the diagnosis of benign disease or cancer in thyroid nodules with indeterminate cytology be established by molecular testing instead of diagnostic surgery?

Findings This prospective, blinded, multicenter cohort study of a multigene genomic classifier (ThyroSeq v3) test included 257 indeterminate cytology thyroid nodules with informative test results. It demonstrated a high sensitivity (94%) and reasonably high specificity (82%), with 61% of the nodules yielding a negative test result and only 3% residual cancer risk in these nodules.

Meanings Up to 61% of patients with indeterminate cytology thyroid nodules may avoid diagnostic surgery by undergoing multigene genomic classifier testing.

IMPORTANCE Approximately 20% of fine-needle aspirations (FNA) of thyroid nodules have indeterminate cytology, most frequently Bethesda category III or IV. Diagnostic surgeries can be avoided for these patients if the nodules are reliably diagnosed as benign without surgery.

OBJECTIVE To determine the diagnostic accuracy of a multigene classifier (GC) test (ThyroSeq v3) for cytologically indeterminate thyroid nodules.

DESIGN, SETTING, AND PARTICIPANTS Prospective, blinded cohort study conducted at 10 medical centers, with 782 patients with 1013 nodules enrolled. Eligibility criteria were met in 256 patients with 286 nodules; central pathology review was performed on 274 nodules.

INTERVENTIONS A total of 286 FNA samples from thyroid nodules underwent molecular analysis using the multigene GC (ThyroSeq v3).

MAIN OUTCOMES AND MEASURES The primary outcome was diagnostic accuracy of the test for thyroid nodules with Bethesda III and IV cytology. The secondary outcome was prediction of cancer by specific genetic alterations in Bethesda III to V nodules.

RESULTS Of the 286 cytologically indeterminate nodules, 206 (72%) were benign, 69 (24%) malignant, and 11 (4%) noninvasive follicular thyroid neoplasms with papillary-like nuclei (NIFTP). A total of 257 (90%) nodules (154 Bethesda III, 93 Bethesda IV, and 10 Bethesda V) had informative GC analysis, with 61% classified as negative and 39% as positive. In Bethesda III and IV nodules combined, the test demonstrated a 94% (95% CI, 86%-98%) sensitivity and 82% (95% CI, 75%-87%) specificity. With a cancer/NIFTP prevalence of 28%, the negative predictive value (NPV) was 97% (95% CI, 93%-99%) and the positive predictive value (PPV) was 66% (95% CI, 56%-75%). The observed 3% false-negative rate was similar to that of benign cytology, and the missed cancers were all low-risk tumors. Among nodules testing positive, specific groups of genetic alterations had cancer probabilities varying from 59% to 100%.

CONCLUSIONS AND RELEVANCE In this prospective, blinded, multicenter study, the multigene GC test demonstrated a high sensitivity/NPV and reasonably high specificity/PPV, which may obviate diagnostic surgery in up to 61% of patients with Bethesda III to IV indeterminate nodules, and up to 82% of all benign nodules with indeterminate cytology. Information on specific genetic alterations obtained from FNA may help inform individualized treatment of patients with a positive test result.

Inadequate FNA Specimen & Gene Testing

30

- Approximately 20%of fine-needle aspirations (FNA) of thyroid nodules have indeterminate cytology, most frequently Bethesda category III or IV.
- Diagnostic surgeries can be avoided for these patients if the nodules are reliably diagnosed as benign without surgery.
- A new multigene genomic classifier test (112-gene test) demonstrated a high sensitivity and reasonably high specificity when identifying cancer-related point mutations, gene fusions and gene expression alterations.
- Negative test results may avoid diagnostic surgery in up to 61% of patients with Bethesda III to IV indeterminate nodules, and up to 82%of all benign nodules with indeterminate cytology.
- Information on specific genetic alterations obtained from FNA may help inform individualized treatment of patients with a positive test result.

Source: *JAMA Oncol*. doi:10.1001/jamaoncol.2018.4616

Inadequate FNA Specimen & Gene Testing

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Table 3. Probability of Cancer/NIFTP in Specific Molecular Alteration Groups

Group	Molecular Alterations, No.	Prevalence in Test-Positive Samples, No. (%)	Histopathologic Diagnosis, %		Cancer Type/ NIFTP (%)
			Cancer/ NIFTP	Benign	
High-risk group	*TERT* (and *HRAS*) (1) *TP53* (and *MEN1*) (1)	2 (2)	100	0	Papillary carcinoma (50) Follicular carcinoma (50)
BRAF-like group	*BRAF V600E* (9) *NTRK3* fusions (2) *RET* fusions (1) *BRAF* fusions (1)	13 (12)	100	0	Classical papillary carcinoma (92) Follicular variant papillary carcinoma (8)
RAS-like group	*NRAS* (21) *HRAS* (18) *KRAS* (5) *EIF1AX* (5) *BRAF K601E* (3) *PTEN* (1) *IDH2* (1) *DICER1* (1) *PPARG* fusions (4) *THADA* fusions (4)	60 (57)	62	38	Follicular variant papillary carcinoma (22) Papillary carcinoma, other variants (17) NIFTP (15) Follicular carcinoma (3) Hürthle cell carcinoma (5)
Copy number alterations group	Copy number alterations	22 (21)	59	41	Hürthle cell carcinoma (32) Follicular variant papillary carcinoma (14) Papillary carcinoma, other variants (9) NIFTP (5)
Gene expression alterations group	Gene expression alterations	8 (8)	75	25	Classical papillary carcinoma (37) NIFTP (13) Other cancers (MTC, mRCC) (25)

Source: *JAMA Oncol.* doi:10.1001/jamaoncol.2018.4616

Genomic Taxonomy of Thyroid Cancers

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Table 2: Genomic Taxonomy of Thyroid Cancers

Thyroid Malignancy	Common Molecular Alteration Site (Penetrance)	MTT
PTC	*BRAF* (40%–45%)	Sorafenib,* vemurafenib, dabrafenib
	RET (10%–20%)	Vandetanib
FTC	*RAS* (40%–53%)	Tipifarnib
	PAX8/PPARG translocation (30%–60%)	PPARγ agonist
MTC	*RET* (sporadic, 40%–50%; familial, >95%)	Vandetanib*
ATC	*TP53* (50%–60%)	Gene therapy
	CTNNB1 (5%–60%)	None
	PI3K/AKT1 pathway (5%–20%)	mTOR inhibitor

Note.—mTOR = mechanistic target of rapamycin, PI3K = phosphatidylinositol 3′-kinase.
*Drugs approved by the U.S. Food and Drug Administration (FDA).

