Pathology of tumors
Neoplasia 5.

Diagnosis, Grade, Stage, Prognosis,
Treatment modalities

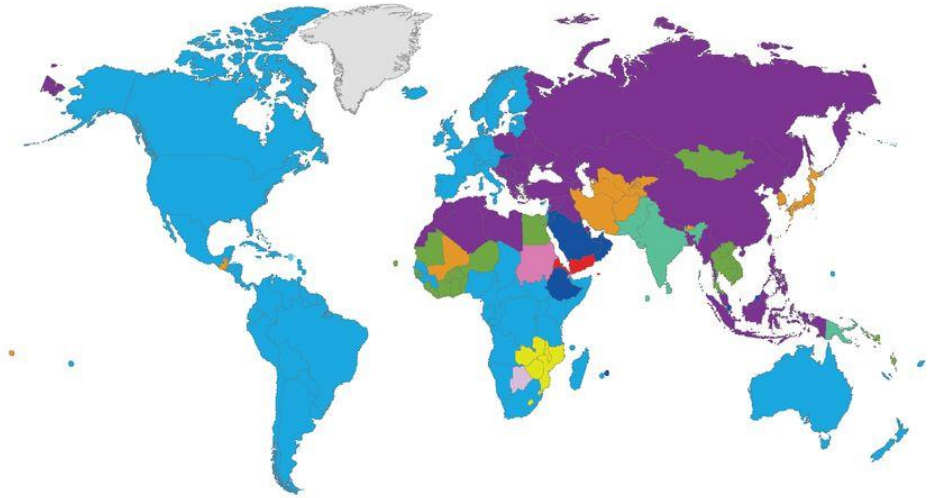
Dr. Janina Kulka

2nd Department of Pathology

30 October 2019

250 years of EXCELLENCE in medical education, research & innovation and healthcare

Males

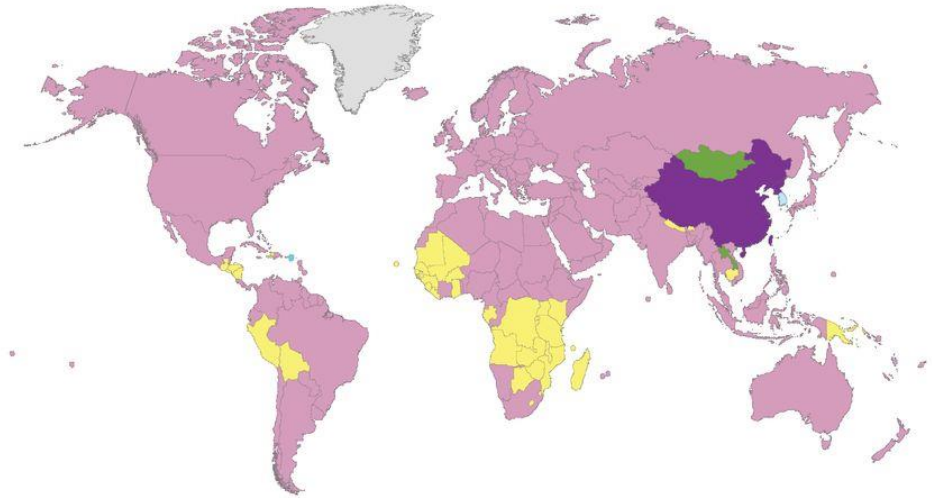


Most common cancer site: males

Colorectum | Kaposi sarcoma | Lip, oral cavity | Lung | Prostate | No data

Esophagus | Leukemia | Liver | Non-Hodgkin lymphoma | Stomach

Females



Most common cancer site: females

Breast | Cervix uteri | Liver | Lung | Thyroid | No data

Most commonly diagnosed cancers, 2012. (Compiled from GLOBOCAN 2012.)

Lindsay et al.
Cancer Epidemiol Biomarkers Prev; 2016;25(1)16-27

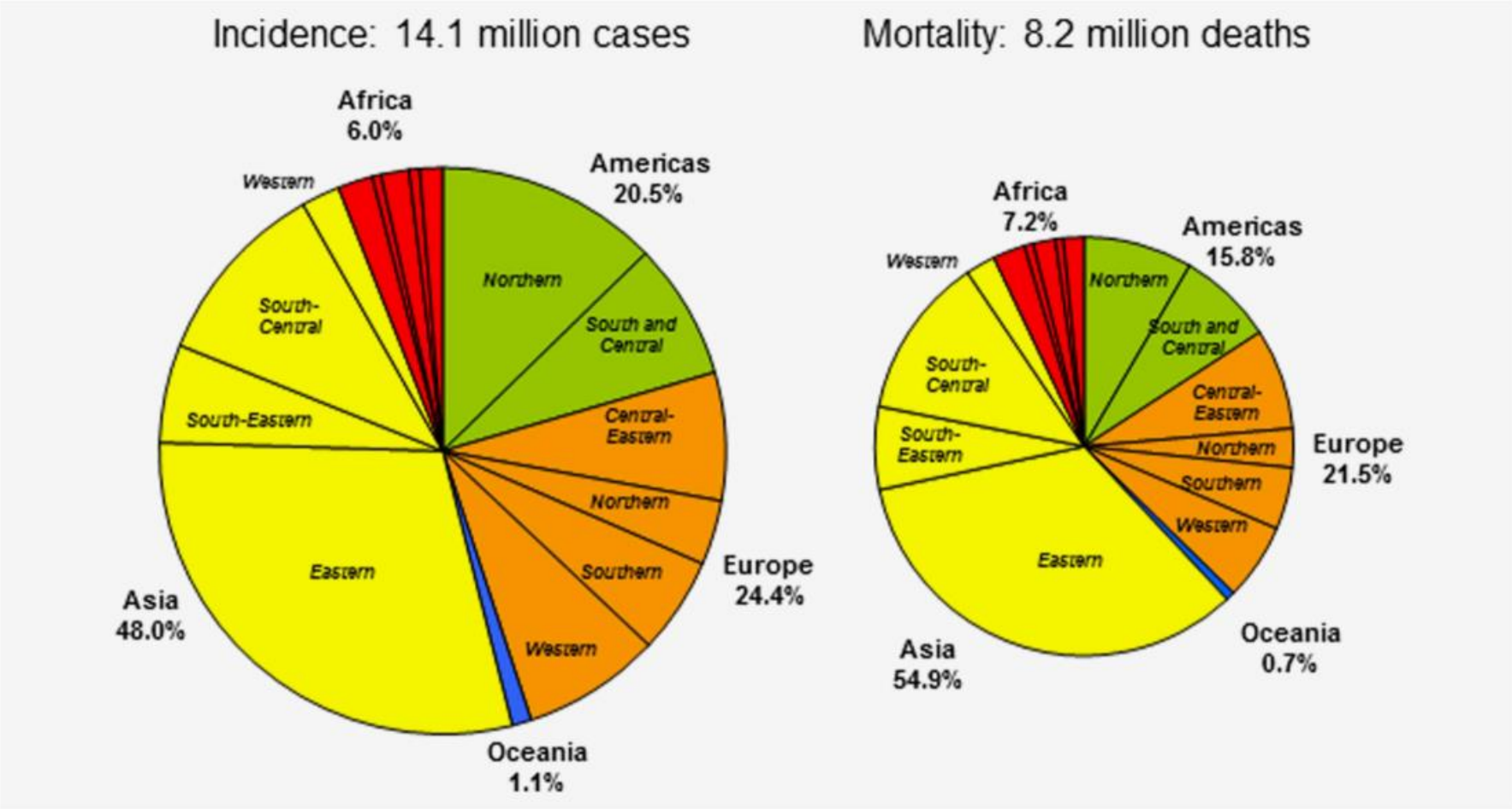
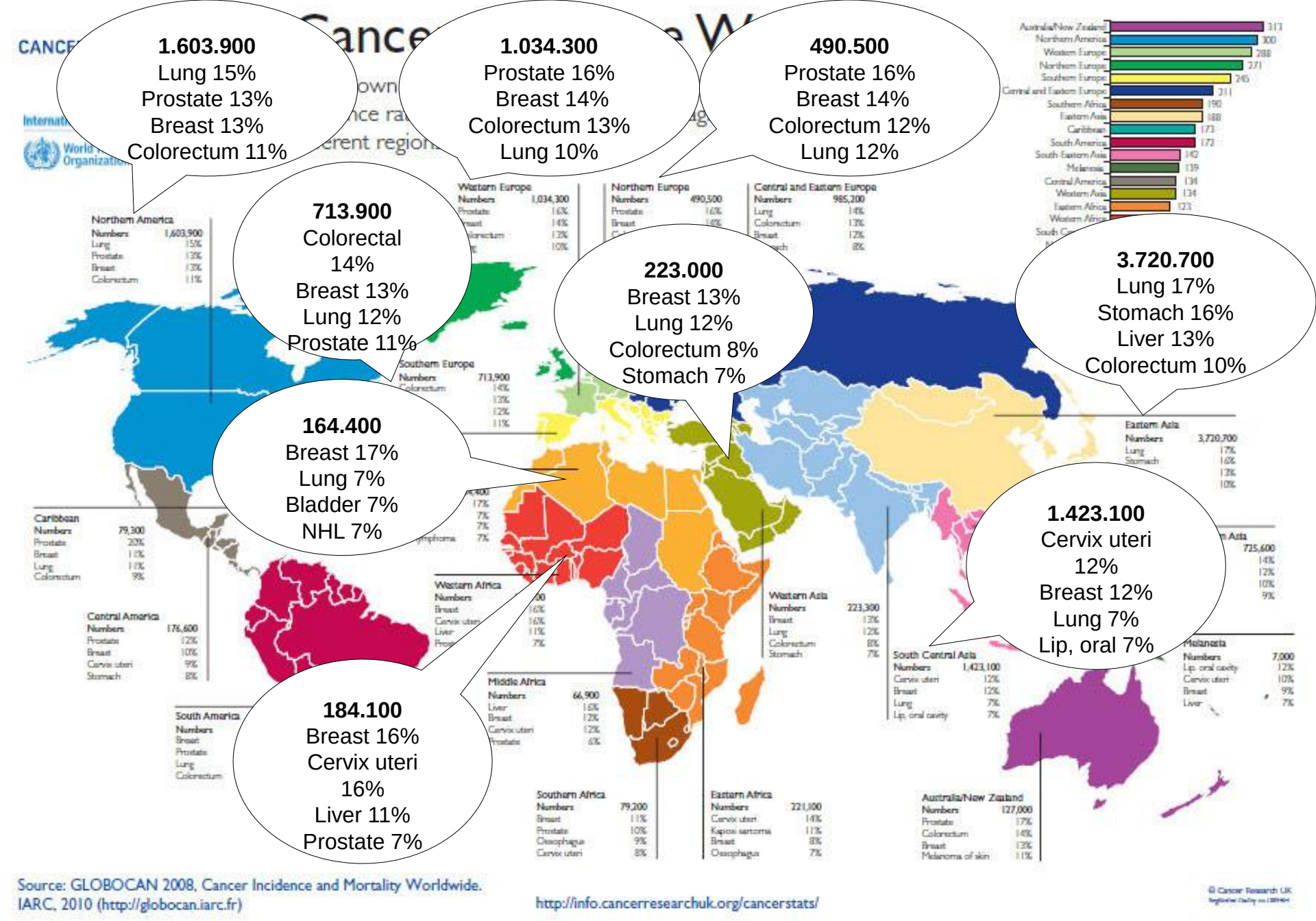


Figure 5. Estimated global numbers of new cases and deaths with proportions by world regions, both sexes combined, 2012. The area of the pie is proportional to the number of new cases or deaths.



http://kch.illinois.edu/Research/Labs/CancerEpidemiology/

Terms often used

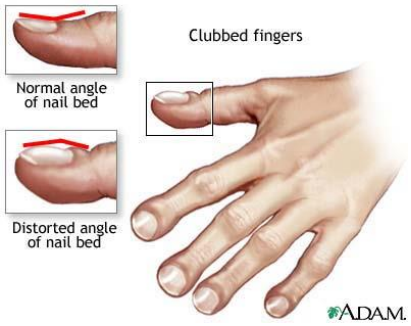
- **Incidence**: the number of ***newly diagnosed*** cases during a specific time period.
- **Prevalence**: The proportion of individuals in a population having a disease - a statistical concept referring to the ***number of cases of a disease that are present*** in a particular population at a given time.
- **Mortality rate**: the number of deaths due to a disease divided by the total population.

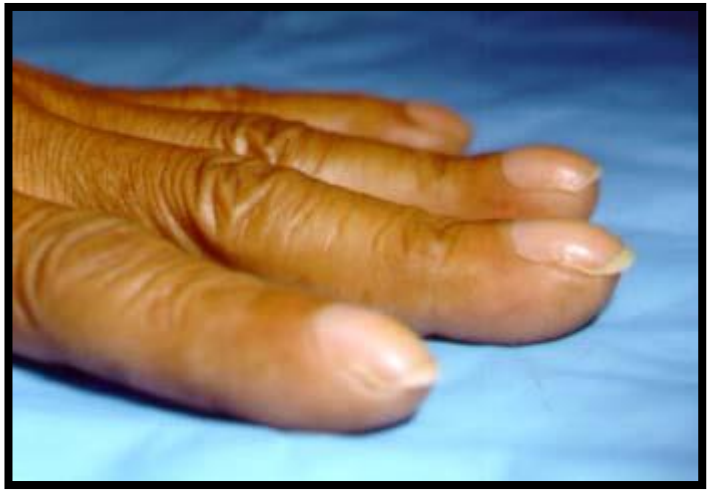
Preoperative (pretreatment) diagnosis

- **Symptoms**
- **Laboratory**: We, Hb-Htcr, blood test, liver function test, CEA, PSA, other tumor markers
- **Imaging**: rtg,isotope, UH, CT, MRI, PET….
- **Endoscopy**:laryngo-, gastro-, colono-, irrigo-, recto-, cysto-, mediastino-, pleuro-….
- **Cytology**:
  Body cavity fluids
  Exfoliative (cervix,bronchus)
  Aspiration (solid organs)
- **Core biopsy**:breast, liver, prostate, kidney…
- **Endoscopic biopsy**
- **Surgical biopsy**

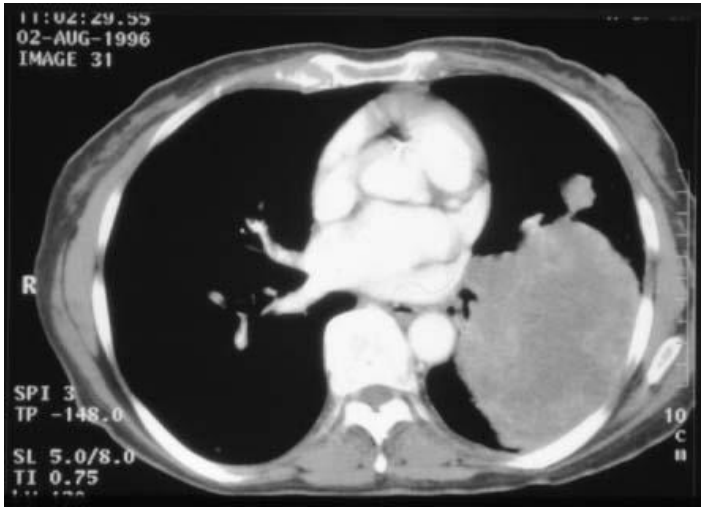
Paraneoplastic syndromes

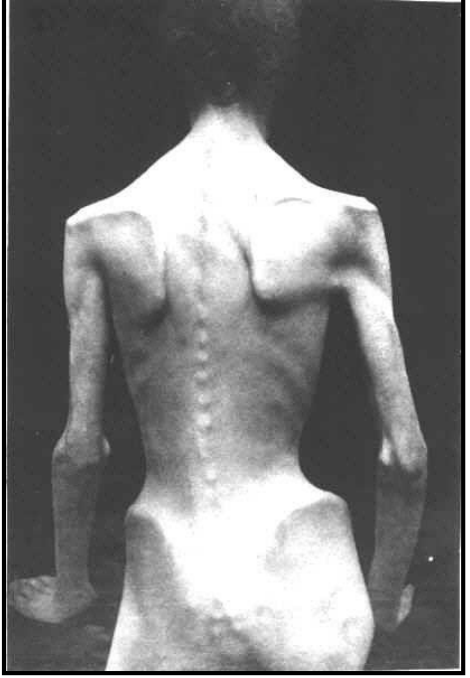
Cachexia
Endocrinopathies– ectopic hormone production
   ACTH, PTHrP, etc.
Neuromyopathies
   polymyopathia, myastenia gravis like symptoms
Hypertrophic osteoarthropathy
   (clubbing fingers+arthritis+periosteal neo-osteogenesis)
Thrombosis
   Trousseau sign, abacterial endocarditis
Acanthosis nigricans
Multiple seborrhoic keratoses (Leser-Trelat syndrome)

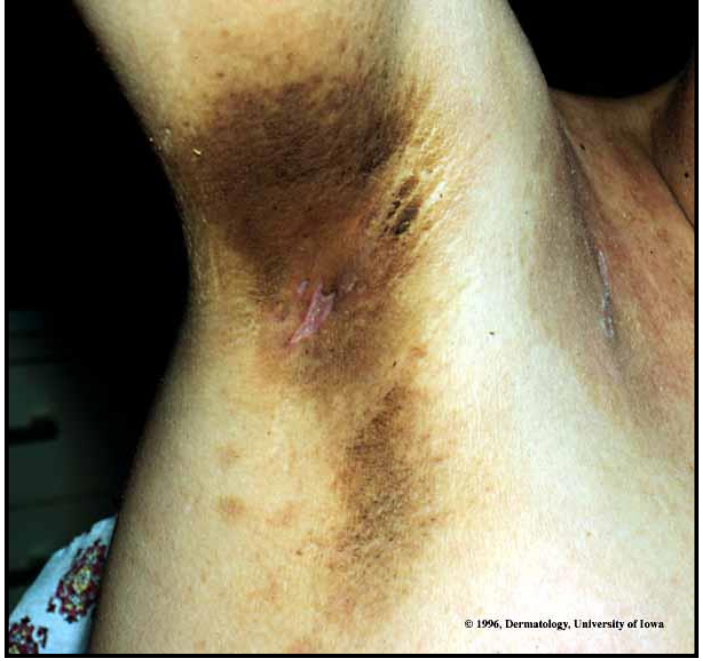


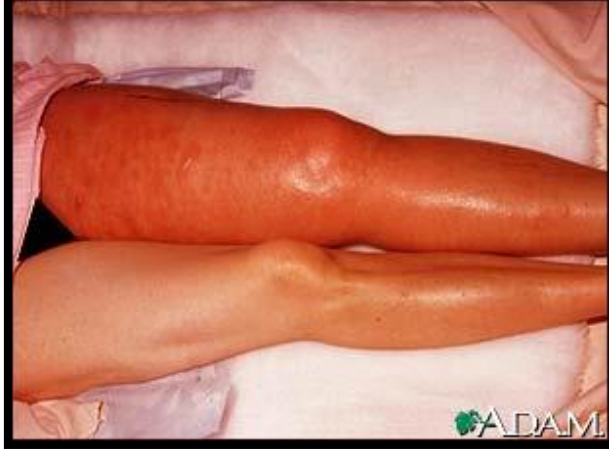


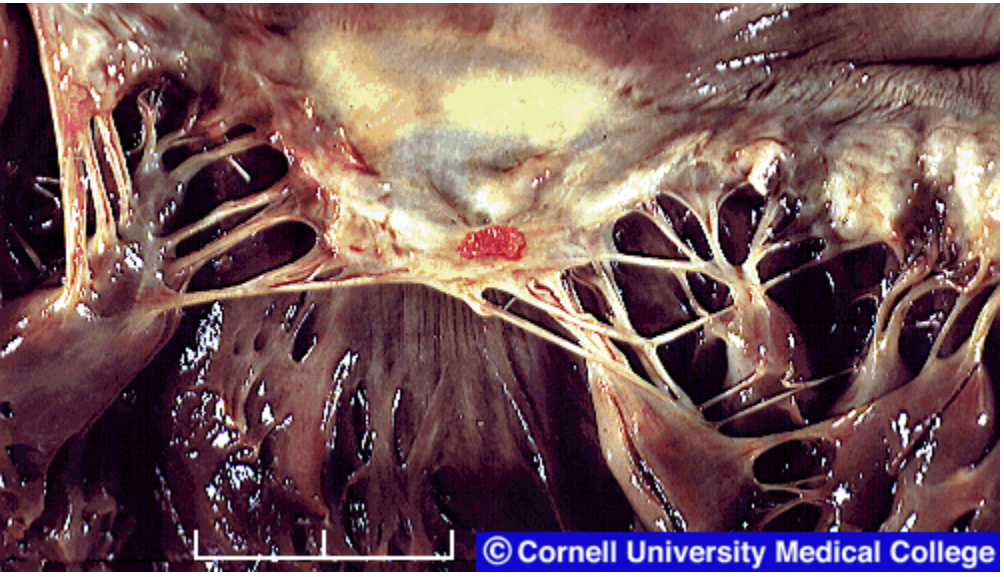
Because of the patient's history of bone pain, evidence of digital clubbing, and radiographic finding of a lung mass, the diagnosis of hypertrophic pulmonary osteoarthropathy was entertained. Hypertrophic pulmonary osteoarthropathy consists of the clinical triad of digital clubbing, active synovitis, and periostitis of the tubular long bones. **It is most frequently associated with intrathoracic malignancies, in particular, large squamous cell carcinomas.** Although the exact mechanism is unclear, the periostitis is believed to result from increased periostial blood flow and new bone formation.

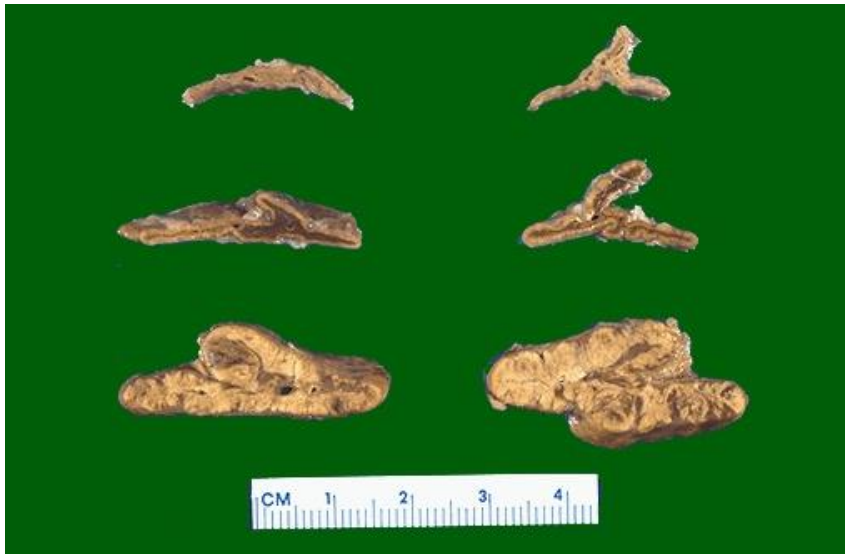










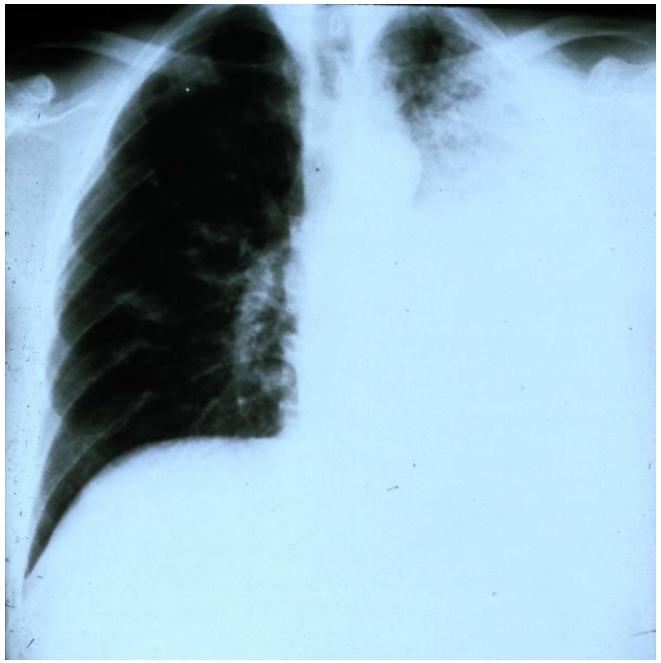


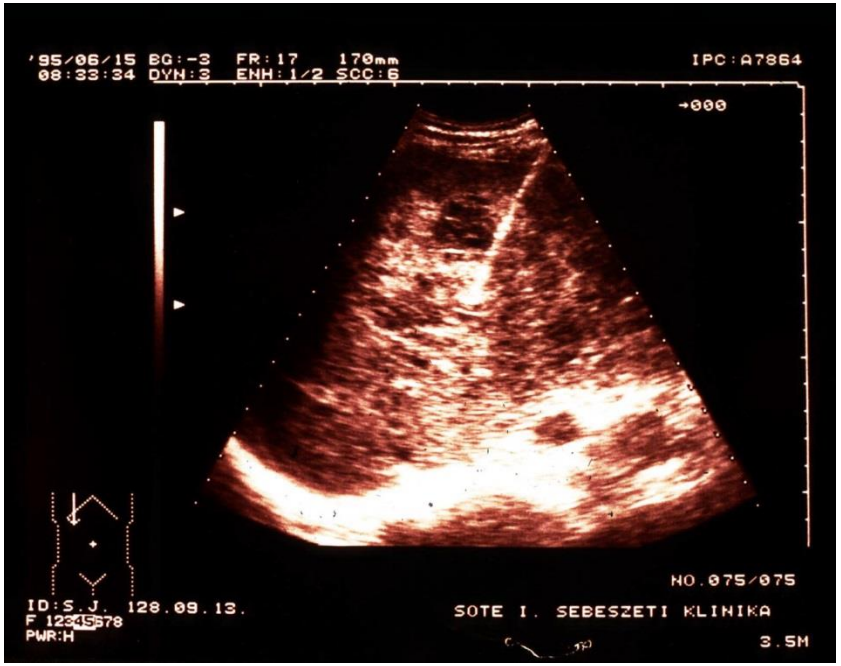
Paraneoplastic syndromes

Tumor markers

CEA	Colon (other common cancers as well)
CA125	Ovary
HE4	Ovary
CA15-3	Breast, ovary, pancreas
CA27.29	Breast
CA19-9	Pancreas, bile duct, gastric
Calcitonin	Medullary thyroid cancer
Chromogranin A	Neuroendocrine tumors
AFP	Liver ca, germ cell tumors
PSA	Prostate cancer
β-HCG	Choriocarcinoma
ACTH	Small cell lung cancer (SCLC)
CYFRA 21.1	Non small cell lung cancer (NSCLC)
Immunoglobulins	Myeloma multiplex

