The Role of the Surgeon in the Interdisciplinary Management of Early Breast Cancer:

A Review of a National Patterns of Care Study of US-Based General Surgeons and Breast Cancer Surgical Investigators

Proceedings and Interviews from a CME Symposium at the 9th Annual Meeting of The American Society of Breast Surgeons

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The Role of the Surgeon in the Interdisciplinary Management of Early Breast Cancer

A Continuing Medical Education Program

OVERVIEW OF ACTIVITY/TARGET AUDIENCE

Historically, surgery has represented the primary method for treating breast cancer. More recently, however, the diagnostic, surgical and medical management of breast malignancies has escalated in complexity due to advancements and availability of novel technology, pharmaceuticals and clinical experience. Thus, the direction of breast cancer care has evolved toward a multifaceted approach necessitating the input from a variety of multidisciplinary experts. This paradigm shift has created the opportunity for extensive knowledge exchange among interrelated oncologic subspecialties, and the challenge of ensuring major clinical advances influencing the selection of local and systemic breast cancer treatment algorithms are effectively disseminated among all multidisciplinary team members. To bridge the gap between research and patient care, this CME activity utilizes one-on-one interviews and a panel discussion with leading breast cancer investigators. By providing access to the latest research developments and expert perspectives, this program assists breast surgeons in the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Compare management strategies of community-based general surgeons and breast cancer surgical specialists for the treatment of early breast cancer, and apply relevant information to clinical practice.
- Evaluate issues related to the accuracy, reliability and interpretation of the ER and HER2 status of breast tumors, in the context of local laboratory practices and national guidelines.
- Identify the rationale for and benefits of extended adjuvant endocrine therapy, and utilize this approach for patients with hormone receptor-positive breast cancer.
- Describe the evidence-based risks and benefits of adjuvant trastuzumab therapy, and implement a plan for the initial treatment for patients with HER2-positive early breast cancer.
- Evaluate the utility of tissue-based genomic assays for therapeutic decision-making and, when applicable, use these in the selection of individualized treatment regimens for patients with early breast cancer.
- Review emerging research data evaluating the utility and long-term impact of sentinel lymph node biopsy, and translate these findings to current practice.
- Discuss the risks and benefits of partial breast irradiation and the clinical trials evaluating this technique with appropriately selected patients.
- Utilize magnetic resonance imaging in appropriately selected patients with breast cancer.

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FACULTY — **Dr Dixon** had no real or apparent conflicts of interest to disclose. The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process: **Dr Pegram** — Advisory Committee: Amgen Inc, Bristol-Myers Squibb Company, Genentech BioOncology, Genomic Health Inc, GlaxoSmithKline, Pfizer Inc; Speakers Bureau: Genentech BioOncology, GlaxoSmithKline, Sanofi-Aventis. **Dr Ravdin** — Consulting Agreement: Genomic Health Inc; Speakers Bureau: AstraZeneca Pharmaceuticals LP; Stock Ownership: Adjuvant! Inc, Bristol-Myers Squibb Company, Pfizer Inc, Wyeth. **Dr Whitworth** — Advisory Committee, Consulting Agreements and Speakers Bureau: Genomic Health Inc, Novartis Pharmaceuticals Corporation; Paid Research: AstraZeneca Pharmaceuticals LP, GlaxoSmithKline.

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EDITOR'S NOTE

Neil Love, MD

State of the art 2008

Welcome to another adventure in cancer education, and special thanks to the co-chair of this project, Dr Pat Whitworth, and collaborator Dr Monica Morrow.

Although many physicians know the audio programs produced by our group in Miami, we have also been *surveying* docs for more than two decades about how they take care of patients with cancer. In recent years, our team has conducted many national Patterns of Care surveys, mostly of medical oncologists but also of radiation oncologists and urologists (**www.PatternsOfCare.com**). This year, as a lead-in to a special satellite symposium at The American Society of Breast Surgeons meeting, we conducted our first Patterns of Care study of surgeons (Figure 1).

The focus was the management of early invasive breast cancer, and in February 2008, our team randomly recruited 100 practicing general surgeons and 28 breast cancer surgical investigators to complete an online Patterns of Care survey, which focused on both local and systemic therapeutic modalities. The major rationale for conducting this study was to obtain a better understanding of the current practice patterns of surgeons as part of interdisciplinary management and simultaneously to identify any differences in treatment approaches between general surgeons and breast cancer specialists. Our ultimate goal was to utilize the results from this project to create a dynamic and relevant discussion platform specifically for a unique live education event at The American Society of Breast Surgeons meeting.

1 **Breast Cancer Patterns of Care Survey: February 2008**

28 surgical clinical investigators (CIS)

100 general surgeons (GS)

As part of the typical survey procedure we utilize for these studies, after a web-based survey instrument was developed, we asked five docs to go through it and note whether the questions were clear and the interactivity satisfactory. These presurvey participants were also asked to provide qualitative comments, and the first surgeon's reaction was of great interest (Figure 2). This comment only heightened our anticipation of the survey results.

