BHARATHIDASAN UNIVERSITY

Tiruchirappalli- 620024,
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Programme: M.Sc., Biomedical science

Course Title : Cancer Biology

Course Code : 18BMS59C16

Unit-IV

TOPIC: Tumor Staging & Grading

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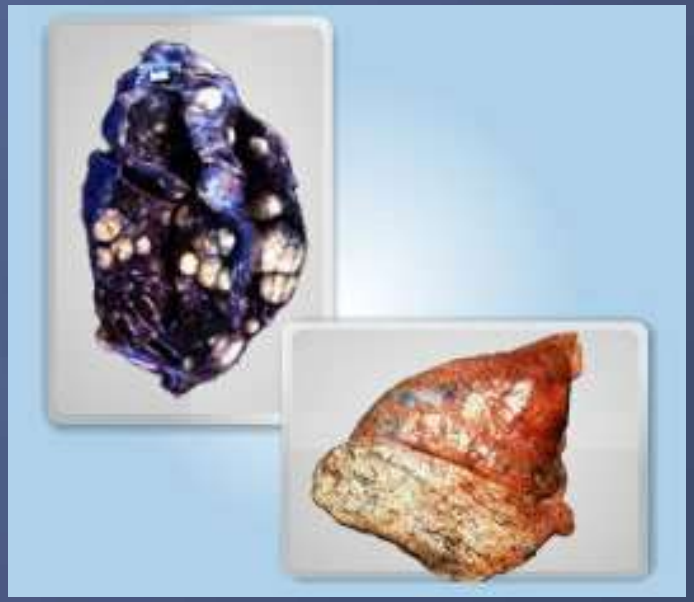
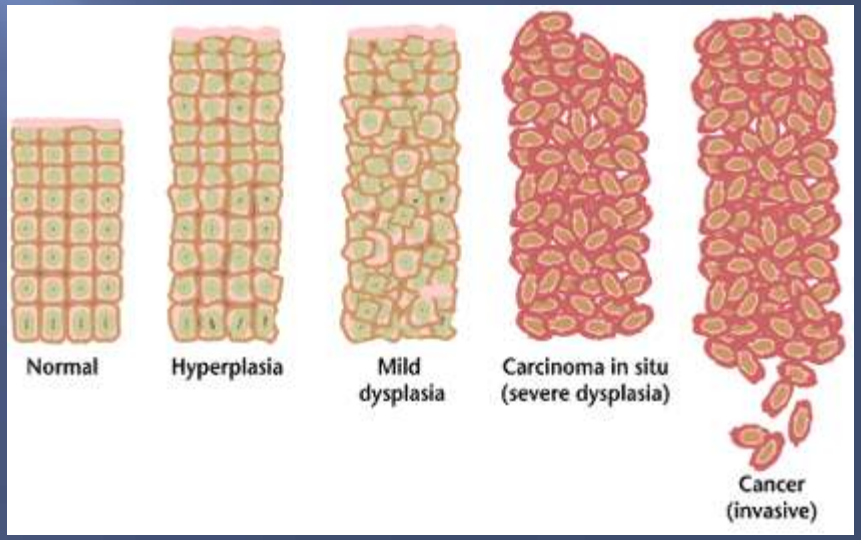
Types of Cancer

- Cancer can affect almost any tissue type in the body.
  - Lung cancer
  - Skin Cancer
  - Liver Cancer
  - Breast Cancer
  - Cervical Cancer
  - Prostate Cancer





Tumor Classification

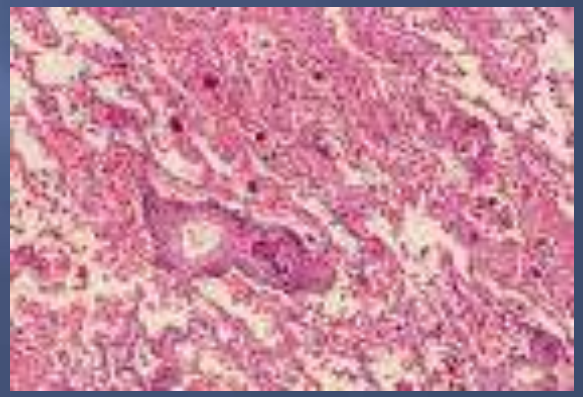
- Anatomical Site
- Cell of Origin
- Biological behavior

- There are a large variety of tumors because tumors can originate from any cell type.

Types of Differentiation

- 1. **Well differentiated**
  - closely resemble the cell of origin
  - easily classified by histology

- 2. **Undifferentiated**
  - do not resemble normal cells
  - more difficult to classify
  - also called “anaplastic”



Cancer terminology

Classification by tissue type:

- carcinoma
  epithelial cell
  90% of all tumours
  derived from ectoderm (mostly) or endoderm (some)
- sarcoma
  connective tissue
  2% of all tumours
  derived from mesoderm
- leukaemia
  circulatory or lymphatic
  8% of all tumours
  derived from mesoderm

Classification by the type of cells:

- Adenomatous cells
  ductal or glandular cells
- Squamous cells
  flat cells
- Myeloid
  blood cell
- Lymphoid
  lymphocytes or macrophages

Epidemiology

- The study of disease incidence.
- Statistical databases identifying patterns of cancer occurrence.
- Researchers use this information and determine incidence of cancer in a general population.

Use factors such as age,gender, race, geographical location.

Staging- Defining Tumor Size and Extension at Point of Diagnosis

- Reason it's important
  - -provides a means of communication about tumors
  - -provides a basis for comparison between tumors
  - -helps in determining best treatment
  - -Aids in predicting prognosis
  - -provides a means for continuing research

Surveillance, Epidemiology and End Results (SEER) Program

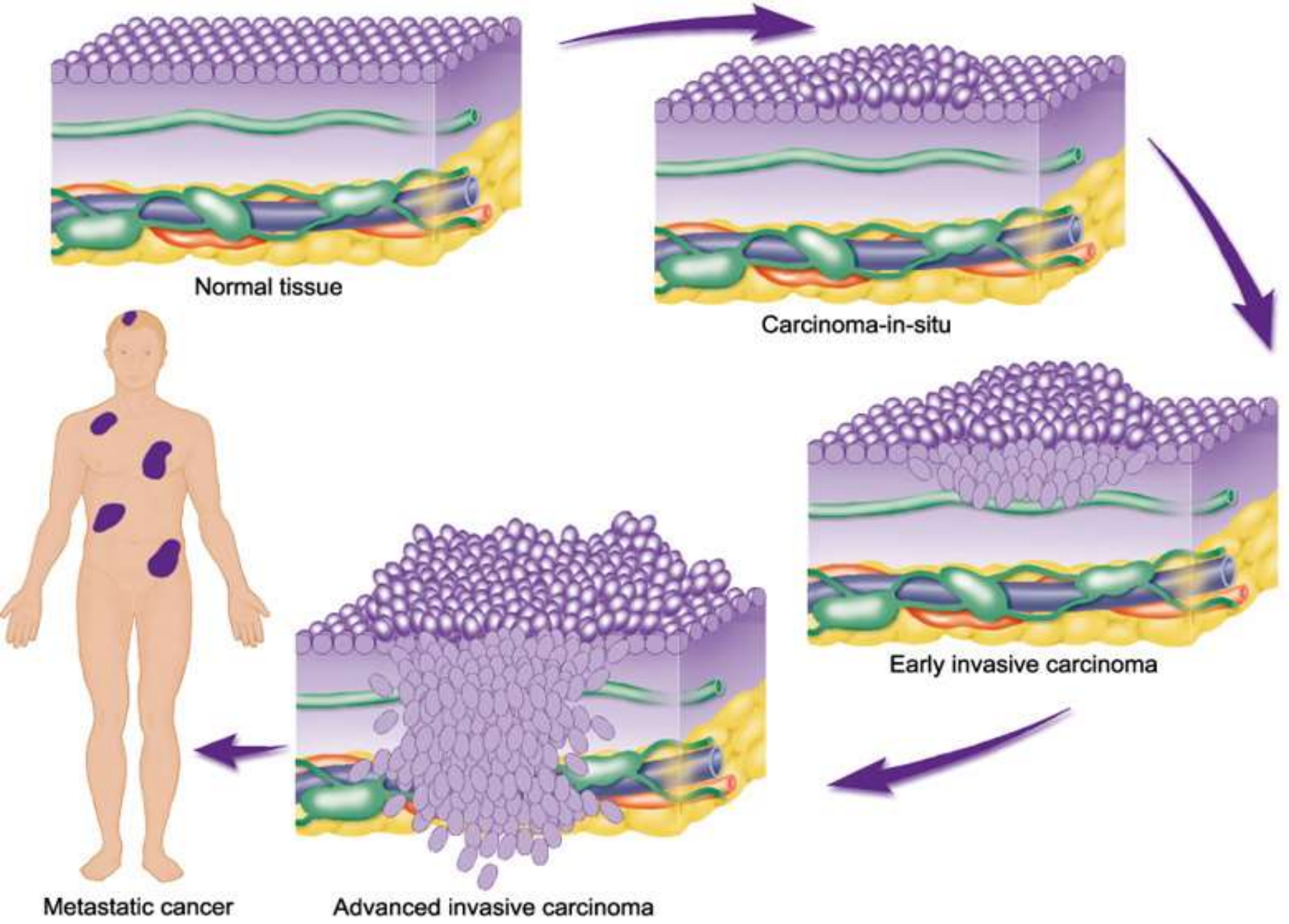
- As technologies advance staging systems change
- **TNM**- is the current staging system used by the International Union Against Cancer and American Joint Committee on Cancer
- Extent of Disease (EOD)
- Summary Stage (SS)- General **Staging**, California **Staging**, and**SEER Staging**.-combination of the most precise clinical and pathological documentation of the extent of disease

