BCU SURGEONS | 2012 VOL 11 | ISSUE 1

Breast Cancer® UPDATE

An Audio Review Journal for Surgeons

Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS

Monica Morrow, MD
Harold J Burstein, MD, PhD
Kelly K Hunt, MD
Lawrence J Solin, MD

EDITOR

Neil Love, MD

CONTENTS

2 Audio CDs

CME Certified

Subscribe to Podcasts or download MP3s of this program at ResearchToPractice.com/BCUS112

Follow us at Facebook.com/ResearchToPractice Follow us on Twitter @DrNeilLove

Breast Cancer Update for Surgeons
A Continuing Medical Education Audio Series

OVERVIEW OF ACTIVITY

Historically, surgery has been the primary mode of treatment for early breast cancer. The diagnostic, surgical and medical management of breast cancer, however, have escalated in complexity because of numerous advances in novel technologies and available adjunctive medical therapies. Hence, the multifaceted treatment of breast cancer now requires the input of an interdisciplinary group of expert care providers. This paradigm shift has created the challenge of ensuring that major clinical advances in local and systemic breast cancer therapy are 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 breast cancer investigators to efficiently distill the latest research developments in the field so that they may be incorporated into clinical practice where 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

- Use case-based learning to aid in the formulation of individualized treatment strategies for patients with breast cancer.
- Formulate an evidence-based approach to the surgical management of breast cancer in patients with a positive sentinel lymph node biopsy.
- Determine the utility of genomic assays in counseling patients with DCIS or ER-positive early breast cancer about their risk of recurrence and the potential benefits of radiation therapy or adjuvant chemotherapy, respectively.
- Evaluate the long-term outcomes associated with the use of radiation therapy following breast-conserving surgery for patients with pathologically confirmed node-negative or node-positive disease.
- Describe current disease management strategies and ongoing clinical trials comparing partial breast irradiation to standard or conventional whole breast radiation therapy.
- Identify appropriate patients for the use of magnetic resonance imaging and screening in the management of breast cancer.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 2.75 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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 CDs, complete the Post-test with a score of 75% 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/BCUS112/CME**.

This activity is supported by an educational grant from Genomic Health Inc.

Last review date: July 2012; Release date: July 2012; Expiration date: July 2013

TABLE OF CONTENTS

FACULTY INTERVIEWS

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantor.

EDITOR

Neil Love, MD
Research To Practice
Miami, Florida

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

FACULTY — **Drs Morrow**, **Burstein** and **Hunt** 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 Solin** — Advisory Committee: Genomic Health Inc.

EDITOR — Dr Love is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: Abbott Laboratories, Allos Therapeutics, Amgen Inc, ArQule Inc, Astellas, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals/Onyx Pharmaceuticals Inc, Biodesix Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, EMD Serono Inc, Genentech BioOncology, Genomic Health Inc, ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, Incyte Corporation, Lilly USA LLC, Medivation Inc, Millennium: The Takeda Oncology Company, Mundipharma International Limited, Novartis Pharmaceuticals Corporation, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Spectrum Pharmaceuticals Inc and Teva.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no real or apparent conflicts of interest to disclose.

Have Questions or Cases You Would Like Us to Pose to the Faculty?

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

Monica Morrow, MD — **Tracks 1-15**

Dr Morrow is Anne Burnett Windfohr Chair of Clinical Oncology, Chief of Breast Service in the Department of Surgery at Memorial Sloan Kettering Cancer Center and Professor of Surgery at Weill Medical College of Cornell University in New York, New York.

