Journal of Breast Imaging, 2019, Vol. 1, Issue 1, 2–8
doi:10.1093/jbi/wby016
Science of Screening

Science of Screening

Antecedents: A Half-Century of Imaging the Breast

Daniel B. Kopans, MD, FACR, FSBI*

Harvard Medical School, Department of Radiology, Waban, MA (D.B.K.).

*Address correspondence to D.B.K. (e-mail: dkopans@verizon.net).

Abstract

The field of Breast Imaging evolved because a fairly small number of dedicated individuals realized the lifesaving potential of detecting breast cancer earlier. They persevered despite persistent efforts to curtail screening. From the first attempts to produce X-ray images of the breast to magnetic resonance and digital breast tomosynthesis, investigators have worked continuously to develop better ways to detect breast cancer at a time when cure is possible, while working continuously to preserve access for women to screening. Consequently, the death rate from breast cancer has declined by more than 40%. Therapy has improved, but therapy saves lives when breast cancers are treated early.

Key words: Breast; breast imaging; history.

Introduction

Much of what follows is based on the history of breast imaging in the United States (U.S.), and even this is constricted. There have been major contributions from other countries. Lungren in Sweden first described the mediolateral oblique projection (1) that permitted the inclusion of more breast tissue. The benefits from screening mammography were proven in Sweden by the enormous efforts of Andersen et al. (2) and Bjurstam et al. (3), whose randomized, controlled trials proved that screening saved lives, including for women in their forties; and, especially, Laszlo Tabár (4), who not only performed one of the major randomized, controlled trials that provided conclusive proof that earlier detection saves lives (5) but also taught us all how to perform high-quality mammography screening. Without their efforts, there would be little reason to image the breast, and the major decline in breast cancer deaths that we have seen would never have happened. Tabár's most recent analysis shows therapy has probably reduced deaths among women who did not participate in screening, but it is clearly much more effective among women who participated in screening, whose death rate declined by 60% at 10 years and 47% at 20 years compared to those who did not participate (6).

Breast imaging as a discipline did not exist in the 1970s. At that time, the handful of radiologists who drew the "short straw" and had to read the mammograms, were often the newest and youngest members of a department. Mammography was often in the basement. No one cared about what we were doing as long as the handful of mammograms was read each day. We were the "Rodney Dangerfields" of radiology (7). Most of our patients had "signs or symptoms." We performed a clinical breast examination, as well as the mammogram, with an occasional needle localization, taking a whole day to provide care for 8 to 10 women. We hoped and thought that a cure for breast cancer would be discovered soon, but while we waited, we recognized the important potential of what we were doing as we began to find small, clinically occult cancers. The American College of Radiology's (ACR) "Breast Task Force" was a subcommittee of a subcommittee. It was not until the ACR realized that we were far ahead of the rest of radiology (actually, all of medicine), having developed a systematic approach to our work (Breast Imaging Reporting and Data System [BI-RADS]) along with an auditing system that required us to follow-up on our findings and monitor outcomes, that the College, in 2005, finally accorded us "commission" status under Carol Lee.

Saving Lives

Not long after Roentgen discovered X-rays, investigators thought of looking for breast cancer (8). They imaged mastectomies. Later Gershon Cohen began imaging patients and developing diagnostic

Key Messages

- Breast imaging and, specifically mammography screening, is the main reason that the death rate from breast cancer, unchanged for the 50 years before screening, has declined by over 40%.
- The history of breast imaging has been a continuous effort to develop scientific evidence to refute misinformation designed to reduce access to screening.
- The foundation of breast imaging is solid, with a firm emphasis on innovation. We need to improve on advances from the past to continue to drive down the death rate from breast cancer.

