Tumor, node, metastasis (TNM) staging classification for breast cancer

AUTHOR: Harold J Burstein, MD, PhD
SECTION EDITOR: Anees B Chagpar, MD, MSc, MA, MPH, MBA, FACS, FRCS(C)
DEPUTY EDITOR: Sadhna R Vora, MD

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Oct 2023.**
This topic last updated: **Apr 15, 2022.**

INTRODUCTION

The tumor, node, metastasis (TNM) staging system for breast cancer is an internationally accepted system used to determine the disease stage. This disease stage is used to determine prognosis and guide management. It is also used to facilitate discussions about treatment and prognosis between collaborating providers, as well as between providers and patients.

The TNM staging system correlates important tumor characteristics with survival data to help estimate and follow outcomes. It is based upon a retrospective analysis of survival in diverse samples of patients representing all stages of disease. It reflects the clinical evaluation methods and treatments that are applied to the particular study population. While an individual patient's clinical course and outcome cannot be predicted with certainty, available survival data can help direct treatment decisions and provide an estimate of the likely prognosis.

Periodic revisions are necessary because advanced imaging techniques and treatments evolve and impact survival. The eighth edition of the TNM staging system, which is effective as of January 1, 2018, includes anatomic stage groups (table 1) as well as two prognostic stage groups, a pathologic (table 2) and a clinical (table 3) prognostic stage group [1]. Staging has traditionally relied on tumor size, involvement of lymph nodes, and presence of metastatic disease. The eighth edition incorporates biologic markers, which improve prognostic discrimination over anatomic staging alone. Outside of the United States, the

Union for International Cancer Control (UICC) implemented the eighth edition changes as of January 1, 2017.

The rationale and data supporting the eighth edition of the TNM staging system are discussed here. The initial evaluation, clinical manifestations, diagnosis, treatment, and prognosis of breast cancer are reviewed elsewhere. (See "Overview of the treatment of newly diagnosed, invasive, non-metastatic breast cancer" and "Clinical features, diagnosis, and staging of newly diagnosed breast cancer".)

REVISIONS IN STAGING FROM THE SEVENTH TO THE EIGHTH EDITIONS

The eighth edition of the American Joint Committee on Cancer (AJCC) staging manual, effective January 1, 2018, outlines a new prognostic staging system that relies not only on the anatomic extent of disease, but also on prognostic biomarkers. A clinical prognostic stage table for use in all patients has been developed, based on history, physical examination, imaging studies if performed, and relevant biopsies. It incorporates T, N, M, and tumor grade; and human epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), and progesterone receptor (PR) status. For those who undergo surgical resection as their initial treatment (before receipt of any systemic or radiation therapy), a pathologic prognostic table has been developed and assigns stage based on all clinical information, biomarker data, and findings from surgery and resected tissue. (See 'Prognostic stage groupings' below.)

In areas in which biomarker testing is performed, prognostic stage groups should be utilized. Although the prognostic staging system provides refined information regarding outcomes, the anatomic staging was retained to allow a common lexicon for patients treated worldwide who may not have access to biomarker testing. Additionally, the anatomic staging system provides a link to cases treated historically, staged using previous editions of the TNM system.

The biomarkers utilized in the eighth edition staging system and supporting data are discussed in detail below. (See 'Incorporation of biologic prognostic factors' below and 'Validation' below.)

Modest changes were made to the anatomic staging system and are discussed in the relevant sections below. (See 'The eighth edition TNM staging system' below.)

Incorporation of biologic prognostic factors — The following were incorporated into the prognostic staging system of the eighth edition of the AJCC staging manual:

- **Estrogen receptor (ER) and progesterone receptor (PR) expression –** Testing for ER and PR is typically performed using immunohistochemistry. A tumor is considered ER or

PR positive if 1 percent or greater of tumor cells stain for the respective protein, regardless of the strength of staining. (See "Hormone receptors in breast cancer: Clinical utility and guideline recommendations to improve test accuracy", section on 'Assays for ER and PR'.)

- **Human epidermal growth factor receptor 2 (HER2) –** HER2 is assayed using either immunohistochemistry to assess protein levels or fluorescent in situ hybridization (FISH) to quantify gene copy number. (See "HER2 and predicting response to therapy in breast cancer", section on 'Testing for HER2 expression'.)

- **Histologic grade –** The grade of a tumor is determined by assessing morphologic features (ie, formation of tubules, mitotic count, and variability and the size and shape of cellular nuclei), assigning a score between 1 (most favorable) and 3 (least favorable) for each feature, and totaling the scores. Grade 1 corresponds to combined scores between 3 and 5, grade 2 corresponds to a combined score of 6 or 7, and grade 3 corresponds to a combined score of 8 or 9.

- **Recurrence Score (RS) –** The results of a multigene assay should be incorporated into the prognostic staging for patients with hormone receptor-positive, HER2-negative, node-negative tumors that are <5 cm. Specifically, for such patients, an RS <11 on Oncotype Dx denotes a prognosis similar to those with T1a to b N0M0 tumors, and they are assigned a prognostic stage of IA.

