

# TNM Staging System: General Principles

**Jae Y. Ro, M.D., Ph.D.**

*March 16, 2018*

**Cornell University**



THE UNIVERSITY OF TEXAS  
**MD ANDERSON**  
**CANCER CENTER**  
*Making Cancer History™*



**Do your BeST!**

Category 1 prognostic factors

March 16, 2018

# **Excel my Diagnostic Skills**

- 1) Normal histology**
- 2) Stage**
- 3) Knowing my limitation  
with Enjoy**

**March 16, 2018**

# Contents

## Tumor Staging and Grading

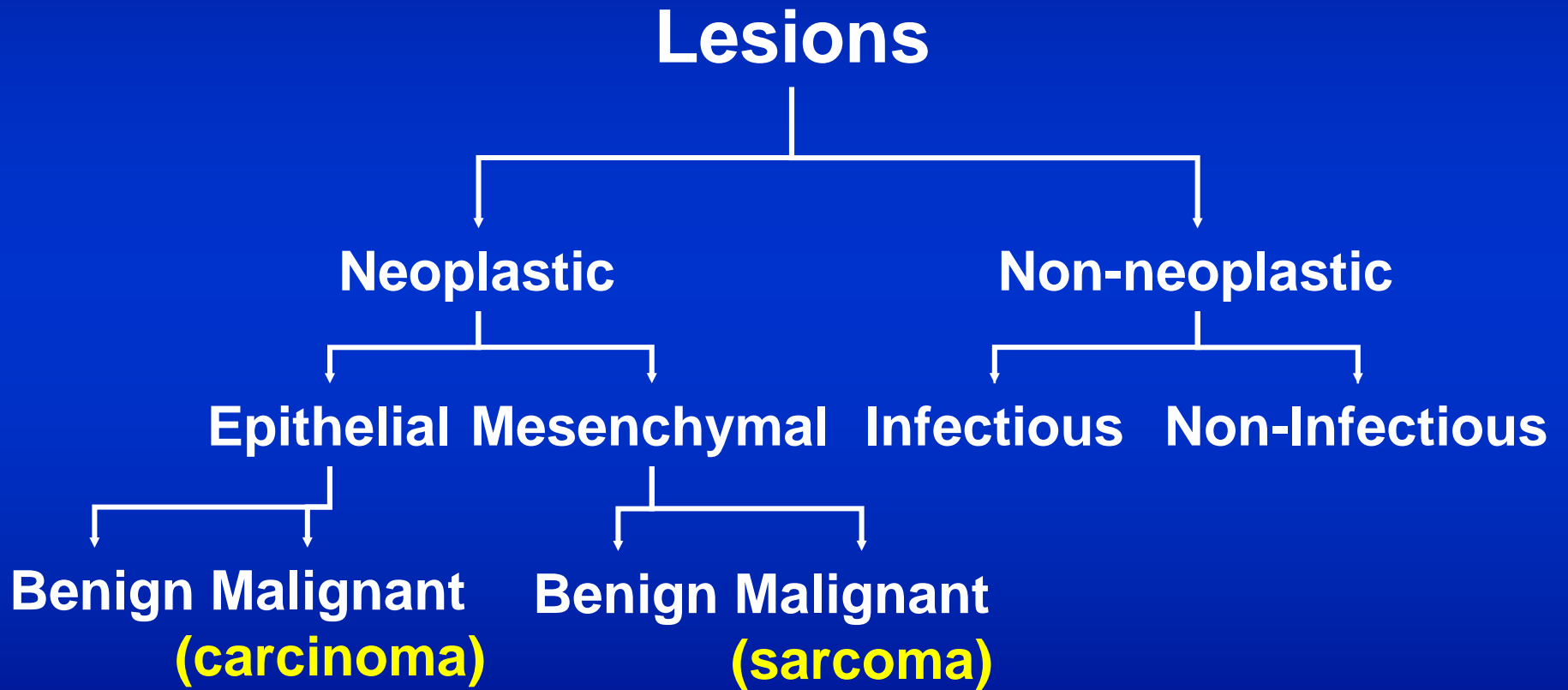
- 1) Basic
- 2) (effort) Study
- 3) Think
- 4) Enjoy

March 16, 2018

# 1. Basic

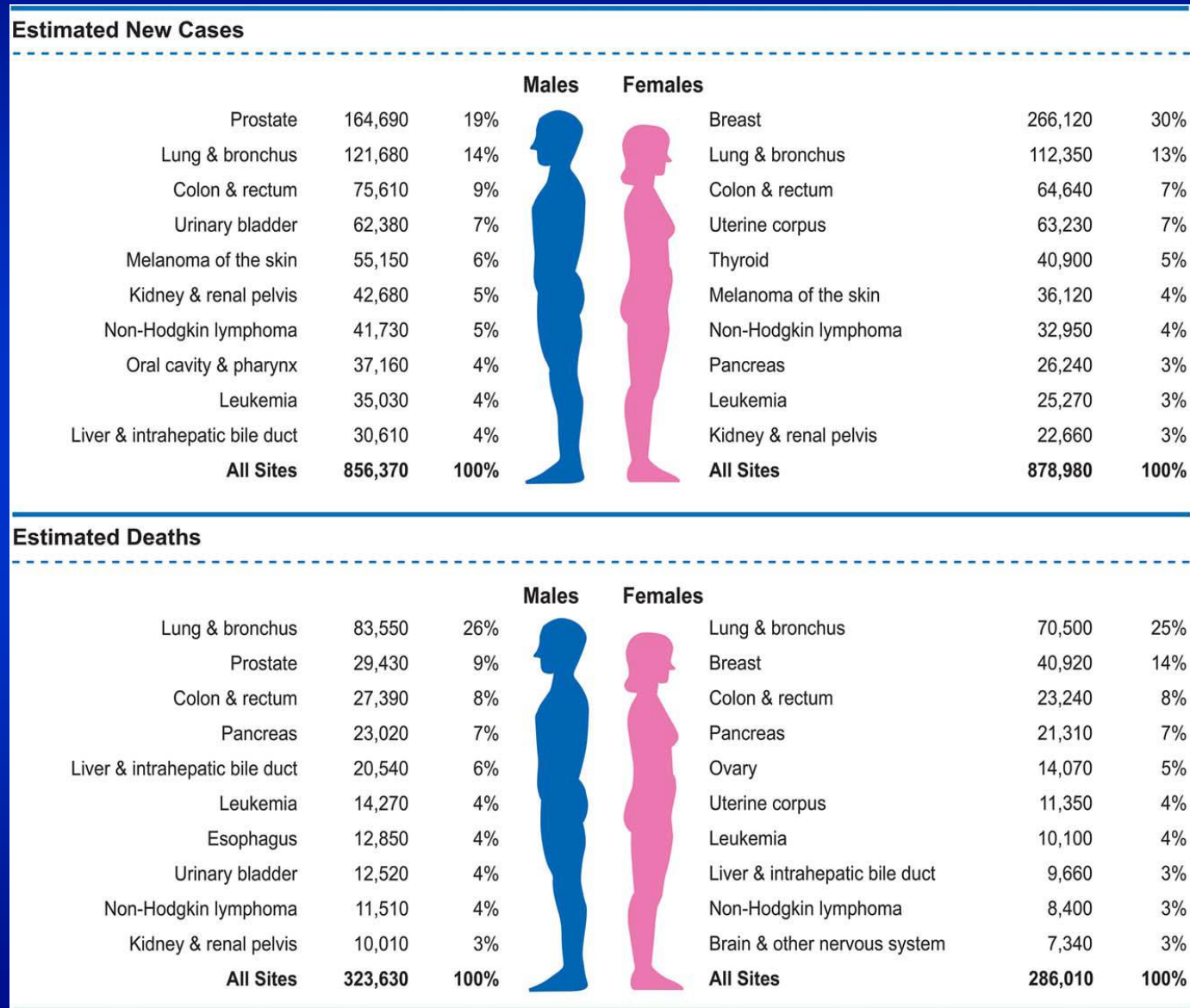
- Tumor characters and diagnosis
- Incidence
- Prognostic factors
- ✓ Stage (TNM, UICC) and Grade
- **I CARE (integrity, compassion, accountability, respect, excellence) value**
- **3C (consultation, communication, and collaboration) practice**

# Diagnostic Approach





# Ten Leading Cancer Types for the Estimated New Cancer Cases and Deaths By Sex, United States, 2018.







# 2. Study

- **Speed, accuracy and decision**
- **Prognostic factors**
  - **Category 1 prognostic factors**
    - ✓ **Stage and grade**
    - ✓ **Non-anatomic prognostic factors (e.g., age, PSA, grade, serum tumor markers, etc)**

# Prognostic Factors

- ❖ **Category I (well supported): stage, grade (non-anatomical factors; PSA, age, serum markers)**
- ❖ **Category II (extensively studied but not well established): DNA ploidy, nuclear proliferation, angiogenesis, apoptosis, tumor suppressor gene**
- ❖ **Category III (currently studying): other oncogenes, cytogenetic analysis, growth factors, detection of circulating tumor cells in blood**

# Tumor Grade

- malignant tumors (Arabic no. 1,2,-- )
  - ▣ **Histologic grade (overall proportional)**
    - ⊙ original Broders' grading (4 tier)
    - ⊙ modified Broders' grading (3 tier)
    - ⊙ high and low grade (2 tier)
  - ▣ **Nuclear grade (worst areas)**
    - ⊙ Black NG for breast ca.
    - ⊙ Fuhrman's NG for renal cell ca.
  - ▣ **Combined: FIGO grade**

# Histologic grade

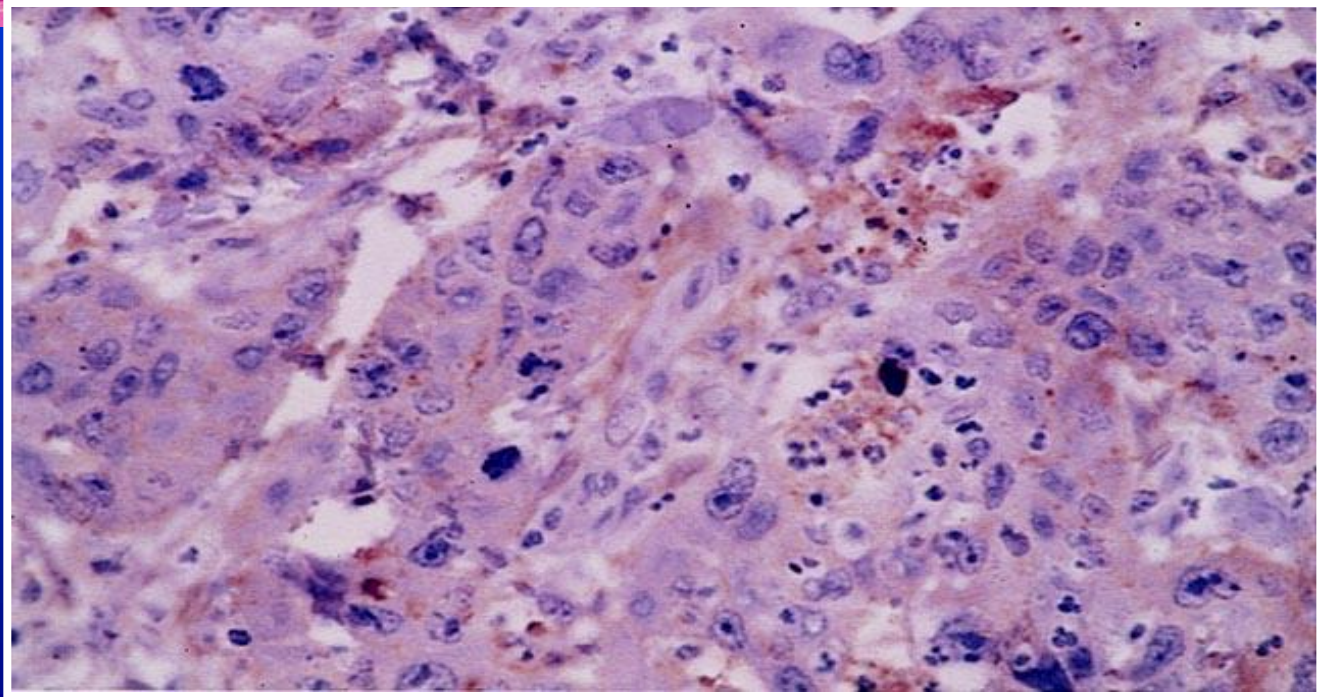
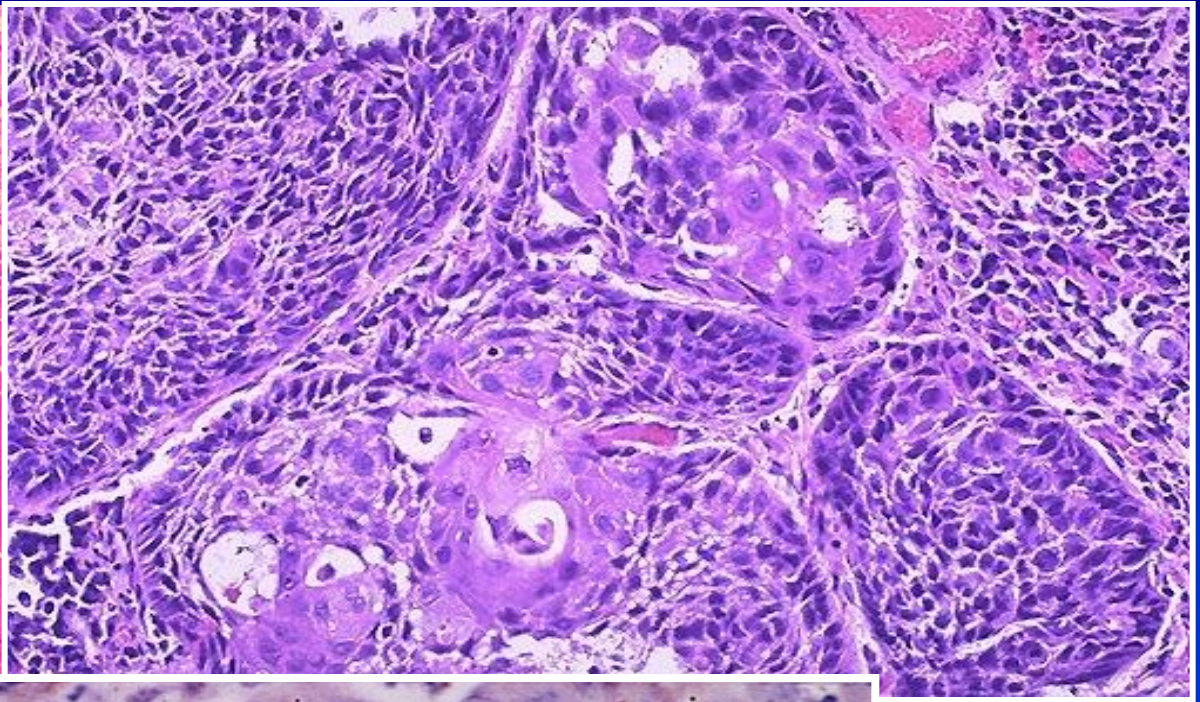
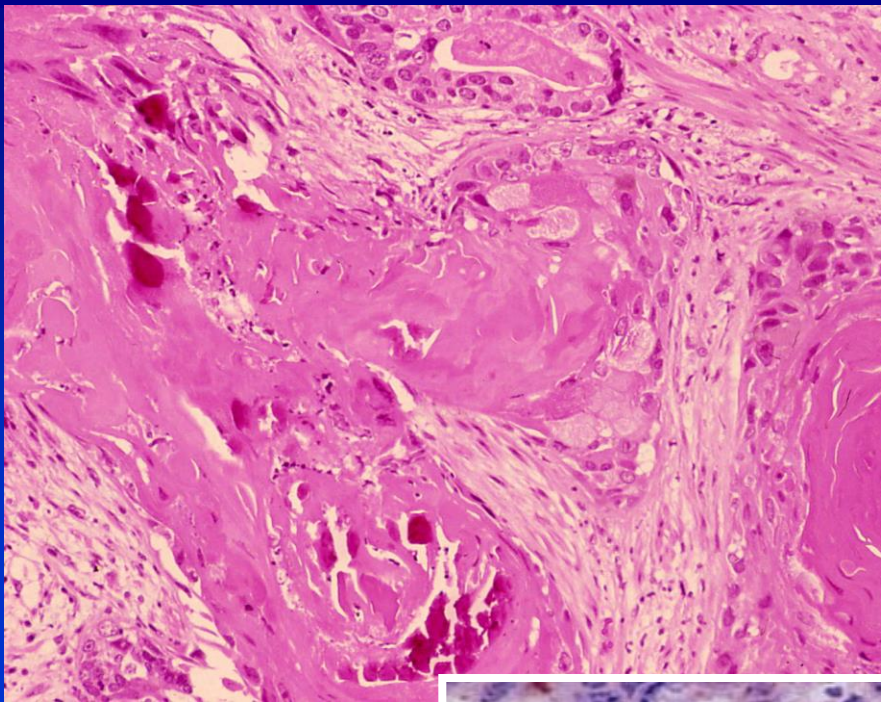
## Original Broders' grade, 4 tier