IMAGING

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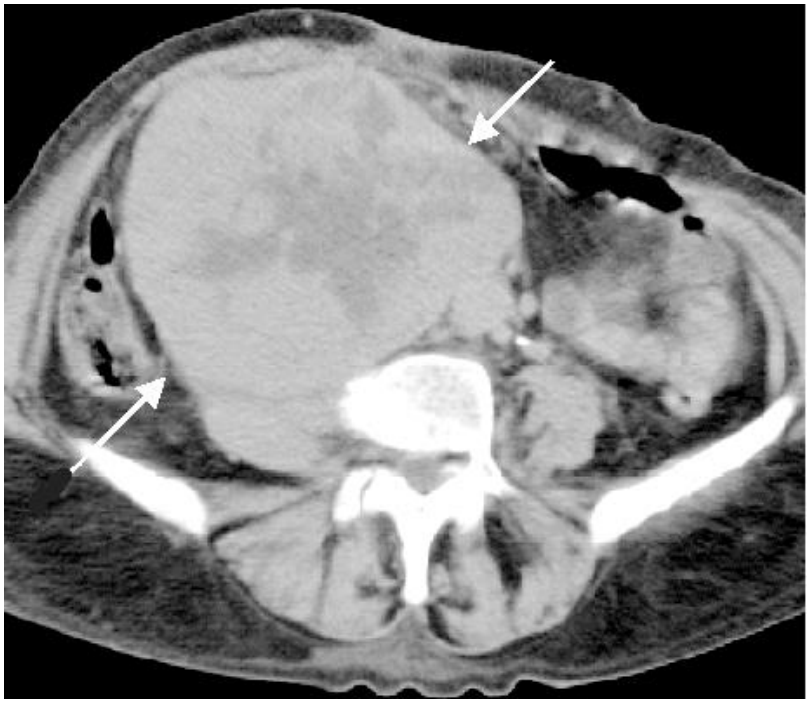

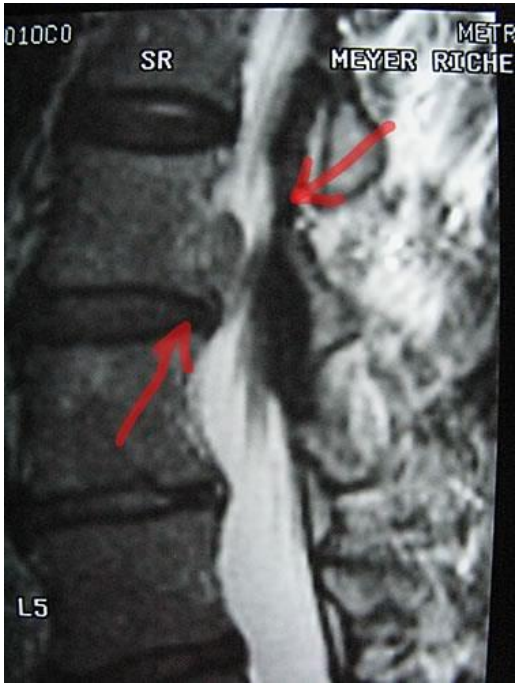
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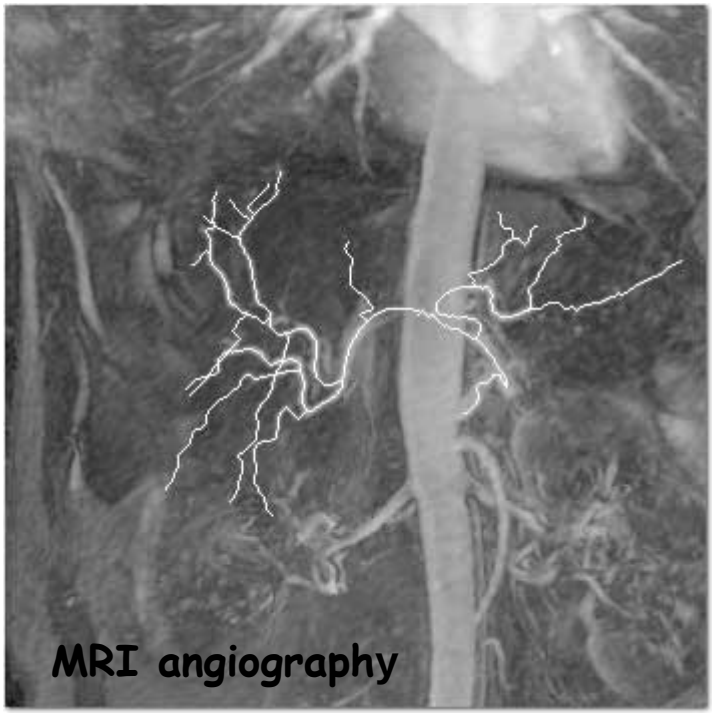
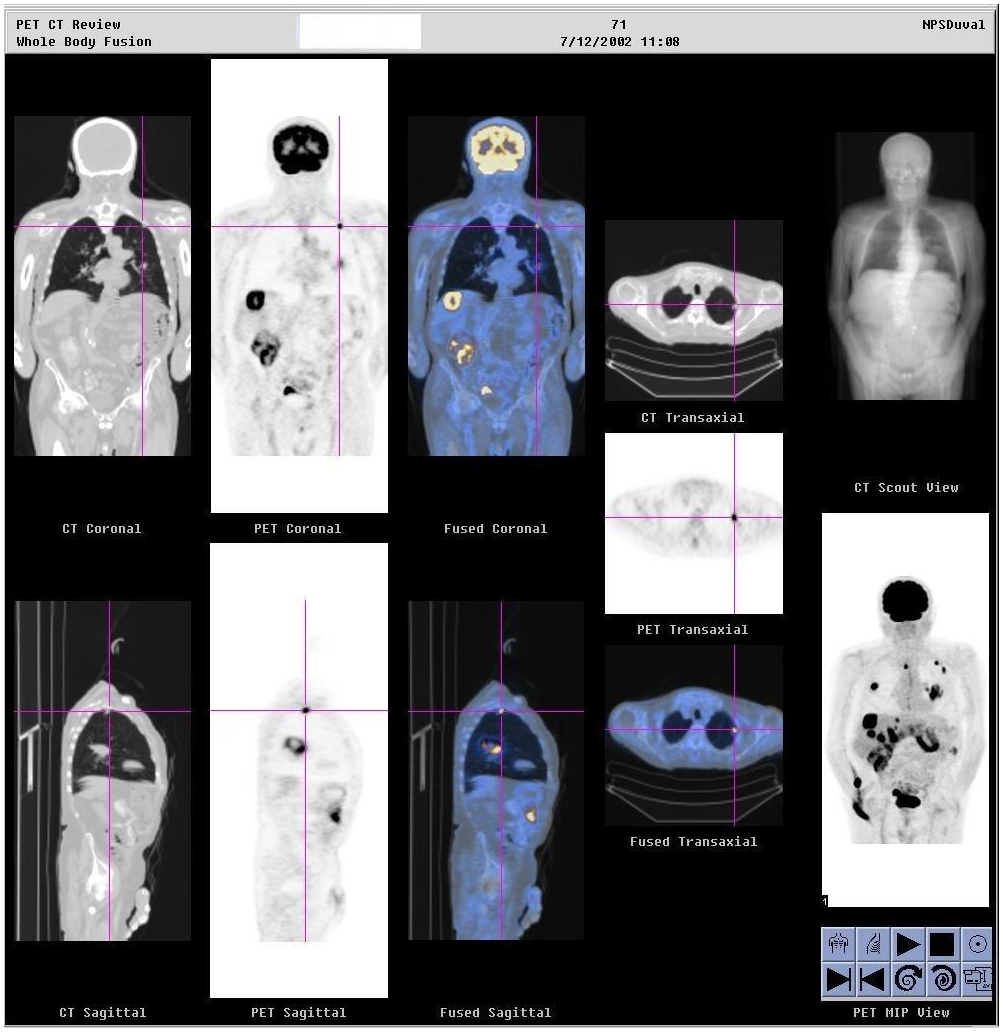
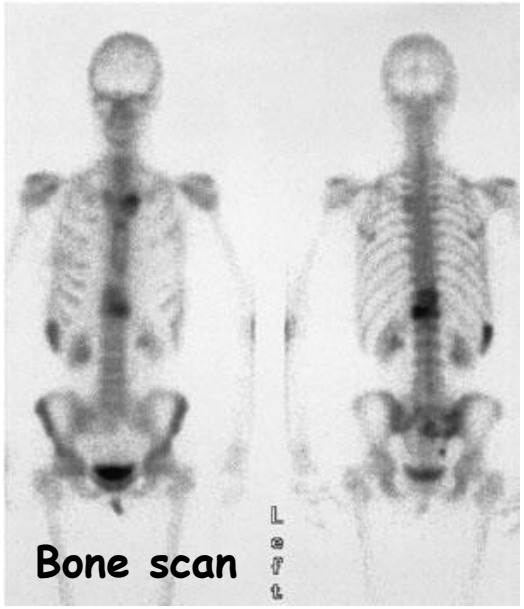
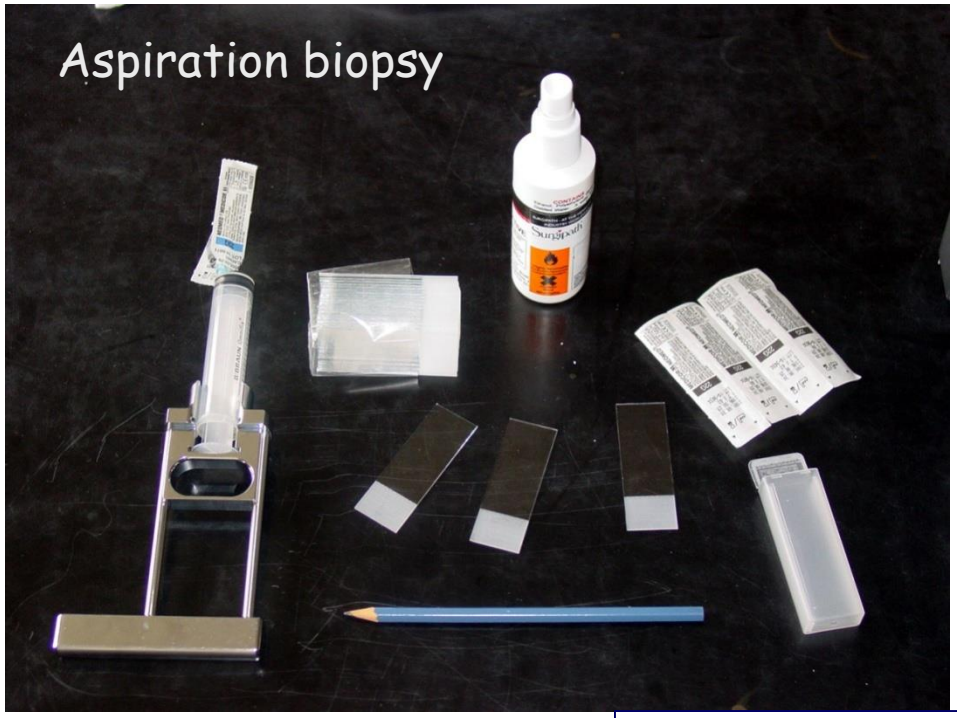

MRI angiography


PET CT Review
Whole Body Fusion
71
7/12/2002 11:08
NPSDuval
CT Coronal
PET Coronal
Fused Coronal
CT Transaxial
CT Scout View
PET Transaxial
Fused Transaxial
CT Sagittal
PET Sagittal
Fused Sagittal
PET MIP View

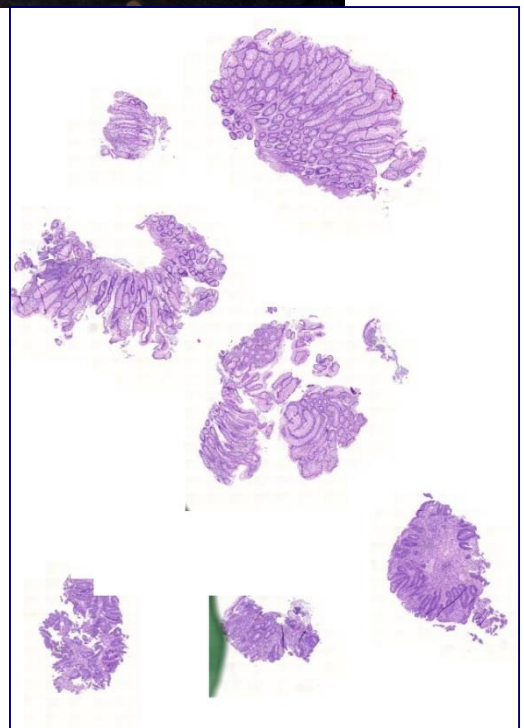
PET scan


Bone scan

Aspiration biopsy



Endoscopic biopsy



Core needle biopsy

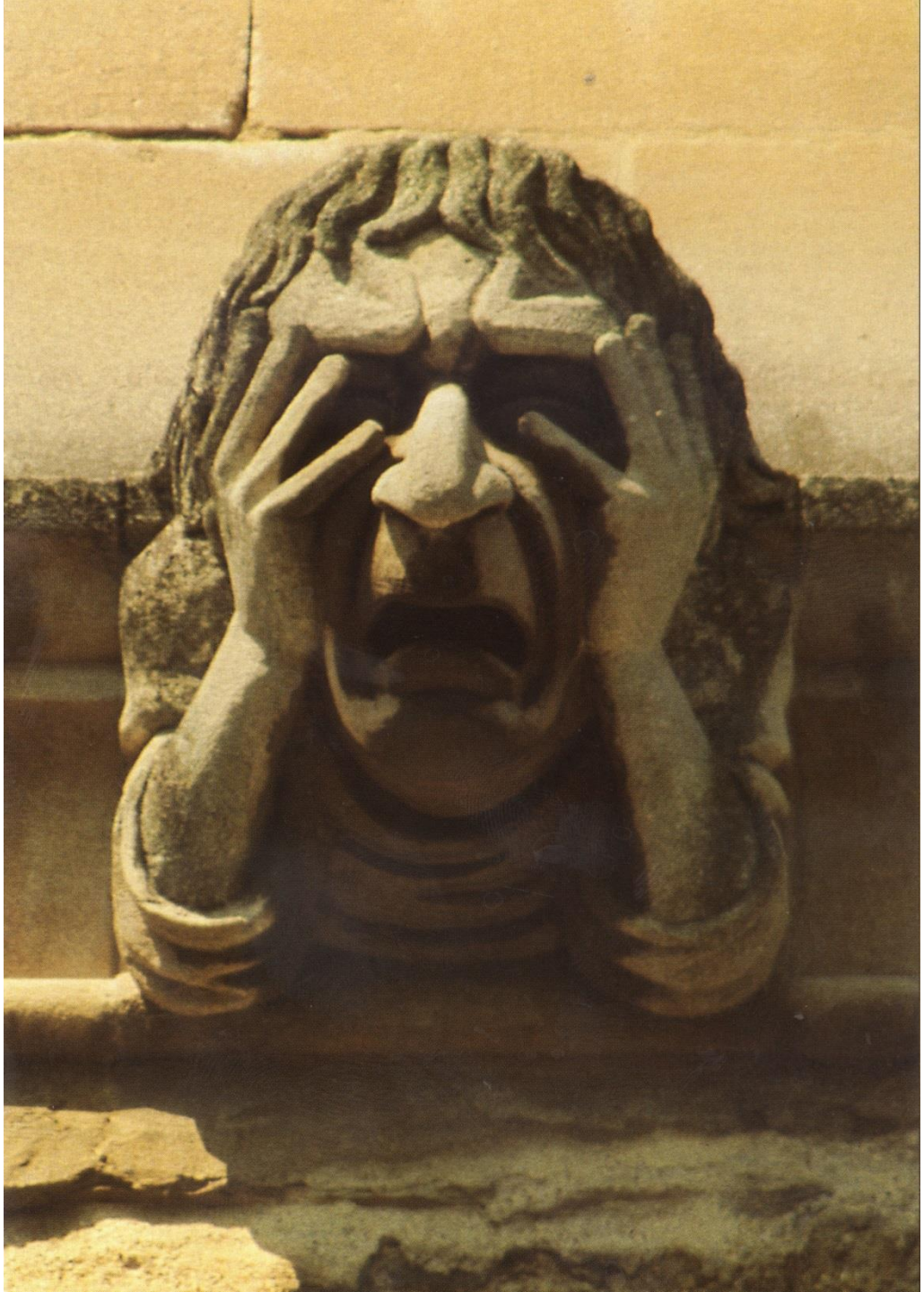
IMPORTANT

message to those students who will become clinicians

- Relevant clinical data should always be written on the Request Form that accompanies the specimen

HISTOPATHOLOGY

TISSUE OF ORIGIN	BENIGN	MALIGNANT
I. Composed of One Parenchymal Cell Type		
A. Mesenchymal tumors		
1. Connective tissue and derivatives	Fibroma	Fibrosarcoma
	Lipoma	Liposarcoma
	Chondroma	Chondrosarcoma
	Osteoma	Osteogenic sarcoma
2. Endothelial and related tissues		
Blood vessels	Hemangioma	Angiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Synovium		Synovial sarcoma
Mesothelium		Mesothelioma
Brain coverings	Meningioma	Invasive meningioma
3. Blood cells and related cells		
Hematopoietic cells		Leukemias
Lymphoid tissue		Malignant lymphomas
4. Muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma
B. Epithelial tumors		
1. Stratified squamous	Squamous cell papilloma	Squamous cell or epidermoid carcinoma
2. Basal cells of skin or adnexa		Basal cell carcinoma
3. Epithelial lining		
Glands or ducts	Adenoma	Adenocarcinoma
	Papilloma	Papillary carcinoma
	Cystadenoma	Cystadenocarcinoma
4. Respiratory passages		Bronchogenic carcinoma
		Bronchial "adenoma" (carcinoid)
5. Neuroectoderm	Nevus	Malignant melanoma
6. Renal epithelium	Renal tubular adenoma	Renal cell carcinoma
7. Liver cells	Liver cell adenoma	Hepatocellular carcinoma
8. Urinary tract epithelium (transitional)	Transitional cell papilloma	Transitional cell carcinoma
9. Placental epithelium (trophoblast)	Hydatidiform mole	Choriocarcinoma
10. Testicular epithelium (germ cells)		Seminoma
		Embryonal carcinoma
II. More Than One Neoplastic Cell Type—Mixed Tumors		
1. Salivary glands	Pleomorphic adenoma (mixed tumor of salivary origin)	Malignant mixed tumor of salivary gland origin
2. Breast	Fibroadenoma	Malignant cystosarcoma phyllodes
3. Renal anlage		Wilms' tumor
III. More Than One Neoplastic Cell Type Derived From More Than One Germ Layer—Teratogenous		
1. Totipotential cells in gonads or in embryonic rests	Mature teratoma, dermoid cyst	Immature teratoma, teratocarcinoma



Methods used that can help

- Special stains
- Immunohistochemistry
- Molecular techniques
  - ISH (in situ hybridisation techniques)
  - Other molecular techniques

Markers used in immunohistochemical reactions

Cytokeratin	Epithelium
(different CK-s)	(different epithelia and epithelial tumors)
Epithelial Membrane Antigen	Epithelial tumors, epithelioid sarcomas
Vimentin	Mesenchymal tissues
Leukocyte Common Antigen (LCA)	Lymphoid tissue/lymphoma
Desmin, Myogenin	Striated muscle
Smooth Muscle Actin, Smooth Muscle Myosin	Smooth muscle
Synaptophysin, Chromogranin-A	Neuroendocrine cells
S100	Melanoma, Schwann cells
HMB45, Melan A	Melanoma
TTF1	Lung, thyroid

.....many more

Organ-specific antibodies

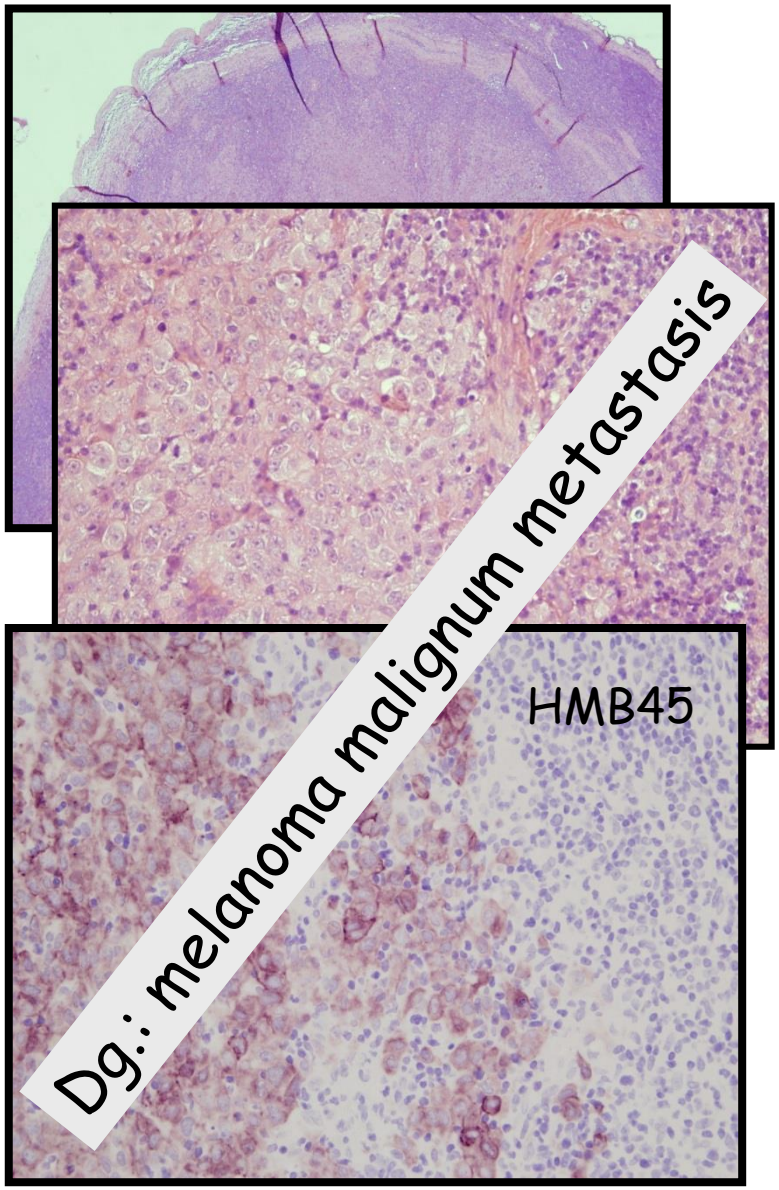
- Mammaglobin: BREAST
- HEP-PAR1: LIVER
- Napsyn: LUNG
- Thyreoglobulin: THYROID
- CDX2: INTESTINE (but also positive in tumors showing intestinal differentiation, e.g. certain mucinous cancers of the ovaries)
- Uroplakin: BLADDER mucosa

Cell-type specific antibodies

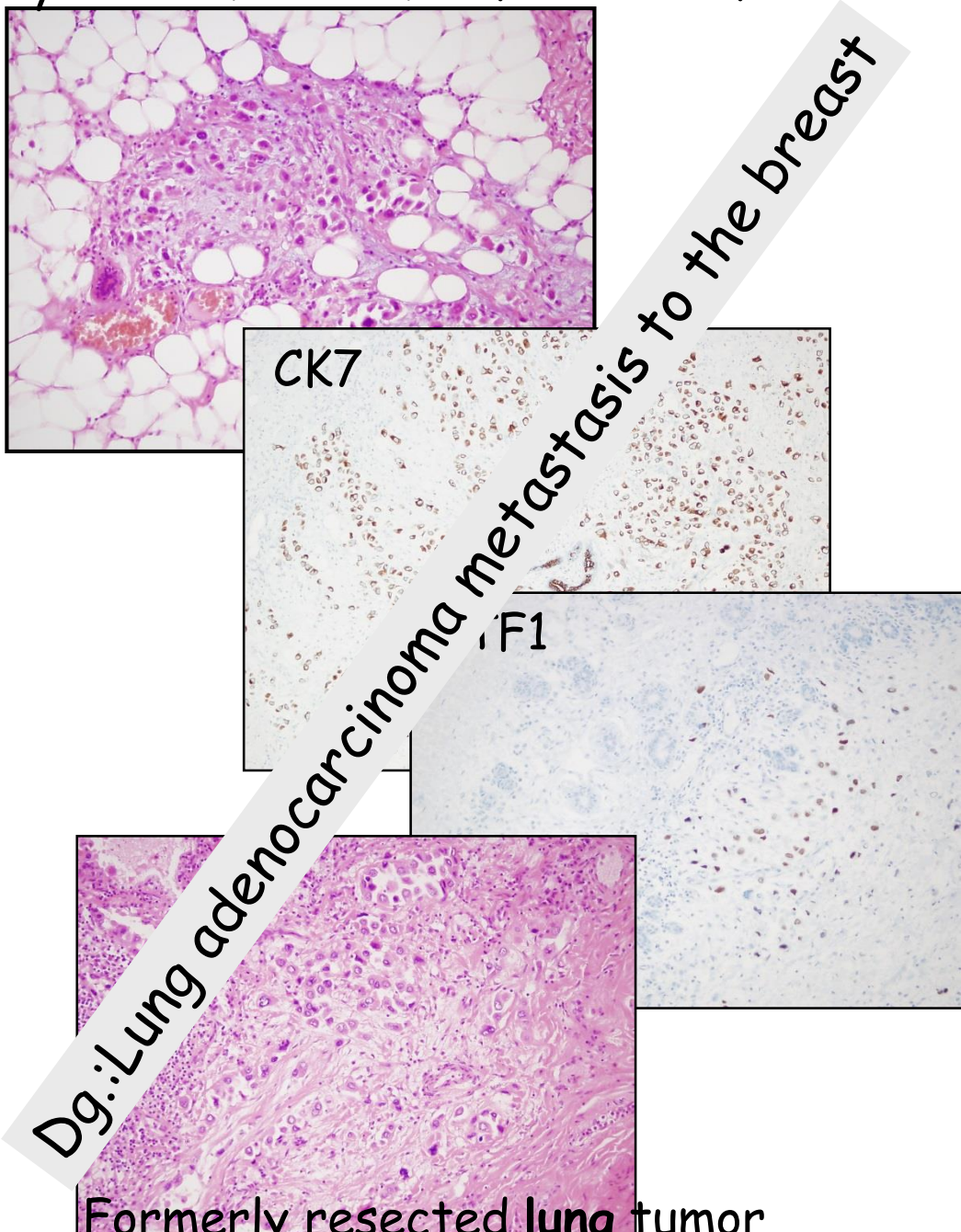
(examples; need to evaluate in the specific context)

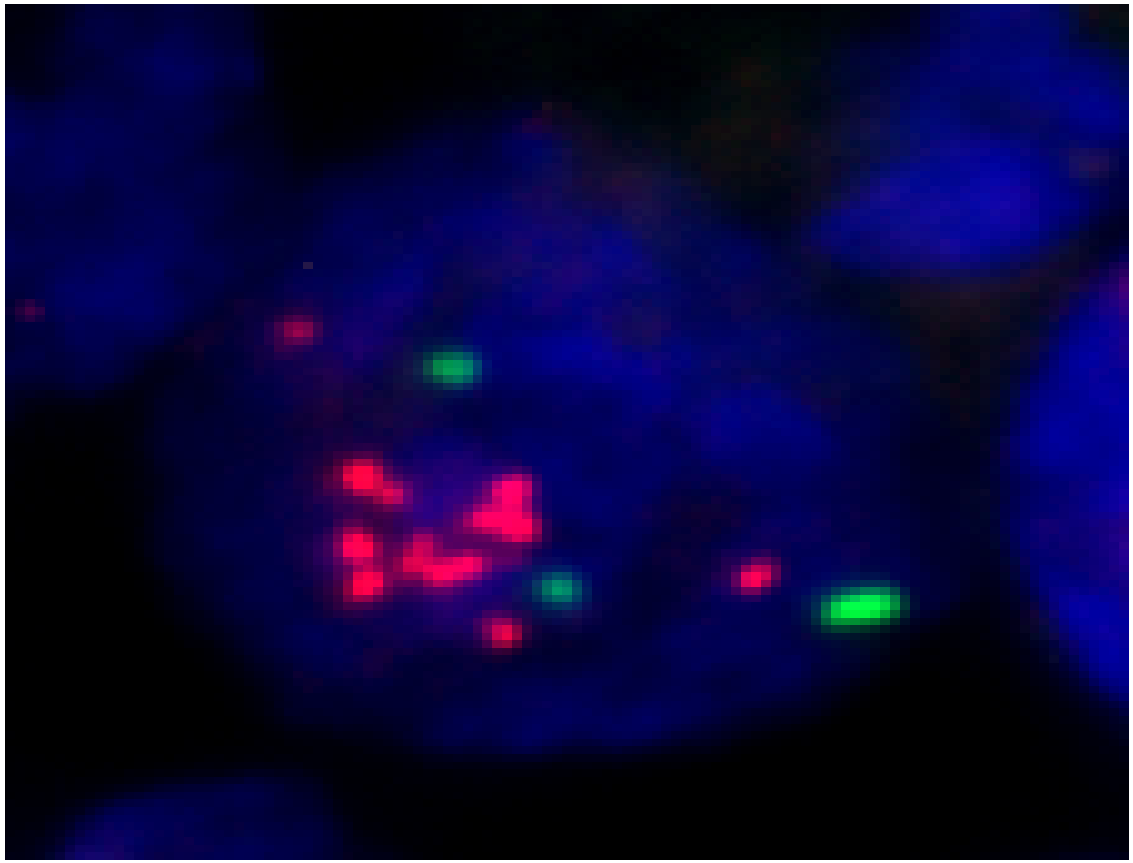
- p63: squamous cells, myoepithelial cells
- GCDFP-15: apocrine cells
- CD10: endometrial stromal cells, renal tubular cells
- Calretinin: mesothelial cells

33 y old male patient.
Metastatic tumor found in a cervical lymph node.

