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Beyond Mammography: New Frontiers in Breast Cancer Screening

Jennifer S. Drukteinis, MD, Blaise P. Mooney, MD, Chris I. Flowers, MBBS, Robert A. Gatenby, MD

H. Lee Moffitt Cancer Center and Research Institute, Tampa, Fla.

ABSTRACT

Breast cancer screening remains a subject of intense and, at times, passionate debate. Mammography has long been the mainstay of breast cancer detection and is the only screening test proven to reduce mortality. Although it remains the gold standard of breast cancer screening, there is increasing awareness of subpopulations of women for whom mammography has reduced sensitivity. Mammography also has undergone increased scrutiny for false positives and excessive biopsies, which increase radiation dose, cost, and patient anxiety. In response to these challenges, new technologies for breast cancer screening have been developed, including low-dose mammography, contrast-enhanced mammography, tomosynthesis, automated whole breast ultrasound, molecular imaging, and magnetic resonance imaging. Here we examine some of the current controversies and promising new technologies that may improve detection of breast cancer both in the general population and in high-risk groups, such as women with dense breasts. We propose that optimal breast cancer screening will ultimately require a personalized approach based on metrics of cancer risk with selective application of specific screening technologies best suited to the individual's age, risk, and breast density.

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It is generally accepted that early detection of breast cancer increases the probability of cure, and mammography has been shown to reduce breast cancer mortality in population-based screening programs.[1] However, mammography has limitations, and some investigators propose that the benefits do not always outweigh the risks. The sensitivity of mammography is highly variable, ranging from 98% in women with fatty breast parenchyma to 36% in women with dense breasts.[2,3] Thus, women who undergo annual mammography may still present with cancers found only on physical examination. False-positive rates in breast cancer screening also are a significant limitation, as high callback rates and unnecessary biopsies increase cost, radiation dose, and patient anxiety. Concern for long-term sequelae of radiation exposure remains, as recent studies suggest that mammography may actually contribute to an increased incidence of breast cancer in certain high-risk populations.[4] These concerns understandably may decrease compliance with screening recommendations.[5]

More successful breast cancer screening requires increased sensitivity and specificity, ideally, limiting both financial cost and radiation burden. Some of this may be obtained through new technological development. However, we propose that optimal patient care will ultimately require a new paradigm, with adoption of patient-specific

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Requests for reprints should be addressed to Jennifer S. Drukteinis, MD, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, Tampa, FL 33612.

E-mail address: jennifer.drukteinis@moffitt.org

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screening strategies tailored to risk assessment based on family history, age, genetic profiles, and breast density. The goal in this approach is development of personalized imaging algorithms that maximize specificity and sensitivity while minimizing cost and radiation exposure. In this article we discuss both current practices and imaging techniques that may be combined in novel ways to achieve optimal, personalized imaging strategies for detecting breast cancer.

SCREENING MAMMOGRAPHY RECOMMENDATIONS

Controversies surrounding mammography and breast cancer screening have led to uncertainty about optimal screening strategies. In 2009, the United States Preventive Services Task Force (USPSTF), a panel of health care professionals that reviews published research and makes recommendations about preventive health care, issued revised mammography guidelines. These included the recommendation for screening mammograms every 2 years beginning at age 50 years for women at average risk of breast cancer. They recommended against routine screening mammograms before age 50 years. This recommendation ignited an ongoing, often passionate debate about optimal screening strategies.

At present, the USPSTF is the only group or consensus panel in the US that recommends screening to begin at age 50 years (**Table 1**). Most such groups recommend breast cancer screening to begin at age 40 years, and women with a first-degree relative diagnosed with breast cancer should begin annual mammography 10 years before the age of diagnosis of that relative.[6]

Table 1 Screening Mammography Guidelines from Major Consensus Groups and Organizations in the United States

	Begin Screening Age (Years)	Interval (Years)
American Cancer Society	40	1
National Cancer Institute	40	1 to 2
American Medical Association	40 (discussion)*	1 to 2
American College of Surgeons	40	1
American College of Physicians	40 (discussion)*	1 to 2
American College of Radiology	40	1
American College of Obstetrics and Gynecology	40	1
United States Preventive Services Task Force	50	2

*Recommends that the patient have a discussion with their medical provider about the risks and benefits prior to undergoing mammography at age 40.

CLINICAL SIGNIFICANCE

- Mammography is the only screening test that reduces breast cancer mortality.
- Mammography has decreased sensitivity in women with dense breasts.
- New technologies for breast cancer screening include low-dose mammography, contrast-enhanced mammography, tomosynthesis, automated whole breast ultrasound, and magnetic resonance imaging.
- Optimal breast cancer screening will require a personalized approach, with selective application of screening technologies best suited to the individual's age, risk, and breast density.

Limitations of Mammography and the Need for an Adjunctive Screening Tool

There is clear evidence that mammography detects early breast cancers and that screening large populations reduces mortality. However, mammography is an imperfect screening tool. The sensitivity of mammography is inversely proportional to breast density.[7] Among women with heterogeneously dense or extremely dense breast parenchyma, full-field digital mammography (FFDM) has been shown to be more sensitive than film-screen mammography.[8] Unfortunately, the sensitivity of both digital and analog mammography remains low in women with dense breast parenchyma,[2,3] limiting its usefulness in high-risk younger women.

Radiation Risks and Low-dose Mammography

While the absorbed radiation dose received by the breast during mammography represents a relatively small component of the lifetime-accumulated dose from medical imaging and other sources, the popular press and medical literature frequently raise concerns about the radiation risks from mammography. According to the National Research Council of the National Academies Biologic Effects of Ionizing Radiation (BEIR) VII study; the average mean glandular dose (MGD) from digital mammography is 3.7 mGy. This is estimated to have a lifetime attributable risk of fatal breast cancer of 1.3 per 100,000 women aged 40 years at exposure and <1 case per 1,000,000 women aged 80 years at exposure.[9] It also has been estimated that for the same cohort, 292 lives would be saved as a result of annual screening.[10] While this favorable risk-benefit ratio seems clear, many women and physicians remain concerned.

Strategies are being investigated to lower radiation dose and alleviate patient fears without compromising cancer detection. Spectral imaging or photon counting is a promising new technology in digital mammography aimed at lowering the MGD to the breast. The image is acquired by a scanning method that utilizes a multislit collimator, eliminating 97% of scattered radiation, significantly lowering the absorbed dose.[11] The direct capture of individual X-ray studies occurs without the analog-to-digital conversion steps, increasing efficiency. Recently, the US Food and