- Grade 1:  $> 75\%$
- Grade 2:  $> 50\%, \leq 75\%$
- Grade 3:  $> 25\%, \leq 50\%$
- Grade 4:  $\leq 25\%$

## Modified Broders' grade, 3 tier

- Well, moderate and poorly

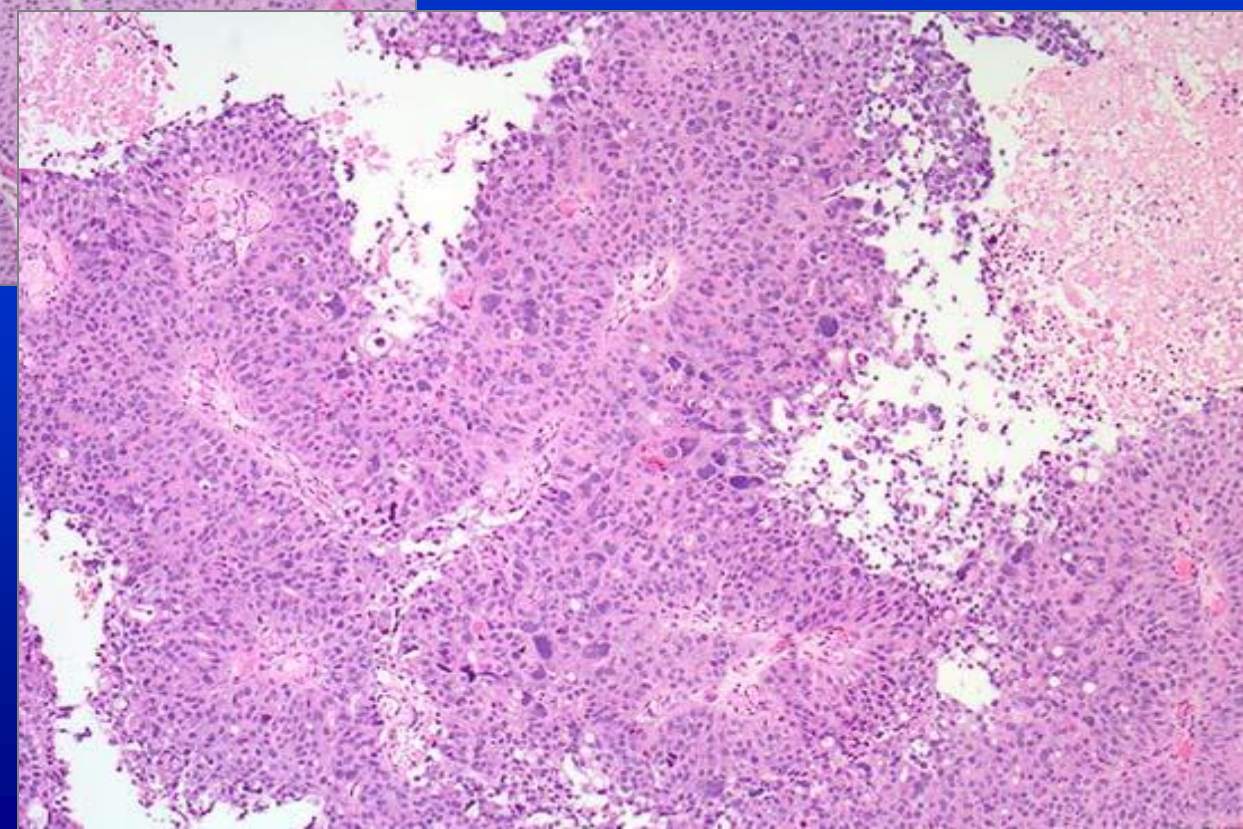
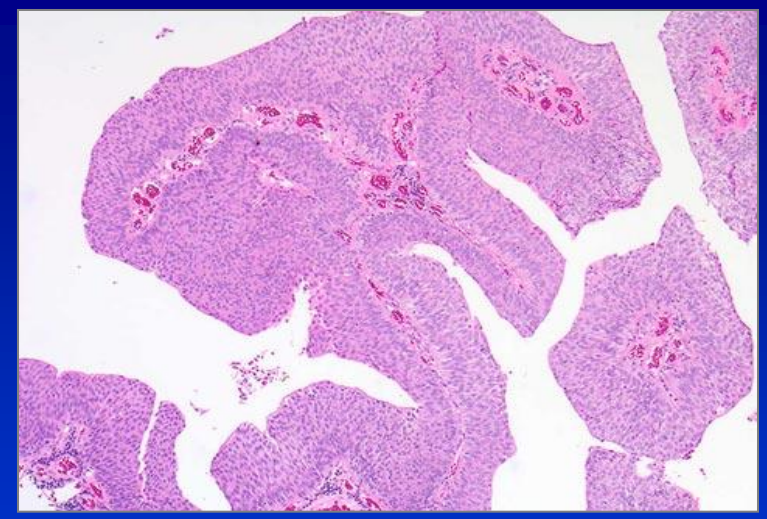
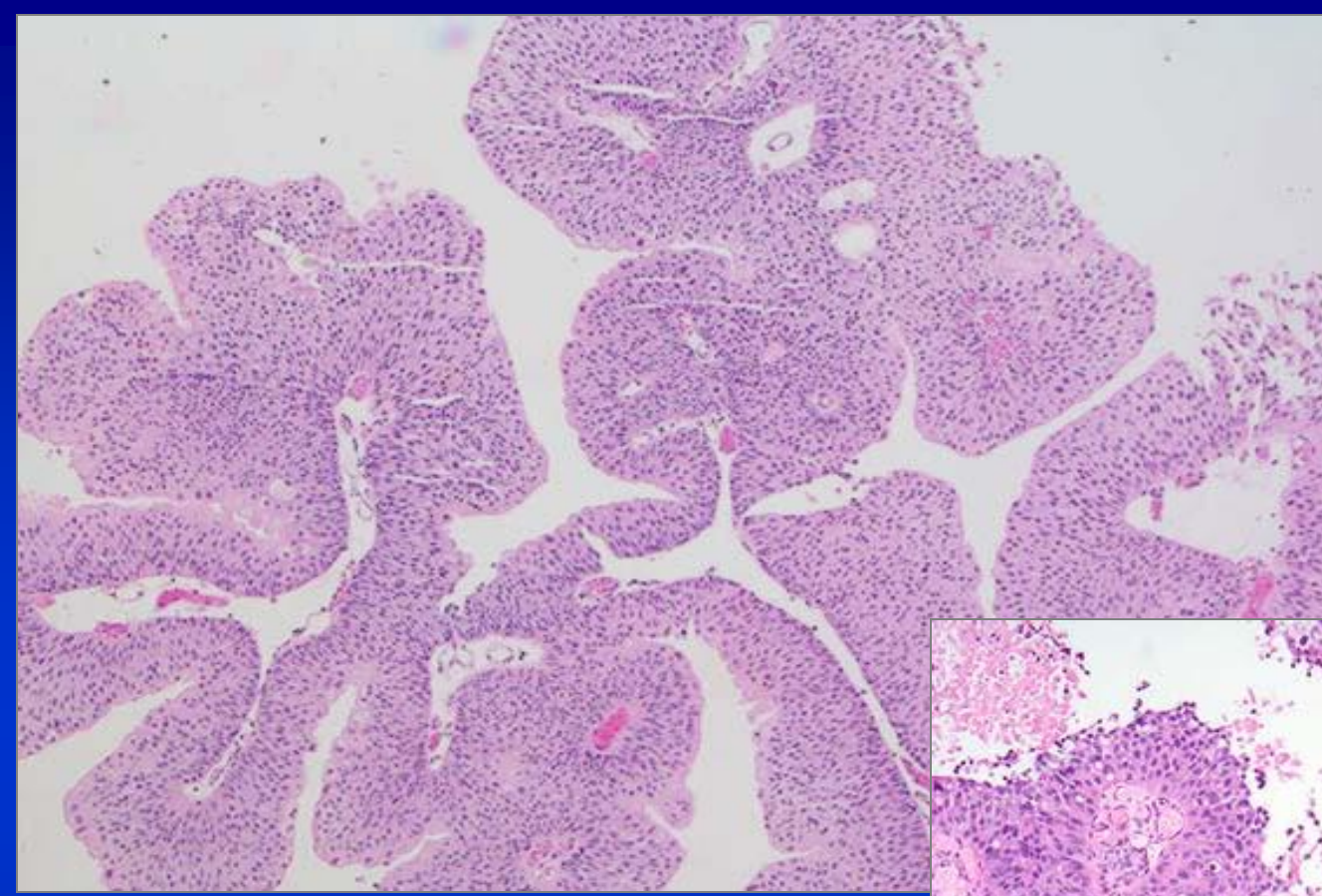






# Tumor Grade

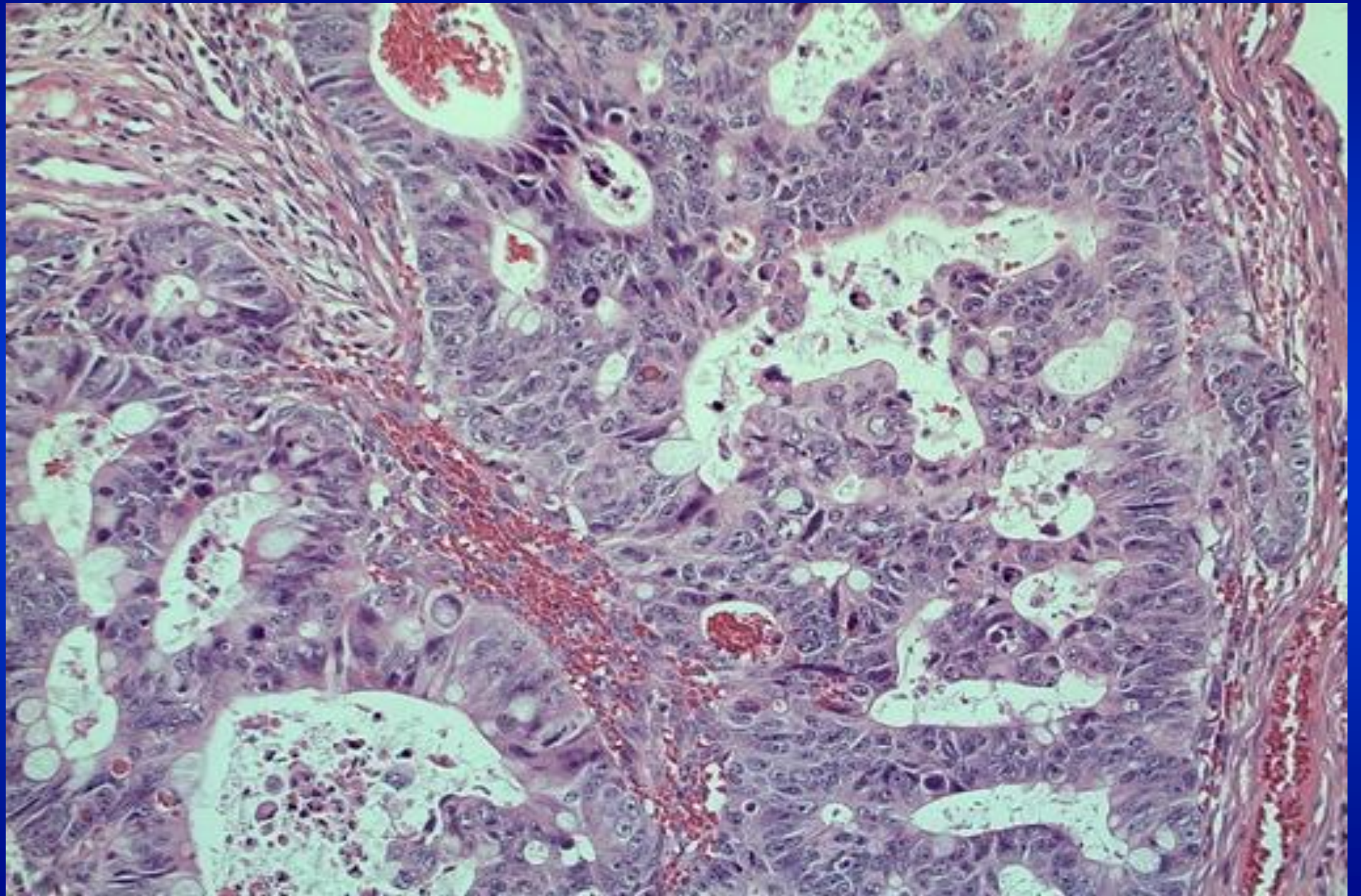
- **High and low grade (2 tier)**
  - **Urothelial carcinoma**
  - **Colon Cancer (AJCC, 7<sup>th</sup> edition): return to 4 tier system in AJCC, 8<sup>th</sup> edition**