The dean of breast cancer surgery, Dr Bernard Fisher of the NSABP, would argue that the disease is primarily systemic, and any surgeon treating such patients must be familiar and involved with these issues. In fact, what we see in the survey

2

Comment from Patterns of Care Presurvey Testing

Presurvey test participant 1

Wow! That is a very in-depth survey. This is a survey designed for surgeons that are in a breast center with multidisciplinary treatments in an academic location. I'm a more rural surgeon. I treat many patients with breast cancer with surgery. Most adjuvant care is through the medical oncologists and most of these questions would be deferred to them. If all I did was breast surgery, perhaps I would take more of a role in addressing the issues in this survey. Questions about new assays and comparing them is beyond my scope of understanding. I'm afraid that you might be disappointed in the results of this survey if you are asking a population of general surgeons that are not specialists in breast surgery or are not in academic centers.

findings, in contrast to the rural surgeon's predictions, is a high degree of awareness and information in most surgeons about systemic issues.

— Neil Love, MD
DrNeilLove@ResearchToPractice.com
July 29, 2008

SELECT PUBLICATIONS

Bartelink H. **Systemic adjuvant therapies and radiotherapy to the conserved breast: Strategies revisited.** *Breast* 2007;16(Suppl 2):84-8. **Abstract**

Fallowfield LJ et al. **Psychological outcomes of different treatment policies in women with early breast cancer outside a clinical trial.** *BMJ* 1990;301(6752):575-80. **Abstract**

Franceschini G et al. **Update in the treatment of locally advanced breast cancer: A multidisciplinary approach.** *Eur Rev Med Pharmacol Sci* 2007;11(5):283-9. **Abstract**

Gralow JR et al. **Preoperative therapy in invasive breast cancer: Pathologic assessment and systemic therapy issues in operable disease.** *J Clin Oncol* 2008;26(5):814-9. **Abstract**

Love N. **Patterns of care in cancer of the breast, colon, lung and prostate.** Available at: **www.PatternsOfCare.com**.

Mandelblatt JS et al. **Patterns of care in early-stage breast cancer survivors in the first year after cessation of active treatment**. *J Clin Oncol* 2006;24(1):77-84. **Abstract**

Mariotto AB et al. **Dissemination of adjuvant multi-agent chemotherapy and tamoxifen for breast cancer in the United States using estrogen receptor information: 1975-1999.** *J Natl Cancer Inst Monogr* 2006;(36):7-15. **Abstract**

Newman LA. **Surgical issues and preoperative systemic therapy.** *Cancer Treat Res* 2008;141:79-98. **Abstract**

Pierce LJ et al. **1998-1999 patterns of care study process survey of national practice patterns using breast-conserving surgery and radiotherapy in the management of stage I-II breast cancer.** *Int J Radiat Oncol Biol Phys* 2005;62(1):183-92. **Abstract**

Waljee JF, Newman LA. **Neoadjuvant systemic therapy and the surgical management of breast cancer.** *Surg Clin North Am* 2007;87(2):399-415. **Abstract**

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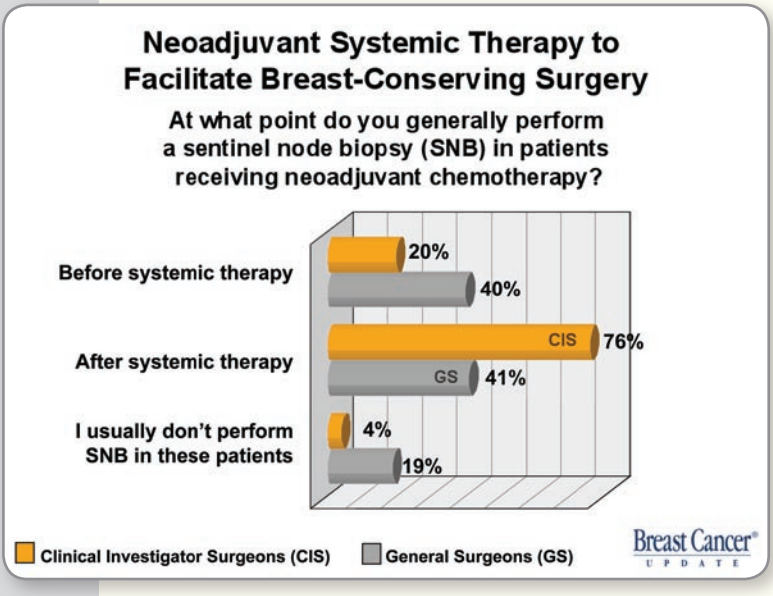
SENTINEL LYMPH NODE BIOPSY (SLNB) RELATIVE TO NEOADJUVANT SYSTEMIC THERAPY



FACULTY COMMENTS

DR WHITWORTH: The performance of SLNB after neoadjuvant therapy is a recent trend among surgical investigators. The timing of SLNB is a complex issue. The initial question was whether SLNB was accurate after neoadjuvant therapy.

Was it possible to sterilize disease in the sentinel node, but not another node, and derive an incorrect answer? In 2005 and 2006, studies began to demonstrate that SLNB was accurate in this setting, particularly in the studies performed by the NSABP. So accuracy is not an issue.

The second question is more problematic and is particularly vexing for radiation oncologists: How do we know how many nodes were positive and who should receive postmastectomy radiation therapy? Is SLNB after neoadjuvant therapy suppressing information that is critically important to treatment decision-making?

Neoadjuvant Systemic Therapy to Facilitate Breast-Conserving Surgery

40 yo B cup-sized breasts: 3-cm, ER+++, PR+++, HER2-negative IDC: Unacceptable cosmetic outcome with lumpectomy. What would you recommend?

