AJCC Staging: Insights into New 2024 Version 9 Protocols

Donna M. Gress, RHIT, ODS-C

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AJCC Vulva Version 9 – 2024

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Vulva: Major Changes

- T1 category depth of invasion has NEW method of measurement
  - Critical for pathologists to note new depth of invasion measurement
  - May change assignment of T1a and T1b based on measurement
  - Description and illustrations in Note T: Primary Tumor
- T4 category has been added
- N category reduced, now only N1 & N2
- p16 collected for HPV-associated or HPV-independent cancers
  - Affects treatment choice, improved response to radiation therapy
  - Affects survival

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Vulva: Important Information

- Based on FIGO 2021 Vulva update
  - AJCC representatives provided data to FIGO and participated in decisions
- Note I: Imaging provides extensive descriptions of T and N categories
- Perineal lesions present a challenge – considered vulvar or anal
  - Explanation and illustration in Note S: Identification of Primary Site

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Vulva: Clinical/Pathological Staging & Workup

DIAGNOSTIC WORKUP	DESCRIPTION	SPECIFIC CONTRIBUTION TO TNM CA
Clinical Exam		
Inspection and palpation	Size, local spread	T1–T3
Biopsy	Microscopic confirmation	T1a–T4
Exam under anesthesia (EUA), cystourethroscopy, proctoscopy	Size, spread to surrounding structures	T1a–T4
Fine needle aspiration (FNA), core needle biopsy, sentinel node biopsy	Microscopic assessment of lymph nodes	N0–N2
Imaging		
CT	Chest/abdomen/pelvis	T1a–T4, N
MRI	Pelvis – define extent of local disease	T1a–T4, N
PET/CT	Base of neck to mid-thigh	T1a–T4, N
Ultrasound	Local nodal assessment	T1a–T4, N
Laboratory Studies		
p16	Immunohistochemistry (IHC), microscopy	Histopath

CATEGORY	SPECIMEN	PATHOLOGIST	MANAGING PHYSICIAN (Stage Documented by Cancer Registry)
General Information		• Assignment of pTNM categories is based on surgical resection **specimen,** as well as intraoperative findings, biopsy procedures and clinical evaluation up to the point of definitive surgical treatment, if available • All other surgical procedure specimens use cTNM; for example, biopsy of a positive regional lymph node without surgical resection of the primary carcinoma is classified as cN1	• Assignment of pTNM categories for the **patient** requires use of information from all biopsy procedures performed during the clinical evaluation up to and including definitive surgical treatment • Requires information from clinical assessment or imaging studies or intraoperative findings to assign pTNM categories (may not change pTNM, but must be considered)
pTX		Not for use by pathologist; assignedonly by managing physician	May assign if unable to determine pT category after surgical resection
pT0		No tumor found in specimen and never identified on diagnostic biopsies	No tumor found in specimen and never identified on diagnostic biopsies
pT1	Radical vulvectomy	Pathologic information from surgical specimen, size of tumor and stromal invasion	Pathology reports +/- appropriate clinical exam, imaging studies, and intraoperative findings
pT1a			
pT1b			
pT2		Extension to adjacent structures	
pT3			
pT4		May not receive specimen of disease fixed to pelvic bone	Pathology reports +/- appropriate clinical exam, imaging studies, and intraoperative findings
pNX		Not for use by pathologist; assigned only by managing physician	May assign if unable to determine pN category

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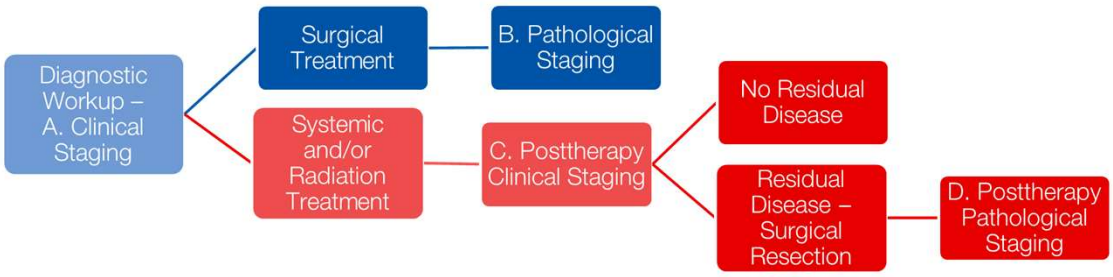
Vulva: Staging Rules