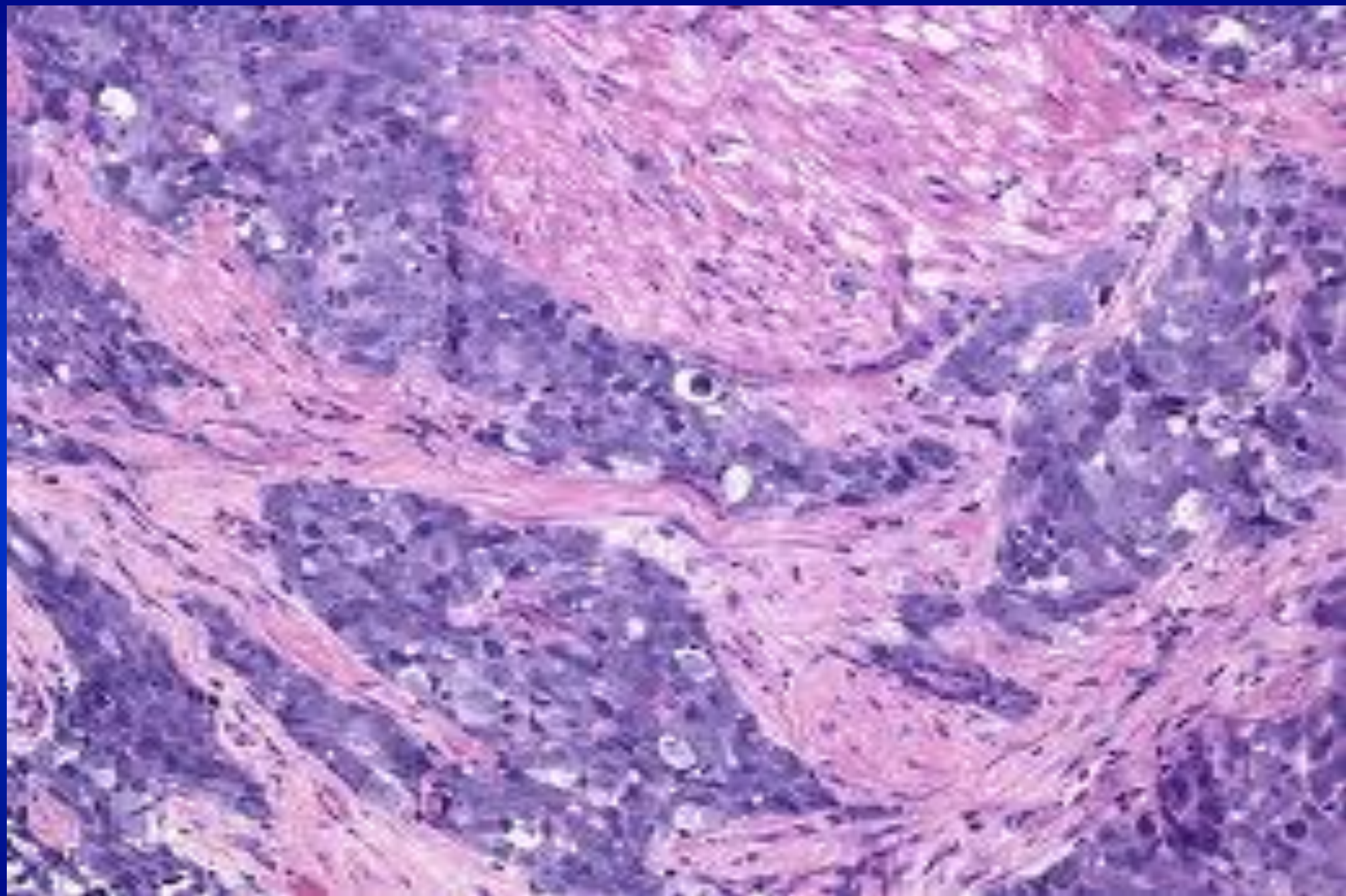
# Tumor Grade

- **Colon cancer (2010 7<sup>th</sup> ed, 2 tier: 2017 8<sup>th</sup> AJCC, back to 4-tier)**
- Low grade (G1, G2)/high grade (G3, G4)
- 4 tier grading system:
  - ✓ G1: Well differentiated
  - ✓ G2: Mod differentiated
  - ✓ G3: Poorly differentiated
  - ✓ G4: Undifferentiated carcinoma
- GX: Grade cannot be assessed