	CIS	GS
Neoadjuvant therapy	82%	52%
Chemotherapy	64%	42%
Endocrine therapy	0%	0%
Endocrine or chemotherapy	18%	10%
Partial mastectomy	11%	13%
Mastectomy	7%	35%

Breast Cancer® UPDATE

Neoadjuvant Systemic Therapy to Facilitate Breast-Conserving Surgery

70 yo B cup-sized breasts: 3-cm, ER+++, PR+++, HER2-negative IDC: Unacceptable cosmetic outcome with lumpectomy. What would you recommend?

	CIS	GS
Neoadjuvant therapy	75%	20%
Chemotherapy	18%	5%
Endocrine therapy	57%	13%
Endocrine or chemotherapy	0%	2%
Partial mastectomy	14%	6%
Mastectomy	11%	74%

Breast Cancer® UPDATE

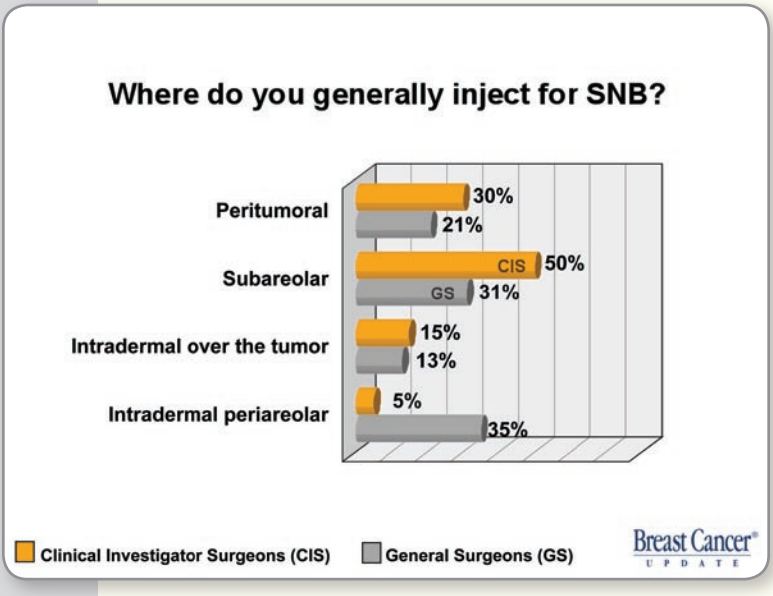
FACULTY COMMENTS

DR DIXON: Semiglazov and colleagues randomly assigned patients to neoadjuvant chemotherapy versus an aromatase inhibitor and reported similar response rates, with significantly more women achieving breast-conserving surgery with endocrine therapy. The reason is that pathologic changes within a tumor are different with endocrine therapy versus chemotherapy.

From our studies we learned that the longer you treat, the better response you obtain. We've been treating patients for longer durations with endocrine therapy — nine months to one year instead of three to four months. You can eventually convert approximately 70 percent of these patients — with strongly ER-positive, usually PR-positive disease — from requiring a mastectomy for locally advanced breast cancer to candidates for breast-conserving surgery.

The other point here relates to the pathology of response with neoadjuvant endocrine therapy treatment — you see a central scar as opposed to the scattered cell pattern with chemotherapy. The cancer implodes, so the size of the tumor after treatment is the size of the piece of tissue that you need to remove.

SENTINEL NODE BIOPSY INJECTION SITE



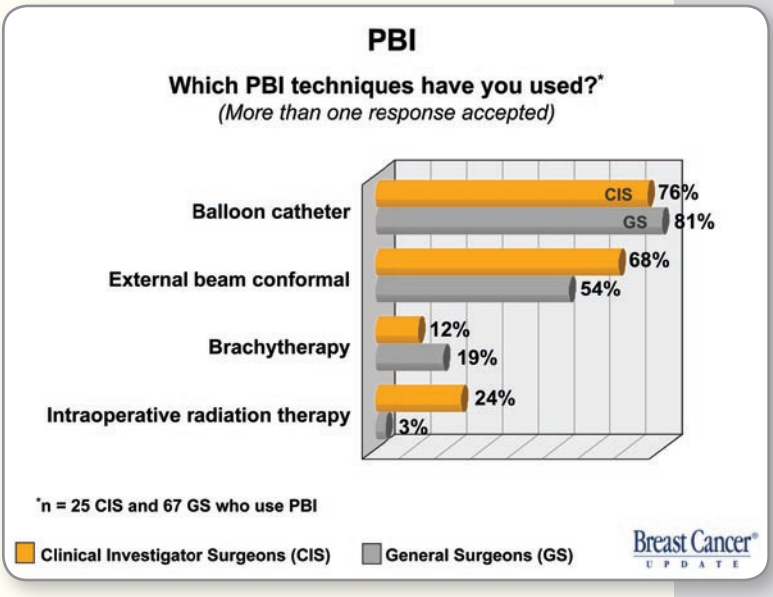
FACULTY COMMENTS

DR DIXON: The science behind injection site location for lymphatic mapping is not clear. Studies suggest that if you inject technetium in the subareolar region and blue dye around the tumor, the injections drain to the same sentinel nodes. I'm not convinced utilizing two injection sites provides benefit. Furthermore, I find injecting peritumorally to be messy when performing surgery, especially when I want to see what's going on, to see the bleeding. When I first started, I injected peritumorally but have since converted to subareolar.

Subareolar injection is easy, straightforward and more commonly practiced, which is especially important when considering the issue of so many impalpable tumors. The radiologist injects the radioisotope around the tumor, and evidence shows this works quite well.