- Common staging scenario
  - Most vulvar cancers are treated surgically, staging is A and B in figure
  - Less commonly, primary radiation and concurrent chemotherapy
    - Cases that are locally advanced, or nodal involvement not amendable to resection
    - Staging is A and C in the figure
    - If residual tumor and it is resected, staging is D in the figure
- Illustrates appropriate staging based on patient care

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AJCC Neuroendocrine Tumors Version 9 – 2024

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AJCC Neuroendocrine Tumors Version 9

- Six protocols in this series
  - Neuroendocrine Tumors of the Stomach
  - Neuroendocrine Tumors of the Duodenum and Ampulla of Vater
  - Neuroendocrine Tumors of the Jejunum and Ileum
  - Neuroendocrine Tumors of the Appendix
  - Neuroendocrine Tumors of the Colon and Rectum
  - Neuroendocrine Tumors of the Pancreas

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Clinical Staging and Workup

- Similar tables
- Slight differences due to anatomic considerations

DIAGNOSTIC WORKUP	DESCRIPTION	SPECIFIC CONTRIBUTION TO TNM CATEGORY
Clinical Exam		
Esophagogastroduodenoscopy (EGD)	Description of tumor(s), size number of lesions	None
Biopsy	Provide histologic diagnosis	None
Imaging		
Endoscopic ultrasound (EUS)		
CT (contrast enhanced)		
MRI (multiphasic and multiplanar)		
Somatostatin receptor (SSTR) PET or PET/MRI		
Stomatostatin scintigraphy (Octreotide scan)		
FDG PET/CT or PET/MRI		
Laboratory Studies		
Biochemical evaluation		
Genetic testing		

DIAGNOSTIC WORKUP	DESCRIPTION	SPECIFIC CONTRIBUTION TO TNM CATEGORY
Clinical Exam		
Digital rectal examination	Assess tumor size, texture	T1-T4
Physical examination, including abdominal examination	Detect lymphadenopathy or hepatomegaly	N1, M1
Colonoscopy with biopsy		
Colonoscopy with polypectomy		
Imaging		
Endorectal ultrasound		
MRI of rectum		
MRI (multiphasic and multiplanar)		
CT (multiphasic and multiplanar)		
Somatostatin receptor (SSTR) PET or PET/MRI		

DIAGNOSTIC WORKUP	DESCRIPTION	SPECIFIC CONTRIBUTION TO TNM CATEGORY
Clinical Exam		
Endoscopic ultrasound (EUS)	Tumor size	T1-T4
Biopsy	Provide histologic diagnosis	None
Imaging		
CT (pancreas protocol)	Chest/abdomen/pelvis – define extent of local disease, nodal involvement, metastasis	T3-T4, N1, M1a-c
MRI (multiphasic and multiplanar)	Abdomen/pelvis – define extent of local disease, nodal involvement, metastasis. Hepatobiliary contrast preferred for liver lesions.	T3-T4, N1, M1a-c
Somatostatin receptor (SSTR) PET/	Skull base to mid-thigh – define	T3-T4, N1, M1a-c

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Pathological Staging and Workup

- Similar tables
- Slight differences due to treatment

CATEGORY	SPECIMEN	PATHOLOGIST	MANAGING PHYSICIAN (Stage Documented by Cancer Registry)
General Information			
pTX			
pT0			
pT1	Endoscopic resection, local resection, gastrectomy		
pT2			
pT3			
pT4			
pNX			

CATEGORY	SPECIMEN	PATHOLOGIST	MANAGING PHYSICIAN (Stage Documented by Cancer Registry)
General Information			
pTX			
pT0			
pT1	Appendectomy, cecectomy, or right hemicolectomy		
pT2			
pT3			
pT4			

