Microinvasive breast carcinoma

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INTRODUCTION

Microinvasive breast carcinoma is defined as invasive carcinoma of the breast with no invasive focus measuring more than 1 mm [1]. It is most commonly encountered in the setting of ductal carcinoma in situ (DCIS); thus, it is usually referred to as DCIS with microinvasion. It is less frequently seen in association with lobular carcinoma in situ (LCIS) or in the absence of carcinoma in situ.

The epidemiology, clinical presentation, pathology, and treatment of microinvasive breast carcinoma will be reviewed here. DCIS and LCIS are presented separately.

- (See "Ductal carcinoma in situ: Treatment and prognosis".)
- (See "Breast ductal carcinoma in situ: Epidemiology, clinical manifestations, and diagnosis".)
- (See "Atypia and lobular carcinoma in situ: High-risk lesions of the breast".)
- (See "Pathology of breast cancer".)

OVERVIEW

Data about the epidemiology and clinical significance of microinvasive breast carcinoma have been limited by its uncommon incidence and the historical lack of a standardized definition.

Epidemiology — The incidence of microinvasive breast carcinoma appears to have increased in parallel with the rising incidence of ductal carcinoma in situ (DCIS), which has been attributed primarily to the introduction of breast cancer screening programs as well as more thorough sampling of breast tissue specimens.

Nevertheless, pure microinvasive breast carcinoma (without associated DCIS) remains an uncommon disease, estimated as accounting for less than 1 percent of all breast cancers [2,3]. As with invasive breast cancer, microinvasive breast carcinoma is predominantly ductal in histologic type.

Risk factors for microinvasive breast carcinoma appear to be similar to those associated with DCIS, such as nulliparity and family history of breast cancer [2,3]. It occurs over a wide age range (30 to 85 years of age), with the average age in the 50 to 60s [3,4]. Case series have also suggested that patients diagnosed with microinvasive breast carcinoma have a high incidence of other high-risk lesions, including concurrent breast carcinoma and other malignancies, present at the time of diagnosis [2,3].

The epidemiology of DCIS is presented separately. (See "Breast ductal carcinoma in situ: Epidemiology, clinical manifestations, and diagnosis".)

Definition, pathology, and staging — Microinvasive breast carcinoma is defined by the American Joint Committee on Cancer and the International Union for Cancer Control (AJCC-UICC) as invasive carcinoma of the breast with no focus measuring more than 1 mm [5]. It is most commonly encountered in the setting of DCIS, where small foci of tumor cells have invaded through the basement membrane into the surrounding stroma. It is rarely seen in association with lobular carcinoma in situ (LCIS) or in the absence of carcinoma in situ [4]. Where associated with LCIS, the microinvasive component is usually lobular or occasionally tubular in histologic type.

According to the eighth edition Tumor, Node, Metastasis staging system as well as the preceding seventh edition, microinvasive breast carcinoma is designated as T1mi, as presented in the respective tables (table 1 and table 2). In cases with multiple foci of microinvasion (where no focus is larger than 1 mm), the number of foci and range of sizes should be reported. Note that the sizes of individual foci of microinvasion are not added together. Since microinvasive breast carcinoma may present with multiple foci of invasion, the pathologic specimen should be carefully examined for additional foci [6,7].

Histopathologically, microinvasive breast carcinoma tends to be associated with high-grade DCIS and comedo-type necrosis [2,8-10]. There is also evidence that the risk of microinvasion increases with larger-size DCIS lesions and multicentric DCIS [8-10]. (See "Pathology of breast cancer".)

There is little information about biologic markers such as estrogen receptor (ER) and progesterone receptor (PR) status and human epidermal growth factor receptor 2 (HER2) overexpression in microinvasive breast carcinoma [2,11,12]. In a study including 30 patients who had complete hormone receptor testing of both the invasive and in situ components, ER/PR positivity was 100 percent concordant in both microinvasive and in situ disease; ER negativity was 83 percent concordant. HER2 status was 100 percent concordant [13]. Contrary to invasive breast cancer, the limited data suggest that receptor expression has little prognostic significance in microinvasive breast cancer. (See 'Prognosis' below.)

Clinical presentation — Microinvasive breast carcinoma commonly presents within a palpable mass that represents an area of DCIS with stromal desmoplasia [2-4,8,9,14-16]. The microinvasion in and of itself is not palpable. Nipple discharge rarely may also occur.