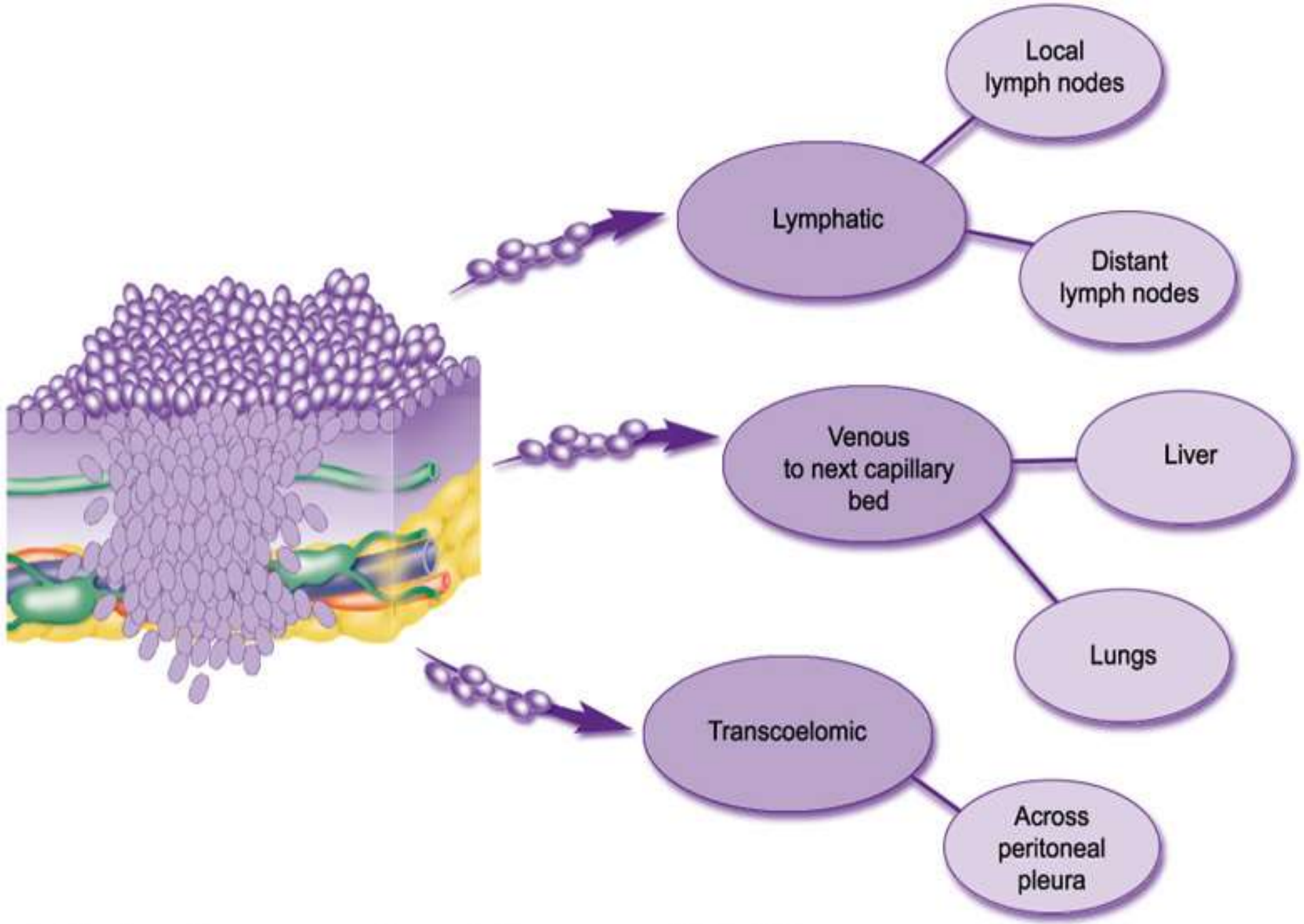
Extent of Disease (EOD)

- The EOD coding scheme consists of a ten-digit code.
- Three digits for the size and/or involvement of the primary tumor,
- Two for the extension of the tumor,
- One more as a general code for lymph node involvement.
- Four more digits are used after these six: two for the number of pathologically positive regional lymph nodes and two more for the number of regional lymph nodes that are pathologically examined.

How Cancer Spreads

- Local invasion
- Direct extension
- Lymphatic metastases
- Blood-borne metastases
- Intra-cavitary





Summary Staging

- 0 – in situ
- 1 – localized
- 2 – regional by direct extension only
- 3 – regional lymph nodes involved only
- 4 – regional by both direct extension and lymph node involvement
- 5 – regional, NOS (not otherwise specified)
- 7 - distant site(s)/node(s) involved
- 9 – unknown (unstaged, unknown or unspecified)

What is TNM Staging?

- Developed by physicians (AJCC)
- Uniform staging system to determine treatment, prognosis & end results
- T = Tumor
- N = Nodes
- M = Metastasis
- Group Stage = summary of TNM

Pierre Denoix

TNM staging system for all solid tumours was devised by Pierre Denoix between 1943 and 1952

TNM Staging
T=Tumor, N=Node, M=Metastasis

- T-size and extent of primary tumor is assigned a number 0-4
  - T0(zero)-no evidence of disease
  - T1-confined to organ of origin, not invading other tissue
  - T2-Deep extension into nearby structures or tissues
  - T3-Confined to region of origin, rather than organ.
  - T4-massive lesion extending into other tissues and organs causing fistulas in hollow organs and making a sinus in solid organs.

N=node Designates the status of lymph nodes and the extent of lymph node involvement

- 0-4 designates the status of lymph nodes and the extent of lymph node involvement.
- N0 (zero)- no positive nodes are present.
- N1-palpable movable nodes in first drainage station the same site of the tumor (1-2 cm).
- N2-larger nodes 3-5 cm invading into capsule.
- N3-Nodes are fixed to bone, muscle, skin, or blood vessels usually 6 cm in size.
- N4- Positive nodes at more distant nodal sites beyond first station.

M=Metastasis, the presence and/or extent of.

- M0(zero) –no metastasis
- M1- One metastasis in one organ or site
- M2-multiple metastatic lesions in one organ system.
- M3- Multiple organs involved with little or no impairment of function.
- M4- Multiple organs with impairment of function.
- MX – unable to access
- Large numbers are more advanced

Many more staging systems, but TNM is widely used.

Common Metastatic Sites of Primary Tumors (Table 1 -7)

Primary Site	*Metastatic Site*
Lung	Liver, adrenal glands, bone, brain
Breast	Lungs, bone, brain
Stomach	Liver
Anus	Liver and lungs
Bladder	Lungs, bone, liver
Prostate	Bone, liver, lungs
Uterine Cervix	Lungs, bone, liver

Group Stage

- Is the general reference point of comparison
- Tis = Stage 0
- Stage I, Stage II, Stage III, Stage IV

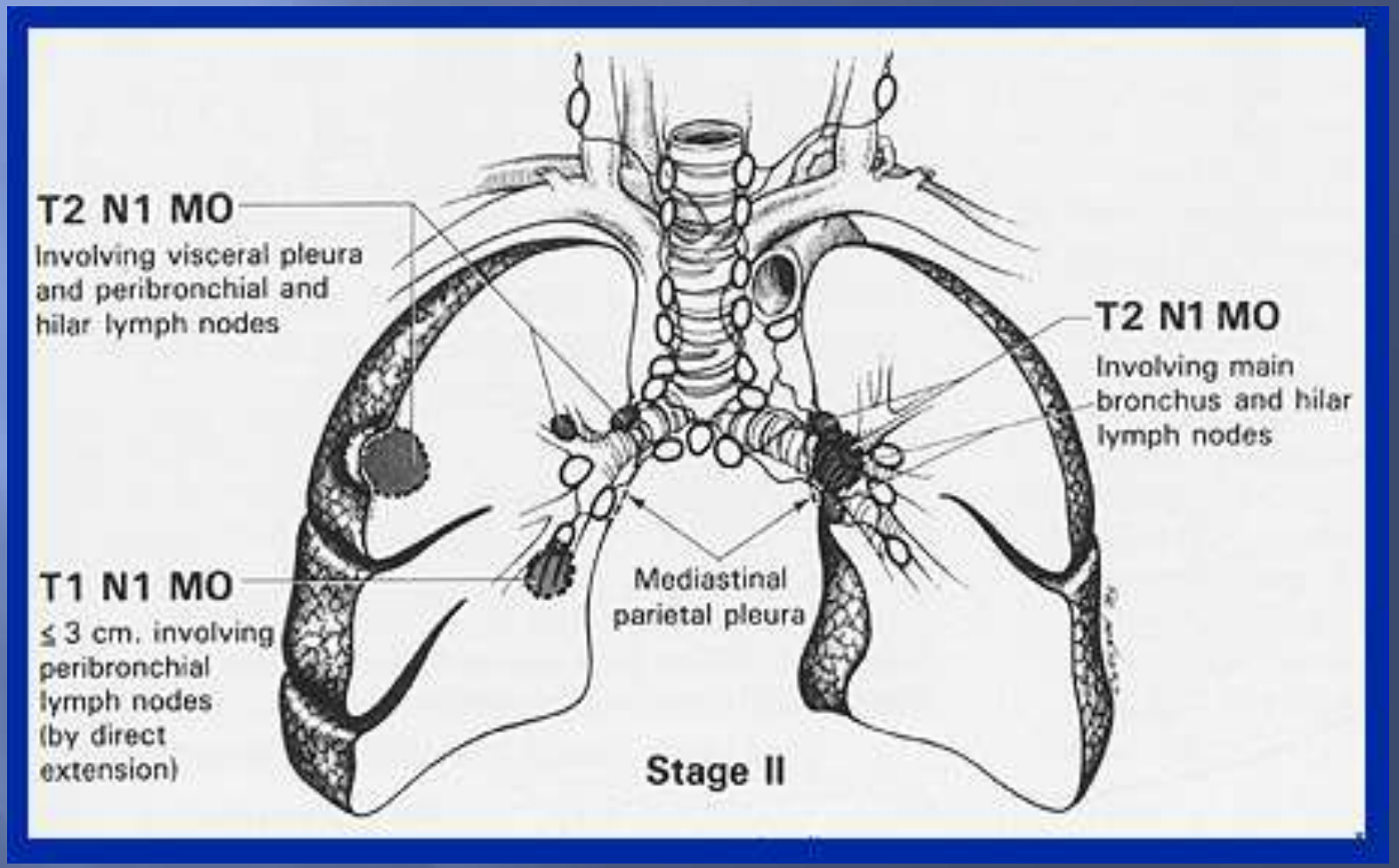
Descriptors

		Indication	
Suffix	m	Presence of multiple primary T	pT(m)NM
Prefix	y	Post initial treatment (staging after preop treatment)	ycTNM or ypTNM
	r	Recurrent tumor after a disease free interval	rTNM
	a	Autopsy	aTNM

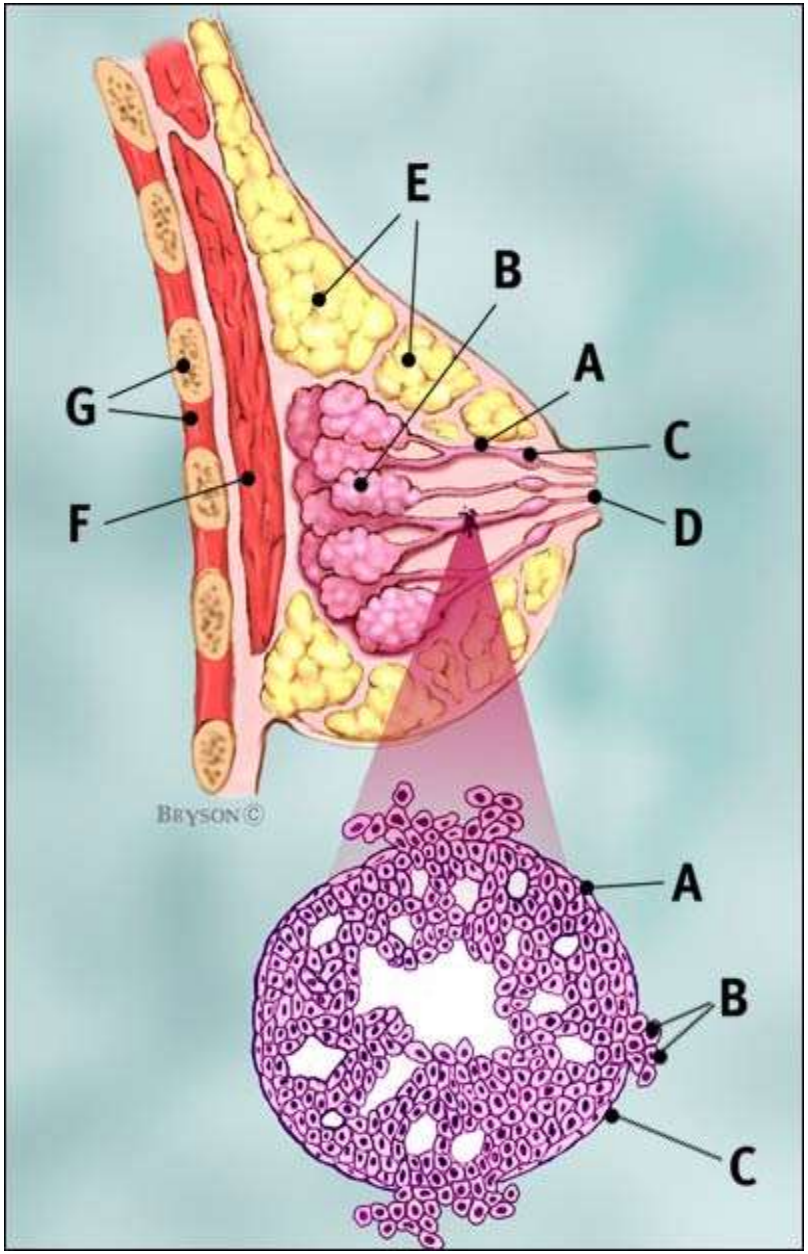
Clinical, Pathologic, Collaborative Staging

