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Breast Cancer® UPDATE

An Audio Review Journal for Surgeons

Bridging the Gap between Research and Patient Care

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Breast Cancer Update for Surgeons
A Continuing Medical Education Audio Series

STATEMENT OF NEED/TARGET AUDIENCE

Breast cancer is one of the most rapidly evolving fields in oncology. Published results from a plethora of ongoing clinical trials lead to the continuous emergence of new therapeutic techniques, agents and changes in the indications for existing treatments. In order to offer optimal patient care — including the option of clinical trial participation — the practicing breast surgeon must be well informed of these advances. To bridge the gap between research and patient care, *Breast Cancer Update* for Surgeons utilizes one-on-one discussions with leading breast cancer investigators. By providing access to the latest research developments and expert perspectives, this CME program assists breast surgeons in the formulation of up-to-date clinical management strategies.

GLOBAL LEARNING OBJECTIVES

- Critically evaluate the clinical implications of emerging clinical trial data in breast cancer in order to incorporate these data into management strategies in adjuvant and neoadjuvant disease.
- Counsel appropriately selected patients about the availability of ongoing clinical trials.
- Counsel postmenopausal patients with ER-positive breast cancer about the risks and benefits of aromatase inhibitors in the adjuvant and neoadjuvant settings and of switching to or sequencing aromatase inhibitors after tamoxifen.
- Counsel appropriately selected patients about emerging clinical trial data and ongoing trials in the prevention and treatment of noninvasive (DCIS) and invasive breast cancer.
- Describe the computerized risk models and genetic markers to determine prognostic information on the quantitative risk of breast cancer relapse, and when applicable, utilize these to guide therapy decisions.
- Counsel appropriately selected patients about availability and applicability of emerging research data on sentinel lymph node biopsy.
- Discuss the risks and benefits of partial breast irradiation and the clinical trials evaluating this technique with appropriately selected patients.

PURPOSE OF THIS ISSUE OF *BREAST CANCER UPDATE* FOR SURGEONS

The purpose of Issue 2 of *Breast Cancer Update* for Surgeons is to support these global objectives by offering the perspectives of Drs Morrow, Fox, Julian, Carlson and Elledge on the integration of emerging clinical research data into the management of breast cancer.

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UPCOMING EDUCATIONAL EVENTS

31st ESMO Congress
September 29-October 3, 2006
Istanbul, Turkey
Event website: **esmo.org**

NSABP Fall Meeting
October 13-16, 2006
Baltimore, Maryland
Event website: **nsabp.pitt.edu/Future_Meetings.asp**

48th Annual Meeting of the American Society for Therapeutic Radiology and Oncology
November 5-9, 2006
Philadelphia, Pennsylvania
Event website: **astro.org**

29th San Antonio Breast Cancer Symposium
December 14-17, 2006
San Antonio, Texas
Event website: **sabcs.org**

Miami Breast Cancer Conference
February 21-24, 2007
Miami Beach, Florida
Event website: **cancerconf.com**

Society of Surgical Oncology Annual Meeting
March 15-18, 2007
Washington, DC
Event website: **surgonc.org**

American Association of Cancer Research Annual Meeting
April 14-18, 2007
Los Angeles, California
Event website: **aacr.org**

ASCO 2007 Annual Meeting
June 1-5, 2007
Chicago, Illinois
Event website: **asco.org**

INTERVIEW

Monica Morrow, MD

Dr Morrow is Professor of Surgery at Temple University School of Medicine, Chairman of the Department of Surgical Oncology and G Willing Pepper Chair in Cancer Research at Fox Chase Cancer Center in Philadelphia, Pennsylvania.

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Track 2

DR LOVE: Can you discuss your recent study examining decision-making for patients undergoing surgical treatment for breast cancer?

DR MORROW: The adoption of breast conservation has been relatively slow, and people have made the assumption that surgeons either are not in favor of breast conservation or are inappropriately advising patients.

We used the SEER registries from Detroit and Los Angeles to identify women within an average of six months after diagnosis, which is a time when they would have fairly active memory of decisions made during the treatment process (Hawley 2006). In that patient sample, we saw that approximately 70 percent of women were treated with breast-conserving therapy, so those numbers have increased when compared to historical studies.