CATEGORY	SPECIMEN	PATHOLOGIST	MANAGING PHYSICIAN (Stage Documented by Cancer Registry)
General Information		• Assignment of pTNM categories are based on an endoscopic, transanal, or surgical resection specimen, as well as intraoperative findings, biopsy procedures and clinical evaluation up to the point of definitive surgical treatment, if available • All other surgical procedure specimens use cTNM; for example, biopsy of a positive regional lymph node without surgical resection of the primary carcinoma is classified as cN1	• Assignment of pTNM categories for the patient requires use of information from all biopsy procedures performed during the clinical evaluation up to and including definitive surgical treatment • Requires information from clinical assessment or imaging studies or interoperative findings to assign pTNM categories (may not change pTNM, but must be considered)
pTX		Not for use by pathologist; assigned only by managing physician	May assign if unable to determine pT category after surgical resection
pT0		No tumor found in specimen and never identified on diagnostic biopsies	No tumor found in specimen and never identified on diagnostic biopsies
pT1	Endoscopic, transanal, or surgical resection	Pathological information from resection specimen only	Pathology report +/- appropriate clinical exam, imaging studies, and intraoperative findings
pT1a			

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NETs Endoscopic Resection and Methods

- Endoscopic resections for NETs
  - Stomach
  - Duodenum & Ampulla of Vater
  - Colon & Rectum
- Endoscopic resection (ER) methods include
  - Endoscopic mucosal resection (EMR)
  - Endoscopic submucosal dissection (ESD)
  - Endoscopic full thickness resection (EFTR)
- Not used for jejunum/ileum, appendix, pancreas

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Surgical Diagnostic Workup Vs. Surgical Treatment

- For AJCC staging, what is surgical treatment?
  - Not just removing some, most, all of tumor
    - Old registry rules that are outdated
  - It is performing resection to give patient best chance of good outcome, of living!
    - May be referred to as definitive, curative intent
- NETs: workup Vs. treatment depends on clinical stage
  - Endoscopic resections and appendectomy
    - Treatment in low stages or small tumor size
    - Diagnostic workup in mid and higher stages, or low stage with larger tumors
- Assign clinical & pathological staging using these principles

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Surgical Diagnostic Workup Vs. Surgical Treatment

- What if diagnostic procedure removes most of tumor?
  - Does ***not*** make it treatment for AJCC staging
  - Don't know if residual tumor exists
  - Residual will continue to grow and jeopardize patient's life
  - If surgical treatment resection has no residual tumor
    - Diagnostic procedure is still diagnostic
    - Don't know if all tumor removed without doing surgical treatment
- How to think about this – diagnostic Vs. treatment
  - Would you gamble with your life, roll the dice, and say I don't want surgical treatment resection in case diagnostic procedure may have removed cancer?
  - Presume physicians & patients wouldn't do this either
  - Follow treatment guidelines, not old registry rules, for AJCC staging

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Staging Rules for NETs – 3 Different Graphics

- Stomach
- Duodenum & Ampulla of Vater

- Colon & Rectum

- Jejunum & Ileum
- Appendix
- Pancreas

NOTE: Neoadjuvant therapy is not current standard of care. Therefore, no AJCC yc or yp staging in graphic.

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Assigning Stage with NX in Limited NET Cases

- Based on survival data, AJCC allows the use of NX in limited cases
  - Workup does not include nodal assessment
  - Type of resection does not include regional nodes
  - Only allowed due to data that is Level of Evidence: I
- T1 NX M0 Stage I
  - NET Stomach
  - NET Duodenum & Ampulla of Vater
  - NET Colon & Rectum
- T1 NX M0 Stage I and T2 NX M0 Stage II
  - NET Appendix

