

# **Breast Cancer Staging**

MANOSMED BREAST DIPLOMA COURSE

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Accurate staging is necessary to:

1. Evaluate the results of treatments and clinical trials.
2. Facilitate the exchange and comparison of information among treatment centers.
3. Serve as a basis for clinical and translational cancer research.

- The extent or stage of cancer at the time of diagnosis is a key factor that defines prognosis and is a critical element in determining appropriate treatment based on the experience and outcomes of groups of prior patients with similar stage.
- Several cancer staging systems are used worldwide.
- Differences among these systems stem from the needs and objectives of users in clinical medicine and in population surveillance.
- The most clinically useful staging system is the tumor node metastasis (TNM) system maintained collaboratively by the American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC).

## History

- The TNM classification of cancer was developed between 1943 and 1952 by Prof. Pierre Denoix at the Institute Gustave-Roussy.
  - A little later, the American Joint Committee for Cancer (AJCC) began 1959 publishing separate definitions of TNM categories.
  - The UICC subsequently 1960 established a Special Committee on Clinical Stage Classification under the Chairmanship of Dr Denoix.
  - Revisions to the staging system were updated in 1962
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- The TNM system classifies cancers by the size and extent of the primary tumor (T), involvement of regional lymph node (N), and the presence or absence of distant metastases (M), supplemented in recent years by carefully selected nonanatomic prognostic factors.
  - There is a TNM staging algorithm for cancers of virtually every anatomic site and histology, with the primary exception in this manual being staging of pediatric cancers.

## History

- The Committee and its direct descendant, the UICC TNM Prognostic Factors Project, continued to develop the TNM Classification.
- At the same time as the UICC was developing the TNM Classification, the International Federation of Gynecology and Obstetrics (FIGO) developed the FIGO Classification for Gynecological malignancies.
- In 1987 the UICC and the AJCC TNM classifications were unified.

## Philosophy of TNM Revision

The AJCC and UICC periodically modify the TNM system in response to

1. Newly acquired clinical data
2. Improved understanding of cancer biology and factors affecting prognosis.

The revision cycle for TNM staging is 6–8 years.

## Breast cancer staging

Edition	Publication	Dates effective for cancer diagnosed
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- till present

### *AJCC Cancer Staging Manual* editions

- Since 1905, several systems of classification have been adopted.
- Steintal described the first pure clinical estimation of the stage or the extent of disease at the time of treatment.
- In 1940, the four stage system for clinical evaluation was adopted at the Christi Hospital in Manchester.
- This classification was widely accepted, and is still in use in many centers all over the world.

### Manchester staging system

- **Stage 1:** The growth is confined to the breast.
- **Stage 2:** The growth is confined to the breast, but palpable, mobile lymph nodes are present in the axilla.
- **Stage 3:** The growth extends beyond the mammary parenchyma: (a) skin invasion or fixation over an area large in relation to the size of the breast or skin ulceration; (b) tumor fixation to the underlying muscle or fascia; axillary nodes, if present, are mobile.
- **Stage 4:** The growth extends beyond the breast area as shown by fixation or matting of the axillary nodes, complete fixation of the tumor to chest wall, deposits in supraclavicular nodes or in the opposite breast, or distant metastases.

### TNM staging system

- In 1972, according to Denoix, and the committee of clinical staging of the UICC.
- The new method of clinical staging was widely used by different centers.
- The Manchester system is a simple clinical staging system, while the TNM classification provides a more accurate assessment and is useful in clinical trials.

## 7<sup>th</sup> Edition of TNM staging system

- TX Primary tumor cannot be assessed.
- T0 No evidence of primary tumor.
- Tis Carcinoma in situ.
- Tis (DCIS) DCIS.
- Tis (LCIS) LCIS.
- Tis (Paget) Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted.

