OVERVIEW OF ACTIVITY
Historically, surgery has been the primary mode of treatment for early breast cancer (BC). The diagnostic, surgical and medical management of BC, however, have escalated in complexity because of numerous advances in novel technologies and available adjunctive therapies. Hence, the multifaceted treatment of BC now requires the input of an interdisciplinary group of expert care providers. This paradigm shift has created the challenge of ensuring that knowledge of major clinical advances in local and systemic BC therapy is effectively disseminated among all members of the cross-functional team. To bridge the gap between research and patient care, *Breast Cancer Update for Surgeons* uses one-on-one interviews with leading BC investigators to efficiently distill the latest research developments so they may be incorporated into clinical practice as appropriate. By providing access to cutting-edge data and expert perspectives, this CME program assists breast surgeons in the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES
- Develop an understanding of the histopathologic characteristics and responsiveness to chemotherapy of invasive lobular carcinomas.
- Appreciate the information provided by genomic platforms to assess risk and individualize therapy for patients with ductal carcinoma in situ and early BC.
- Individualize the selection of evidence-based neoadjuvant and adjuvant chemobiologic regimens for patients with HER2-positive and triple-negative early BC.
- Describe the importance of adequate surgical margins in mitigating local recurrence risk for women with ductal carcinoma in situ treated with breast-conserving surgery and whole-breast irradiation.
- Develop an evidence-based approach to the management of the axilla in patients with localized BC and a positive sentinel lymph node biopsy.
- Counsel appropriately selected patients with BC about participation in ongoing clinical trials.

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HOW TO USE THIS CME ACTIVITY
This CME activity contains an audio component. To receive credit, the participant should review the CME information, listen to the audio tracks, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located in the back of this booklet or on our website at [ResearchToPractice.com/BCUS117/CME](http://ResearchToPractice.com/BCUS117/CME).

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EDITOR

Neil Love, MD
Research To Practice
Miami, Florida

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FACULTY — Drs Gradishar, King and Khan had no relevant conflicts of interest to disclose. The following faculty (and his spouse/partner) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process: Dr Sparano — Advisory Committee: AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Celgene Corporation, Genentech BioOncology, Merck, Novartis Pharmaceuticals Corporation, Pfizer Inc; Consulting Agreements: Celldex Therapeutics, Genentech BioOncology, Lilly; Contracted Research: Deciphera Pharmaceuticals LLC, Eisai Inc, Genentech BioOncology, MedImmune Inc, Merck, Novartis Pharmaceuticals Corporation, Prescient Therapeutics; Ownership Interest: MetaStat Inc.


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Submit them to us via Facebook or Twitter and we will do our best to get them answered for you

Facebook.com/ResearchToPractice or Twitter @DrNeilLove
**Interview with William J Gradishar, MD**

**Tracks 1-6**

| Track 1 | **Case discussion:** A 37-year-old woman with a 3.5-cm, ER/PR-low, HER2-positive, clinically node-negative breast cancer (BC) |
| Track 2 | **Case discussion:** A 58-year-old woman with T1cN1, ER-positive, HER2-negative BC and a 21-gene Recurrence Score® (RS) of 12 |
| Track 3 | MINDACT trial: Utility of the 70-gene signature in selecting patients with BC and 0 to 3 positive nodes for adjuvant chemotherapy |
| Track 4 | Fertility issues in early BC |
| Track 5 | Targeting the androgen receptor in patients with triple-negative BC (TNBC) |
| Track 6 | Adjuvant bisphosphonates for early BC |