criteria (9). Egan described standard and reproducible methods for X-ray imaging the breast using industrial film (10), making it possible to detect preclinical breast cancer. Recognizing that the only way to prove screening could save lives was through a randomized, controlled trial (RCT), radiologist Phillip Strax and biostatistician Sam Shapiro performed the first RCT in the 1960s, within the Health Insurance Plan of New York (HIP). In the HIP they randomly invited 32,000 women to annual mammography and a clinical breast examination, and compared them to 32,000 unscreened (find your lump and see your doctor) women ages 40 to 64 years, proving that earlier detection could reduce deaths from breast cancer (11). This was followed by other RCT, primarily in Sweden (the Edinburgh Trial and the Canadian National Breast Screening Studies were compromised by biased allocation) that proved that mammography screening could reduce deaths by 20% to 30% among women "invited to be screened" (12), with even greater reduction in deaths for women who actually participated in screening. Numerous observational studies have shown that women in the general population who have access to screening have many fewer deaths than those who do not (13–29), despite theoretically all women having access to modern therapy. This was dramatically confirmed by the recent study by Tabár et al., showing that the major decline in breast cancer deaths is linked to participation in screening (6). In the Harvard hospitals, 71% of women who died from breast cancer, despite having access to modern therapy, were among the 20% of women who were not participating in screening (30).

Efforts to Curtail Screening

A detailed discussion of the screening issues is beyond this article, but dating back to the 1970s, there has been an almost nonstop effort to reduce access to screening through the creation of "alternative facts" (31). The main events included a radiation scare in the mid1970s, the 1989 "Consensus Guidelines," supporting screening starting at the age of 40 (32), followed by the 1993 International Workshop on Screening for Breast Cancer, in which the National Cancer Institute (NCI) using, inappropriate, unplanned, retrospective, subgroup analysis (33) falsely claimed that there was no benefit from screening before the age of 50 years and dropped support for women ages 40 to 49 years (34, 35). Under pressure from the ACR and the American Cancer Society (ACS), a Consensus Development Conference (CDC) was held in 1997, which also falsely claimed no benefit from screening women in their forties (36), despite direct evidence to the contrary (37). Ignoring the CDC results, the NCI once again supported screening women in their forties. However, in 2007, the American College of Physicians took a step backward and (with no scientific support) recommended waiting until age 50 years and then screening women every 2 years (38), despite admitting that the most lives are saved by screening starting at the age of 40 years (39). This was followed by the U.S. Preventive Services Task Force (USPSTF) in 2009, making the same scientifically unsupported argument that women should wait until the age of 50 years to be screened and then be screened every 2 years thereafter (40).

There are absolutely no data that support the use of the age of 50 years as a threshold, but the USPSTF reinforced these guidelines in 2016, ignoring their own results from the 6 NCI/CISNET computer models that all agreed that the most lives would be saved by starting annual screening at the age of 40 years (41). In 2015, the ACS, long a supporter of annual screening starting at the age of 40 years (42), argued for an intermediate starting point (age 45 years) and ultimately longer time between screens all the while, also agreeing that the most lives are saved by starting annual screening at the age of 40 years (43). The CISNET models show that if women now in their thirties wait until the age of 50 years to be screened every 2 years, as many as 100,000 lives will be lost that could have been saved by starting annual screening at the age of 40 years (44). The American College of Radiology and the Society of Breast Imaging, both driven by science and evidence, have always supported annual screening starting at the age of 40 years.

Mammography screening has been studied in more ways than any other test and has been proven by the RCT to reduce deaths from breast cancer for women ages 40 to 74 years. The death rate from breast cancer had been unchanged for decades before the start of screening in the mid1980s. In 1990, deaths began to decline. There are now more than 40% fewer women dying from breast cancer each year (45), primarily because of early detection (6).

The purpose of this summary is to provide the background for this major decline in deaths. We are certainly not declaring an end to breast cancer deaths, but it is important to understand where we have been in order to help direct where we are going. It is outrageous that so little money is being spent on developing improved methods to detect breast cancer at a time when cure is possible, in light of the millions spent on creating what are, essentially, toxins to primarily delay, but not eliminate deaths.

Our Origins

There were only a handful of individuals performing mammography in the 1960s. Plain "industrial film" was replaced in the 1970s by the Xeroradiographic technique, derived from copy machine technology, using a semiconductor plate, electrical charge, and toner powder. John Wolfe promoted the technology and developed the 4 categories of tissue "parenchymal patterns." He was the first to identify a link between dense breast tissue and risk of developing breast cancer (46). Most (not all) modern full-field digital mammography systems (FFDM) rely on the Xeroradiographic principles, but the charge is read directly from the plates without using toner.