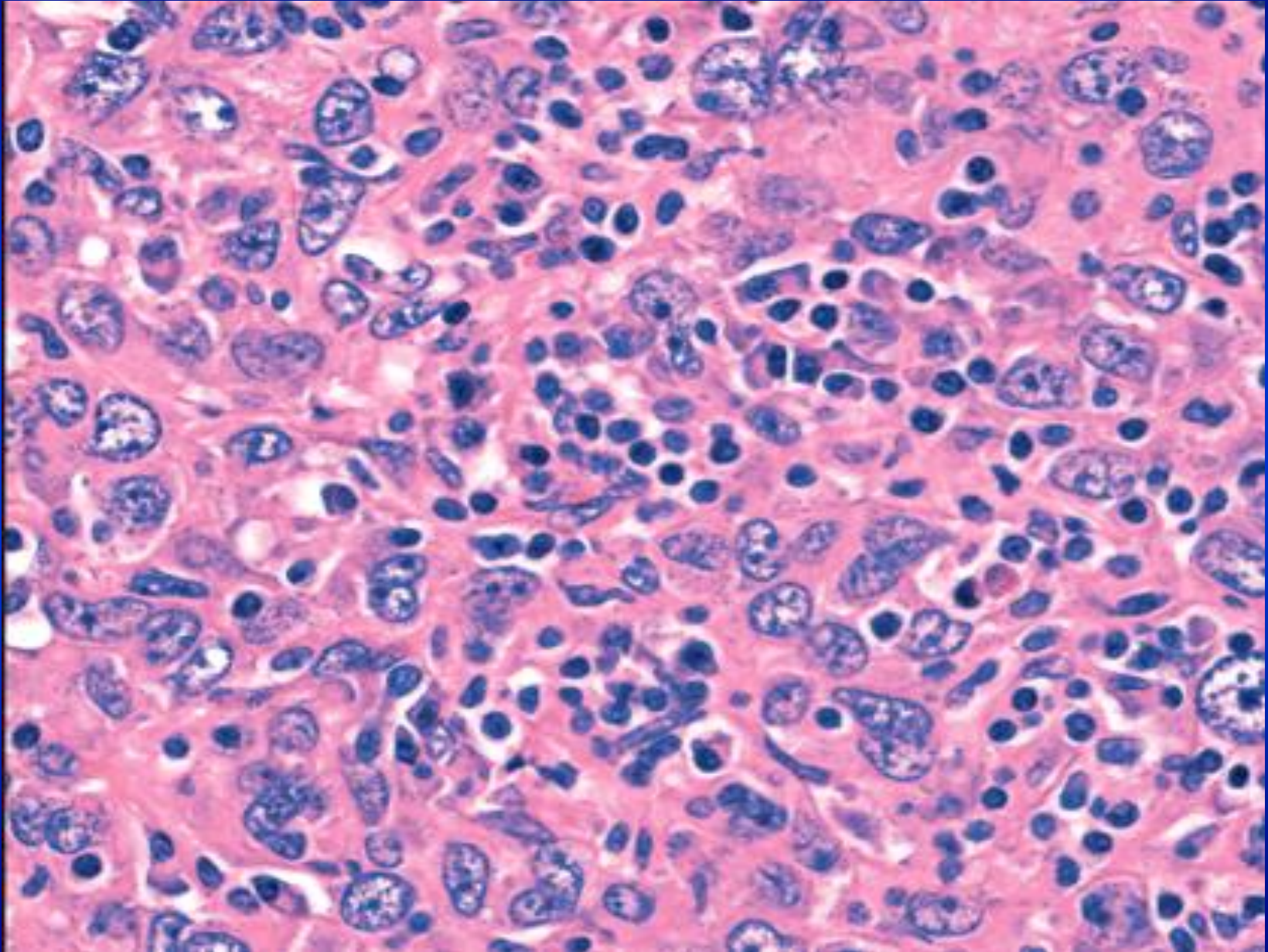




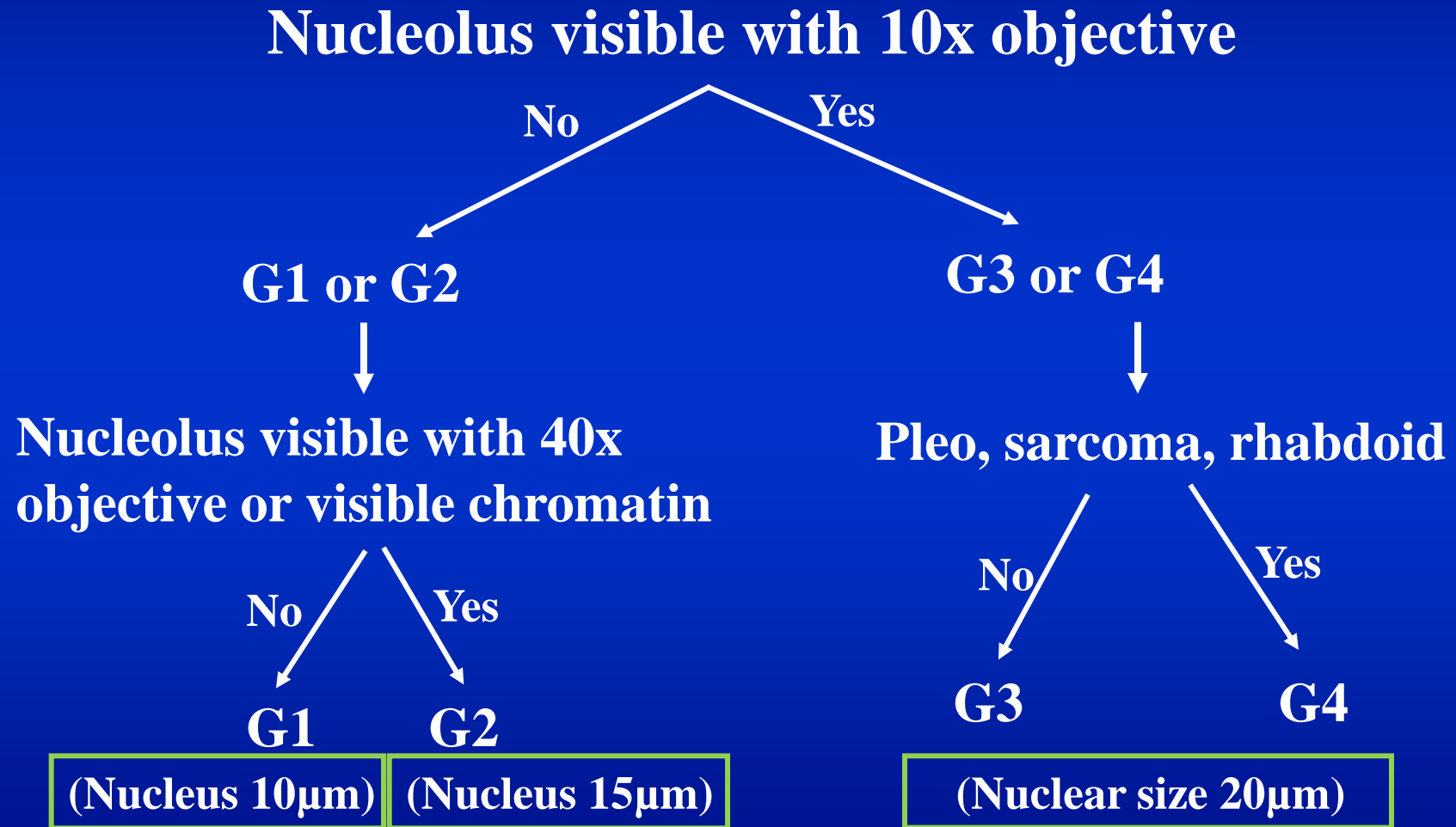




# Nuclear Grade

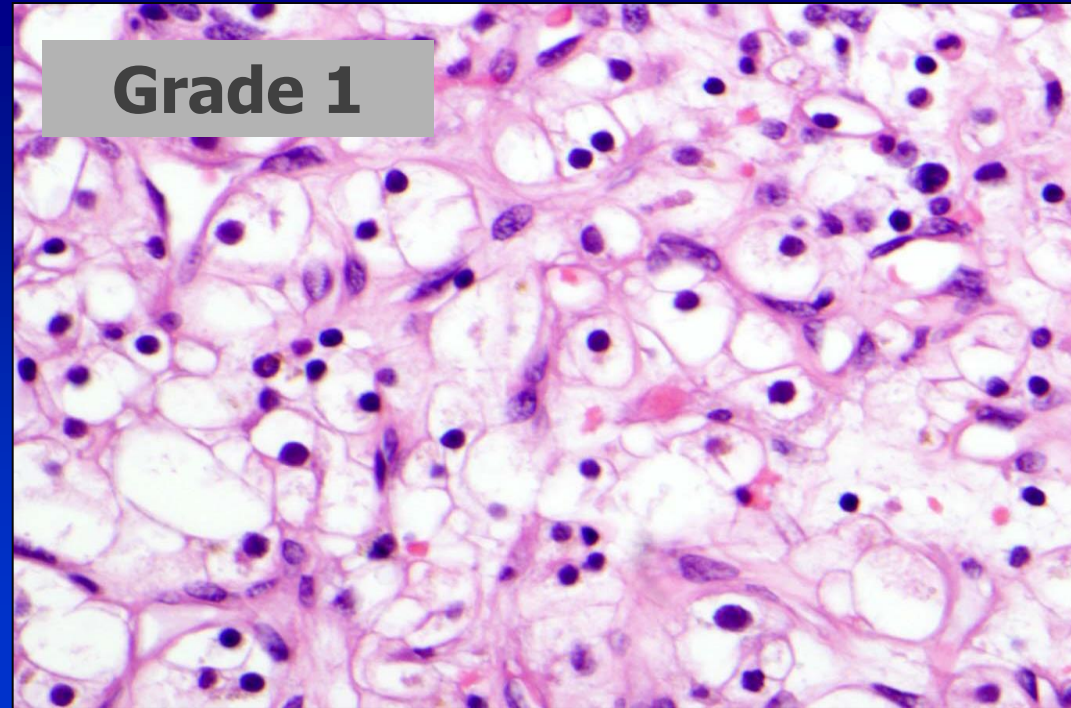


# WHO/ISUP (Fuhrman's) Nuclear Grade

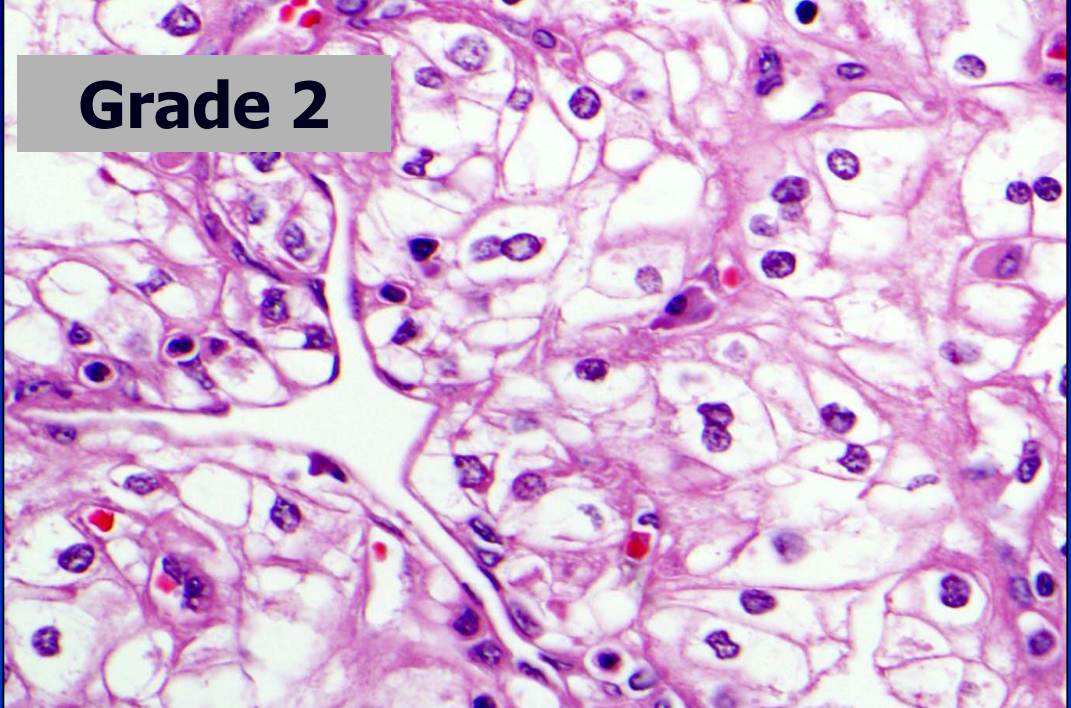




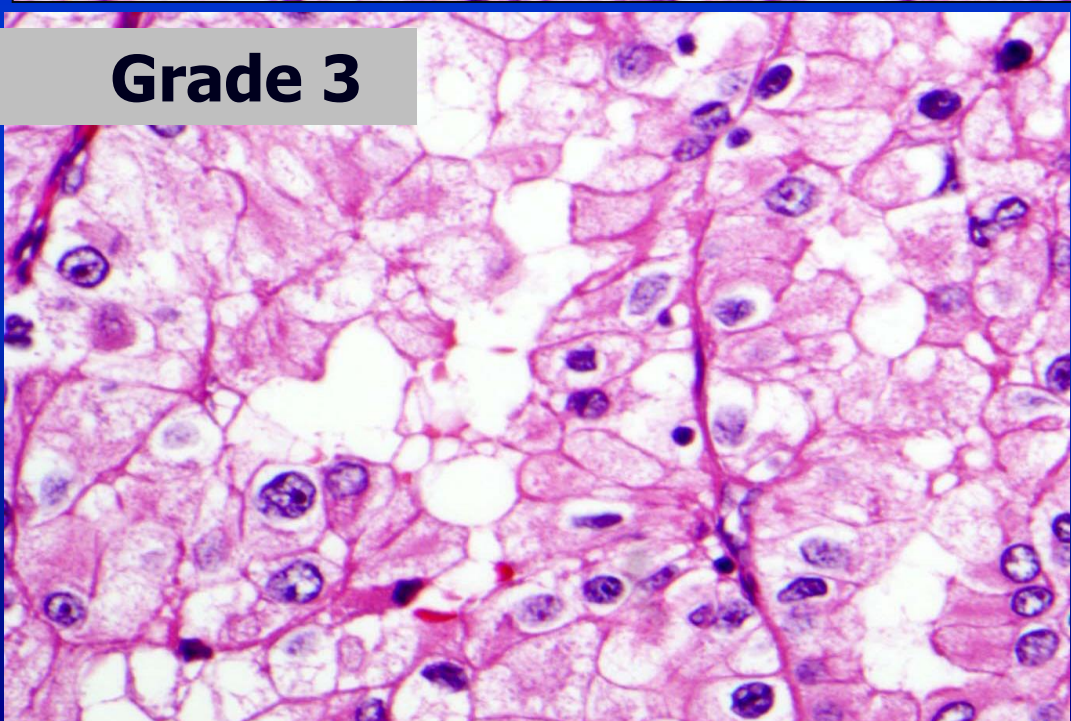
**Grade 1**



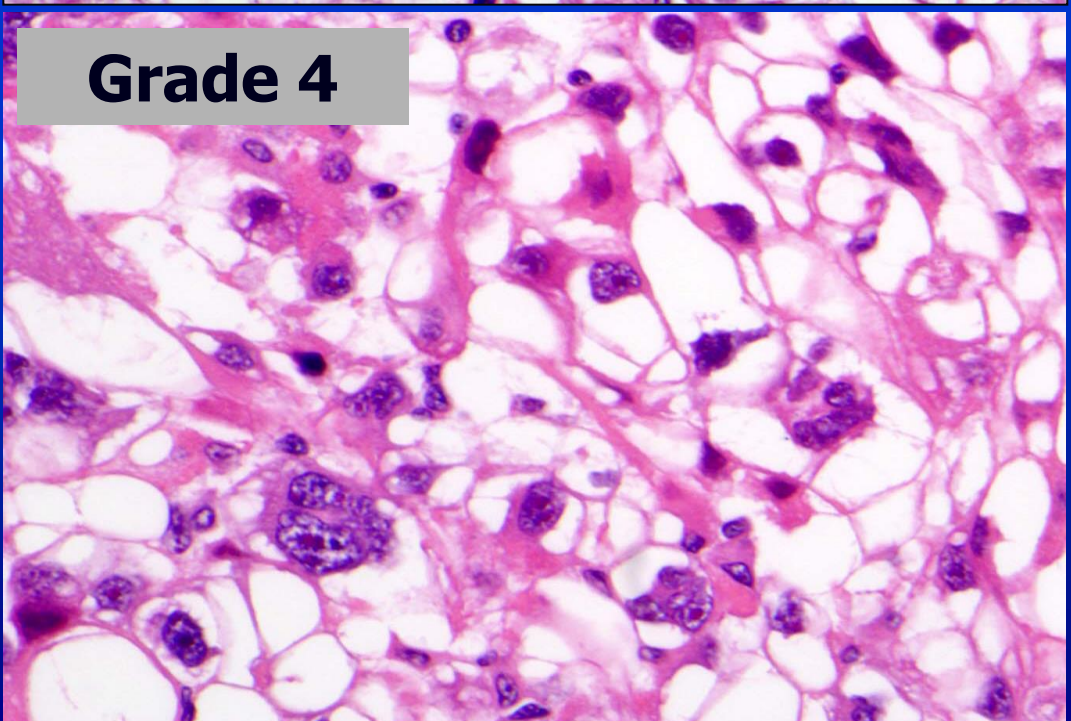
**Grade 2**



**Grade 3**



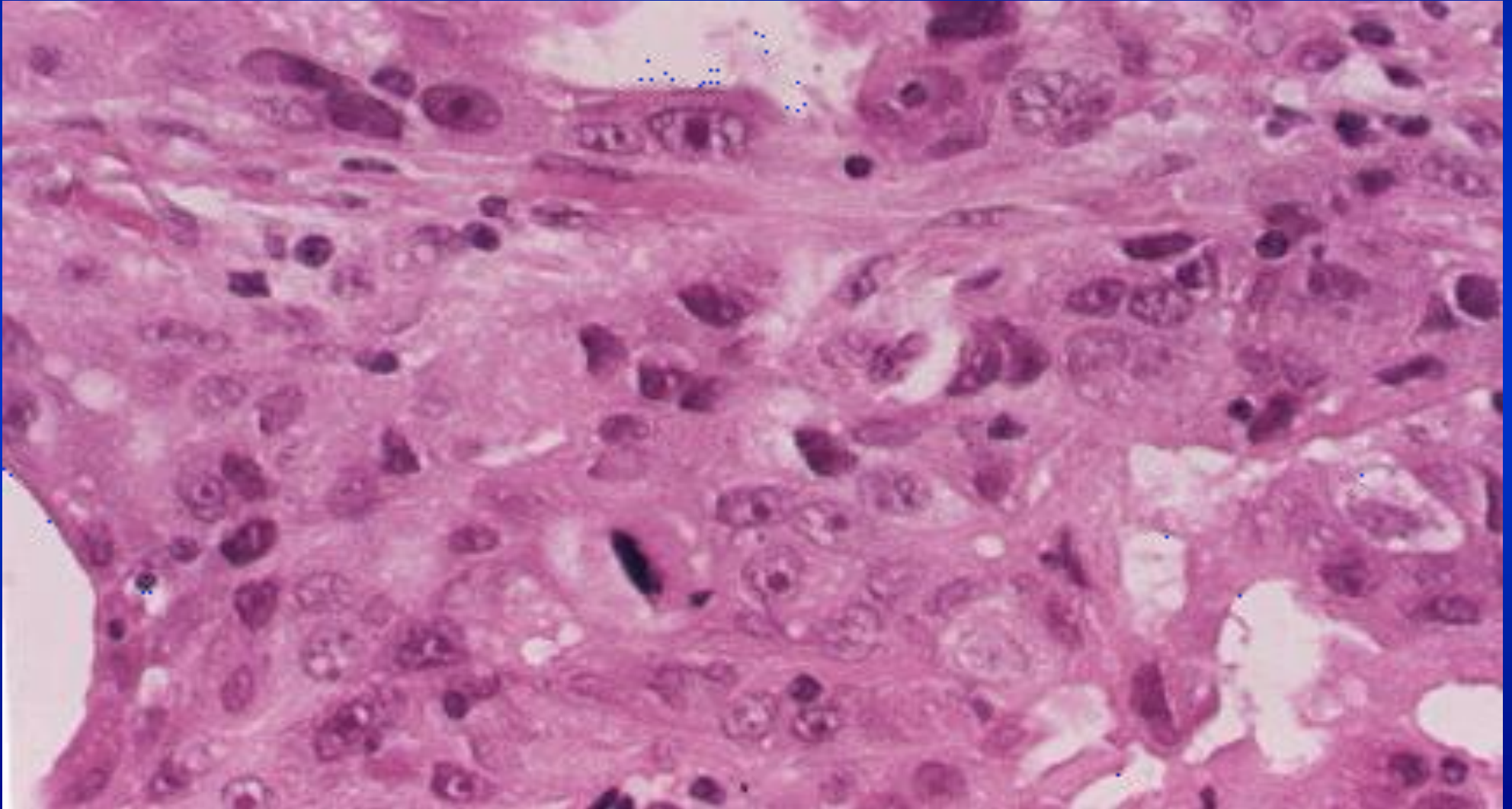
**Grade 4**





# Black Nuclear grade:

nuclear size, chromatin, nucleolus, pleomorphism, mitoses



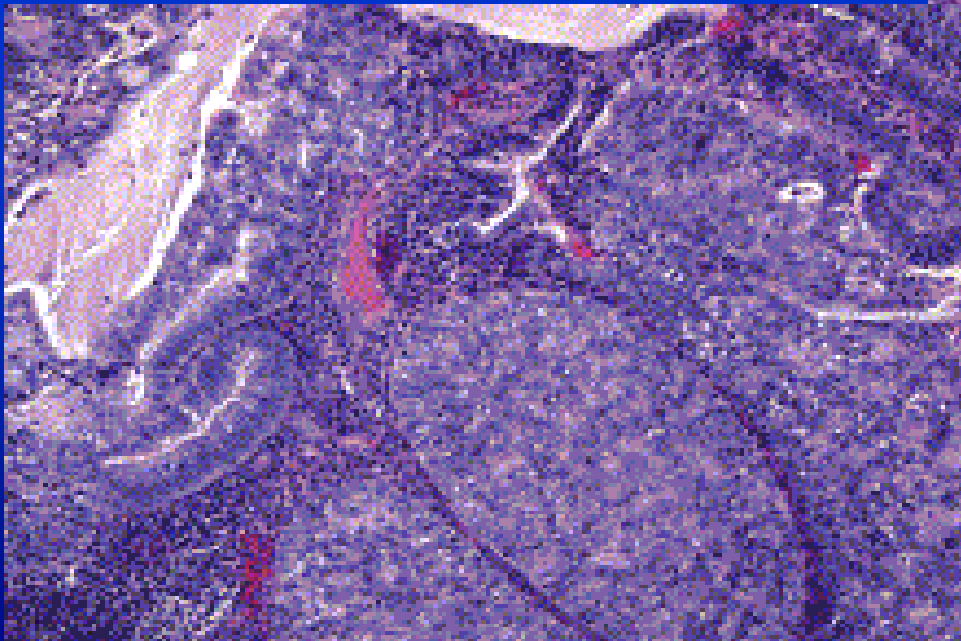
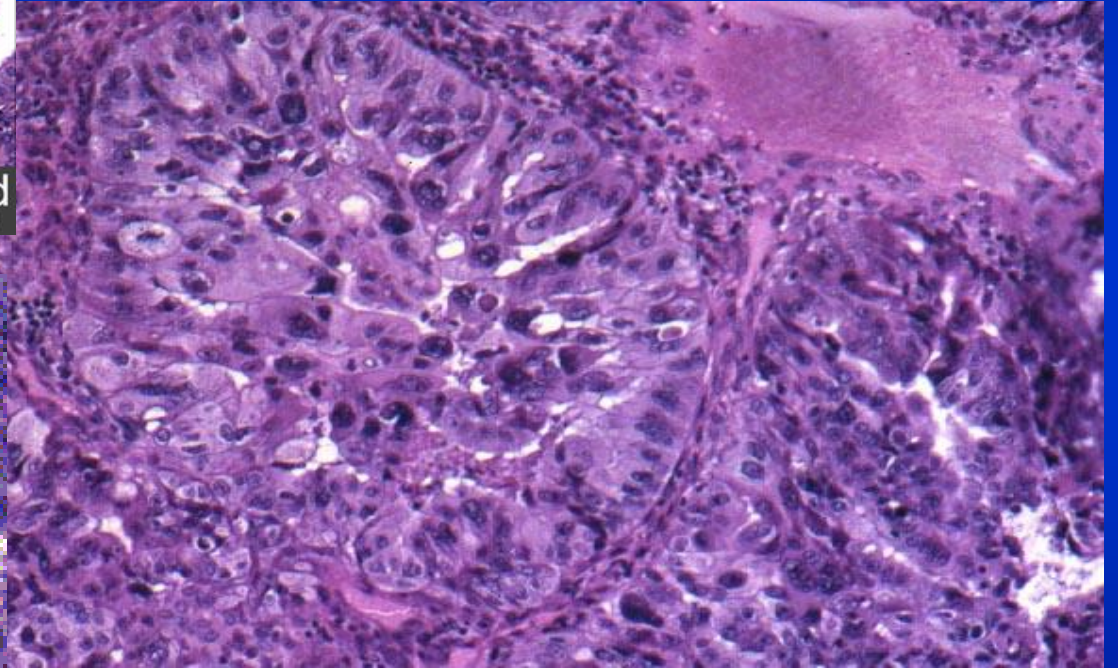
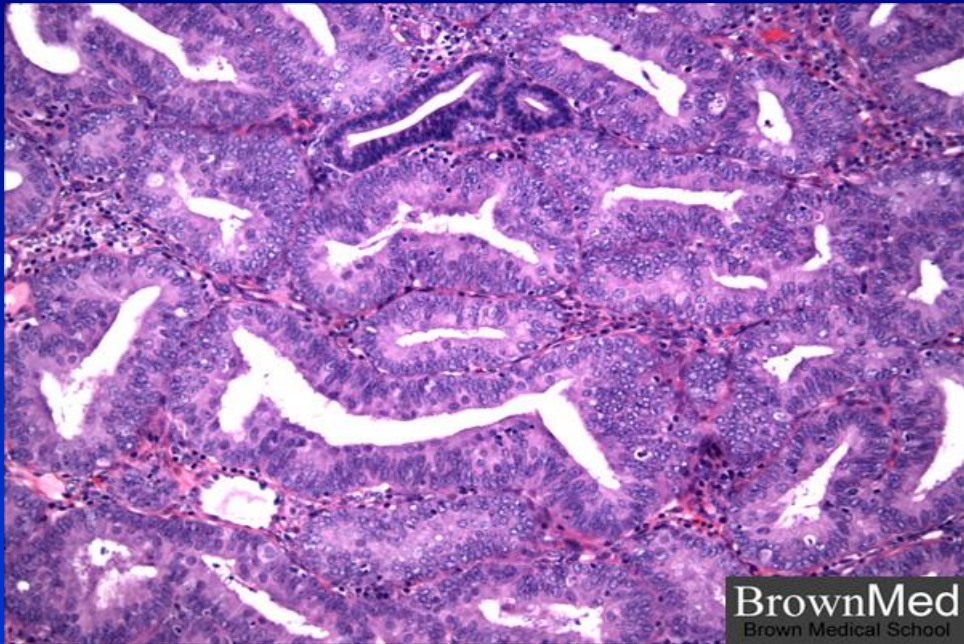
# Combined grade