When we asked patients, "Did you, your surgeon or you and your surgeon in collaboration make the decision about surgery?" we saw a highly statistically significant correlation between greater patient involvement in the decision-making process and higher mastectomy rates. Yet in response to the question, "Did your surgeon recommend a treatment to you?" patients overwhelmingly said their surgeons recommended breast-conserving therapy.

We asked patients what was driving their decision and discovered two big issues. One concern was recurrence, and since it's always been clear that the rate of distant recurrence with mastectomy and breast conservation is the same, this is a local recurrence issue. The second issue was concern about the use of radiation therapy.

To me, probably the most alarming outcome of this study was that when we asked patients a series of true-false questions to assess the knowledge they would need to make an informed decision, only 50 percent of them correctly answered that their chances of surviving after breast-conserving therapy or mastectomy were equal.

I believe this tells us that we are not clearly getting this information to patients, and they are choosing what they perceive to be a safer or more aggressive cancer treatment.

Shared decision-making is certainly a good idea and one I endorse, but patients need to have an appropriate understanding of the key facts, and our study suggests that's still a problem.

Track 8

DR LOVE: I'm curious what your thoughts are about the Onco*type* DX assay.

DR MORROW: The Onco*type* DX assay is an examination of a selected panel of 21 genes. A great advantage is that it can be performed on paraffin specimens, so it's widely applicable and clinically available in practice.

The initial important validation of this assay was seen in patients on the NSABP-B-14 trial, which randomly assigned patients with ER-positive, node-negative disease to tamoxifen or a placebo (Paik 2004). This study showed that you could look at a recurrence score, which was designated as low, medium or high based on numeric cutoffs, and identify outcomes of patients. Most importantly, it showed that you could identify which patients who had received tamoxifen would not benefit from the addition of chemotherapy.

Subsequently, this was examined again in other NSABP data sets and some non-NSABP data sets, and the initial findings were basically confirmed. The studies confirmed that patients with low recurrence scores who received chemotherapy did not experience any additional benefit.

This is useful information, because when you use the traditional prognostic

measures — tumor size, histologic grade — you end up treating many women with receptor-positive disease who already have a good prognosis and will mostly gain only the toxicity of chemotherapy.

In addition, the assay can identify a subset of women who traditionally would not be considered candidates for chemotherapy — tumors less than a centimeter in size, node-negative — who, in fact, fall into a high-risk group.

DR LOVE: Do you use the Onco*type* DX clinically?

DR MORROW: We apply this in our practice after we ask ourselves the question, "Would we change how we're going to treat this patient based on the results of this assay?"

Track 11

DR LOVE: How do you feel about the use of aromatase inhibitors after five years of adjuvant tamoxifen, and have you integrated this strategy into your practice?

DR MORROW: It is important for women who have been treated in the past or who are coming to the end of five years of tamoxifen to know that adding an aromatase inhibitor prolongs disease-free survival and, in node-positive subsets, overall survival.

The only group for which I would question the use of an aromatase inhibitor after five years of tamoxifen is patients with very low-risk tumors. For that group, I don't know the risk-benefit balance of administering an aromatase inhibitor for another five years, but for the vast majority of women with breast cancer, this strategy makes perfect sense.

DR LOVE: If you see a postmenopausal woman who has completed adjuvant tamoxifen, do you prescribe an aromatase inhibitor or send her to an oncologist?

DR MORROW: I definitely believe it's something that needs to be addressed with patients in this day and age, and I advise them to discuss it with their oncologist. ■

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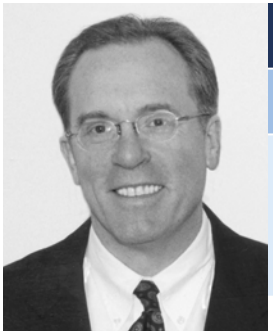

INTERVIEW

Kevin R Fox, MD

Dr Fox is Director of Rena Rowan Breast Center and Associate Professor of Medicine at the University of Pennsylvania Cancer Center in Philadelphia, Pennsylvania.

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Track 3 SWOG trial of chemotherapy with or without ovarian suppression for patients with ER-negative disease

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Track 16 Future clinical research questions regarding patients with ER-positive, PR-positive tumors

Select Excerpts from the Interview

Track 6

DR LOVE: What options are available for patients diagnosed with breast cancer who want to preserve their fertility?