Track 1 ACOSOG-Z0011: A randomized trial of axillary lymph node dissection (ALND) in women with clinical T1-2N0M0 breast cancer (BC) who have a positive sentinel lymph node (SLN)

Track 2 Clinical application of the ACOSOG-Z0011 trial results

Track 3 Adverse effects and complications of ALND versus SLN biopsy

Track 4 Use of the Onco*type* DX® DCIS Score™ to identify patients who will not benefit from radiation therapy (RT)

Track 5 **Second opinion:** Preoperative magnetic resonance imaging (MRI) and surgical management of nonpalpable BC

Track 6 Appropriate use of MRI screening for patients with known BRCA mutations or family history of BC

Track 7 **Second opinion:** Impact of surgical margins on local recurrence in women with early-stage invasive BC treated with breast-conserving therapy (BCT)

Track 8 Risk of local recurrence for patients with invasive breast cancer and DCIS who do not undergo RT

Track 9 Clinical decision-making regarding surgery based on histopathologic grading

Track 10 **Case discussion:** A 56-year-old woman with a 6-cm, T3N1, Grade III triple-negative invasive ductal carcinoma (IDC)

Track 11 Use of MRI to plan breast-conserving surgery after neoadjuvant chemotherapy

Track 12 Neoadjuvant treatment algorithm for patients who desire BCT

Track 13 **Case discussion:** A 42-year-old woman with a 3-cm, Grade II, ER/PR-positive, HER2-negative, node-negative IDC and an Onco*type* DX Recurrence Score® (RS) of 10

Track 14 Applicability of the Onco*type* DX assay

Track 15 **Case discussion:** A 55-year-old postmenopausal woman undergoes lumpectomy for a Grade II, ER-positive, mixed, solid and cribriform DCIS

INTERVIEW

Harold J Burstein, MD, PhD — **Tracks 1-12**

Dr Burstein is Associate Professor of Medicine at Harvard Medical School and is affiliated with the Breast Oncology Center at Dana-Farber Cancer Institute in Boston, Massachusetts.

Track 1 **Case discussion:** A 66-year-old woman who underwent treatment for node-positive BC in 1985 presents with ER-positive, HER2-negative recurrent disease 16 years later

Track 2 Predictors of late recurrence after adjuvant endocrine therapy for BC

Track 3 Multidisciplinary management of loco-regional recurrence

Track 4 Use of partial breast irradiation in clinical practice

Track 5 Isolated skull metastases after long-term disease control with "pseudoadjuvant" chemotherapy

Track 6 Importance of rebiopsy at initial diagnosis of metastatic disease

Track 7 BOLERO-2 results: Exemestane with or without everolimus in ER-positive locally advanced or metastatic BC refractory to nonsteroidal aromatase inhibitors (AIs)

Track 8 **Case discussion:** A 62-year-old woman with a 1.3-cm, Grade II, ER-positive, HER2-negative BC with an SLN metastasis and a RS of 27

Track 9 Use of the Onco*type* DX assay in decision-making for patients with node-positive BC outside of a trial setting

Track 10 Viewpoint on next-generation tests for making individualized treatment decisions in the neoadjuvant setting

Track 11 Lack of available guidelines to determine patient selection for molecular profiling

Track 12 Influence of Onco*type* DX RS on the selection of chemotherapy for a patient with ER-positive BC and SLN metastases

INTERVIEW

Kelly K Hunt, MD — **Tracks 1-14**

Dr Hunt is Hamill Foundation Distinguished Professor of Surgery in Honor of Dr Richard G Martin Sr and Chief of the Surgical Breast Section in the Department of Surgical Oncology at The University of Texas MD Anderson Cancer Center in Houston, Texas.

Track 1 Impact of lymphedema after ALND on quality of life

Track 2 Treatment decision-making regarding ALND for patients with positive SLN biopsy

Track 3 Perspective on the design and results of the ACOSOG-Z0011 trial

Track 4 IBCSG 23-01: A Phase III trial evaluating ALND for patients with node-negative BC and micrometastases in the sentinel node

Track 5 Results of Phase III trials evaluating the prognostic value of SLN micrometastases in predicting overall survival in BC

Track 6 **Second opinion:** Decision-making regarding MRI use, necessity of ALND and decision-making regarding adjuvant chemotherapy