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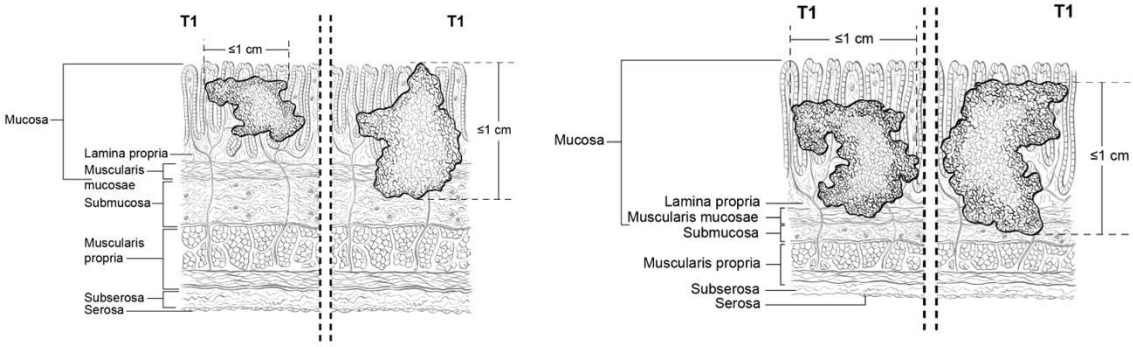
NETs Arise from Deep Mucosa

- Compare to T1 illustrations for other histologies



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NET Grade

- Mitotic count and Ki-67 index are indicators of tumor proliferation
  - Used to grade NETs
  - Cellular pleomorphism is not useful feature
- Mitotic count has changed to per 2 mm^2
  - No longer using per 10 HPF as it varied with different microscopes
- Use highest grade if disparity between mitotic count & Ki-67 index
- Remember, well-differentiated NET is histology, NOT grade

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NET Stomach: Major Changes

- T1 NX M0 added to stage I
  - Most early gastric NETs treated endoscopically with no nodes removed
  - Early gastric NETs rarely have nodal involvement
  - No difference in survival between T1N0M0 and T1NXM0
- Prognostic tumor characteristics
  - Removed chromogranin A
  - Added type of gastric NETs (Type 1, 2, 3, or PPI-associated)
- Emerging Factors
  - Clinical history of proton pump inhibitor (PPI) use

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NET Stomach: Important Information

- Table of key features by gastric NET type 1, 2, 3, and PPI-associated
  - Includes demographics and frequency
  - Clinical findings including type of tumor seen on endoscopy
  - Pathology including grading, invasion depth, and gastric mucosa
  - 5-year survival
- Note T: Primary Tumor describes T categories, sampling, & treatment
  - cT1 may be treated with endoscopic resection
  - > cT1 usually treated with surgical techniques such as wedge resection
- Note N: Regional Lymph Nodes
  - Rare nodal involvement in T1

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NET Duodenum & Ampulla of Vater: Major Changes

- T1 NX M0 added to stage I
  - Most early duodenal/ampullary NETs treated endoscopically with no nodes removed
  - No difference in survival between T1N0M0 and T1NXM0
- Modalities used for diagnosis and staging
  - New section in Version 9
  - Highlights endoscopic management for small duodenal NETs
- Prognostic tumor characteristics
  - Removed associated genetic syndrome and chromogranin A

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NET Duodenum & Ampulla of Vater: Important Information

- Table of key features of four subtypes
  - Nonfunctional NOS, gastrinoma, somatostatinoma, CoGNET
  - Clinical findings of location, size, multiplicity, genetic syndromes
  - Pathology including histologic features, biomarkers
  - Nodal and metastatic involvement
- Endoscopic ultrasound (EUS) plays central role in staging
  - Accuracy rates from 80-100%
  - Evaluates depth of invasion, nodal involvement
  - Determines candidacy for endoscopic resection

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NET Jejunum & Ileum: Major Changes

- Identification of primary site
  - Added C17.8 overlapping lesions of small intestine
  - Added C17.9 small intestine, NOS
- Rationale for staging small intestine NETs with this protocol
  - Small intestine most common primary location
  - Terminal ileum most common tumor site
    - But only most distant portion of terminal ileum easily assessed by colonoscopy
    - Therefore primary tumors in ileum are difficult to identify
- Prognostic tumor characteristics
  - Removed chromogranin A, plasma pancreastatin, plasma serotonin level
  - Added mesenteric fibrosis

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NET Jejunum & Ileum: Important Information