  The Oncotype Dx is a genomic assay of 21 genes assessed by reverse transcription polymerase chain reaction (RT-PCR). A score <11 denotes a favorable prognosis, with the TAILORx trial demonstrating a five-year distant recurrence-free survival of 99.3 percent for such patients with endocrine therapy alone [2]. (See "Deciding when to use adjuvant chemotherapy for hormone receptor-positive, HER2-negative breast cancer", section on 'Recurrence Score'.)

The clinical prognostic staging system assumes that the patient is receiving effective therapy. Thus, HER2-positive tumors are "downstaged" in this system because of the assumption that effective anti-HER2 treatment will improve outcomes. Similarly, staging stratification by RS assumes that the patient is taking effective antiestrogen treatments. In clinical situations where the patient will not or cannot receive effective adjuvant therapy, the prognostic value of the clinical prognostic staging criteria is markedly affected.

In addition to the above, the AJCC expert panel identified several other factors that may also yield prognostic information, but are not formally included in the staging system:

- **Ki-67 –** Ki-67 is a nuclear protein associated with cellular proliferation assessed by immunohistochemistry, although a uniform methodology is lacking. Standard cutoffs for high, intermediate, or low Ki-67 scores do not exist.

- **Multigene expression assays other than RS –** RS was the only multigene expression panel supported by level I evidence, and therefore was included in the eighth edition of the TNM staging system. Other multigene expression panels, however, including MammaPrint, EndoPredict, PAM50 Risk of Recurrence (ROR), and the Breast Cancer Index are supported by level II evidence and may be incorporated into future editions of the TNM staging system when high-level data are available. (See "Prognostic and predictive factors in early, non-metastatic breast cancer", section on 'Receptor status' and "Deciding when to use adjuvant chemotherapy for hormone receptor-positive, HER2-negative breast cancer".)

- **Risk assessment models –** The AJCC evaluated 30 prognostication tools for breast cancer and found that two tools, Adjuvant! Online and PREDICT-Plus, met all of the predefined inclusion criteria and none of the exclusion criteria. These tools provide estimates of outcomes among women treated for early breast cancer and indicate the relative benefit of adjuvant treatments. They were externally validated and have acceptable levels of predictive accuracy.

- **Circulating tumor cells (CTCs) –** CTCs are cancer cells that separate from solid tumors and enter the blood stream. The US Food and Drug Administration (FDA) has approved the CellSearch assay for detection of CTCs in metastatic breast cancer, in which they are a poor prognostic indicator. This assay uses ferrofluid nanoparticles with antibodies that target epithelial cell adhesion molecules, allowing for magnetic separation and subsequent immunohistochemical staining of cancer cells. For metastatic breast cancer, the cutoff for an unfavorable prognosis is ≥5 cells/7.5 mL. Although the use of this assay in primary breast cancer has been explored, an expert panel from the American Society of Clinical Oncology (ASCO) concluded that there are insufficient data to support its use in this setting. (See "Prognostic and predictive factors in metastatic breast cancer", section on 'Circulating tumor cells' and "Prognostic and predictive factors in early, non-metastatic breast cancer", section on 'Disseminated and circulating tumor cells'.)

- **Disseminated tumor cells (DTCs) –** DTCs in the bone marrow provide prognostic information regarding the likelihood of relapse at the time of initial tumor resection. The relevant cutoff is ≥1 cell. Although DTCs may provide prognostic information and are included as an additional factor for clinical care in the eighth edition AJCC manual, an ASCO expert panel on tumor markers in breast cancer concluded that the available data were insufficient to recommend their use in clinical decision-making. (See "Prognostic and predictive factors in early, non-metastatic breast cancer", section on 'Disseminated and circulating tumor cells'.)

Validation — Two independent groups demonstrated that incorporation of biologic markers would improve prognostic discrimination over anatomic staging alone.

Clinical prognostic stage groups for the eighth edition were established based on a study of 334,243 patients enrolled in the National Cancer Database between 2010 and 2012, representing over 70 percent of breast cancers diagnosed in the United States [1]. A second analysis using 305,519 patients who received surgical resection as initial treatment was also conducted and forms the basis of the pathologic prognostic stage groupings. In these analyses, survival calculations were performed based on anatomic stage, grade, HER2, and ER/PR status. Patients with any-grade, triple-negative tumor and those with grade 3, HER2-negative tumors that were negative for either ER or PR had decreased survival, comparable to patients with at least one stage higher disease based on anatomic staging alone. Incorporation of grade, HER2, and hormone receptor status for both clinical and pathologic prognostic staging groups led to reassignment of stage in more than 35 percent of cases compared with the AJCC seventh edition staging system.

Similarly, in a study of approximately 3700 patients enrolled in a database from the University of Texas MD Anderson Cancer Center, ER and PR status and grade were found to refine anatomic staging most precisely [1]. When compared with anatomic stage alone, incorporation of these biomarkers (as part of a "risk profile") resulted in improved discrimination between stages in regards to disease-specific survival (table 4). Given that this analysis predated the use of trastuzumab for patients with HER2-positive breast cancer, a subsequent analysis of roughly 3300 patients found that a staging system that incorporated HER2 status further improved upon the prognostic reliability of the staging system.