DR FOX: Dr Oktay from Cornell has been a driving force behind a strategy to stimulate the ovary to produce eggs for fertilization and cryopreservation (Sonmezer, Oktay 2006).

Dr Oktay's hypothesis is that if a patient is diagnosed with a breast cancer and is desirous of subsequently having children, you can stimulate her ovaries to produce eggs for fertilization before chemotherapy is initiated. Tamoxifen or letrozole is incorporated to stimulate the ovaries. The eggs can be retrieved in large numbers and can be fertilized, cryopreserved, and then implanted at a later time.

The concerns are whether this stimulatory strategy prior to chemotherapy will put the patient in harm's way and whether the delay in chemotherapy, even by a few weeks, increases the patient's risk of recurrence.

Even though it's very early follow-up — approximately 18 months — and the number of patients is relatively small, he demonstrated as convincingly as one can in a small cohort that no precipitous increase in relapse rates occurred during that time interval.

We don't yet know the fertility success rate. With only 18 months of data, those numbers are just beginning to develop.

Track 11

DR LOVE: Can you provide an update of clinical research on adjuvant hormonal therapy for premenopausal patients?

DR FOX: The biggest challenge in developing new therapeutic strategies for premenopausal women with hormone receptor-positive breast cancers is related to the issue of ovarian suppression. We are participating in one of the largest clinical trials addressing this issue — the SOFT trial (2.1).

This trial randomly assigns premenopausal women with receptor-positive cancers to receive tamoxifen alone, ovarian suppression for five years with tamoxifen or ovarian suppression for five years with exemestane.

I don't know of a more important question in clinical research on breast cancer in younger patients at the moment. The irony is that it's been enormously

2.1 **Trials of Adjuvant Endocrine Therapy with Ovarian Suppression**

Study	N	Eligibility	Randomization
IBCSG-24-02 (SOFT trial)	3,000 (Open)	Premenopausal ER ≥ 10% and/or PgR ≥ 10%	T x 5y OFS + T x 5y OFS + E x 5y
IBCSG-25-02 (TEXT trial)	1,845 (Open)	Premenopausal ER ≥ 10% and/or PgR ≥ 10%	Triptorelin ± chemotherapy + T x 5y Triptorelin ± chemotherapy + E x 5y

T = tamoxifen; OFS = ovarian function suppression with triptorelin, surgical oophorectomy or ovarian irradiation; E = exemestane

SOURCES: ibcsg.org; NCI Physician Data Query, July 2006.

difficult to get patients to participate in this trial, and accrual to the SOFT trial has been sluggish at best.

In the summary of recommendations of the 2005 St Gallen meeting, a little section appears at the end on the treatment of premenopausal women, worded in a very interesting way. It basically says that despite the absence of available data, the use of ovarian function suppression in premenopausal women is acceptable.

My feeling is that it certainly is acceptable. But acceptability notwithstanding, this is something that we at Penn have not offered to patients on a consistent basis for the simple reason that I am uncomfortable in the absence of supporting data.

I will say that, outside of a clinical trial like the SOFT or TEXT trial, we have not consistently offered ovarian suppression to patients in addition to their tamoxifen therapy. I still believe tamoxifen is the standard of care.

Track 13

DR LOVE: What are your thoughts about the aromatase inhibitor clinical trials in postmenopausal patients and current implications for clinical practice?

DR FOX: At the moment, you have to look at patients based on where they happen to be in their course of treatment.

The ATAC trial addresses treatment of the newly diagnosed postmenopausal patient with estrogen receptor-positive breast cancer, and I believe this trial gives irrefutable evidence that anastrozole is superior to tamoxifen with respect to reducing the risk of recurrence. So for the newly diagnosed patient, the available data suggest that five years of an aromatase inhibitor is the best therapy (Howell 2005).

The preliminary information with letrozole in the BIG 1-98 study gives the same message (Thürlimann 2005). The follow-up is shorter — a little over two years versus six in ATAC — but the apparent reduction in the risk of recurrence is on the order of that seen with anastrozole. I think that most of us believe them to be likely equivalent. The preferential prescription of anastrozole at the moment is based on more maturity of data.