# Combined grade

- **FIGO endometrial carcinoma**
  - **$\leq 5\%$  nonsquamous or nonmorular solid growth**
  - **6-50% nonsquamous or nonmorular solid growth**
  - **$> 50\%$  nonsquamous or nonmorular solid growth**
  - **One up grade based on nuclear features**
- **No grading for non-endometrioid carcinoma (type 2 cancers)**





AJCC  
American Joint Committee on Cancer

# AJCC Cancer Staging Manual

*Eighth Edition*


Copyright © 2010

**ajcc**

## Cancer Staging Handbook





*From the AJCC  
Cancer Staging  
Manual*

SEVENTH  
EDITION

 Springer

Copyright © 2010



<p><b>Tumor size</b></p> <p><b>T</b></p>	<p>Tumor size &lt; 2 cm</p>  <p><b>T1</b></p>	<p>Tumor size 2-5 cm</p>  <p><b>T2</b></p>	<p>Tumor size &gt; 5 cm</p>  <p><b>T3</b></p>	<p>Tumor extends to skin or chest wall</p>  <p><b>T4</b></p>
<p><b>Lymph Nodes</b></p> <p><b>N</b></p>	<p><b>N0</b></p> <p>No lymph node metastasis</p>	<p><b>N1</b></p> <p>Metastasis to ipsilateral, movable, axillary LNs</p>	<p><b>N2</b></p> <p>Metastasis to ipsilateral fixed axillary, or IM LNs</p>	<p><b>N3</b></p> <p>Metastasis to infraclavicular/supraclavicular LN, or to axillary and IM LNs</p>
<p><b>Metastasis</b></p> <p><b>M</b></p>	<p><b>M0</b></p> <p>No distant metastasis</p>	<p><b>M1</b></p> <p>Distant metastasis</p>	<p><b>احسن اونکولوجیست</b></p> <p><a href="http://www.TheBestOncologist.com">www.TheBestOncologist.com</a></p> <p>© The Best Oncologist™</p> <p>LN= Lymph Nodes; IM= Internal Mammary</p>	

# Staging System

- **AJCC (American Joint Committee on Cancer)**
- **UICC (International Union Against cancer)**
- **Dukes, Jewett/Whitmore, Ann Arbor systems, FIGO staging**



# AJCC Cancer Staging

- **AJCC has become the standard for TNM information and the way cancer is communicated worldwide**
  - ✓ **Validating**
  - ✓ **Revising**
  - ✓ **Restructuring**
  - ✓ **Publishing**
  
- **Widely used by Clinicians**
  - ✓ **Surveillance community & tumor registrars**
  - ✓ **Researchers**
  - ✓ **Patient advocates**
  - ✓ **Patients**

# AJCC Cancer Staging (Roles)

- **Communication**  
*Standardized nomenclature of cancer*
- **Clinical practice**  
*Staging & prognosis*  
*Treatment recommendations*
- **Clinical trials**  
*Eligibility and Stratification*
- **Research at all levels**
- **Reporting – population science**  
*Longitudinal cancer instance*  
*Changing spectrum of disease*  
*Efficacy of treatment*  
*Quality of care*

# TNM Stages

- AJCC first organized in 1959 (c UICC)
- T, N, M: 1<sup>st</sup> edition in 1977 (7<sup>th</sup> ed., 2009):  
revision cycle 6-8 yrs
- Non-anatomical factors integrated (7<sup>th</sup>, 2010)
  - ✓ Histologic grade (prostate, soft tissue, etc)
  - ✓ Serum tumor markers (testis)
  - ✓ Age (thyroid cancer)
  - ✓ Biologic markers, genetic mutations
- WHO blue book, AFIP fascicles
- ICD10, ICD-O3 and SNOMED
- No acceptable TNM staging for CNS, lymphoma, and pediatric tumors



# TNM Stages, 8<sup>th</sup> edition

- No acceptable TNM staging for CNS, lymphoma/leukemia, and pediatric tumors (included in staging book, except for pediatric tumors)
- GU split (Male genital, part XIII; Urinary system, part XIV)
- Digestive system split (upper, part III, lower, part IV and hepatobiliary and exocrine pancreas, part V)
- Neuroendocrine tumor, added as new part (part VI)
- Endocrine added (part XVII)
- Bone and soft tissue sarcoma split (part VIII and IX)
- Lymphoid neoplasms, renamed as hematologic malignancies, leukemia included (part XVIII)

# Changes for 8<sup>th</sup> Edition

- New features

- Levels of Evidence → **Level I-IV**
- Imaging section
- Risk Assessment Models for select cancer sites
- Recommendations for Clinical Trial Stratification
- Prognostic factors
  - Required for prognostic stage grouping
  - Recommended for clinical care
  - Emerging factors



# Examples of AJCC level of evidence

## ➤ Prostate Cancer

- Level I: PSA, Grade group/Gleason score  
**(Integrated in AJCC Prognostic stage groups)**
- Level II: Surgical margin status
- Level III: Histologic types

## ➤ Testis Tumor

- Level I: Serum tumor markers, LVI, International germ cell classification grouping  
(serum tumor markers, visceral met, mediastinal location)



# AJCC Prognostic Stage Groups

<b>T</b>	<b>N</b>	<b>M</b>	<b>PSA</b>	<b>Grade Group</b>	<b>Stage group</b>
cT1a-c	N0	M0	< 10	1	I
cT2a					
pT2	N0	M0	< 10	1	I
cT1-c	N0	M0	≥ 10 < 20	1	IIA
cT2a					
cT2b-c	N0	M0	< 20	1	IIA
T1-2	N0	M0	< 20	2	IIB
T1-2	N0	M0	< 20	3	IIC
T1-2	N0	M0	< 20	4	IIC
T1-2	N0	M0	≥ 20	1-4	IIIA
T3-4	N0	M0	Any	1-4	IIIB
Any T	N0	M0	Any	5	IIIC
Any T	N1	M0	Any	Any	IVA
Any T	N0	M1	Any	Any	IVB

# AJCC prognostic stage groups

Group	T	N	M	S (Serum Tumor Markers)
Stage 0	pTis	N0	M0	S0
Stage I	pT1-4	N0	M0	SX
Stage IA	pT1	N0	M0	S0
Stage IB	pT2	N0	M0	S0
	pT3	N0	M0	S0
	pT4	N0	M0	S0
Stage IS	Any pT/Tx	N0	M0	S1-3 (measured post orchiectomy)

# AJCC Prognostic Stage Groups

<b>Stage II</b>	<b>Any pT/Tx</b>	<b>N1-3</b>	<b>M0</b>	<b>SX</b>
<b>Stage IIA</b>	<b>Any pT/Tx</b>	<b>N1</b>	<b>M0</b>	<b>S0</b>
	<b>Any pT/Tx</b>	<b>N1</b>	<b>M0</b>	<b>S1</b>
<b>Stage IIB</b>	<b>Any pT/Tx</b>	<b>N2</b>	<b>M0</b>	<b>S0</b>
	<b>Any pT/Tx</b>	<b>N2</b>	<b>M0</b>	<b>S1</b>
<b>Stage IIC</b>	<b>Any pT/Tx</b>	<b>N3</b>	<b>M0</b>	<b>S0</b>
	<b>Any pT/Tx</b>	<b>N3</b>	<b>M0</b>	<b>S1</b>



# AJCC Prognostic Stage Groups

Stage III	Any pT/Tx	Any N	M1	SX
Stage IIIA	Any pT/Tx	Any N	M1a	S0
	Any pT/Tx	Any N	M1a	S1
Stage IIIB	Any pT/Tx	N1-3	M0	S2
	Any pT/Tx	Any N	M1a	S2
Stage IIIC	Any pT/Tx	N1-3	M0	S3
	Any pT/Tx	Any N	M1a	S3
	Any pT/Tx	Any N	M1b	Any S

**\*\*\*Non-anatomic factors incorporated**

# Examples of AJCC level of evidence

## ➤ Kidney Cancer

- Level I: beyond T, N, M, no additional factors
- Level II: NG, sarcomatoid/rhabdoid histology, tumor necrosis, LVI

## ➤ Bladder Tumor

- Level I: beyond T, N, M, no additional factors
- Level II: Concurrent CIS, pT1 substages, total # of LNs, histologic types, margin status
- Level III: Extranodal extension, LVI

## ➤ Penile cancer

- Level I: beyond T, N, M, additional factors (Level I: tumor grade, LVI)
- Level II: Total # of LN removed
- Level III: PNI, size of largest LN metastasis

# AJCC Prognostic Stage Groups

## ➤ AJCC Anatomic (Prognostic) Stage Groups

- Only T, N, M with no other level I integrated

## ➤ AJCC Prognostic Stage Groups

- Penile cancer (level I prognostic factors)
- ✓ Differentiation
- ✓ LVI
- But only T, N, M
- Why?
- T1a vs T1b (based on diff, and LVI, **PNI, level of evidence III**)



# Breast Stage Grouping

## ➤ AJCC Anatomic Stage Groups

- Only T, N, M with no other level I integrated

## ➤ AJCC Prognostic Stage Groups

- T, N, M and
- ER and PR status
- Her2/neu
- Histologic grade (Scarff-Bloom-Richardson System- Nottingham Modification)
- Oncotype Dx

# Changes for 8<sup>th</sup> Edition

- New paradigms

- HPV (oropharyngeal ca staging systems based on HPV status)

- (Under Part II H&N; chapter 10, p16+; chapter 11, p16-)**

- Separate staging system for patients with neoadjuvant therapy (*yc* or *yp* systems)

- Esophagus and Stomach

- Bone and Soft Tissue Sarcoma **(part VIII and IX)**

- Separate staging systems based on anatomic sites (in bone and soft tissue sarcomas)



# Changes for 8<sup>th</sup> Edition

- New chapters/staging systems

- Cervical Lymph Nodes and Unknown Primary Tumors of the Head and Neck **(Part II, Ch 6)**
- Pharynx - HPV-Mediated Oropharynx Cancer (p16+) **Ch 10; p16-, Ch 11**
- Cutaneous Squamous Cell Carcinoma of the Head and Neck **(chapter 15)**
- Thymus **(Part VII, under thorax, chapter 35)**
- Bone: Appendicular Skeleton/Trunk/Skull/Face, Pelvis, and Spine **Part VIII**
- Soft Tissue Sarcoma of the Head and Neck **Ch40**
- Soft Tissue Sarcoma of the Trunk and Extremities **Ch 41**
- Soft Tissue Sarcoma of the Abdomen and Thoracic Visceral Organs **Ch 42**
- Soft Tissue Sarcoma of the Retroperitoneum **Ch 44**
- Soft Tissue Sarcoma – Unusual Histologies and Sites **Ch 45**
- Parathyroid **Part XVII, under Endocrine, Ch 75**
- Leukemia **Part XVIII, Hematologic malignancy, Ch 83**



**\*\*\*GIST, Ch 43**





# Changes for 8<sup>th</sup> Edition

- Split chapters

- p16 negative oropharynx and hypopharynx (previously pharynx)
- Nasopharynx (previously pharynx) **Ch 9**
- Pancreas – exocrine (previously endocrine/exocrine pancreas) **Pa V, Ch 28**
- Pancreas – endocrine (previously endocrine/exocrine pancreas)
- Neuroendocrine Tumors of the Stomach **Ch 29**
- Neuroendocrine Tumors of the Duodenum and Ampulla of Vater **Ch 30**
- Neuroendocrine Tumors of the Jejunum and Ileum **Ch 31**
- Neuroendocrine Tumors of the Appendix **Ch 32**
- Neuroendocrine Tumors of the Colon and Rectum **Ch 33**
- Neuroendocrine Tumors of the Pancreas **Ch 34**
- Thyroid – Differentiated and Anaplastic **Ch 73**
- Thyroid – Medullary **Ch 74**
- Adrenal Cortical Carcinoma **Ch 76**
- Adrenal – Neuroendocrine **Ch 77**

**Part  
VI**

**Part  
XII**



# Changes for 8<sup>th</sup> Edition

- Merged chapters
  - Ovary, Fallopian Tube, and Primary Peritoneal Carcinoma **Pa XII, Ch 55**  
In 7<sup>th</sup> ed: Ovary and primary peritoneal **Pa VIII, Ch 37**  
Fallopian tube separately **Pa VIII, Ch 38**
- Deleted chapters
  - Cutaneous Squamous Cell Carcinoma and Other Cutaneous Carcinomas
    - See cutaneous carcinoma of the head and neck