- Clinical (cT, cN, cM)
  - Before initiation of primary treatment
  - Important in deciding primary treatment
- Pathologic (pT, pN, pM)
  - From resected tissues
- Collaborative Stage (CS) allows combined pathological and clinical "mixed" or "best" stages to be captured.
  - Implemented by the cancer registries
  - Stage derived through computer algorithms

Staging



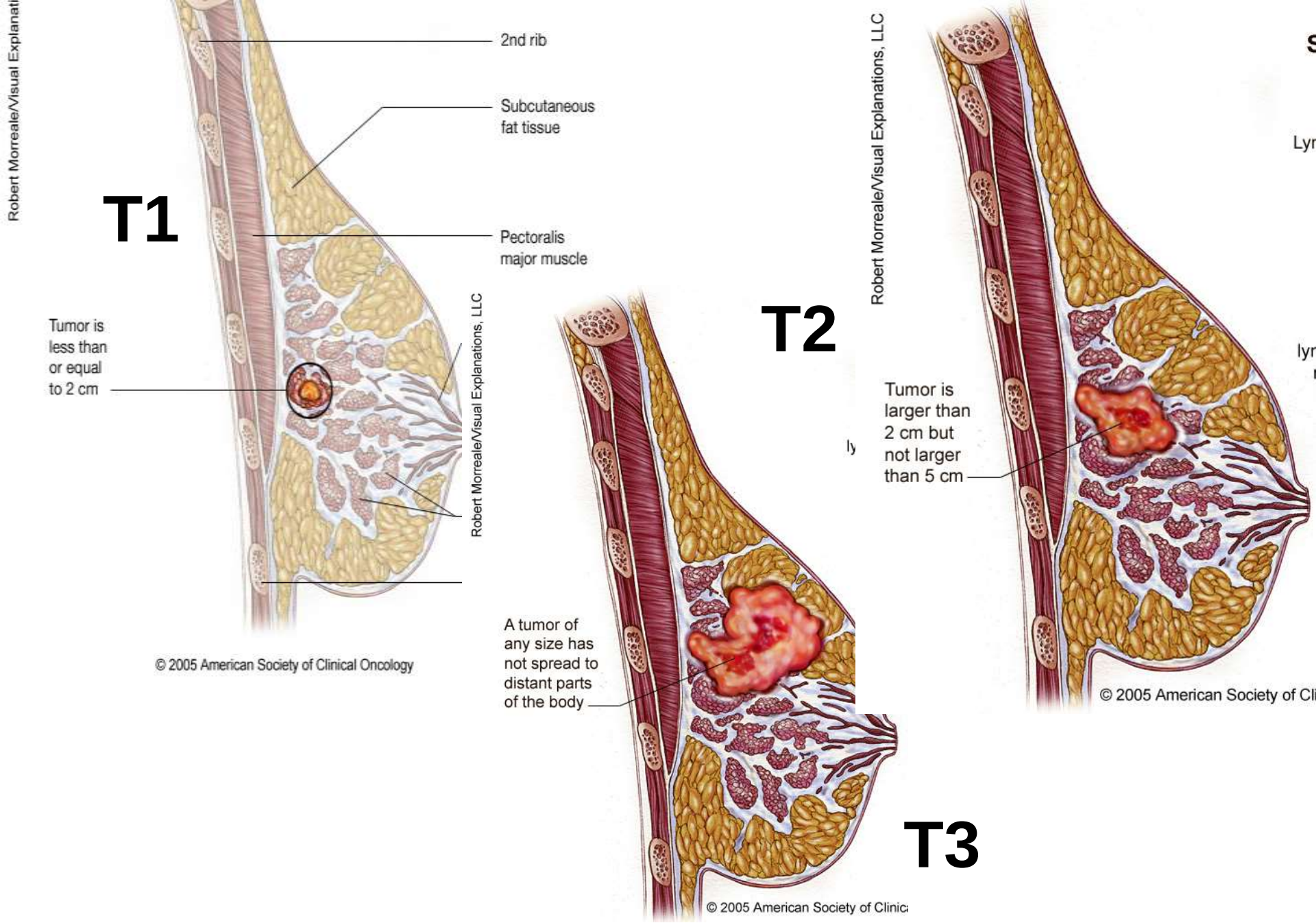
www.vh.org/.../Staging/ Images/TNM008.jpg



Breast profile:

A ducts,
B lobules,
C dilated section of duct to hold milk
D nipple,
E fat,
F pectoralis major muscle, **G** chest wall/rib cage

Enlargement:
A normal duct cells,
B ductal cancer cells breaking through the basement membrane
C basement membrane


Robert Morreale/Visual Explanations, LLC
2nd rib
Subcutaneous fat tissue
T1
Pectoralis major muscle
Tumor is less than or equal to 2 cm
Robert Morreale/Visual Explanations, LLC
© 2005 American Society of Clinical Oncology
T2
A tumor of any size has not spread to distant parts of the body
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Robert Morreale/Visual Explanations, LLC
Tumor is larger than 2 cm but not larger than 5 cm
T3
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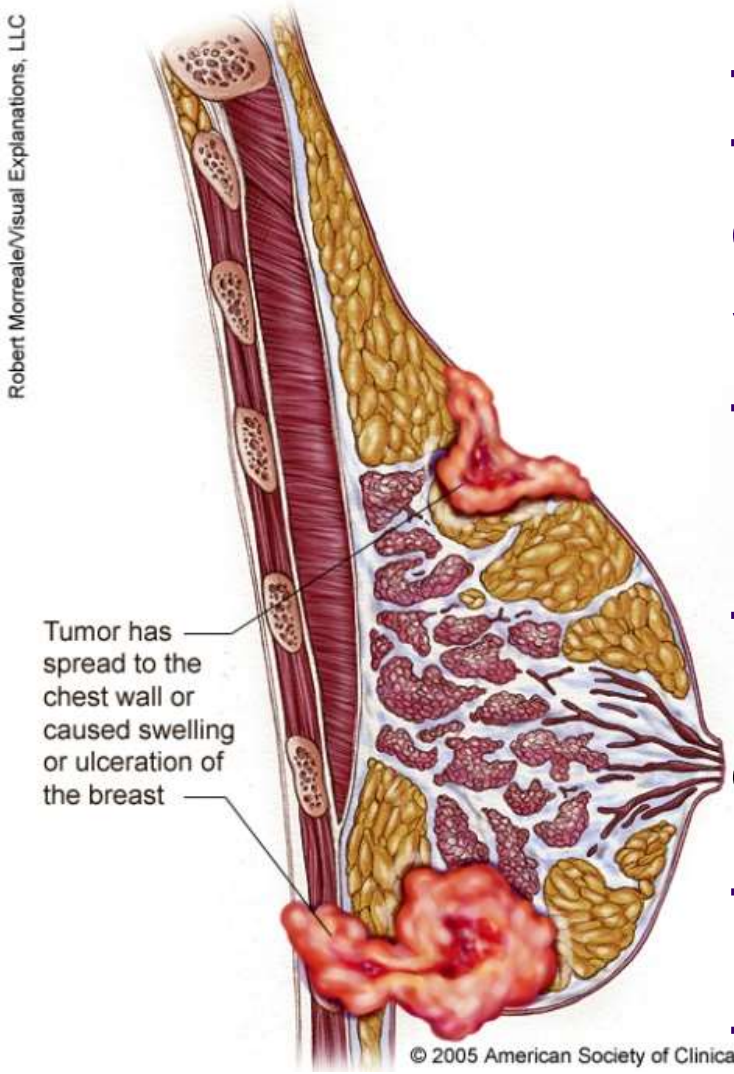


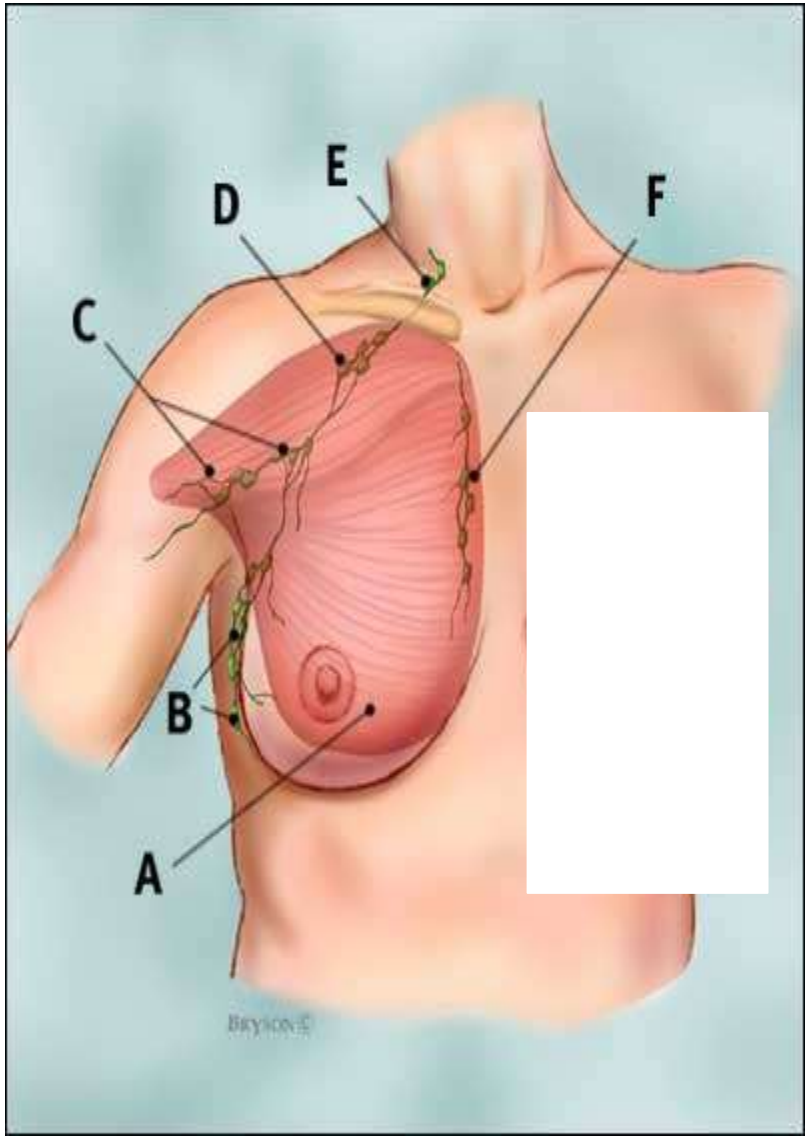
T4
Tumor of any size with direct extension to (a) chest wall or (b) skin

T4a **Extension to chest wall, not including pectoralis muscle**

T4b **ulceration of the skin of the breast, or satellite skin nodules confined to the same breast**