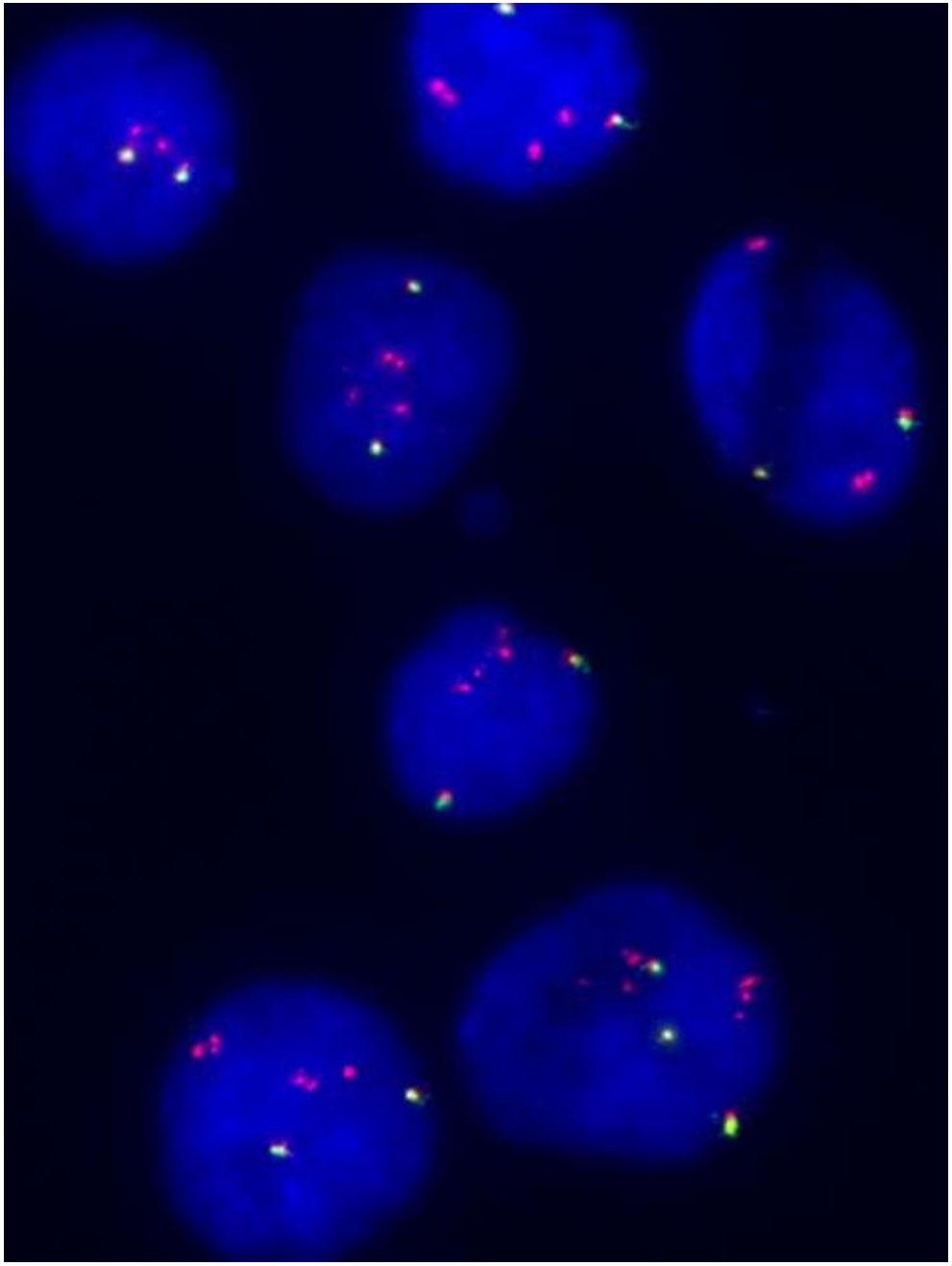


54 y old woman. Tumor found in left **breast**





FISH: gene amplification
(this case: HER2, breast cancer)



Dr. Christine Lovly, Vanderbilt University

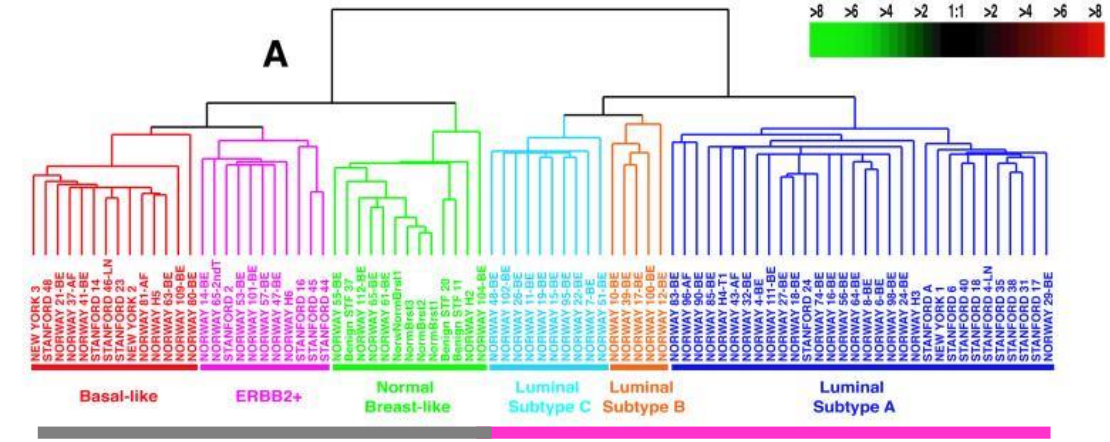
EML4-ALK fusion gene
(following translocation)
in lung adenocarcinoma cells

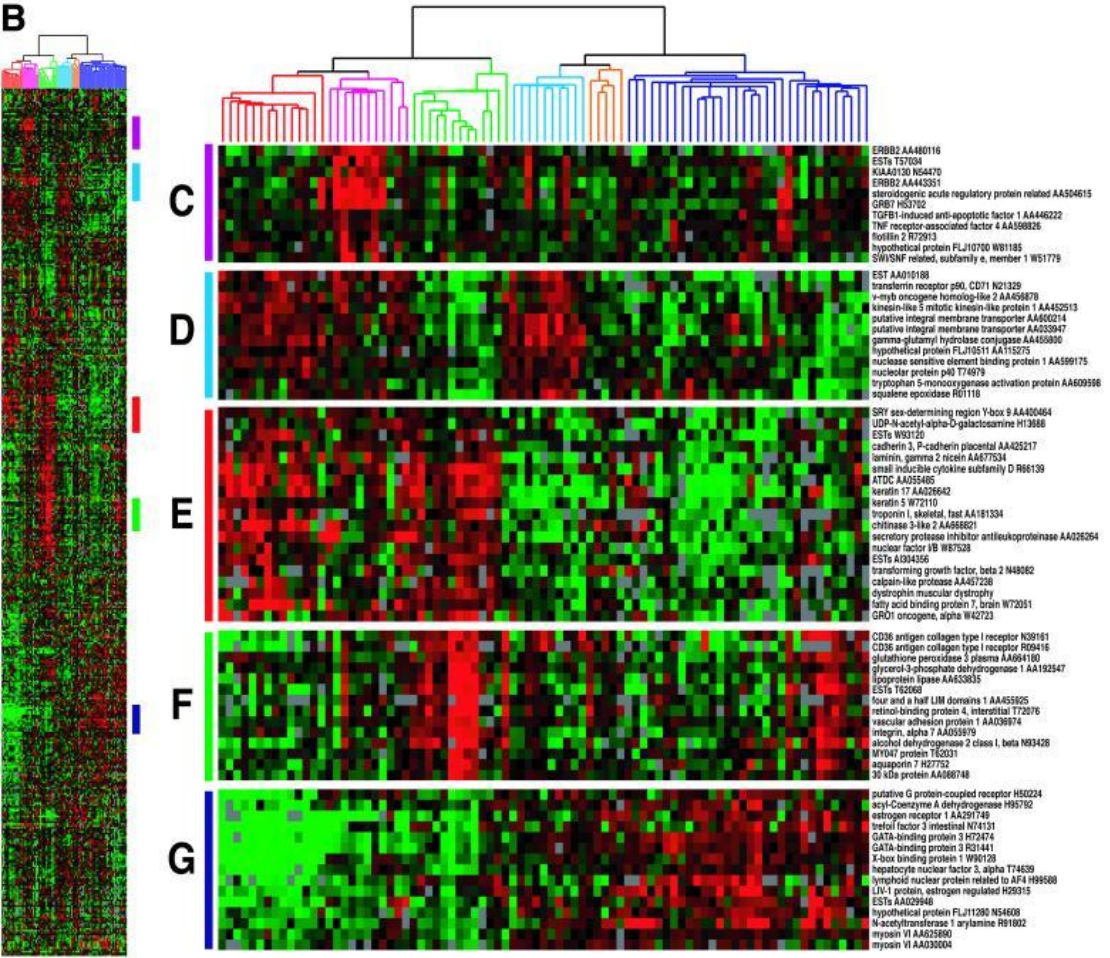
Molecular genetic studies

DNS “chip”: genetic profile – MOLECULAR CLASSIFICATION

Classification of breast carcinomas based on genetic profile

M. Perou et al.





Estrogen receptor positive

Luminal type

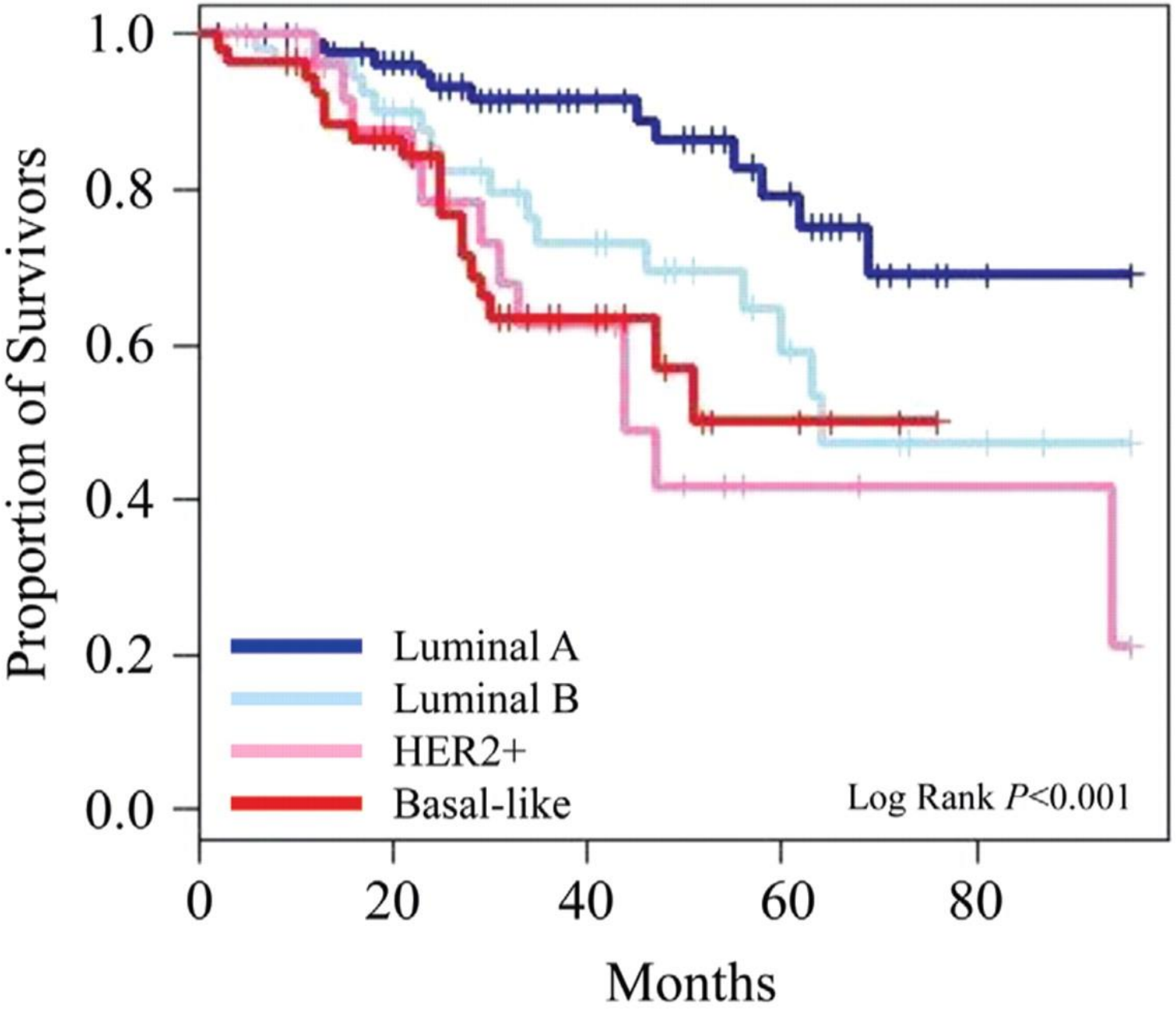
- -A
- -B

Estrogen receptor negative

Basal type

Her2/neu positive

Normal breast type



Sandhu R et al Lab Med June 2010;6:364-372

Classification of colorectal carcinomas based on gene expression profiling: Consensus Molecular Subtypes

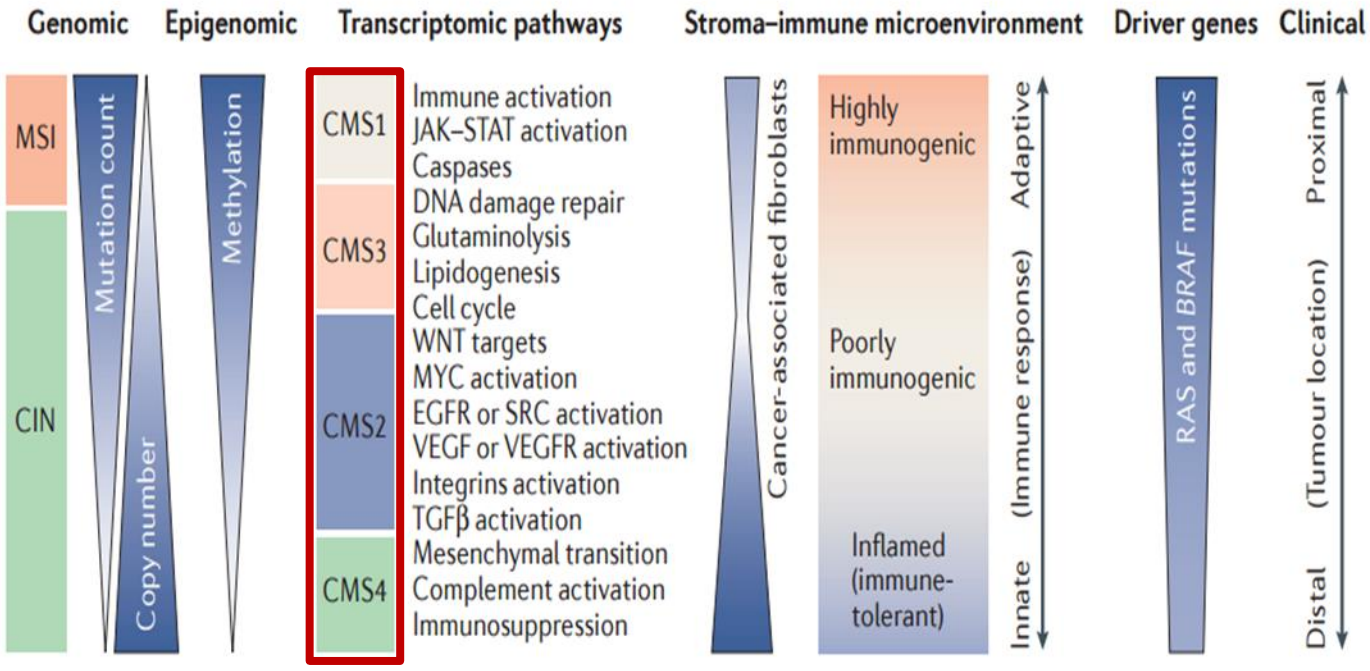
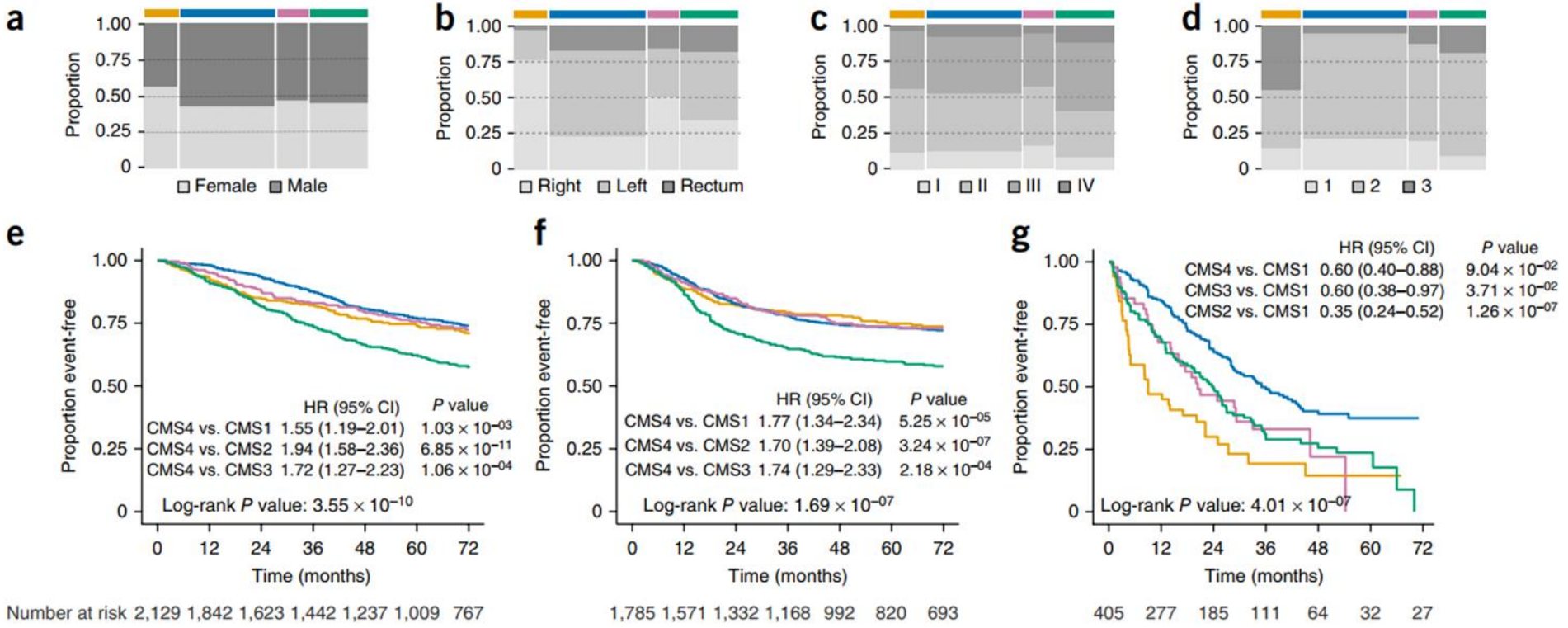


Figure 1 | **Schematic representation of CRC subtypes.** Microsatellite instability (MSI) is linked to hypermutation, hypermethylation, immune infiltration, activation of RAS, *BRAF* mutations, and locations in the proximal colon. Tumours with chromosomal instability (CIN) are more heterogeneous at the gene-expression level, showing a spectrum of pathway activation ranging from epithelial canonical (consensus molecular subtype 2 (CMS2)) to mesenchymal (CMS4). Tumours with CIN are mainly diagnosed in left colon or rectum, and their microenvironment is either poorly immunogenic or inflamed, with marked stromal infiltration. A subset of CRC tumours enriched for RAS mutations has strong metabolic adaptation (CMS3) and intermediate levels of mutation, methylation and copy number events. EGFR, epidermal growth factor receptor; JAK, Janus kinase; STAT, signal transducer and activator of transcription; TGFβ, transforming growth factor-β; VEGF, vascular endothelial growth factor; VEGFR, VEGF receptor.

Nat Rev Cancer. 2017 Feb;17(2):79-92.