THE EIGHTH EDITION TNM STAGING SYSTEM

The anatomic and prognostic stage groups, which incorporate biomarkers, are shown in the respective tables (table 1 and table 3 and table 2), with relevant classifications according to the American Joint Committee on Cancer (AJCC) discussed below [1].

Clinical versus pathologic staging — Each characteristic of a tumor (size, nodal involvement, metastases) can be evaluated and reported either clinically, using physical exam, with or without imaging, and incorporating any biopsy results (if available); or pathologically, which uses all the data from clinical staging, plus data from surgical resection. Pathologic examination must include excision of the primary carcinoma with no macroscopic tumor at any margins.

At diagnosis, most patients are assigned to a pathologic stage based on T and N and M status. Then it can be useful to adjust their prognostic status by anticipated treatment and

tumor subset.

Pathologic staging is generally considered to be more accurate than clinical staging (table 2 and table 3). However, there are instances in which the clinical staging is useful for making initial treatment recommendations, particularly in regards to neoadjuvant therapy and determining eligibility for clinical trials. Subsequent pathology may alter the clinical TNM classification. (See "General principles of neoadjuvant management of breast cancer".)

Primary tumor classification — The definitions for tumor classification are the same whether assessed clinically or pathologically. A designation of cT or pT is used to indicate whether the staging is based on clinical or pathologic criteria. Pathologic classification is preferred when available.

- Tx – Primary tumor is unable to be assessed.
- T0 – No evidence of primary tumor.
- Tis – Carcinoma in situ.
  - **Tis (DCIS) –** Ductal carcinoma in situ.
  - **Tis (Paget) –** Paget disease of the nipple **not** associated with invasive carcinoma and/or DCIS in the underlying breast parenchyma. Carcinoma in the breast parenchyma associated with Paget disease is categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget 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 (round any measurement 1.0 to 1.9 mm to 2 mm).
  - **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 ≤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 the skin (ulceration or macroscopic 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 peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma.
- **T4c –** Both (T4a and T4b).
- **T4d –** Inflammatory carcinoma**.

*Invasion of the dermis alone does not qualify as T4.

**Inflammatory carcinoma is restricted to cases with typical skin changes involving one-third or greater 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. (See "Inflammatory breast cancer: Clinical features and treatment", section on 'Diagnostic criteria'.)

Changes in tumor (T) classification — Changes in T staging between the seventh and eighth editions are summarized here:

- Lobular carcinoma in situ (LCIS) is now considered a benign entity and is no longer classified as Tis. (See "Atypia and lobular carcinoma in situ: High-risk lesions of the breast".)
- Tumors >1 mm and <2 mm should now be rounded to 2 mm, so as not to classify tumors between 1 and 1.5 mm as microinvasive (T1mi) carcinomas.
- The eighth edition confirmed that small, microscopic, satellite tumor foci around a primary should not be added to the maximum tumor size.
- It also clarified that the T size for multiple synchronous tumors is that of the largest tumor, but the suffix "m" should be appended to the T score.
- It defined T4b lesions as macroscopic satellite tumor nodules to the skin that are separate from the primary tumor. Microscopic skin and dermal tumor satellite nodules do not qualify and should be classified based on tumor size.

Regional lymph nodes (N) — Lymph node classification criteria differ depending on whether the nodes are clinically or pathologically assessed. A designation of cN or pN is used to make the distinction. Pathologic classification is preferred when available.

Regional lymph nodes include axillary nodes, ipsilateral intramammary nodes, internal mammary nodes, and supraclavicular nodes. Intramammary nodes reside within the breast

tissue and are coded as axillary lymph nodes for staging purposes. Supraclavicular lymph nodes are classified as regional lymph nodes for staging purposes. Metastases to any other lymph node, including cervical, or contralateral axillary lymph nodes are classified as distant (M1).

Clinical classification of regional lymph nodes

- cNX* – Regional lymph nodes cannot be assessed (eg, previously removed).
- cN0 – No regional lymph node metastases (neither by imaging nor clinical exam).
- cN1 – Metastasis to movable ipsilateral level I, II axillary lymph nodes(s).
  - cN1mi** – Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm).
- cN2 – Metastasis to ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in ipsilateral internal mammary nodes in the absence of clinically evident axillary node metastases.
  - **cN2a** – Metastasis to ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures.
  - **cN2b** – Metastasis only in ipsilateral internal mammary nodes, and in the absence of clinically evident axillary node metastases.
- cN3 – Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement.
  - **cN3a** – Metastasis to ipsilateral infraclavicular lymph node(s).
  - **cN3b** – Metastasis to ipsilateral internal mammary lymph node(s) and axillary lymph nodes.
  - **cN3c** – Metastasis in ipsilateral supraclavicular lymph node(s).

*The cNX category is used sparingly in cases where regional lymph nodes have previously been surgically removed or where there is no documentation of physical examination of the axilla.

**cN1mi is rarely used but may be appropriate in cases where sentinel node biopsy is performed before tumor resection (such as in certain cases treated neoadjuvantly).

The suffixes (sn) and (f) should be added to the N descriptor to note confirmation by sentinel lymph node biopsy or fine needle aspiration/core needle biopsy, respectively.