- Small bowel NETs
  - Most common location for all gastroenteropancreatic (GEP) NETs
  - Diagnostic challenge since screening colonoscopy cannot reach
  - Usually small but may be multicentric tumors
  - Clinical symptoms often absent in early disease
    - Older studies reported symptoms
    - Increasingly being diagnosed in asymptomatic patients incidentally
  - Imaging used to
    - Assess regional/distant mets
    - Relation to mesenteric vessels to determine resectability
- Duodenal NETs not included with small bowel
  - Duodenum behaves biologically differently from small bowel (jejunum/ileum)
  - Staged with ampulla of Vater due to behavioral similarities

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NET Appendix: Major Changes

- T1 NX M0 added to stage I
  - Small size early stage treated with appendectomy with no nodes removed
  - Early appendiceal NETs rarely have nodal involvement
  - No difference in survival between T1N0M0 and T1NXM0
- T2 NX M0 added to stage II
  - For patients not undergoing lymphadenectomy
  - No difference in survival between T2N0M0 and T2NXM0
- Note CE: Clinical Examination & Rationale for Changes/Future Directions
  - No routine usage of chromogranin A
  - Data on emerging prognostic tools: PPQ and Clinical Score

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NET Appendix: Important Information

- Appendiceal NETs
  - While rare across all NETs, represent 85% of all appendiceal neoplasms
  - Most found during incidental appendectomy
  - Separate staging system from other appendiceal neoplasms
    - No apparent in situ state, arise in deep mucosa
    - Tumor size more important than depth of invasion
- T1 and T2 categories differ from small bowel and colon/rectum
  - Size, not depth of invasion
- Treatment
  - Appendectomy for <1cm
  - Appendectomy Vs. more aggressive resection for >1cm but ≤ 2cm
  - Right hemicolectomy for >2cm (appendectomy would be diagnostic)

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NET Colon & Rectum: Major Changes

- T1 NX M0 added to stage I
  - Most early colorectal NETs treated endoscopically with no nodes removed
  - Increasing tumor size associated with increasing risk of nodal involvement
  - No difference in survival between T1N0M0 and T1NXM0
- Modalities used for diagnosis and staging
  - New section in Version 9
  - Imaging including endorectal ultrasound
  - Highlights types of endoscopic and transanal management for small NETs
- Prognostic tumor characteristics
  - Removed chromogranin A
  - Added lymphovascular invasion

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NET Colon & Rectum: Important Information

- Colorectal NETs
  - Rectum most frequent site for gastroenteropancreatic (GEP) NETs
  - Most incidentally found on screening colonoscopy
- Treatment
  - Endoscopic resection for <1cm
  - Surgical resection for >2cm, partly due to high risk of nodal involvement
  - Modified endoscopic mucosal resection (EMR) for 1-2cm
  - Endoscopic submucosal dissection (ESD) for 1-2cm
  - Transanal endoscopic microsurgery is next most intensive procedure

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NET Pancreas: Major Changes

- Modalities used for diagnosis and staging
  - New section in Version 9
  - Somastatin receptor PET scans
  - More detail in Clinical Staging and Workup table
- Prognostic tumor characteristics
  - Potential biomarkers: *DAXX/ATRX, ARX, PDX1*
  - New non-tumor factors
- Introduction
  - Discussion of latest treatment options

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NET Pancreas: Important Information

- Pancreatic NETs (PanNETs)
  - Most are sporadic with risk factors poorly understood
  - Certain genes associated with a poor prognosis
- Table of syndromes associated with pancreatic NETs
  - Divided by most common and less common
  - Information includes tumor location and symptoms/signs
- Surgical treatment
  - Depends on tumor size, grade, location, comorbidities
  - Left sided lesion: distal pancreatectomy with possible splenectomy
  - Right sided lesion: pancreaticoduodenectomy (Whipple procedure)
  - Central pancreatectomy or enucleation in selected cases

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Sneak Peek - AJCC Version 9 for 2025

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AJCC Version 9 for 2025

- Will be released this fall
- Thoracic
  - Thymus
  - Lung
  - Diffuse Pleural Mesothelioma
- Head & Neck
  - Nasopharynx