Source: RadioGraphics 2016; 36:1478–1493

CAP Biomarker Checklist – Thyroid

33

- BRAF Mutation (V600E, K601E, Other)
- TERT Mutation (1-124 or 1-146, Other)
- NRAS Mutation – Q61R
- HRAS Mutation – Q61R, G12V
- KRAS Mutation – G12D
- AKT1 Mutation – E17K
- TP53 Mutation
- PIK3CA Mutation – H1047R
- CTNNB1 Mutation – S33a
- RET Mutation – M918T and Mutation Type
- ALK Rearrangement – STRN/ALK or EML4/ALK
- NTRK1 Rearrangement – NTRK1/TPM3 or NTRK1/TFG
- NTRK3 Rearrangement – NTRK3/ETV6
- RET Rearrangement – RET/PTC1 or RET/PTC3
- PPAR gamma Rearrangement – PAX8/PPAR gamma or CREB3L2/PPAR gamma
- Other Markers

ICD-O-3 Updates - 2018

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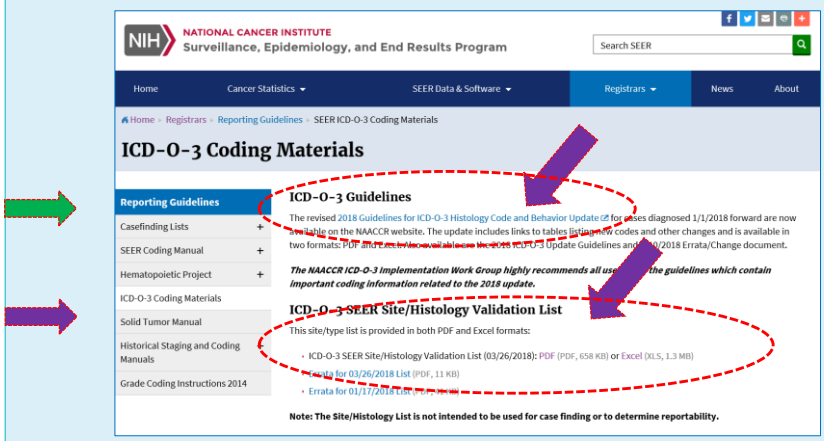
https://seer.cancer.gov/icd-o-3/



ICD-O-3 Coding Resources

35

- ICD-O-3 Manual – use your current manual
- ICD-O-3 Errata & 2011 Updates
  - http://www.who.int/classifications/icd/updates/icdo3updates/en/
- ICD-O-3 Updates for 2018
  - https://seer.cancer.gov/icd-o-3/
- 2018 Solid Tumor MP/H Rules
  - https://seer.cancer.gov/tools/solidtumor
- Hematopoietic Database On Line
  - https://seer.cancer.gov/seertools/hemelymph/
- 2018 Site-Specific Grade Instructions
  - https://www.naaccr.org/SSDI/Grade-Manual.pdf
- 2018 SEER Site/Type Validation List
  - https://seer.cancer.gov/icd-o-3/

New Reporting Requirements - Thyroid

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- The changes to classification of thyroid neoplasms will result in incorrect and inconsistent coding by medical records and billing departments for thyroid.
- Some may be coded as benign, some malignant, some borderline malignant – wide variation seen.
- Include benign and borderline ICD-10-CM codes while coders learn about coding new classifications.
  - D34 – benign neoplasm of thyroid gland
  - D44 – neoplasm of uncertain behavior thyroid gland
  - E04.1 – single thyroid nodule
  - E04.2 – multiple thyroid nodules
  - E04.2 – multinodular goiter

ICD-O-3 Updates - Thyroid

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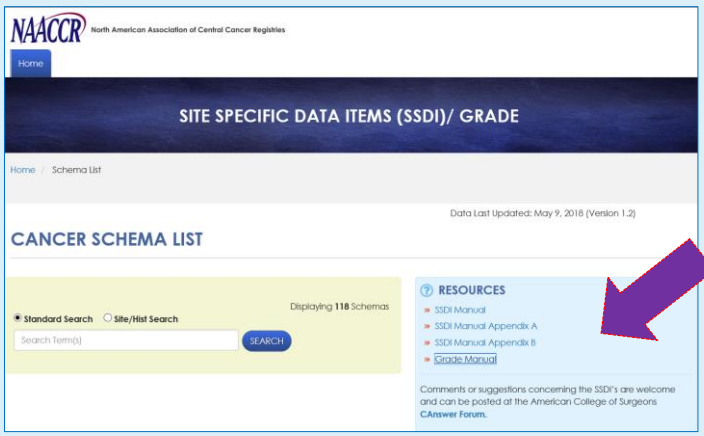
New code/term	8339/3	**Follicular thyroid carcinoma (FTC), encapsulated angioinvasive (C73.9)**	Y	
New Term	8343/3	Invasive encapsulated follicular variant of papillary thyroid carcinoma (invasive EFVPTC) **(C73.9)**	Y	Cases diagnosed 1/1/2017 forward
New Term	8343/3	Encapsulated follicular variant of papillary thyroid carcinoma, NOS (EFVPTC, NOS) **(C73.9)**	Y	Cases diagnosed 1/1/2017 forward
New Term	8345/3	Medullary thyroid carcinoma (C73.9)	Y	For thyroid 2018+. For breast use 8510.
New Term	8343/2	Non-invasive EFVPTC **(C73.9)**	Y	Cases diagnosed 1/1/2017 forward
New Term	8343/2	Non-invasive encapsulated follicular variant of papillary thyroid carcinoma (non-invasive EFVPTC) **(C73.9)**	Y	Cases diagnosed 1/1/2017 forward
New Term	8343/2	Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) **(C73.9)**	Y	Cases diagnosed 1/1/2017 forward
New Term	8343/2	Non-invasive FTP **(C73.9)**	Y	Cases diagnosed 1/1/2017 forward