T4c **Both T4a and T4b**

T4d **Inflammatory carcinoma**



Lymph Node Areas Adjacent to Breast Area

A- Pectoralis major muscle

B- Axillary LN: levels I

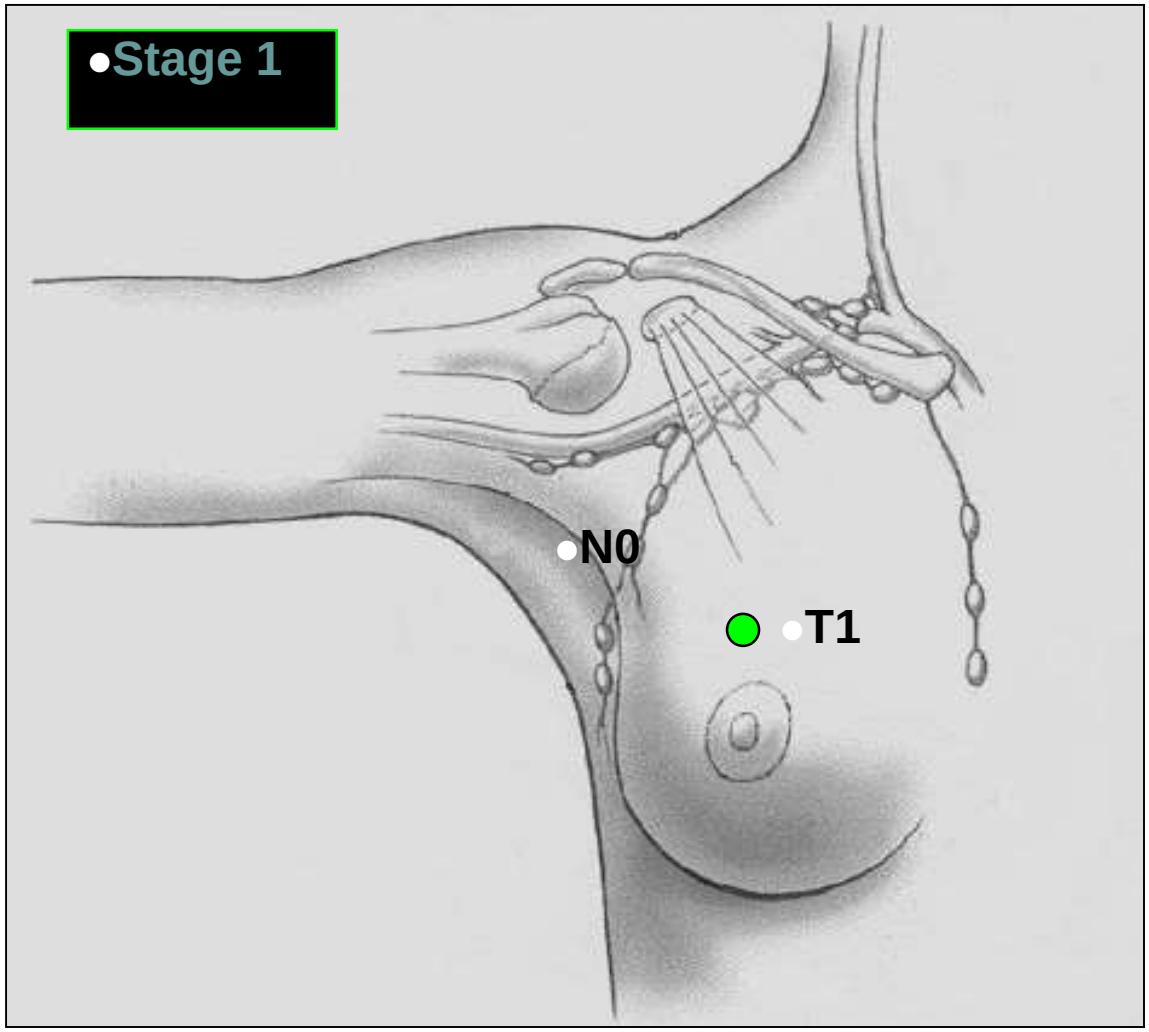
C -AxillaryLN: levels II

D- Axillary LN: levels III

E- Supraclavicular LN

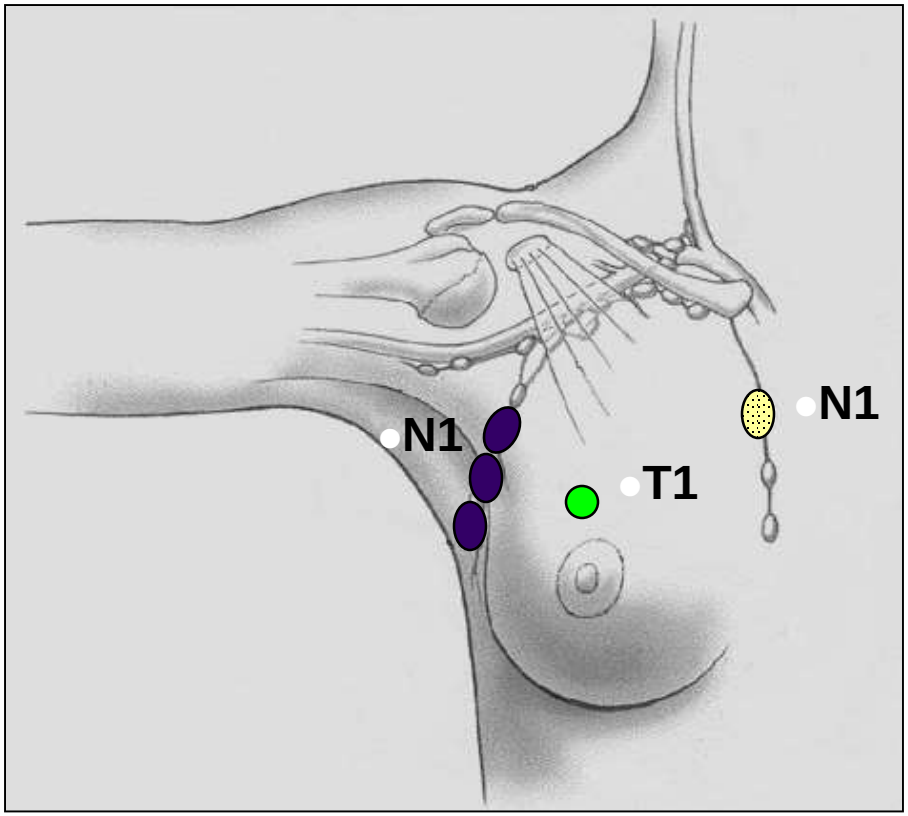
F -Internal mammary LN

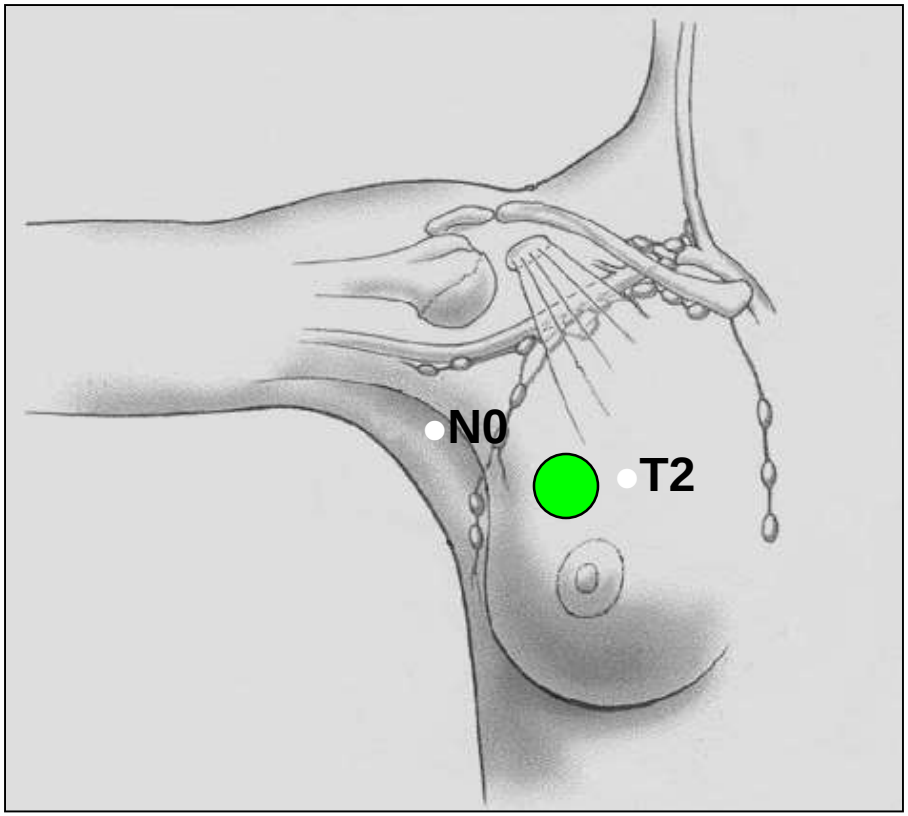
Breast Cancer Staging
Stage I



Breast Cancer Staging
Stage IIA

- Stage IIA

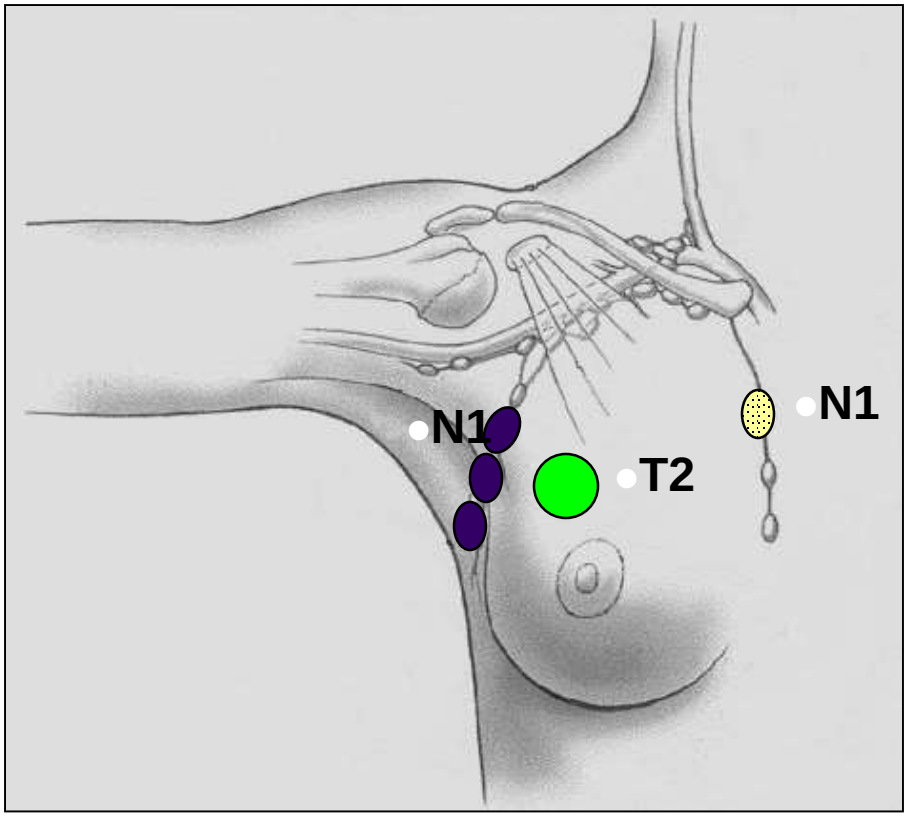


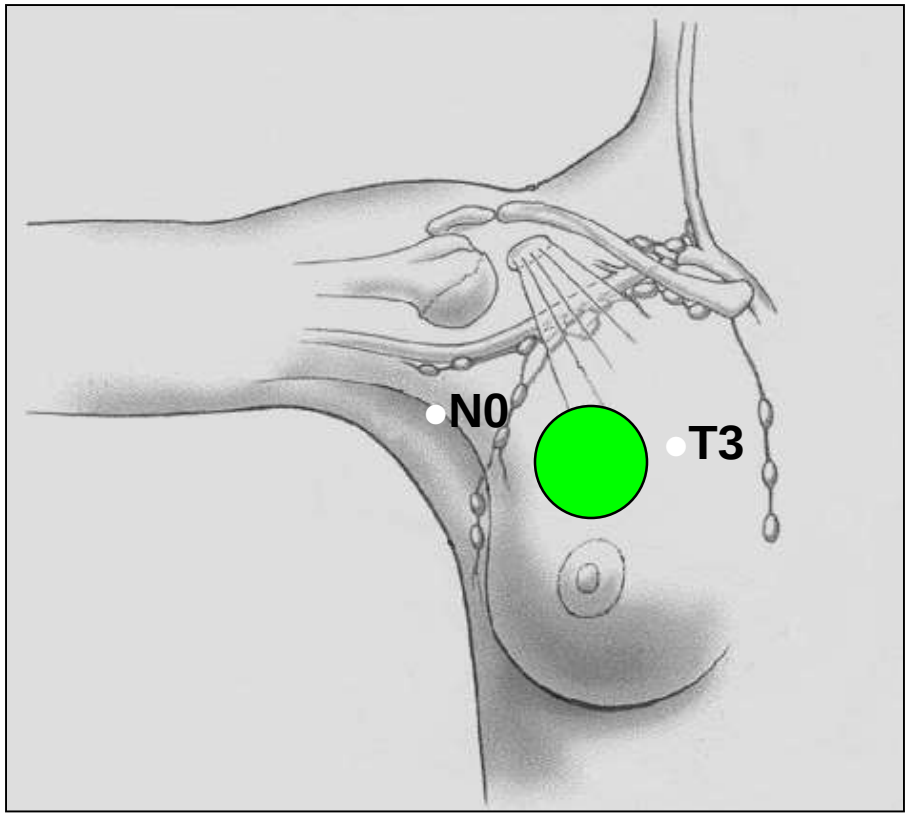


Stage IIa may also describe cancer in the axillary lymph nodes with no evidence of a tumor in the breast