The second situation is that of the patient in the middle of a course of therapy. This was evaluated in the international exemestane group trial and the trials of anastrozole, which were similarly constructed (Coombes 2005; Boccardo 2005; Jakesz 2005). These trials were designed to capture patients at the midpoint of a course of therapy and measure outcomes from the point of changing treatment, randomly assigning patients to continue tamoxifen or take an aromatase inhibitor for the balance of the five-year period.

For the patient in the middle of a course of tamoxifen therapy or the premenopausal woman who's become amenorrheic from chemotherapy and has

been on tamoxifen and amenorrheic for two years, it is appropriate to change her to an aromatase inhibitor.

A third situation is that of the patient who has completed five years of tamoxifen. MA17 demonstrates that letrozole produces a small but measurable reduction in the risk of recurrence and an indication of a survival benefit among women with node-positive disease (Goss 2005, 2006).

If you evaluate patients with respect to where they fall in time and follow the data that exist, these are the three scenarios and the three approaches I would take. ■

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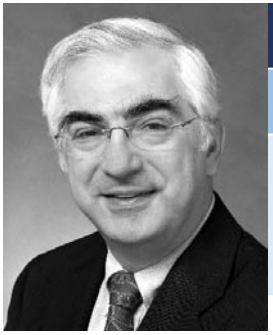

INTERVIEW

Thomas B Julian, MD

Dr Julian is Associate Professor of Human Oncology at the Drexel University College of Medicine and Associate Director of the Breast Care Center at Allegheny Cancer Center in Pittsburgh, Pennsylvania.

Tracks 1-11

Select Excerpts from the Interview

Track 2

DR LOVE: Can you describe the NSABP-B-32 trial?

DR JULIAN: NSABP-B-32 was one of our largest trials. Women with clinically node-negative disease were randomly assigned to receive a sentinel node biopsy with an axillary node dissection or a sentinel node biopsy alone. In the group assigned to a sentinel node biopsy alone, if the sentinel node biopsy was negative, the patient was observed, and if the sentinel node biopsy was positive, the patient went on to have an axillary dissection (Julian 2004).

The trial accrued 5,611 patients in a little less than five years, something that was not thought to be possible at the time. The first technical report came out at the 2004 San Antonio Breast Cancer Symposium. In both groups, we reported a sentinel node identification rate of about 97 percent, and the positive sentinel node rate was 26 percent. In the group assigned to sentinel node biopsy and axillary dissection, the false-negative rate was 9.7 percent (Julian 2004).

Tracks 7-8

DR LOVE: Can you review the work that's been done with the NSABP and led by Soon Paik evaluating the Onco*type* DX assay?

DR JULIAN: The Onco*type* DX is a great story of using molecular technology and taxonomy to try to select patients who should or should not receive chemotherapy, where previously we may have just used a best-guess estimate to advise them (Paik 2004). This is a very important step in the march toward individualizing treatment for patients.

In fact, it's even been carried one step further because Terry Mamounas reported data at San Antonio this past year (Mamounas 2005) evaluating the ability of using that type of molecular assay to predict for local recurrences. If you have a high recurrence score, then there's a strong likelihood that you will have an in-breast local recurrence as well.

DR LOVE: Is there a patient in your practice who you could present in a deidentified way that would make the point about the practical utility of the Onco*type* assay?

DR JULIAN: I evaluated a woman in her mid-forties. She had a lesion that was identified mammographically, and she was totally asymptomatic. You could not palpate the lesion, and she was clinically node-negative. She had her core biopsy, and it was an invasive, estrogen receptor-positive, progesterone receptor-positive, HER2-negative ductal cancer. She went on to have a partial mastectomy, and we performed a sentinel node biopsy at the same time.

The tumor was roughly 1.2 centimeters in diameter, and the two sentinel nodes were both negative on final H&E analysis. She did not have any lymphovascular invasion in her tumor, and there were no other tumor parameters that looked worrisome. But, given her age and premenopausal status, we subjected the tumor to an Onco*type* DX, and it came back with a recurrence score of 38, which was in the high range. That was important because normally this is a patient who might have gotten a very strong benefit of just being placed on tamoxifen. For her, the recommendation was, "You should also receive adjuvant chemotherapy," and she's very much in favor of doing that.