Others have found that, similar to DCIS, the most frequent imaging appearance is calcifications [2]. These different results are likely due to differences between studies in the definition of microinvasive breast carcinoma used, which imaging studies were performed (ie, mammography or ultrasonography), and degree of tissue sampling. For example, a retrospective review of 37 patients with microinvasive breast cancer and 44 patients with intraductal carcinoma found that the most dominant magnetic resonance imaging (MRI) finding of both lesions was heterogeneous enhancement of non-mass-like lesions [17].

Most diagnostic biopsies are performed as core needle biopsies. As such, pathology results may only reveal DCIS or DCIS with a focus "suspicious for" microinvasion. It is only when the entire lesion is removed that a complete evaluation can be performed and a final diagnosis of invasive or microinvasive breast carcinoma can be rendered.

TREATMENT

Management of the breast — There are no randomized trials to inform the optimal surgical treatment for microinvasive breast carcinoma. Breast-conserving surgery (BCS) followed by radiation therapy (RT) for most patients with microinvasive breast carcinoma is appropriate. However, mastectomy (without RT) may be preferred for patients in whom the ductal carcinoma in situ (DCIS) component is large, high grade, with or without comedo necrosis **and** in whom clean margins cannot be definitively obtained with BCS.

BCS may be associated with an increased risk of local recurrence; RT after BCS minimizes this risk. For those with pure microinvasive carcinoma, margin requirements are the same as for those with invasive carcinoma (ie, no tumor on ink); however, for microinvasive carcinoma associated with DCIS, the larger margin requirements needed for DCIS are required. (See "Adjuvant radiation therapy for women with newly diagnosed, non-metastatic breast cancer"

and "Ductal carcinoma in situ: Treatment and prognosis" and "Breast-conserving therapy" and "Mastectomy".)

As with DCIS and early invasive breast cancer, BCS for microinvasive breast carcinoma appears to achieve excellent outcomes [13,18]. In a retrospective study of 321 patients with DCIS and 72 patients with microinvasion treated with BCS, the presence of microinvasion did not correlate with local recurrence rate, distant relapse-free survival, or overall survival at almost nine years of follow-up [18]. The improved outcomes in contemporary series may be due at least in part to the use of adjuvant endocrine therapy for patients whose disease is estrogen receptor positive.

The risk of recurrence following BCS for microinvasive disease appears to be increased with:

- Positive excision margins [13,19] (see 'Prognosis' below)
- Size of the DCIS component [3,4]
- Unfavorable histopathologic characteristics of the associated DCIS component (ie, presence of comedo necrosis and high nuclear grade) [9]

As described above, these characteristics are common with microinvasive breast carcinoma. (See 'Overview' above.)

Management of the axilla — The reported incidence of axillary lymph node involvement in microinvasive breast carcinoma ranges from 0 to 20 percent but is generally 5 percent or less for properly defined microinvasive breast carcinoma [4,8,19-28]. The likelihood of axillary node involvement is greater in cases where stromal invasion is demonstrated by clusters of cells rather than single cells [6,8,14,15].

Although the majority of patients with microinvasive breast carcinoma are likely to have negative axillary lymph nodes, we proceed with a sentinel lymph node biopsy for patients in whom the assessment of axillary lymph node status will influence adjuvant therapy decisions. Omission of the sentinel lymph node for select older women with hormone-positive disease is discussed elsewhere. (See "Overview of the approach to early breast cancer in older women", section on 'Management of the axilla'.)

The importance of identifying nodal metastasis in T1mi patients should be further investigated to determine the impact, if any, on local-regional recurrence or distant disease [27,28]. (See "Overview of sentinel lymph node biopsy in breast cancer" and "Overview of sentinel lymph node biopsy in breast cancer", section on 'DCIS with suspicious features'.)

PROGNOSIS

Microinvasive breast carcinoma has an excellent prognosis, with a five-year overall survival between 97 and 100 percent [9]. Survival seems to be intermediate between pure ductal carcinoma in situ (DCIS) and small invasive carcinomas [11].

For women with microinvasive carcinoma, the risk of recurrence following surgery (breast-conserving therapy or mastectomy) appears to be small. In one study of 83 patients followed for a median of six years, the cumulative incidence of recurrence at five years was 5 percent [13]. The postexcision finding of close or positive margins (≤2 mm) on pathologic evaluation was the only factor associated with an increased risk of a local recurrence, which was diagnosed in 4 of 20 patients who had a close margin versus 2 of 62 who had a negative margin (hazard ratio 8.8, 95% CI 1.6-48.8). This small study also reported that overexpression of human epidermal growth factor 2 was not associated with the risk of axillary node involvement at diagnosis or the risk of recurrence.

IS THERE A ROLE FOR ADJUVANT SYSTEMIC THERAPY?

