Appendix D: Breast Cancer Staging[i]

The stage of a breast cancer can be based either on the results of physical exam, biopsy, and imaging tests (called the *clinical stage*), or on the results of these tests plus the results of surgery (called the *pathologic stage*). The staging described here is the pathologic stage, which includes the findings after surgery, when the pathologist has looked at the breast mass and nearby lymph nodes. Pathologic staging is likely to be more accurate than clinical staging, as it allows the doctor to get a firsthand impression of the extent of the cancer.

The TNM staging system classifies cancers based on their T, N, and M stages:

- The letter T followed by a number from 0 to 4 describes the tumor's size and spread to the skin or to the chest wall under the breast. Higher T numbers mean a larger tumor and/or wider spread to tissues near the breast.
- The letter N followed by a number from 0 to 3 indicates whether the cancer has spread to lymph nodes near the breast and, if so, how many lymph nodes are affected.
- The letter M followed by a 0 or 1 indicates whether the cancer has spread to distant organs -- for example, the lungs or bones.

Primary tumor (T) categories:

- **TX:** Primary tumor cannot be assessed.
- **T0:** No evidence of primary tumor.
- **Tis:** Carcinoma in situ (DCIS, LCIS, or Paget disease of the nipple with no associated tumor mass)
- **T1** (includes T1a, T1b, and T1c)**:** Tumor is 2 cm (3/4 of an inch) or less across.
- **T2:** Tumor is more than 2 cm but not more than 5 cm (2 inches) across.
- **T3:** Tumor is more than 5 cm across.
- **T4** (includes T4a, T4b, T4c, and T4d)**:** Tumor of any size growing into the chest wall or skin. This includes inflammatory breast cancer.

Nearby lymph nodes (N; based on looking at them under a microscope):

Lymph node staging for breast cancer has changed as technology has evolved. Earlier methods were useful in finding large deposits of cancer cells in the lymph nodes, but could miss microscopic areas of cancer spread. Newer methods have made it possible to find smaller and smaller deposits of cancer cells, but experts haven't been sure what to do with the new information. Do tiny deposits of cancer cells affect outlook the same way that larger deposits do? How much cancer in the lymph node is needed to see a change in outlook or treatment?

These questions are still being studied, but for now, a deposit of cancer cells must contain at least 200 cells or be at least 0.2 mm across (less than 1/100 of an inch) for it to change the N stage. An area of cancer spread that is smaller than 0.2 mm (or less than 200 cells) doesn't change the stage, but is recorded with abbreviations that reflect the way the cancer spread was detected. The

abbreviation "i+" means that a small number of cancer cells (called *isolated tumor cells*) were seen in routine stains or when a special type of staining technique, called *immunohistochemistry*, was used.
The abbreviation "mol+" is used if the cancer could only be found using a technique called *RT-PCR*. RT-PCR is a molecular test that can find very small numbers of cells that cannot be seen even using special stains. However, this test is not often used for finding breast cancer cells in lymph nodes because the results do not influence treatment decisions.

If the area of cancer spread is at least 0.2 mm (or 200 cells), but still not larger than 2 mm, it is called a*micrometastasis* (one mm is about the size of the width of a grain of rice). Micrometastases are counted only if there aren't any larger areas of cancer spread. Areas of cancer spread larger than 2 mm are known to affect outlook and do change the N stage. These larger areas are sometimes called *macrometastases*, but are more often just called *metastases*.

NX: Nearby lymph nodes cannot be assessed (for example, if they were removed previously).

N0: Cancer has not spread to nearby lymph nodes.

- **N0(i+):** Tiny amounts of cancer are found in underarm lymph nodes by using either routine or special stains. The area of cancer spread contains less than 200 cells and is smaller than 0.2 mm.
- **N0(mol+):** Cancer cells cannot be seen in underarm lymph nodes (even using special stains), but traces of cancer cells were detected using RT-PCR.

N1: Cancer has spread to 1 to 3 axillary (underarm) lymph node(s), and/or tiny amounts of cancer are found in internal mammary lymph nodes (those near the breast bone) on sentinel lymph node biopsy.

- **N1mi:** Micrometastases (tiny areas of cancer spread) in 1 to 3 lymph nodes under the arm. The areas of cancer spread in the lymph nodes are 2 mm or less across (but at least 200 cancer cells or 0.2mm across).
- **N1a:** Cancer has spread to 1 to 3 lymph nodes under the arm with at least one area of cancer spread greater than 2 mm across.
- **N1b:** Cancer has spread to internal mammary lymph nodes, but this spread could only be found on sentinel lymph node biopsy (it did not cause the lymph nodes to become enlarged).
- **N1c**: Both N1a and N1b apply.

N2: Cancer has spread to 4 to 9 lymph nodes under the arm, or cancer has enlarged the internal mammary lymph nodes (either N2a or N2b, but not both).

- **N2a:** Cancer has spread to 4 to 9 lymph nodes under the arm, with at least one area of cancer spread larger than 2 mm.
- **N2b:** Cancer has spread to one or more internal mammary lymph nodes, causing them to become enlarged.

N3: Any of the following:

- **N3a:** either
    - Cancer has spread to 10 or more axillary lymph nodes, with at least one area of cancer spread greater than 2mm, OR
    - Cancer has spread to the lymph nodes under the clavicle (collar bone), with at least one area of cancer spread greater than 2mm.
- **N3b:** either:
    - Cancer is found in at least one axillary lymph node (with at least one area of cancer spread greater than 2 mm) and has enlarged the internal mammary lymph nodes, OR
    - Cancer has spread to 4 or more axillary lymph nodes (with at least one area of cancer spread greater than 2 mm), and tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy.
- **N3c:** Cancer has spread to the lymph nodes above the clavicle with at least one area of cancer spread greater than 2mm.