Grade Coding Manual

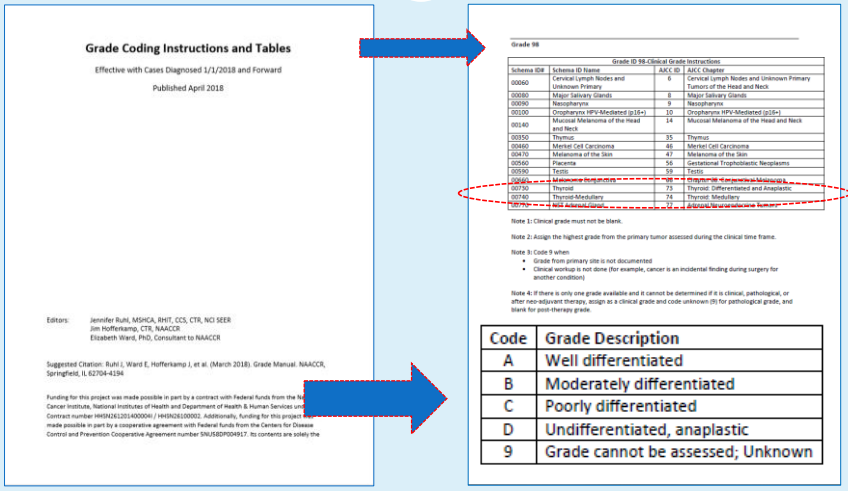
38



https://apps.naaccr.org/ssdi/list/

Grade Coding Manual – Schema ID

39



Grade Coding Instructions and Tables

Effective with Cases Diagnosed 1/1/2018 and Forward

Published April 2018

Editors: Jennifer Ruhl, MSHCA, RHIT, CCS, CTR, NCI SEER
Jim Hofferkamp, CTR, NAACCR
Elizabeth Ward, PhD, Consultant to NAACCR

Suggested Citation: Ruhl J, Ward E, Hofferkamp J, et al. (March 2018). Grade Manual. NAACCR, Springfield, IL 62704-4194

Grade 98

Grade ID 98-Clinical Grade Instructions

Schema ID#	Schema ID Name	AJCC ID	AJCC Chapter
00060	Cervical Lymph Nodes and Unknown Primary	6	Cervical Lymph Nodes and Unknown Primary Tumors of the Head and Neck
00080	Major Salivary Glands	8	Major Salivary Glands
00090	Nasopharynx	9	Nasopharynx
00100	Oropharynx HPV-Mediated (p16+)	10	Oropharynx HPV-Mediated (p16+)
00140	Mucosal Melanoma of the Head and Neck	14	Mucosal Melanoma of the Head and Neck
00350	Thymus	35	Thymus
00460	Merkel Cell Carcinoma	46	Merkel Cell Carcinoma
00470	Melanoma of the Skin	47	Melanoma of the Skin
00560	Placenta	56	Gestational Trophoblastic Neoplasms
00590	Testis	59	Testis
00730	Thyroid	73	Thyroid: Differentiated and Anaplastic
00740	Thyroid-Medullary	74	Thyroid: Medullary

Note 1: Clinical grade must not be blank.

Note 2: Assign the highest grade from the primary tumor assessed during the clinical time frame.

Note 3: Code 9 when
- Grade from primary site is not documented
- Clinical workup is not done (for example, cancer is an incidental finding during surgery for another condition)

Note 4: If there is only one grade available and it cannot be determined if it is clinical, pathological, or after neo-adjuvant therapy, assign as a clinical grade and code unknown (9) for pathological grade, and blank for post-therapy grade.

Code	Grade Description
A	Well differentiated
B	Moderately differentiated
C	Poorly differentiated
D	Undifferentiated, anaplastic
9	Grade cannot be assessed; Unknown

https://www.naaccr.org/SSDI/Grade-Manual.pdf?v=1528898095

2018 Grade - Thyroid

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- **Clinical Grade** - the grade of a solid primary tumor before any treatment. Treatment may include surgical resection, systemic therapy, radiation therapy, or neoadjuvant therapy. NOTE: All surgical procedures are not treatment, e.g. TURB and endoscopic biopsies.
- **Pathological Grade** - the grade of a solid primary tumor that has been surgically resected and for which no neoadjuvant therapy was administered. If AJCC pathological staging is being assigned, the tumor must have met the surgical resection requirements in the AJCC manual. This may include the grade from the clinical workup, as all information from diagnosis (clinical staging) through the surgical resection is used for pathological staging.
- **Post-Therapy Grade** - the grade of a solid primary tumor that has been resected following neoadjuvant therapy. If AJCC post-therapy staging is being assigned, the tumor must have met the surgical resection requirements for yp in the AJCC manual. Neoadjuvant therapy must meet guidelines or standards, and not be that given for variable or unconventional reasons as noted in the AJCC manual.

2018 Grade - Parathyroid

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Grade 25

Grade ID 25-Clinical Grade Instructions			
Schema ID#	Schema ID Name	AJCC ID	AJCC Chapter
00750	Parathyroid	75	Parathyroid

Note 1: Clinical grade must not be blank.

Note 2: Assign the highest grade from the primary tumor assessed during the clinical time frame.

Note 3: Codes L and H take priority over A-D.

Note 4: Code 9 when

- Grade from primary site is not documented
- Clinical workup is not done (for example, cancer is an incidental finding during surgery for another condition)
- Grade checked "not applicable" on CAP Protocol (if available) and no other grade information is available

Note 5: If there is only one grade available and it cannot be determined if it is clinical, pathological, or after neo-adjuvant therapy, assign as a clinical grade and code unknown (9) for pathological grade, and blank for post-therapy grade.

Code	Grade Description
L	LG: Low grade: round monomorphic nuclei with only mild to moderate nuclear size variation, indistinct nucleoli, and chromatin characteristics resembling those of normal parathyroid or of adenoma
H	HG: High grade: more pleomorphism, with a nuclear size variation greater than 4:1; prominent nuclear membrane irregularities; chromatin alterations, including hyperchromasia or margination of chromatin; and prominent nucleoli. High-grade tumors show several discrete confluent areas with nuclear changes.
A	Well differentiated
B	Moderately differentiated
C	Poorly differentiated
D	Undifferentiated, anaplastic
9	Grade cannot be assessed; Unknown

2018 Solid Tumor MP/H Rules

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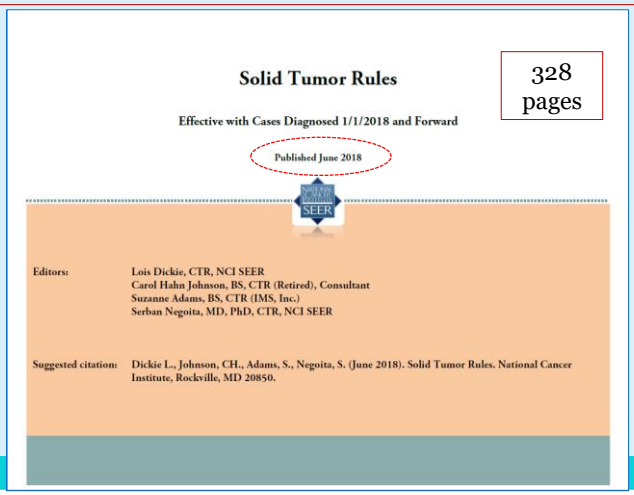
Published June 2018 – but still had MAJOR changes in October 2018 – be sure you have the correct set of rules