Overall survival

Relapse-free survival

Survival after relapse

CMS 1

CMS 2

CMS 3

CMS 4

Nature Medicine 2015;21:1350–1356

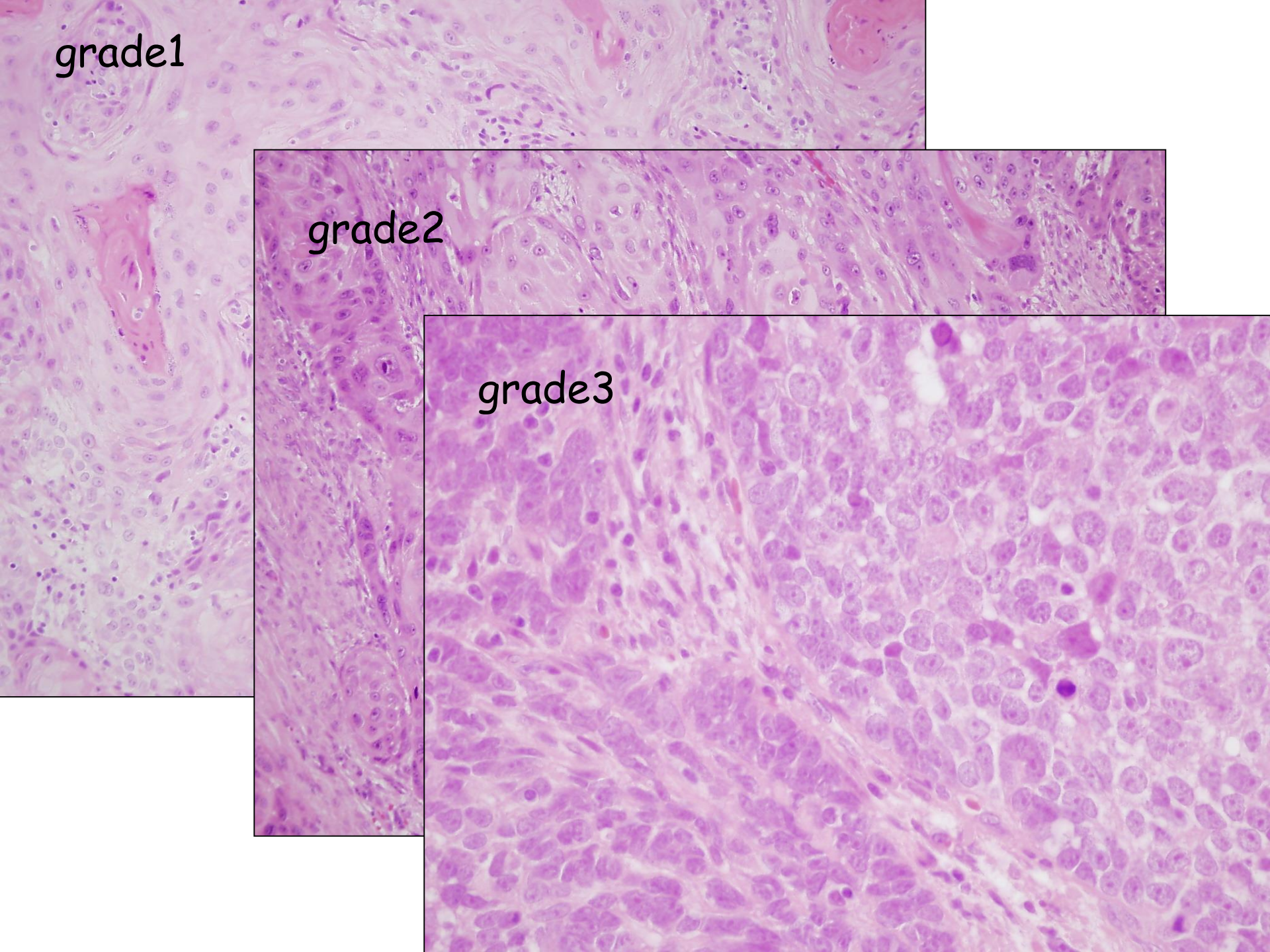
GRADE - generally

Measure of the DIFFERENTIATION

Well differentiated:Grade 1

Moderately differentiated:Grade 2

Poorly differentiated: Grade 3


grade1
grade2
grade3

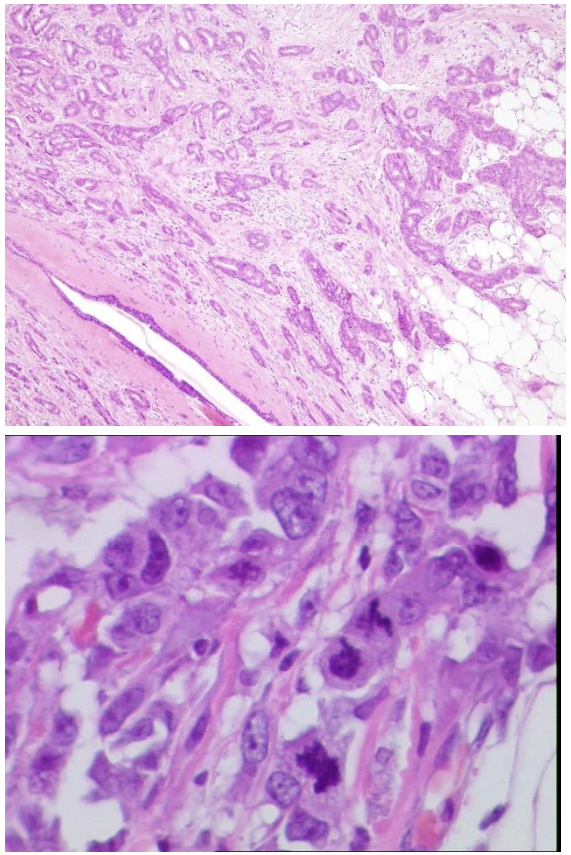
GRADE - special

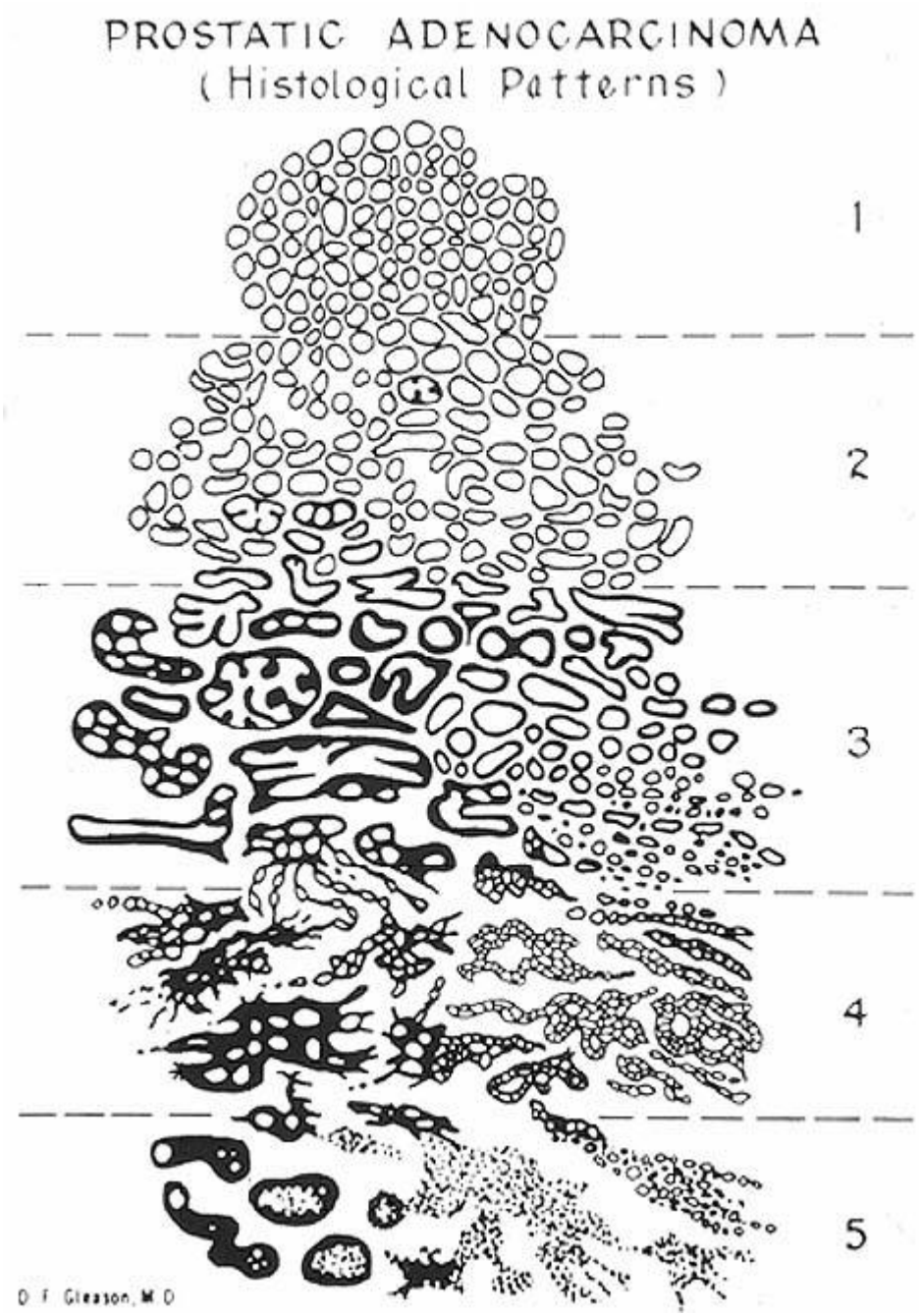
- *Breast carcinoma*:
  - Nottingham grade:
    - nuclear pleiomorphism
    - tubule formation
    - number of mitosis
- *Prostate carcinoma*
  - Gleason grade and score
  - Recently: ISUP grade groups
- *Renal cell carcinoma*
  - Fuhrman grade
  - Recently: ISUP grade

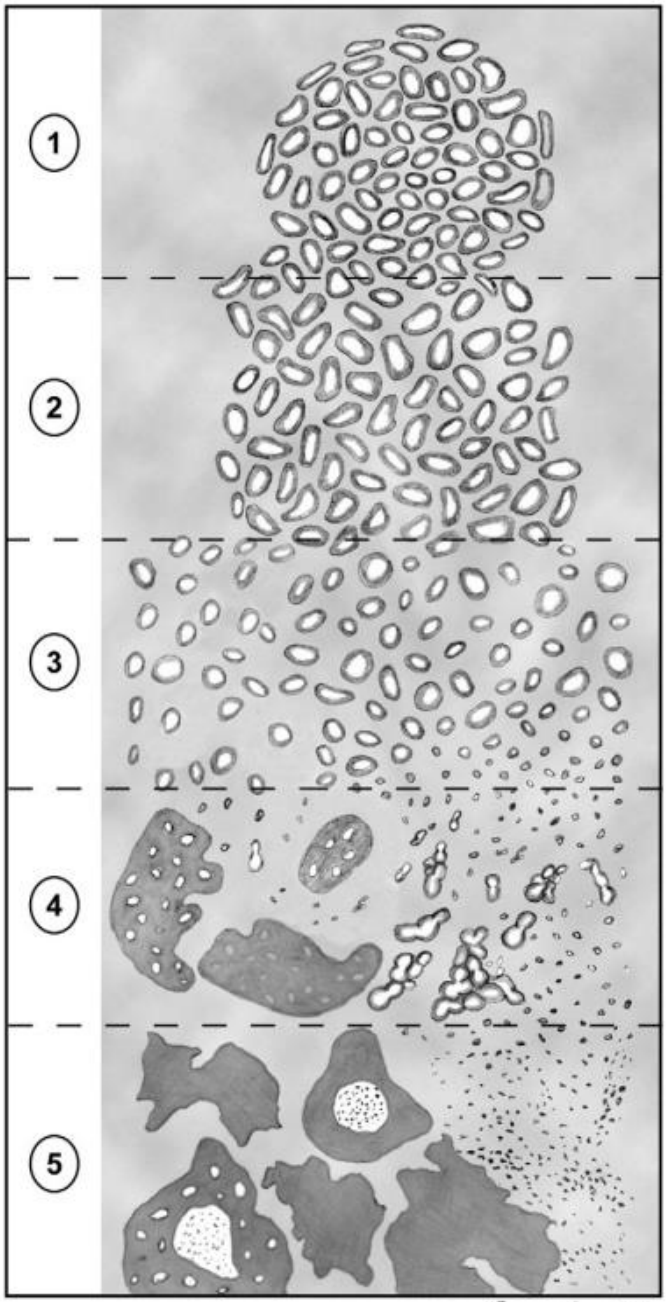
Breast carcinoma grade

Nottingham grade

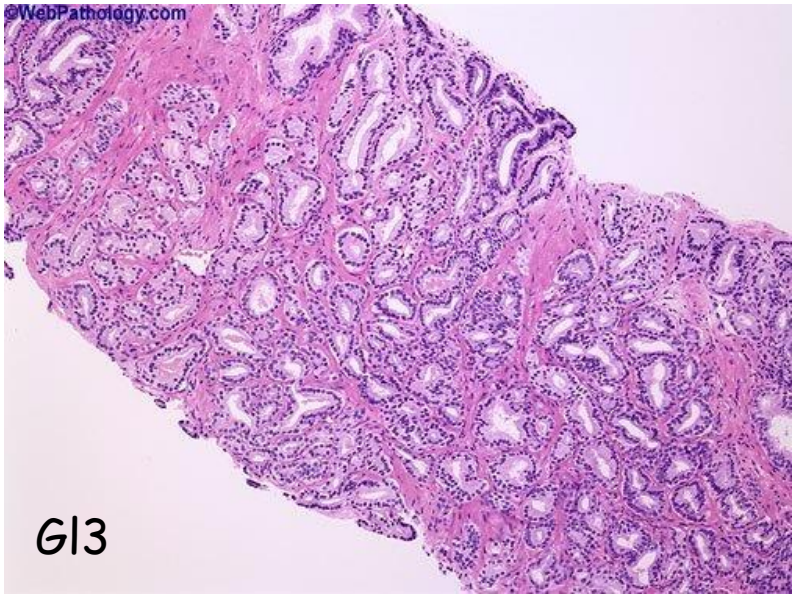
- Tubule formation
  0-10% 10-70% >70%
- Nuclear polymorphism
  slight- moderate- marked
- Mitosis
  /10 high power field







Epstein, 2010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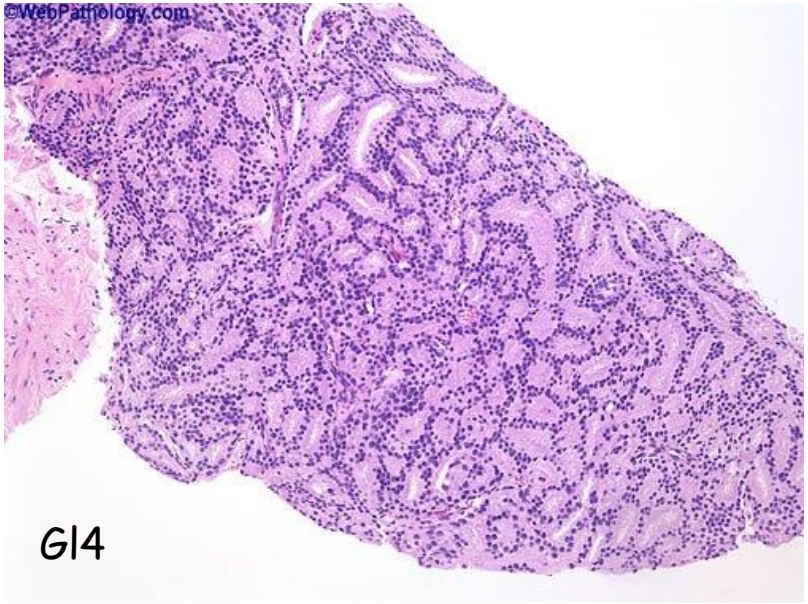
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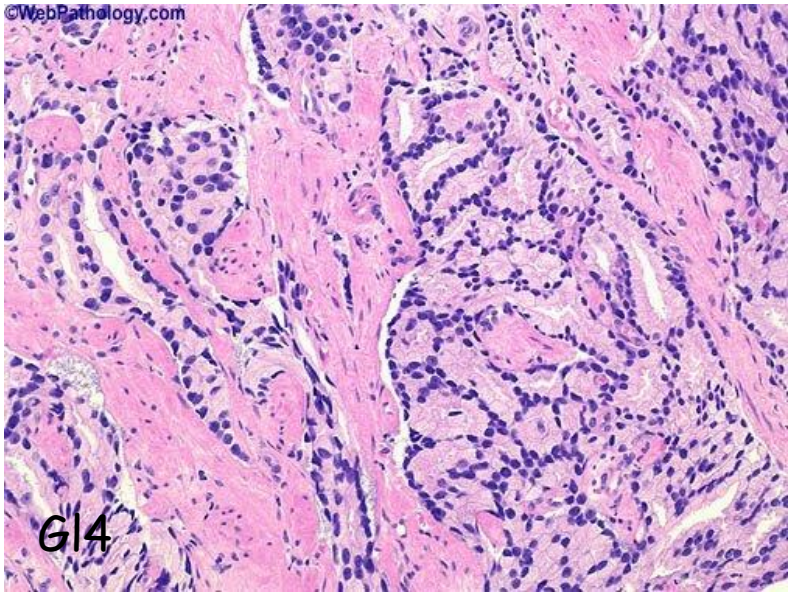
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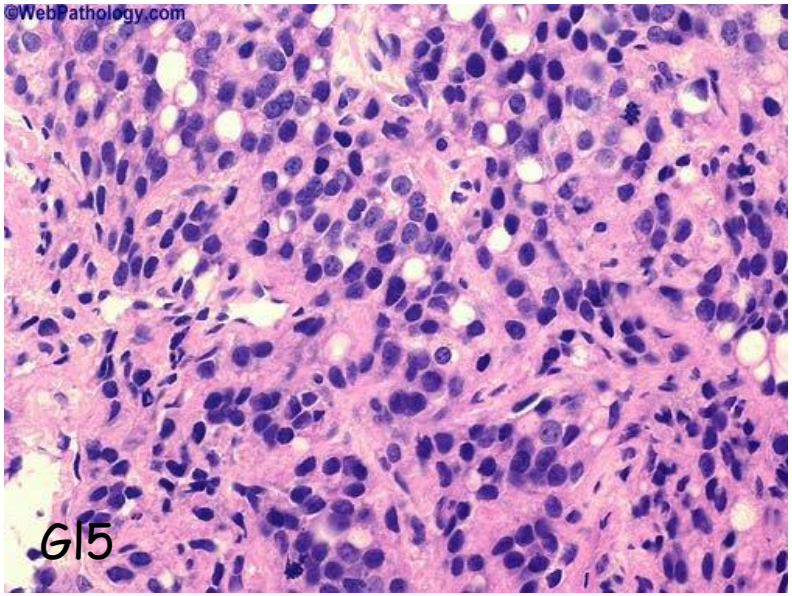
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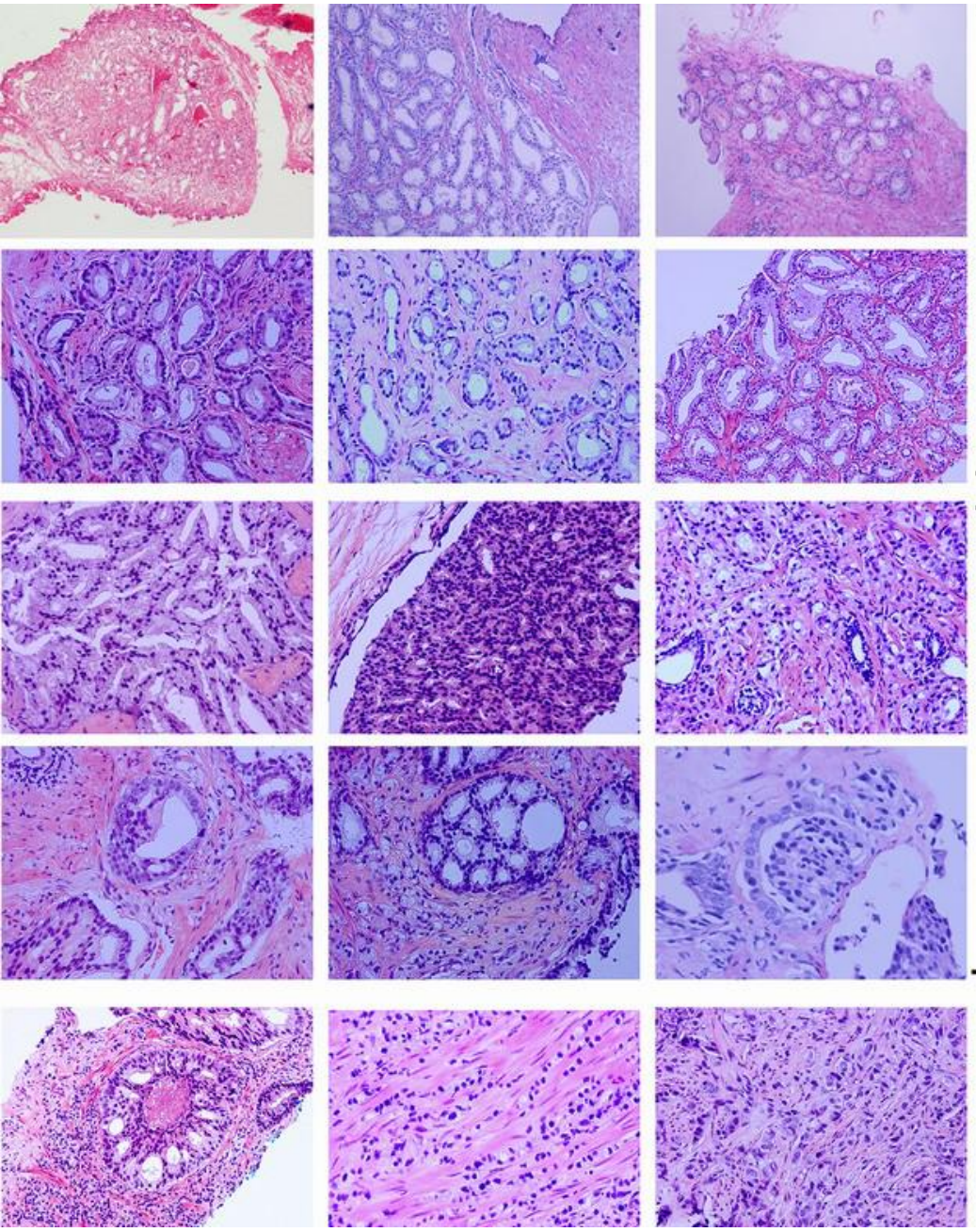
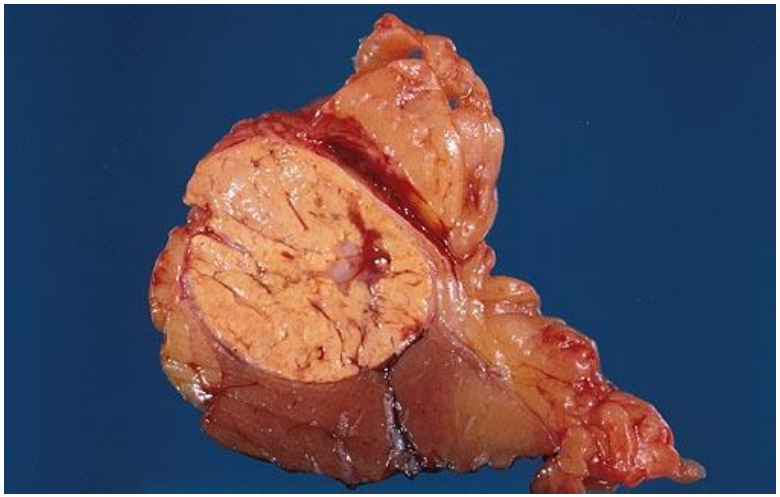
Gl5

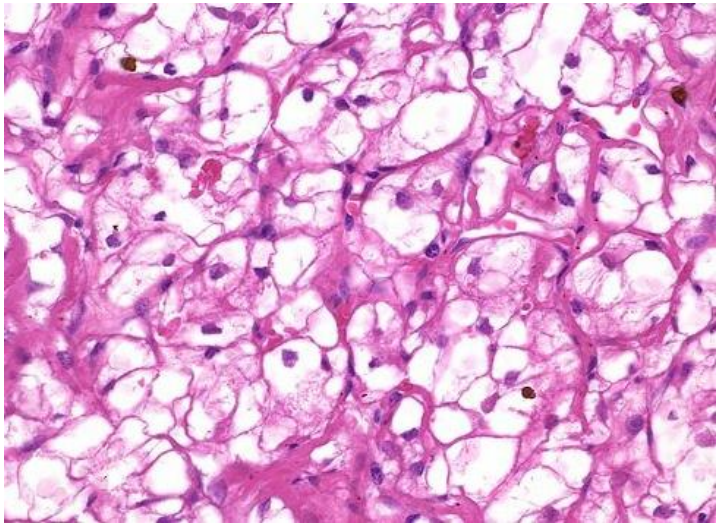


Gleason patterns 1–3 distinct, discrete, individual glands	**Gleason score ≤6**	**Grade group I**
	Gleason score 3+4=7	**Grade group II**
Gleason pattern 4 fused, cribriform, or poorly-formed glands, or glomerularion	**Gleason score** 4+3=7	**Grade group III**
	Gleason score 4+4=8 3+5=8 5+3=8	**Grade group IV**
Gleason pattern 5 comedo necrosis, cords, sheets, solid nests, single cells	**Gleason score** 4+5=9 5+4=9 5+5=10	**Grade group V**

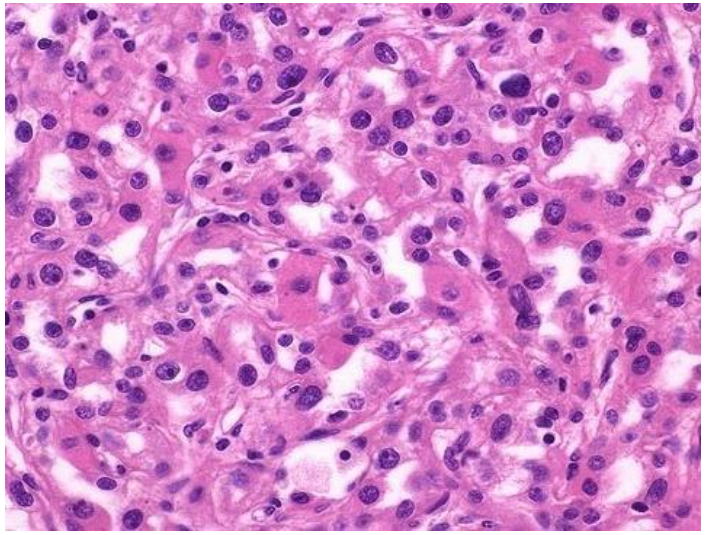
http://cjcr.amegroups.com/article/view/9260/9985

Renal cell carcinoma





Fuhrman grade 1



Fuhrman grade 3

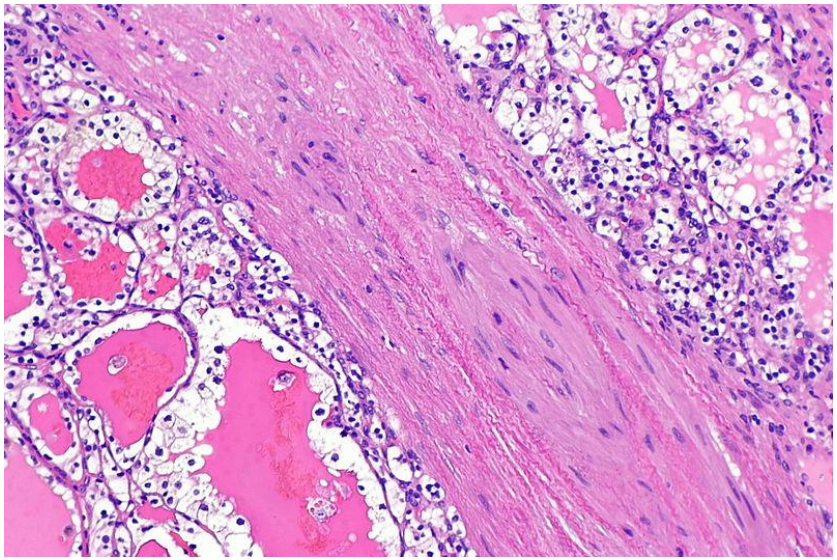
ISUP renal cell carcinoma Grade definitions

Grade 1 - nucleoli absent/very small at 400x.

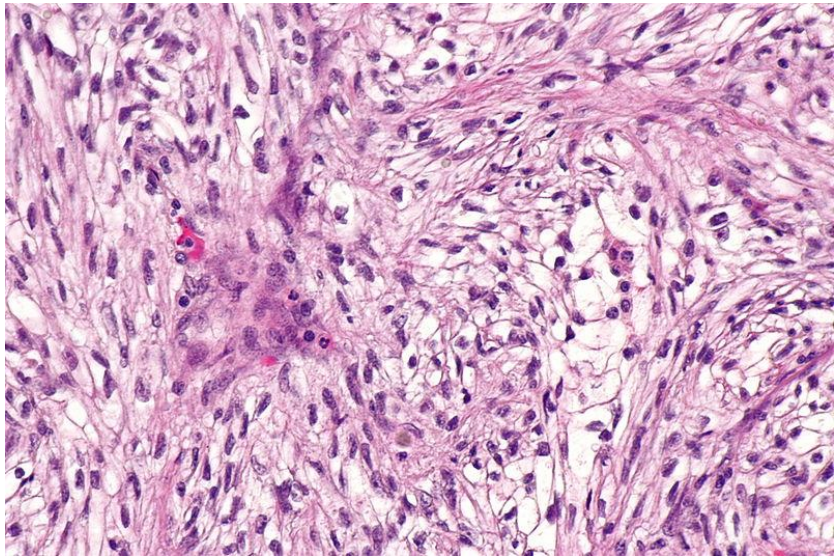
Grade 2 - nucleoli seen with 400x, but not at 100x.