In the 1970s, the Breast Cancer Detection Demonstration Project recruited more than 250,000 women and proved that screening could efficiently find small clinically occult cancers (47) and ad hoc screening began to find cancers at curable sizes that surgeons were unable to feel (48).

Efforts were made to block screening, particularly for women in their forties (49). Myron "Mike" Moskowitz almost single handily preserved access to screening (50, 51). He taught a small cadre of radiologists how to understand the statistical issues that allowed us

to go "toe to toe" with epidemiologists, who had limited experience in breast care.

In 1974, the wives of the president and vice president of the U.S. diagnosed with breast cancer led to a flurry of ad hoc screening and a jump in "incidence" in the first year of the Surveillance, Epidemiology, and End Results database of the NCI. After 1974, incidence fell as few women continued to participate in screening. Fear was generated in 1976, when John Bailar claimed that mammography screening would cause more breast cancers than would be cured (52). Stephen Feig did analyses that challenged Bailar's estimates and allowed us to continue to screen more and more women (53). Evaluations that are more recent show little if any risk for women ages 40 years and over.

In the 1970s, it was thought that thermography could find early cancer and as a passive measure of skin temperature, would be completely safe. However, since it is only a measure of skin temperature, and the breast is a good insulator, only large cancers or those immediately under the skin were detectable, and studies like those by Feig et al. (54) showed the lack of efficacy for thermography.

In the 1970s, it was also claimed that shining flashlights through the breast could find breast cancers (diaphanography), but it soon became clear that this was of little value. Laser transillumination has been tried in an effort to detect breast cancers by finding oxygenated and deoxygenated hemoglobin, but even linking this with proven technologies such as digital breast tomosynthesis (DBT) (55) has not proven efficacious because even laser light is scattered and diffused by the breast.

The radiation scare (56) spurred efforts to reduce radiation dose for mammography. Fluorescent screens converted the X-rays to light-exposing film more efficiently and provided high-quality images at much lower doses, and screen/film combinations replaced Xeroradiography in the 1980s.

Dedicated mammography systems allowed more breast tissue to be held in the field of view, using small focal spots and the more appropriate lower energy, "soft" X-rays for high contrast. Rigid compression was promoted by Wendy Logan (contradictory to the notion that men developed breast compression) to even out the breast thickness, providing uniform exposures and high- quality images at lower doses (57).

Tabár took film/screen systems to their pinnacle by developing best methods for positioning the breast and developing the images (58). We learned how batch reading could improve efficiency and permit the "double reading" that reduced the false negative rate (59).

Sickles developed magnification mammography (60) and principles that remain valid today. He argued in support of 2-view mammography (61), and developed and provided the scientific support for BI-RADS 3: "short-interval follow-up" (62).

In 1985, major mortality reduction in Tabár's "Two County" RCT (63), triggered the start of screening in the U.S. Soon after, in 1990, the death rate from breast cancer began to fall for the first time in more than 50 years. Therapy had improved, but therapy saves lives when breast cancer is treated early, as reflected in the observational studies. The data suggest that approximately 20% of women participated in the mid1980s, plateauing at approximately 70% at the end of the 1990s. Women in the U.S. have not been participating consistently likely because of all of the confusion attributable to the misinformation that has been promulgated about screening (64).

In the 1970s, General Electric (GE) (Boston, MA) built 2 prototype breast CT scanners. The Mayo clinic found no use for the system, and GE pulled the prototypes. Chang, however, found that breast cancer "enhanced" with IV contrast, and did studies using chest CT to evaluate the breasts (65). We found CT useful for locating (and localizing for surgery) lesions deep in the breast (66, 67). Chang's work presaged the need for intravenous contrast using magnetic resonance imaging (MRI) since iodine and gadolinium have similar biodistributions. Later using FFDM, Loren Niklason, in my group (68), as well as Martin Yaffe and Roberta Jong in Canada (69), did preliminary work on temporal subtraction using contrast material, but these images were compromised by even small amounts of motion. John Lewin reduced the motion problem using intravenous iodinated contrast and dual energy subtraction to reveal the "blush" of tumor neovascularity (70), now named contrast-enhanced spectral mammography.

