Foreword: *Radiology* Select Volume 8—Breast Imaging: Beyond Mammographic Screening

Dear *Radiology* Select Reader:

In 2013, our fourth volume of *Radiology* Select was introduced, Breast Cancer Screening. This offering was hugely successful, and many readers made use of the continuing medical education (CME) offerings that were specific to breast imaging. But CME offerings eventually "sunset," and in an ever-evolving subject area such as breast imaging, there is always more to learn. Thus, as we considered potential topics for our next issue of *Radiology* Select, it was clear that breast imaging was a topic ripe with clinically relevant research of immediate use to our imaging community. We are pleased to introduce *Radiology* Select Volume 8: Breast Imaging—Beyond Mammographic Screening. We chose as our guest editors two breast imagers from Memorial Sloan Kettering Cancer Center (MSKCC) and Weill Cornell Medical College, Elizabeth Morris, MD (who is professor of radiology and chief of breast imaging at MSKCC), and Donna D'Alessio, MD (who is assistant professor of radiology and director of the Breast Imaging Interventional Program at MSKCC). These breast imaging and research experts then chose to focus their collection on the broad areas of Breast Density, Tomosynthesis, Ultrasonography, Biomarkers, and MR Imaging in Breast Disease Management.

Drs Morris and D'Alessio had the difficult task of reviewing original research and reviews recently published in *Radiology* and selecting articles for inclusion in this compilation. We are limited in the number of articles we can include to have a compilation of reasonable size, so the final list of articles is, of necessity, subjective. The contents of this volume reflect a somewhat personal view of which are the key articles—not the result of a quantitative determination. Furthermore, it must be recognized that *Radiology* has published many more fine articles on the subject area than can be condensed into this 32-article volume. Some excellent and clinically important articles, therefore, had to be passed over and not included.

We believe that this collection of key articles will be a valuable resource for breast imagers and other providers of women's health care. Having the key articles together will allow the reader to identify the relationships between articles and to follow the development of trends in breast imaging research over time.

Self-assessment CME (SA-CME) is an important aspect of clinical practice in radiology. Recent American Board of Radiology diplomates, in addition to needing CME, also need SA-CME for recertification. We believe that *Radiology* Select offers a perfect vehicle to provide up-to-date SA-CME to our readers and will help them better understand how research evolves and translates into clinical practice. Therefore, Drs Morris and D'Alessio identified key articles that were thought to be valuable for CME. The corresponding authors of selected articles were then contacted and asked to supply questions for CME. The Online Educational Edition includes 17 tests with an opportunity to earn 17 SA-CME credits. This enduring material can be applied toward the American Board of Radiology self-assessment requirement, allowing for focused learning in breast imaging.

The online era provides multimedia opportunities for publications. We exploit this capability by providing audio and video conversations with authors to explore their views on the effect of their work and the work of others in the field with the benefit of hindsight. These conversations also allow experts to share their thoughts on future developments and the effect of their work on these. In this volume of *Radiology* Select, Drs Morris and D'Alessio have conversations with several groups of authors to discuss the pertinent topics in Breast Imaging—Beyond Mammographic Screening.

In keeping with the trend of increasing reliance on electronic publishing, we are offering *Radiology* Select in two formats: HTML on the Internet and print on demand. Print on demand is a bound printed compilation of the articles for those who prefer reading hard copy. The online edition is an HTML version for viewing with a Web browser. Individual PDFs can be downloaded, and readers can listen to and view the audio and video conversations. The SA-CME activities are available only through the online version.

We thank Drs Morris and D'Alessio for reviewing and selecting the articles collected in this volume. We are especially grateful to the authors of the articles, without whom *Radiology* Select would not be possible.

Sincerely,
Deborah Levine, MD, Series Editor, *Radiology* Select
Herbert Y. Kressel, MD, Editor, *Radiology*

Video
Online Educational Edition of *Radiology* Select includes a video with series editor Deborah Levine, MD.

Introducing *Radiology* Select: Breast Imaging—Beyond Mammographic Screening

Elizabeth Morris, MD
Donna D. D'Alessio, MD

The role of breast imaging in diagnosing and treating breast cancer is evolving and has greatly expanded beyond detection. Many factors have contributed to this growth. Breast imaging has moved beyond the mammogram, particularly for women at increased risk of the disease. Demands in patient-tailored imaging and advances in therapy have increased utilization of breast imaging techniques. Advancing technology has emphasized breast imaging as an integral player in breast disease detection, diagnosis, and management.

