Breast Cancer; Mastectomy with Neoadjuvant and Adjuvant Therapy

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OVERVIEW OF BREAST CANCER THERAPY

Once a diagnosis of breast cancer is made

The type of therapy is determined by :

The stage of the disease

The biologic subtype and

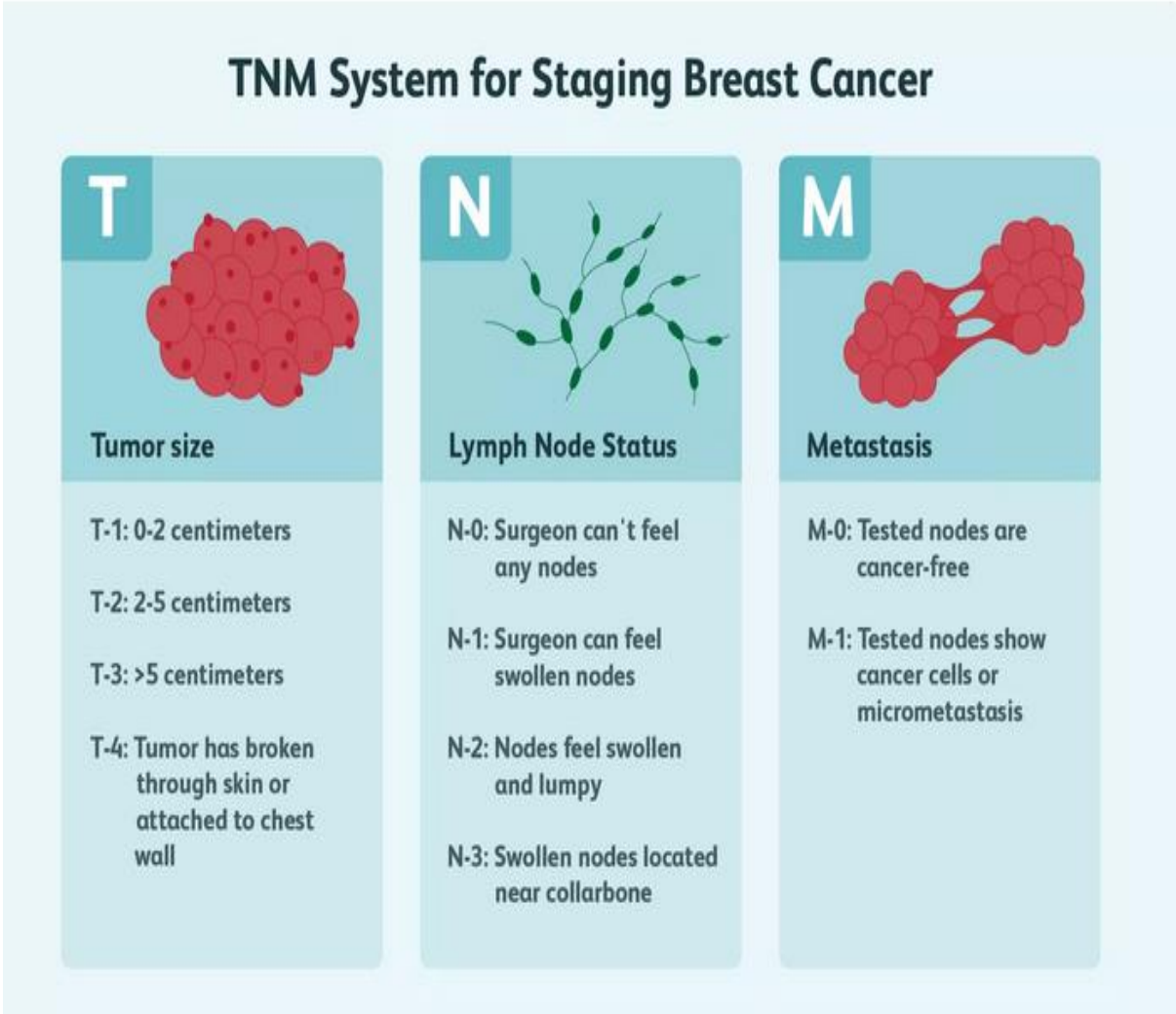
The general health status of the individual.

Diagnostic studies for breast cancer patients

	CANCER STAGE				
	0	I	II	III	IV
History & physical	X	X	X	X	X
Complete blood count, platelet count			X	X	X
Liver function tests and alkaline phosphatase level			X	X	X
Chest radiograph			X	X	X
Bilateral diagnostic mammograms, ultrasound as indicated	X	X	X	X	X
Hormone receptor status	X	X	X	X	X
HER-2/*neu* expression		X	X	X	X
Bone scan				X	X
Abdominal (without or without pelvis) computed tomographic scan or ultrasound or magnetic resonance imaging				X	X

TNM stage groupings

STAGE 0	TIS	N0	M0
Stage IA	T1[a]	N0	M0
Stage IB	T0	N1mi	M0
	T1[a]	N1mi	M0
Stage IIA	T0	N1[b]	M0
	T1[a]	N1[b]	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1[a]	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1



In Situ Breast Cancer (Stage 0)

Lobular carcinoma in situ (LCIS)

- ***Lobular carcinoma in situ (LCIS)***
- The current treatment options include:
- observation,
- chemoprevention,
- bilateral total mastectomy.