**Interview with Tari King, MD**

**Tracks 1-10**

| Track 1 | **Case discussion:** A 42-year-old woman with strongly ER/PR-positive, HER2-negative, node-negative multifocal invasive ductal carcinoma (IDC) and a 21-gene RS of 19 |
| Track 2 | Pathologic features and risks of developing BC for patients with lobular carcinoma in situ |
| Track 3 | Comprehensive molecular portrait of invasive lobular BC |
| Track 4 | **Case discussion:** A 36-year-old woman with a 4-cm, triple-negative IDC who wishes to have breast-conserving surgery (BCS) receives neoadjuvant cisplatin on a clinical trial |
| Track 5 | Effect of ER and HER2 status on the use of neoadjuvant chemotherapy |
| Track 6 | Use of the 21-gene RS to guide neoadjuvant therapy decision-making |
| Track 7 | **Case discussion:** A 50-year-old perimenopausal woman who presents with a small group of microcalcifications in the right breast undergoes stereotactic biopsy and is diagnosed with intermediate-grade ER-positive ductal carcinoma in situ (DCIS) |
| Track 8 | Benefits and limitations of the DCIS Score™ |
| Track 9 | Consensus guidelines on margins for BCS with whole-breast irradiation in patients with DCIS |
| Track 10 | Complexities, challenges and advances in the treatment of DCIS |

**Interview with Joseph A Sparano, MD**

**Tracks 1-12**

| Track 1 | POSITIVE: An intergroup study evaluating pregnancy outcomes and safety of interrupting endocrine therapy for young women with endocrine-responsive BC who desire pregnancy |
| Track 2 | The DCIS Score as a tool for identifying risk of BC recurrence |
| Track 3 | Use of the DCIS Score to facilitate decision-making regarding radiation therapy |
| Track 4 | **Case discussion:** A 56-year-old woman with Stage IIIB (T3N1M0) ER/PR-positive, HER2-positive IDC initially treated with neoadjuvant docetaxel/carboplatin/trastuzumab/pertuzumab |
Interview with Dr Sparano (continued)

Track 5  **Case discussion:** A 47-year-old premenopausal woman with Stage IIB (T2N1M0) ER/PR-positive, HER2-negative IDC and a 21-gene RS of 13 elects to receive endocrine therapy alone

Track 6  **TAILORx:** Results of the low-risk registry of a prospective trial of adjuvant systemic therapy for patients with ER-positive, HER2-negative BC based on the 21-gene RS

Track 7  Results of the Phase III West German Study Group PlanB trial: Effect of the 21-gene RS and concordance of prognostic markers in ER-positive, HER2-negative high-risk node-negative and node-positive BC

Track 8  Critical evaluation of the MINDACT trial results

Track 9  Perspective on the utility of the 70-gene signature in clinical practice

Track 10  Results of a prospective registry of patients with early BC for whom treatment decisions in clinical practice were made incorporating the 21-gene RS

Track 11  BC-specific survival in patients with ER-positive, node-negative invasive BC and 21-gene signature results in the SEER database

Track 12  **Case discussion:** A 50-year-old postmenopausal woman with Stage IIA, ER/PR-positive, HER2-negative IDC

Interview with Seema A Khan, MD, MPH

Tracks 1-12

Track 1  **Case discussion:** A 52-year-old postmenopausal woman with ER/PR-positive, HER2-negative, node-negative IDC and an RS of 12 undergoes BCS

Track 2  Role of the 21-gene signature in neoadjuvant decision-making

Track 3  **Case discussion:** A 43-year-old woman with triple-negative, BRCA-negative IDC who deferred treatment for 1 year

Track 4  Adjuvant capecitabine in patients with HER2-negative BC and pathologic residual invasive disease after neoadjuvant chemotherapy

Track 5  Viewpoint on performing sentinel lymph node biopsy (SLNB) prior to the administration of neoadjuvant chemotherapy

Track 6  SLNB after neoadjuvant chemotherapy in patients with node-negative versus node-positive BC

Track 7  Approach to BRCA mutation testing in patients with TNBC

Track 8  **Second opinion:** Surgical resection of an intact primary tumor in a 49-year-old woman with ER/PR-negative, HER2-positive metastatic BC after complete response of a solitary liver metastasis to paclitaxel/trastuzumab/pertuzumab

Track 9  Status of ECOG-E2108: A Phase III trial evaluating early surgery versus standard palliative therapy in treating Stage IV BC

Track 10  **Second opinion:** A 41-year-old woman with ER/PR-positive, HER2-negative, clinically node-negative BC: Distinction between locally advanced and inflammatory disease

Track 11  **Second opinion:** Role of SLNB in the setting of recurrent BC

Track 12  Results from the Phase III CALOR (IBCSG 27-02, NSABP-B-37, BIG 1-02) trial: Adjuvant chemotherapy prolongs survival for patients with isolated local or regional recurrence of BC
SELECT PUBLICATIONS