328 pages

General Instructions

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- TEXT ONLY RULES INCLUDE:
  - General Instructions PLUS
  - 10 Sets of Solid Tumor MP/H Rules
  - Each Module includes Multiple Sections (Notes/Site/MP/Histology)
- Code subtypes/variants when definitively described (no modifiers)
- Do Not Use Ambiguous Terminology to Code Histology
- Ambiguous terminology is used to determine "case reportability"
- Ambiguous terminology is not to be used to determine histology
- Ambiguous terminology such as "with features of", etc. are no longer used to determine a subtype OR to determine which histology should be coded. See the following histology rules for instructions on coding multiple histologies.
- Use the Histology (H) Rules to determine when to use or not use any ambiguous terminology when an ambiguous term is used to describe a histologic type – sometimes you use the ambiguous term to code a subtype or variant or mixed histology -- and sometimes you do not.

General Instructions

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- Introduction
- Changes from 2007 MPH Rules
- Definitions
- Equivalent or Equal Terms
- Terms that are NOT Equivalent or Equal
- Table and Instructions for Coding Primary Site
- Table: Specific Histologies, NOS and Subtypes Variants
- Table: Combination/Mixed Histology Codes
- Table: Histologies Not Reportable for This Site
- Illustrations
- Multiple Primary Rules
- Histology Coding Rules

General Instructions

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How to Use the Solid Tumor Rules

Note: The rules do not apply to hematopoietic primaries (lymphoma and leukemia) of any site. Use the Hematopoietic & Lymphoid Neoplasm Coding Manual and Database for histologies M9590-M9992.

1. Use the following site-specific rules for tumors diagnosed 1/1/2018 and forward:
   - Malignant CNS and Peripheral Nerves
   - Non-Malignant CNS
   - Breast
   - Colon
   - Head and neck
   - Kidney
   - Lung
   - Urinary sites
2. Use the following site-specific rules for tumors diagnosed 1/1/2007 through 12/31/2018:
   - Malignant melanoma of the skin (not updated for 2018)
   - Other Sites (not updated for 2018) for solid tumors which occur in primary sites not covered by the site-specific rules.
3. 2007 MPH Rules and 2018 Solid Tumor Rules are used based on **date of diagnosis**.
   - Tumors diagnosed 01/01/2007 through 12/31/2017: Use 2007 MPH Rules
   - Tumors diagnosed 01/01/2018 and later: Use 2018 Solid Tumor Rules
   - An original tumor diagnosed before 1/1/2018 and a subsequent tumor diagnosed 1/1/2018 or later **in the same primary site**: Use the 2018 Solid Tumor Rules
4. The Solid Tumor Rules are **not used** to determine case reportability, stage, or tumor grade.
5. Other staging systems are **not used** to determine the number of primaries or histology.
6. Use rules in the following order:
   A. General Instructions
   B. Equivalent Terms and Definitions
   C. Multiple Primary rules
   D. Histology rules
7. The Solid Tumor Rules are available in text format.
8. **Notes and examples** are included with some of the rules to highlight key points or to add clarity to the rules.
9. Rules are in **hierarchical** order within each module. Use the first rule that applies and

STOP

General Instructions

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How to Use the Histology Rules

Note 1: Do not use these rules to determine case reportability.
Note 2: First use the Multiple Primary Rules to determine whether this is a single primary or multiple primaries. Determine the histology for each case.

1. Rules are divided into two sections: Single Tumor and Multiple Tumors Abstracted as a Single Primary
   A. Each section is a complete set of rules.
   B. Within each section, the rules are hierarchical. Use the first rule that applies and **STOP**. Do not continue through the rules.
2. Code the histology diagnosis prior to **neoadjuvant therapy.** Neoadjuvant therapy can change the histological profile of the tumor.
3. A list of terms which can be used and terms which cannot be used to code histology precede each set of histology rules.
4. Do not code histologies or subtypes/variants described by **ambiguous terms**:

Apparently	Most likely
Appears	Presumed
Comparable with	Probable
Compatible with	Suspect(ed)
Consistent with	Suspicious (for)
Favor(s)	Typical (of)
Malignant-appearing	

Note: Histology described by ambiguous terminology is coded **ONLY** when a case is accessioned based on ambiguous terminology and no other histology information is available/documented.

Ambiguous terminology from the SEER Manual and CoC Manual is used to determine reportability, not to determine histology.

Multiple Primary Rules – Remember: Most People Have Only One Cancer

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Some People or Their Families Have More Than One Cancer

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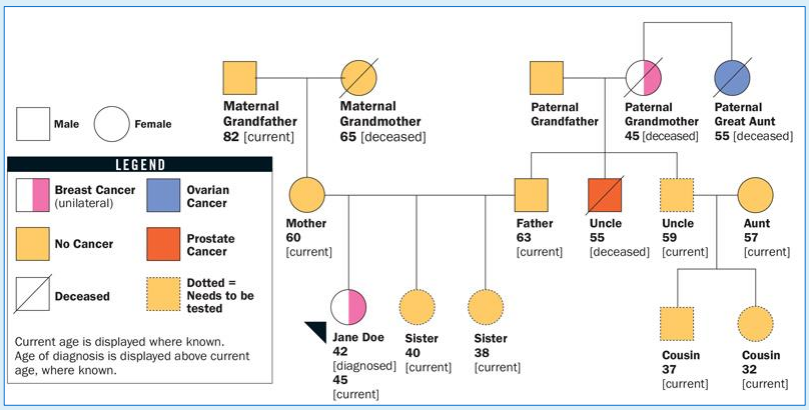

https://www.curetoday.com/journey/cancer-guides/at-diagnosis/

2018 Solid Tumor Rules – Other Sites

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Column 1: Required Histology	Column 2: Combined with Histology	Column 3: Combination Term	Column 4: Code
Gyn malignancies with two or more of the histologies in column 2	Clear cell Endometrioid Mucinous Papillary Serous Squamous Transitional (Brenner)	Mixed cell adenocarcinoma	8323
Papillary and Follicular		Papillary carcinoma, follicular variant	8340
Medullary	Follicular	Mixed medullary-follicular carcinoma	8346
Medullary	Papillary	Mixed medullary-papillary carcinoma	8347

Rule M6 Follicular and papillary tumors in the **thyroid** within 60 days of diagnosis are a single primary. *

Rule M10 Tumors diagnosed **more than one (1) year** apart are multiple primaries.

