

## CODING REGIONAL LYMPH NODES FOR BREAST

Coding regional lymph node involvement for breast cancers is more complex than for many other sites, especially when dealing with isolated tumor cells (ITCs) and micrometastases. The following may help clarify the reasons behind the codes in CS Lymph Nodes and Site-Specific Factors 3-5. For a more detailed explanation, see the section in the breast chapter of the *AJCC Cancer Staging Manual*, 6<sup>th</sup> ed., called “Considerations for Evidence-Based Changes to the *AJCC Cancer Staging Manual*, 6<sup>th</sup> Edition” beginning on page 229.

**Isolated Tumor Cells (ITCs).** Pathologists can detect isolated tumor cells (ITCs) spread from a breast cancer into regional lymph nodes. These are very small deposits of tumor cells, so small that they are **not** considered significant for assigning stage. They usually do not show evidence of malignant activity in the nodes, such as proliferation or stromal reaction. To be considered ITCs, they must be single tumor cells or small clusters not more than 0.2 mm. As more data are collected about these ITCs, their prognostic significance may be better understood. **At this time, nodes with only these ITCs are not considered positive nodes.** These ITCs are most often found using immunohistochemistry tests on sentinel lymph node specimens. The ITCs may sometimes also be seen on routine H&E-stained sections.

**Hematoxylin and Eosin (H & E).** (from “ ‘Hematoxylin & Eosin’: (The Routine Stain)), by H. Skip Brown, BA, HT(ASCP), from:

<http://www.sigmaaldrich.com/img/assets/7361/Primer-H&Emay04.pdf>

In histology, the standard or ‘**routine stain**’ is the **hematoxylin and eosin** stain, better known as the ‘**H&E**’ stain. With rare exceptions, every specimen being examined will first receive an H&E stain to give the laboratorian a visible look at the nucleus of the cells and their present state of activity. With most disease states there is abnormal growth and/or division in the nucleus of the cells. The hematoxylin and eosin stain uses two separate dyes, one staining the nucleus and the other staining the cytoplasm and connective tissue. Hematoxylin is a dark purplish dye that will stain the chromatin (nuclear material) within the nucleus, leaving it a deep purplish-blue color. Eosin is an orangish-pink to red dye that stains the cytoplasmic material including connective tissue and collagen, and leaves an orange-pink counterstain. This counterstain acts as a sharp contrast to the purplish-blue nuclear stain of the nucleus, and helps identify other entities in the tissues such as cell membrane (border), red blood cells, and fluid.

**Immunohistochemistry (IHC).** Immunohistochemistry (IHC) tests use antibodies to stain for proteins of interest in tissue specimens. The IHC test for metastatic breast cancer in lymph nodes uses antibodies to cytokeratin, so the test may be called “cytokeratin staining”. Other IHC tests are used on the primary breast tumor, rather than the lymph nodes, to assess estrogen and progesterone receptors and HER-2 neu (human epidermal growth factor receptor). In SSF 4, code only IHC results for ITCs in lymph nodes.

**Molecular Study: Reverse Transcriptase/Polymerase Chain Reaction (RT-PCR).** An even more sensitive test used to detect ITCs in lymph nodes is RT-PCR, a molecular test looking for expression of genes of interest. This test is rarely done.

**Micrometastasis.** When the tumor deposits in the lymph nodes are larger than 0.2 mm but not larger than 2.0 mm, they are defined as micrometastasis. **Nodes with micrometastasis are considered positive for staging.**

In coding CS Lymph Nodes and Site-Specific Factors 3-5, the important things to abstract are the size of the tumor detected in the lymph nodes and the methods of detection. The table below may help in coding this information. Note that the table includes codes for axillary nodes only, not internal mammary nodes. The table is followed by examples to illustrate likely coding situations.

To use the table, identify the group (numbered I-V) of applicable rows based on the information in column 2 that best represents the information in the case. Within that group, find the row or rows that represent the information in the case, and read right to the last four columns to find the codes to use. The group numbers are for convenience in using this chart only, and do not correlate with any anatomic groups of nodes.

