CANCER FACTS

National Cancer Institute • National Institutes of Health
Department of Health and Human Services

Questions and Answers About NCI's Sentinel Node Biopsy Trials

The National Cancer Institute (NCI) is sponsoring two large randomized clinical trials (research studies) comparing sentinel lymph node biopsy with conventional axillary lymph node dissection for breast cancer. The trials are being carried out by the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the American College of Surgeons-Oncology Group (ACOS-OG). NSABP and ACOS-OG are both NCI-sponsored Clinical Trials Cooperative Groups, which are networks of institutions and physicians across the country who jointly conduct trials.

Below is general information about sentinel node biopsy followed by details of the two trials.

1. What is a sentinel node?

A sentinel node is the first lymph node to which a tumor drains, and therefore is the first place to which cancer is likely to spread. In some cases, there can be more than one sentinel node. In breast cancer, the sentinel node is usually located in the axillary nodes, the group of lymph nodes under the arm; however, in a small percentage of cases, the sentinel node is found elsewhere in the lymphatic system of the breast. If a doctor can feel lymph nodes during a physical exam of the breast and underarm area that he or she suspects may be cancerous, the patient is diagnosed as "clinically node-positive." If a patient is clinically node-negative, surgery and a laboratory analysis must be performed to determine whether there is microscopic evidence of cancer in the lymph nodes.

2. What is the conventional surgical treatment for breast cancer?

Standard treatment usually involves removing a breast tumor by either lumpectomy or mastectomy and removing most of the axillary nodes (axillary node dissection). Several complications can arise from removing the axillary nodes; some reports indicate that more than 80 percent of women who undergo a complete axillary dissection have at least one complication after surgery. These complications are of varying severity, but can include lymphedema (swelling in the arm caused by excess fluid buildup), numbness, a persistent burning sensation, infection, and limited movement of the shoulder.

3. What information is provided by the sentinel node biopsy procedure?

Previous research has suggested that the sentinel node can be used to determine if cancer cells have spread to the lymph nodes. In sentinel node biopsy, only one or a few lymph nodes are removed for laboratory analysis when a patient has a lumpectomy or mastectomy. Preliminary studies suggest that if an analysis finds no cancer cells in the sentinel node, the patient is unlikely to have tumor cells in the remaining axillary nodes.

4. How is the sentinel node found?

There are two methods for finding the sentinel node. One is to inject a blue dye near the breast tumor and track its path through the lymph nodes. The dye accumulates in the sentinel node. In a similar technique, doctors inject a safe, small amount of a radioactive solution near the tumor and then use a gamma detector to find the "hotspot," or the node in which the solution has accumulated. These two techniques can also be used together. Surgeons participating in the NSABP trial will use both methods together, and surgeons participating in the ACOS-OG trial may use either of the techniques or the combination.

5. Why is sentinel node biopsy being studied?

The sentinel node may provide valuable information about the status of a woman's cancer without the complications associated with axillary dissection. While several studies have examined the correlation between the sentinel node and the remaining axillary nodes, these are the first two randomized trials that will compare the long-term results of sentinel node dissection with full axillary node dissection. The two trials, while different in design, have similar goals. Both trials will examine the effect of sentinel node biopsy and full axillary dissection on long-term survival and disease-free survival. Both trials will also compare the side effects of the different surgeries.

6. Is sentinel node biopsy a new procedure?

Some surgeons already perform sentinel node biopsies in patients with breast cancer, although it is still considered an investigational procedure. The concept of mapping the sentinel node was first reported in 1977 by a researcher studying cancer of the penis. The technique was later used to study drainage patterns of melanoma, and was first reported for breast cancer in 1993. Since then, researchers have improved methods for finding the sentinel node, and several studies have shown that when the sentinel node is negative, the remaining nodes are also negative in a majority of cases. These studies were done in a small number of centers and overall survival was not examined in these trials. Surgeons participating in both the NSABP and ACOS-OG trials must be specially trained in identifying sentinel nodes and performing sentinel node biopsies. Side effects of sentinel node biopsy can include minor pain or bruising at the biopsy site and the rare possibility of an allergic reaction to the blue dye used in finding the sentinel node.

7. Why is the NCI supporting two different trials?

The two trials are asking different but important questions, and can be viewed as complementary. The NSABP study is examining whether sentinel lymph node biopsy can replace axillary lymph node dissection in the approximately 70 percent of breast cancer patients with negative sentinel nodes while the ACOS-OG study is examining the same issue in women with positive sentinel nodes.

NSABP Study of Sentinel Node Biopsy in Node-Negative Women

8. What will the NSABP study do?

This trial is designed to determine whether sentinel node biopsy provides the same information, control of the disease in the area around the breast, and survival as conventional axillary dissection while significantly reducing complications.

The study will randomize about 4,000 breast cancer patients who have clinically negative nodes into two groups. Group 1 will undergo sentinel node biopsy followed by axillary dissection. Group 2 will undergo sentinel node biopsy followed by axillary dissection only if the sentinel node is positive for cancer. If the sentinel node is negative, women in this group will have no further axillary dissection.

9. What surgical procedures are involved?

All patients will undergo breast-conserving surgery (lumpectomy), or mastectomy and removal of the sentinel nodes. Some will also have additional underarm lymph nodes removed, as described above.