Conversely, other studies have found that "The deep aspects of the breast and the parenchyma drain differently to the subareolar region." However, we've done a fairly large study on subareolar injection and have shown highly effective sentinel node mapping with a low false-negative rate.

PARTIAL BREAST IRRADIATION (PBI)



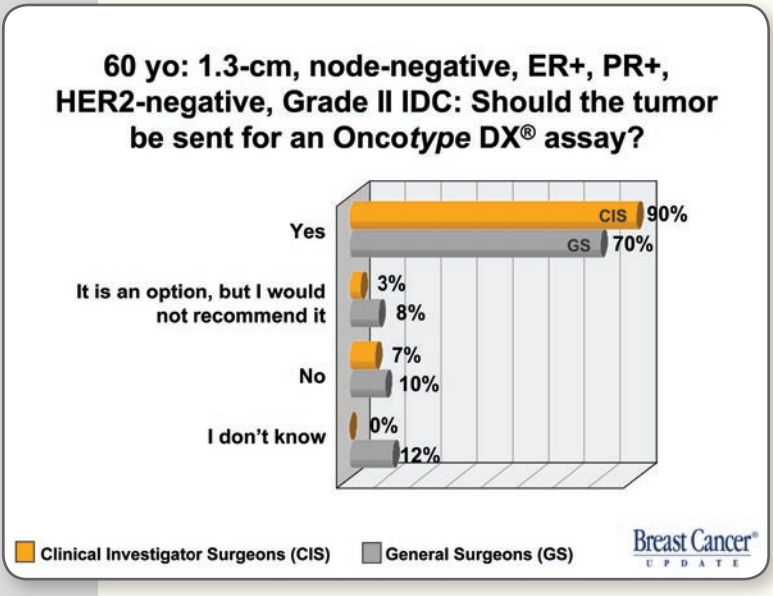
FACULTY COMMENTS

DR WHITWORTH: If you reconsider the NSABP-B-06 trial, it's clear that whole breast irradiation therapy resulted in zero benefit in any quadrant other than the primary tumor quadrant. So we have reason to believe the NSABP-B-39 trial will show equivalent benefit with PBI and whole breast irradiation, even in the patients at higher risk.

However, I would wait to use PBI therapy outside of the B-39 trial for patients who are at higher risk — those who have positive nodes, tumors larger than three centimeters or age younger than 45 to 50.

DR DIXON: PBI is not widely used in the United Kingdom. I did a pretty comprehensive systematic review of the whole literature on local recurrence, and surprisingly, most studies have shown that size and positive nodes are not as important as relative contraindications. However, young age is important, and the major factor, of course, is what we always talk about — the margins seem to matter. So I believe we have studies going on that will be interesting during the next few years.

GENOMIC ASSAYS: PREDICTION OF BENEFIT FROM CHEMOTHERAPY



American Society of Clinical Oncology 2007 Update of Recommendations for the Use of Tumor Markers in Breast Cancer

Harris L et al. *J Clin Oncol* 2007;25(33):5287-312. Abstract

For newly diagnosed patients with node-negative, estrogen receptor-positive breast cancer, the Onco*type* DX assay can be used to:

- **Predict the risk of recurrence for patients treated with tamoxifen**
- **Identify patients who are predicted to obtain the most therapeutic benefit from adjuvant tamoxifen and may not require adjuvant chemotherapy**

Breast Cancer® UPDATE

Impact of Adding Chemotherapy According to the Onco*type* DX Recurrence Score® in ER+, Node+ Early Breast Cancer

	10-year disease-free survival estimates	
	Tamoxifen (n = 148)	CAF → tamoxifen (n = 219)
Low Recurrence Score (<18)	60%	64%
Midrange Recurrence Score (18-30)	49%	63%
High Recurrence Score (≥31)	43%	55%

SOURCE: Albain K et al. San Antonio Breast Cancer Symposium 2007;Abstract 10.

Breast Cancer® UPDATE

In about what percent of patients does the Onco*type* DX assay change the decision about using chemotherapy?

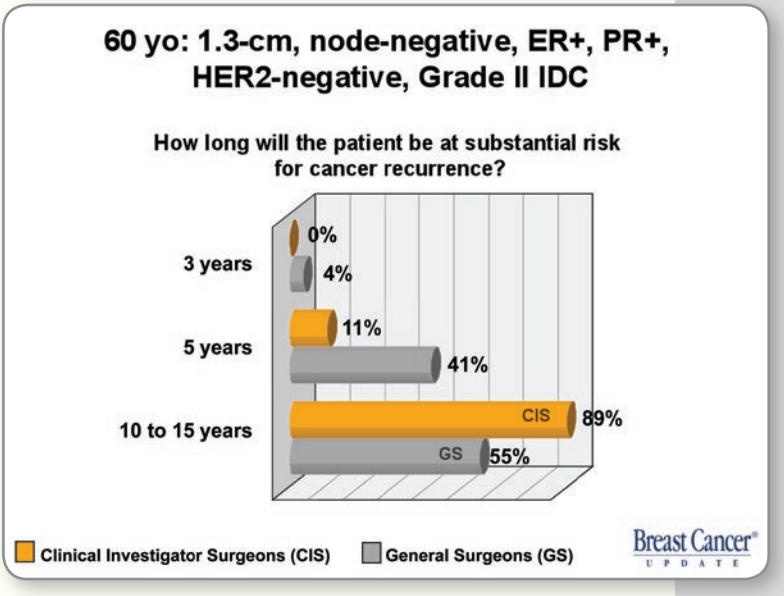
	CIS	GS
Mean	**29%**	**31%**
% responding "I don't know"	**14%**	**46%**