GIVEN THIS INFORMATION . . .			USE THESE CODES . . .				
		Row Num-ber	IHC and/or Mol Studies Done, or Method of Detection/Verification	CS Lymph Nodes	SSF 3 (# pos ax)	SSF 4 (IHC)	SSF 5 (mol)
I.	Clinical information only; no pathological information used to code CS Lymph Nodes; no nodes examined pathologically	1.	None; does not apply	00, 50, 60, or 99	098	000	000
II.	Nodes examined pathologically, nodes negative; no Isolated Tumor Cells (ITCs)  <b>NOTE:</b> SSF 4 and 5 are coded independently of each other.	2.	Immunohistochemistry (IHC) (cytokeratin staining) not done, <b>OR</b> unknown if done	00	000	000	
		3.	IHC done, neg for tumor	00	000	001	
		4.	Molecular studies not done, <b>OR</b> unknown if done	00	000		000
		5.	Molecular studies done, neg for tumor	00	000		001
		6.	H&E (routine stained slides)	05	000	888	888
III.	Nodes examined pathologically, Isolated Tumor Cells (ITCs) ONLY; Single tumor cells, or clusters $\leq 0.2\text{mm}$ <b>OR</b> Immunohistochemistry (IHC) pos, NOS  <b>NOTE:</b> SSF 4 and 5 are coded independently of each other.	7.	H&E neg, immunohistochemistry (IHC) (cytokeratin staining) not done, <b>OR</b> unknown if done	00	000	000	
		8.	H&E neg, IHC done, neg for ITCs	00	000	001	
		9.	H&E neg, IHC done, pos for ITCs	00	000	002	
		10.	H&E neg, IHC done, pos but size of deposits not stated	00	000	009	
		11.	H&E neg, molecular studies not done, or unknown if done	00	000		000
		12.	H&E neg, molecular studies done, neg for tumor	00	000		001
		13.	H&E neg, molecular studies done, pos for ITCs	00	000		002
		IV.	Nodes examined pathologically Tumor > 0.2mm, < 2.0mm (Micrometastasis)	14.	H&E neg, micromets on IHC (cytokeratin staining) ONLY	13	001-097
15.	H&E pos for micromets			15	001-097	888	888
V.	Nodes examined pathologically Tumor > 2.0mm; positive lymph nodes	16.	Does not apply	25 or higher	001-097	888	888

## Examples for Each Group:

### Group I Examples

1. Nodes clinically negative, patient refused further workup. [Row number 1]
2. Fixed and matted ipsilateral axillary nodes clinically, patient had pre-op chemotherapy. Subsequent modified radical mastectomy showed negative axillary nodes. (CS Reg Nodes Eval = 5 in this case.) [Row number 1]

### Group II Examples

1. Sentinel nodes neg on H&E. IHC (cytokeratin stain) performed, negative for ITCs. Molecular studies not done. [Rows 3 and 4]
2. Modified radical mastectomy, path report with 12 lymph nodes neg for tumor, no special stains, cytokeratin, IHC, or molecular studies performed on lymph nodes. [Rows 2 and 4]
3. Sentinel nodes neg on H&E. Unknown if IHC done. RT-PCR done, negative for ITCs. [Rows 2 and 5]

### Group III Examples

1. Sentinel nodes neg on H&E. IHC (cytokeratin stain) performed, positive for ITCs. Unknown if molecular studies done. [Rows 9 and 11]
2. Sentinel nodes initially neg on H&E. IHC performed, positive for ITCs. No molecular studies done. ITCs then verified on H&E slides of the sentinel nodes. [Row 6 ONLY]
3. Class 3 case abstracted from clinical history. Sentinel nodes neg on H&E. IHC on sentinel nodes was positive, NOS. Molecular studies not mentioned. [Rows 10 and 11]
4. Sentinel nodes neg on H&E. Cytokeratin stain showed clusters of tumor cells in the node up to 0.15 mm. RT-PCR was pos for ITCs. [Rows 9 and 13]
5. Sentinel nodes neg on H&E. Unknown if IHC performed. RT-PCR study done, neg for ITCs. [Rows 7 and 12]
6. Sentinel nodes neg on H&E. IHC and RT-PCR negative for tumor. [Rows 8 and 12]

### Group IV Examples:

1. Path report, final diagnosis: "Lymph Nodes: one of three sentinel lymph nodes positive for capsular micrometastases." Microscopic description: "Sections of the first submitted sentinel lymph node demonstrate normal nodal architecture, however, on cytokeratin stain, micrometastases are noted in the capsule." [Row 14]
2. Path report, final diagnosis: "Lymph Nodes: one of three sentinel lymph nodes positive for capsular micrometastases." Microscopic description: "Sections of the first submitted sentinel lymph node demonstrate micrometastases in the capsule." No special studies are mentioned in the report. [Row 15]

### Group V Examples

1. Axilla neg on palpation. Modified radical mastectomy, 2/14 nodes positive. Largest metastasis 0.8 cm. [Row 16]