- ***There is no benefit to excising LCIS***
- the disease diffusely involves both breasts
- the risk of developing invasive cancer is equal for both breasts.

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
Tis (DCIS)	Ductal carcinoma in situ
Tis (LCIS)	Lobular carcinoma in situ
Tis (Paget's)	Paget's 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's disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget's disease should still be noted
T1	Tumor ≤20 mm in greatest dimension
T1mi	Tumor ≤1 mm in greatest dimension
T1a	Tumor >1 mm but ≤5 mm in greatest dimension
T1b	Tumor >5 mm but ≤10 mm in greatest dimension
T1c	Tumor >10 mm but ≤20 mm in greatest dimension
T2	Tumor >20 mm but ≤5 cm 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 chest wall, not including only pectoralis muscle adherence/invasion
T4b	Ulceration and/or ipsilateral satellite nodules and/or edema (including peaud'orange) of the skin, which do not meet the criteria for inflammatory carcinoma
T4c	Both T4a and T4b
T4d	Inflammatory carcinoma**
	*Note: Invasion of the dermis alone does not qualify as T4
	**Note: Inflammatory carcinoma is restricted to cases with typical skin changes involving a third or more of the skin of the breast. While the histologic presence of invasive carcinoma invading dermal lymphatics is supportive of the diagnosis, it is not required, nor is dermal lymphatic invasion without typical clinical findings sufficient for a diagnosis of inflammatory breast cancer.

- ***Ductal Carcinoma in Situ (DCIS)***

- **evidence of extensive disease:**
  Tumor size >4 cm of disease
  more than one quadrant
- *usually require mastectomy*

- **Limited disease**
- lumpectomy and radiation therapy

- **Nonpalpable DCIS**
- needle localization
  image-guided techniques are used to guide the surgical resection.

- Since it is not feasible to perform sentinel node dissection after mastectomy, most surgeons will recommend the use of sentinel node dissection at the time of mastectomy for DCIS

Early Invasive Breast Cancer (Stage I, IIA, or IIB)

- ***lumpectomy and radiation therapy(WBI)***
- The preferred method of treatment :
- women who have unifocal disease
- who are not known BRCA mutation carriers

- **Some studies suggest:**
- *radiation can be avoided in early-stage breast cancer*
- patients over the age of 70 years
- when are diagnosed with T1, N0,
- ER-positive breast cancer

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Stage IIA	T0	N1[b]	M0
	T1[a]	N1[b]	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0

- ***Accelerated partial breast irradiation (APBI):***

- selected patients with DCIS and early stage breast cancer.
- recurrences after breast conservation: in or adjacent to the tumor bed

- There has been interest in limiting the radiation to the area of the primary tumor bed with a margin of normal tissue.

- patients “suitable” for APBI
- women 60 years of age or older with a unifocal,
- T1,
- ER-positive tumor with no lymphovascular invasion
- margins of at least 2 mm.

- Multiple RCT with follow-up of up to 20 years :
- BCT is safe and has survival outcomes equivalent to mastectomy in stage I and II breast cancer.

- A few earlier trials reported higher rates of locoregional recurrence (LRR) following BCT than were seen after mastectomy (10-22%)
- Much lower LRR rates are reported in contemporary studies.