### Modifications of T stage since the 6<sup>th</sup> Edition

- Designation changed from T1mic to T1mi
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- T1 Tumor  $\leq 20$  mm in greatest dimension.  
**T1mi Tumor  $\leq 1$  mm in greatest dimension.**  
T1a Tumor  $>1$  mm but  $\leq 5$  mm in greatest dimension.  
T1b Tumor  $>5$  mm but  $\leq 10$  mm in greatest dimension.  
T1c Tumor  $>10$  mm but  $\leq 20$  mm in greatest dimension.
- T2 Tumor  $>20$  mm but  $\leq 50$  mm in greatest dimension.
- T3 Tumor  $>50$  mm in greatest dimension.
- T4 Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules).  
T4a Extension to the chest wall, not including only pectoralis muscle adherence/invasion.  
T4b Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma.  
T4c Both T4a and T4b.  
T4d Inflammatory carcinoma.

### Recommendations of T stage in the 7th Edition

- **Inflammatory Carcinoma** Term is restricted to cases with typical skin changes involving a third or more of the breast (**Decreased from majority of skin to a third or more**).
- Demonstration of **dermal lymphatic involvement** by tumor **not necessary for diagnosis** of IBC (Change from tissue proven necessary to not required).

## Recommendations of T stage in the 7th Edition

- Identified specific **imaging modalities** that can be used to estimate clinical tumor size, including mammography, ultrasound, and magnetic resonance imaging (MRI).

## Recommendations of T stage in the 7th Edition

- Made the recommendation to **estimate the size of noninvasive carcinomas (DCIS and LCIS)**, even though it does not currently change their T classification, because noninvasive cancer size may influence therapeutic decisions, acknowledging that providing a precise size for LCIS may be difficult.
- Acknowledged that the prognosis of **microinvasive carcinoma is generally thought to be quite favorable**, although the clinical impact of multifocal microinvasive disease is not well understood at this time.

## Recommendations of T stage in the 7th Edition

- Acknowledged **“ductal intraepithelial neoplasia” (DIN)** as uncommon, and still not widely accepted, terminology encompassing both DCIS and ADH, and clarification that only cases referred to as DIN containing **DCIS ( $\pm$ ADH)** are classified as **Tis (DCIS)**.
- Acknowledged **“lobular intraepithelial neoplasia” (LIN)** as uncommon, and still not widely accepted, terminology encompassing both LCIS and ALH, and clarification that only cases referred to as LIN containing **LCIS ( $\pm$ ALH)** are classified as **Tis (LCIS)**.
- Clarified that only **Paget’s disease NOT associated** with an underlying **noninvasive (that is, DCIS and/or LCIS) or invasive breast cancer** should be classified as **Tis (Paget’s)** and that Paget’s disease associated with an underlying cancer be classified according to the underlying cancer (Tis, T1, and so on).

## Recommendations of T stage in the 7th Edition

- Recommend that **all invasive cancer** should be graded using **the Nottingham combined histologic grade (Elston-Ellis modification of Scarff–Bloom Richardson grading system)**.

## Elston-Ellis modification of Scarff-Bloom-Richardson grading system

- Formation of tubules
- Degree of anaplasia
- Number of mitoses

**3-5 points: Low grade**

**6-7 points: Intermediate grade**

**8-9 points: High grade**

- **N3** Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement. OR Metastases in clinically detected ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph nodes metastases. OR Metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement.

**N3a** Metastases in ipsilateral infraclavicular lymph node(s).

**N3b** Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node(s).

**N3c** Metastases in ipsilateral supraclavicular lymph node(s).

## N stage 7<sup>th</sup> Edition

- **NX** Regional lymph nodes cannot be assessed (e.g., previously removed).
- **N0** No regional lymph node metastases.
- **N1** Metastases to movable ipsilateral level I, II axillary lymph node(s).
- **N2** Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted. OR Metastases in clinically detected ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases.
  - N2a** Metastases in ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures.
  - N2b** Metastases only in clinically detected ipsilateral internal mammary nodes and in the absence of clinically evident level I, II axillary lymph node metastases.

## Pathologic Classification (pN)

- **pNx** Regional lymph nodes cannot be assessed (e.g., previously removed or not removed for pathologic study)
  - **pN0** No regional lymph node metastases histologically
  - **pN0 (i)** No regional lymph node metastases histologically, negative IHC
  - **pN0 (i+)** Malignant cells in regional lymph node(s) no greater than 0.2 mm (detected by H&E or IHC including ITC)
  - **pN0 (mol)** No regional lymph node metastasis histologically, negative molecular findings (reverse transcriptase polymerase chain reaction [RT-PCR])
  - **pN0 (mol+)** Positive molecular findings (RT-PCR), but no regional lymph node metastases detected by histology or IHC.