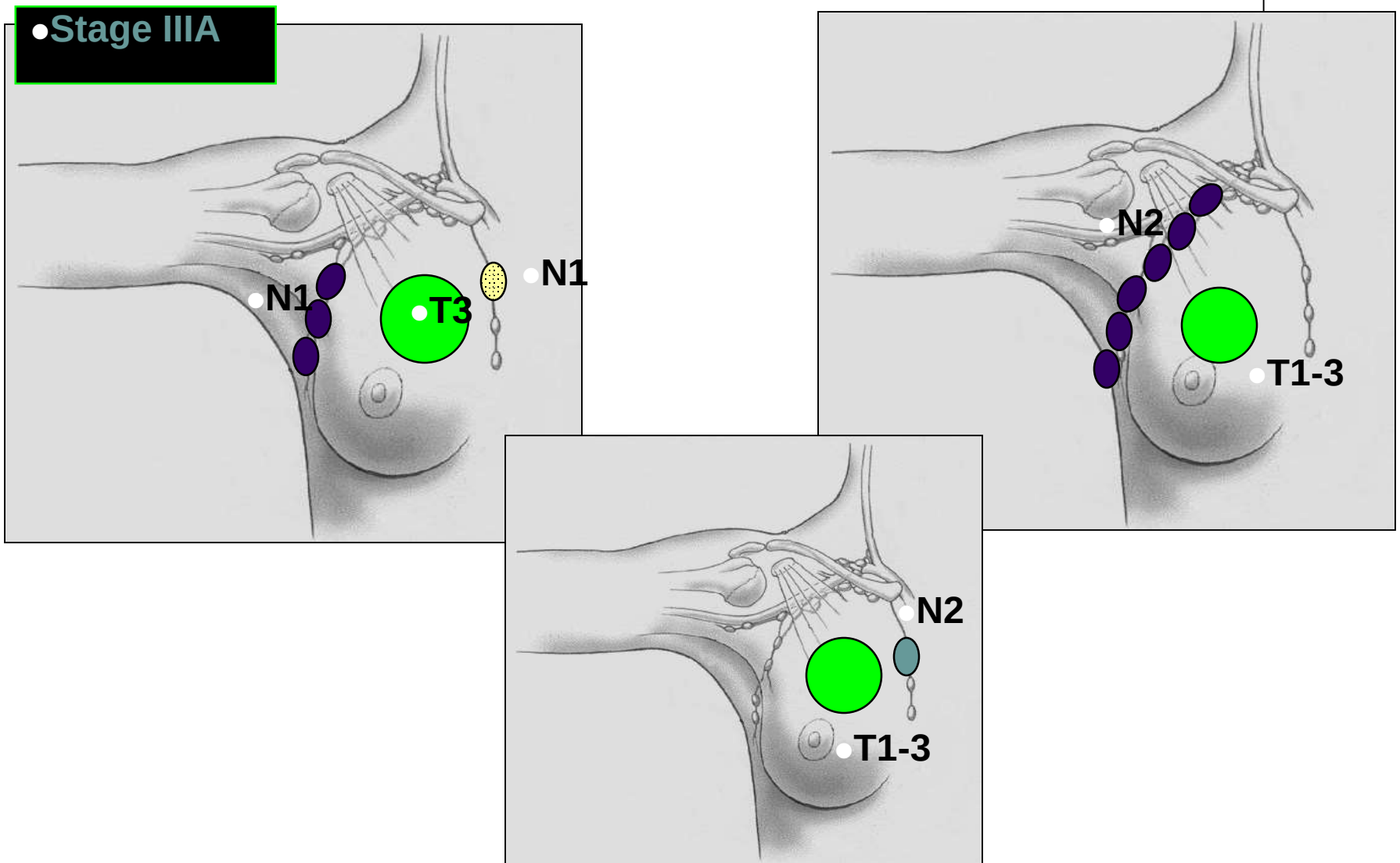
Breast Cancer Staging
Stage IIB

- Stage IIB

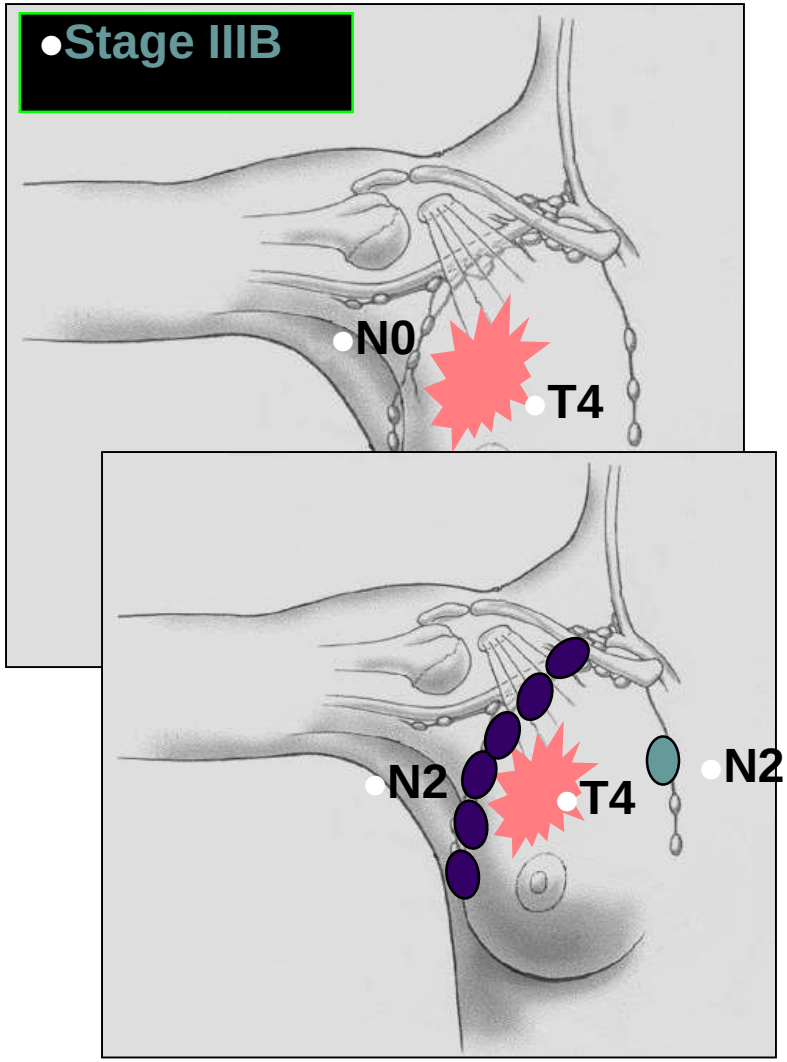


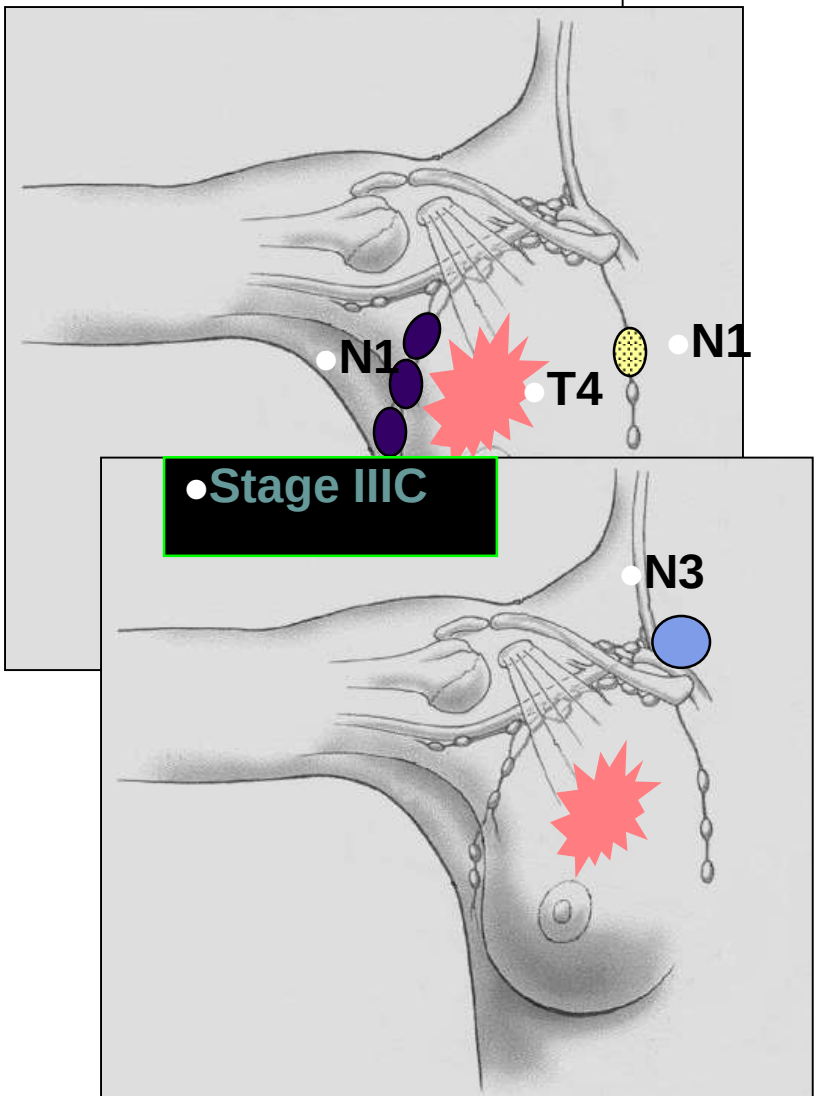


Breast Cancer Staging
Stage IIIA



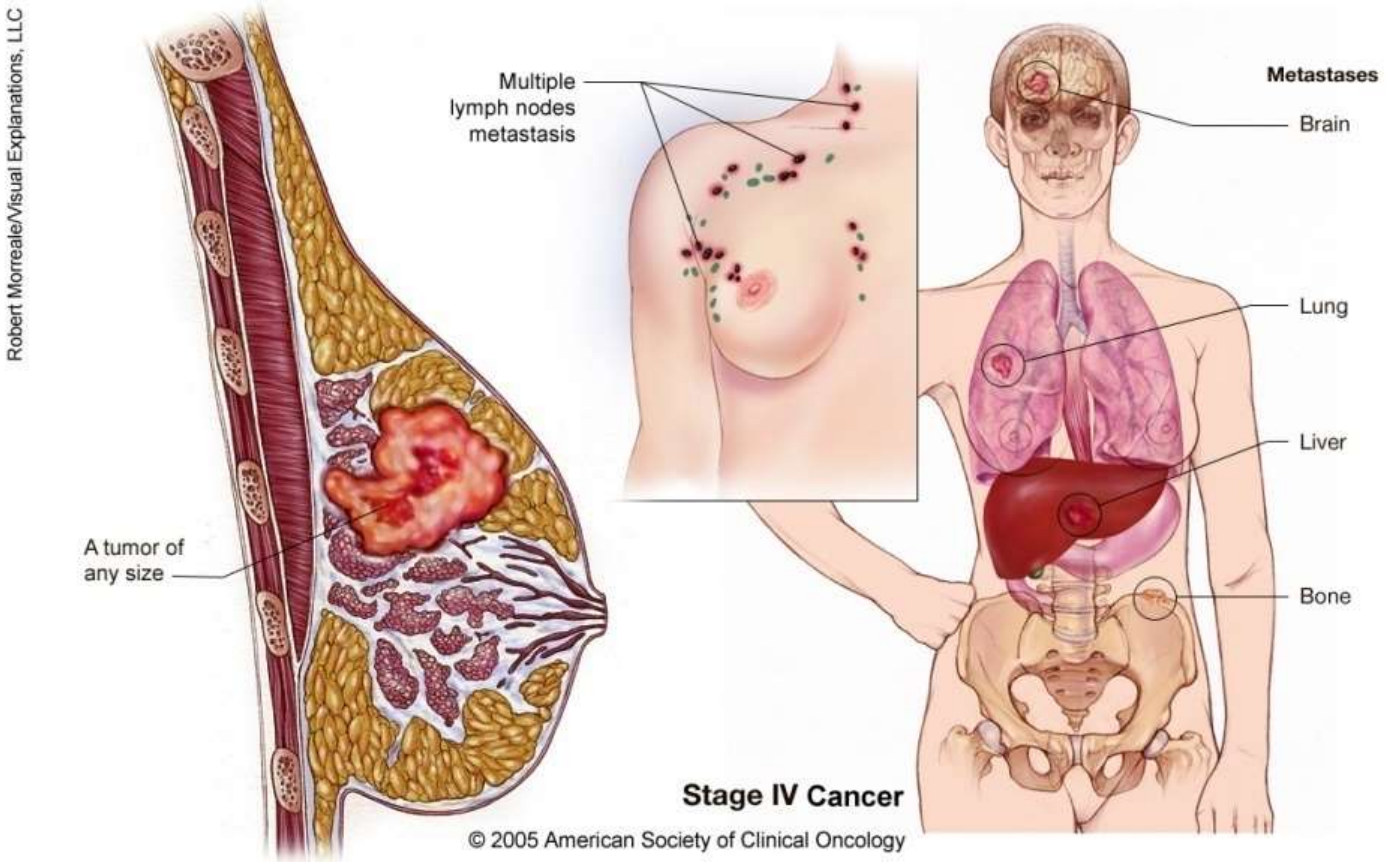
Breast Cancer Staging
Stage IIIB, IIIC





Stage IV Breast Cancer

- Stage IV breast cancer can be any size and has spread to distant sites in the body, usually the bones, lungs or liver, or chest wall



AJCC Staging System (anatomic)

T	N	M	Stage
1	0	0	I
0-2	0-1	0	IIa
2-3	0-1	0	IIb
0-3	1-2	0	IIIa
4 or 0-1	1-2	0	IIIb
Any	3	0	IIIc
any	any	1	IV