- *It is now understood that local control:*

  tumor subtype

  administration of systemic therapy

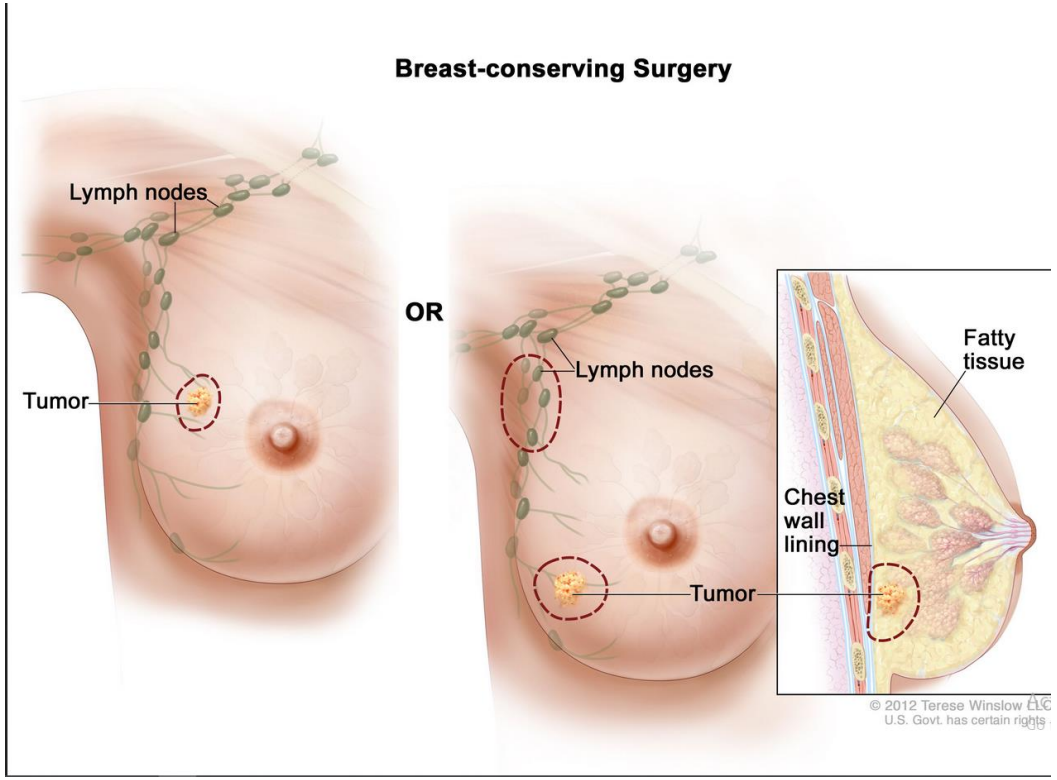
Currently, mastectomy with axillary staging and breast conserving surgery with axillary staging and radiation therapy.

equivalent treatments for patients with stage I and II breast cancer

Breast conservation is considered for all patients

cosmetic advantages and

equivalent survival outcomes



not advised in women who are known BRCA mutation carriers due to the high lifetime risk for development of additional breast cancers

Breast-conserving therapy (BCT)

- Excision of the tumor (lumpectomy) followed by adjuvant whole breast irradiation (WBI).
- excise the tumor to negative margins
- with an acceptable cosmetic outcome
- the patient must be able to receive radiotherapy,
- the breast must be suitable for follow-up to allow prompt detection of local recurrence.

- ***Relative contraindications to BCT include***

- (a) prior radiation therapy to the breast or chest wall,
- (b) persistently positive surgical margins after reexcision,
- (c) multicentric disease
- (d) scleroderma or lupus erythematosus.
- (e) The presence of diffuse suspicious or malignant appearing calcifications
- (f)Can not be resected to negative margins with a satisfactory cosmetic result

- *Young age, aggressive tumor subtype (HER2 positive and triple negative), and lobular histology are not contraindications to BCT*

- Local recurrence rates are highest among patients with hormone receptor (HR) negative, HER2 negative cancers (“triple negative”), and lowest among patients with HR positive, HER2 negative cancers

- In smaller, node-negative breast cancers (mammographic screening)
- routine use of ALND for axillary staging not necessary.
- ***up to 75% operable breast cancer presenting with a negative axilla at the time of screening.***

- ***(NCCN) guidelines:***
  no OS difference for patients with 1 or 2 positive
  SLNs treated with breast conserving surgery who underwent completion ALND vs. those who had no further axillary surgery

- patients with axillary lymphadenopathy
- FNA or core biopsy confirmed the metastatic disease
- SLN dissection is not necessary

Directly ALND or be considered for preoperative systemic therapy

- ***The American Society of Clinical Oncology has included SLN dissection as appropriate for axillary staging:***
- larger primary tumors (T3)
- treated with neoadjuvant chemotherapy.

- *If a SLN cannot be identified:*
- ALND is generally performed for appropriate staging.

- Completion ALND is indicated in patients with 3 or more positive sentinel lymph nodes and those found to have matted nodes intraoperatively.

- Preoperative axillary imaging in clinically node-negative patients should be reserved for those undergoing mastectomy where the finding of any nodal disease is an indication for ALND or preoperative chemotherapy to downstage the axilla.

Adjuvant chemotherapy for patients with early-stage:

- node-positive cancers,
- cancers that are >1 cm, and
- node-negative cancers of >0.5 cm when adverse prognostic features are present.

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- ***Adverse prognostic factors:***
- blood vessel or lymph vessel invasion,
- high nuclear grade,
- high histologic grade,
- *HER*-2/*neu* overexpression or amplification,
- negative hormone receptor status

Neoadjuvant chemotherapy

- *NAC has been used in operable tumors:*
- To downstage disease in the breast and axilla with the intention of facilitating breast conservation and, in some instances, avoiding ALND.