DR LOVE: Did you feel that in your discussions with her that the Onco*type* DX was going to decide whether she was going to receive chemotherapy?

DR JULIAN: It was really to provide guidance to her and the medical oncologist because this is a tumor that very easily could have just been treated in the past with antihormonal therapy and, of course, breast irradiation, especially if patients were somewhat hesitant to receive chemotherapy because of the concern about side effects or toxicities. This is a tool that now presents them with very dramatic evidence to say, "It is important for you to know that you've got this very strong chance that this cancer will come back beyond what we could predict by using a computerized model."

Track 9

DR LOVE: Can you discuss the background and design of NSABP-B-35, which compares anastrozole to tamoxifen in patients with DCIS?

DR JULIAN: The background includes the prior two DCIS trials — NSABP-B-17 and NSABP-B-24. NSABP-B-17 showed the benefit of whole breast radiation therapy with lumpectomy as opposed to lumpectomy alone in reducing the rate of both invasive and noninvasive cancer in the treated breast (Fisher 1998). NSABP-B-24 carried that one step further with the comparison of tamoxifen versus placebo in patients receiving radiation therapy following their lumpectomy (Fisher 1999).

NSABP-B-24 showed a decrease in all breast cancer events with the use of tamoxifen and a reduction in invasive cancers in the ipsilateral breast. Based on those trials and the work performed by Craig Allred suggesting that the impact of the tamoxifen was the greatest in patients with ER-positive disease (Allred 2002), we then carried it one step further to evaluate the use of an aromatase inhibitor in postmenopausal women with DCIS.

The ATAC trial demonstrated a reduction in invasive breast cancers in both the ipsilateral and the contralateral breast with the use of anastrozole compared to tamoxifen (Howell 2005). We believed that the next step would be to compare an aromatase inhibitor to tamoxifen for DCIS in a randomized setting. That was the background and basis for launching NSABP-B-35.

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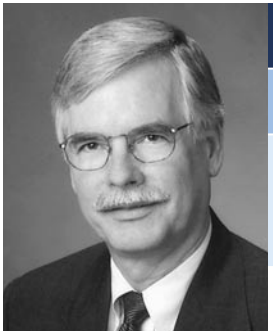


INTERVIEW

Robert W Carlson, MD

Dr Carlson is Professor of Medicine in the Division of Oncology and Stanford Medical Informatics at Stanford University Medical Center in Stanford, California.

Tracks 1-7

Select Excerpts from the Interview

Track 2

DR LOVE: Can you comment on the controversy about whether all postmenopausal women with ER-positive tumors should be started on an aromatase inhibitor or whether some patients can be identified who would derive greater benefit from a sequential strategy of two to three years of tamoxifen followed by an aromatase inhibitor?

DR CARLSON: The strategies have never truly been studied in a randomized fashion. The BIG 1-98 trial will give us the first look at directly comparing these strategies (Thürlimann 2005). The issue is whether tamoxifen is doing something biologically to the tumor that primes it or sensitizes it to profound estrogen deprivation, which characterizes the activity of an aromatase inhibitor.

DR LOVE: That would kick in after two to three years, but there would be more recurrences during the first two to three years.

DR CARLSON: That's correct. And is that priming by tamoxifen — if it happens, and I think that's questionable — great enough that, over the ensuing period of time with the aromatase inhibitor, that you "catch up" with the

women who have experienced recurrences during the first two to three years? The question is: Is there really something that tamoxifen is doing to prime the breast cancer cells, which then makes the aromatase inhibitor more effective? Or is it, rather, that the population of women and the characteristics of their breast cancer, specifically, change over time in a way that we would expect to make the aromatase inhibitors, or any hormonal therapy, more effective?

I believe there is a substantial amount of data that would support the "selection bias theory" — the population of breast cancers is changing over time. You would expect the endocrine-resistant, receptor-positive breast cancers to recur earlier. So those women are removed from the denominator, and if you really do have a sensitive population and an insensitive population of hormone receptor-positive tumors, you should expect — even if there's no difference in efficacy between the hormonal therapies — to see an increasing effect the later in time you initiate the therapy.

DR LOVE: So what would you recommend for practical purposes?