Pathologic classification of regional lymph nodes

- pNX – Regional lymph nodes cannot be assessed (eg, previously removed, or not removed for pathologic study).
- pN0 – No regional lymph node metastases.
  - **pN0** – No regional lymph node metastasis identified or isolated tumor cells (ITCs) only.
  - **pN0(i+)** – Malignant cells in regional lymph node(s) no greater than 0.2 mm (detected by hematoxylin and eosin stain [H&E] or immunohistochemistry [IHC] including ITCs).
  - **pN0(mol+)** – Positive molecular findings (reverse transcription polymerase chain reaction [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 clinically negative internal mammary nodes with micro- or macrometastases detected by sentinel lymph node biopsy.
  - **pN1mi** – Micrometastases (approximately 200 cells, greater than 0.2 mm, but none greater than 2.0 mm).
  - **pN1a** – Metastases in one to three axillary lymph nodes, with at least one metastasis greater than 2.0 mm.
  - **pN1b** – Metastases in ipsilateral internal mammary sentinel nodes, excluding ITCs.
  - **pN1c** – pN1a and pN1b combined.
- pN2 – Metastases in four to nine axillary lymph nodes, or positive ipsilateral internal mammary lymph nodes by imaging 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** – Metastasis only in clinically detected internal mammary nodes with or without microscopic confirmation; with pathologically negative axillary nodes.
- pN3 – Metastases in 10 or **more** axillary lymph nodes; or in infraclavicular (level III axillary) lymph nodes; or in ipsilateral internal mammary lymph nodes by imaging 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.

- **N3a –** 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 –** pN1a or pN2a in the presence of cN2b (positive internal mammary nodes by imaging); or pN2a in the presence of pN1b.

- **pN3c –** Metastases in ipsilateral supraclavicular lymph nodes.

The suffixes (sn) and (f) should be added to the N descriptor to note confirmation by sentinel lymph node biopsy or fine needle aspiration/core needle biopsy, respectively, with **no** further resection of lymph nodes.

Changes in nodes (N) classification — The eighth edition clarified that the largest contiguous tumor deposit should define pN. Dimensions of satellite deposits are not added.

Furthermore, clarification was added that cNX should only be used when a nodal basin has been removed and cannot be examined by imaging or clinical exam. cN0 is assigned to tumors in which nodal exam and imaging, if obtained, are negative.

Distant metastasis (M)

- M0 – No clinical or radiographic evidence of distant metastases (no pathologic M0; imaging studies are not required to assign the cM0 category).

  - cM0(i+) – No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells that are no larger than 0.2 mm are present in circulating blood, bone marrow, or other nonregional nodal tissue 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 metastases larger than 0.2 mm.

Changes in metastases (M) classification — In the eighth edition, clarification was added that pM0 should not be used. Cases are either cM0 or cM1, and if cM1 disease is confirmed by biopsy, then pM1 should be used.

Clarifications regarding postneoadjuvant staging — Postneoadjuvant pathologic T and N categories (ypT and ypN) are based on the largest focus of residual tumor at the primary site

or lymph nodes, respectively. Treatment-related fibrosis is not included in these measurements. If multiple foci of residual tumor are present at the primary site, the suffix "m" is appended to the T stage. If a cancer was categorized as M1 prior to neoadjuvant therapy, it remains M1 after treatment, regardless of response.

Anatomic stage groupings — The anatomic stage groupings are found in the table (table 1).

Prognostic stage groupings — The clinical prognostic stage applies to all patients with breast cancer (table 3). It is the primary prognostic staging system for patients who receive neoadjuvant treatment or for those who do not receive surgery. It is based on clinical T, N, and M; grade; and HER2 and hormone receptor status and does not include genomic profile information.

For patients who receive surgical resection as initial treatment, a pathologic prognostic stage should be assigned (table 2). It is based on pathologic T, N, and M; grade; HER2 and hormone receptor status; and for T1 to T2 N0, ER-positive, HER2-negative disease, the result of genomic testing.

THE SEVENTH EDITION TNM STAGING SYSTEM

The previous edition of the TNM staging system was the seventh edition, which was in effect between January 1, 2010 and December 31, 2017 (table 5). This system was based on observed survival rates for 211,645 breast cancer cases diagnosed in the years 2001 to 2002 and entered into the National Cancer Database (Commission on Cancer of the American College of Surgeons and the American Cancer Society). It included anatomic staging only, without incorporation of biomarkers.

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles

on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: Breast cancer guide to diagnosis and treatment (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **The tumor, node, metastasis (TNM) staging system –** The TNM staging system for breast cancer is an internationally accepted system used to determine the disease stage. The eighth edition of the TNM staging system, effective as of January 1, 2018, is the most recent version and includes anatomic stage groups as well as clinical and pathologic prognostic stage groups, which incorporate biomarker testing. (See 'Anatomic stage groupings' above and 'Prognostic stage groupings' above.)

- **Anatomic staging system –** The TNM anatomic staging system for breast cancer classifies tumors on the basis of the primary tumor type (invasive or in situ) and size (T), the presence or absence of regional lymph node involvement (N), and the presence or absence of distant metastases (M). The overall anatomic stage of the tumor (stage I through IV) depends upon the particular combination of T, N, and M characteristics. (See 'The eighth edition TNM staging system' above.)