**pN1** Micrometastases or metastases in one to three axillary lymph nodes, and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected\*

- **pN1mi** Micrometastases (greater than 0.2 mm, and/or more than 200 cells, but none greater than 2.0 mm)
- **pN1a** Metastases in one to three axillary lymph nodes, at least one metastasis greater than 2.0 mm
- **pN1b** Metastases in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected
- **pN1c** Metastases in 1–3 axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected

**pN3** Metastases in 10 or more axillary lymph nodes, or in infraclavicular (level III) lymph nodes, or clinically detected\*\* ipsilateral internal mammary lymph nodes in the presence of one or more positive level I,II axillary lymph nodes, or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected\*\* or in ipsilateral supraclavicular lymph nodes

- **pN3a** Metastases in 10 or more axillary lymph nodes (at least one tumor deposit greater than 2.0 mm), or metastases to the infraclavicular (level III axillary lymph) nodes
- **pN3b** Metastases in clinically detected ipsilateral internal mammary lymph nodes in the presence of one or more positive axillary lymph nodes, or in more than three axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected.
- **pN3c** Metastases in ipsilateral supraclavicular lymph nodes.

**pN2** Metastases in four to nine axillary lymph nodes, or in clinically detected\*\* internal mammary lymph nodes in the absence of axillary lymph node metastases

- **pN2a** Metastases in four to nine axillary lymph nodes (at least one tumor deposit greater than 2.0 mm)
- **pN2b** Metastases in clinically detected internal mammary lymph nodes in the absence of axillary lymph node metastasis

## Recommendations of N stage in the 7th Edition

- Classification of **isolated tumor cell clusters** and **single cells** is more stringent. Small clusters of cells not greater than 0.2 millimeters, or nonconfluent or nearly confluent clusters of cells not exceeding 200 cells in a single histologic lymph node cross section are classified as isolated tumor cells.
- Use of the **(sn) modifier** has been clarified and restricted. When six or more sentinel nodes are identified on gross examination of pathology specimens the (sn) modifier should be omitted.
- Stage I breast tumors have been subdivided into Stage IA and Stage IB; **Stage IB** includes small tumors (T1) with **exclusively micrometastases in lymph nodes (N1mi)**.

## M stage 7<sup>th</sup> Edition

- **M0** : No clinical or radiographic evidence of distant metastases.
- **cM0(i+)** : No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells in circulating blood, bone marrow, or other non-regional nodal tissue that are  $\leq 0.2$  mm in a patient without symptoms or signs of metastases.
- **M1** : Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven  $>0.2$  mm.

## Recommendations of M stage in the 7th Edition

- Created new **M0(i+)** category, defined by presence of either disseminated tumor cells detectable in bone marrow or circulating tumor cells or found incidentally in other tissues (such as ovaries removed prophylactically) if not exceeding 0.2 millimeters.
- However, this category does not change the stage grouping. Assuming that they do not have clinically and/or radiographically detectable metastases, patients with M0(i+) are staged according to T and N.

## TNM Stage Groups

Stage:	Combinations:
0	• Tis, N0, M0,
1A	• T1, N0, M0
1B	• T0 or T1, N1mic, M0
2A	• T0, N1, M0 or T1, N1, M0 or T2, N0, M0
2B	• T2, N1, M0 or T3, N0, M0
3A	• T0-3, N2, M0 or T3, N1, M0
3B	• T4, N0-2, M0
3C	• Any T, N3, M0
4	• And T, any N, M1

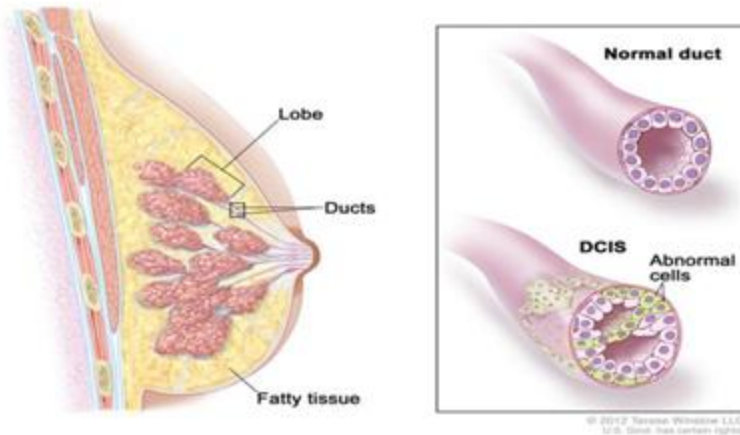
## Stage 0 (carcinoma in situ)

