Kathy D. Miller, MD began her new position as Chair of the ECOG-ACRIN Breast Committee on January 1, 2014, after serving as Co-Chair since 2011. Dr. Miller succeeds Joseph A. Sparano, MD, who after serving as Co-Chair and Chair of the Breast Committee since 2002 became Vice Chair of ECOG-ACRIN last year (see story in May 2013 newsletter).

In ECOG-ACRIN, each of the 11 broad tumor areas is organized into a scientific committee or working group, whose leadership is a team of three members, two representing the therapeutic disciplines and the other representing the diagnostic disciplines. The other two Breast Committee leaders are Christopher E. Comstock, MD, the Committee’s Imaging Chair, who was appointed to that role immediately following the merger of ECOG (Eastern Cooperative Oncology Group) and ACRIN (American College of Radiology Imaging Network), and Antonio C. Wolff, MD, who is replacing Dr. Miller as Co-Chair of the Committee.

ECOG-ACRIN Group Co-Chairs, Robert L. Comis, MD and Mitchell D. Schnall, MD, PhD made the appointments.

The Breast Committee’s research activities span the disease continuum from screening through treatment of advanced disease. Its current research directions are to:

- Integrate agents targeting novel biological pathways in early through advanced-stage disease
- Apply and refine the clinical use of prognostic and predictive biomarkers
- Integrate advanced and experimental imaging as a predictive and pharmacodynamic biomarker or as an improved anatomic delineation of disease extent
- Develop and validate biomarkers predictive of treatment response and toxicity
- Validate single nucleotide polymorphisms (SNPs) that predict neurotoxicity from adjuvant taxane therapy and other SNPs that predict aromatase-inhibitor-associated arthralgia, as defined by patient-reported measures
- Define, assess, and understand the needs and preferences of patients throughout their entire cancer journey and minimize short- and long-term adverse consequences of cancer therapy

Following are brief descriptions of the three leaders, their history with ECOG-ACRIN, and their associated research contributions. Links to their full institutional biographies are posted on the Therapeutic Studies webpage.

Dr. Miller was introduced to ECOG while a fellow at the Indiana University (IU) between 1991 and 1994, and again later while working at the Community Cancer Oncology Program in North Dakota. Her involvement with ECOG increased substantially when she returned to the IU faculty in early 1999; IU, along with its Melvin and Bren Simon Cancer Center, has been an ECOG member institution since 1986. She became the IU principal investigator to ECOG-ACRIN in 2013.

Dr. Miller is notable as study chair for three ECOG trials exploring the role of the antiangiogenic agent bevacizumab in breast cancer. E2100 was the seminal phase III trial that demonstrated that the use of bevacizumab could double progression-free survival in metastatic breast cancer (Miller NEJM 2007). Additionally, through E2100, investigators identified candidate SNPs in the VEGFA gene for bevacizumab-induced hypertension and efficacy. Bryan Schneider, MD of Indiana University conducted this work (Schneider JCO 2008).

The second trial, E2104, was a pilot safety/feasibility trial that established the cardiac safety of adjuvant bevacizumab given concurrently with doxorubicin (Miller Ann Oncol 2011). These results led to E5103, a double-blind placebo-controlled study to determine whether there is a role for bevacizumab in lymph node-positive and high-risk lymph node-negative disease; results are forthcoming. E5103 is a US Food and Administration (FDA) registration trial.

The combined work with these trials led to Dr. Miller being named the recipient of the Young Investigator Award in 2007 from the ECOG Research and Education Foundation.
Christopher E. Comstock, MD became associated with ACRIN in 2004 when he was awarded its two-year Fellowship in Clinical Trials of Medical Imaging while Section Chief of Breast Imaging at the University of California, San Diego. He was appointed its Chair in 2012. As mentioned above, he transitioned seamlessly into the role of Imaging Chair, ECOG-ACRIN Breast Committee, following the merger. Dr. Comstock also served as the ACRIN Institutional Participants Committee Chair and as a member its Quality Assurance Committee.

Dr. Comstock leads ACRIN 6694, the companion imaging portion for A011104, the randomized trial evaluating the effect of preoperative breast magnetic resonance imaging (MRI) on surgical outcomes, costs, and quality of life. The trial compares the rates of local-regional recurrence following attempted breast conserving therapy in a cohort of 488 women with either triple negative or HER2 (human epidermal growth factor receptor) amplified breast cancer randomized to standard preoperative staging with mammography or standard plus breast MRI. A011104 is being conducted by the Alliance for Clinical Trials in Oncology.

Antonio C. Wolff, MD began working on ECOG studies during his medical oncology fellowship at Johns Hopkins University in the early 1990s. Since then, he has led, co-led, or co-authored studies with various investigators from the Breast Committee, including E8193 (single agent topotecan as first-line therapy), E1195 (phase II study of doxorubicin and paclitaxel), E1199 (adjuvant phase III trial of doxorubicin/cyclophosphamide followed by a taxane), and E3198 (liposomal doxorubicin/docetaxel and trastuzumab). He represented ECOG in North American Breast Cancer Group studies including CALGB 49907 (phase III adjuvant combination vs. single agent chemotherapy in older women) and the ongoing ALTTO (adjuvant trastuzumab and/or lapatinib) trial in HER2-positive breast cancer.

He was instrumental in establishing the breast cancer clinical research infrastructure at Hopkins, an institutional member of ECOG-ACRIN since 1970, for the conduct of cooperative group studies. He also established the infrastructure to support biospecimen-intensive multicenter studies through the Translational Breast Cancer Research Consortium, and has co-chaired guideline panels co-sponsored by the American Society of Clinical Oncology and the College of American Pathologists to improve the quality of predictive biomarker testing-HER2 and ER/PR (estrogen receptors/progesterone receptors) in clinical practice and clinical research. He was honored with a Cancer Clinical Investigator Team Leadership Award from the National Cancer Institute (NCI) in 2009.

More About the Breast Committee and its Accomplishments

The Breast Committee has played a leading role in developing, validating, and/or refining the role of multiparameter gene expression assays in breast cancer management that may result in the sparing of chemotherapy in invasive disease (TAILORx) or selection of radiation in ductal carcinoma in situ (DCIS) score validation study using E5194 samples. TAILORx (Trial Assigning Individualized Options for Treatment) will inform the optimal management of patients with a mid-range Oncotype DX® recurrence score in ER-positive, node-negative breast cancer, a common clinical scenario in which there is a therapeutic equipoise about the role of chemotherapy.

Breast Committee members include investigators from both treatment and diagnostic-imaging disciplines, who together pursue scientific objectives related to drug interventions and imaging technologies. Importantly, the committee includes multi-disciplinary representation from physicians, scientists, nurses, clinical research associates, patient advocates/patient representatives, and other healthcare professionals devoted to performing research into therapeutic interventions.

The Breast Committee is currently working in concert with the National Cancer Institute, FDA, and pharmaceutical companies on two trials designed for regulatory drug approval: bevacizumab (Roche) as adjuvant therapy (E5103) and entinostat (Syndax) in metastatic breast cancer (E2112). Dr. Miller is the lead investigator for E5103. Roisin Connolly, MB, BCh, Assistant Professor of Oncology at Johns Hopkins University, is the lead investigator under the mentorship of Dr. Miller for E2112, the first phase III trial of epigenetic therapy in metastatic disease. E2112 will open soon to patient enrollment.