- **Prognostic staging systems –** The TNM prognostic staging system for breast cancer relies on the anatomic extent of disease as well as grade, hormone and human epidermal growth factor 2 (HER2) receptor status, and, for those with T1 to 2 N0M0, hormone-receptor positive, HER2-negative, node-negative tumors, the result of genomic testing. If testing for these biomarkers is available, patients should be staged using the prognostic staging systems.

  - The clinical prognostic staging system applies to all patients.

  - For those in whom surgery is the initial cancer treatment, a pathologic prognostic stage should be assigned. (See 'Revisions in staging from the seventh to the eighth editions' above.)

  - The clinical prognostic staging system assumes that the patient is receiving effective therapy. Thus, HER2-positive tumors are "downstaged" in this system because of the assumption that effective anti-HER2 treatment will improve outcomes. Similarly, staging stratification by recurrence score assumes that the patient is taking effective antiestrogen treatments. In clinical situations where the patient will not or cannot receive effective adjuvant therapy, the prognostic value of the clinical prognostic staging criteria is markedly affected.

ACKNOWLEDGMENT

Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original sources for this material are the AJCC Cancer Staging Manual, Seventh Edition (2010) and Eighth Edition (2017) published by the AJCC and Springer.

REFERENCES

1. AJCC (American Joint Committee on Cancer) Cancer Staging Manual; 8th edition, 3rd printing, Amin MB, Edge SB, Greene FL, et al (Eds), Springer, Chicago 2018.
2. Sparano JA, Gray RJ, Makower DF, et al. Prospective Validation of a 21-Gene Expression Assay in Breast Cancer. N Engl J Med 2015; 373:2005.

Topic 800 Version 35.0

GRAPHICS

Breast carcinoma TNM anatomic stage group AJCC UICC 8th edition

When T is...	And N is...	And M is...	Then the stage group is...
Tis	N0	M0	0
T1	N0	M0	IA
T0	N1mi	M0	IB
T1	N1mi	M0	IB
T0	N1	M0	IIA
T1	N1	M0	IIA
T2	N0	M0	IIA
T2	N1	M0	IIB
T3	N0	M0	IIB
T0	N2	M0	IIIA
T1	N2	M0	IIIA
T2	N2	M0	IIIA
T3	N1	M0	IIIA
T3	N2	M0	IIIA
T4	N0	M0	IIIB
T4	N1	M0	IIIB
T4	N2	M0	IIIB
Any T	N3	M0	IIIC
Any T	Any N	M1	IV

- The anatomic stage group table should only be used in global regions where biomarker tests are not routinely available.

- Cancer registries in the US must use the prognostic stage group table for case reporting.

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

Graphic 110848 Version 8.0

Breast carcinoma TNM pathologic prognostic stage groups AJCC UICC 8th edition

When TNM is…	And grade is…	And HER2 status is…	And ER status is…	And PR status is…	Then the pathological prognostic stage group is…
Tis N0 M0	Any	Any	Any	Any	0
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G1	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G2	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G3	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
T0 N1¶ M0	G1	Positive	Positive	Positive	IA
				Negative	IB

T1* N1¶ M0 T2 N0 M0			Negative	Positive	IB
				Negative	IIA
		Negative	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IIA
T0 N1¶ M0 T1* N1¶ M0 T2 N0 M0	G2	Positive	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IIA
		Negative	Positive	Positive	IA
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
T0 N1¶ M0 T1* N1¶ M0 T2 N0 M0	G3	Positive	Positive	Positive	IA
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
T2 N1Δ M0 T3 N0 M0	G1	Positive	Positive	Positive	IA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
T2 N1Δ M0 T3 N0 M0	G2	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB

		Negative	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
T2 N1[Δ] M0 T3 N0 M0	G3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIA
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G1	Positive	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G2	Positive	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G3	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIB
				Negative	IIIA

			Negative	Positive	IIIA
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G1	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G2	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G3	Positive	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIC
			Negative	Positive	IIIC
				Negative	IIIC
Any T Any N M1	Any	Any	Any	Any	IV

NOTES:

1. For cases with lymph node involvement with no evidence of primary tumor (eg, T0 N1, etc) or with breast ductal carcinoma *in situ* (eg, Tis N1, etc), the grade, HER2, ER, and PR information from the tumor in the lymph node should be used for assigning stage group.
2. For cases where HER2 is determined to be "equivocal" by ISH (FISH or CISH) testing under the 2013 ASCO/CAP HER2 testing guidelines, the HER2 "negative" category should be used for staging in the pathological prognostic stage group table.

3. The prognostic value of these prognostic stage groups is based on populations of persons with breast cancer that have been offered and mostly treated with appropriate endocrine and/or systemic chemotherapy (including anti-HER2 therapy).

Genomic profile for pathologic prognostic staging

When OncotypeDx score is less than 11...