There are 3 types of breast carcinoma in situ:

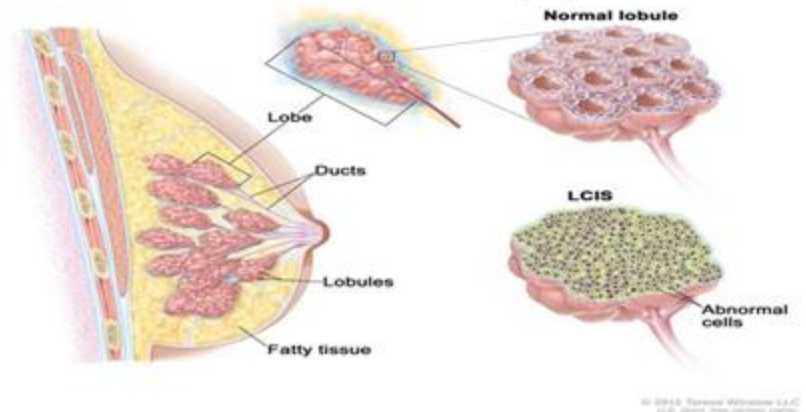
- **Ductal carcinoma in situ (DCIS)** is a noninvasive condition in which abnormal cells are found in the lining of a breast duct. The abnormal cells have not spread outside the duct to other tissues in the breast.
- **Lobular carcinoma in situ (LCIS)** is a condition in which abnormal cells are found in the lobules of the breast. This condition seldom becomes invasive cancer.
- **Paget disease of the nipple** is a condition in which abnormal cells are found in the nipple only.



## Ductal Carcinoma In Situ (DCIS)



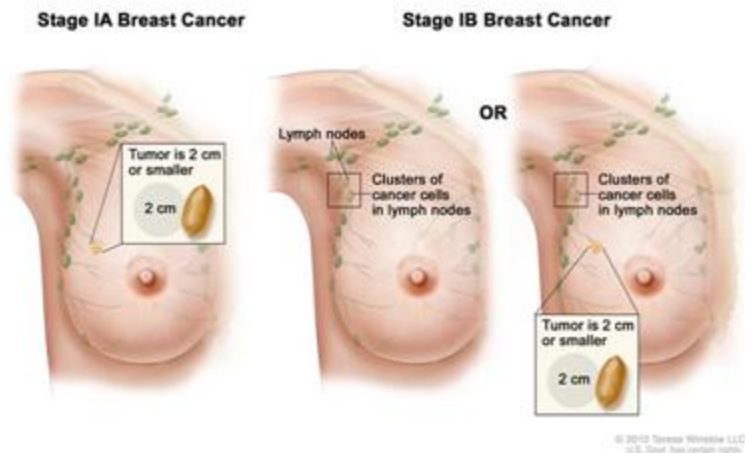
## Lobular Carcinoma In Situ (LCIS)



## Stage Groups : Stage I breast cancer

- **In stage IA**, the tumor is 2 centimeters or smaller and has not spread outside the breast.
- **In stage IB**, no tumor is found in the breast **or** the tumor is 2 centimeters or smaller. Small clusters of cancer cells (larger than 0.2 millimeter but not larger than 2 millimeters) are found in the lymph nodes.