In the early 1970s, breast biopsies for clinically occult lesions were excisional and were performed by surgeons using general anesthesia in main operating rooms. Not knowing the exact location of a nonpalpable lesion, frequently an entire quadrant was removed for what often proved to be a benign lesion. Gerald Dodd described putting a hypodermic needle into the area that contained the lesion to guide the surgeon (71). Often, the needle was not very close to the target or it would fall out in the operating room. In 1976, surgeon Howard Frank and radiologist Ferris Hall bent a wire into a hook at one end, passing it through a small skin incision to fix into the tissue near a lesion (you only got one shot), with the wire protruding from the skin (72). I developed a wire localization system with a spring hook wire that could be "after loaded" through a needle to permit very safe and accurate positioning in or at the lesion (73–75) it, improving guidance for surgeons (76). These allowed much safer outpatient biopsies using local anesthesia, with much less cosmetic damage (77), addressing the complaints being used to curtail screening. A number of other guides have been developed. All are being challenged by radiofrequency transmitters, magnetic markers, and radioactive seeds—which are an order of magnitude more expensive (not to mention that your site becomes a nuclear accident if you lose a seed!)—but may be more convenient for surgeons.

In the 1970s, Kossof and Jellins were among the first to use ultrasound (US) to image the breast (78). Kobayshi defined the fundamental parameters for analyzing breast lesions (79). Black and white, bi-stable devices were replaced by grayscale and "real- time" high-frequency transducers, which provided improved imaging. More radiologists used US, for cyst/solid differentiation. Experts like Bruno Fornage developed criteria for improved analysis of solid lesions (80). In the 1980s, US began to be used for guiding interventional procedures (81).

As a response to radiation concerns, there were early efforts to substitute US for screening. "Whole breast" scanners were built. Others and we showed that the technology of the 1980s was not able to routinely detect small cancers (82, 83), but the technology continued to improve. Tom Kolb was among the first in the U.S. to detect a large number of small cancers that were not seen on mammography (84). Paula Gordon in Canada developed US-guided fine-needle aspiration techniques (85). Ultrasound technology improved to the point where we were able to see the needle and the lesion, facilitating safe, accurate, and less traumatic cytological and then confirm imaging-detected lesions histologically. Ultimately, Wendy Berg did the randomized trial that showed US to be a viable second-level screening test (86).

A prone table developed in Sweden to permit stereotactic-guided biopsy of nonpalpable breast lesions was pioneered by Robert Schmidt in the U.S. (87). Steve Parker promoted the idea of

image-guided core needle biopsies, providing histological information (88). To replace fine-needle aspiration and surgical biopsies in the U.S., DBT-guided needle biopsies are now available.

In the late 1970s, US, CT, MRI, and nuclear medicine ("molecular imaging") were being used for body imaging. My institution debated as to whether we should rename our Radiology Department the Department of Imaging. Traditions were strong, and the idea was tabled. However, since no one really cared what I did with my "Xeroradiography Division," and acknowledging the fact that we were using multiple methods for evaluating the breast in 1978, I renamed my division Breast Imaging. I used the name in teaching programs and meetings ("The Team Approach to Breast Imaging"). My talks carried the title "Breast Imaging." More and more radiologists who ran "mammography" divisions adopted the name. I believe that the first paper to explain our nascent field was one that we published in 1984 in the *New England Journal of Medicine* (89). The new name spread, and in 1985, Mark Homer organized the Society of Breast Imaging.

In the late 1970s and early 1980s, personal computers became available, and Sickles, at the University of California, San Francisco, and I, along with Richard Moore, at the Massachusetts General Hospital, developed computer systems for our groups that organized and structured our reporting (no more stream of consciousness reports). We tracked our results, monitored outcomes, and learned from the expanding data. Sickles developed the "Medical Audit" (90). My reporting system, with its final assessment categories (91, 92), became the basis for the ACR BI-RADS, while Carl D'Orsi's work with Bolt, Beraneck, and Newman (a think tank) led to the selection of terms that we all now know as the BI-RADS Lexicon. We developed structured reporting and outcomes monitoring in breast imaging long before any others in radiology did. Ed Hendrick, who would also develop much of the scientific support for screening, guided the ACR in developing the criteria for quality mammography practice. Support by Marie Zinninger and Pamela Wilcox, at the ACR, was critical for advancing the specialty. Technologists Rita Heinlein, Debra Diebel, and Louise Miller, along with Dorothy McGrath, elevated the importance of the X-ray technologist on the Breast Imaging team, and taught generations of technologists the importance of proper mammographic positioning.