When TNM is...	And grade is...	And HER2 status is...	And ER status is...	And PR status is...	Then the pathological prognostic stage group is...
T1 N0 M0 T2 N0 M0	Any	Negative	Positive	Any	IA

NOTES:

1. Obtaining genomic profiles is NOT required for assigning pathological prognostic stage. However genomic profiles may be performed for use in determining appropriate treatment. If the OncotypeDx test is performed in cases with a T1N0M0 or T2N0M0 cancer that is HER2-negative and ER-positive, and the recurrence score is less than 11, the case should be assigned pathological prognostic stage group IA.
2. If OncotypeDx is not performed, or if it is performed and the OncotypeDx score is not available, or is 11 or greater for patients with T1-2 N0 M0 HER2-negative, ER-positive cancer, then the prognostic stage group is assigned based on the anatomic and biomarker categories shown above.
3. OncotypeDx is the only multigene panel included to classify pathologic prognostic stage because prospective level I data supports this use for patients with a score less than 11. Future updates to the staging system may include results from other multigene panels to assign cohorts of patients to prognostic stage groups based on the then available evidence. Inclusion or exclusion in this staging table of a genomic profile assay is not an endorsement of any specific assay and should not limit appropriate clinical use of any genomic profile assay based on evidence available at the time of treatment.

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

* T1 includes T1mi.

¶ N1 does not include N1mi. T1 N1mi M0 and T0 N1mi M0 cancers are included for prognostic staging with T1 N0 M0 cancers of the same prognostic factor status.

Δ N1 includes N1mi. T2, T3, and T4 cancers and N1mi are included for prognostic staging with T2 N1, T3 N1, and T4 N1, respectively.

---

printing, 2017.

Graphic 117141 Version 7.0

Breast carcinoma TNM clinical prognostic stage groups AJCC UICC 8th edition

When TNM is…	And grade is…	And HER2 status is…	And ER status is…	And PR status is…	Then the clinical prognostic stage group is…
Tis N0 M0	Any	Any	Any	Any	0
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G1	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G2	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IB
T1* N0 M0 T0 N1mi M0 T1* N1mi M0	G3	Positive	Positive	Positive	IA
				Negative	IA
			Negative	Positive	IA
				Negative	IA
		Negative	Positive	Positive	IA
				Negative	IB
			Negative	Positive	IB
				Negative	IB

T0 N1[¶] M0 T1* N1[¶] M0 T2 N0 M0	G1	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
T0 N1[¶] M0 T1* N1[¶] M0 T2 N0 M0	G2	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
T0 N1[¶] M0 T1* N1[¶] M0 T2 N0 M0	G3	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIA
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
T2 N1[Δ] M0 T3 N0 M0	G1	Positive	Positive	Positive	IB
				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
T2 N1[Δ] M0	G2	Positive	Positive	Positive	IB

T3 N0 M0				Negative	IIA
			Negative	Positive	IIA
				Negative	IIB
		Negative	Positive	Positive	IIA
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIIB
T2 N1[Δ] M0 T3 N0 M0	G3	Positive	Positive	Positive	IB
				Negative	IIB
			Negative	Positive	IIB
				Negative	IIB
		Negative	Positive	Positive	IIB
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G1	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0	G2	Positive	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIA
				Negative	IIIA
			Negative	Positive	IIIA
				Negative	IIIB
T0 N2 M0 T1* N2 M0	G3	Positive	Positive	Positive	IIB
				Negative	IIIA

T2 N2 M0 T3 N1[Δ] M0 T3 N2 M0			Negative	Positive	IIIA
				Negative	IIIA
		Negative	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G1	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G2	Positive	Positive	Positive	IIIA
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIC
T4 N0 M0 T4 N1[Δ] M0 T4 N2 M0 Any T N3 M0	G3	Positive	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
				Negative	IIIB
		Negative	Positive	Positive	IIIB
				Negative	IIIC
			Negative	Positive	IIIC
				Negative	IIIC
Any T Any N M1	Any	Any	Any	Any	IV

NOTES:

1. Because N1mi categorization requires evaluation of the entire node, and cannot be assigned on the basis of an FNA or core biopsy, N1mi can only be used with the clinical prognostic staging when clinical staging is based on a resected lymph node in the absence of resection of the primary cancer, such as the situation where sentinel node biopsy is performed prior to receipt of neoadjuvant chemotherapy or endocrine therapy.
2. For cases with lymph node involvement with no evidence of primary tumor (eg, T0 N1, etc) or with breast ductal carcinoma *in situ* (eg, Tis N1, etc), the grade, HER2, ER, and PR information from the tumor in the lymph node should be used for assigning stage group.
3. For cases where HER2 is determined to be "equivocal" by ISH (FISH or CISH) testing under the 2013 ASCO/CAP HER2 testing guidelines, the HER2 "negative" category should be used for staging in the clinical prognostic stage group table.
4. The prognostic value of these prognostic stage groups is based on populations of persons with breast cancer that have been offered and mostly treated with appropriate endocrine and/or systemic chemotherapy (including anti-HER2 therapy).

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control.

* T1 includes T1mi.

¶ N1 does not include N1mi. T1 N1mi M0 and T0 N1mi M0 cancers are included for prognostic staging with T1 N0 M0 cancers of the same prognostic factor status.

Δ N1 includes N1mi. T2, T3, and T4 cancers and N1mi are included for prognostic staging with T2 N1, T3 N1, and T4 N1, respectively.