10. What other treatments will patients receive?

In accordance with standard guidelines for cancer treatment, patients may receive chemotherapy and/or hormonal therapy following mastectomy or lumpectomy. Patients undergoing lumpectomy will also receive breast radiation treatments. Patients undergoing mastectomy who have positive sentinel nodes may receive radiation treatments to the chest wall or to the nodes under the arm at the discretion of their physician.

11. What issues will be examined?

The primary goals of this study are to determine if: 1) control of the regional spread of breast cancer is equivalent between the two procedures, 2) the overall survival and number of years without recurrence are comparable, and 3) the side effects associated with sentinel node removal are less severe than those from conventional axillary dissection.

The trial will also examine whether the sentinel node is as effective as the axillary nodes at determining if cancer has spread and whether sentinel nodes can properly identify patients with an increased risk of having their cancer recur. Investigators will use a special technique (immunohistochemistry or IHC) to detect very small amounts of cancer cells (micrometastases) in biopsy specimens from negative nodes. These micrometastases are not found during routine examination of biopsy specimens. With the IHC results, researchers hope to learn whether micrometastases are associated with breast cancer recurrence.

12. Who is eligible for the NSABP study?

Breast cancer patients may be eligible if:

- They have been diagnosed with breast cancer removable by lumpectomy or mastectomy.
- Their axillary lymph nodes cannot be felt during a physical exam.
- They have not had any treatment for their current breast cancer.
- They have a life expectancy of at least 10 years.

13. What is the National Surgical Adjuvant Breast and Bowel Project (NSABP)?

The NSABP is a cooperative group with a 40-year history of designing and conducting clinical trials, the results of which have changed the way breast cancer is treated. Results of research studies conducted by NSABP researchers have been the dominant force in altering the standard surgical treatment of breast cancer from radical mastectomy to lumpectomy plus radiation. This group was also the first to demonstrate that adjuvant therapy could alter the natural history of breast cancer, thus increasing survival rates.

ACOS-OG Study of Sentinel Node Biopsy in Women with Positive Biopsies

14. What will the ACOS-OG study do?

This trial will examine whether long-term survival for patients with positive sentinel nodes who do not receive an axillary node dissection or axillary radiation is any different from survival of those who do undergo a complete dissection.

For this trial, ACOS-OG is seeking to enroll about 7,600 women with early breast cancer. The researchers anticipate that about 1,900 of these patients will have positive sentinel node biopsies. These women with positive sentinel nodes will be randomized into two groups. One group will have a complete axillary node dissection, and the other group will have no further lymph nodes removed and no radiation to the axilla. For the women with negative sentinel nodes, no further axillary surgery will be performed.

15. What surgical procedures are involved?

All women in this trial will undergo breast-conserving surgery (lumpectomy) and sentinel lymph node biopsy. About half of the patients with positive sentinel nodes, as explained above, will have a complete axillary node dissection, while half will have no further axillary surgery.

16. What other treatments will patients receive?

Following standard guidelines for cancer treatment, women in both groups of the study will have breast radiation therapy, and may have chemotherapy and/or hormonal therapy as well.

17. What issues will be examined?

This trial is designed to determine if overall survival for patients with positive sentinel nodes who do not undergo axillary node dissection is different from survival for sentinel node-positive patients who do receive a complete axillary node dissection. The study will also compare the side effects of the two procedures. For women with negative sentinel nodes, recurrence of cancer in the breast and surrounding area will be monitored.

In addition, participants' sentinel nodes will be analyzed with special studies that are not routinely performed (immunohistochemistry) to search for any cancer cells that were not detected with routine methods. In this way, researchers hope to learn if minute amounts of tumor in the lymph nodes—micrometastases—have any significance in terms of the patient's outcome.

18. Is it dangerous to leave axillary lymph nodes in place if the sentinel node is positive?

This is a major unanswered question in breast cancer treatment. There is no firm evidence that removing involved lymph nodes improves survival, even though it is standard practice. Randomized studies suggest that lymph node removal may not improve survival, although it is valuable in determining the stage of the cancer. Sentinel node biopsy can be used to determine stage, so it may be all that is necessary, even in node-positive women. One of the aims of this study is to resolve the issue of whether axillary lymph node removal is necessary in node-positive women and justifies its long-term side effects. (Also, it is important to note that patients in the ACOS-OG study will receive post-surgical radiation therapy to the breast and may have chemotherapy and/or hormonal therapy as well.)

19. Who is eligible for the ACOS-OG study?

Breast cancer patients may be eligible if:

- They have stage I or II breast cancer with a tumor that can be removed by lumpectomy.

- Their axillary lymph nodes cannot be felt during a physical exam.
- They have not been previously treated with chemotherapy for their current breast cancer.
- They have a life expectancy of at least 10 years.

20. What is the American College of Surgeons (ACOS)?

ACOS is the largest professional organization of surgeons in the world. Established in 1913, it has for many years provided its members with standards of practice, credentialing for specialists, and educational materials. In a new venture in 1998, it formed the Oncology Group (ACOS-OG) which will perform clinical trials sponsored by the National Cancer Institute. The Group will be able to draw upon the organization's nationwide membership and its long experience with medical education. The sentinel node trial is one of the first clinical trials the group is conducting.

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1–800–4–CANCER (1–800–422–6237)
TTY (for deaf and hard of hearing callers): 1–800–332–8615

NCI Online

Internet

Use http://cancer.gov to reach the NCI's Web site.

LiveHelp

Cancer Information Specialists offer online assistance through the *LiveHelp* link on the NCI's Web site.

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