Breast Cancer® UPDATE

FACULTY COMMENTS

DR RAVDIN: During the past two years, the issue of smaller, ER-positive, HER2-negative, node-negative tumors has become an area of contention and enormous expectation. Ordinarily, these patients with ER-positive disease would most likely receive endocrine therapy, but the question is, would they benefit from chemotherapy in addition to hormone therapy? The idea is that we'll be able to identify patients who will obtain a particularly low degree of benefit from chemotherapy and be able to prevent overtreatment. The hope is that we will revolutionize treatment for patients with ER-positive disease who are at low risk.

One line of thought is that molecular markers will allow us to use the multigene assays as in the NSABP-B-20 study, which demonstrated that patients with low Onco*type* Recurrence Scores did not benefit from chemotherapy. More recently, SWOG presented a node-positive trial at San Antonio evaluating patients who received tamoxifen and were then randomly assigned to chemotherapy or not. Again, the low-risk molecular signature identified patients who obtained no risk reduction from chemotherapy.



FACULTY COMMENTS

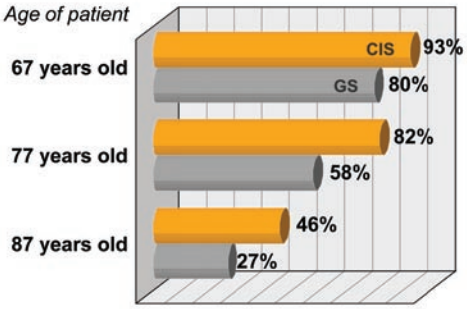
DR RAVDIN: We have all seen disappointing circumstances in which disease recurs after 10 years. The data indicate that recurrence risk is stable during the first five years, with a substantial risk in years five to 10.

Between years five and 10, patients with node-positive disease have approximately a 20 percent risk of recurrence, while those with node-negative disease have a 10 percent risk. This is true for patients with hormone receptor-positive tumors, but it's not true for those with hormone receptor-negative tumors, who experience most of their recurrences within the first five years.

DR DIXON: MA17 was a seminal study that reeducated us that among patients with hormone receptor-positive breast cancer, more events occur from years five to 15 than in the first five years.

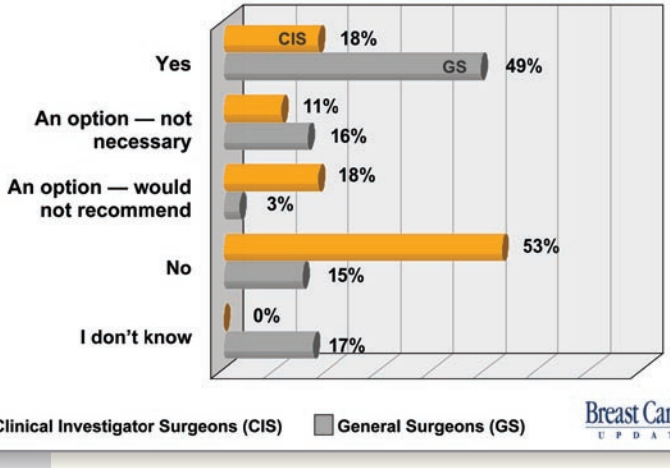
I believe that everyone is more aware now that the risk of recurrence is almost lifelong. The rate of contralateral or second breast primaries in treated patients continues at the same rate almost forever.

For a patient originally with 3 positive nodes who has just completed 5 years of tamoxifen, would you start an AI? *(% answering "yes")*

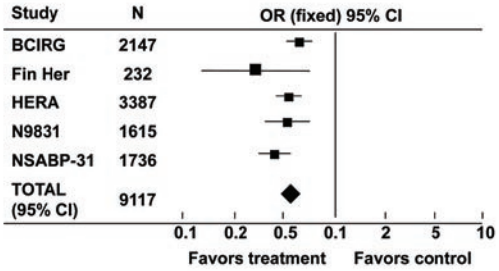


ASSESSMENT OF HER2 STATUS

60 yo: 1.3-cm, node-negative, ER+, PR+, Grade II IDC.
HER2 testing by IHC is 1+.
Should a FISH assay be done?



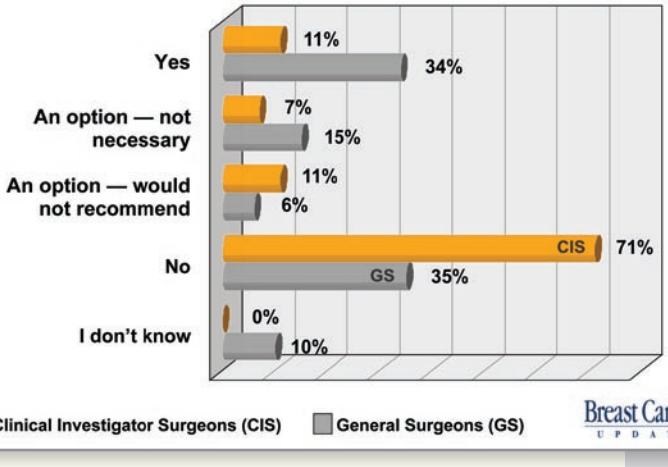
Disease-Free Survival in Published Randomized Trials of Adjuvant Trastuzumab