Rule M15 An **invasive** tumor **following** an **in situ** tumor more than 60 days after diagnosis is a multiple primary.

Rule M17 Tumors with ICD-O-3 **histology** codes that are **different** at the first (**x**xxx), second (x**x**xx) or third (xx**x**x) number are multiple primaries.

2018 Solid Tumor Rules - Thyroid

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Column 1: Required Histology	Column 2: Combined with Histology	Column 3: Combination Term	Column 4: Code
Gyn malignancies with two or more of the histologies in column 2	Clear cell Endometrioid Mucinous Papillary Serous Squamous Transitional (Brenner)	Mixed cell adenocarcinoma	8323
Papillary and Follicular		Papillary carcinoma, follicular variant	8340
Medullary	Follicular	Mixed medullary-follicular carcinoma	8346
Medullary	Papillary	Mixed medullary-papillary carcinoma	8347

Rule H14 Code papillary carcinoma of the thyroid to papillary adenocarcinoma, NOS (8260).

Rule H15 Code follicular and papillary carcinoma of the thyroid to papillary carcinoma, follicular variant (8340).

Rule H30 Code the appropriate combination/mixed code (Table 2) when there are multiple specific histologies or when there is a non-specific histology with multiple specific histologies.

2018 SEER Summary Stage

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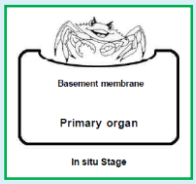
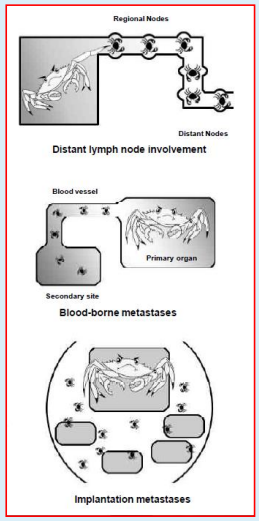
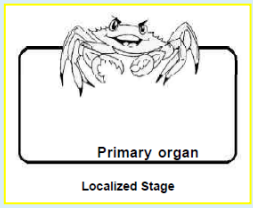
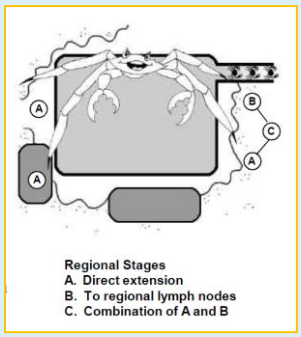


Purpose of Staging
Biochemical Tumor Markers
Molecular Tumor Markers
Genetic Mutations/Variations
Risk Stratification







Source: SEER Summary Staging Manual 2018

Thyroid Cancer Staging – SS2018

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ENDOCRINE SYSTEM

THYROID

8000-8700, 8720-8790, 9700-9701

C739
C739 Thyroid gland

SUMMARY STAGE

0 In situ: noninvasive, intraepithelial

1 Localized only (localized, NOS)

- Confined to thyroid, NOS
- Into thyroid capsule, but not beyond
- Multiple foci confined to thyroid
- Single invasive tumor confined to thyroid

2 Regional by direct extension only

- Blood vessel(s) (major)
  - Carotid artery (encased)
  - Jugular vein
  - Thyroid artery or vein
- Cricoid cartilage
- Esophagus
- Extrathyroidal extension (microscopic, macroscopic, NOS)
- Larynx
- Nerves
  - Recurrent laryngeal
  - Vagus nerve
- Parathyroid
- Pericapsular soft tissue/conn
- Sternocleidomastoid muscle
- Strap muscle(s)
  - Omohyoid
  - Sternohyoid
  - Sternothyroid
  - Thyrohyoid
- Subcutaneous soft tissue
- Thyroid cartilage
- Trachea
- Tumor described as "FIXED

3 Regional lymph node(s) involved only

- Level I
  - Level IA - Submental
  - Level IB - Submandibular (submaxillary), sublingual
- Level II - Upper jugular
  - Jugulodigastric (subdigastric)
  - Upper deep cervical
  - Level IIA - Anterior
  - Level IIB - Posterior
- Level III - Middle jugular
  - Middle deep cervical
- Level IV - Lower jugular
  - Jugulo-omohyoid (supraomohyoid)
  - Lower deep cervical
  - Virchow node
- Level V - Posterior triangle group
  - Posterior cervical
  - Level VA - Spinal accessory

Thyroid Cancer Staging – SS2018

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- Level VB - Transverse cervical, supraclavicular
- Level VI - Anterior compartment group
  - Laterotracheal
  - Paralaryngeal
  - Paratracheal - above suprasternal notch
  - Perithyroidal
  - Precricoid (Delphian)
  - Prelaryngeal
  - Pretracheal - above suprasternal notch
  - Recurrent laryngeal
- Level VII - Superior mediastinal group (for other mediastin
  - Esophageal groove
  - Paratracheal - below suprasternal notch
  - Pretracheal - below suprasternal notch
- Other groups
  - Cervical, NOS
  - Deep cervical, NOS
  - Facial
    - Buccinator (buccal)
    - Mandibular
    - Nasolabial
  - Internal jugular, NOS
  - Parapharyngeal
  - Parotid
    - Infrauricular
    - Intraparotid
    - Periparotid
    - Preauricular
  - Retroauricular (mastoid)
  - Retropharyngeal
  - Suboccipital
- Regional lymph node(s), NOS
  - Lymph node(s), NOS

4 Regional by BOTH direct extension AND regional lymph node(s) involved

- Codes (2) + (3)

7 Distant site(s)/lymph node(s) involved

- Distant site(s) (including further contiguous extension)
  - Gross extrathyroidal extension invading
    - Bone
    - Mediastinal tissues
    - Prevertebral fascia
    - Skeletal muscle, other than strap or sternocleidomastoid muscle
- Distant lymph node(s), NOS
- Distant metastasis, NOS
  - Carcinomatosis
  - Distant mets WITH or WITHOUT distant lymph node(s)

9 Unknown if extension or metastasis

ParaThyroid Cancer Staging – SS2018

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PARATHYROID

8000-8700, 8720-8790, 9700-9701

C750
C750 Parathyroid

SUMMARY STAGE

0 In situ, intraepithelial, noninvasive

- Atypical parathyroid neoplasm (neoplasm of uncertain malig

1 Localized only (localized, NOS)

- Confined to parathyroid
- Extension to soft tissue

2 Regional by direct extension only

- Adjacent lymph nodes
- Esophagus
- Recurrent laryngeal nerve
- Thymus
- Thyroid gland
- Trachea
- Skeletal muscle