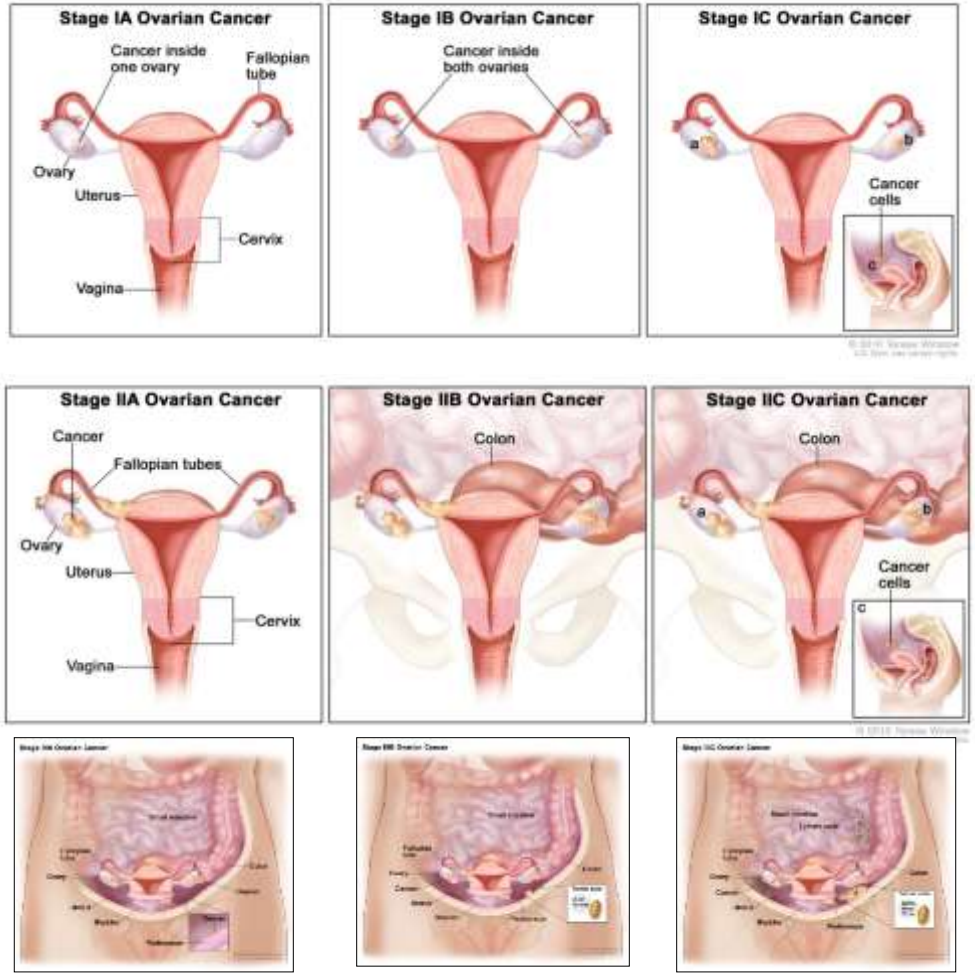
Ovarian cancer

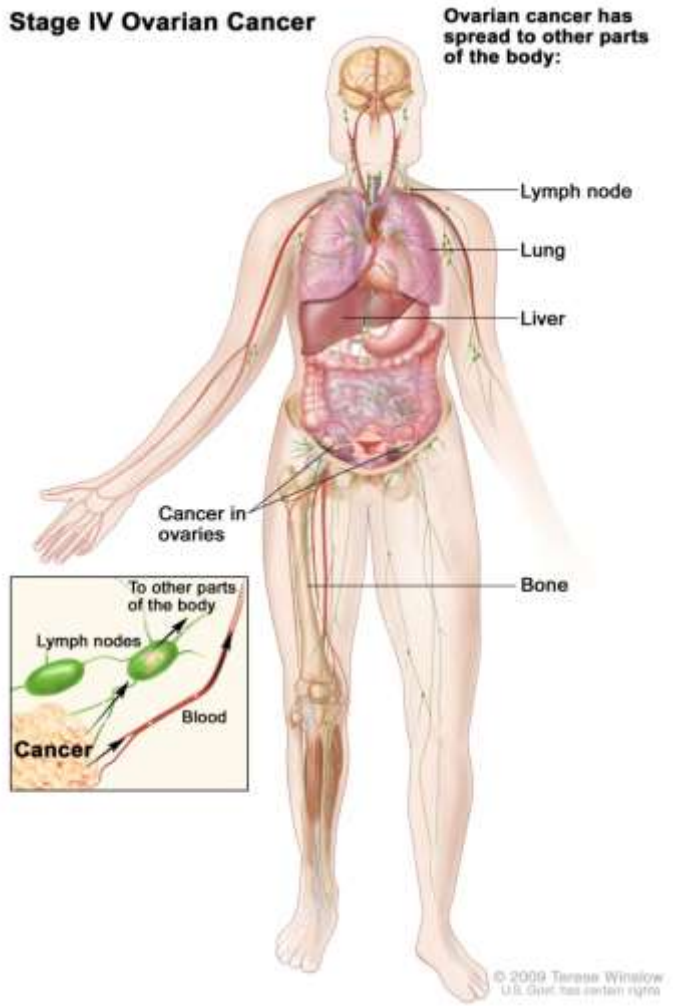
- Ovarian cancer: is the fifth leading cause of cancer related death and the leading cause of death from gynecological malignancies.
- Difficult to diagnose
- Late diagnosis: Stage 3 cancer of the ovary
- 80% of Ovarian cancer present with omental metastasis
- Screening test: CA 125 (50%) accuracy, late marker
- Standard treatment : no change in survival rate

Scenario in India

- ✓Massive surge in cancer cases in India
- ✓ As per WHO, 500,000 people die of cancer and
- expected to rise to 700,000 by 2015.