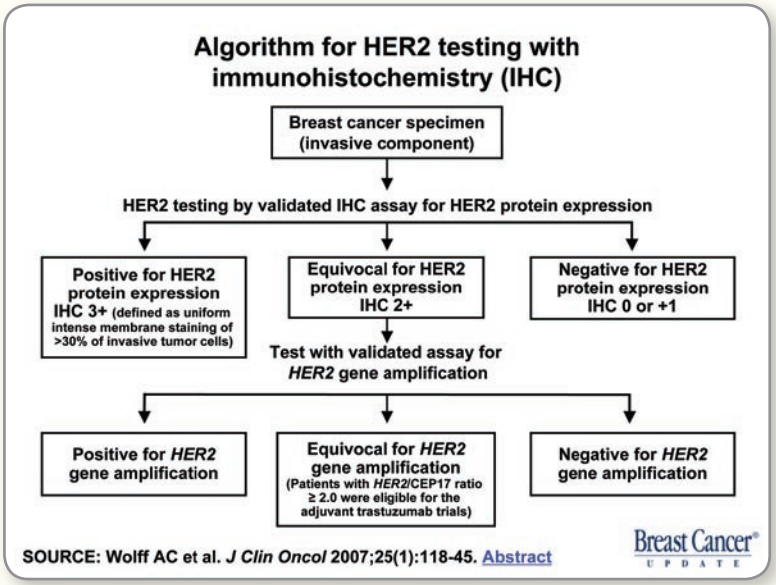
SOURCE: Viani GA et al. *BMC Cancer* 2007;7:153. Abstract

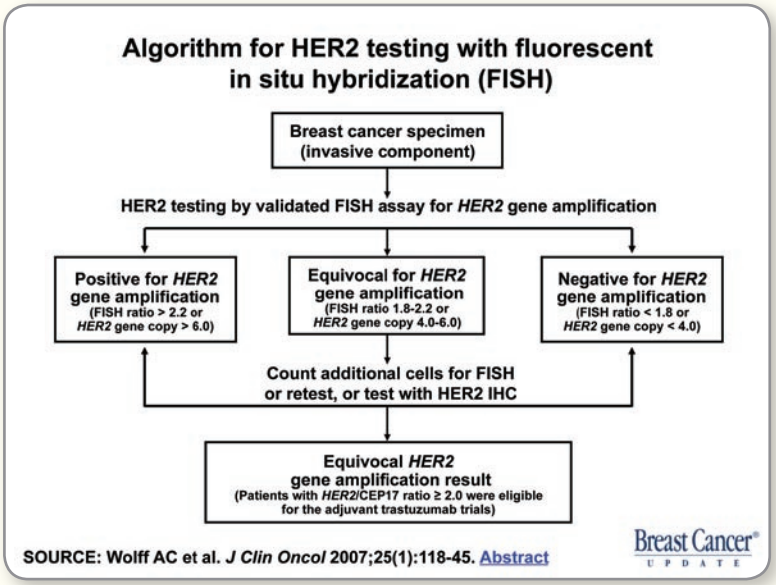
Breast Cancer® UPDATE

38 yo: 2.1-cm, ER+, PR+ IDC with 3 positive nodes. HER2 is 3+ by IHC. *Should a FISH assay be done?*



Breast Cancer® UPDATE


Algorithm for HER2 testing with immunohistochemistry (IHC)
Breast cancer specimen (invasive component)
HER2 testing by validated IHC assay for HER2 protein expression
Positive for HER2 protein expression IHC 3+ (defined as uniform intense membrane staining of >30% of invasive tumor cells)
Equivocal for HER2 protein expression IHC 2+
Negative for HER2 protein expression IHC 0 or +1
Test with validated assay for HER2 gene amplification
Positive for HER2 gene amplification
Equivocal for HER2 gene amplification (Patients with HER2/CEP17 ratio ≥ 2.0 were eligible for the adjuvant trastuzumab trials)
Negative for HER2 gene amplification
SOURCE: Wolff AC et al. J Clin Oncol 2007;25(1):118-45. Abstract
Breast Cancer UPDATE


Algorithm for HER2 testing with fluorescent in situ hybridization (FISH)
Breast cancer specimen (invasive component)
HER2 testing by validated FISH assay for HER2 gene amplification
Positive for HER2 gene amplification (FISH ratio > 2.2 or HER2 gene copy > 6.0)
Equivocal for HER2 gene amplification (FISH ratio 1.8-2.2 or HER2 gene copy 4.0-6.0)
Negative for HER2 gene amplification (FISH ratio < 1.8 or HER2 gene copy < 4.0)
Count additional cells for FISH or retest, or test with HER2 IHC
Equivocal HER2 gene amplification result (Patients with HER2/CEP17 ratio ≥ 2.0 were eligible for the adjuvant trastuzumab trials)
SOURCE: Wolff AC et al. J Clin Oncol 2007;25(1):118-45. Abstract
Breast Cancer UPDATE

SELECT PUBLICATIONS

Albain K et al. **Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal, node-positive, ER-positive breast cancer (S8814,INT0100).** San Antonio Breast Cancer Symposium 2007;**Abstract 10**.

