Management of the Axilla

A series of classic randomized trials — including NSABP B-04 — formed the basis for level I and II axillary node dissection becoming a standard of care for invasive breast cancer. The emergence of sentinel lymph node biopsy (SLNB) as an initial staging procedure has led to a new generation of trials evaluating the need for axillary dissection in women with both pathologically negative nodes and positive nodes. A critical related question is the interpretation of micrometastases in both the sentinel lymph node and bone marrow. The value of treating the axilla in elderly women is also being examined, as well as the potential for treating the axilla with radiotherapy.

PHASE III PROGNOSTIC STUDY OF SENTINEL NODE AND BONE MARROW MICROMETASTASES IN WOMEN WITH STAGE I OR IIA BREAST CANCER

Open Protocol

Protocol IDs: ACOSOG-Z0010, GUMC-00152
Projected Accrual: 5,300 patients

Eligibility	Stage I or IIA breast carcinoma within 60 days of planned sentinel lymph node dissection

Protocol: Bilateral anterior iliac crest bone marrow aspiration to test for micrometastases → lumpectomy + SLND

→ Sentinel node + → ACOSOG - Z0011

All patients receive whole breast radiotherapy (excluding a supraclavicular field) 5 days a week, for a maximum of 8 weeks, and systemic adjuvant therapy as indicated.

Patients with no sentinel node identified intraoperatively and patients with sentinel node metastases identified by H & E who choose not to be registered to ACOSOG-Z0011 undergo ALND.

Study Contact:
Armando E Giuliano, Chair. Tel: 310-829-8089
American College of Surgeons Oncology Group

SOURCE: NCI Physician Data Query, January 2003

PHASE III RANDOMIZED STUDY OF AXILLARY LYMPH NODE DISSECTION IN WOMEN WITH STAGE I OR IIA BREAST CANCER WHO HAVE A POSITIVE SENTINEL NODE — Open Protocol

Protocol IDs: ACOSOG-Z0011, GUMC-00153
Projected Accrual: 1,900 patients

Eligibility	Positive sentinel node from ACOSOG Z-10 trial (Z-10 requires breast conservation therapy)
ARM 1	ALND involving removal of at least level I and II nodes, followed by whole breast radiotherapy (exclusive of a third supraclavicular field) 5 days a week, for a maximum of 7 weeks
ARM 2	Breast radiotherapy only as in ARM 1

Patients in both arms may receive adjuvant systemic therapy at the discretion of the treating physician.

Study Contact:
Armando E Giuliano, Chair. Tel: 310-829-8089
American College of Surgeons Oncology Group

SOURCE: NCI Physician Data Query, January 2003

PHASE III RANDOMIZED STUDY OF SENTINEL NODE DISSECTION WITH OR WITHOUT CONVENTIONAL AXILLARY DISSECTION IN WOMEN WITH CLINICALLY NODE-NEGATIVE BREAST CANCER — Open Protocol

Protocol ID: NSABP-B-32
Projected Accrual: 5,400 patients

Eligibility	Clinically node-negative breast cancer
ARM 1	Sentinel lymph node biopsy (SLNB) with axillary dissection
ARM 2	SLNB → positive → axillary dissection; negative → no axillary dissection

Note: If no sentinel node is identified, then patients undergo axillary dissection. Patients with cytologically negative but histologically positive sentinel nodes undergo axillary dissection.

Study Contact:
David N Krag, Chair. Ph: 802-656-5830
National Surgical Adjuvant Breast and Bowel Project

SOURCE: NCI Physician Data Query, January 2003

TRIALS EVALUATING AXILLARY DISSECTION

Protocol ID	Eligibility	Schema
EORTC-10981, EORTC-10981-AMAROS	T0-2, N0; clinically negative axilla; Sentinel node+	ARM 1: Complete ALND ARM 2: Axillary node radiotherapy
CNR-9502, EU-95020	Age 65-80, postmenopausal, stage I, ER-positive	ARM 1: Quadrantectomy with level I & II ALND ARM 2: Quadrantectomy without ALND
EU-93013, IBCSG-10-93, NCI-F93-0008	Age ≥60, postmenopausal, stage I or IIA, no prior axillary clearance or biopsy allowed	ARM 1: Mastectomy, lumpectomy or quadrantectomy with axillary clearance, SLNB optional ARM 2: Surgery as in Arm 1 without axillary clearance

ALND=axillary lymph node dissection
SLNB=sentinel lymph node biopsy

SOURCE: NCI Physician Data Query, January 2003

SELECT PUBLICATIONS

Clarke D et al. **Sentinel node biopsy in breast cancer: ALMANAC trial.** *World J Surg* 2001;25(6):819-22.