Grade 3 - nucleoli seen at 100x,

Grade 4 - extreme nuclear pleomorphism (esp. nuclear enlargement) *or sarcomatoid differentiation*



Grade 2

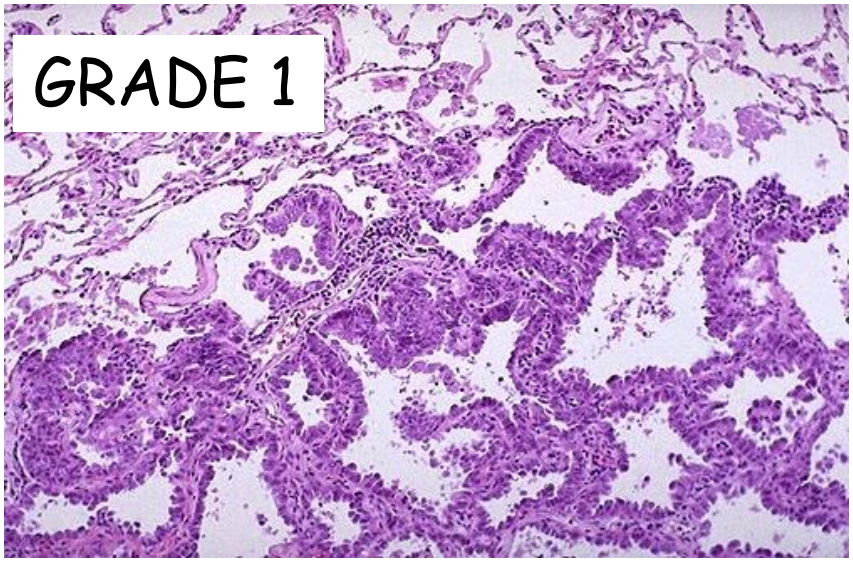


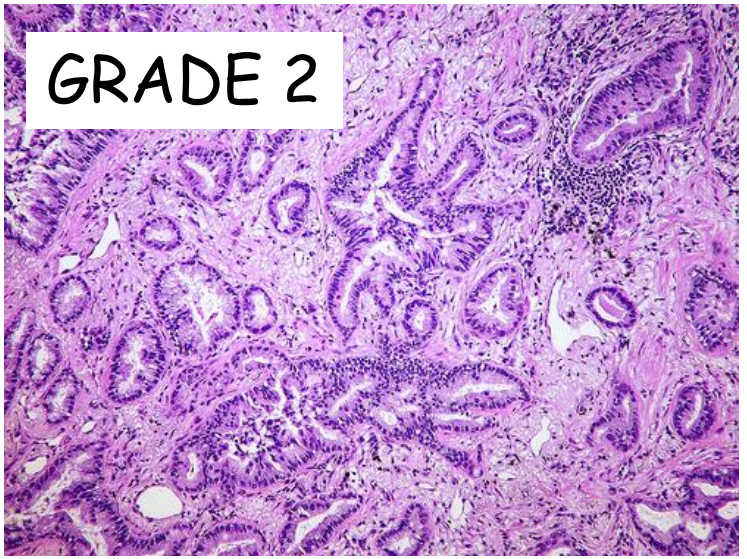
Grade 4

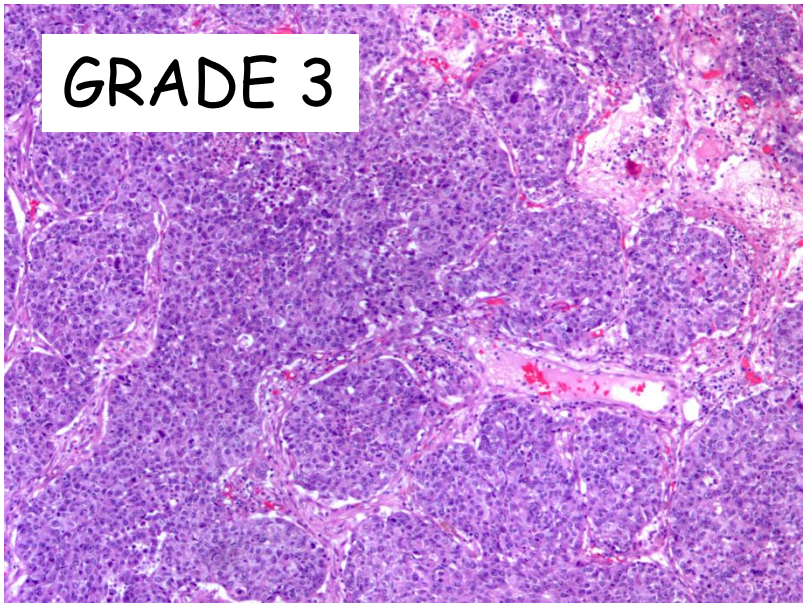
Lung adenocarcinoma

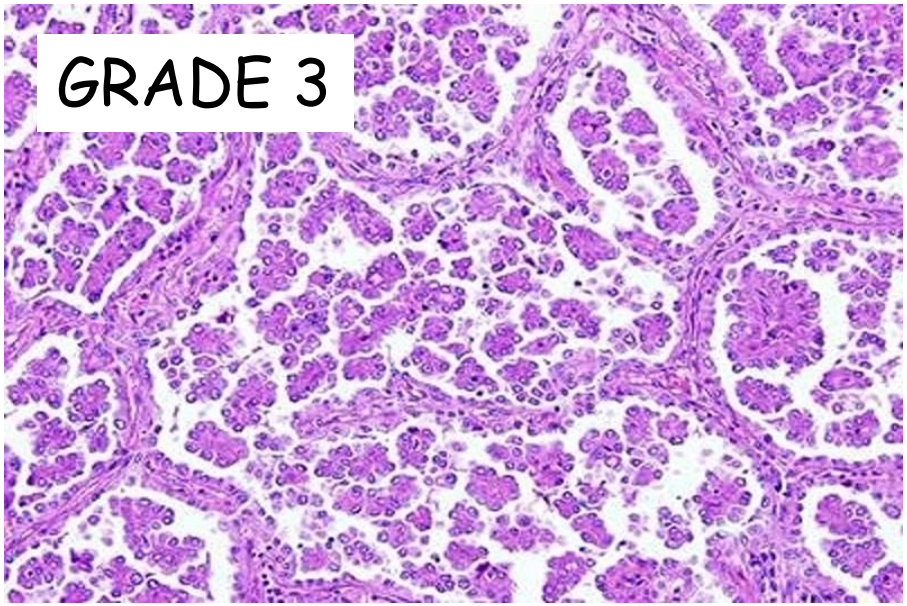
- ARCHITECTURAL GRADE: „...grading according to the single most predominant pattern appears to be a simple and sufficient approach. „
- GRADE 1 *„lepidic" growth pattern*
- GRADE 2 *acinar and papillary*
- GRADE 3 *solid and micropapillary*

Travis et al . Journal of Thoracic Oncology 1243 ® • Volume 10, Number 9, September 2015


GRADE 1


GRADE 2


GRADE 3


GRADE 3

T - N - M

Tumor - Node - distant Metastasis

Defines the EXTENT of the tumor or the systemic neoplastic disease

- T: Size/extent of the primary tumor
- N: Regional lymph node metastasis
- M: Distant metastasis

UICC International Union Against Cancer

global cancer control

TNM

Classification of Malignant Tumours

SEVENTH EDITION

EDITED BY

LESLIE SOBIN | MARY GOSPODAROWICZ | CHRISTIAN WITTEKIND

UICC

UNION FOR INTERNATIONAL CANCER CONTROL

TNM Classification of MALIGNANT TUMOURS

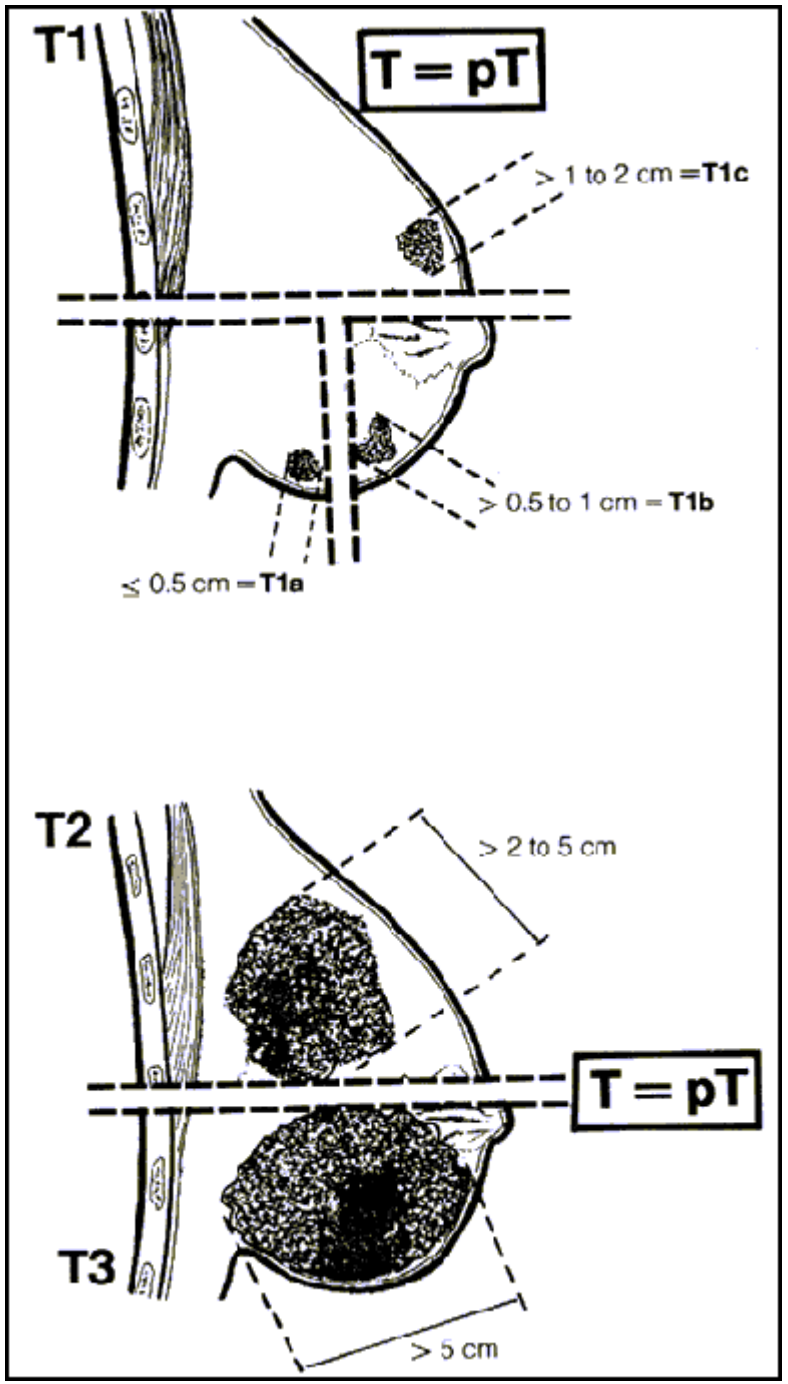
Eighth Edition

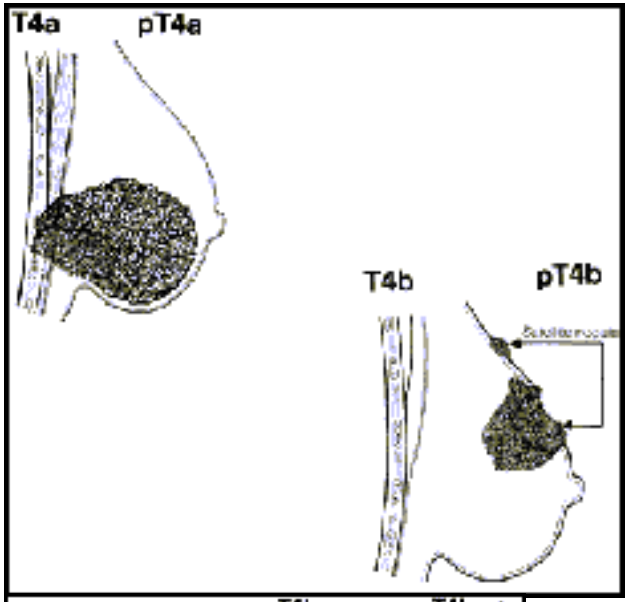
Edited by James D. Brierley, Mary K. Gospodarowicz and Christian Wittekind

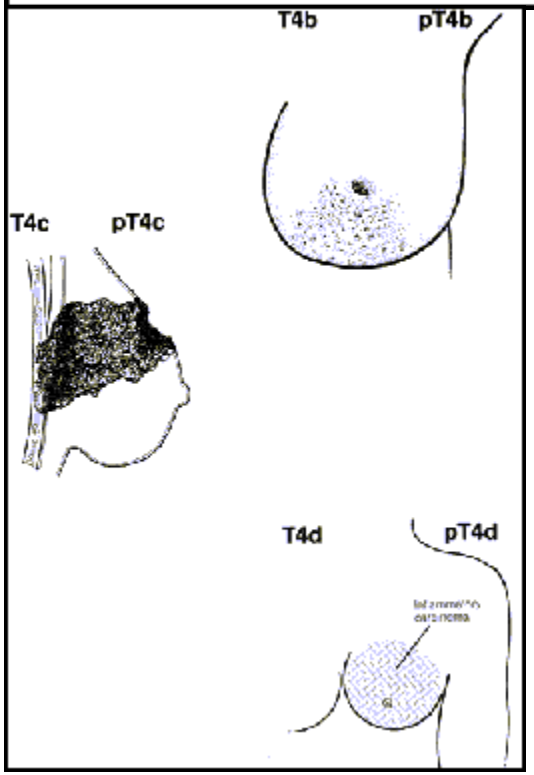
WILEY Blackwell

- (TX) T0, Tis, T1, T2, T3, T4
- (NX) N0, N1, N2, N3
- (MX) M0, M1

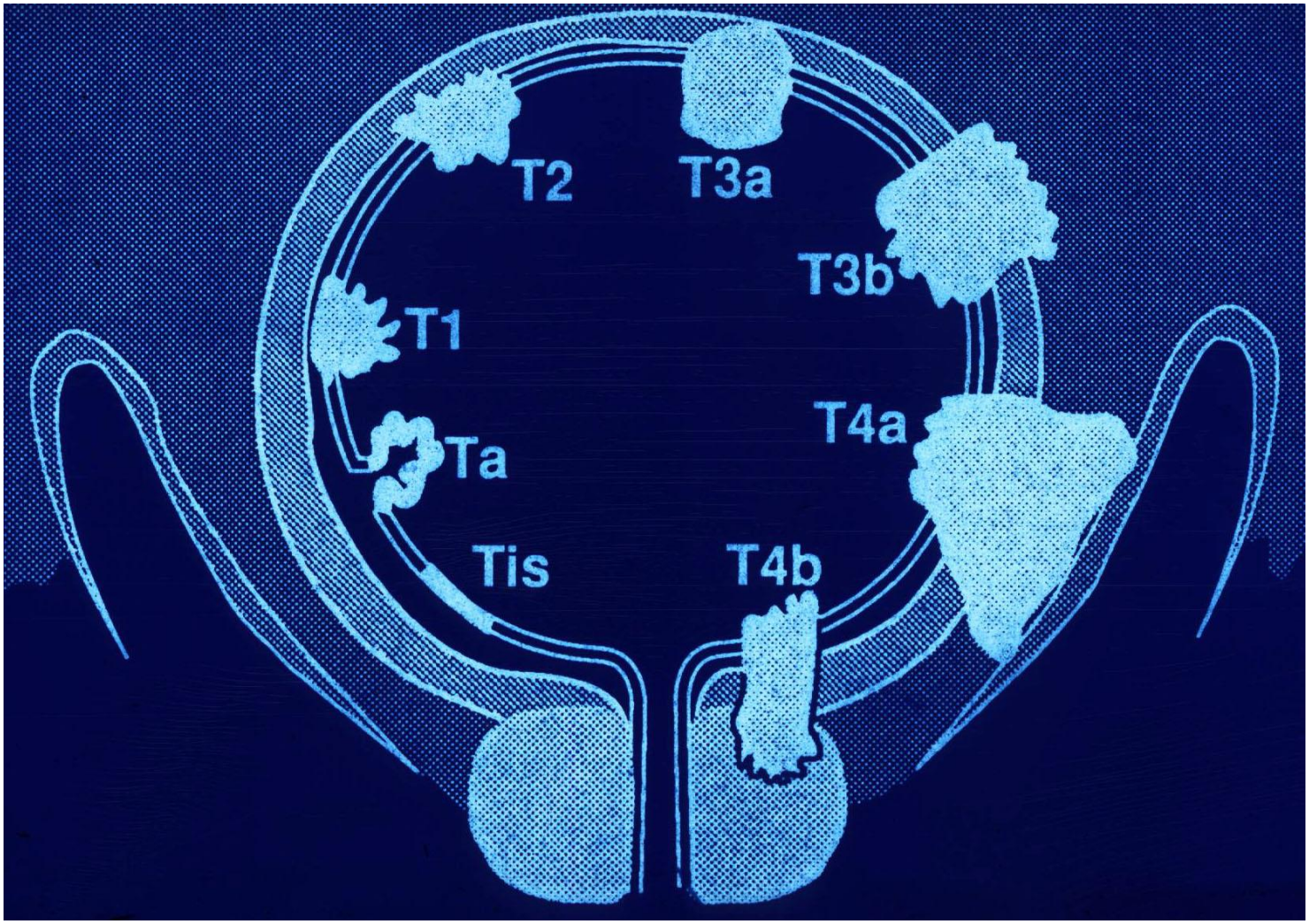
- cTNM: clinical
- pTNM: pathological
- rTNM: recurrent tumor
- aTNM: autopsy
- y TNM: following primary systemic oncotherapy
- (m): multiplex primary tumor


T1
T = pT
> 1 to 2 cm = T1c
> 0.5 to 1 cm = T1b
≤ 0.5 cm = T1a
T2
> 2 to 5 cm
T = pT
T3
> 5 cm

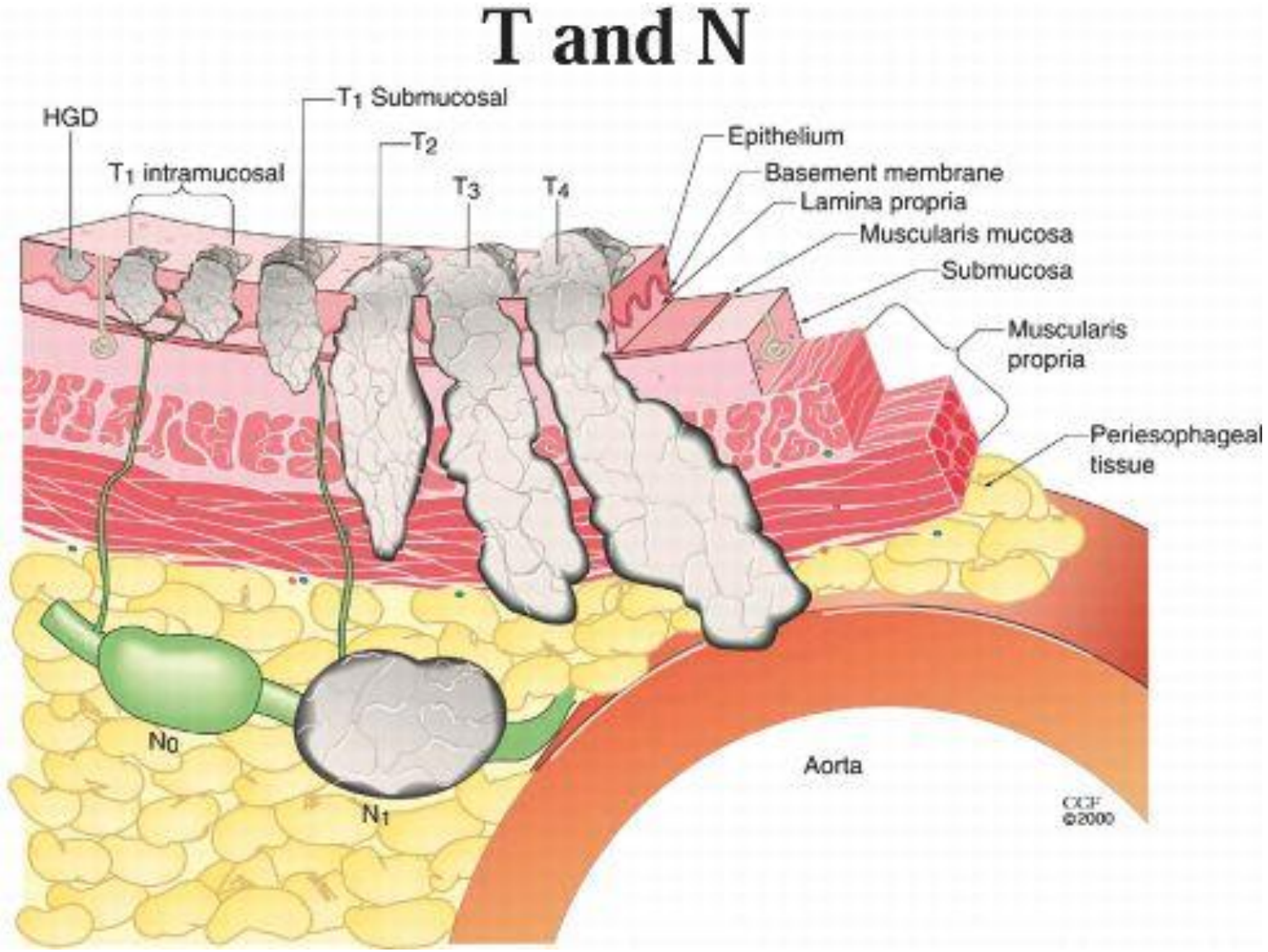

T4a
pT4a
T4b
pT4b


T4b
pT4b
T4c
pT4c
T4d
pT4d

pT

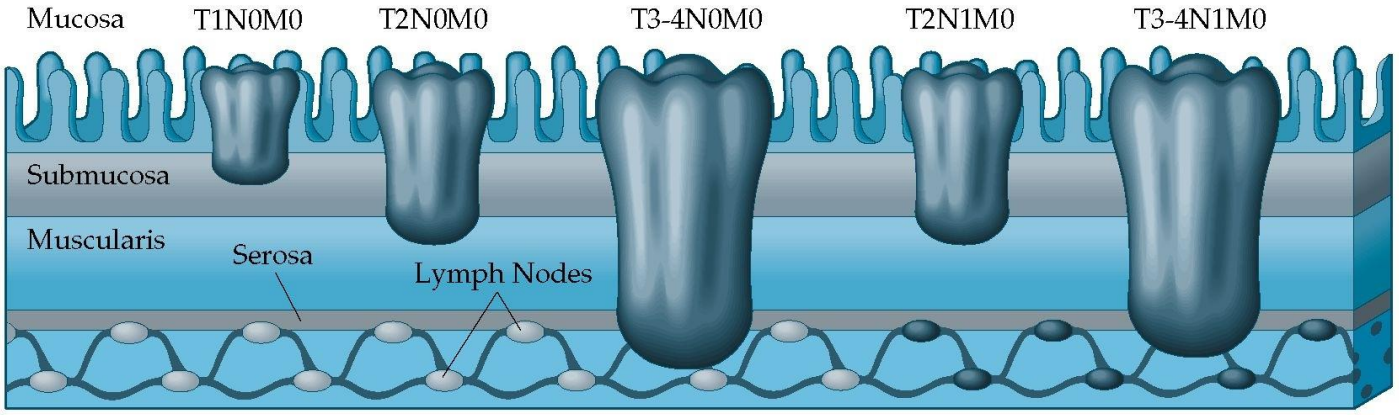


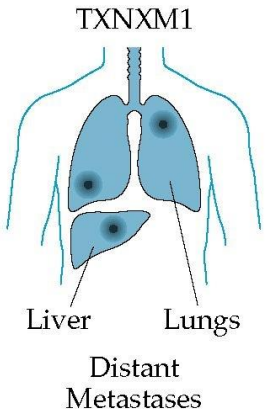
Urinary bladder cancer



Esophageal cancer

http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/hematology-oncology/esophageal-cancer/

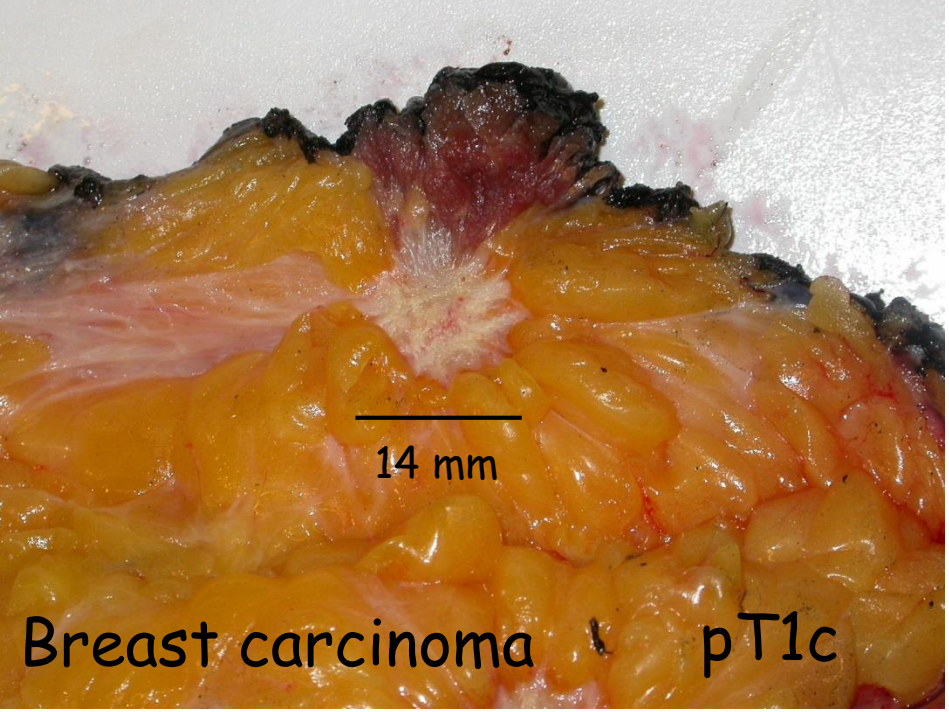




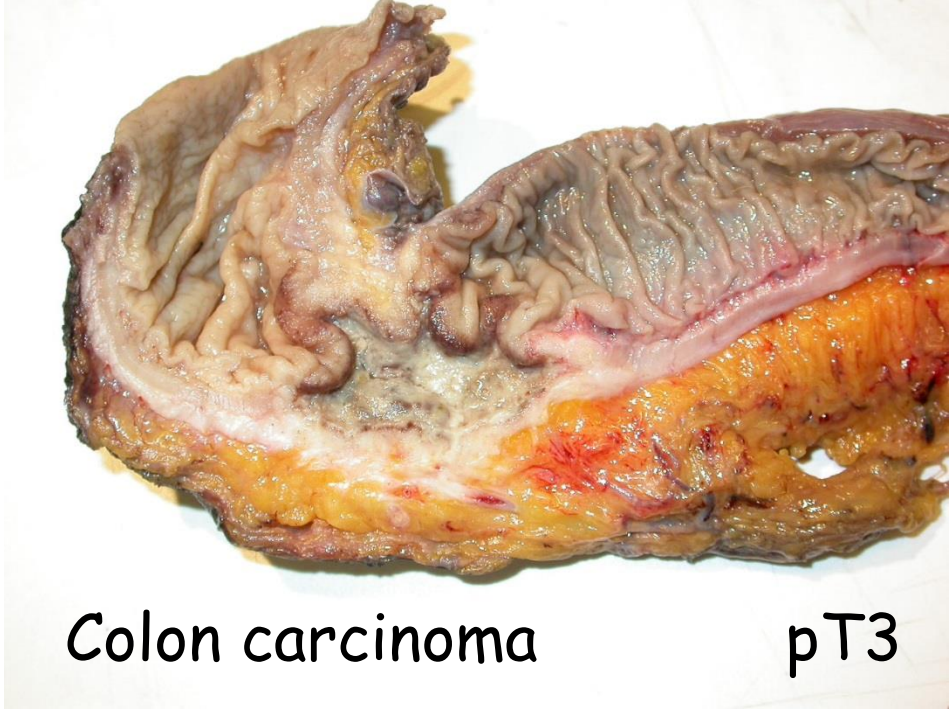
TNM Stage	*Description*
T1N0M0	Infiltration no deeper than submucosa
T2N0M0	Infiltration of muscularis; no penetration through colonic wall; no lymph node involvement
T3-4N0M0	Extension through colonic wall; no lymph node involvement
T2N1M0	Infiltration of muscularis; no penetration through colonic wall; lymph node involvement
T3-4N1M0	Extension through colonic wall; lymph node involvement
AnyT AnyN M1	Distant metastases