Different stages of ovarian cancer





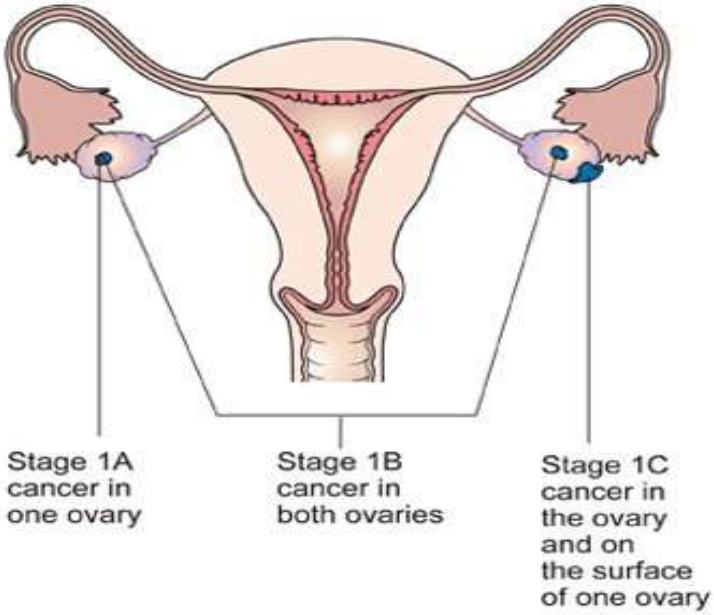


Diagram showing stage
1 ovarian cancer

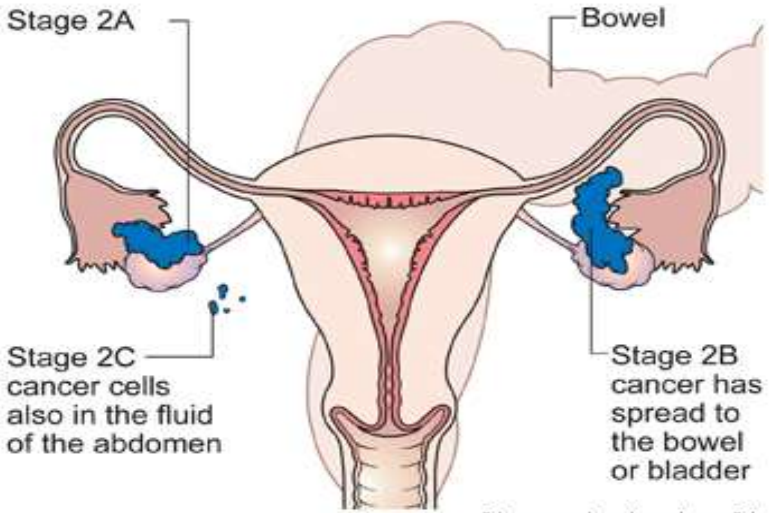


Diagram showing stage 2A
to 2C ovarian cancer

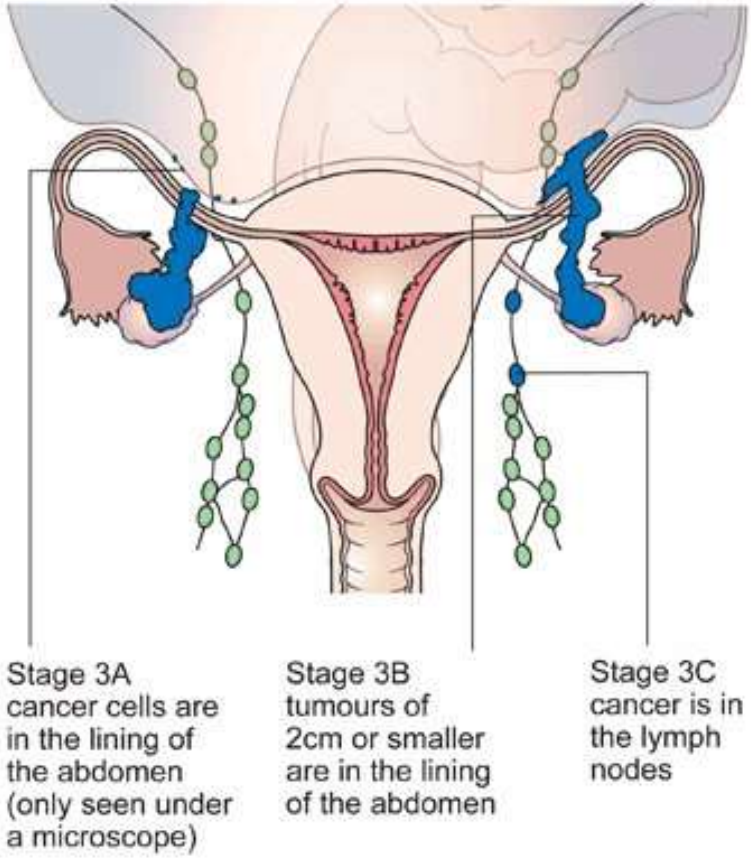


Diagram showing stage
3A to 3C ovarian cancer

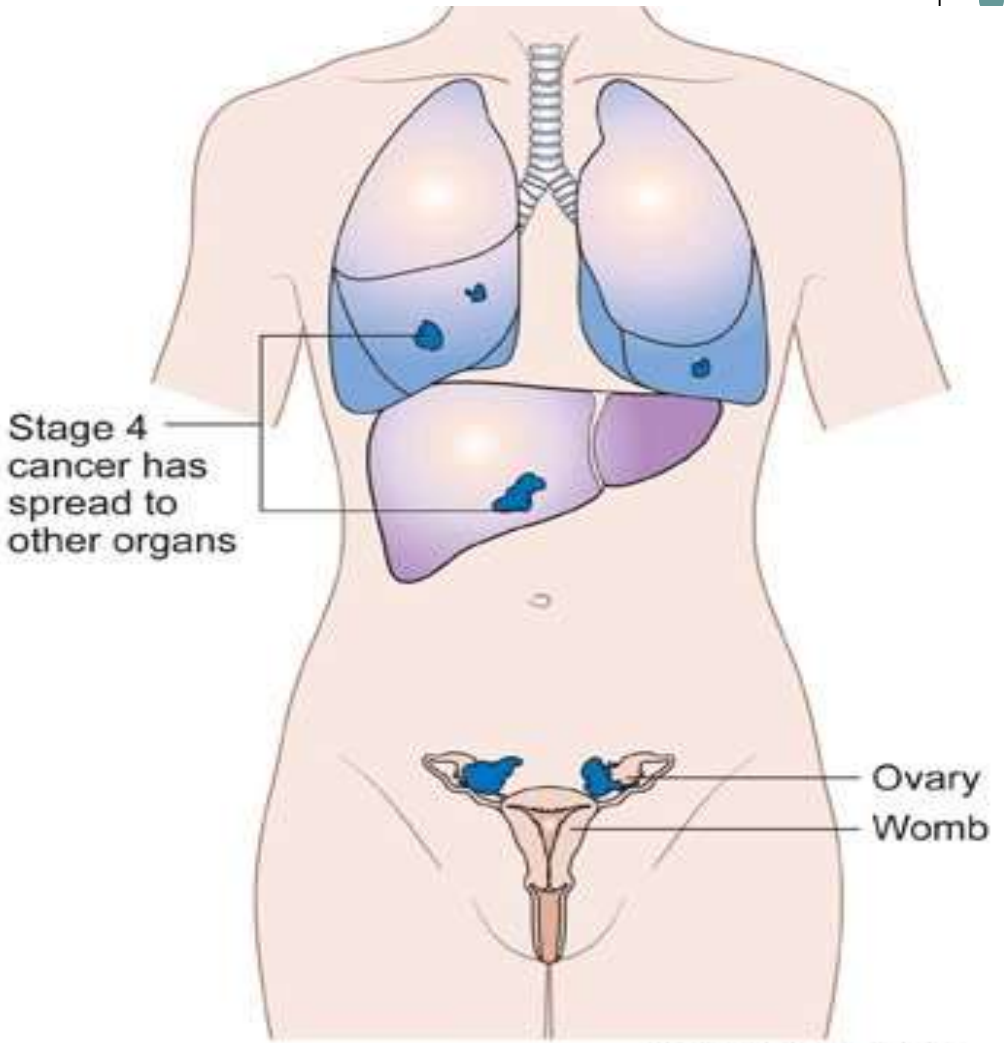


Diagram showing stage
4 ovarian cancer

Grade
provides info about the tumors aggressiveness

- Grade is based on the degree of differentiation (histology).
- Grading can also be described as the degree of malignancy.
  - G1-Well differentiated
  - G2-Moderately well differentiated
  - G3- Poorly differentiated
  - G4- Very poorly differentiated

The degree of malignancy is determined by the proportion of poorly differentiated to well differentiated cells.

The more undifferentiated a tumor is the more likely it is to metastasize.

*Differentiation may be different throughout the tumor.

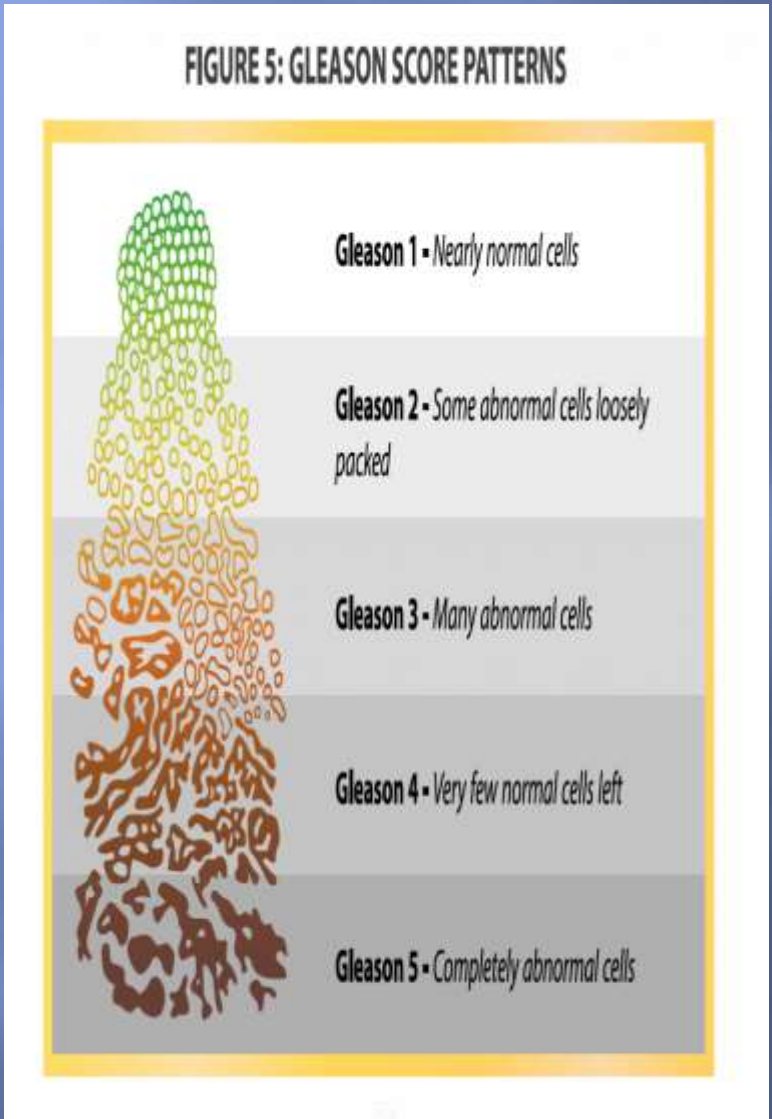
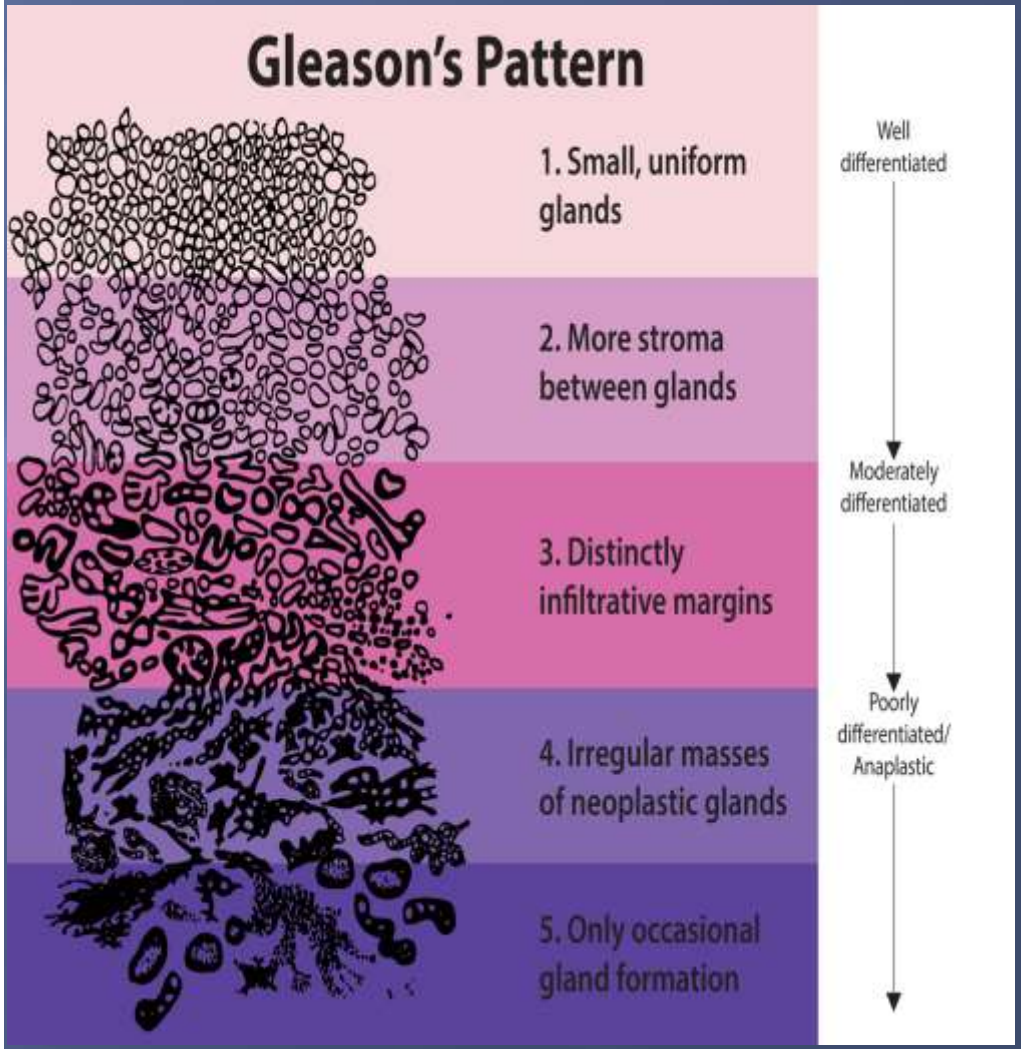