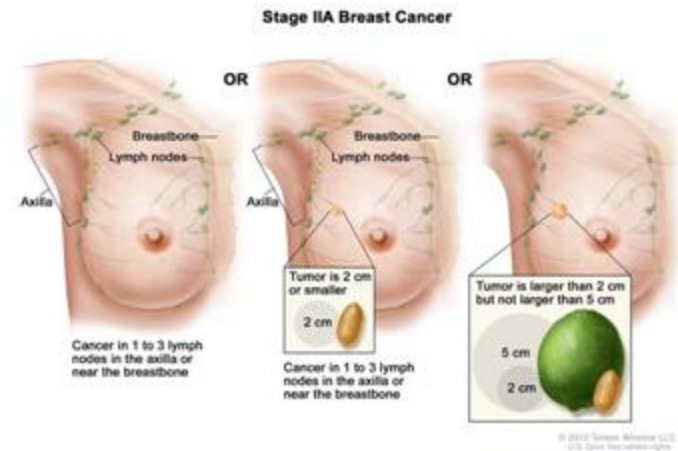
## Stage I A and I B Groups



## Stage Groups : Stage II breast cancer

- **In stage IIA:** no tumor is found in the breast or the tumor is 2 centimeters or smaller. Cancer (larger than 2 millimeters) is found in 1 to 3 axillary lymph nodes); or the tumor is larger than 2 centimeters but not larger than 5 centimeters. Cancer has not spread to the lymph nodes.

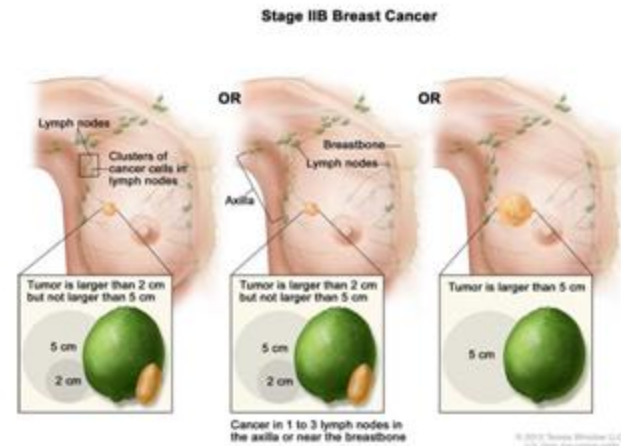
## Stage II A



**In stage IIB,** the tumor is:

- larger than 2 centimeters but not larger than 5 centimeters. Small clusters of breast cancer cells (larger than 0.2 millimeter but not larger than 2 millimeters) are found in the lymph nodes; or
- larger than 2 centimeters but not larger than 5 centimeters. Cancer has spread to 1 to 3 axillary lymph nodes or to the lymph nodes near the breastbone; or
- larger than 5 centimeters. Cancer has not spread to the lymph nodes.

## Stage II B

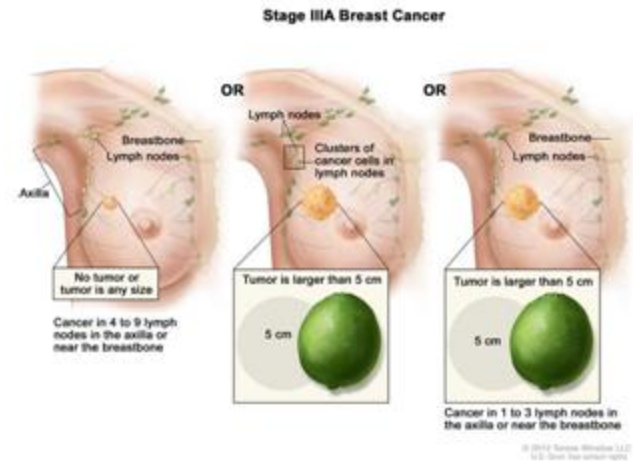


## Stage Groups : Stage III breast cancer

### In stage IIIA:

- no tumor is found in the breast or the tumor may be any size. Cancer is found in 4 to 9 axillary lymph nodes; or
- the tumor is larger than 5 centimeters. Small clusters of breast cancer cells (larger than 0.2 millimeter but not larger than 2 millimeters) are found in the lymph nodes; or
- the tumor is larger than 5 centimeters. Cancer has spread to 1 to 3 axillary lymph nodes.