Colorectal cancer

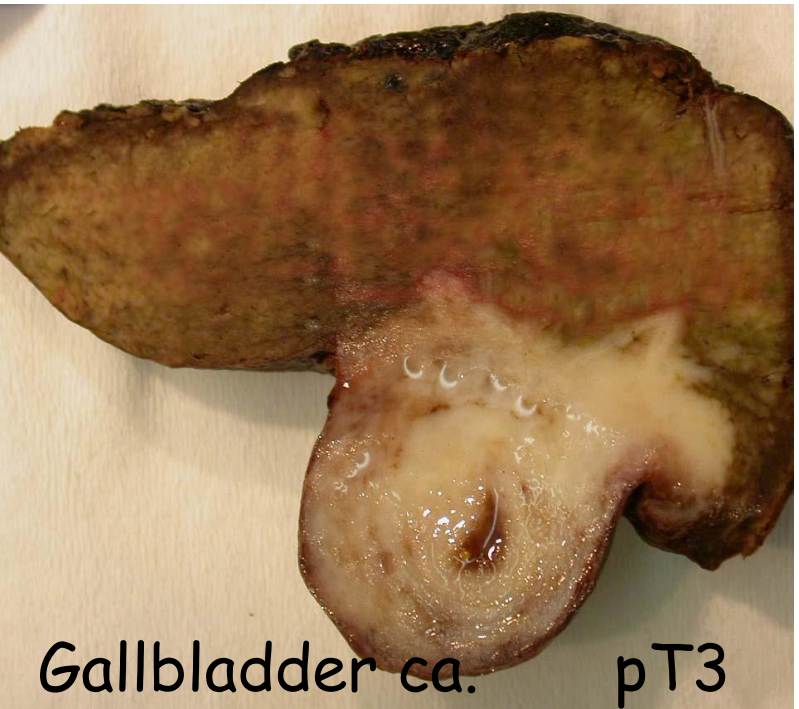
acp-medicine/colorectal-cancer-part-3



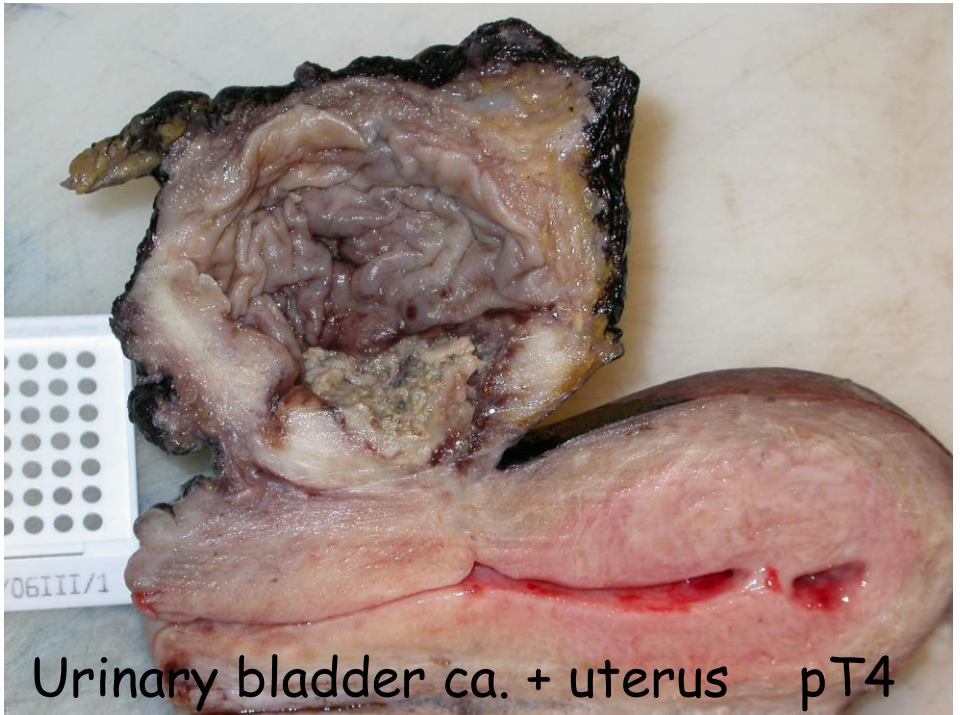
Breast carcinoma pT1c



Colon carcinoma pT3



Gallbladder ca. pT3



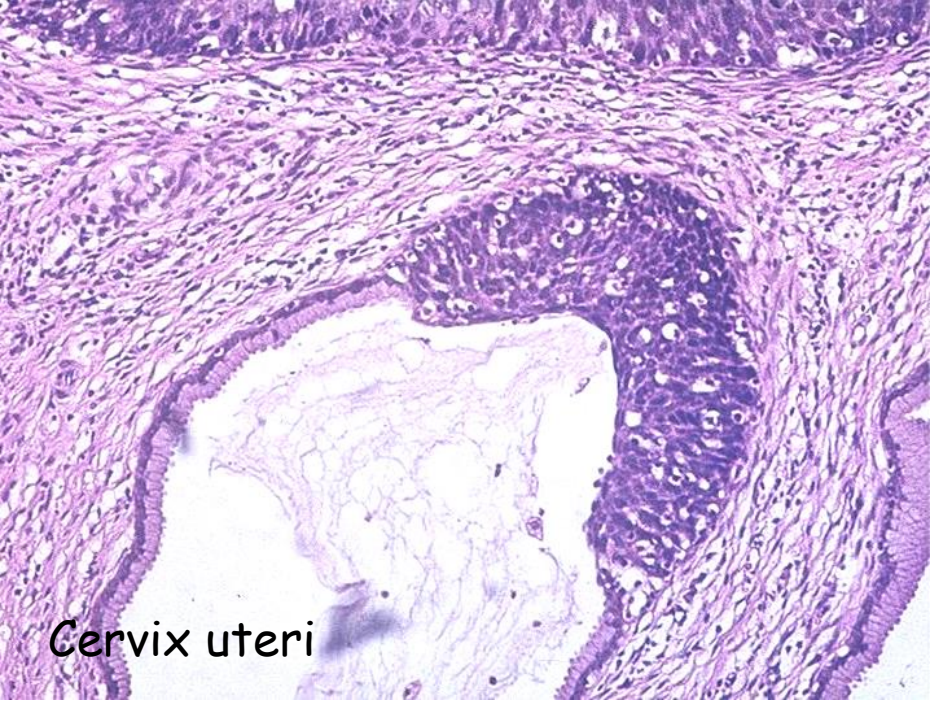
Urinary bladder ca. + uterus pT4

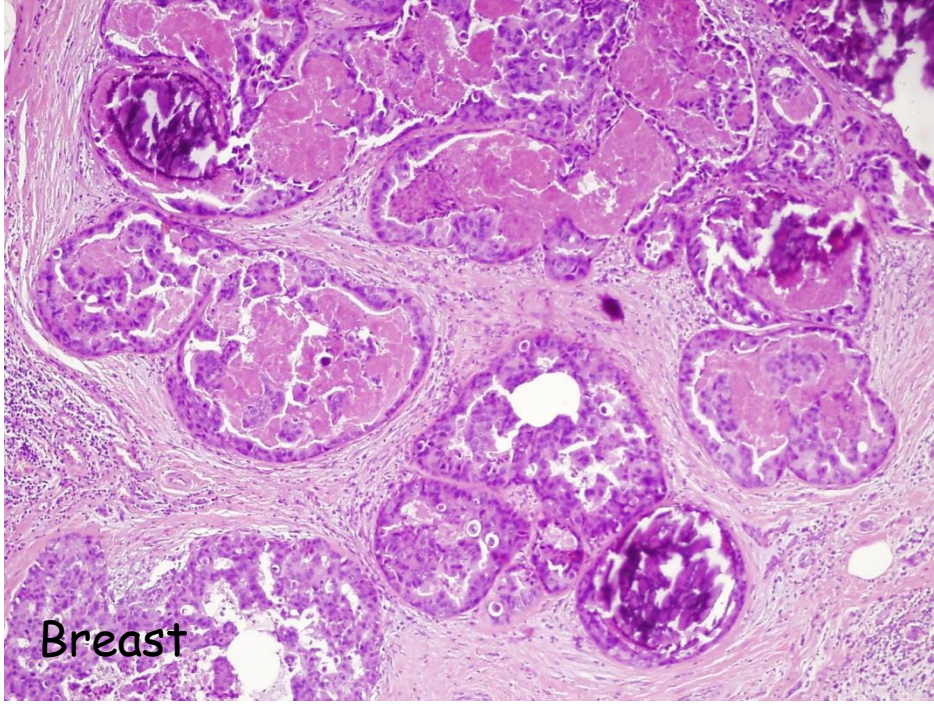
Tis: Carcinoma in situ

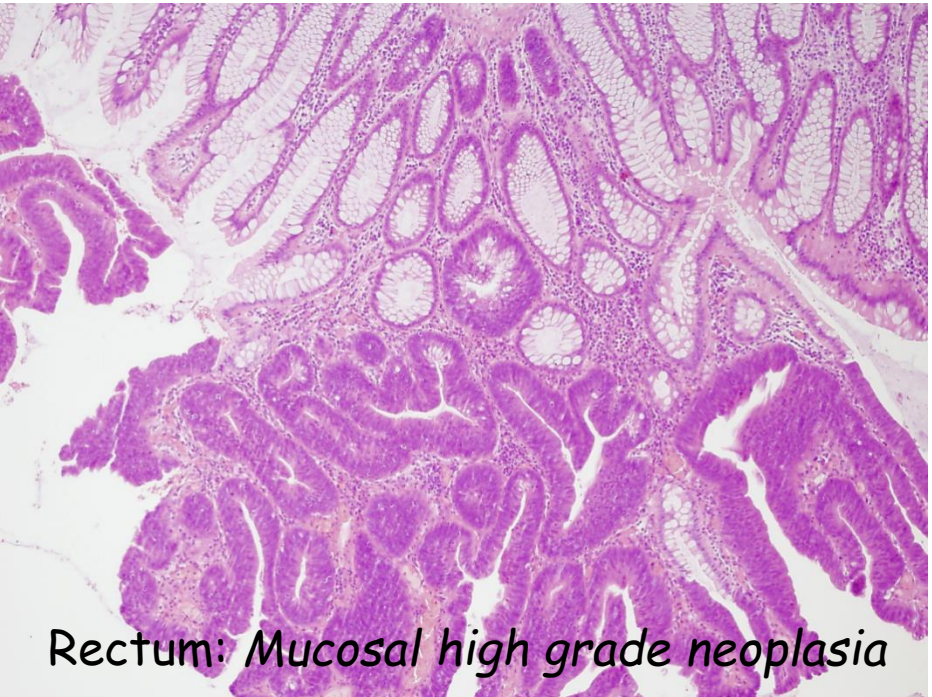
Carcinoma is confined to the epithelium - the basement membrane is intact

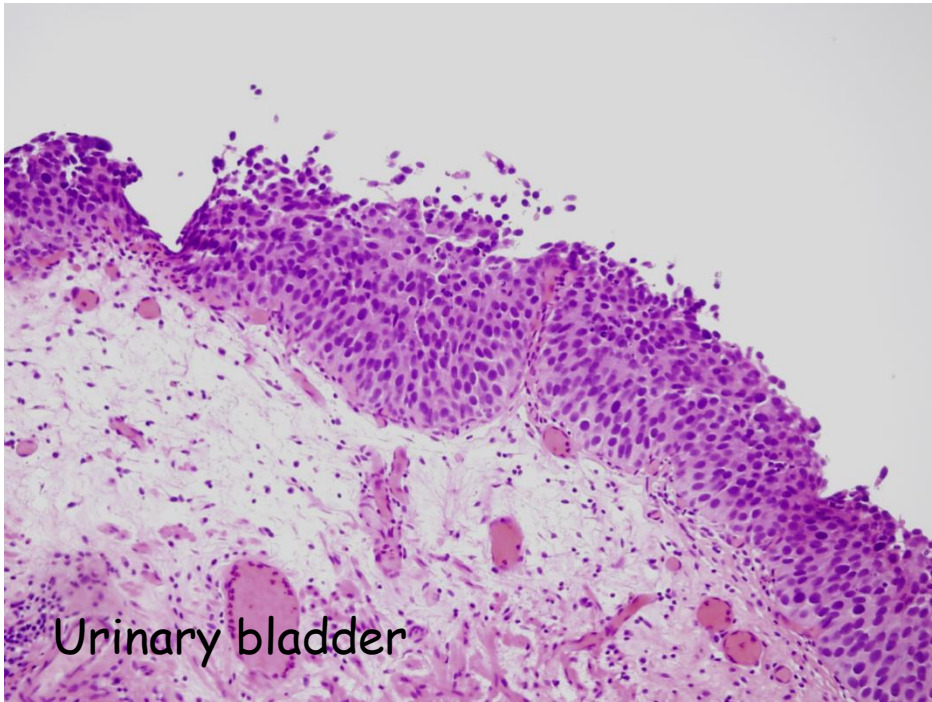
- Cytologically malignant
- Does not infiltrate
- Does not metastasise

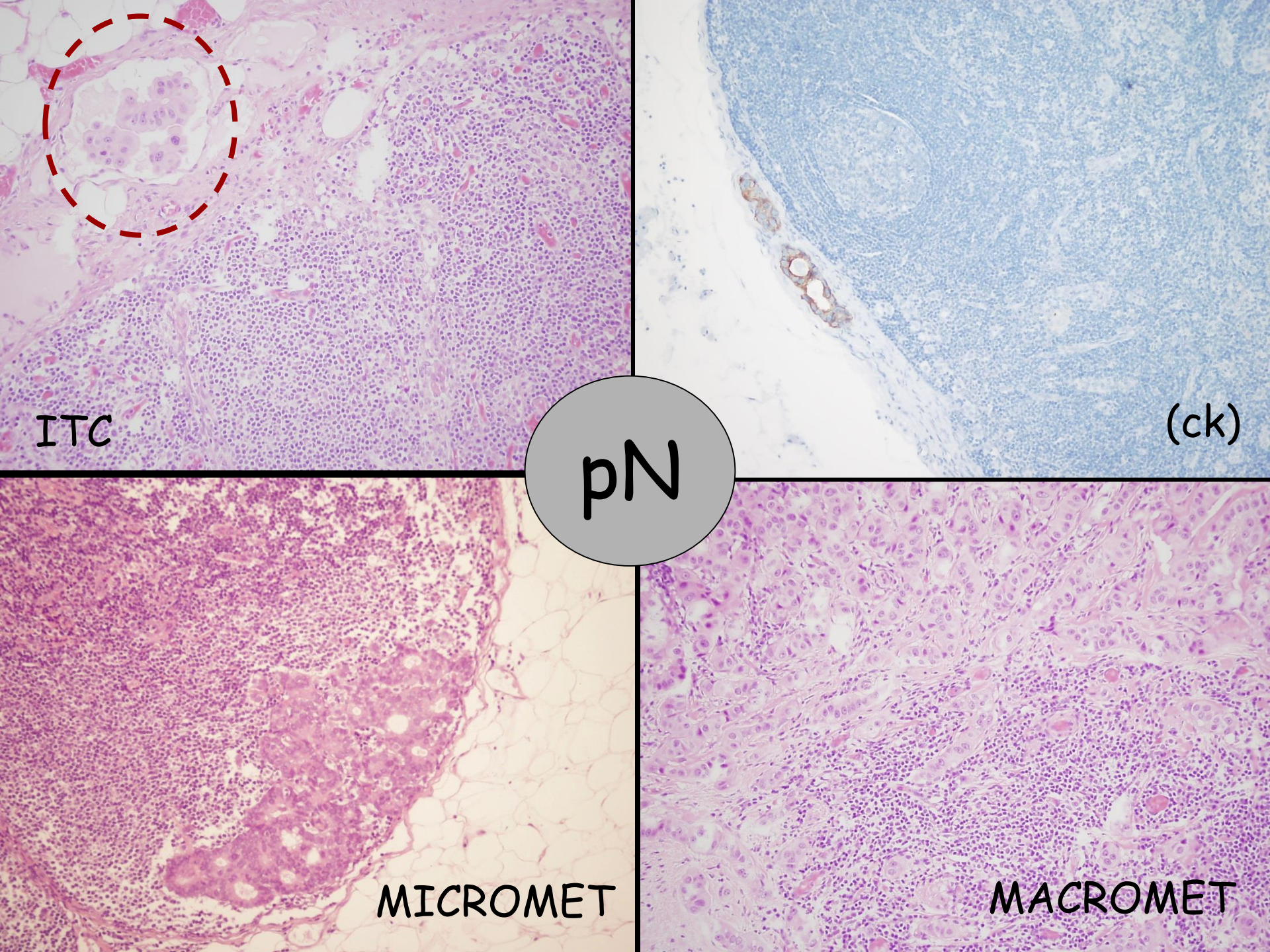
Importance of SCREENING: cervix, breast, colon, skin, prostate, stomach


Cervix uteri

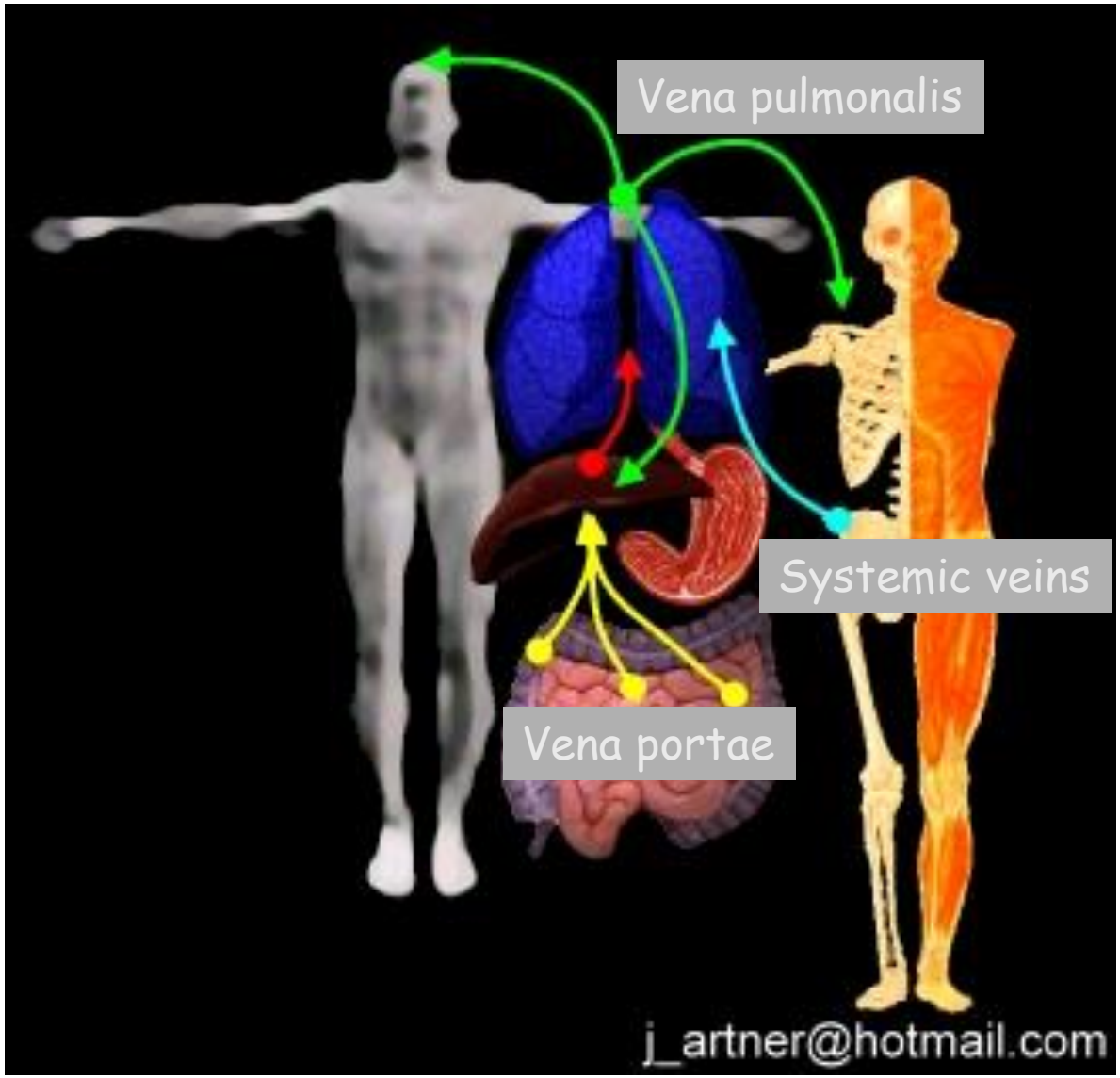

Breast

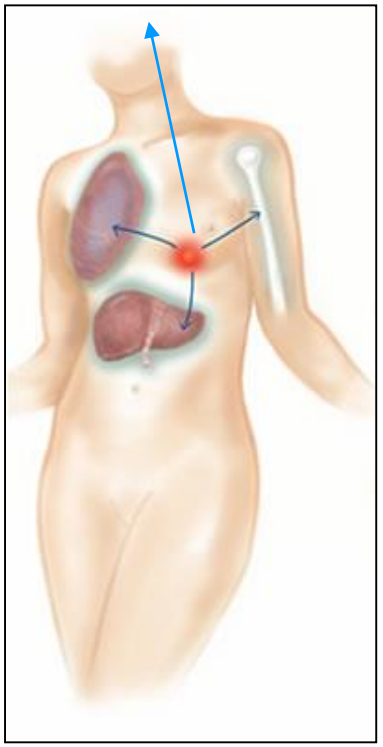

Rectum: *Mucosal high grade neoplasia*


Urinary bladder


ITC
(ck)
pN
MICROMET
MACROMET

M

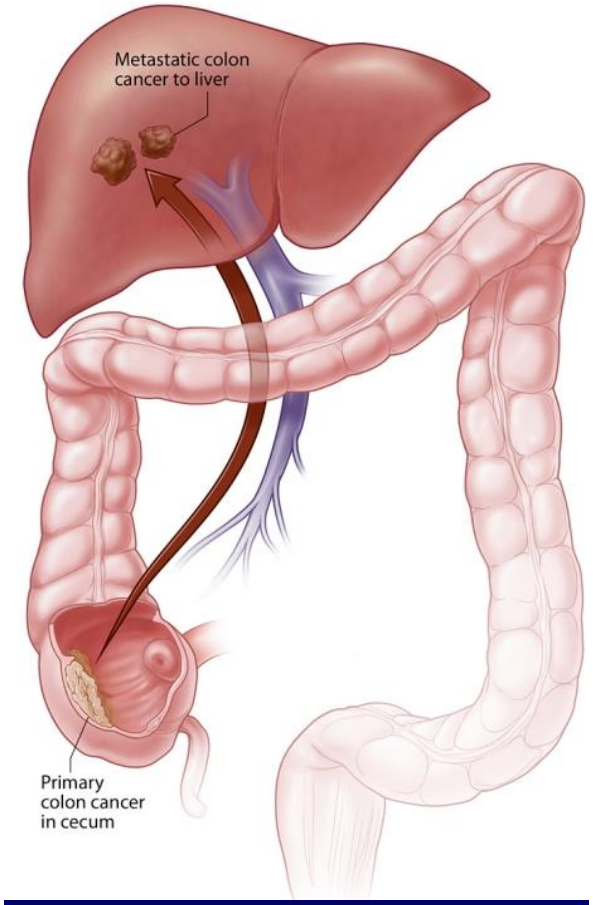

Vena pulmonalis
Systemic veins
Vena portae
j_artner@hotmail.com

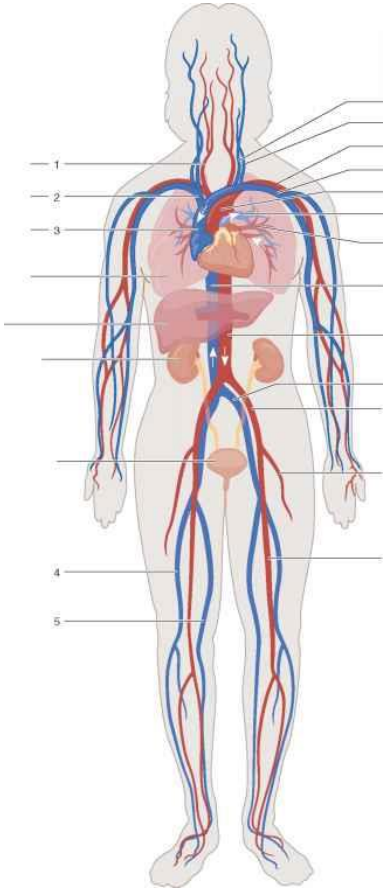


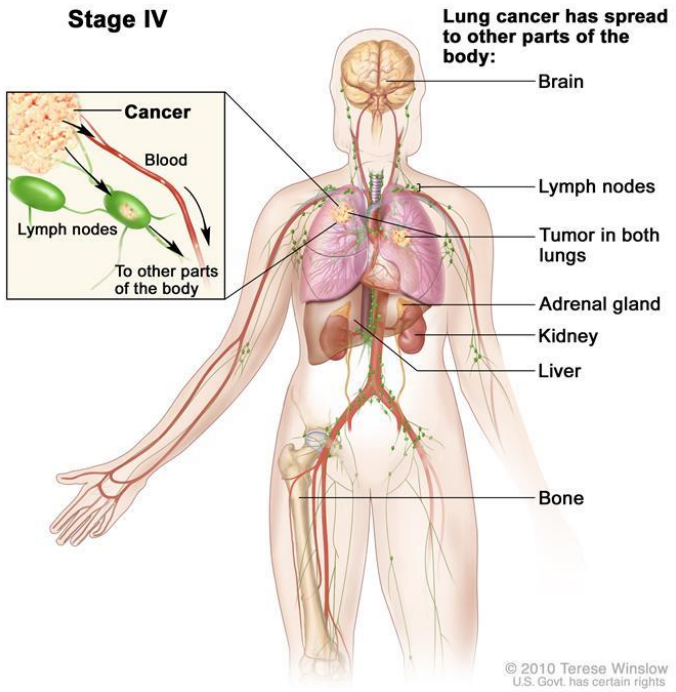
Portal vein

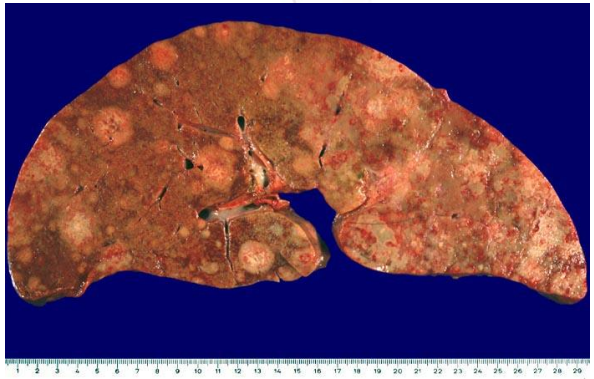
Vena cava – RV - Pulmonal artery

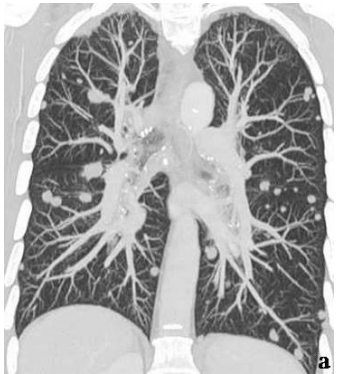
Vena pulmonalis – LV - Systemic arteries