FIGURE 5: GLEASON SCORE PATTERNS
Gleason 1 - Nearly normal cells
Gleason 2 - Some abnormal cells loosely packed
Gleason 3 - Many abnormal cells
Gleason 4 - Very few normal cells left
Gleason 5 - Completely abnormal cells


Gleason's Pattern
1. Small, uniform glands
2. More stroma between glands
3. Distinctly infiltrative margins
4. Irregular masses of neoplastic glands
5. Only occasional gland formation
Well differentiated
Moderately differentiated
Poorly differentiated/ Anaplastic

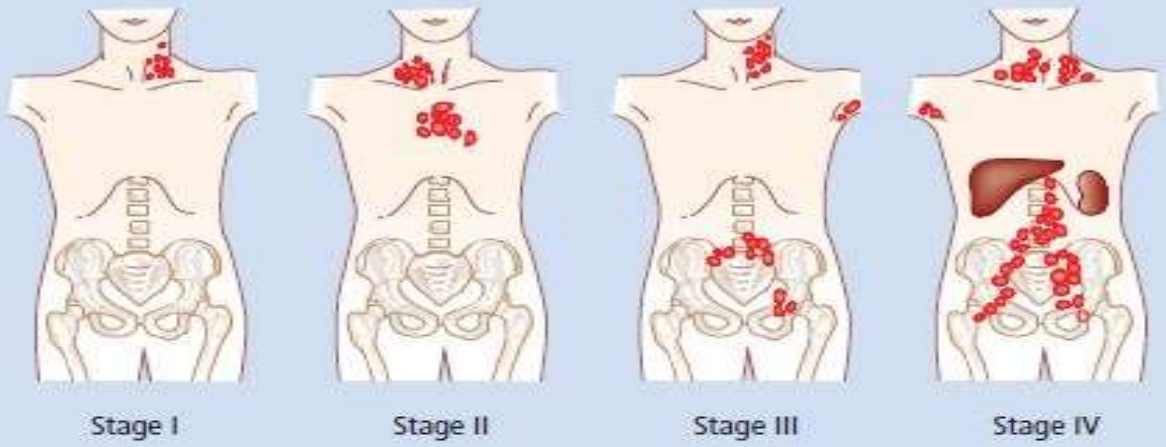
Grading & Staging

- Together, the stage and grade offer an accurate picture of the tumor and its behavior.
- This allows physicians to make better, more effective, treatment decisions

Grading	vs	Staging
• How abnormal the cells are • 1, 2, 3,4 • Based on – Tubule formation – Size and shape of cells – Mitotic division • Measures the likely aggressiveness of the cells		• How far the cancer has spread • I, II, III, IV • Based on – Size of tumor – Invasive vs non invasive – Spread to lymph nodes – Spread to other parts of the body

OTHER CLASSIFICATION

Ann Arbour → lymphomas



A = without symptoms
B = with symptoms including unexplained weight loss (≥10% in 6 months prior to diagnosis), unexplained fever, and drenching night sweats.

Stage I	one lymph node area
Stage II	two or more lymph node areas but confined to one side of the diaphragm
Stage III	lymph nodes above and below the diaphragm – spleen involvement is included
Stage IV	outside the lymph node areas, e.g. bone marrow, liver and other extranodal sites

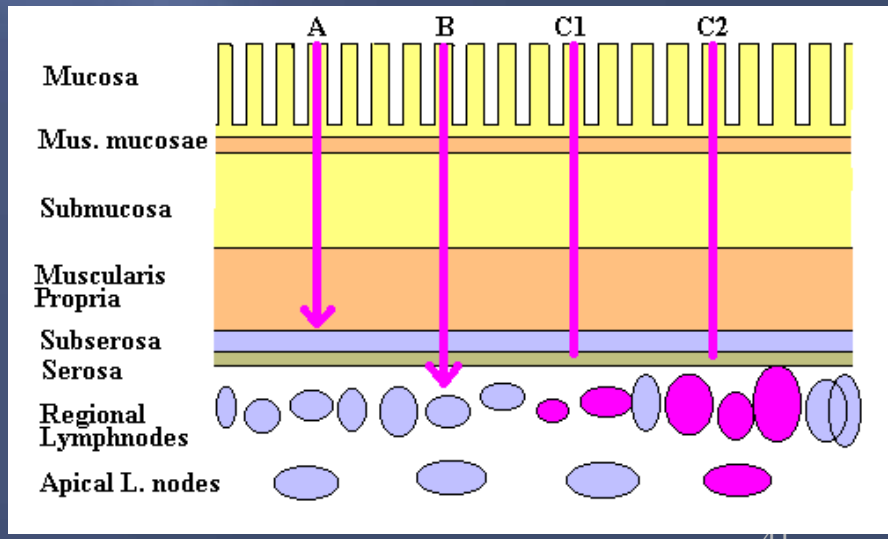
Duke's classification → colon cancer

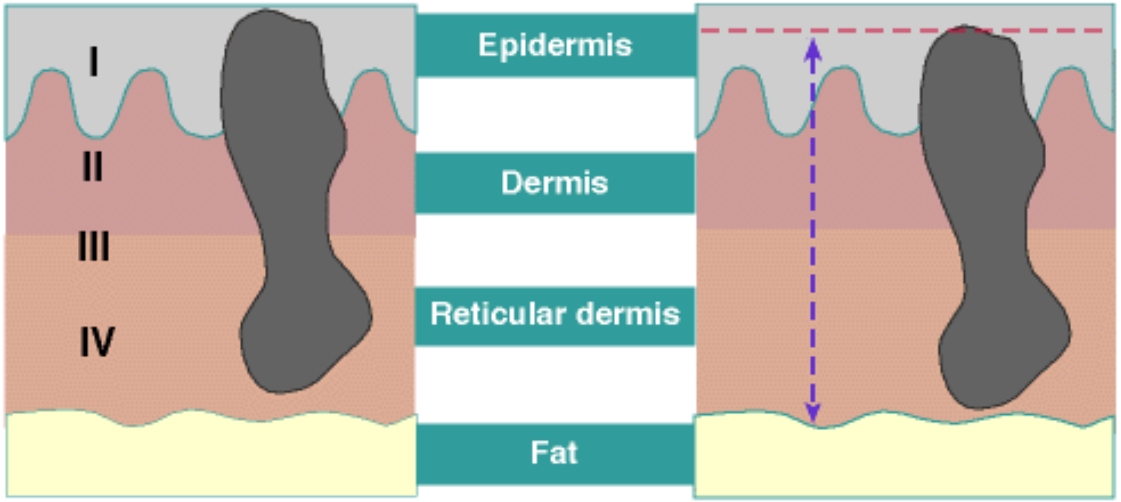
TNM stage	Modified dukes stage	Description
T1N0M0	A	Limited to submucosa
T2N0M	B1	Limited to muscularis propria
T3N0M0	B2	Transmural extension
T2N1M0	C1	T2, enlarged mesenteric nodes
T3N1M0	C2	T3, enlarged mesenteric nodes
T4	C2	Invasion of adjacent organs
Any T, M1	D	Distant metastases present

Modified from the American Joint Committee on Cancer. TNM: Tumor node metastasis

Stage	Features	5-year survival
A	Tumor confined to the mucosa	90–95%
B1	Tumor growth into muscularis propria	75–80%
B2	Tumor growth through muscularis propria and serosa (full thickness)	60%
C1	Tumor spread to 1–4 regional lymph nodes	25–30%
C2	Tumor spread to more than 4 regional lymph nodes	
D	Distant metastases (liver, lung, bones)	<1%

Cuthbert Dukes





Dr. Breslow suggested measuring from the top of the granular layer to the bottom of the melanoma using an occular micrometer within the microscope. This method is highly reproducible and now widely used.

Breslow scale and Clark's level → melanoma

TABLE 2
Clark and Breslow staging and risk[11]

Clark scale (level of invasion)		Breslow scale (vertical thickness)	Risk for metastasis
I	Epidermis (in situ)	in situ	None
II	Invades papillary dermis	<0.75 mm	Minimal (excellent prognosis)
III	Fills the papillary dermis to papillary-reticular junction	0.75–1.5 mm	Significant/medium
IV	Invades reticular dermis	1.51–4.0 mm	High
V	Invades subcutaneous fat/tissue	>4.0 mm	Extremely high

Types of Diagnostic Exams

Normal Chest X-ray

- Chest x-ray
- CT
- Colonoscopy
- MRI
- US

MRI of Glioblastoma Multiforme

Pathology reports → biopsy, cytology

Surgical reports

Lung Cancer

Laboratory tests → blood, urine, AST/ALT, tumor markers (CA19-9,CA19-5….)

computerized tomography **scan**

positron emission tomography **(PET)**

Thanks for your Attention

Acknowledgement

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- Thanks are due to all the original contributors and entities whose pictures were used in the creation of this presentation.