Metastasis (M):

- **MX:** Distant spread (metastasis) cannot be assessed.
- **M0:** No distant spread is found on x-rays (or other imaging procedures) or by physical exam.
    - **cM0(i +):** Small numbers of cancer cells are found in blood or bone marrow (found only by special tests), or tiny areas of cancer spread (no larger than 0.2 mm) are found in lymph nodes away from the breast.
- **M1:** Cancer has spread to distant organs. (The most common sites are bone, lung, brain, and liver.)

Breast cancer stage grouping

Once the T, N, and M categories have been determined, this information is combined in a process called *stage grouping*. Cancers with similar stages tend to have a similar outlook and are often treated in a similar way. Stage is expressed in Roman numerals from stage I (the least advanced stage) to stage IV (the most advanced stage). Non-invasive cancer is listed as stage 0.

Stage 0:

Tis, N0, M0: This is *ductal carcinoma in situ (DCIS)*, a pre-cancer of the breast. Many consider DCIS the earliest form of breast cancer. In DCIS, cancer cells are still within a duct and have not invaded deeper into the surrounding fatty breast tissue. *Lobular carcinoma in situ (LCIS)* sometimes also is classified as stage 0 breast cancer, but most oncologists believe it is not a true cancer or pre-cancer. Paget disease of the nipple (without an underlying tumor mass) is also stage 0. In all cases the cancer has not spread to lymph nodes or distant sites.

Stage IA: T1, N0, M0:

The tumor is 2 cm (about 3/4 of an inch) or less across (T1) and has not spread to lymph nodes (N0) or distant sites (M0).

Stage IB: T0 or T1, N1mi, M0:

The tumor is 2 cm or less across (or is not found) (T0 or T1) with micrometastases in 1 to 3 axillary lymph nodes (the cancer in the lymph nodes is greater than 0.2mm across and/or more than 200 cells but is not larger than 2 mm)(N1mi). The cancer has not spread to distant sites (M0).

Stage IIA: One of the following applies:

T0 or T1, N1 (but not N1mi), M0: The tumor is 2 cm or less across (or is not found) (T1 or T0) and either:

- It has spread to 1 to 3 axillary lymph nodes, with the cancer in the lymph nodes larger than 2 mm across (N1a), OR
- Tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy (N1b), OR
- It has spread to 1 to 3 lymph nodes under the arm and to internal mammary lymph nodes (found on sentinel lymph node biopsy) (N1c).

OR

- **T2, N0, M0:** The tumor is larger than 2 cm but less than 5 cm across (T2) but hasn't spread to the lymph nodes (N0).
- The cancer hasn't spread to distant sites (M0).

Stage IIB: One of the following applies:

T2, N1, M0: The tumor is larger than 2 cm but less than 5 cm across (T2). It has spread to 1 to 3 axillary lymph nodes and/or tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy (N1). The cancer hasn't spread to distant sites (M0).

OR

T3, N0, M0: The tumor is larger than 5 cm across but does not grow into the chest wall or skin and has not spread to lymph nodes (T3, N0). The cancer hasn't spread to distant sites (M0).

Stage IIIA: One of the following applies:

T0 to T2, N2, M0: The tumor is not more than 5 cm across (or cannot be found) (T0 to T2). It has spread to 4 to 9 axillary lymph nodes, or it has enlarged the internal mammary lymph nodes (N2). The cancer hasn't spread to distant sites (M0).

OR

T3, N1 or N2, M0: The tumor is larger than 5 cm across but does not grow into the chest wall or skin (T3). It has spread to 1 to 9 axillary nodes, or to internal mammary nodes (N1 or N2). The cancer hasn't spread to distant sites (M0).

Stage IIIB: T4, N0 to N2, M0:

The tumor has grown into the chest wall or skin (T4), and one of the following applies:

- It has not spread to the lymph nodes (N0).
- It has spread to 1 to 3 axillary lymph nodes and/or tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy (N1).
- It has spread to 4 to 9 axillary lymph nodes, or it has enlarged the internal mammary lymph nodes (N2).

The cancer hasn't spread to distant sites (M0).

Inflammatory breast cancer is classified as T4d and is at least stage IIIB. If it has spread to many nearby lymph nodes (N3) it could be stage IIIC, and if it has spread to distant lymph nodes or organs (M1) it would be stage IV.

Stage IIIC: any T, N3, M0:

The tumor is any size (or can't be found), and one of the following applies:

- Cancer has spread to 10 or more axillary lymph nodes (N3).
- Cancer has spread to the lymph nodes under the clavicle (collar bone) (N3).
- Cancer has spread to the lymph nodes above the clavicle (N3).
- Cancer involves axillary lymph nodes and has enlarged the internal mammary lymph nodes (N3).
- Cancer has spread to 4 or more axillary lymph nodes, and tiny amounts of cancer are found in internal mammary lymph nodes on sentinel lymph node biopsy (N3)

The cancer hasn't spread to distant sites (M0).

Stage IV: any T, any N, M1:

The cancer can be any size (any T) and may or may not have spread to nearby lymph nodes (any N). It has spread to distant organs or to lymph nodes far from the breast (M1). The most common sites of spread are the bone, liver, brain, or lung.

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[i] The American Cancer Society. How is breast cancer staged. Last Revised: 06/10/2015. Available: http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-staging. Accessed: October 2015.