A randomized phase III trial of the value of early local therapy for the intact primary tumor in patients with metastatic breast cancer. NCT01242800

ALTERNate approaches for clinical stage II or III Estrogen Receptor positive breast cancer NeoAdjuvant TrEatment (ALTERNATE) in postmenopausal women: A Phase III study (A011106). NCT01953588


Love N et al. HER2 and estrogen receptor status drive decisions regarding the use of neoadjuvant chemotherapy. San Antonio Breast Cancer Symposium 2015;Abstract P1-14-20.
Miller K et al. Improved clinical outcomes on enzalutamide observed in patients with PREDICT AR+ triple-negative breast cancer: Prognosis or prediction? San Antonio Breast Cancer Symposium 2015;Abstract P3-07-25.


Stemmer SM et al. Real-life analysis evaluating 1594 NO/Nmic breast cancer patients for whom treatment decisions incorporated the 21-gene Recurrence Score result: 5-year KM estimate for breast cancer specific survival with Recurrence Score results <30 is >98%, San Antonio Breast Cancer Symposium 2015;Abstract P5-08-02.
QUESTIONS (PLEASE CIRCLE ANSWER):

1. Tumors classified as invasive lobular carcinoma are typically of which subtype?
   a. ER-negative, HER2-negative
   b. ER-negative, HER2-positive
   c. ER-positive, HER2-negative
   d. ER-positive, HER2-positive

2. The goal of the MINDACT trial, for which initial results were recently published, was to evaluate the benefit of genomic profiling with the __________ in addition to standard clinical-pathological criteria for patients with early BC and 0 to 3 positive lymph nodes who might safely forgo chemotherapy without compromising outcome.
   a. PAM50 assay
   b. 70-gene signature
   c. 21-gene signature

3. A recent meta-analysis evaluating the use of adjuvant bisphosphonates for women with early BC pointed toward a reduction in the odds of disease recurrence in women who were __________ when they began treatment.
   a. Premenopausal
   b. Postmenopausal

4. The SSO-ASTRO-ASCO Consensus Guideline on Margins for Breast-Conserving Surgery with Whole-Breast Irradiation in Ductal Carcinoma in Situ states that clear margins wider than 2 millimeters result in significantly lower rates of recurrence.
   a. True
   b. False

5. The ongoing POSITIVE study is evaluating recurrence risk of interrupting endocrine therapy for young women with endocrine-responsive BC who desire pregnancy.
   a. True
   b. False

6. The DCIS Score for patients with DCIS who have undergone local excision is predictive of __________.
   a. The risk of DCIS recurrence
   b. The risk of invasive BC
   c. Both a and b

7. Results of the low-risk registry of the TAILORx trial, which is evaluating adjuvant endocrine therapy with or without chemotherapy for patients with ER-positive, HER2-negative BC based on the 21-gene signature, reported an approximate __________ risk of distant recurrence at 5 years for patients with a low RS of less than 11 who received endocrine therapy alone without chemotherapy.
   a. 0.1%
   b. 1.0%
   c. 10.0%

8. The Phase III __________ study randomly assigns patients with hormone receptor-positive, HER2-negative BC, 1 to 3 positive nodes and a 21-gene RS of 25 or lower to adjuvant endocrine therapy with or without chemotherapy.
   a. ECOG-E2108
   b. POSITIVE
   c. RxPONDER

9. Results of the Phase III West German Study Group PlanB trial demonstrated a 5-year disease-free survival rate of 94% in patients with ER-positive, HER2-negative, __________ BC who did not receive adjuvant chemotherapy based on an RS of 11 or lower.
   a. High-risk node-negative
   b. Node-positive
   c. Both a and b

10. The Phase III CALOR trial evaluating adjuvant chemotherapy for isolated local or regional recurrence of BC demonstrated a significant improvement in survival for patients who received chemotherapy.
    a. True
    b. False
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 1 — Please tell us about your experience with this educational activity**