DiFronzo LA et al. **Does sentinel lymphadenectomy improve staging and alter therapy in elderly women with breast cancer?** *Ann Surg Oncol* 2000;7(6):406-410.

Giuliano AE et al. **Prospective observational study of sentinel lymphadenectomy without further axillary dissection in patients with sentinel node-negative breast cancer.** *J Clin Oncol* 2000;18:2553-2559.

Grube BJ, Giuliano AE. **Observation of the breast cancer patient with a tumor-positive sentinel node: Implications of the ACOSOG Z0011 trial.** *Semin Surg Oncol* 2001;20(3):230-237.

Harlow SP, Krag DN. **Sentinel lymph node — Why study it: Implications of the B-32 study.** *Sem Surg Oncol* 2001;20:224-229.

Krag DN et al. **Radiolabeled sentinel node biopsy: Collaborative trial with the National Cancer Institute.** *World J Surg* 2001;25(6):823-828.

Lucci A Jr et al. **National practice patterns of sentinel lymph node dissection for breast carcinoma.** *J Am Coll Surg* 2001;192(4):453-458.

McMasters KM et al. **Sentinel lymph node biopsy for breast cancer: A suitable alternative to routine axillary dissection in multi-institutional practice when optimal technique is used.** *J Clin Oncol* 2000;18:2560-2566.

Morrow M et al. **Learning sentinel node biopsy: Results of a prospective randomized trial of two techniques.** *Surgery* 1999;126(4):714-20; discussion 720-7222.

RATIONALE FOR AXILLARY DISSECTION

There are three reasons to do axillary dissection: regional control, staging and to improve survival. For staging, we have enough literature from around the world to tell us the accuracy of sentinel node biopsy. For regional control, surgery results in almost 100% control, as does radiation therapy, so before we abandon something that works very well, we have to be very careful. We don't have any long-term data on regional control for sentinel node. Regarding survival — there may be a survival advantage in controlling the axilla. The few studies that looked at this were done in an era when we randomized hundreds of patients, not thousands of patients, so the statistical power was not there.

I've personally never done a sentinel node procedure in a breast cancer case outside of a clinical trial. I'm not going to say that it shouldn't be done — this is a judgment call. But in terms of making the claim that sentinel node is as good as axillary dissection, we don't have the data and we are in an era of evidence-based medicine.

—David Krag, MD

RATIONALE FOR ACOS Z-11 TRIAL

Many surgeons believe that axillary dissection is therapeutic, and they are reluctant not to perform axillary dissection in sentinel node-positive patients. However, a number of randomized studies failed to show that axillary dissection improves survival. In sentinel node-positive women, the sentinel node may be enough because often it's the only involved node.

Virtually all node-positive women in this country receive adjuvant systemic therapy, and many patients are also receiving opposed tangential field radiation. In studies where patients received lumpectomy with radiation and no axillary dissection, the axillary recurrence rate was extraordinarily low. I think ACOS Z-11 is a very important, very justifiable and ethical trial. For an operation that's been used for 100 years, it's time to answer the question about the need for axillary dissection.

—Armando Giuliano, MD

CLINICAL TRIALS OF SLNB

NSABP trial B-04 showed no difference in survival outcome between axillary dissection at the time of diagnosis and delayed axillary dissection if clinically positive nodes developed. Since that trial didn't show a survival difference, is it reasonable to expect that NSABP B-32 would? I think that's a very open question. However, B-32 will tell us about the clinical false-negative rate when many surgeons do sentinel node biopsy, which is an important issue to inform patients about. The ACOS trial addresses the much more controversial question of whether to remove axillary nodes after the patient has been staged as node-positive. It challenges the dogma that people have had for years.

—Monica Morrow, MD

ACCRUAL TO SENTINEL NODE TRIALS

In some ways, sentinel node mapping is becoming a victim of its own success. As surgeons realize that it is not a terrific technical feat to learn, and as more patients become aware of it through the Internet and other sources, it will become harder and harder to find both patients and physicians willing to participate in these randomized clinical trials.

—Patrick Borgen, MD