Goss PE et al. **Late extended adjuvant treatment with letrozole improves outcome in women with early-stage breast cancer who complete 5 years of tamoxifen.** *J Clin Oncol* 2008;26(12):1948-55. **Abstract**

Harlow SP et al. **Prerandomization surgical training for the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-32 trial: A randomized phase III clinical trial to compare sentinel node resection to conventional axillary dissection in clinically node-negative breast cancer.** *Ann Surg* 2005;241(1):48-54. **Abstract**

Harris L et al; American Society of Clinical Oncology. **American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer.** *J Clin Oncol* 2007;25(33):5287-312. **Abstract**

Kennecke H et al. **Risk of early recurrence among postmenopausal women with estrogen receptor-positive early breast cancer treated with adjuvant tamoxifen.** *Cancer* 2008;112(7):1437-44. **Abstract**

Krag D et al. **Breast cancer and the NSABP-B-32 sentinel node trial**. *Breast Cancer* 2004;11(3):221-4. No abstract available

Mamounas EP et al. **Sentinel node biopsy after neoadjuvant chemotherapy in breast cancer: Results from National Surgical Adjuvant Breast and Bowel Project Protocol B-27.** *J Clin Oncol* 2005;23(12):2694-702. **Abstract**

Muss HB et al. **Efficacy, toxicity, and quality of life in older women with early-stage breast cancer treated with letrozole or placebo after 5 years of tamoxifen: NCIC CTG Intergroup trial MA.17.** *J Clin Oncol* 2008;26(12):1956-64. **Abstract**

Paik S et al. **Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer.** *J Clin Oncol* 2006;24(23):3726-34. **Abstract**

Povoski SP et al. **Prospective randomized clinical trial comparing intradermal, intra-parenchymal, and subareolar injection routes for sentinel lymph node mapping and biopsy in breast cancer.** *Ann Surg Oncol* 2006;13(11):1412-21. **Abstract**

Semiglazov VF et al. **Phase 2 randomized trial of primary endocrine therapy versus chemotherapy in postmenopausal patients with estrogen receptor-positive breast cancer.** *Cancer* 2007;110(2):244-54. **Abstract**

Sparano JA, Paik S. **Development of the 21-gene assay and its application in clinical practice and clinical trials.** *J Clin Oncol* 2008;26(5):721-8. **Abstract**

Thomas JS et al. **Histopathology of breast carcinoma following neoadjuvant systemic therapy: A common association between letrozole therapy and central scarring.** *Histopathology* 2007;51(2):219-26. **Abstract**

Wolff AC et al. **American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer.** *J Clin Oncol* 2007;25(1):118-45. **Abstract**

POST-TEST

The Role of the Surgeon in the Interdisciplinary Management of Early Breast Cancer

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **Most breast cancer clinical investigator surgeons _____.**
   a. Perform SLNB before neoadjuvant systemic therapy
   b. Perform SLNB after neoadjuvant systemic therapy
   c. Do not perform SLNB in patients undergoing neoadjuvant therapy

2. **The most commonly reported site of tracer injection by clinical investigator surgeons was _____.**
   a. Peritumoral
   b. Subareolar
   c. Intradermal over the tumor
   d. Intradermal periareolar

3. **In a study by Semiglazov and colleagues, neoadjuvant endocrine therapy and chemotherapy resulted in similar response rates, but endocrine therapy resulted in a _____.**
   a. Higher rate of breast-conserving surgery
   b. Lower rate of breast-conserving surgery

4. **The most commonly used partial breast irradiation technique by US-based general surgeons and clinical investigator surgeons was _____.**
   a. Balloon catheter
   b. External beam conformal
   c. Brachytherapy
   d. Intraoperative radiation therapy

5. **In the ASCO 2007 update of recommendations for the use of tumor markers in breast cancer, which of the following roles were identified for the Onco*type* DX assay?**
   a. Predict the risk of recurrence for patients treated with tamoxifen
   b. Identify patients who are predicted to obtain the most benefit from adjuvant tamoxifen and may not require adjuvant chemotherapy
   c. Neither a nor b
   d. Both a and b

6. **TAILORx is a Phase III study of adjuvant chemotherapy and hormonal therapy versus adjuvant hormonal therapy alone in patients with a _____ Recurrence Score on the Onco*type* DX assay.**
   a. Low
   b. Midrange
   c. High

7. **The ASCO/College of American Pathologists guidelines for HER2 testing recommend that patients whose tumors are 1+ for HER2 by IHC should have their tumors reanalyzed by FISH.**
   a. True
   b. False

8. **In the Patterns of Care survey, the majority of clinical investigator surgeons would recommend that patients whose tumors are 3+ for HER2 by IHC should have their tumors reanalyzed by FISH.**
   a. True
   b. False

9. **In patients with hormone receptor-positive, node-positive early breast cancer who completed five years of adjuvant endocrine therapy, the risk of recurrence between years five and 10 is approximately _____.**
   a. Four percent
   b. Eight percent
   c. 12 percent
   d. 20 percent

10. **The MA17 trial evaluated _____ after completion of five years of adjuvant tamoxifen for postmenopausal women with hormone receptor-positive early breast cancer.**
    a. Letrozole versus control
    b. Letrozole versus anastrozole
    c. Letrozole versus tamoxifen

11. **Clinical trials of adjuvant trastuzumab for HER2-positive early breast cancer have demonstrated a significant survival benefit of ____ percent.**
    a. Eight
    b. 15
    c. 19
    d. 33

Post-test answer key: 1b, 2b, 3a, 4a, 5d, 6b, 7b, 8b, 9d, 10a, 11d

EDUCATIONAL ASSESSMENT AND CREDIT FORM

The Role of the Surgeon in the Interdisciplinary Management of Early Breast Cancer

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART ONE — Please tell us about your experience with this educational activity

BEFORE completion of this activity, how would you characterize your level of knowledge on the following topics?