This *Radiology* Select collection covers research relevant to advances in breast imaging technology between 2011 and 2015 and is limited to 32 articles. Many outstanding articles are not included in this collection. Articles were chosen to represent five key topics in breast imaging and to represent findings from centers in and outside of the United States. When possible, multicenter, prospective trials were emphasized. The five sections are Breast Density, Tomosynthesis, Ultrasonography, Biomarkers, and MR Imaging in Breast Disease Management.

The articles selected for the Breast Density section include those related to legislation surrounding breast density in mammography, in addition to studies investigating advances in breast imaging techniques for women with dense breasts (1-6). There is an increasing demand for improved breast cancer detection, both by the medical community and the general public because of the known limitations of mammography and an increase in breast cancer awareness (1). Mammography is the only screening test that has been shown to reduce breast cancer mortality. However, the overall sensitivity of mammography ranges from 70% to 90% and can be as low as 30%–48% in women with dense breasts (1). Dense tissue is a common finding and is currently classified by the subjective visual assessment of the interpreting physician into four categories as defined by the American College of Radiology's Breast Imaging Reporting and Data System (BI-RADS) (2). On the basis of large-scale population-based data from a representative sample of mammography practices in the United States, approximately 50% of women who undergo screening mammography have dense breasts (2,3). Women with dense breasts have an associated three-to-five times greater risk of developing breast cancer (4). In 2009, Connecticut enacted a law

Video
Online Educational Edition of *Radiology* Select includes videos with guest editors Elizabeth Morris, MD and Donna D. D'Alessio, MD.

mandating patient and referring physician notification when the pattern of fibroglandular tissue on a patient's mammogram was considered dense by the interpreting radiologist. Since then, breast density notification laws have been put into effect in more than half of the states, which emphasizes the risk associated with heterogeneously dense or extremely dense breast tissue at mammography (5). Demand for advances in breast imaging techniques to aid in supplemental evaluation of women with dense breasts has led to research involving screening ultrasonography (US) and tomosynthesis in patients with mammographically dense breasts, some of which is represented in this section of the collection.

The second section of this collection includes articles and research in digital breast tomosynthesis (DBT) (7–14). Mammography is limited in women with dense breasts for whom cancers may be masked by overlapping breast tissue (7). The type of supplemental screening, if any, that should be recommended for women with dense breasts remains unclear. U.S. Food and Drug Administration approval for DBT was obtained in 2011. Tomosynthesis, in contrast to US and magnetic resonance (MR) imaging, may offer operational and ease-of use advantages, because it is an integrated part of newer-generation mammography units (6). With DBT, mammographic projections are acquired at different angles to generate a three-dimensional image of the breast during the standard mammographic compression. It is of particular interest for evaluation of women with dense breast tissue because it partially overcomes the masking effect seen with mammography. Two European prospective population-based screening studies and two North American–based retrospective analyses have shown that adjunct tomosynthesis increases cancer detection rates while decreasing recall rates (7–14). Articles included in this section focus on DBT in the screening and diagnostic setting, as well as on technique, including the use of synthetically reconstructed projections compared with DBT performed with full-field digital mammography.

The next section, Ultrasonography, includes articles investigating the use of US in breast disease (15–18). US has long been used in the diagnostic setting. As a screening tool, US is attractive because it is widely available, is performed without a contrast agent, and is well tolerated in women (15). In the American College of Radiology Imaging Network (ACRIN) 6666 study, screening US had a sensitivity of 76% and a specificity of 84% in women with dense breasts and elevated risk (16). In women with dense breasts and negative mammograms, screening US yielded an incremental cancer detection rate of 2.3–4.6 cancers per 1000 women screened (15,17). Most breast cancers detected with screening US tend to be node-negative small invasive cancers (18). The majority of breast cancers detected at screening US are obscured by overlapping dense breast tissue at mammography; however, other factors contribute to the lack of detection with mammography (19). Breast density inform legislation is increasingly widespread, and, in response, interest in strategies for implementing supplemental screening modalities, including screening breast US, continues to grow. While the ACRIN 6666 protocol demonstrated that screening breast US yielded a greater cancer-detected rate in that population, there was also an increase in number of false-positive findings and an increased percentage of the women studied subjected to biopsies and short-term follow-up (3,16). The articles in this section address issues surrounding breast US technique, management of findings at supplemental screening, and the challenges involved with implementing such a program. One prospective study by Barr et al evaluates predefined breast US BI-RADS category 3 criteria in a multicenter setting in an elevated risk population to determine the prevalence and rate of malignancy in this subgroup and addresses the issues related to supplemental screening with US (16).