DR CARLSON: The majority of my patients are given a prescription for an aromatase inhibitor; typically, that would be anastrozole in my practice.

Track 4

DR LOVE: What about the issue of hormone therapy for premenopausal women who become postmenopausal after receiving chemotherapy?

DR CARLSON: None of the published aromatase inhibitor trials have enrolled women who were rendered postmenopausal by the treating oncologist. Therefore, this is a population of women who do not meet the eligibility criteria for the aromatase inhibitor trials.

My expectation is that such a strategy is going to be highly effective. If we look at the studies that have examined ovarian suppression and aromatase inhibition in metastatic premenopausal breast cancer with positive hormone receptors, we can expect to see high rates of clinical benefit and long durations of disease control.

This is what we found in our trial at Stanford conducted with investigators from MD Anderson. It is a Phase II trial designed for premenopausal women with hormone receptor-positive, measurable metastatic breast cancer who have not received a prior aromatase inhibitor.

Currently, we have 29 patients of a planned 30 enrolled. We're seeing quite surprisingly high rates of clinical benefit, in the 75 to 80 percent range, and significantly long durations of disease control, and the time to progression is well beyond six months.

SELECT PUBLICATIONS

Thürlimann B et al. **A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer.** *N Engl J Med* 2005;353:2747-57. **Abstract**

INTERVIEW

Richard M Elledge, MD

Dr Elledge is Medical Director at the Breast Care Center and Associate Professor of Medicine at Baylor College of Medicine in Houston, Texas.

Tracks 1-6

Track 1	Introduction
Track 2	Utility and benefit of the Onco*type* DX assay
Track 3	Case discussion: A 72-year-old woman with ER-positive, PR-positive, node-negative breast cancer
Track 4	Use of Onco*type* DX to facilitate decision-making about adjuvant chemotherapy
Track 5	Quality control in ER and HER2 testing
Track 6	Importance of obtaining accurate ER and HER2 status

Select Excerpts from the Interview

Tracks 2-4

DR LOVE: Can you comment on the Onco*type* DX assay?

DR ELLEDGE: I believe it is a very useful tool. I would strongly endorse community oncologists using it in situations in which they are trying to decide whether to use chemotherapy. The strengths of the Onco*type* DX assay are its standardization and reproducibility.

The assay uses a collection of genes that were combed from the world's literature over the last 30 years and found to be associated with outcome in breast cancer. They were combined in an assay and tested retrospectively in databases to see how they predicted for the natural history of the disease after local therapies (Paik 2004; [4.1]) and for response to adjuvant chemotherapy (Paik 2006; [4.2]).

The Onco*type* DX assay offers prognostic information about the risk of recurrence. It presents a visual representation of where your patient lies along a spectrum. It will assign a score, which some people "trichotomize" into a low, intermediate or high score. Patients who are on the lower end of the spectrum will have a lower absolute risk of recurrence and much lower benefit from chemotherapy (4.1, 4.2).

4.1

Estimates of Recurrence Rate Based on Multigene Assay in Patients Who Received Tamoxifen on NSABP-B-14 (N = 668)

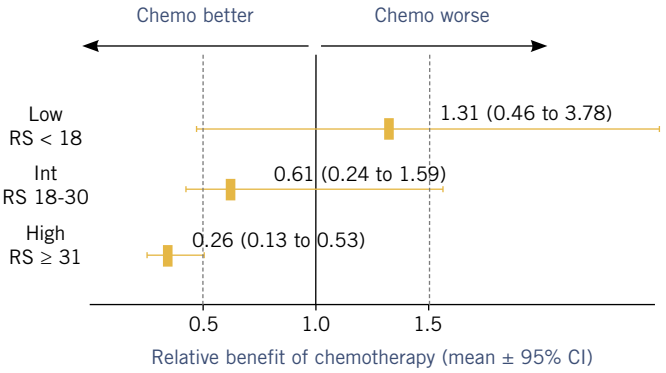
Risk group	Percent of patients	10-year distant recurrence rate	95% confidence interval
Low (RS < 18)	51	6.8%	4.0-9.6
Intermediate (RS = 18-30)	22	14.3%	8.3-20.3
High (RS ≥ 31)	27	30.5%	23.6-37.4

RS = recurrence score
$p < 0.001$ for comparison between high- and low-risk groups

SOURCE: Paik S et al. *N Engl J Med* 2004;351(27):2817-26. **Abstract**

4.2

Adjuvant Chemotherapy Benefit According to the Oncotype DX Recurrence Score



SOURCE: Paik S et al. *J Clin Oncol* 2006;[Epub ahead of print]. **Abstract**

Tracks 5-6

DR LOVE: Can you comment on the issue of quality control with ER and HER2 testing?