# Summary

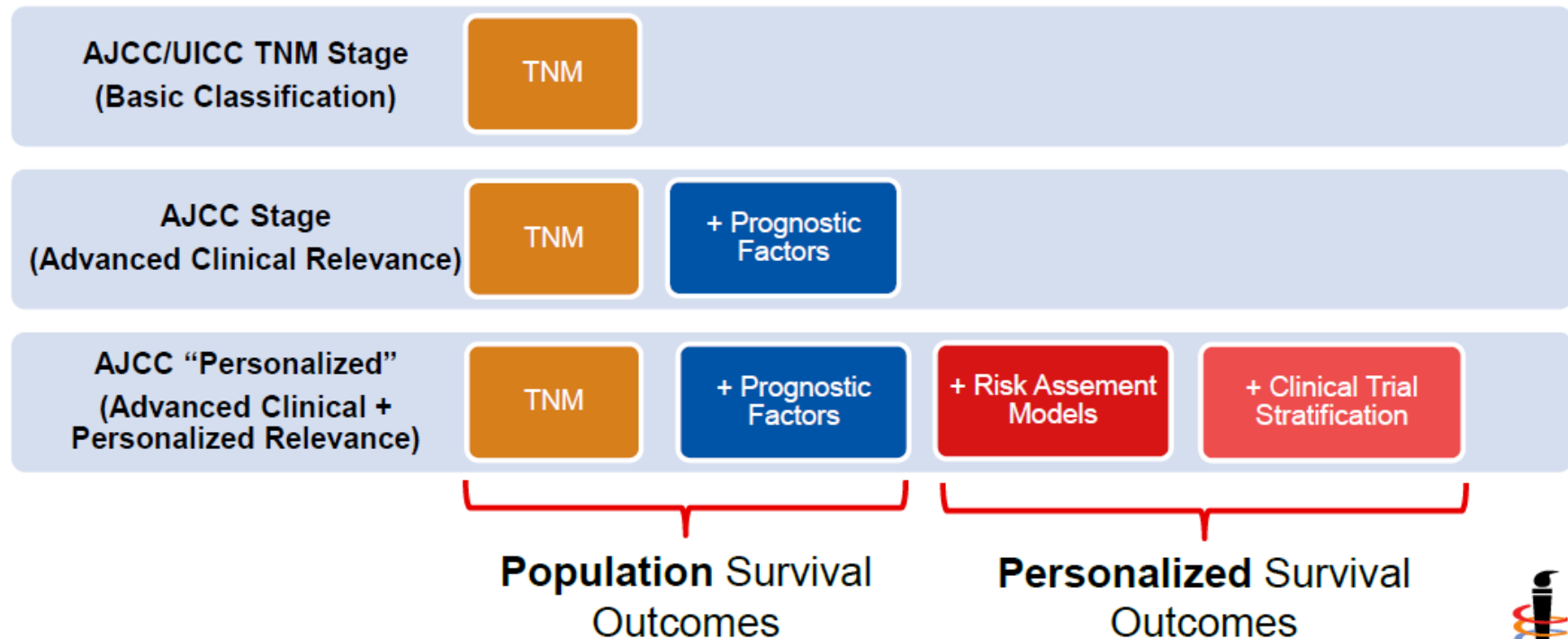
- 8<sup>th</sup> edition is a significant step forward
- Education planned for physicians and registrars
- Significant disease site changes will be communicated
- AJCC Web site will provide a roadmap for information on 8<sup>th</sup> edition
- Congratulations to Cancer Registrars on 8<sup>th</sup> edition dedication





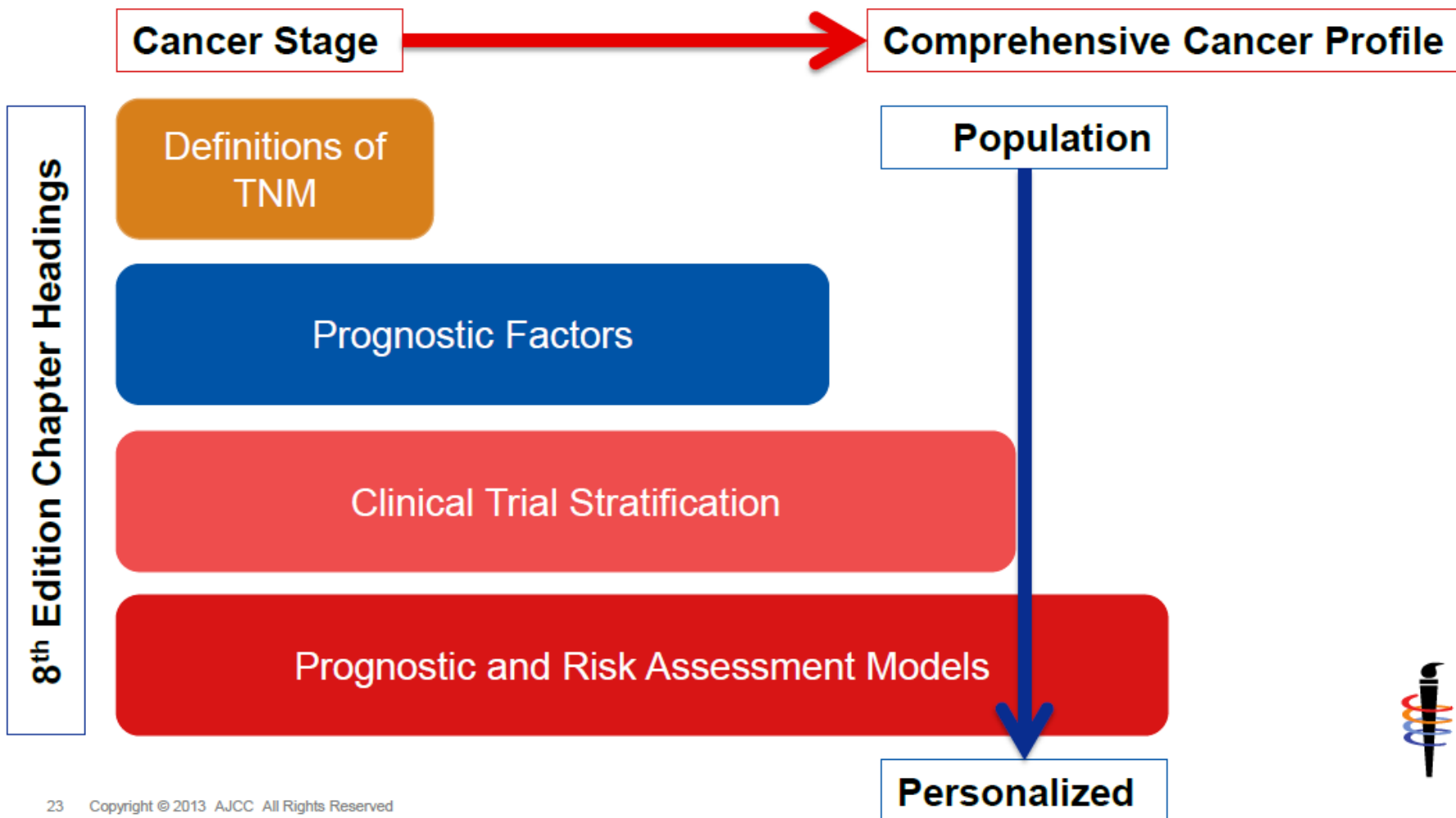
# AJCC Vision

## The Transition from Population Based to a more “Personalized” Approach



# AJCC Vision

...and Where It Fits in the 8<sup>th</sup> Edition:



# AJCC Cancer Staging Manual Editions: revision cycle 6-8 years

<u>Edition</u>	<u>Publication</u>	<u>dates effective for Dx</u>
1	1977	1978- 1983
2	1983	1984- 1988
3	1988	1989- 1992
4	1992	1993- 1997
5	1997	1998- 2002
6	2002	2003- 2009
7	2009	2010- 2017
8	2016	2017, postponed to 2018

# AJCC Cancer Staging Manual editions

Edition	Publication	Effective dates for cancer diagnoses
1 <sup>st</sup>	1977	1978 - 1983
2 <sup>nd</sup>	1983	1984 - 1988
3 <sup>rd</sup>	1988	1989 - 1992
4 <sup>th</sup>	1992	1993 - 1997
5 <sup>th</sup>	1997	1998 - 2002
6 <sup>th</sup>	2002	2003 - 2009
7 <sup>th</sup>	2009	2010 - 2016
8 <sup>th</sup>	2016	2017 -





# TNM revision

- Periodically modified in response to newly acquired clinical/pathological data and improved understanding of cancer biology and factors affecting prognosis
- Makes TNM system most clinically useful staging system and accounts for use worldwide
- To avoid difficulty to compare outcome of current and past, makes revision carefully and only based on best possible evidence

# TNM Stages

- Define prognosis
- Determining appropriate treatment
- Evaluate the results of treatment and clinical trials
- Serve as a basis for clinical and translational cancer research
- Facilitate exchange and comparison of information among treatment centers
- ✓ **cTNM, pTNM, yTNM (rTNM, aTNM)**

# Staging Classification

<u>Classification</u>	<u>Data source</u>	<u>Usage</u>
cTNM	symptoms, PE, image endoscopy, bx 1 <sup>st</sup> site, single/sentinel LN <u>c</u> cT	Define prog Initial Rx
	Surg explo s resection	<u>Popu comp</u>
pTNM	Surgical resection & pathology	Precise prog <u>Subseq Rx</u>
yc/ypTNM	systemic chemo/XRT before surg or other Rx	Resp to RX <u>Subseq Rx</u>
<u>rTNM</u>	<u>Retreatment for recur</u>	<u>Define Rx</u>
aTNM	Determine at autopsy	Identify at A

# TNM staging

- Clinical staging: extent of cancer before initiation of definitive treatment or **within 4 months after the date of diagnosis**
  - ✓ Essential to select therapy
  - ✓ Critical for comparison of different groups of cases (surgery, neoadjuvant chemo, no Rx)
- Pathologic staging: after completion of definitive surgery as part of first course of treatment or **within 4 months after diagnosis**
- Post treatment (y): tumor regression grade
  - ✓ Recurrent/retreatment (r) and autopsy (a)



# TNM Classification

T (tumor), N (node) & M (metastasis)

Primary tumor (T)

**TX** Primary tumor cannot be assessed

**T0** No evidence of primary tumor

**Tis** Carcinoma in situ

**T1-T4** Increasing size and/or local extent  
(depth of invasion) of tumor

**T4a (resectable/moderately advanced)**  
and **T4b (unresectable/very advanced)**

## Sixth edition

- 1 - Epithelium
- 2 - Subepithelial connective tissue
- 3 - Muscle
- 4 - Perivesical fat

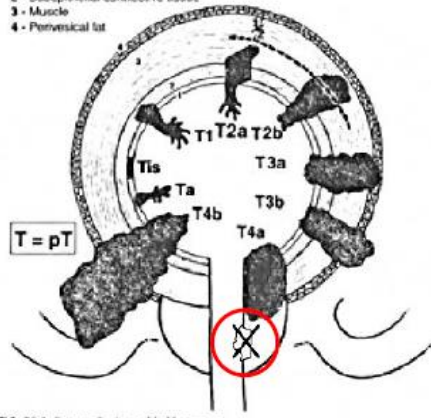


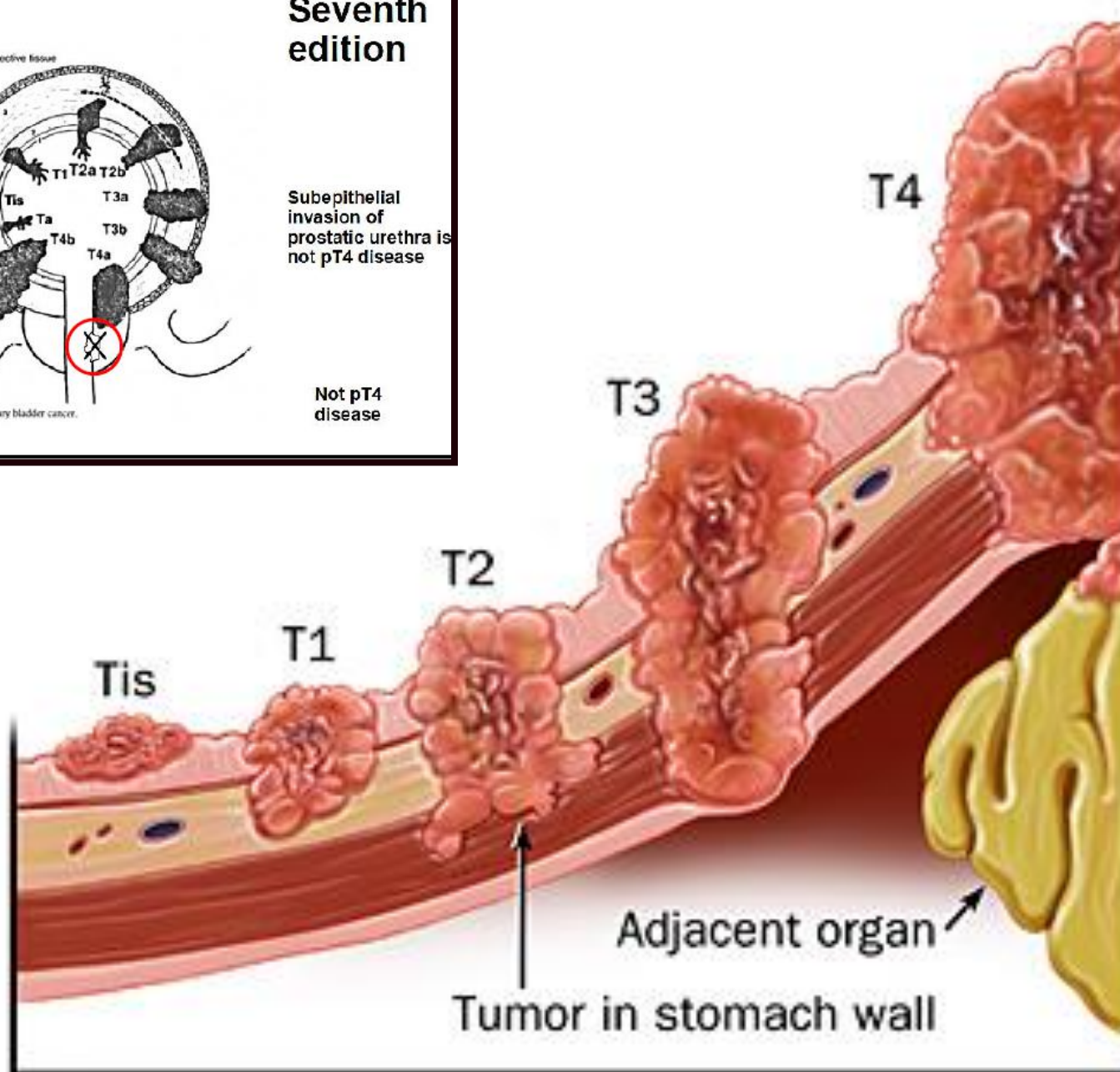
FIG. 36.1. Extent of primary bladder cancer.