Graphic 110851 Version 11.0

Risk profile and associated survival outcomes, MD Anderson validation of biomarkers in TNM 8th edition staging

	Five-year DSS (%)	Univariate analysis		Multivariate analysis 2		Assigned points
		HR	*p*	HR	*p*	
Pathological stage						
I	99.1	Referent		Referent		0
IIA	98.0	2.8	0.002	2.3	0.01	1
IIB	95.6	4.8	<0.0001	4.0	<0.0001	2
IIIA	95.4	6.8	<0.0001	7.2	<0.0001	3
IIIC	79.5	26.6	<0.0001	19.9	<0.0001	4
Nuclear grade						
I	99.8	Referent		Referent		0
II	98.9	5.0	0.1	4.0	0.2	0
III	95.3	25.0	0.001	13.1	0.01	1
ER status						
Positive	98.8	Referent		Referent		0
Negative	92.9	4.9	<0.0001	2.5	0.001	1
PR status						
Positive	98.8	Referent		Referent		
Negative	95.2	4.0	<0.0001		NS	
HER2 status						
Positive	97.5	Referent		Referent		0
Negative	98.0	0.8	0.5	2.2	0.04	1

Factor	**0 points**	**1 point**
Grade	Grade 1/2	Grade 3
ER status	ER positive	ER negative
HER2 status	HER2 positive	HER2 negative

Stage	**Risk profile**	**N**	**Five-year DSS (%)**	**95% CI**	**Five-year OS (%)**	**95% CI**
I (IA and IB)	0	36	100		97	80.4-99.6
	1	1173	99.4	98.7-99.7	96.7	95.4-97

	2	274	98.8	96.4-99.6	94.6	91-96.8
	3	119	96.6	91.1-98.7	93.8	87.5-97
IIA	0	31	100		96.8	79.2-99.5
	1	634	99.4	97.5-99.8	97.1	94.7-98.4
	2	236	97.5	93.2-99.1	94.1	88.7-97
	3	98	91	81.8-95.7	88.2	78.5-93.8
IIB	0	11	100		100	
	1	309	96.9	92.6-98.8	94.6	89.6-97.2
	2	107	92.9	83.6-97.1	89.3	80.1-94.4
	3	40	91.5	75.6-97.2	91.5	75.6-97.2
IIIA	0	3	100		100	
	1	134	98.3	88.2-99.8	91.5	82.6-96
	2	50	92.2	77.2-97.5	90.3	75.7-96.3
	3	7	68.6	21.3-91.2	68.6	21.3-91.2
IIIC	0	0				
	1	39	92.2	72.1-98.0	84.4	63.7-93.9
	2	16	80.8	51.4-93.4	80.8	51.4-93.4
	3	10	33.3	6.3-64.6	33.3	6.3-64.6

TNM: tumor, node, metastasis; AJCC: American Joint Committee on Cancer.

Graphic 110850 Version 9.0

Breast carcinoma TNM staging AJCC UICC 2010

Primary tumor (T)*¶Δ	
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 (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'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 ≤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§
Posttreatment ypT.¥ The use of neoadjuvant therapy does not change the clinical (pretreatment) stage. Clinical (pretreatment) T will be defined by clinical and radiographic findings, while y pathologic (posttreatment) T will be determined by pathologic size and extension. The ypT will be measured as the largest single focus of invasive tumor, with the modifier "m" indicating multiple foci. The measurement of the largest tumor focus should not include areas of fibrosis within the tumor bed.	
Regional lymph nodes (N)	
Clinical	
NX	Regional lymph nodes cannot be assessed (eg, 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 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
N3	Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected‡ ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node 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)
Pathologic (pN)†**	
pNX	Regional lymph nodes cannot be assessed (eg, previously removed, or not removed for pathologic study)
pN0	No regional lymph node metastasis identified histologically
pN0(i-)	No regional lymph node metastases histologically, negative immunohistochemistry (IHC)
pN0(i+)	Malignant cells in regional lymph node(s) no greater than 0.2 mm (detected by H&E or IHC including isolated tumor cell clusters (ITC))
pN0(mol-)	No regional lymph node metastases histologically, negative molecular findings (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 1-3 axillary lymph nodes; and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected ΔΔ
pN1mi	Micrometastases (greater than 0.2 mm and/or more than 200 cells, but none greater than 2.0 mm)
pN1a	Metastases in 1-3 axillary lymph nodes, at least one metastasis greater than 2 mm
pN1b	Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected ΔΔ

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
pN2	Metastases in 4-9 axillary lymph nodes; or in clinically detected◇◇ internal mammary lymph nodes in the *absence* of axillary lymph node metastases
pN2a	Metastases in 4-9 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 metastases
pN3	Metastases in ten or more axillary lymph nodes; or in infraclavicular (level III axillary) lymph nodes; or in 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 ΔΔ; or in ipsilateral supraclavicular lymph nodes
pN3a	Metastases in ten 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 ΔΔ
pN3c	Metastases in ipsilateral supraclavicular lymph nodes
Posttreatment ypN	
▪ Post-treatment yp "N" should be evaluated as for clinical (pretreatment) "N" methods above. The modifier "sn" is used only if a sentinel node evaluation was performed after treatment. If no subscript is attached, it is assumed that the axillary nodal evaluation was by axillary node dissection (AND).	
▪ The X classification will be used (ypNX) if no yp posttreatment SN or AND was performed	
▪ N categories are the same as those for pN	
Distant metastasis (M)	
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 nonregional nodal tissue that are no larger than 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 larger than 0.2 mm

