

**Alberta Breast Cancer Program - February 2011  
Breast Cancer Staging / Recommended Investigations**

**Recommended Investigations for Asymptomatic, Newly Diagnosed Breast Cancer**

The Alberta Breast Cancer Program has made the following guideline recommendations for staging investigations in breast cancer. This guideline is a consensus document and has been created after review of the available evidence and in discussion with the group membership.

**These guidelines were made in an effort to standardize clinical practice across the province and to expedite subsequent assessment and treatment of patients at the cancer centers.**

**These recommendations are not meant to be proscriptive and/or to replace the clinical judgment of any medical practitioner.** Any patients with symptoms, physical findings or lab results suspicious for metastatic disease should undergo further directed staging investigations in addition to those as outlined below.

**The following investigations are recommended for asymptomatic, biopsy confirmed breast cancer and should be initiated prior to referral to the cancer center. Laboratory and/or baseline cardiac investigations (if required) for subsequent adjuvant therapy can be arranged at the time of cancer center triage review.**

Unless metastatic disease is suspected from symptoms and/or physical exam, then staging tests can be done post-surgery.

**All staging tests will be reviewed at the cancer center and subsequently followed up as required based upon the results of the tests.**

All patients should have and appropriate medical history and physical examination performed by a qualified health care practitioner

<b>Stage</b>	<b>Recommended Investigations</b>
0	<ul style="list-style-type: none"> <li>• Bilateral Mammography</li> </ul>
I	<ul style="list-style-type: none"> <li>• Bilateral Mammography,</li> <li>• Laboratory investigations<sup>†</sup></li> </ul>
II	<ul style="list-style-type: none"> <li>• Bilateral Mammography, Chest X-ray</li> <li>• Laboratory Investigations<sup>†</sup></li> </ul> If LN+ → Bone Scan (Abdominal imaging optional)
III	<ul style="list-style-type: none"> <li>• Bilateral Mammography</li> <li>• Chest (Chest X-ray or *CT)</li> <li>• Abdominal Imaging (US or *CT) and</li> <li>• Bone Scan</li> <li>• Laboratory investigations<sup>†</sup></li> </ul> *CT scan preferred in cases of Inflammatory Breast Cancer
IV	<ul style="list-style-type: none"> <li>• Chest (Chest X-ray or CT), Abdominal Imaging (US or CT) and Bone Scan</li> <li>• Laboratory investigations<sup>†</sup></li> </ul>

<sup>†</sup> Laboratory Investigations = CBC, ALT, Alkaline Phos, Total Bilirubin, Albumin, Calcium, LDH

<b>Anthracycline-based chemotherapy (e.g. LN+) or trastuzumab candidate (HER2+)</b>	<b>MUGA or ECHO</b>
<b>Adjuvant chemotherapy candidate (LN+, high risk LN-) or Stage III or Stage IV</b>	<b>CBC, ALT, Alkaline Phosphatase, Total Bilirubin, Albumin, Calcium, LDH</b>

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### **Breast Cancer Staging**

(Adapted from NCI 2011 website)

<http://www.cancer.gov/cancertopics/pdq/treatment/breast/HealthProfessional/page3>

The American Joint Committee on Cancer (AJCC) staging system provides a strategy for grouping patients with respect to prognosis.

Therapeutic decisions are formulated in part according to staging categories but primarily according to tumor size, lymph node status, estrogen-receptor and progesterone-receptor levels in the tumor tissue, human epidermal growth factor receptor 2 (HER2/neu) status, menopausal status, and the general health of the patient.

### **Definitions of TNM**

The AJCC has designated staging by TNM classification to define breast cancer.[1] When this system was modified in 2002, some nodal categories that were previously considered stage II were reclassified as stage III.[2] As a result of the stage migration phenomenon, survival by stage for case series classified by the new system will appear superior to those using the old system.[3]

### **References**

[1] Breast. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 347-76.

[2] Singletary SE, Allred C, Ashley P, et al.: Revision of the American Joint Committee on Cancer staging system for breast cancer. J Clin Oncol 20 (17): 3628-36, 2002.

[3] Woodward WA, Strom EA, Tucker SL, et al.: Changes in the 2003 American Joint Committee on Cancer staging for breast cancer dramatically affect stage-specific survival. J Clin Oncol 21 (17): 3244-8, 2003.

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<b>Table 1. Primary Tumor (T)<sup>a,b</sup></b>	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
Tis	Carcinoma in situ.
Tis (DCIS)	DCIS.
Tis (LCIS)	LCIS.
Tis (Paget)	Paget disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget disease are categorized based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted.
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). <sup>c</sup>
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.
DCIS = ductal carcinoma in situ; LCIS = lobular carcinoma in situ.	
<sup>a</sup> Reprinted from AJCC: Breast. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 347-76.	
<sup>b</sup> The T classification of the primary tumor is the same regardless of whether it is based on clinical or pathologic criteria, or both. 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. For example, a reported size of 1.1 mm is reported as 1 mm, or a size of 2.01 cm is reported as 2.0 cm. 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.	
<sup>c</sup> Invasion of the dermis alone does not qualify as T4.	

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**Table 2. Regional Lymph Nodes (N)<sup>a</sup>**

Clinical	
NX	Regional lymph nodes cannot be assessed (e.g., previously removed).
N0	No regional lymph node metastases.
N1	Metastases to movable ipsilateral level I, II axillary lymph node(s).
N2	Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted.
	OR
	Metastases in clinically detected <sup>b</sup> 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 <sup>b</sup> 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
	Metastases in clinically detected <sup>b</sup> 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).