3 Regional lymph node(s) involved only

- Level I
  - Level IA - Submental
  - Level IB - Submandibular (submaxillary), sublingual
- Level II - Upper jugular
  - Jugulodigastric (subdigastric)
  - Upper deep cervical
  - Level IIA - Anterior
  - Level IIB - Posterior
- Level III - Middle jugular
  - Middle deep cervical
- Level IV - Lower jugular
  - Jugulo-omohyoid (supraomohyoid)
  - Lower deep cervical
  - Virchow node
- Level V - Posterior triangle group
  - Posterior cervical
  - Level VA - Spinal accessory
  - Level VB - Transverse cervical, supraclavicular
- Level VI - Anterior compartment group
  - Laterotracheal
  - Paralaryngeal
  - Paratracheal - above suprasternal notch
  - Perithyroidal
  - Precricoid (Delphian)
  - Prelaryngeal
  - Pretracheal - above suprasternal notch
  - Recurrent laryngeal
- Level VII - Superior mediastinal group (for other mediastinal n
  - Esophageal groove
  - Paratracheal - below suprasternal notch
  - Pretracheal - below suprasternal notch
- Other groups
  - Cervical, NOS

ParaThyroid Cancer Staging – SS2018

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- Deep cervical, NOS
- Facial
  - Buccinator (buccal)
  - Mandibular
  - Nasolabial
- Internal jugular, NOS
- Parapharyngeal
- Parotid
  - Infraauricular
  - Intraparotid
  - Periparotid
  - Preauricular
- Retroauricular (mastoid)
- Retropharyngeal
- Suboccipital

- Regional lymph node(s), NOS
  - Lymph node(s), NOS

4 Regional by BOTH direct extension AND regional lymph node(s) invol

- Codes (2) + (3)

7 Distant site(s)/lymph node(s) involved

- Distant site(s) (including further contiguous extension)
  - Bone
  - Diaphragm
  - Liver
  - Lung
  - Pancreas
  - Spleen
- Distant lymph node(s), NOS
- Distant metastasis, NOS
  - Carcinomatosis
  - Distant metastasis WITH or WITHOUT distant lymph node(s)

9 Unknown if extension or metastasis

Thyroid Staging – AJCC TNM Criteria

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- Chapter 73 –Differentiated & Anaplastic Carcinoma
  - Papillary Carcinoma (8260/3)
  - Follicular Carcinoma (8330/3)
  - Hurthle Cell Carcioma (8290/3)
  - NIFTP (8343/2) – non-invasive
  - EFVPTC (8343/2) – non-invasive
  - Anaplastic/Undifferentiated Carcinoma (8020/3)
- Chapter 74 – Medullary Carcinoma
  - Medullary Carcinoma (8345/3)
  - Mixed Medullary and Follicular Carcinoma (8346/3)
  - Mixed Medullar and Papillary Carcinoma (8347/3)
- Chapter 75 – Parathyroid
  - See List in AJCC Manual

AJCC
American Joint Committee on Cancer

Thyroid Staging – AJCC TNM Criteria

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- AJCC Prognostic Stage Group is Further Divided by;
  - Histology
    - Papillary & Follicular
    - Anaplastic/Undifferentiated
    - Medullary
    - Mixed Medullary
  - Behavior
    - Non-Invasive Histology (/2)
    - Invasive Histology (/3)
  - Age at Diagnosis
  - Restaged at Recurrence for Risk Assessment

AJCC
American Joint Committee on Cancer

Major Changes - Thyroid

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AJCC
American Joint Committee on Cancer

TABLE 1. MAJOR CHANGES TO THE AJCC/TNM STAGING OF DIFFERENTIATED AND ANAPLASTIC THYROID CANCERS IN THE EIGHTH EDITION

Differentiated	1.	The age cutoff used for staging was increased from 45 to 55 years of age at diagnosis.
	2.	Minor extrathyroidal extension detected only on histological examination was removed from the definition of T3 disease and therefore has no impact on either T category or overall stage.
	3.	N1 disease no longer upstages a patient to stage III. If <55 years of age at diagnosis, N1 disease is stage I. If ≥55 years of age, N1 disease is stage II.
	4.	T3a is a new category for tumors >4 cm confined to the thyroid gland.
	5.	T3b is a new category for tumors of any size demonstrating gross extrathyroidal extension into strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles).
	6.	Level VII lymph nodes, previously classified as lateral neck lymph nodes (N1b), were reclassified as central neck lymph nodes (N1a) to be more anatomically consistent and because level VII presented significant coding difficulties for tumor registrars, clinicians, and researchers.
	7.	In differentiated thyroid cancer, the presence of distant metastases in older patients is classified as stage IVB disease rather than stage IVC disease. Distant metastasis in anaplastic thyroid cancer continues to be classified as stage IVC disease.
Anaplastic	1.	Unlike previous editions where all anaplastic thyroid cancers were classified as T4 disease, anaplastic cancers will now use the same T definitions as differentiated thyroid cancer.
	2.	Intrathyroidal disease is stage IVA, gross extrathyroidal extension or cervical lymph node metastases is stage IVB, and distant metastases are stage IVC.

Major Changes - Thyroid

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TABLE 3. A CLINICALLY BASED APPROACH TO STAGING IN DIFFERENTIATED THYROID CANCER USING THE EIGHTH EDITION AJCC/TNM UPDATE

	Distant metastasis	*Gross ETE present?*	*Structures involved with gross ETE*	*T category*	*N category*	*Stage*
<55 years	No	Yes or no	Any or none	Any	Any	I
	Yes	Yes or no	Any or none	Any	Any	II
≥55 years	No	No	None	≤4 cm (T1–2)	N0/Nx	I
					N1a/N1b	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

AJCC TNM – T Category Codes

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Definition of Primary Tumor (T)

For Papillary, Follicular, Poorly differentiated, Hurthle cell and Anaplastic Thyroid Carcinoma

T Category	*T Criteria*
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 2 cm in greatest dimension limited to the thyroid
T1a	Tumor ≤ 1 cm in greatest dimension limited to the thyroid
T1b	Tumor > 1 cm but ≤ 2 cm in greatest dimension, limited to the thyroid
T2	Tumor > 2 cm but ≤ 4 cm in greatest dimension limited to the thyroid
T3*	Tumor > 4cm limited to the thyroid, or gross extrathyroidal extension invading only strap muscles
T3a*	Tumor > 4 cm limited to the thyroid
T3b*	Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) from a tumor of any size
T4	Includes gross extrathyroidal extension into major neck structures
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing carotid artery or mediastinal vessels from a tumor of any size
Note: All categories may be subdivided: (s) solitary tumor and (m) multifocal tumor (the largest tumor determines the classification).	