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Information and Questions on AJCC Staging

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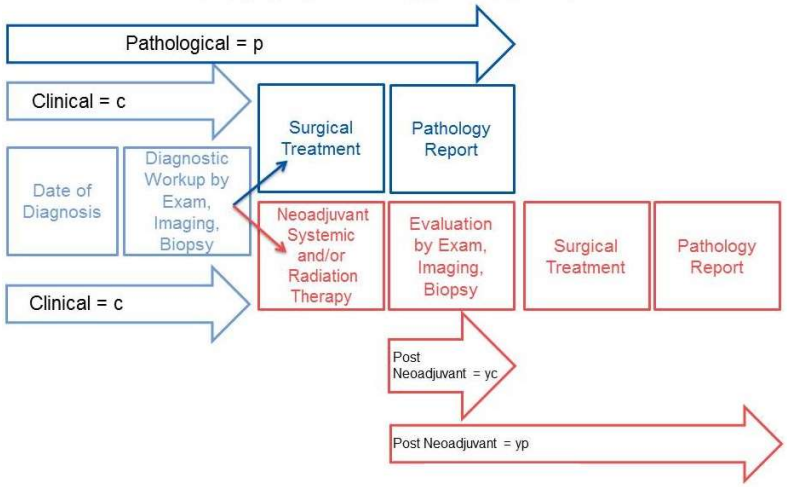
Timing is Everything

AJCC Stage Classifications

Defining Time Frame and Criteria



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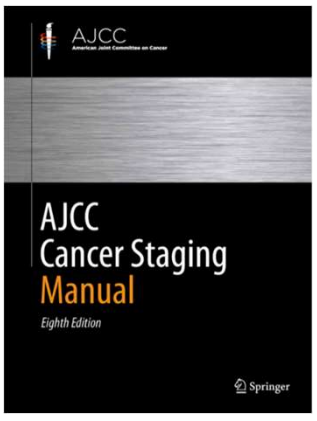
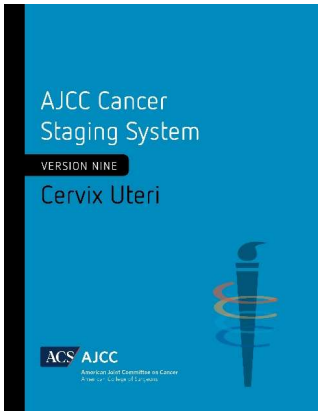
AJCC Web Site

- https://**cancerstaging.org**
- https://www.facs.org/quality-programs/cancer-programs/american-joint-committee-on-cancer/

- General information
  - Overview
  - AJCC Staging Online
  - Version 9
  - Cancer Staging Systems
    - AJCC 8th edition Chapter 1: Principles of Cancer Staging
  - Cancer Staging Education
  - FAQ & Resources





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NEW AJCC Webinars Posted Fall 2023

- Principles of Cancer Staging
  - Blank Vs. X Definitions and Data Interpretation for AJCC Staging
  - Do Not Use Registry Ambiguous Terminology for AJCC Staging
- AJCC 8th Edition Staging
  - Breast
  - Colorectal
  - Lung
  - Melanoma
  - Prostate
- Critical Clarifications
  - AJCC 8th Edition Melanoma Staging – 1-page resource highlighting rules

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AJCC Staging Online

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CAnswer Forum

- Submit questions to AJCC Forum
  - Version 9 Forum
  - 8th Edition Forum
  - Located within CAnswer Forum
  - Provides information for all
  - Allows tracking for educational purposes
- http://cancerbulletin.facs.org/forums/

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Summary

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Summary

- Discussed key points of seven new AJCC Version 9 protocols
  - Understanding strategies of new staging systems
- Dissect changes in new staging systems
  - Identified areas of change
  - Explored the rationale
- Examine workup tables and disease-specific staging rules
  - New features of AJCC protocols
  - Usage from a registrar's point of view
  - Customization compared/contrasted to Timing is Everything graphic

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Donna M. Gress, RHIT, ODS-C

Manager, Cancer Staging and Registry Operations
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