Posttreatment yp M classification. The M category for patients treated with neoadjuvant therapy is the category assigned in the clinical stage, prior to initiation of neoadjuvant therapy. Identification of distant metastases after the start of therapy in cases where pretherapy evaluation showed no metastases is considered progression of disease. If a patient was designated to have detectable distant metastases (M1) before chemotherapy, the patient will be designated as M1 throughout.			
Anatomic stage/prognostic groups[§§]			
0	Tis	N0	M0
IA	T1[¥¥]	N0	M0
IB	T0	N1mi	M0
	T1[¥¥]	N1mi	M0
IIA	T0	N1[‡‡]	M0
	T1[¥¥]	N1[‡‡]	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1[¥¥]	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

* The T classification of the primary tumor is the same regardless of whether it is based on clinical or pathologic criteria, or both. Designation should be made with the subscript "c" or "p" modifier to indicate whether the T classification was determined by clinical (physical examination or radiologic) or pathologic measurements, respectively. In general, pathologic determination should take precedence over clinical determination of T size.

¶ Size should be measured to the nearest millimeter. If the tumor size is slightly less than or greater than a cutoff for a given T classification, it is recommended that the size be rounded to the millimeter reading that is closest to the cutoff.

Δ Multiple simultaneous ipsilateral primary carcinomas are defined as infiltrating carcinomas in the same breast, which are grossly or macroscopically distinct and measurable. T stage is based only on the largest tumor. The presence and sizes of the smaller tumor(s) should be recorded using the "(m)" modifier.

◇ Invasion of the dermis alone does not qualify as T4; dimpling of the skin, nipple retraction, or any other skin change except those described under T4b and T4d may occur in T1, T2, or T3 without changing the classification. The chest wall includes ribs, intercostal muscles, and serratus anterior muscle, but not the pectoralis muscles.

§ Inflammatory carcinoma is a clinical-pathologic entity characterized by diffuse erythema and edema (peau d'orange) involving a third or more of the skin of the breast. These skin changes are due to lymphedema caused by tumor emboli within dermal lymphatics. Although dermal lymphatic involvement supports the diagnosis of inflammatory breast cancer, it is neither necessary nor sufficient, in the absence of classical clinical findings, for the diagnosis of inflammatory breast cancer.

¥ If a cancer was designated as inflammatory before neoadjuvant chemotherapy, the patient will be designated to have inflammatory breast cancer throughout, even if the patient has complete resolution of inflammatory findings.

‡ *Clinically detected* is defined as detecting by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration biopsy with cytologic examination. Confirmation of clinically detected metastatic disease by fine needle aspiration without excision biopsy is designated with an (f) suffix, for example, cN3a(f). Excisional biopsy of a lymph node or biopsy of a sentinel node, in the absence of assignment of a pT, is classified as a clinical N, for example, cN1. Information regarding the confirmation of the nodal status will be designated in site specific factors as clinical, fine needle aspiration, core biopsy, or sentinel lymph node biopsy. Pathologic classification (pN) is used for excision or sentinel lymph node biopsy only in conjunction with a pathologic T assignment.

† Classification is based on axillary lymph node dissection with or without sentinel lymph node biopsy. Classification based solely on sentinel lymph node biopsy without subsequent axillary lymph node dissection is designated (sn) for "sentinel node," for example, pN0(sn).

** Isolated tumor cell clusters (ITC) are defined as small clusters of cells not greater than 0.2 mm, or single tumor cells, or a cluster of fewer than 200 cells in a single histologic cross-section. ITCs may be detected by routine histology or by immunohistochemical (IHC) methods. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification but should be included in the total number of nodes evaluated.

¶¶ RT-PCR: reverse transcriptase/polymerase chain reaction.

ΔΔ "Not clinically detected" is defined as not detected by imaging studies (excluding lymphoscintigraphy) or not detected by clinical examination.

◇◇ "Clinically detected" is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathologic macrometastasis based on fine needle aspiration biopsy with cytologic examination.

§§ Anatomic stage:

- M0 includes M0(i+).
- The designation pM0 is not valid; any M0 should be clinical.
- 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 the "y" prefix. For patients with a pathologic complete response (pCR) to neoadjuvant therapy, no stage group is assigned (ie, yT0N0M0).

¥¥ T1 includes T1mi.

‡‡ T0 and T1 tumors with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.

Graphic 65393 Version 14.0

Contributor Disclosures

Harold J Burstein, MD, PhD No relevant financial relationship(s) with ineligible companies to disclose. **Anees B Chagpar, MD, MSc, MA, MPH, MBA, FACS, FRCS(C)** Consultant/Advisory Boards: Guardant Health [Breast cancer]; Merck [Breast cancer]; Novartis [Breast cancer]; Protean BioDiagnostics [Breast cancer]; Sanofi-Aventis [Breast cancer]. Speaker's Bureau: Merck [Breast cancer]. All of the relevant financial relationships listed have been mitigated. **Sadhna R Vora, MD** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→