<sup>a</sup> Reprinted from AJCC: Breast. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 347-76.

<sup>b</sup>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. 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.

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<b>Table 3. Pathologic (pN)<sup>a,b</sup></b>	
pNX	Regional lymph nodes cannot be assessed (e.g., previously removed or not removed for pathologic study).
pN0	No regional lymph node metastasis identified histologically.
Note: ITCs are defined as small clusters of cells $\leq 0.2$ mm, or single tumor cells, or a cluster of $< 200$ cells in a single histologic cross-section. ITCs may be detected by routine histology or by 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.	
pN0(i-)	No regional lymph node metastases histologically, negative IHC.
pN0(i+)	Malignant cells in regional lymph node(s) $\leq 0.2$ mm (detected by H&E or IHC including 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
	Metastases in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected. <sup>c</sup>
pN1mi	Micrometastases ( $> 0.2$ mm and/or $> 200$ cells but none $> 2.0$ mm).
pN1a	Metastases in 1–3 axillary lymph nodes, at least one metastasis $> 2.0$ mm.
pN1b	Metastases in internal mammary nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected. <sup>c</sup>
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
	Metastases in clinically detected <sup>d</sup> internal mammary lymph nodes in the absence of axillary lymph node metastases.
pN2a	Metastases in 4–9 axillary lymph nodes (at least 1 tumor deposit $> 2$ mm).
pN2b	Metastases in clinically detected <sup>d</sup> internal mammary lymph nodes in the absence of axillary lymph node metastases.

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pN3	Metastases in $\geq 10$ axillary lymph nodes.
	OR
	Metastases in infraclavicular (level III axillary) lymph nodes.
	OR
	Metastases in clinically detected <sup>c</sup> ipsilateral internal mammary lymph nodes in the presence of one or more positive level I, II axillary lymph nodes.
	OR
	Metastases in $>3$ axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected. <sup>c</sup>
	OR
pN3a	Metastases in $\geq 10$ axillary lymph nodes (at least 1 tumor deposit $>2.0$ mm).
	OR
	Metastases to the infraclavicular (level III axillary lymph) nodes.
pN3b	Metastases in clinically detected <sup>d</sup> ipsilateral internal mammary lymph nodes in the presence of one or more positive axillary lymph nodes;
	OR
	Metastases in $>3$ axillary lymph nodes and in internal mammary lymph nodes with micrometastases or macrometastases detected by sentinel lymph node biopsy but not clinically detected. <sup>c</sup>
pN3c	Metastases in ipsilateral supraclavicular lymph nodes.
Post-treatment = 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 AND.	
– The X classification will be used (ypNX) if no yp posttreatment SN or AND was performed.	
– N categories are the same as those used for pN.	
AND = axillary node dissection; H&E = hematoxylin and eosin stain; IHC = immunohistochemical; ITC = isolated tumor cells; RT-PCR = reverse transcriptase/polymerase chain reaction.	
<sup>a</sup> Reprinted from AJCC: Breast. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 347-76.	
<sup>b</sup> 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).	
<sup>c</sup> "Not clinically detected" is defined as not detected by imaging studies (excluding lymphoscintigraphy) or not detected by clinical examination.	
<sup>d</sup> "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.	

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**Table 4. Distant Metastases (M)<sup>a</sup>**

<sup>a</sup> Reprinted with permission from AJCC: Breast. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 347-76.

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 ≤0.2 mm in a patient without symptoms or signs of metastases.
M1	Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven >0.2 mm.

Post treatment 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.[1]

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**Table 5. Anatomic Stage/Prognostic Groups<sup>a,b</sup>**

Stage	T	N	M
0	Tis	N0	M0
IA	T1 <sup>b</sup>	N0	M0
IB	T0	N1mi	M0
	T1 <sup>b</sup>	N1mi	M0
IIA	T0	N1c	M0
	T1 <sup>b</sup>	N1c	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1 <sup>b</sup>	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

<sup>a</sup> Reprinted from AJCC: Breast. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 347-76.

<sup>b</sup> T1 includes T1mi.

<sup>c</sup> T0 and T1 tumors with nodal micrometastases only are excluded from Stage IIA and are classified Stage IB.

– M0 includes M0(i+).

– The designation pM0 is not valid; any M0 should be clinical.

– 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.

– Post neoadjuvant therapy is designated with "yc" or "yp" prefix. Of note, no stage group is assigned if there is a complete pathologic response (CR) to neoadjuvant therapy, for example, ypT0ypN0cM0.

**References**

- [1] Breast. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 347-76.
- [2] Singletary SE, Allred C, Ashley P, et al.: Revision of the American Joint Committee on Cancer staging system for breast cancer. J Clin Oncol 20 (17): 3628-36, 2002.
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- The above is a summary of breast cancer staging guideline discussions of the Alberta Breast Cancer Program (ABCP).
- Original discussions occurred among the ABCP Breast Executive (Radiation Oncology / Medical Oncology / Surgical Oncology representation) from May – October 2010.
- A draft document was subsequently created, distributed for review and discussed with the general membership at the ABCP Annual Meeting in January 2011.
- Recommendations were agreed to and based upon group consensus after review of other existing staging guideline recommendations from Alberta, BC, Ontario and NCCN.