## Stage IIIA

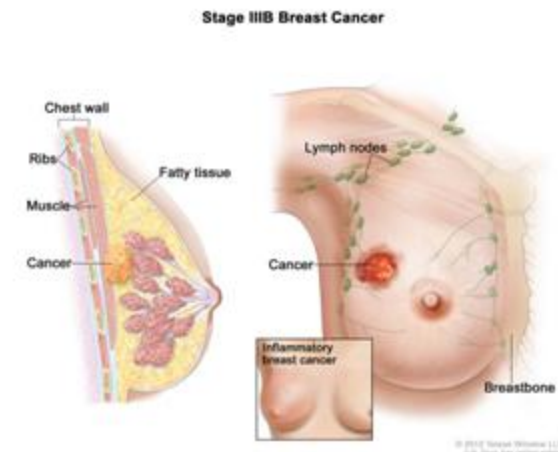


- **In stage IIIB**, the tumor may be any size and cancer has spread to the chest wall and/or to the skin of the breast and caused swelling or an ulcer. Also, cancer may have spread to:

- up to 9 axillary lymph nodes; or
- the lymph nodes near the sternum.

Cancer that has spread to the skin of the breast may be inflammatory breast cancer.

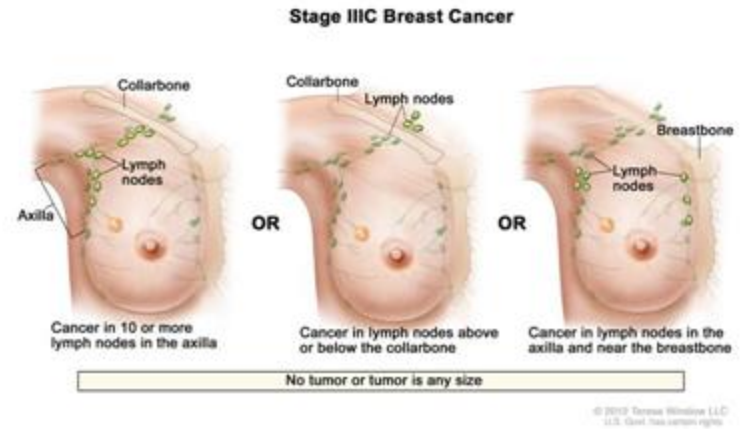
## Stage IIIB



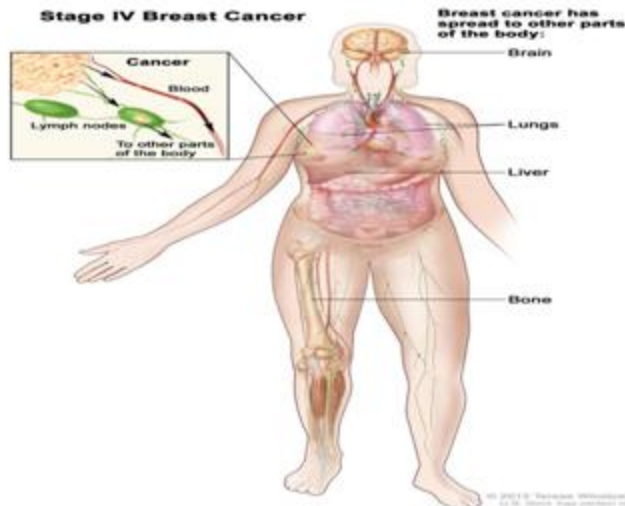
## Stage IIIC

### In stage IIIC,

- no tumor is found in the breast or the tumor may be any size. Cancer may have spread to the skin of the breast and caused swelling or an ulcer and/or has spread to the chest wall. Also, cancer has spread to:
  - 10 or more axillary lymph nodes; or
  - lymph nodes above or below the clavicle; or
  - axillary lymph nodes and lymph nodes near the sternum.



**In stage IV,** cancer has spread to other organs of the body, most often the bones, lungs, liver, or brain.



## Remarks

- T1 includes T1mi.
- T0 and T1 tumors with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.
- M0 includes M0(i+).
- The designation pM0 is not valid; any M0 should be clinical.
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# Remarks

- If a patient presents with M1 prior to neoadjuvant systemic therapy, the stage is considered Stage IV and remains Stage IV regardless of response to neoadjuvant therapy.
- Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.
- Postneoadjuvant therapy is designated with "yc" or "yp" prefix. Of note, no stage group is assigned if there is a complete pathologic response (CR) to neoadjuvant therapy, for example, ypT0ypN0cM0

**Thank you**