T4: tumor invades prostate, uterus, and vagina

## Seventh edition

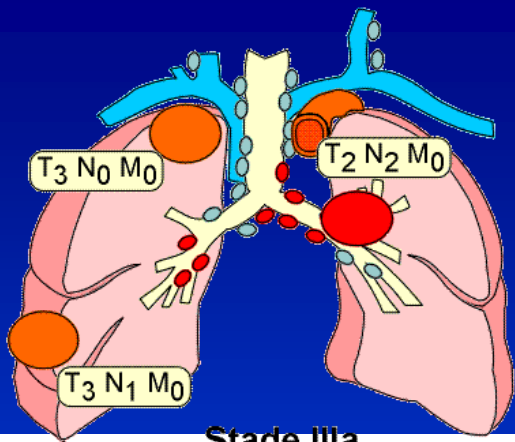
Subepithelial invasion of prostatic urethra is not pT4 disease

Not pT4 disease

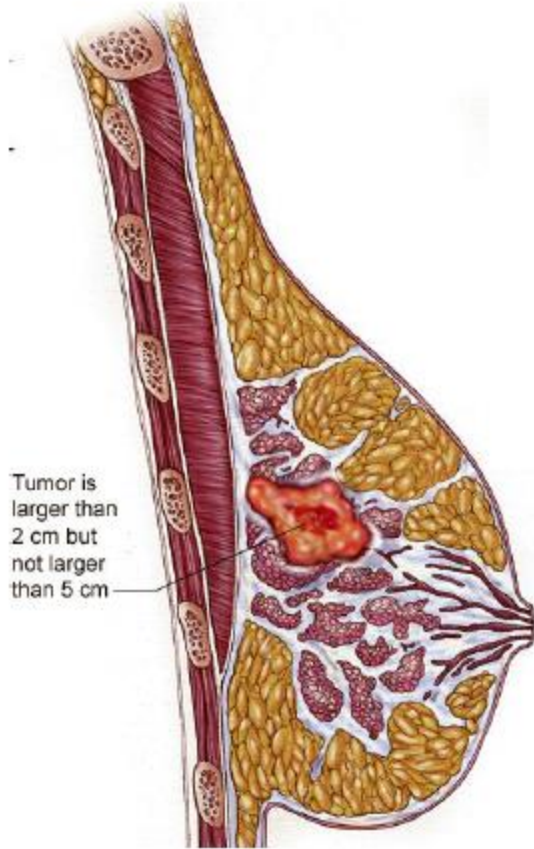


Tumor in stomach wall

Adjacent organ



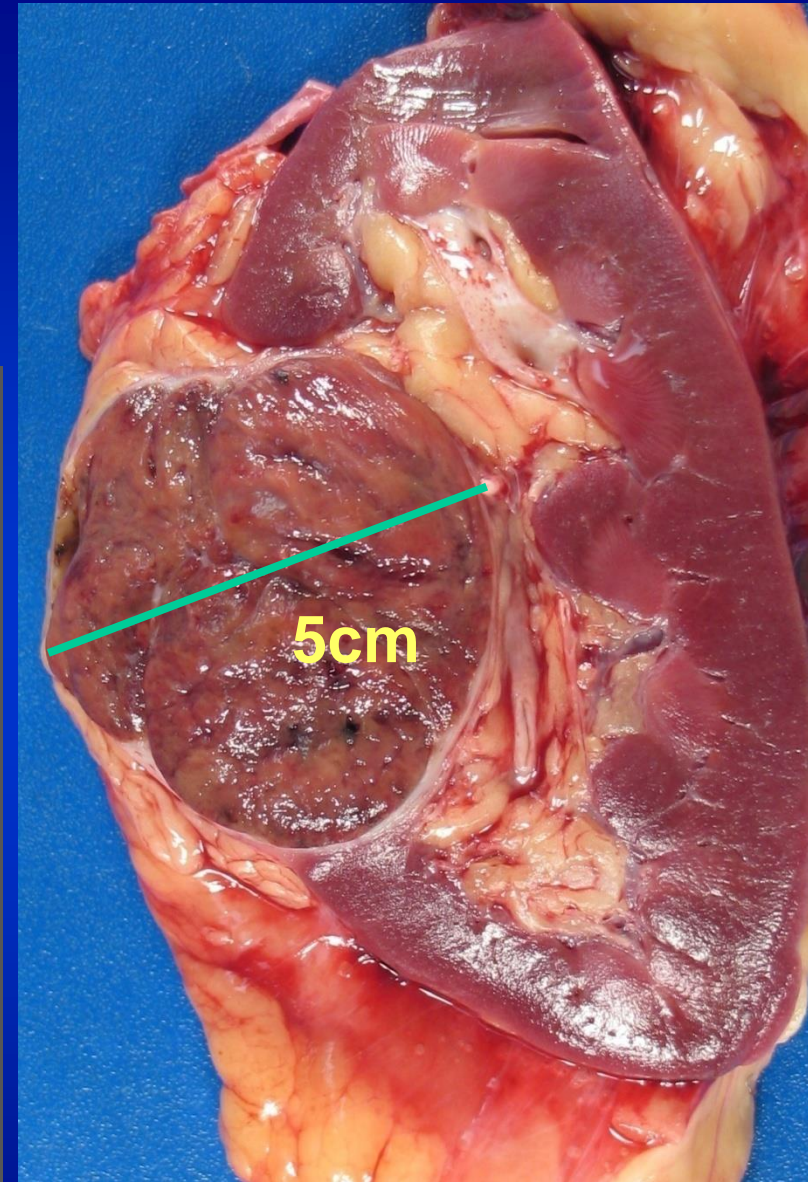
Stade IIIa



Tumor is larger than 2 cm but not larger than 5 cm

**T2**

Tumor more than 2 cm but not more than 5 cm in greatest dimension





# T Classification Rules

- Site specific rule based on size/local extension (solid vs. hollow viscus)
- Clinical assessment (cT) based on physical exam, image, endoscopy, **biopsy**, surgical exploration with no resection
- Pathologic assessment (pT), resection or **biopsy** if it assigns the highest T category
- > 1 specimens, estimate size/local extension
- Tumor size as whole mm c round up (e.g., 1.2mm - 1mm; 1.7mm - 2mm)
- **LVI in T system in 3 organs (liver, testis, penis)**



# TNM Classification

## Regional lymph nodes (N)

**NX** Regional LNs cannot be assessed

**N0** No regional LN metastasis

**N1-N3** Number, size, location of regional LNs involvement

**\*** Direct extension of tumor into a LN classified as a LN metastasis

**\*\*** Met in other than regional LNs classified as “Met (M1)”

**\*\*\*** Satellites/ in-transit metastases (Melanoma/Merkel)

**\*\*\*\*** TD in subserosa, mesentery, nonperitonealized pericolic/perirectal tissue without LN met (N1c)  
(discontinuous spread, VI c extravascular, or replaced LN)

## Distant metastasis (M)

**MX** no MX in 7<sup>th</sup> and 8<sup>th</sup> editions:

**M0** No distant metastasis (no pM0)

**M1** Distant metastasis (M1a, M1b, M1c)

# N Classification rule

- Disease specific rule based on number and location, size of tumor met (not size of LN), and ENE
- Minimum expected # of LNs ( $\geq 12$ ); LN surgery performed, classify as pN even minimum # not examined
- Sentinel LN, pN0 (sn), pN1 (sn): up to 5 LN
- ITC only, pN0 (i+, or mol+);  $\leq 0.2\text{mm}$ ,  $\leq 200$  cells
- ✓ **Melanoma sentinel node exception**

# M Classification Rules

- Clinical M (cM), only history and exam, not require imaging of distant organs
- MX not valid category
- **pM1 requires positive biopsy**: biopsy negative on suspected met, cM0, not pM0
- pM1 regardless **clinical or pathologic** status, stage IV
- ITC (CTCs, DTCs) in bone marrow, cM0(i+)

# General Rules for TNM Stages

- Tumor size: 1.2mm - 1mm; 1.7mm - 2mm  
e.g.: 1.47 cm--1.5 cm; 2.43 cm—2.4 cm
- No met in LNs, even number of examined LNs less than suggested—classify **pN0**
- **Isolated tumor cells (ITC)**: single tumor cells or clusters  $\leq 0.2$  mm in LN or distant sites—classify N0, M0 (also for flow or DNA detected cells ) (e,g,,  $\leq 200$  cells): **pN0 (i+, or mol+)**
- **MX category eliminated** (dropped M component from pathology template): **no pM0**



# General Rules of TNM Stages

- All cases should be confirmed microscopically: in rare cases with no pathologic diagnosis—analyzed separately, **not included in overall disease survival analysis**
- Five classification:
  - Clinical: cTNM, TNM (for primary Rx)
  - Pathological: pTNM (for adjuvant Rx, estimation of prognosis, end result)
  - Restage after treatment: yTNM (ycTNM or ypTNM)
  - Recurrent (retreatment) tumor: rTNM (recur after disease free)
  - Autopsy: aTNM (found at autopsy)

# General Rules for TNM Stages

- Multiple synchronous tumors (**met excluded**): tumor with highest T category – T (m) or T (5)
- Metachronous tumor: new TNM (**not y or r**)
- Bilateral or multiple organs tumor: separate as independent tumors
- Unknown 1<sup>st</sup> :**e.g., +axillary LN (T0N1M0)\*, consider as breast cancer**
- If uncertainty present (N1 vs. N2), non-anatomic factor (Gleason), use lower value
- **Pure unknown primary: TXN1M0 or TXN0M1**

# General Rules for TNM Stages

- Specified type of grading, 2 tier, 3 or 4 tier
- Histologic grade
  - GX grade cannot be assessed
  - G1 well diff; G2 mod diff
  - G3 poorly diff: G4 undifferentiated
- 3 tier: G1, G2 and G3-G4 (grade together)
- 2 tier: high and low grade (in 7<sup>th</sup> ed, colon ca)
- Urothelial ca, prostate, breast (own grading sys)
- No grading: thyroid, eyelids, testis, melanoma
- By definition grade 4: small cell ca, LCC of lung, Ewing sarcoma, rhabdomyosarcoma

# General Rules for TNM Stages

- **Lymph-vascular invasion (LVI)**
  - **Lymphatic invasion**
  - **Vascular invasion**
  - **Lymph-vascular invasion**
- **Residual tumor (R): RX, R0, R1 (micro), R2 (macro)**
- **Margins: negative, micro, macro, not assessed**



# Perineural invasion

## **Pn**

- **PnX**
- **Pn0**
- **Pn1**

## **Perineural invasion**

**Perineural invasion cannot  
be assessed**

**No perineural invasion**

**Perineural invasion present**

# Stage grouping

- Separate clinical, pathologic group (c, pTNM)
- ✓ may combine as “working” stage
- Avoid and minimize TX, NX (unstageable), except for TX or NX with M1 (stage IV)
- Non-anatomic factors missing---use lowest category (e.g., markers, Gleason grading)
- pT, pN, cM0 or cM1 (pathologic stage group)
- cT, cN, pM1 (clinical & pathologic group)
- pTis,cN0,cM0 (stage 0 for both group)
- ✓ ypT0,ypN0, cM0, do not use as Stage 0 (need pretreatment clinical stage)

# AJCC Prognostic Stage Groups

<b>T</b>	<b>N</b>	<b>M</b>	<b>PSA</b>	<b>Grade Group</b>	<b>Stage group</b>
cT1a-c	N0	M0	< 10	1	I
cT2a					
pT2	N0	M0	< 10	1	I
cT1-c	N0	M0	≥ 10 < 20	1	IIA
cT2a					
cT2b-c	N0	M0	< 20	1	IIA
T1-2	N0	M0	< 20	2	IIB
T1-2	N0	M0	< 20	3	IIC
T1-2	N0	M0	< 20	4	IIC
T1-2	N0	M0	≥ 20	1-4	IIIA
T3-4	N0	M0	Any	1-4	IIIB
Any T	N0	M0	Any	5	IIIC
Any T	N1	M0	Any	Any	IVA
Any T	N0	M1	Any	Any	IVB

# AJCC prognostic stage groups

<b>Group</b>	<b>T</b>	<b>N</b>	<b>M</b>	<b>S (Serum Tumor Markers)</b>
<b>Stage 0</b>	<b>pTis</b>	<b>N0</b>	<b>M0</b>	<b>S0</b>
<b>Stage I</b>	<b>pT1-4</b>	<b>N0</b>	<b>M0</b>	<b>SX</b>
<b>Stage IA</b>	<b>pT1</b>	<b>N0</b>	<b>M0</b>	<b>S0</b>
<b>Stage IB</b>	<b>pT2</b>	<b>N0</b>	<b>M0</b>	<b>S0</b>
	<b>pT3</b>	<b>N0</b>	<b>M0</b>	<b>S0</b>
	<b>pT4</b>	<b>N0</b>	<b>M0</b>	<b>S0</b>
<b>Stage IS</b>	<b>Any pT/Tx</b>	<b>N0</b>	<b>M0</b>	<b>S1-3 (measured post orchiectomy)</b>

# AJCC Prognostic Stage Groups

<b>Stage II</b>	<b>Any pT/Tx</b>	<b>N1-3</b>	<b>M0</b>	<b>SX</b>
<b>Stage IIA</b>	<b>Any pT/Tx</b>	<b>N1</b>	<b>M0</b>	<b>S0</b>
	<b>Any pT/Tx</b>	<b>N1</b>	<b>M0</b>	<b>S1</b>
<b>Stage IIB</b>	<b>Any pT/Tx</b>	<b>N2</b>	<b>M0</b>	<b>S0</b>
	<b>Any pT/Tx</b>	<b>N2</b>	<b>M0</b>	<b>S1</b>
<b>Stage IIC</b>	<b>Any pT/Tx</b>	<b>N3</b>	<b>M0</b>	<b>S0</b>
	<b>Any pT/Tx</b>	<b>N3</b>	<b>M0</b>	<b>S1</b>



# AJCC Prognostic Stage Groups

<b>Stage III</b>	<b>Any pT/Tx</b>	<b>Any N</b>	<b>M1</b>	<b>SX</b>
<b>Stage IIIA</b>	<b>Any pT/Tx</b>	<b>Any N</b>	<b>M1a</b>	<b>S0</b>
	<b>Any pT/Tx</b>	<b>Any N</b>	<b>M1a</b>	<b>S1</b>
<b>Stage IIIB</b>	<b>Any pT/Tx</b>	<b>N1-3</b>	<b>M0</b>	<b>S2</b>
	<b>Any pT/Tx</b>	<b>Any N</b>	<b>M1a</b>	<b>S2</b>
<b>Stage IIIC</b>	<b>Any pT/Tx</b>	<b>N1-3</b>	<b>M0</b>	<b>S3</b>
	<b>Any pT/Tx</b>	<b>Any N</b>	<b>M1a</b>	<b>S3</b>
	<b>Any pT/Tx</b>	<b>Any N</b>	<b>M1b</b>	<b>Any S</b>

**\*\*\*Non-anatomic factors incorporated**

# AJCC Prognostic Stage Groups

• Stage 0	Tis	N0	M0
• Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
• Stage IIA	T1	N1	M0
Stage IIB	T2 (T3)	N1 (N0)	M0
• Stage IIIA	T1-T3	N1, N2	M0
Stage IIIB	Any T	N3	M0
	T4	Any N	M0
• Stage IV	Any T	Any N	M1