There have been no clinical trials specifically addressing the role of adjuvant endocrine therapy, chemotherapy, and/or trastuzumab in the treatment of microinvasive breast carcinoma. In the absence of definitive data, we treat microinvasive cancer similarly to ductal carcinoma in situ (DCIS), specifically:

- Adjuvant endocrine therapy is appropriate for most women with hormone receptor (HR)-positive microinvasive breast cancer. In this instance, the role of endocrine therapy is as "chemoprevention" either for the remaining breast tissue or the contralateral side, since the odds of distant recurrence and mortality from the microinvasive carcinoma are so low. The approach to these patients is similar to that for women with DCIS. (See "Ductal carcinoma in situ: Treatment and prognosis", section on 'Endocrine therapy'.)

- Given that by definition these patients have a primary breast tumor ≤1 mm, chemotherapy is not administered in the absence of nodal involvement. For patients who have microinvasive disease in the breast who are found concurrently to have metastatic disease in the lymph nodes, decisions regarding chemotherapy depend on receptor status and risk factors of the cancer. (See "Deciding when to use adjuvant chemotherapy for hormone receptor-positive, HER2-negative breast cancer" and "ER/PR negative, HER2-negative (triple-negative) breast cancer", section on 'Non-metastatic disease' and "Adjuvant systemic therapy for HER2-positive breast cancer".)

- The prognostic significance of hormone and/or human epidermal growth factor 2 (HER2) receptor expression is uncertain due to the paucity of available data. Often, there is not enough tissue for hormone and HER2 analysis. (See 'Prognosis' above.)

The evidence underlying these recommendations for adjuvant therapy for early-stage breast cancer is discussed separately. (See "Overview of the treatment of newly diagnosed, invasive, non-metastatic breast cancer".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Ductal carcinoma in situ".)

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.)

- Basics topic (see "Patient education: Ductal carcinoma in situ (DCIS) (The Basics)")

SUMMARY AND RECOMMENDATIONS

Microinvasive breast carcinoma is defined as invasive carcinoma of the breast with no focus measuring more than 1 mm; it is invariably encountered in the setting of ductal carcinoma in situ (DCIS).

- **Overview** – The risk of microinvasive breast carcinoma increases with larger-size DCIS lesions and multicentric DCIS. It tends to be associated with high-grade DCIS and DCIS with comedo necrosis and in that setting is more likely to present with multiple foci of microinvasion. (See 'Overview' above.)

  According to the eighth edition American Joint Committee on Cancer and the International Union for Cancer Control Tumor, Node, Metastasis staging system,

microinvasive breast carcinoma is designated as T1mi. (See 'Overview' above.)

- **Management of the breast –** The optimal treatment for microinvasive breast cancer is undefined. We suggest breast-conserving surgery (BCS) followed by radiation therapy to reduce the risk of local recurrence (**Grade 2B**). However, mastectomy may be preferred for patients at high risk of local recurrence with breast-conserving therapy, including those with extensive, multicentric, high-grade DCIS, with or without comedo necrosis and for those patients when histologically clear margins cannot be obtained with BCS. (See 'Management of the breast' above.)

- **Management of the axilla –** We proceed with sentinel lymph node biopsy (SLNB) for patients with confirmed microinvasive breast carcinoma in whom the assessment of axillary lymph node status will influence adjuvant therapy decisions (see 'Management of the axilla' above). Omission of SLNB for older women with hormone receptor-positive breast cancer is discussed elsewhere. (See "Overview of the approach to early breast cancer in older women", section on 'Management of the axilla'.)

- **Prognosis –** Microinvasive breast carcinoma has an excellent prognosis, with a greater than 95 percent five-year overall survival. (See 'Prognosis' above.)

- **Adjuvant systemic therapy –** Adjuvant endocrine therapy is appropriate for most women with hormone receptor (HR)-positive microinvasive breast cancer. In this instance, the role of endocrine therapy is as "chemoprevention" either for the remaining breast tissue or the contralateral side, since the odds of distant recurrence and mortality from microinvasive carcinoma are so low. The approach to these patients is similar to that for women in invasive HR-positive breast cancer. (See "Adjuvant endocrine and targeted therapy for postmenopausal women with hormone receptor-positive breast cancer".)

  Given that by definition these patients have a primary breast tumor ≤1 mm, chemotherapy is not administered in the absence of nodal involvement. For patients who have microinvasive disease in the breast who are found concurrently to have macrometastatic disease to the lymph nodes, decisions regarding chemotherapy depend on receptor status and risk factors of the cancer. (See "Selection and administration of adjuvant chemotherapy for HER2-negative breast cancer" and "Adjuvant systemic therapy for HER2-positive breast cancer".)

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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 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

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