AJCC TNM – N & M Category Codes

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Definition of Regional Lymph Node (N)

N Category	*N Criteria*
NX	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph nodes metastasis
N0a*	One or more cytological or histologically confirmed benign lymph node
N0b*	No radiologic or clinical evidence of locoregional lymph node metastasis
N1*	Metastasis to regional nodes
N1a*	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian or upper mediastinal) lymph nodes. This can be unilateral or bilateral disease.
N1b*	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (Levels I, II, III, IV, or V) or retropharyngeal lymph nodes

Definition of Distant Metastasis (M)

M Category	*M Criteria*
M0	No distant metastasis
M1	Distant metastasis

AJCC TNM – Stage Group Derivagtion

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Differentiated thyroid cancer

When age at diagnosis is…	*And T is…*	*And N is…*	*And M is…*	*Then the stage group is…*
< 55 yrs	Any T	Any N	M0	I
	Any T	Any N	M1	II
≥ 55 yrs	T1	N0/NX	M0	I
	T1	N1	M0	II
	T2	N0/NX	M0	I
	T2	N1	M0	II
	T3a/T3b	Any N	M0	II
	T4a	Any N	M0	III
	T4b	Any N	M0	IVA
	Any T	Any N	M1	IVB

Anaplastic thyroid cancer

T is…	*And N is…*	*And M is…*	*Then the stage group is…*
T1-T3a	N0/NX	M0	IVA
T1-T3a	N1	M0	IVB
T3b	Any N	M0	IVB
T4	Any N	M0	IVB
Any T	Any N	M1	IVC

AJCC TNM – Medullary Carcinoma

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Primary tumor (pT) for medullary thyroid carcinomas:
- **TX - T3:** *Definitions are similar to the above*
- **T4:** Advanced disease
  - **T4a:** Moderately advanced disease; tumor of any size with gross extrathyroidal extension into the nearby tissues of the neck, including subcutaneous soft tissue, larynx, trachea, esophagus or recurrent laryngeal nerve
  - **T4b:** Very advanced disease; tumor of any size with extension toward the spine or into nearby large blood vessels, invading the prevertebral fascia or encasing the carotid artery or mediastinal vessels

Regional lymph node (pN):
- **NX:** Regional lymph nodes cannot be assessed
- **N0:** No evidence of regional lymph node metastasis
  - **N0a*:** One or more cytologic or histologically confirmed benign lymph nodes
  - **N0b*:** No radiologic or clinical evidence of locoregional lymph node metastasis
- **N1*:** Metastasis to regional nodes
  - **N1a*:** Metastasis to level VI or VII (pretracheal, paratracheal, prelaryngeal / Delphian or up
    bilateral disease
  - **N1b*:** Metastasis to unilateral, bilateral or contralateral lateral neck lymph nodes (levels I, I

Distant metastasis (M):
- **M0:** No distant metastasis
- **M1:** Distant metastasis

Medullary thyroid cancer:

Stage I:	T1	N0	M0
Stage II:	T2	N0	M0
	T3	N0	M0
Stage III:	T1 - 3	N1a	M0
Stage IVA:	T4a	any N	M0
	T1 - 3	N1b	M0
Stage IVB:	T4b	any N	M0
Stage IVC:	any T	any N	M1

Introduction to SSDI Manual

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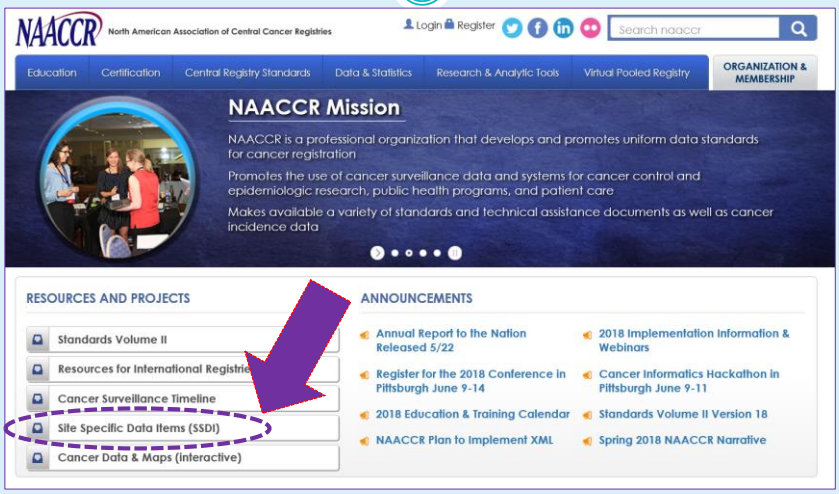

https://apps.naaccr.org/ssdi/list/

Introduction to SSDI Manual

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Site-Specific Data Item (SSDI) Manual

Effective with Cases Diagnosed 1/1/2018 and Forward

Published May 2018

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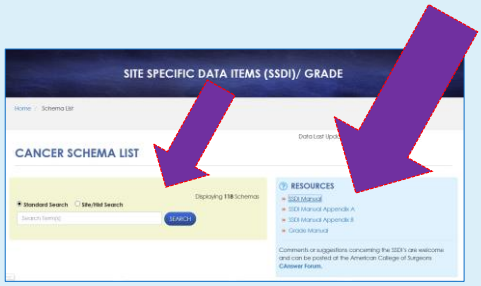

https://apps.naaccr.org/ssdi/list/

Types of Site Specific Data Items

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- Prognostic Factors "Required for Stage Grouping" (All Cases)
  - Not ALL SSDIs Labeled "Required for Stage Grouping" are actually required for staging.
  - Some "Required for Stage Grouping" Items have "Prognostic Significant" and are Required.
- Additional Factors Recommended for Clinical Care (CoC/NCDB and SEER)
- Emerging Factors for Clinical Care (Web Only – Not Required)
- May Include Molecular or Protein Biomarkers, Genetic Markers, Lab Test Value, Interpretation of Lab Value, Clinical Factors such as Size of Lymph Node, Alternate Staging such as FIGO, Measured Depth of Invasion (Breslow Depth), Site Specific Grade Detail (Gleason), Cytogenetics, Immunochemistry, Surgical Margin Details, MSI or Microsatellite Instability and More
- You may not see the SSDIs that clinicians reference and think are important today…the reason is that it takes time for cancer registry standards to catch up with present day technology and testing – particularly for genetic factors.
- Your Cancer Program can define any additional SSDIs you would like to capture for your physicians – genetic markers for lung for example - approve these through your Cancer Committee and carefully define user-defined instructions and codes