DR ELLEDGE: Quality control is crucial in measuring these markers. We do not have good quality control throughout the United States. That has been clearly shown multiple times objectively, for both ER and HER2.

For instance, at the beginning of NSABP-B-31, the NCI and Soon Paik showed that the risk of an error in HER2 assessment was 24 percent, especially from smaller labs (Paik 2002). For ER, studies in the United States and Europe have shown that ER testing is inaccurate in the 20 percent range, especially for ER negativity. This has clouded the results of our studies and

our thinking. So standardization is extremely important.

It's very difficult for community oncologists to become involved because this is a pathology issue. In terms of practical advice, I tell them that I would insist that their patients' breast tumors be sent to large reference labs. I believe that if you measure ER and HER2 accurately and ER is clearly positive and HER2 is clearly negative, the benefits from chemotherapy are modest at best and may be nonexistent.

DR LOVE: The flip side is the patient who is not receiving therapy because of inaccuracies in how her tumor was studied — women who are said to have ER-negative tumors when in fact their tumors are ER-positive and they don't receive hormone therapy and, likewise, patients who are said to have HER2-negative disease when they have HER2-positive disease and who don't receive trastuzumab. It surprises me that people aren't more upset about this.

DR ELLEDGE: It has surprised me too. In my editorial published in the *JCO*, I calculated that up to 1,000 women per year die because of inaccurate ER assays (Elledge 2006; [4.3]).

4.3

Estimated Annual Deaths Related to Inaccurate ER Testing

"Mismeasurement of ER is a lethal medical error. In the United States, 190,000 patients are diagnosed with breast cancer annually, and approximately 50,000 are classified as ER negative. If 20% of these patients were actually ER positive, this would be some 10,000 patients. In this group, 3,000 deaths will occur. Conservatively, tamoxifen, when administered appropriately, could have prevented 1,000 to 1,500 of these deaths."

SOURCE: Elledge RM. *J Clin Oncol* 2006;24(9):1323-5. No abstract available

SELECT PUBLICATIONS

Colleoni M et al; International Breast Cancer Study Group. **Tamoxifen after adjuvant chemotherapy for premenopausal women with lymph node-positive breast cancer: International Breast Cancer Study Group Trial 13-93.** *J Clin Oncol* 2006;24(9):1332-41. **Abstract**

Elledge RM. **Tales from a targeted therapy.** *J Clin Oncol* 2006;24(9):1323-5. No abstract available

Fisher B et al. **Tamoxifen and chemotherapy for axillary node-negative, estrogen receptor-negative breast cancer: Findings from National Surgical Adjuvant Breast and Bowel Project B-23.** *J Clin Oncol* 2001;19(4):931-42. **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;[Epub ahead of print]. **Abstract**

Paik S et al. **A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer.** *N Engl J Med* 2004;351(27):2817-26. **Abstract**

Paik S et al. **Real-world performance of HER2 testing — National Surgical Adjuvant Breast and Bowel Project experience.** *J Natl Cancer Inst* 2002;94(11):852-4. **Abstract**