- *NAC is most likely to allow BCT in the woman:*

  Unicentric cancer which is large relative to the size of her breast

  HER2 positive

  Triple negative breast cancers.

- Accurate evaluation of response to therapy and the feasibility of BCT can be problematic.
- MRI is more accurate than mammography or ultrasound in predicting the extent of residual disease,
- *Normal MRI does not exclude the presence of scattered foci of viable carcinoma which may preclude BCT.*

Advanced Local-Regional Breast Cancer (Stage IIIA or IIIB)

Advanced local-regional breast cancer

No clinically detected distant metastases.

- *It should be noted that most of these patients will already have distant metastasis which is often highlighted by radiological evidence when bone scans, PET &/or CT scans are performed*

Even when they are negative, elevated serum tumor markers may be another indicator that distant spread has already occurred

Stage IIIA	T0	N2	M0
	T1[a]	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0

- ***An important part of the initial clinical evaluation :***
- Identify clinical criteria of unresectibility which necessitate the use of neoadjuvant therapy.
- ***These include :***
- Inflammatory carcinoma(T4)
- Fixation of the tumor to the bony chest wall(ribs, sternum)(T4)
- Extensive skin involvement with ulceration or satellite skin nodules,
- Fixed/matted axillary lymphadenopathy(N3)
- Involvement of neurovascular structures of the axilla, or lymphedema of the ipsilateral arm.

- ***All of these findings are readily identifiable on physical examination and should prompt an imaging evaluation for distant metastases***

- ***The initial management:***

- Preoperative (also known as neoadjuvant) chemotherapy
  especially estrogen receptor negative tumors.

- Surgical therapy :
- *modified radical mastectomy, followed by adjuvant radiation therapy*

- *Chemotherapy is used to maximize distant disease-free survival, whereas radiation therapy is used to maximize local-regional control and disease-free survival.*

- Selected patients with stage IIIA cancer:

- *preoperative chemotherapy can reduce the size of the primary cancer and permit breast-conserving surgery*

Selected patients with stage IIIA cancer:

preoperative chemotherapy can reduce the size of the primary cancer and permit breast-conserving surgery

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	T1[a]	N2	M0
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Stage IIIC	Any T	N3	M0

N-0	The surgeon cannot feel any swollen nodes.
N-1	The surgeon can feel some swelling and thinks the nodes are positive (cancerous).
N-2	The lymph nodes feel like they are quite swollen, lumpy, and bunched together.
N-3	Swollen lymph nodes are near the collarbone.

- patients who presented with nodal metastases and became clinically node negative after NAC had a nodal pathologic complete response and 3 or more identifiable sentinel nodes, and were able to avoid axillary dissection.
- In patients who remain node positive, completion ALND is standard. The question of whether or not axillary radiation can be substituted for a completion ALND in the setting of a positive axillary sentinel node after NAC is currently being addressed in the Alliance A011202 tria

- ***In both stage IIIA and IIIB disease, surgery is followed by adjuvant radiation therapy***

Postmastectomy radiation (PMRT)

- *Patients with 4 or more positive axillary lymph nodes*
- 25% or greater risk of developing an LRR.
- *Tumor size ≥ 5 cm*
- an increased risk of chest wall recurrence of > 20%.
- For this reason, PMRT has been considered standard in these patients for many years.
- *PMRT in women with 1-3 positive lymph nodes and T1-2 breast cancers is an area of ongoing debate.*

PMRT is recommended following NAC:

patients who present with clinical T3-4 tumors
N2-3 nodal involvement
who have persistent nodal disease following NAC.

The benefit of PMRT in clinical T1-2, N1 patients who have a pathologic complete response is an area of ongoing study

T-1	0 to 2 centimeters (cm)
T-2	2 to 5 cm
T-3	Greater than 5 cm
T-4	Tumor of any size that has broken through (ulcerated) the skin or is attached to the chest wall

N-0	The surgeon cannot feel any swollen nodes.
N-1	The surgeon can feel some swelling and thinks the nodes are positive (cancerous).
N-2	The lymph nodes feel like they are quite swollen, lumpy, and bunched together.
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Internal Mammary Lymph Nodes

- Metastatic disease to internal mammary lymph nodes
- may be occult,
- may be evident on CXR or CT scan
- painless parasternal mass with or without skin involvement.

Need for internal mammary lymph node radiation therapy ??

- at increased risk for occult involvement (cancers involving the medial aspect of the breast, axillary lymph node involvement) but who show no signs of internal mammary lymph node Involvement.

NO CONSENSUS

Distant Metastases (Stage IV)

- Not curative but may prolong survival and enhance a woman’s quality of life.
- Several reports have suggested that women who undergo resection of the primary tumor have improved survival over those who do not.