**\*\*\*Non-anatomic factors not incorporated**

# Collaborative Stage (CS) Data (AJCC)

- **Tumor** CS tumor size (in mm)  
CS extension  
CS tumor size/extension eval.
- **Nodes** CS LNs  
CS LN eval (method of eval)  
LN +, # LN examined
- **Metastases** CS mets at Dx  
CS mets eval
- **Site specific factors (non-anatomic factors)**

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# CAP Electronic Cancer Checklists (CAP eCC) Overview

An International Implementation of SNOMED CT®



## SOFT TISSUE SARCOMA STAGING FORM

CLINICAL <i>Extent of disease before any treatment</i>	STAGE CATEGORY DEFINITIONS	PATHOLOGIC <i>Extent of disease during and from surgery</i>
<input type="checkbox"/> y clinical-staging completed after neoadjuvant therapy but before subsequent surgery	<b>TUMOR SIZE:</b> _____ <b>LATERALITY:</b> <input type="checkbox"/> left <input type="checkbox"/> right <input type="checkbox"/> bilateral	<input type="checkbox"/> y pathologic - staging completed after neoadjuvant therapy AND subsequent surgery
<input type="checkbox"/> TX <input type="checkbox"/> T0 <input type="checkbox"/> T1 <input type="checkbox"/> T1a <input type="checkbox"/> T1b <input type="checkbox"/> T2 <input type="checkbox"/> T2a <input type="checkbox"/> T2b	<b>PRIMARY TUMOR (T)</b> Primary tumor cannot be assessed No evidence of primary tumor Tumor 5 cm or less in greatest dimension Superficial tumor Deep tumor Tumor more than 5 cm in greatest dimension Superficial tumor Deep tumor  Note: Superficial tumor is located exclusively above the superficial fascia without invasion of the fascia; deep tumor is located either exclusively beneath the superficial fascia, superficial to the fascia with invasion of or through the fascia, or both superficial yet beneath the fascia.	<input type="checkbox"/> TX <input type="checkbox"/> T0 <input type="checkbox"/> T1 <input type="checkbox"/> T1a <input type="checkbox"/> T1b <input type="checkbox"/> T2 <input type="checkbox"/> T2a <input type="checkbox"/> T2b
<input type="checkbox"/> NX <input type="checkbox"/> N0 <input type="checkbox"/> N1*	<b>REGIONAL LYMPH NODES (N)</b> Regional lymph nodes cannot be assessed No regional lymph node metastasis Regional lymph node metastasis  *Note: Presence of positive nodes (N1) in M0 tumors is considered Stage III	<input type="checkbox"/> NX <input type="checkbox"/> N0 <input type="checkbox"/> N1
<input type="checkbox"/> M0 <input type="checkbox"/> M1	<b>DISTANT METASTASIS (M)</b> No distant metastasis (no pathologic M0; use clinical M to complete stage group) Distant metastasis	<input type="checkbox"/> M1
ANATOMIC STAGE • PROGNOSTIC GROUPS		
	<b>CLINICAL</b>	<b>PATHOLOGIC</b>
<b>GROUP</b>	<b>T</b> <b>N</b> <b>M</b> <b>Grade</b>	<b>GROUP</b> <b>T</b> <b>N</b> <b>M</b> <b>Grade</b>
<input type="checkbox"/> IA	T1a    N0    M0    G1, GX T1b    N0    M0    G1, GX	<input type="checkbox"/> IA    T1a    N0    M0    G1, GX <input type="checkbox"/> IA    T1b    N0    M0    G1, GX
<input type="checkbox"/> IB	T2a    N0    M0    G1, GX T2b    N0    M0    G1, GX	<input type="checkbox"/> IB    T2a    N0    M0    G1, GX <input type="checkbox"/> IB    T2b    N0    M0    G1, GX
<input type="checkbox"/> IIA	T1a    N0    M0    G2, G3 T1b    N0    M0    G2, G3	<input type="checkbox"/> IIA    T1a    N0    M0    G2, G3 <input type="checkbox"/> IIA    T1b    N0    M0    G2, G3
<input type="checkbox"/> IIB	T2a    N0    M0    G2 T2b    N0    M0    G2	<input type="checkbox"/> IIB    T2a    N0    M0    G2 <input type="checkbox"/> IIB    T2b    N0    M0    G2
<input type="checkbox"/> III	T2a, T2b    N0    M0    G3 Any T    N1    M0    Any G	<input type="checkbox"/> III    T2b    N0    M0    G3 <input type="checkbox"/> III    Any T    N1    M0    Any G
<input type="checkbox"/> IV	Any T    Any N    M1    Any G	<input type="checkbox"/> IV    Any T    Any N    M1    Any G
<input type="checkbox"/> Stage unknown		<input type="checkbox"/> Stage unknown

HOSPITAL NAME/ADDRESS	PATIENT NAME/INFORMATION
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## SOFT TISSUE SARCOMA STAGING FORM

### PROGNOSTIC FACTORS (SITE-SPECIFIC FACTORS)

**REQUIRED FOR STAGING:** Grade \_\_\_\_\_

**CLINICALLY SIGNIFICANT:**

Neurovascular invasion as determined by pathology: \_\_\_\_\_

Bone invasion as determined by imaging: \_\_\_\_\_

If pM1, source of pathologic metastatic specimen: \_\_\_\_\_

**Histologic Grade (G)** (also known as overall grade)

- | Grading system   | Grade                                   |
|--|---|
| <input type="checkbox"/> 2 grade system                          | <input type="checkbox"/> Grade I or 1   |
| <input type="checkbox"/> 3 grade system                          | <input type="checkbox"/> Grade II or 2  |
| <input type="checkbox"/> 4 grade system                          | <input type="checkbox"/> Grade III or 3 |
| <input type="checkbox"/> No 2, 3, or 4 grade system is available | <input type="checkbox"/> Grade IV or 4  |

**ADDITIONAL DESCRIPTORS**

**Lymphatic Vessel Invasion (L) and Venous Invasion (V)** have been combined into Lymph-Vascular Invasion (LVI) for collection by cancer registrars. The College of American Pathologists' (CAP) Checklist should be used as the primary source. Other sources may be used in the absence of a Checklist. Priority is given to positive results.

- Lymph-Vascular Invasion Not Present (absent)/Not Identified
- Lymph-Vascular Invasion Present/Identified
- Not Applicable
- Unknown/Indeterminate

**Residual Tumor (R)**

The absence or presence of residual tumor after treatment. In some cases treated with surgery and/or with neoadjuvant therapy there will be residual tumor at the primary site after treatment because of incomplete resection or local and regional disease that extends beyond the limit of ability of resection.

- RX Presence of residual tumor cannot be assessed
- R0 No residual tumor
- R1 Microscopic residual tumor
- R2 Macroscopic residual tumor

**General Notes:**

For identification of special cases of TNM or pTNM classifications, the "m" suffix and "y," "r," and "a" prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

**m suffix** indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

**y prefix** indicates those cases in which classification is performed during or following initial multimodality therapy. The cTNM or pTNM category is identified by a "y" prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The "y" categorization is not an estimate of tumor prior to multimodality therapy.

**r prefix** indicates a recurrent tumor when staged after a disease-free interval, and is identified by the "r" prefix: rTNM.

**a prefix** designates the stage determined at autopsy: aTNM.

**surgical margins** is data field recorded by registrars describing the surgical margins of the resected primary site specimen as determined only by the pathology report.

**neoadjuvant treatment** is radiation therapy or systemic therapy (consisting of chemotherapy, hormone therapy, or immunotherapy) administered prior to a definitive surgical procedure. If the surgical procedure is not performed, the administered therapy no longer meets the definition of neoadjuvant therapy.

Clinical stage was used in treatment planning (describe): \_\_\_\_\_

National guidelines were used in treatment planning  NCCN  Other (describe): \_\_\_\_\_

Physician signature \_\_\_\_\_

Date/Time \_\_\_\_\_

HOSPITAL NAME/ADDRESS

PATIENT NAME/INFORMATION

*(continued from previous page)*



# 3. Think

- Determine prognosis
- Determining treatment
- Results of treatment and clinical trials
- Clinical and translational cancer research
- Exchange and comparison of information among treatment centers

# **Nomenclatures of morphology of cancer**

- **WHO blue books**
- **ICD-O 3<sup>rd</sup> edition**
- **SNOMED (CAP)**
- **Collaborative Stage Data Collection (AJCC)**
- **CAP cancer protocol**
- **caBIG (cancer bioinformatics grid; NCI)**
- **Atlas of tumor pathology (AFIP)**
- **American College of Radiology Appropriateness Criteria**
- **Practice Guideline of National Comprehensive Cancer Network (NCCN)**

# Coding of Tumors

- ICD-O 3<sup>rd</sup> edition
- ICD-10
- SNOMED
- SNOP
- IARC
- ICD-O: Topographic codes C00.0-C80.9  
Morphologic code M8000/0-9989/3  
Grade/Immunophenotypes  
e.g., C34.1 M8070/33



# Example

- **Poorly differentiated squamous carcinoma. Upper lobe of lung**
- **C34.1 M8070/33**
- **Behavior code**
  - /0 benign
  - /1 uncertain/unknown malignancy
  - /2 in situ (non-invasive) carcinoma
  - /3 malignant tumor, primary
  - /6 malignant tumor, metastasis
  - /9 malignant tumor, primary vs. metastasis uncertain

# **Essential to perform multidisciplinary team approach**

- **Recognition of patients' needs**
- **Clarifying responsibility**
- **Respect each other**
- **Keeping “good Team Work”**
  - ✓ **I CARE (integrity, compassion, accountability, respect and excellence)**
  - ✓ **3Cs (communication, collaboration, consultation)**

# Future Medicine (4Ps): Try to make 5Ps

- Prevention
- Prediction and Prognosis
- Personalized Medicine (tailored)
- Participatory Medicine
- 5P (?) Pathology

# Main Themes of 21<sup>st</sup> Century Cancer Research

- **Molecular dissection**
- **Molecular diagnosis**
  - Biomarker
  - Molecular imaging
- **Molecular therapy**
  - Molecular target
  - Gene therapy

# 4. Enjoy

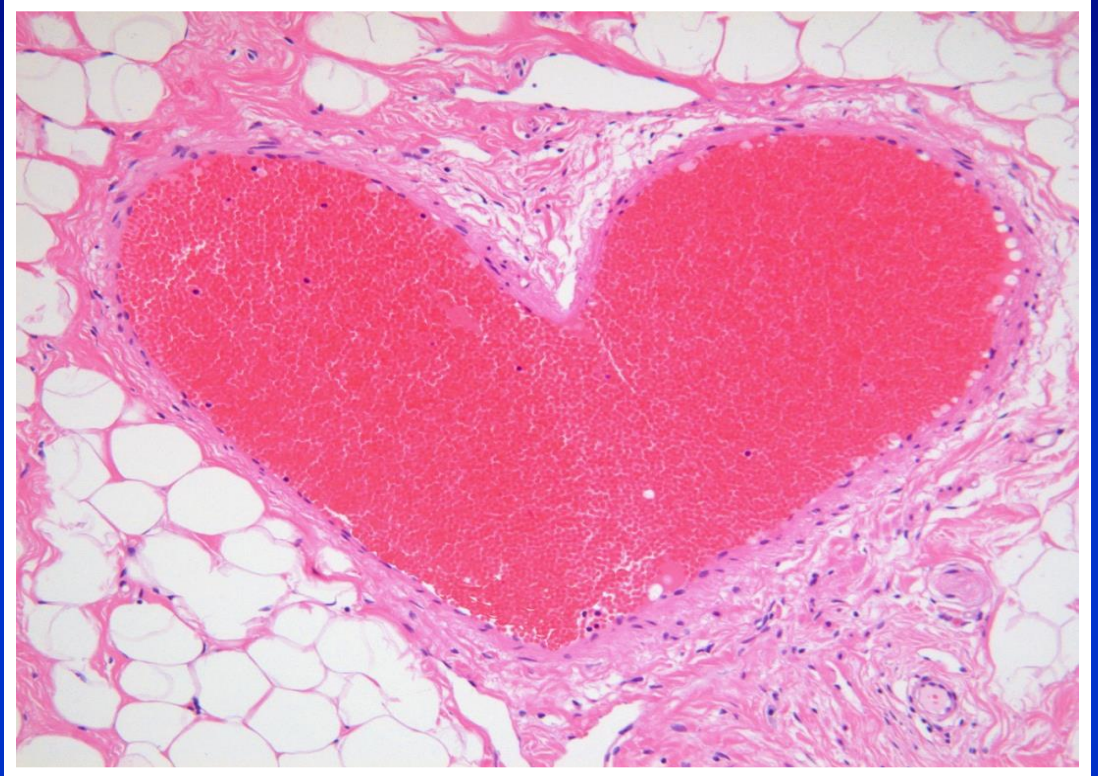
- BeST
- I CARE value
- 3 C practice

**\*\*\*Correct diagnosis and prognosis**

- Right patient, drug, time
- Right doctor and pathologist







**Do your BeST!**

**Tumor stage and grade**

**March 16, 2018**

Outstanding Faculty Award  
To  
Jae Ro, M.D., Ph.D.

In recognition and appreciation of your dedication  
to pathology teaching through 11 years of  
Microscope Conference

Thank you for giving your **BEST** to all.

Houston Methodist Residents, Fellows and Faculty  
2015-16



# In Google: Dr. Ro's BeST

## Dr. Ro's BeST

VIEW SOURCE

SHARE

### BeST

"You must always do your BeST to be a good pathologist."

—Dr. Ro

Besides the literal meaning of best, we have our own "BeST." The "BeST" stands for "B" representing "Basics", "e" for "enjoyment", "S" for "Study" and "T" for "Think".

#### Basics:

The art of pathology is observing and diagnosing tissue or cells that are abnormal or diseased. Obviously, it is impossible to do this without knowing what "normal" looks like in the first place. Dr. Ro often repeats his favorite mantra: "You must study basic histology!" This is usually said after one of his residents confuses breast tissue with prostate, or skin with mucosa. It is an obvious truth that a solid foundational knowledge of basic normal histology is one of the keys to becoming an excellent pathologist. A diagnosis of "no pathologic alteration" (i.e. - normal) is often harder to make than a diagnosis of carcinoma. A pathologist who is well acquainted with histology and all of the unusual variations of morphology that may be seen in "normal" tissues will more easily be able to discern normal from diseased tissue.

#### enjoyment/enthusiasm:

Although it is not strictly necessary to enjoy pathology, it is the defining feature that separates good pathologists from outstanding pathologists. The difference is obvious in the academic setting, where those who are enthusiastic about their work are effective teachers and admired mentors. These pathologists inspire their pupils to learn more, to work harder, and to enjoy the study and practice of pathology. As with any vocation, those who enjoy their work will perform better and have increased job satisfaction. Enjoyment and enthusiasm help to make the sacrifices worth it, make it easier to stay late when necessary, and keep one from exhaustion and burnout. If pathology is not enjoyable, then why do we do it?



**Thank for your attention!**