Track 7 Surgical management of centrally located BC

Track 8 Principles of oncoplastic surgery in the treatment of BC

Track 9 Applications and potential complications of nipple-sparing mastectomy

Track 10 **Case discussion:** A 56-year-old woman with T3N0 ER-positive, HER2-positive BC who receives neoadjuvant chemotherapy with concurrent trastuzumab and BCT and experiences a pathologic complete response

Track 11 **Case discussion:** A 60-year-old woman with T2N0 ER-positive BC enrolls on the Phase III ACOSOG-Z1031 trial and receives neoadjuvant AI therapy → BCT

Track 12 **Case discussion:** A 48-year-old woman with a 5-cm area of calcification biopsy proven to be DCIS who desires BCT

Track 13 **Case discussion:** A 62-year-old postmenopausal woman with a 2.5-cm T2N0, ER-positive IDC who has an Onco*type* DX RS of 6

Track 14 Perspective on the Phase III SWOG-S1007 (RxPONDER) trial of adjuvant endocrine therapy with or without chemotherapy for patients with node-positive BC and an Onco*type* DX RS of 25 or lower

INTERVIEW

Lawrence J Solin, MD — **Tracks 1-10**

Dr Solin is Chairman in the Department of Radiation Oncology at the Albert Einstein Medical Center in Philadelphia, Pennsylvania.

Track 1 Meta-analysis of 17 randomized trials on the effect of RT after BCT

Track 2 Decision-making regarding the use of RT for patients age 70 or older

Track 3 Comparison between partial and whole breast irradiation

Track 4 TARGIT: A Phase III trial comparing targeted intraoperative RT to conventional postoperative RT after BCT for patients with early-stage BC

Track 5 Identification of patients who benefit from postmastectomy RT

Track 6 Potential use of molecular profiling assays in the selection of locoregional therapies

Track 7 Prospective validation of the Onco*type* DX DCIS Score in predicting risk of local recurrence after resection alone for DCIS

Track 8 Current role of the Onco*type* DX DCIS Score as a tool for identifying the risk of BC recurrence

Track 9 Emerging approaches to stratifying risk and individualizing treatment for patients with DCIS

Track 10 Perspective on future studies evaluating the Onco*type* DX DCIS Score

SELECT PUBLICATIONS

Albain KS et al. **Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: A retrospective analysis of a randomised trial.** *Lancet Oncol* 2010;11(1):55-65.

Allred DC et al. **Adjuvant tamoxifen reduces subsequent breast cancer in women with estrogen receptor-positive ductal carcinoma in situ: A study based on NSABP protocol B-24.** *J Clin Oncol* 2012;30(12):1268-73.

Baselga J et al. **Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer.** *N Engl J Med* 2012;366(6):520-9.

Burstein HJ, Griggs JJ. **Deep time: The long and the short of adjuvant endocrine therapy for breast cancer.** *J Clin Oncol* 2012;30(7):684-6.

Giuliano AE et al. **Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: A randomized clinical trial.** *JAMA* 2011;305(6):569-75.

Giuliano AE et al. **ACOSOG Z0011: A randomized trial of axillary node dissection in women with clinical T1-2 N0 M0 breast cancer who have a positive sentinel node.** *Proc ASCO* 2010;**Abstract CRA506**.

Gonzalez-Angulo AM et al. **SWOG S1007: A phase III, randomized clinical trial of standard adjuvant endocrine therapy with or without chemotherapy in patients with one to three positive nodes, hormone receptor (HR)-positive, and HER2-negative breast cancer with recurrence score (RS) of 25 or less.** *Proc ASCO* 2011;**Abstract TPS104**.

Hortobagyi GN et al. **Everolimus for postmenopausal women with advanced breast cancer: Updated results of the BOLERO-2 Phase III trial.** San Antonio Breast Cancer Symposium 2011;**Abstract S3-7**.

Houssami N et al. **Meta-analysis of the impact of surgical margins on local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy.** *Eur J Cancer* 2010;46(18):3219-32.

Martelli G et al. **Axillary dissection versus no axillary dissection in elderly patients with breast cancer and no palpable axillary nodes: Results after 15 years of follow-up.** *Ann Surg Oncol* 2011;18(1):125-33.