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **The ATAC study demonstrated that five years of adjuvant anastrozole was equivalent but not superior to tamoxifen in reducing the number of breast cancer events.**
   a. True
   b. False
2. **In a study that examined shared decision-making with patients undergoing surgical treatment for breast cancer, a statistically significant correlation appeared between greater patient involvement in the decision-making process and _____ mastectomy rates.**
   a. Higher
   b. Lower
3. **In the NSABP-B-39/RTOG-0413 study comparing adjuvant whole breast versus partial breast irradiation, which technique is permitted?**
   a. Brachytherapy
   b. MammoSite®
   c. 3D conformal external beam radiation
   d. Any one of the above
4. **In a study by Dr Julian and colleagues, surgeon's experience with SLNB was related to:**
   a. Identification of the sentinel node
   b. False-negative rate
   c. Both a and b
5. **Among tamoxifen-treated patients with high recurrence scores from the Onco*type* DX assay, chemotherapy reduced the rate of recurrence by approximately _____.**
   a. 25 percent
   b. 50 percent
   c. 75 percent
6. **The MA17 trial demonstrated that letrozole given after five years of adjuvant tamoxifen therapy can prolong disease-free survival and, in node-positive subsets, overall survival.**
   a. True
   b. False
7. **In NSABP-B-32, patients assigned to sentinel lymph node biopsy and axillary dissection had a false-negative rate of approximately 10 percent.**
   a. True
   b. False
8. **In Dr Craig Allred's analysis of ER status in patients with DCIS, those who were determined by a central laboratory to have ER-negative disease did not benefit from tamoxifen.**
   a. True
   b. False
9. **NSABP-B-35 is comparing _____ with tamoxifen in women with DCIS.**
   a. Toremifene
   b. Letrozole
   c. Anastrozole
   d. Exemestane
   e. All of the above
10. **The Onco*type* DX assay can be used to predict the benefit of adjuvant chemotherapy for women with ER-positive breast cancer.**
    a. True
    b. False
11. **Inaccurate ER testing may lead to an estimated _____ excess deaths from breast cancer annually because the patients do not receive hormonal therapy.**
    a. 100
    b. 1,000
    c. 10,000
    d. 1,000,000

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

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Breast Cancer Update for Surgeons — Issue 2, 2006

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To what extent does this issue of *BCU* for Surgeons address the following global learning objectives?

- Critically evaluate the clinical implications of emerging clinical trial data in breast cancer in order to incorporate these data into management strategies in adjuvant and neoadjuvant disease. . . . . 5 4 3 2 1 N/A
- Counsel appropriately selected patients about the availability of ongoing clinical trials. . . . . 5 4 3 2 1 N/A
- Counsel postmenopausal patients with ER-positive breast cancer about the risks and benefits of aromatase inhibitors in the adjuvant and neoadjuvant settings and of switching to or sequencing aromatase inhibitors after tamoxifen. . . . . 5 4 3 2 1 N/A
- Counsel appropriately selected patients about emerging clinical trial data and ongoing trials in the prevention and treatment of noninvasive (DCIS) and invasive breast cancer. . . . . 5 4 3 2 1 N/A
- Describe the computerized risk models and genetic markers to determine prognostic information on the quantitative risk of breast cancer relapse, and when applicable, utilize these to guide therapy decisions. . . . . 5 4 3 2 1 N/A
- Counsel appropriately selected patients about availability and applicability of emerging research data on sentinel lymph node biopsy. . . . . 5 4 3 2 1 N/A
- Discuss the risks and benefits of partial breast irradiation and the clinical trials evaluating this technique with appropriately selected patients. . . . . 5 4 3 2 1 N/A

EFFECTIVENESS OF THE INDIVIDUAL FACULTY MEMBERS

Faculty	Knowledge of subject matter	Effectiveness as an educator
Monica Morrow, MD	5 4 3 2 1	5 4 3 2 1
Kevin R Fox, MD	5 4 3 2 1	5 4 3 2 1
Thomas B Julian, MD	5 4 3 2 1	5 4 3 2 1
Robert W Carlson, MD	5 4 3 2 1	5 4 3 2 1
Richard M Elledge, MD	5 4 3 2 1	5 4 3 2 1

OVERALL EFFECTIVENESS OF THE ACTIVITY

Objectives were related to overall purpose/goal(s) of activity. . . . . 5 4 3 2 1 N/A
Related to my practice needs. . . . . 5 4 3 2 1 N/A
Will influence how I practice. . . . . 5 4 3 2 1 N/A
Will help me improve patient care. . . . . 5 4 3 2 1 N/A
Stimulated my intellectual curiosity. . . . . 5 4 3 2 1 N/A
Overall quality of material. . . . . 5 4 3 2 1 N/A
Overall, the activity met my expectations. . . . . 5 4 3 2 1 N/A
Avoided commercial bias or influence. . . . . 5 4 3 2 1 N/A

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BCUS206

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