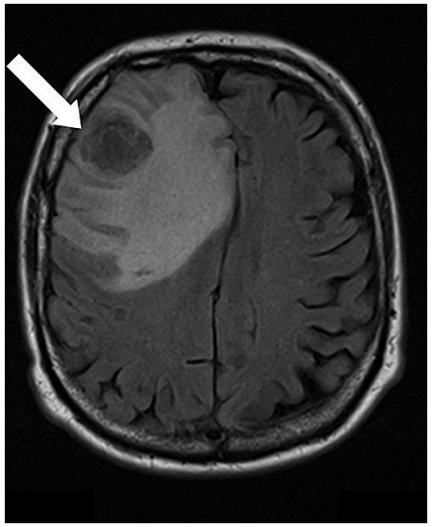


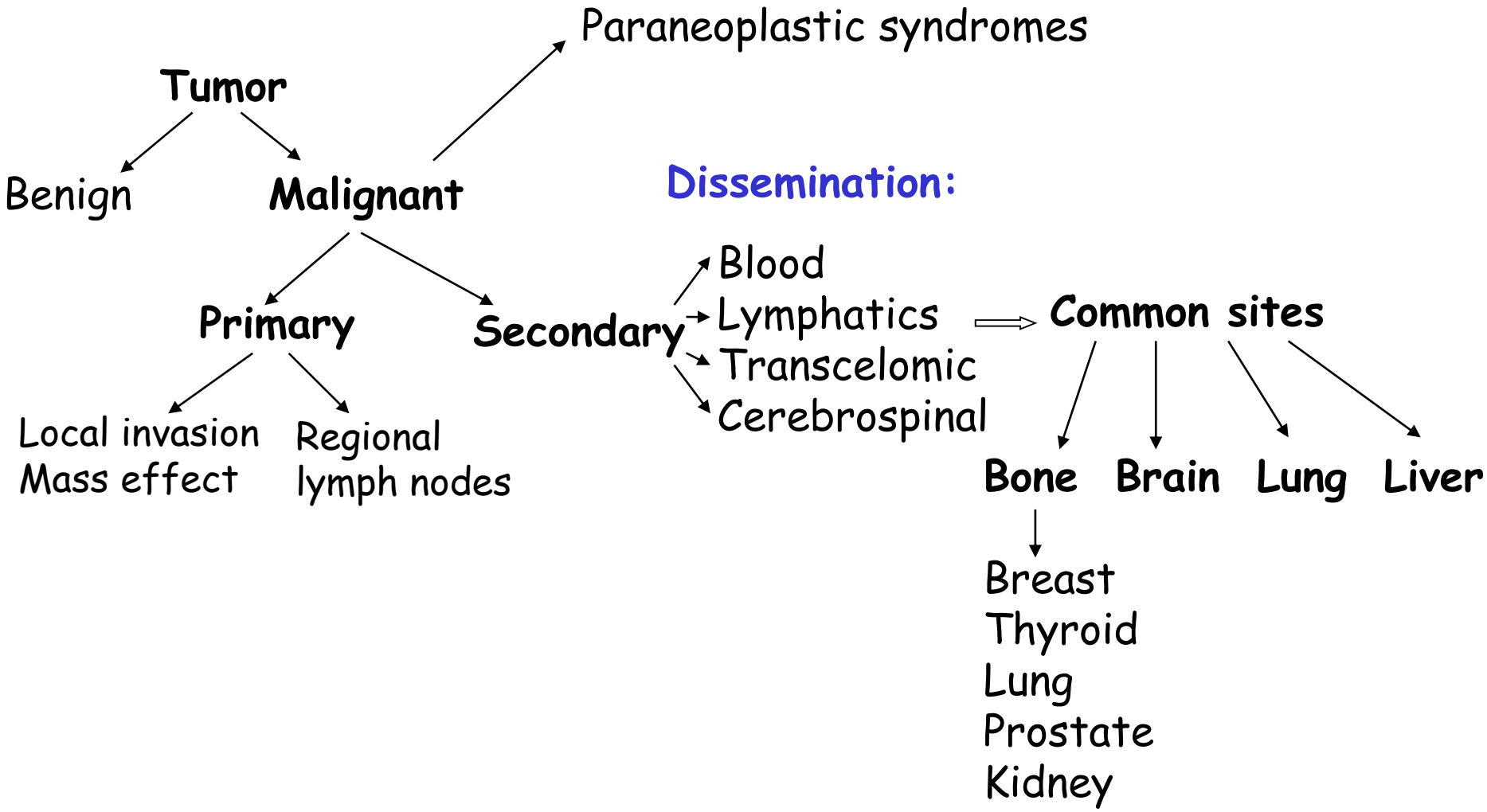




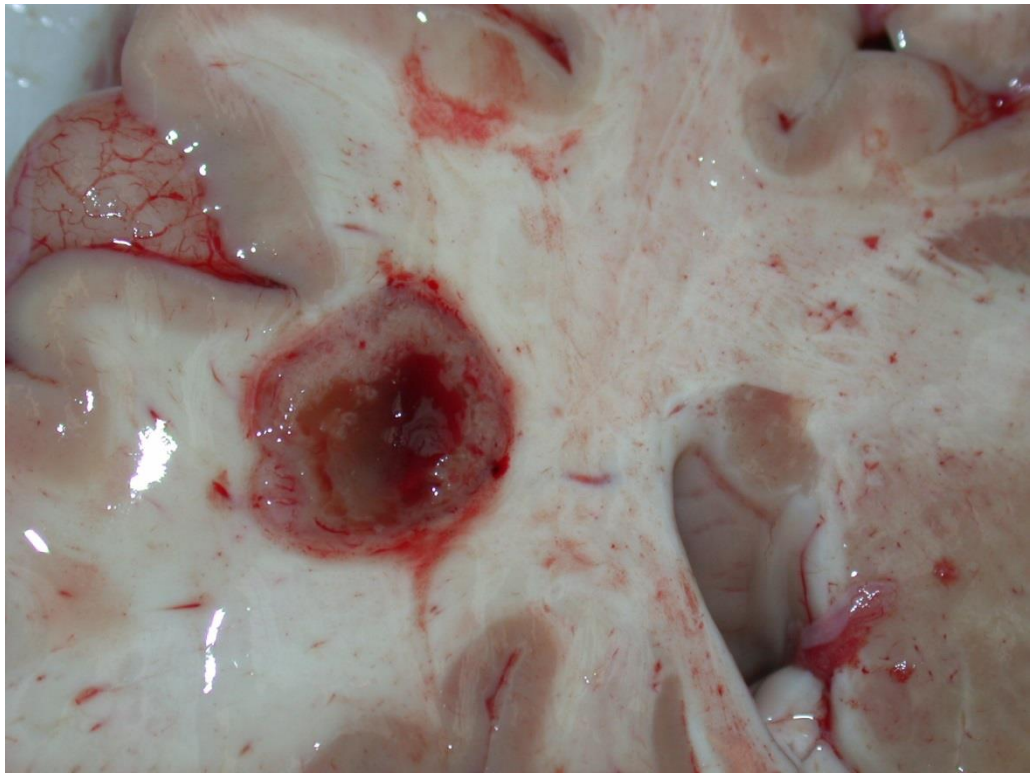






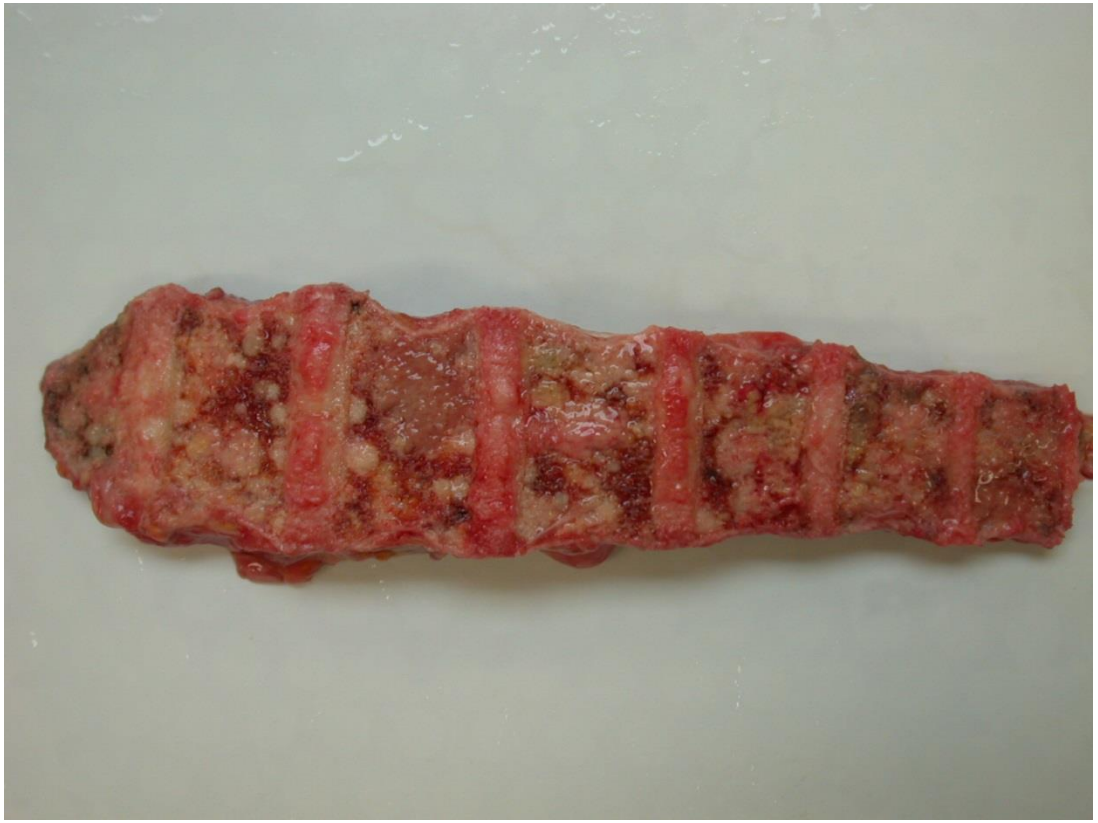

Paraneoplastic syndromes
Tumor
Benign
Malignant
Dissemination:
Primary
Secondary
Blood
Lymphatics
Transcelomic
Cerebrospinal
Common sites
Local invasion
Mass effect
Regional
lymph nodes
Bone
Brain
Lung
Liver
Breast
Thyroid
Lung
Prostate
Kidney

BRAIN METASTASIS



LUNG - and
BREAST CARCINOMA
MALIGNANT MELANOMA

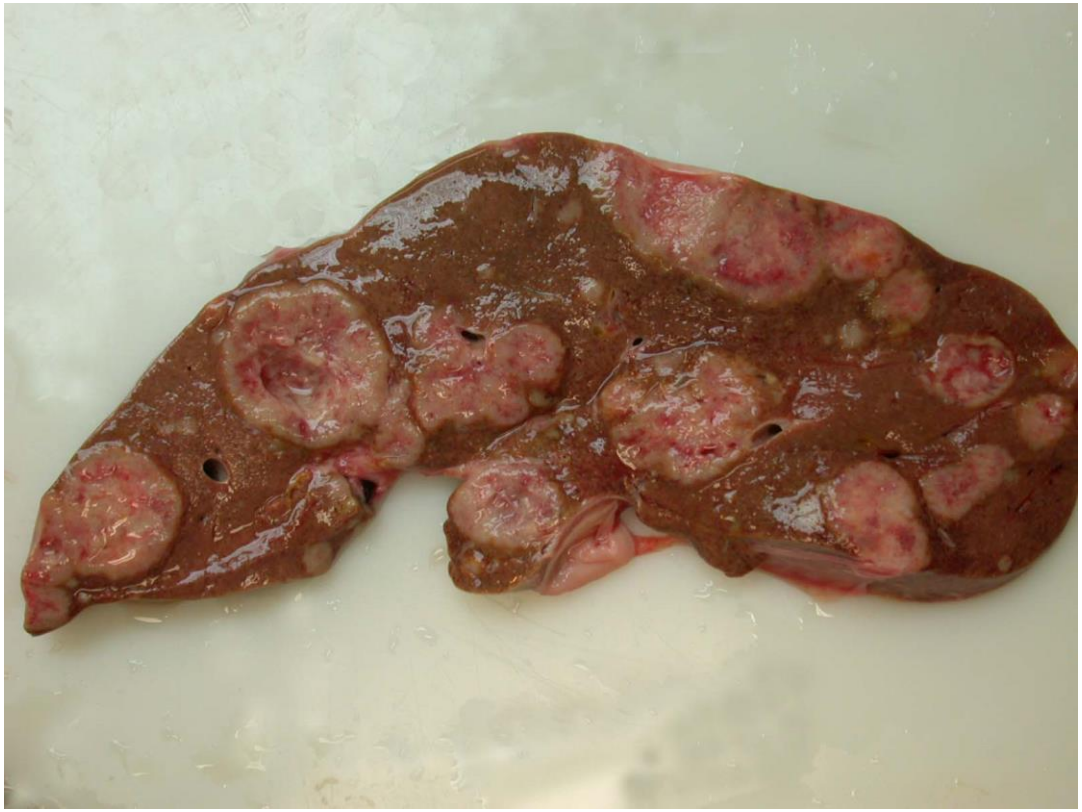
BONE METASTASIS



LUNG –
BREAST –
THYROID –
PROSTATE –
KIDNEY CARCINOMA

Note: prostate carinoma gives vertebral metastases via the Batson veins

LIVER METASTASIS



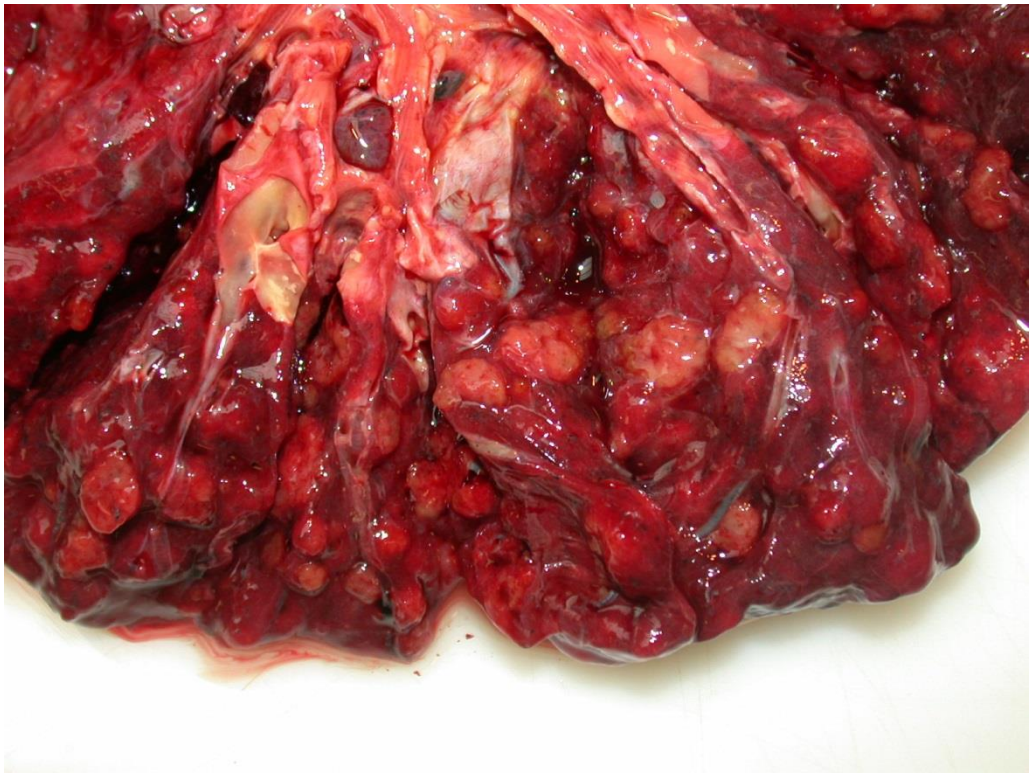
GASTROINTESTINAL –
LUNG –
BREAST CARCINOMA

MELANOMA

NEUROBLASTOMA

etc.

LUNG METASTASIS



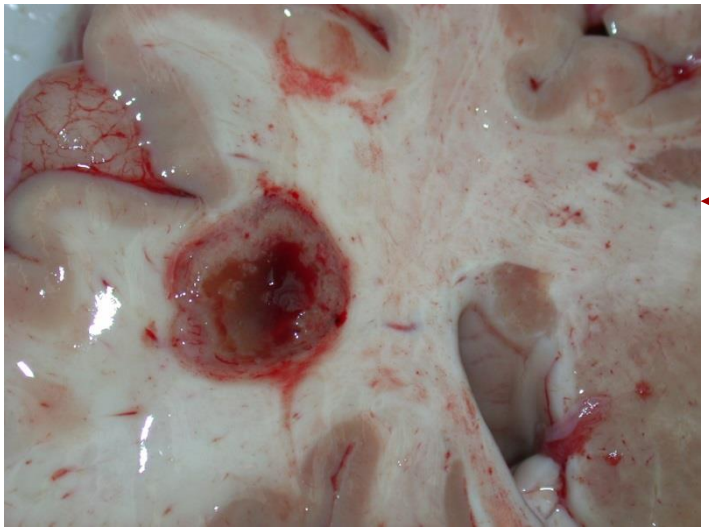
BREAST -
LIVER -
KIDNEY -
RECTUM CARCINOMA

GERM CELL TUMORS

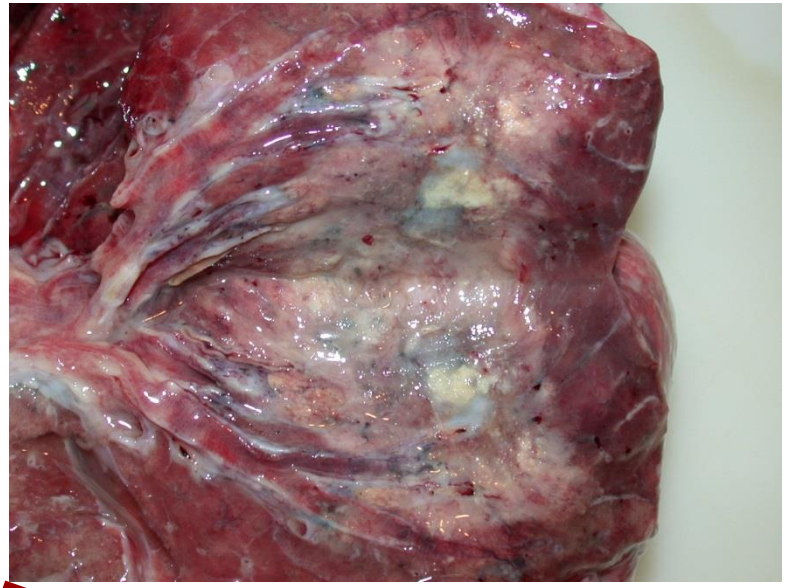
SOFT TISSUE SARCOMAS

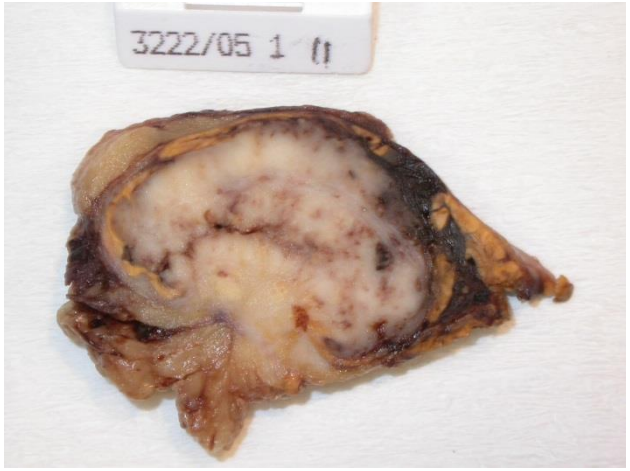
OSTEOSARCOMA

LUNG CANCER



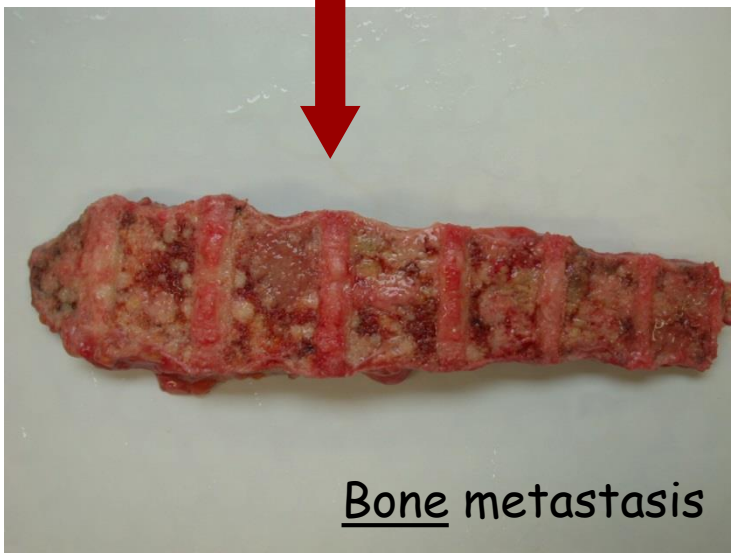
Brain metastasis



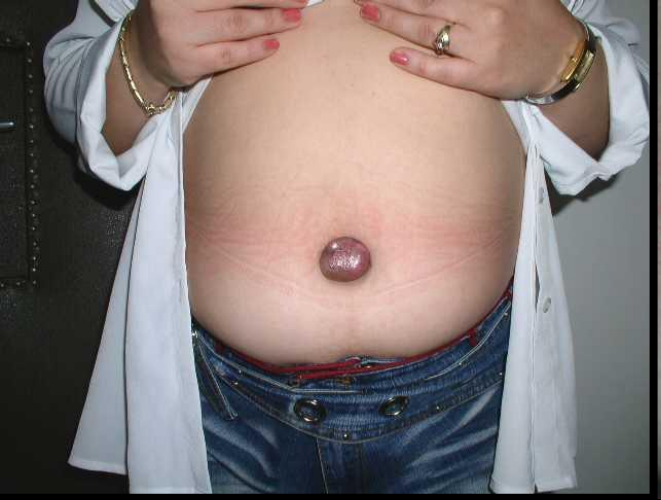


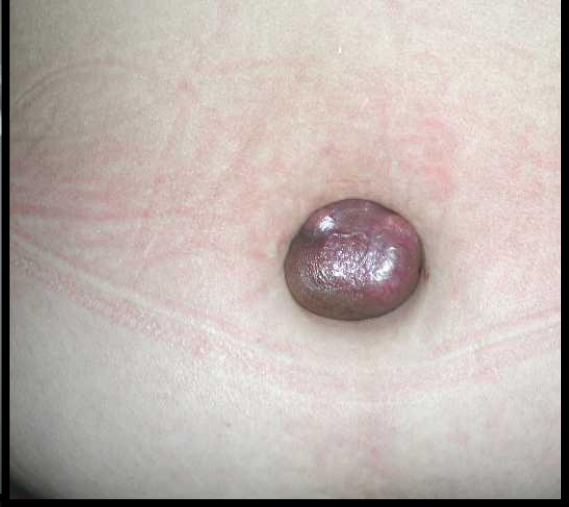
Adrenal metastasis

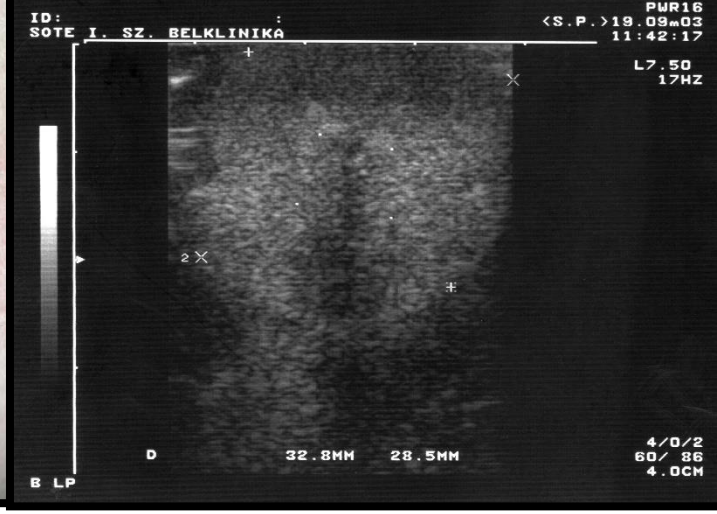
Liver met.