Types of Site Specific Data Items

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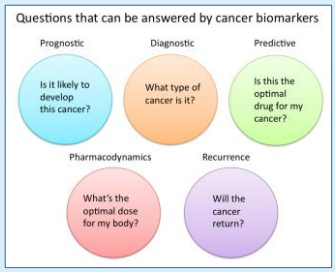
- Molecular Genetics still minimally addressed in 2018 SSDIs
- 2018 SSDIs support TNM data - not biomarkers/molecular markers or genetics
- Most evaluate genetic mutations and/or protein surface markers
- Some have targeted therapy(s) associated with mutation

- Chromosomal Abnormality(s) – Mutation
- Biochemical Abnormality
- Genetic/DNA Mutation

- Prognostic
- Diagnostic
- Predictive
- Tumor Burden
- Pharmacodynamics
- Recurrence Monitoring



2018 SSDIs - Thyroid

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- Only One SSDI – Schema Discriminator 1
- A schema discriminator is used to discriminate between thyroid gland and thyroglossal duct tumors with primary site code C739: Thyroid Gland.
- Code the site in which the tumor arose.
  - Thyroid gland (see code 1)
    - Subsites include: Thyroid, NOS
  - Thyroglossal duct (see code 2)

Code	Description	AJCC Disease ID
1	Thyroid gland Thyroid, NOS	73.1: Thyroid: Differentiated 73.2: Thyroid: Anaplastic 74: Thyroid: Medullary
2	Thyroglossal duct cyst	n/a (not TNM staged)

Treatment Guidelines - Thyroid

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- Most types are highly curable cancers – Factors
  - Patient Age
  - Size of Tumor
  - Type of Tumor
  - (Histology, Behavior and Grade)
  - Stage or Extent of Disease – How far has the tumor spread?
- New Tyrosine Kinase Inhibitors (TKI inhibitor) have shown to shrink tumors and slow growth but no cure
- Primary Treatment is remove all tumor at surgery plus nodes to ensure they are free of cancer. Then the patient is treated with radioactive iodine (I-131) to destroy remaining thyroid tissue or for latter stages of disease.
- Hormone Replacement Therapy is always given after thyroidectomy to bring back into balance the hormones normally produced by the thyroid AND to keep the body from producing thyroid stimulating hormones.
- Long-Term Follow Up Plan Must Be Part of Every Treatment Plan

Treatment Guidelines – No Treatment

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- Papillary Thyroid Cancers – Active Surveillance
- Some physicians may not even biopsy a small tumor
- Avoids Overtreatment of Cancers Unlikely to Cause Medical Problems…
  - Incidental Nodule(s) Found During W/U for Other Reason
  - Small and Asymptomatic Thyroid Cancers
  - Suspected But Not Proven Thyroid Cancers
- …however, patients and physicians and family members may insist on treatment even when it is felt to not be necessary and may lead to harmful side effects
- Patients need support they have made a sound treatment decision for their cancer – not a stupid or crazy decision.

Treatment Guidelines - Surgery

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- Papillary / Follicular Histology – Local/Regional Disease
  - Lobectomy with Level VI Central Node Dissection
  - Total Thyroidectomy with Level VI Central Node Dissection
  - Radioactive Iodine Therapy – I-131
  - Thyroid Suppression Therapy with Thyroid-Stimulating Hormone (TSH)
  - External Beam Radiation Therapy
- Anaplastic Thyroid Cancer
  - Surgery – Lobectomy or Total Thyroidectomy with Central Node Dissection
  - External Beam Radiation Therapy
  - Systemic Therapy or Target Therapy – Sorafenib, Lenvatinib
- Medullary Thyroid Cancer – Localized Disease
  - Total Thyroidectomy with Nodes plus External Beam Radiation Therapy
- Medullary Thyroid Cancer – Locally Advanced/Metastatic
  - Targeted Therapy – Sorafenib, Lenvatinib, Vandetanib, Cabozantinib
  - Palliative Chemotherapy

Treatment Guidelines – Target Drugs

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- Usually only given for metastatic disease or when patient has anaplastic or medullary histology.
- May 25, 2018 - Dabrafenib–Trametinib Combination
  - Anaplastic Histology Only
  - Dabrafenib (Tafinlar) – code as chemo per SEER*Rx
    - Inhibits enzyme over-produced by BRAF V600 gene mutation
  - Trametinib (Mekinist) – code as chemo per SEER*Rx
    - Blocks one of resistance pathways making Tafinlar more effective

Table 3: U.S. FDA–approved MTTs for Thyroid Cancers

MTT	Trade Name	Year of Approval	Targets	Thyroid Malignancy
Vandetanib	Caprelsa	2011	VEGFR, RET, EGFR	MTC
Cabozantinib	Cometriq	2012	VEGFR, c-MET, RET	MTC
Sorafenib	Nexavar	2013	VEGFR-1, -2, -3; PDGFR; RET; BRAF	DTC
Lenvatinib	Lenvima	2015	VEGFR, RET, c-KIT, PDGFR, FGFR	DTC

Note.—FGFR = fibroblast growth factor receptor, PDGFR = platelet-derived growth factor receptor.

Treatment Guidelines – Target Drugs

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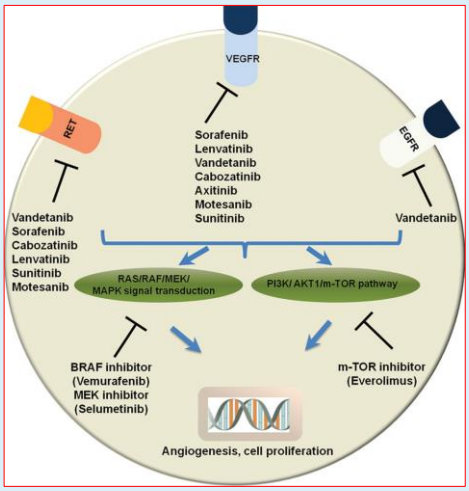

Text Documentation

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- NCRA Informational Text Guidelines for Abstracts – Thyroid – Not Available in the Current Set for Text
- Follow Typical Recommendations for Complete Documentation with Special Focus on Histology, Capsular Invasion, Extra-thyroid Extension, Nodes and Extranodal Extension, and Mets as well as completely documenting Treatment Given
- Be aware there are multiple new histology codes, etc.

Staging Practice - Pending

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References

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Questions

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