McCahill LE et al. **Variability in reexcision following breast conservation surgery.** *JAMA* 2012;307(5):467-75.

Morrow M. **Refining the use of endocrine therapy for ductal carcinoma in situ.** *J Clin Oncol* 2012;30(12):1249-51.

Morrow M et al. **MRI for breast cancer screening, diagnosis, and treatment.** *Lancet* 2011;378(9805):1804-11.

Morrow M, Giuliano AE. **To cut is to cure: Can we really apply Z11 in practice?** *Ann Surg Oncol* 2011;18(9):2413-5.

Motwani SB et al. **Ductal carcinoma in situ treated with breast-conserving surgery and radiotherapy: A comparison with ECOG study 5194.** *Cancer* 2011;117(6):1156-62.

Peters NH et al. **Preoperative MRI and surgical management in patients with nonpalpable breast cancer: The MONET randomised controlled trial.** *Eur J Cancer* 2011;47(6):879-86.

Shak S et al. **Quantitative gene expression analysis in a large cohort of estrogen-receptor positive breast cancers: Characterization of the tumor profiles in younger patients (≤40 yrs) and in older patients (≥70 yrs).** San Antonio Breast Cancer Symposium 2010;**Abstract P3-10-01**.

Solin LJ et al. **A quantitative multigene RT-PCR assay for predicting recurrence risk after surgical excision alone without irradiation for ductal carcinoma in situ (DCIS): A prospective validation study of the DCIS Score from ECOG E5194.** San Antonio Breast Cancer Symposium 2011;**Abstract S4-6**.

Turnbull L et al. **Comparative effectiveness of MRI in breast cancer (COMICE) trial: A randomised controlled trial.** *Lancet* 2010;375(9714):563-71.

Untch M et al. **Neoadjuvant clinical trials for the treatment of primary breast cancer: The experience of the German study groups.** *Curr Oncol Rep* 2012;14(1):27-34.

Whelan TJ et al. **NCIC-CTG MA.20: An intergroup trial of regional nodal irradiation in early breast cancer.** *Proc ASCO* 2011;**Abstract LBA1003**.

Wright PA, Zenilman ME**. Less may be better: Axillary dissection is unnecessary in some patients with a positive sentinel lymph node.** *Arch Surg* 2011;146(8):980-2.

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **The Phase III ACOSOG-Z0011 trial randomly assigned patients with clinical T1-2N0M0 breast cancer and a positive sentinel node to axillary lymph node dissection (ALND) versus no ALND.**
   a. True
   b. False

2. **Common complications associated with ALND include _____.**
   a. Pain
   b. Lymphedema
   c. Prolonged postoperative drainage
   d. Changes in sensation in the upper, inner arm
   e. All of the above

3. **The BOLERO-2 Phase III trial of exemestane with or without everolimus for postmenopausal women with disease refractory to nonsteroidal aromatase inhibitors demonstrated improvements in response rate and progression-free survival with the addition of everolimus to exemestane.**
   a. True
   b. False

4. **The Onco*type* DX DCIS Score was validated in the ECOG-E5194 study, which included only women with small foci of DCIS.**
   a. True
   b. False

5. **ACOSOG-Z1031 was a Phase III study in which _____ patients with ER-positive breast cancer were further selected on the basis of their Allred score before random assignment to 1 of 3 aromatase inhibitors — exemestane, anastrozole or letrozole.**
   a. Postmenopausal
   b. Premenopausal

6. **The Phase III SWOG-S1007 (RxPONDER) study randomly assigns patients with node-positive, ER-positive, HER2-negative breast cancer and Onco*type* DX Recurrence Scores of 25 or lower to adjuvant endocrine therapy with or without chemotherapy.**
   a. True
   b. False

7. **Which of the following toxicities was associated with the addition of everolimus to exemestane for patients with ER/PR-positive metastatic breast cancer refractory to nonsteroidal aromatase inhibitors in the BOLERO-2 trial?**
   a. Stomatitis
   b. Pneumonitis
   c. Dyspnea
   d. All of the above

8. **The Phase III TARGIT trial compares targeted intraoperative radiation therapy to conventional postoperative radiation therapy after breast-conserving therapy for patients with early-stage breast cancer.**
   a. True
   b. False

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Breast Cancer Update for Surgeons — Issue 1, 2012

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?