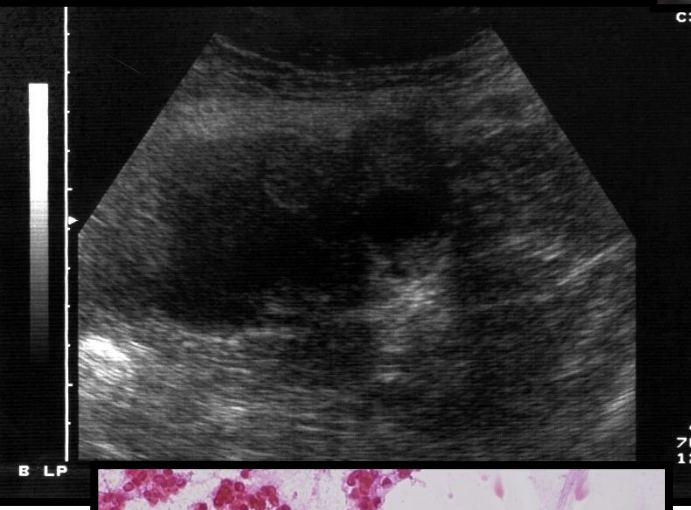


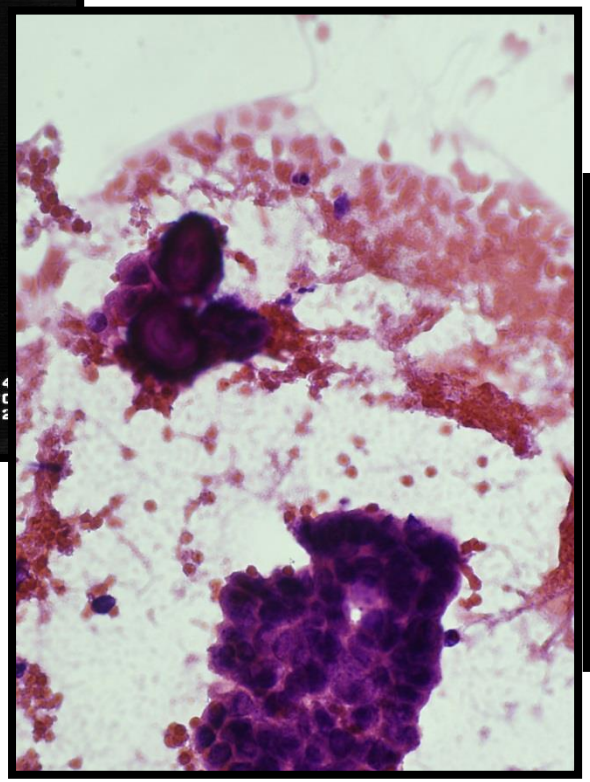
Bone metastasis



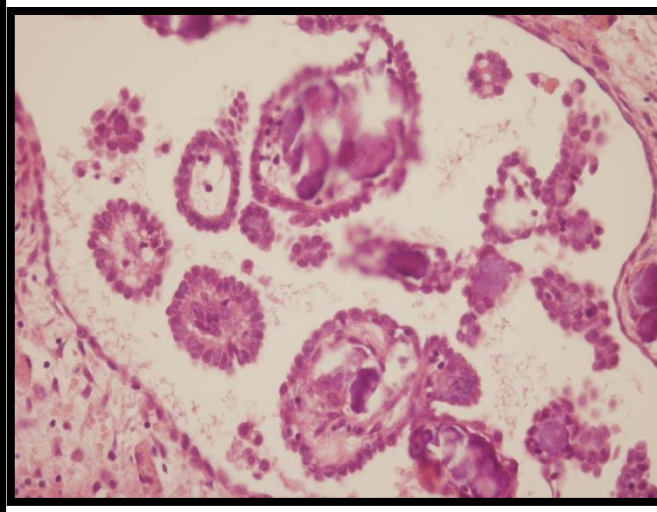


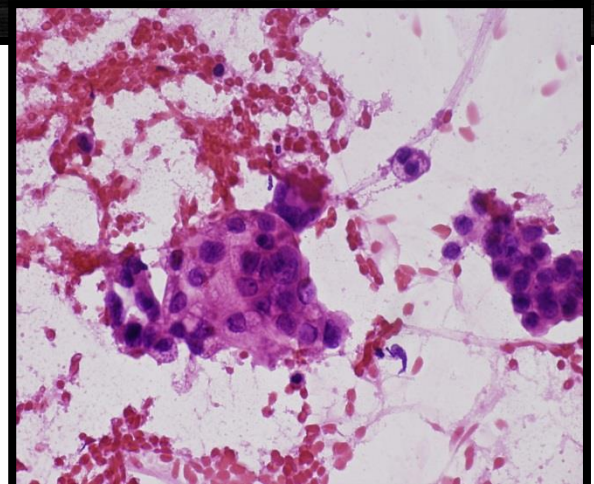






Sister Mary Joseph nodule





STAGE

GENERALLY: I - II - III - IV

STAGE 0 means in situ cancer

STAGE IV means distant metastasis

TNM STAGING OF LUNG CANCER

CHANGES MADE IN TNM 8th!!

Stage IA	T1	N0	M0
Stage IA1	T1mi,T1a	N0	M0
Stage IA2	T1b	N0	M0
Stage IA3	T1c ●	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b	N0	M0
Stage IIB	T1a-c, T2a,b	N1	M0
	T3	N0	M0
Stage IIIA	T1a-c, T2a,b	N2	M0
	T3	N1	
	T4	N0,N1	M0
Stage IIIB	T1a-c, T2a,b	N3	M0
	T3, T4	N2	M0
Stage IIIC	T3, T4	N3	M0
Stage IV	Any T	Any N	M1
Stage IVA	Any T	Any N	●M1a,b
Stage IVB	Any T	Any N	●M1c

M1 : Present
Separate metastatic tumor nodule(s) in the ipsilateral nonprimary-tumor lobe(s) of the lung also are classified M1

Tis : Carcinoma *in situ*

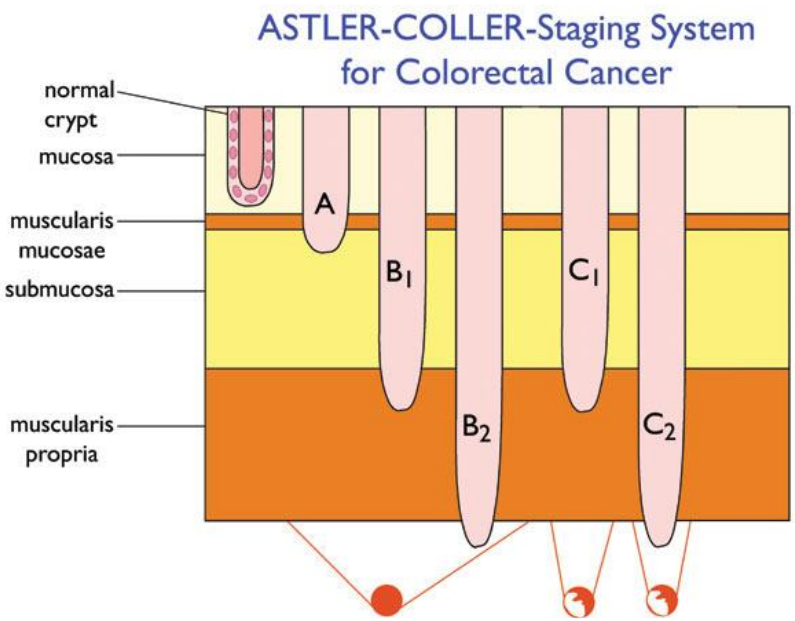
Staging is not relevant for Occult Carcinoma (Tx, N0, M0)

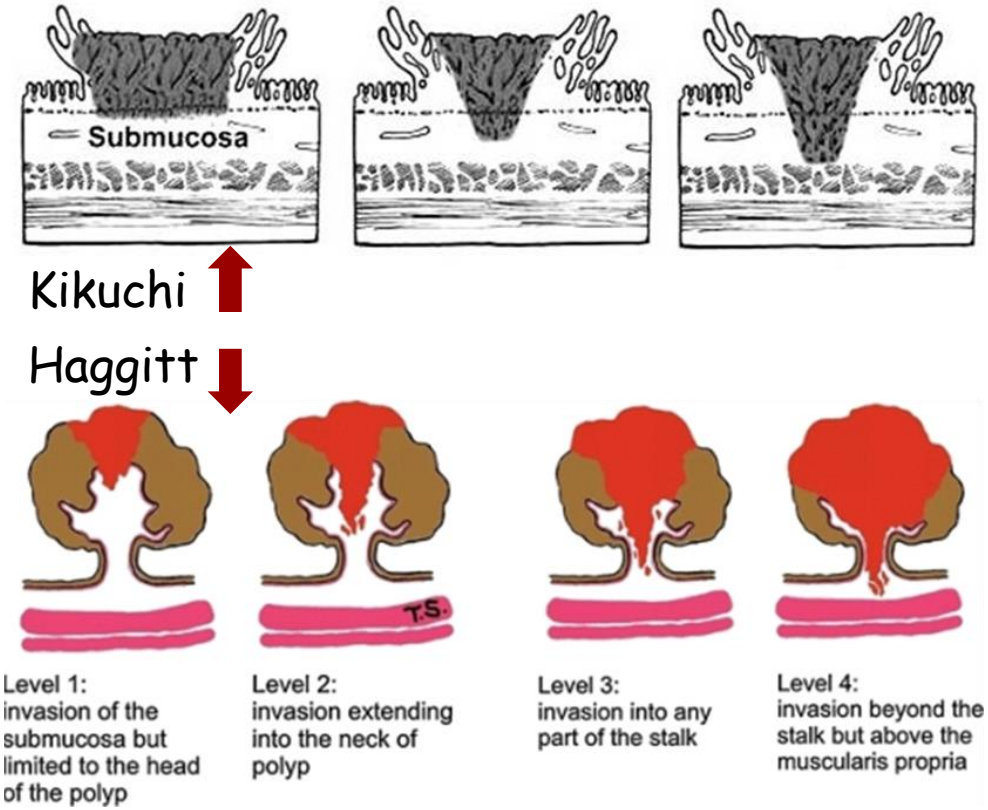
* Including direct extension to intrapulmonary nodes
** Including superior sulcus tumor

(& : and) (/ : or) (&/ : and /or)

surrounded by lung or visceral pleura	Visceral pleura	Chest wall **/ diaphragm/ mediastinal pleura/ parietal pericardium	Mediastinum/ trachea/heart/ great vessels/ esophagus/ vertebral body/ carina	**c. Local Invasion**
–	Atelectasis/ obstructive pneumonitis that extends to the hilar region but doesn't involve the entire lung	Atelectasis/ obstructive pneumonitis of the entire lung	Malignant pleural/peri-cardial effusion or satellite tumor nodule(s) within the ipsilateral primary-tumor lobe of the lung	**d. Other**

- **COLORECTAL CARCINOMA**
  - DUKES A, B, C
  - MODIFIED ASTLER-COLLER (MAC) A, B, C, D
  - Kikuchi: levels of submucosal infiltration in early colorectal cancer: SM1, SM2, SM3
  - Haggitt: levels of invasion within the stalk in case of adenocarcinomas developing in polypoid adenomas





T categorties: MELANOMA MALIGNUM (TNM 8)

Tis. In situ melanoma (epidermis).

T1a Invasive melanoma ≤0.8mm

T1b Invasive melanoma >0.8mm -1mm

T2a. Invasive melanoma >1.0-2.0 mm thick, without ulceration.

T2b. Invasive melanoma >1.0-2.0 mm thick, with ulceration.

T3a. Invasive melanoma >2.0-4.0 mm thick, without ulceration.

T3b. Invasive melanoma >2.0-4.0 mm thick, with ulceration.

T4a. >4.0 mm Invasive melanoma without ulceration.

T4b. >4.0 mm Invasive melanoma with ulceration.

- A recent consensus conference in Lugano suggested a more simplified system putting together **stage I and II as Limited Stage** and **stage III and IV as Advanced Stage** lymphoma.

Limited Stage

- **Stage I**
- **Stage II**
- **Bulky Stage II**

Advanced Stage

- **Stage III**
- **Stage IV**

TNM 8th edition

Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol*. 2014;32: 3059-3068

- **MALIGNANT LYMPHOMA**
  - **Ann-Arbor**

Mandard et al. (15)	Becker et al. (12)	Dworak et al. (14)	Rödel et al. (17)
1. Complete regression (= fibrosis without detectable tissue of tumor)	1a. No residual tumor/tumor bed + chemotherapy effect	0. No regression	0. No regression
2. Fibrosis with scattered tumor cells	1b. <10% Residual tumor/tumor bed + chemotherapy effect	1. Predominantly tumor with significant fibrosis and/or vasculopathy	1. Regression of <25% of tumor mass
3. Fibrosis and tumor cells with preponderance of fibrosis	2. 10–50% Residual tumor/tumor bed + chemotherapy effect	2. Predominantly fibrosis with scattered tumor cells (slightly recognizable histologically)	2. Regression of 25–50% tumor mass
4. Fibrosis and tumor cells with preponderance of tumor cells	3. >50% Residual tumor/tumor bed ± chemotherapy effect	3. Only scattered tumor cells in the space of fibrosis with/without acellular mucin	3. Regression of >50% tumor mass
5. Tissue of tumor without changes of regression		4. No vital tumor cells detectable	4. Complete regression

Staging post chemo- and/or radiotherapy (common situations)

Rectal cancer

Esophageal cancer

Breast cancer

Table 3: Recommended classification of response to chemotherapy

Tumour response

1. Complete pathological response, either (i) no residual carcinoma or (ii) no residual invasive tumour but DCIS present.
2. Partial response to therapy, either (i) minimal residual disease/near total effect (e.g. < 10% of tumour remaining) or (ii) evidence of response to therapy but with 10–50% of tumour remaining or (iii) > 50% of tumour cellularity remains evident, when compared with the previous core biopsy sample, although some features of response to therapy present. Points (ii) and (iii) are somewhat subjective, especially when the core biopsy cannot be reviewed.
3. No evidence of response to therapy.

Nodal response

1. No evidence of metastatic disease and no evidence of changes in the lymph nodes.
2. Metastatic tumour not detected but evidence of response/down-staging, e.g. fibrosis.
3. Metastatic disease present but also evidence of response, such as nodal fibrosis.
4. Metastatic disease present with no evidence of response to therapy.

Prognosis

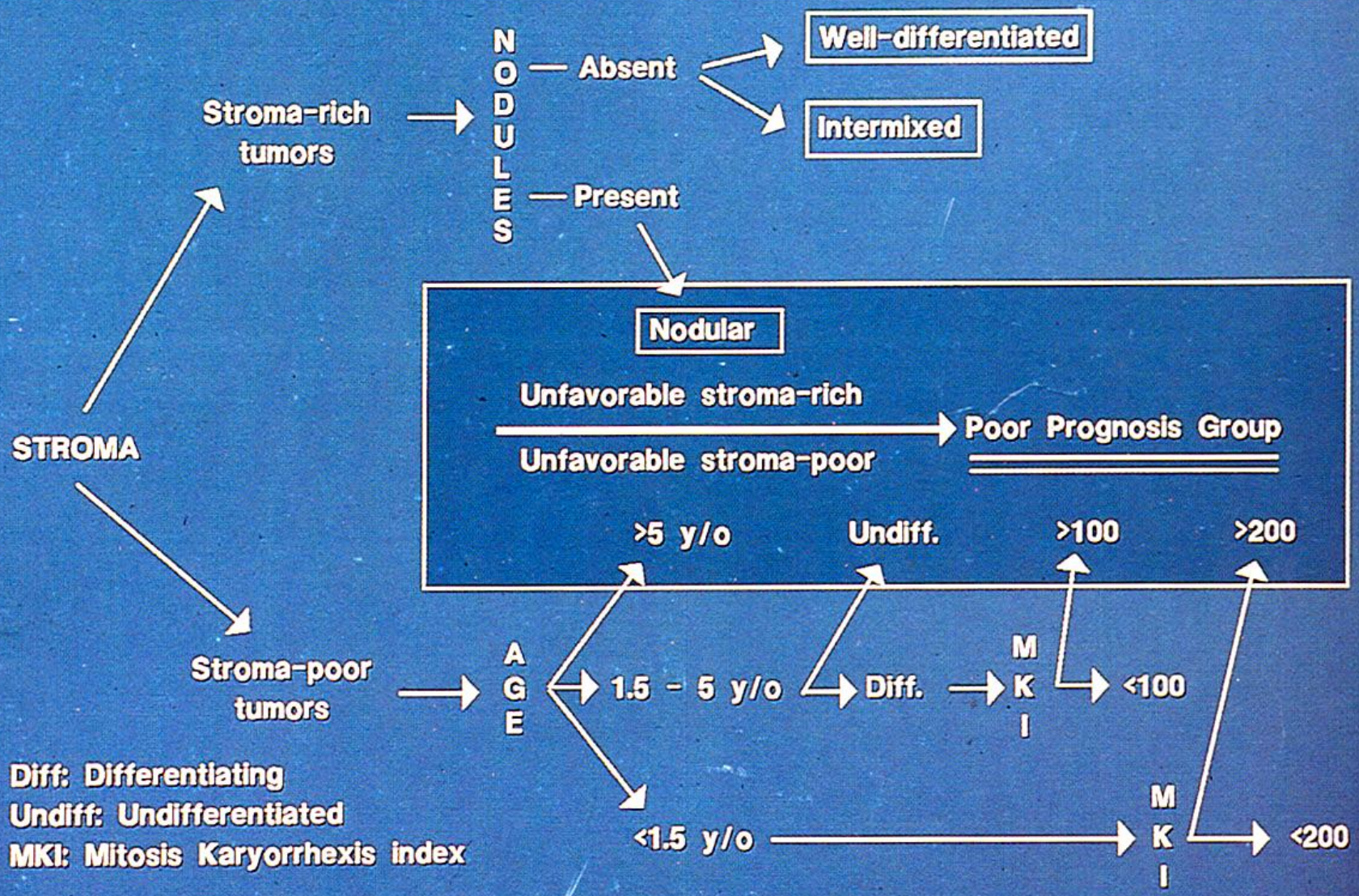
- Survival
  - overall survival
  - disease free survival
- Quality of life

Quality of Life: A multidimensional construct encompassing complete information on the impact of disease or its treatment on a patient's usual or expected physical, psychological, and social well-being

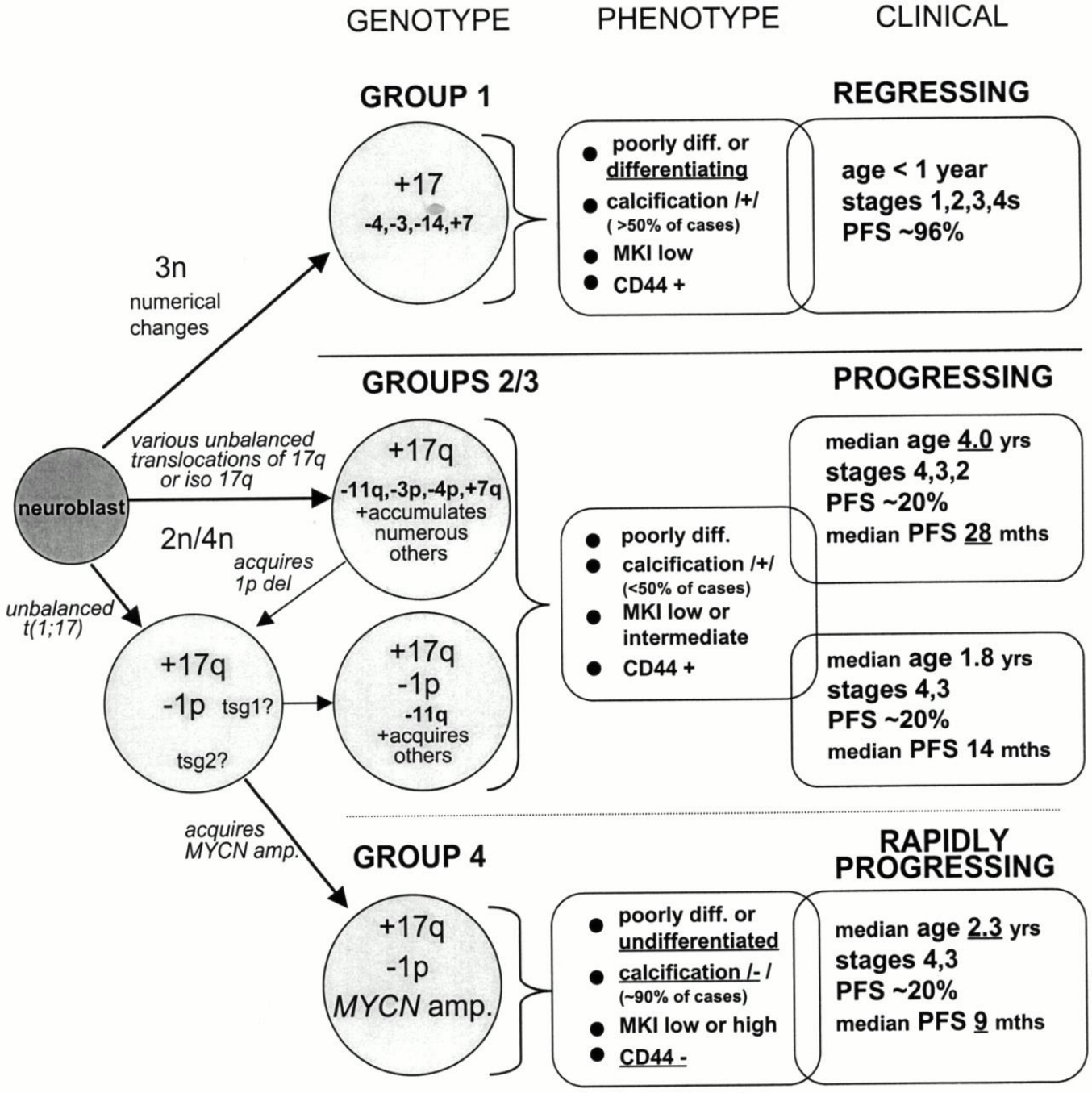
Prognosis is influenced by

- Sex
- Age
- Tumor type - grade - size - stage
- Tumor location
- Genetic profile of the tumor
- Intra/peritumoral immune cell characteristics – antitumor immunity
- Treatment, incl. targeted, tailored therapy

PROGNOSTIC FACTORS IN NEUROBLASTIC TUMORS



Shimada et. al. JNCI, 73:405-416, 1984

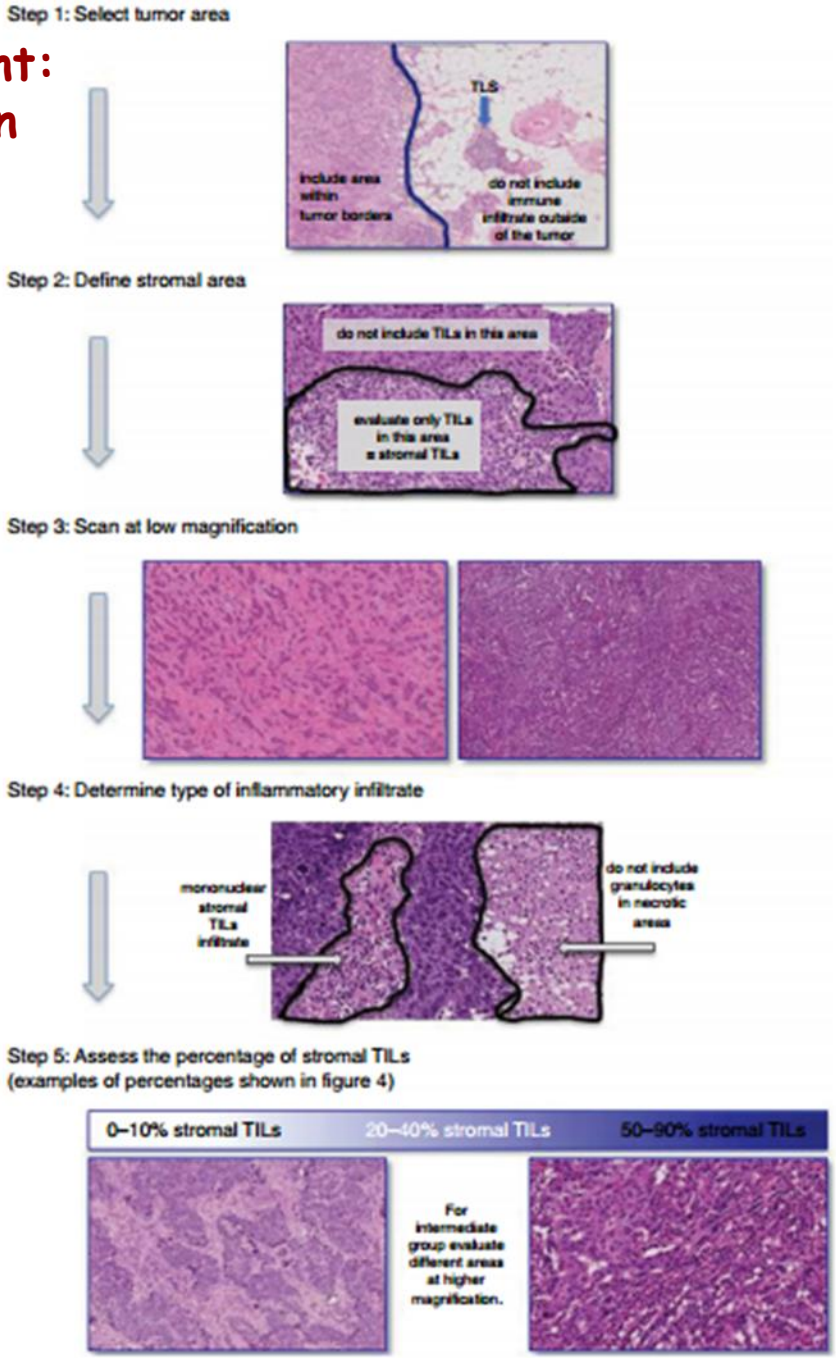


JOURNAL OF CLINICAL ONCOLOGY

Lastowska M et al. JCO 2001;19:3080-3090

Annals of Oncology 26: 259–271, 2015

Tumor microenvironment: Immune cell infiltration



THERAPY

- **Surgical:** curative or palliative
- **Radiation:** pre- or postoperative or exclusively
- **Chemotherapy:** pre- or postoperative or exclusively
- **Endocrine therapy:** hormone sensitive tumors
- **Targeted („biological")-therapy:** needs identification of the TARGET in the tumor tissue
- **Immune therapy:** reactivation of the host immune system against the tumor cells (blocked by the tumor cells)

TARGETED THERAPY

Identification of characteristic molecular-genetic alterations in the tumor

↓

Treatment with specific, targeted agents
(antibody, enzyme blocking, pathway blocking, etc.)

↓

Increased effects, decreased side effects

Examples: colon-,breast- and lung carcinomas, gastrointestinal stromal tumor, chronic myeloid leukaemia

PREVENTION

EARLY DETECTION

are very important

NEOPLASTIC DISEASES REQUIRE

MULTIDISCIPLINARY APPROACH