The section on Biomarkers focuses on studies utilizing breast MR imaging techniques and findings that may shed light on a patient's risk for breast cancer and identifying imaging features that may help determine which cancers may progress or recur (20–26). The mammographic appearance of the breast has been shown to provide valuable information with regard to breast cancer risk. A strong association between mammographic parenchymal pattern and breast cancer risk was proposed by Wolfe in 1976 and has since been validated by using quantitative and qualitative methods (20). Women with mammographically dense breasts have a three-to-five times greater

risk for breast cancer than those with predominantly fatty breasts at mammography (4). This relationship of mammographic breast density and breast cancer risk has driven researchers to study the association of background parenchymal enhancement in breast MR imaging with breast cancer risk. Some of these studies are included in this collection. Evaluating breast imaging findings in the context of risk is one of the many useful ways breast MR imaging plays a role in breast cancer management.

Once breast cancer is detected, determining which cancers will progress or recur is another challenge. Currently, ductal carcinoma in situ (DCIS) accounts for 20%–30% of all newly diagnosed breast cancers in the United States and approximately 20% of cases are detected with mammography (21). An important issue, however, is that one cannot predict whether DCIS will evolve to invasive carcinoma. Therefore, although low-grade DCIS is considered nonlethal, all cases of DCIS are typically treated as though they will become invasive. Unlike adenocarcinoma of the colon which evolves following a single line, benign proliferative breast disease, some low-grade DCIS, most high-grade DCIS, and invasive carcinoma develop through distinct pathways (21). Hence, more accurate grading of DCIS at initial diagnosis may help to customize therapeutic approach. Studies in advances in breast MR imaging techniques, including background parenchymal enhancement ratio, diffusion-weighted imaging, apparent diffusion coefficients, intrinsic imaging phenotypes, and associations with prognostic gene expression profiles are topics represented in this section. One study focuses on the emergence of radiogenomics, which allows for analysis of clinical imaging data and seamless integration with clinical, tissue, cellular, and molecular phenotypes to evaluate these associations with breast cancer disease progression (22).

As breast cancer therapies are constantly being developed, the role breast imaging plays in the management of the disease has evolved in response to this demand. The final section of this collection, MR Imaging in Breast Disease Management, focuses on the advances in breast MR imaging as a critical player in both the surgical and medical management of the disease (27–35). Routine use of breast MR imaging to preoperatively evaluate patients with breast cancer who may qualify for breast conservation therapy is controversial among breast cancer care providers. Recognizing the heterogeneity of breast cancer has led to the differentiation of breast carcinoma into distinct molecular subtypes on the basis of gene expression profiling (23,27). These distinct molecular subtypes respond differently to therapy and confer different prognoses (24). This information may help provide guidance in the decision to pursue preoperative breast MR imaging, and studies evaluating this concept are included in this section.

Systemic chemotherapy is used to treat women with invasive breast cancer to reduce the risk of recurrence after surgery. Clinical trials comparing neoadjuvant chemotherapy (NACT) and adjuvant chemotherapy have shown equivalent relapse-free and overall survival outcomes between the two groups (28). However, women who underwent NACT were more likely to achieve breast conservation than those undergoing chemotherapy after surgery (29). One study included in this collection is the ACRIN 6657/I-SPY Trial. This study was conducted as the imaging component of the multicenter prospective study entitled Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging and Molecular Analysis (I-SPY TRIAL). This ACRIN study was designed to test MR imaging for its ability to help predict response to treatment and to stratify the risk of recurrence in patients with stage II or III breast cancer undergoing NACT. The goal of the study was to compare breast MR imaging and clinical assessment for prediction of pathologic response after NACT (29). Additional prospective trials, including one in England presented in this collection, evaluate the use of breast MR imaging to predict survival in patients undergoing NACT (30). Another study from Korea investigates volume-based metabolic tumor response to NACT and the association with risk of recurrence (31). The studies included in this section demonstrate the increasing role breast MR imaging plays in evaluating patients who have been diagnosed with and who are undergoing treatment for breast cancer.

Breast cancer is a major source of morbidity and mortality for women around the world. Medical therapies and surgical options for managing the disease continue to grow. In turn, breast imaging continues to expand its critical role in helping predict the risk of developing the disease and evaluating for the presence and

extent of the disease, the likelihood of responding to treatment, and the risk of recurrence. The articles presented in *Radiology* Select represent the substantial advances breast imaging has made in breast cancer diagnosis and in evaluating women being treated for the disease. The results of this research should offer guidance in providing the best care for patients.

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