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

	BEFORE	AFTER
Prognostic value of sentinel lymph node micrometastases in predicting overall survival for patients with early-stage breast cancer — NSABP-B-32 and ACOSOG-Z0010 Phase III trials	4 3 2 1	4 3 2 1
SWOG-S1007 (RxPONDER) study: Adjuvant endocrine therapy with or without chemotherapy for patients with node-positive breast cancer and an Onco*type* DX Recurrence Score of 25 or lower	4 3 2 1	4 3 2 1
Prospective validation study of the Onco*type* DX DCIS Score in predicting risk of local recurrence after resection alone for DCIS	4 3 2 1	4 3 2 1
TARGIT: A Phase III trial comparing targeted intraoperative radiation therapy to conventional postoperative radiation therapy after breast-conserving surgery in early-stage breast cancer	4 3 2 1	4 3 2 1

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:

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

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

- Use case-based learning to aid in the formulation of individualized treatment strategies for patients with breast cancer. . . . . 4 3 2 1 N/M N/A
- Formulate an evidence-based approach to the surgical management of breast cancer in patients with a positive sentinel lymph node biopsy. . . . . 4 3 2 1 N/M N/A
- Determine the utility of genomic assays in counseling patients with DCIS or ER-positive early breast cancer about their risk of recurrence and the potential benefits of radiation therapy or adjuvant chemotherapy, respectively. . . . . 4 3 2 1 N/M N/A
- Evaluate the long-term outcomes associated with the use of radiation therapy following breast-conserving surgery for patients with pathologically confirmed node-negative or node-positive disease. . . . . 4 3 2 1 N/M N/A
- Describe current disease management strategies and ongoing clinical trials comparing partial breast irradiation to standard or conventional whole breast radiation therapy. . . . . 4 3 2 1 N/M N/A
- Identify appropriate patients for the use of magnetic resonance imaging and screening in the management of breast cancer. . . . . 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:

.....

As part of our ongoing, continuous quality-improvement effort, we conduct postactivity follow-up surveys to assess the impact of our educational interventions on professional practice. Please indicate your willingness to participate in such a survey.

☐ Yes, I am willing to participate in a follow-up survey.

☐ No, I am not willing to participate in a follow-up survey.

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

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter	Effectiveness as an educator
Monica Morrow, MD	4 3 2 1	4 3 2 1
Harold J Burstein, MD, PhD	4 3 2 1	4 3 2 1
Kelly K Hunt, MD	4 3 2 1	4 3 2 1
Lawrence J Solin, MD	4 3 2 1	4 3 2 1
Editor	**Knowledge of subject matter**	**Effectiveness as an educator**
Neil Love, MD	4 3 2 1	4 3 2 1

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:.....

Research To Practice designates this enduring material for a maximum of 2.75 *AMA PRA Category 1 Credits™*. Physicians should claim only the 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:.....

The expiration date for this activity is July 2013. 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.ResearchToPractice.com/BCUS112/CME.

QID 1002

Breast Cancer®
UPDATE

PRSRT STD
U.S. POSTAGE
PAID
MIAMI, FL
PERMIT #1317

Neil Love, MD
Research To Practice
One Biscayne Tower
2 South Biscayne Boulevard, Suite 3600
Miami, FL 33131

This activity is supported by an educational grant from
Genomic Health Inc.

Research
To Practice®

Sponsored by Research To Practice.

Last review date: July 2012
Release date: July 2012
Expiration date: July 2013
Estimated time to complete: 2.75 hours

This program is printed on MacGregor XP paper, which is manufactured in accordance with the world's leading forest management certification standards.