4 = Very good 3 = Above average 2 = Adequate 1 = Suboptimal

- **Use of neoadjuvant systemic therapy, including timing of sentinel node biopsy and selection of therapy** 4 3 2 1
- **Contraindications to the use of partial breast irradiation** 4 3 2 1
- **Extending adjuvant hormonal therapy beyond five years for patients with ER-positive disease** 4 3 2 1
- **Use of genomic assays to identify appropriate patients for adjuvant chemotherapy** 4 3 2 1
- **Application of guidelines for HER2 testing and resulting impact on treatment choice for adjuvant therapy for HER2-positive breast cancer** 4 3 2 1

AFTER completion of this activity, how would you characterize your level of knowledge on the following topics?

4 = Very good 3 = Above average 2 = Adequate 1 = Suboptimal

- **Use of neoadjuvant systemic therapy, including timing of sentinel node biopsy and selection of therapy** 4 3 2 1
- **Contraindications to the use of partial breast irradiation** 4 3 2 1
- **Extending adjuvant hormonal therapy beyond five years for patients with ER-positive disease** 4 3 2 1
- **Use of genomic assays to identify appropriate patients for adjuvant chemotherapy** 4 3 2 1
- **Application of guidelines for HER2 testing and resulting impact on treatment choice for adjuvant therapy for HER2-positive breast cancer** 4 3 2 1

Was the activity evidence based, fair, balanced and free from commercial bias?

☐ Yes ☐ No

If no, please explain: . . . . . .

Will this activity help you improve patient care?

☐ Yes ☐ No ☐ Not applicable

If no, please explain: . . . . . .

Did the activity meet your educational needs and expectations?

☐ Yes ☐ No

If no, please explain: . . . . . .

Please respond to the following LEARNER statements by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = Learning objective not met N/A = Not applicable

As a result of this activity, I will be able to:

- Compare management strategies of community-based general surgeons and breast cancer surgical specialists for the treatment of early breast cancer, and apply relevant information to clinical practice. . . . . 4 3 2 1 N/M N/A
- Evaluate issues related to the accuracy, reliability and interpretation of the ER and HER2 status of breast tumors, in the context of local laboratory practices and national guidelines. . . . . 4 3 2 1 N/M N/A
- Identify the rationale for and benefits of extended adjuvant endocrine therapy, and utilize this approach for patients with hormone receptor-positive breast cancer. . . . . 4 3 2 1 N/M N/A
- Describe the evidence-based risks and benefits of adjuvant trastuzumab therapy, and implement a plan for the initial treatment for patients with HER2-positive early breast cancer. . . . . 4 3 2 1 N/M N/A
- Evaluate the utility of tissue-based genomic assays for therapeutic decision-making and, when applicable, use these in the selection of individualized treatment regimens for patients with early breast cancer. . . . . 4 3 2 1 N/M N/A
- Review emerging research data evaluating the utility and long-term impact of sentinel lymph node biopsy, and translate these findings to current practice. . . . . 4 3 2 1 N/M N/A
- Discuss the risks and benefits of partial breast irradiation and the clinical trials evaluating this technique with appropriately selected patients. . . . . 4 3 2 1 N/M N/A
- Utilize magnetic resonance imaging in appropriately selected patients with breast cancer . . . . . 4 3 2 1 N/M N/A

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

What other practice changes will you make or consider making as a result of this activity?

.....

What additional information or training do you need on the activity topics or other oncology-related topics?

.....

Additional comments about this activity:

.....

.....

May we include you in future assessments to evaluate the effectiveness of this activity?

☐ Yes ☐ No

PART TWO — Please tell us about the faculty for this educational activity

4 = Very good 3 = Above average 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter	Effectiveness as an educator
J Michael Dixon, MD	4 3 2 1	4 3 2 1
Mark D Pegram, MD	4 3 2 1	4 3 2 1
Peter M Ravdin, MD, PhD	4 3 2 1	4 3 2 1
Pat W Whitworth Jr, MD	4 3 2 1	4 3 2 1

Please recommend additional faculty for future activities:

.....

Other comments about the faculty for this activity:

.....

REQUEST FOR CREDIT — Please print clearly

Name:..... Specialty:.....

Professional Designation:

☐ MD ☐ DO ☐ PharmD ☐ NP ☐ RN ☐ PA ☐ Other.....

Medical License/ME Number:..... Last 4 Digits of SSN (required):.....

Street Address:..... Box/Suite:.....

City, State, Zip:.....

Telephone:..... Fax:.....

Email:.....

Research To Practice designates this educational activity for a maximum of 3.75 *AMA PRA Category 1 Credit(s)™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.
I certify my actual time spent to complete this educational activity to be _____ hour(s).

Signature:..... Date:.....

To obtain a certificate of completion and receive credit for this activity, please complete the Post-test, fill out the Educational Assessment and Credit Form and fax both to (800) 447-4310, or mail both to Research To Practice, One Biscayne Tower, 2 South Biscayne Boulevard, Suite 3600, Miami, FL 33131. You may also complete the Post-test and Educational Assessment online at www.BreastCancerUpdate.com/Surgeons/CME.

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Breast Cancer® UPDATE

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