**How would you characterize your level of knowledge on the following topics?**

<table>
<thead>
<tr>
<th>Topic</th>
<th>BEFORE</th>
<th>AFTER</th>
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<tbody>
<tr>
<td>MINDACT trial: Utility of the 70-gene signature in selecting patients with BC and 0 to 3 positive nodes for adjuvant chemotherapy</td>
<td>4 3 2 1</td>
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<td>Consensus guidelines on margins for BCS with whole-breast irradiation in patients with DCIS</td>
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<tr>
<td>Utility of the DCIS Score in assessing the benefit of radiation therapy after lumpectomy for patients with DCIS</td>
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<td>Targeting the androgen receptor in patients with TNBC</td>
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**Practice Setting:**
- ☐ Academic center/medical school
- ☐ Community cancer center/hospital
- ☐ Group practice
- ☐ Solo practice
- ☐ Government (eg, VA)
- ☐ Other (please specify) ..................................

**Approximately how many new patients with breast cancer do you see per year?** .......................... patients

**Was the activity evidence based, fair, balanced and free from commercial bias?**
- ☐ Yes
- ☐ No
  
  If no, please explain: .............................................................................................................................

**Please identify how you will change your practice as a result of completing this activity (select all that apply).**
- ☐ This activity validated my current practice
- ☐ Create/revise protocols, policies and/or procedures
- ☐ Change the management and/or treatment of my patients
- ☐ Other (please explain): ......................................................................................................................

**If you intend to implement any changes in your practice, please provide 1 or more examples:**
- .............................................................................................................................................................

**The content of this activity matched my current (or potential) scope of practice.**
- ☐ Yes
- ☐ No
  
  If no, please explain: ..................................................................................................................................

**Please respond to the following learning objectives (LOs) by circling the appropriate selection:**

<table>
<thead>
<tr>
<th>Objective</th>
<th>4 = Yes</th>
<th>3 = Will consider</th>
<th>2 = No</th>
<th>1 = Already doing</th>
<th>N/M = LO not met</th>
<th>N/A = Not applicable</th>
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<tbody>
<tr>
<td>As a result of this activity, I will be able to:</td>
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<td>• Develop an understanding of the histopathologic characteristics and responsiveness to chemotherapy of invasive lobular carcinomas</td>
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<td>• Appreciate the information provided by genomic platforms to assess risk and individualize therapy for patients with ductal carcinoma in situ and early BC</td>
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<td>• Individualize the selection of evidence-based neoadjuvant and adjuvant chemobiologic regimens for patients with HER2-positive and triple-negative early BC</td>
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<td>N/M</td>
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<tr>
<td>• Describe the importance of adequate surgical margins in mitigating local recurrence risk for women with ductal carcinoma in situ treated with breast-conserving surgery and whole-breast irradiation</td>
<td>4 3 2 1</td>
<td>N/M</td>
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As a result of this activity, I will be able to:

- Develop an evidence-based approach to the management of the axilla in patients with localized BC and a positive sentinel lymph node biopsy. ................................................................. 4 3 2 1 N/M N/A
- Counsel appropriately selected patients with BC about participation in ongoing clinical trials. ................................................................. 4 3 2 1 N/M N/A

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:

Would you recommend this activity to a colleague?
☐ Yes ☐ No
If no, please explain:

Additional comments about this activity:

PART 2 — Please tell us about the faculty and editor for this educational activity

<table>
<thead>
<tr>
<th>Faculty</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
</tr>
</thead>
<tbody>
<tr>
<td>William J Gradishar, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
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<tr>
<td>Tari King, MD</td>
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<tr>
<td>Joseph A Sparano, MD</td>
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<tr>
<td>Seema A Khan, MD, MPH</td>
<td>4 3 2 1</td>
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</thead>
<tbody>
<tr>
<td>Neil Love, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
</tbody>
</table>

Please recommend additional faculty for future activities:

Other comments about the faculty and editor for this activity:

REQUEST FOR CREDIT — Please print clearly

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

Professional Designation:
☐ MD ☐ DO ☐ PharmD ☐ NP ☐ RN ☐ PA ☐ Other .......................................

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

City, State, Zip: ................................................................................................................

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

Email: ..........................................................................................................................

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I certify my actual time spent to complete this educational activity to be _________ hour(s).

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

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