Although many radiologists rose to the challenge and, despite poor reimbursement, provided screening in the 1980s, some took advantage. In 1987, the ACR initiated a voluntary accreditation program. However, with no mandatory national oversight, media reports of poor-quality mammography led Congress to pass the Mammography Quality Standards Act, introduced in 1994, assigning the FDA to monitor mammography, leading to regulations requiring accreditation and improved quality across the U.S.

In the late 1970s and early 1980s, as others and we began to explore MRI (93), we found that without an intraveneous contrast agent MRI had little value for detecting breast cancers. In the late 1990s, Priscilla Slanetz, at the Massachusetts General Hospital, was the first to show that MRI with gadolinium could detect mammographically occult breast cancers in the contralateral breasts of volunteers with breast cancer (94), suggesting that MRI had the potential to become a major second-level screening test.

Recognizing that all of us, periodically, fail to see cancers that are visible in retrospect, screening groups in Europe introduced "double reading" for mammographic screening, which reduced the false negative rate (95). A few of us adopted the approach in the U.S. A major effort was made in the 1980s and 1990s, to employ Computer Aided Detection (CAD) to help detect breast cancers (96). CAD, using the cues that radiologists use, had great promise (97, 98), but it never really achieved its anticipated potential. Computing power has increased dramatically, and CAD is now being revisited as artificial intelligence or deep learning, to see if computers, using multilayer neural networks, can find their own keys and detect breast cancers.

Mammography has undergone a huge evolution. Industrial film was replaced by Xeroradiography, which itself was replaced and improved by screen/film. In the late 1980s and 1990s, digital imaging began to replace general X-ray imaging. The FDA required FFDM to undergo a premarket approval (PMA) process instead of the simpler and far less expensive 510K process that they required for imaging of other organs. This greatly delayed the development of FFDM. We used the first high-resolution FFDM prototype from American Science and Engineering in 1985, to image volunteers, but it was not until 2000 that GE obtained the first FDA approval for FFDM. It was clear that FFDM was not really better than screen/film, but it was certainly comparable and it had major logistical benefits.

In 1978, I realized that a concept called tomosynthesis (99) would solve the major problems of superimposition of normal structures hiding or simulating a cancer on mammograms, while not increasing dose (100), but I had to wait for digital detectors. In the 1990s, using GE's prototype FFDM system, my development group, led by Richard Moore and Loren Niklason, was able to show that DBT could not only detect cancers that were hidden on conventional 2D mammography, but could also reduce recalls, because 25% of the women we recalled had nothing but superimposed normal tissues that disappeared on DBT (101–104). Our findings have been confirmed in studies involving hundreds of thousands of volunteers (105), and DBT is replacing 2D mammography for all mammography.

We have become better and better at detecting more breast cancers at a curable stage. DBT is replacing conventional 2D mammography, and some are even doing US screening, which detects a few more additional cancers. MRI is clearly the most sensitive way to detect the most cancers at an early size and stage, and abbreviated ("fast") MRI, first promoted by Christian Kuhl (106), can be used to reduce the cost of MRI screening and increase its accessibility for more women. We need to understand the accumulation of gadolinium in the brain better, but if this proves to be of no consequence, MRI screening for the general population may be the ultimate answer to eliminate most deaths from breast cancer. Breast Imaging—and specifically breast cancer screening—has been one of the major health advances of the past 50 years. We all want the "magic bullet" that cures all breast cancers, but we are nowhere near finding such a miracle cure. Early detection is the best way to cure breast cancer, and we need to build on the sturdy foundation that has been created.

Conflict of interest statement

None declared.

References

1. Lundgren B. The oblique view at mammography. *BJR* 1977;50:626–628.
2. Andersson I, Janzon L. Reduced breast cancer mortality in women under 50: update from the malmo mammographic screening program. *Monogr Natl Cancer Inst* 1997;22:63–67.

3. Bjurstam N, Bjorneld L, Duffy S, et al. The Gothenberg breast cancer screening trial: preliminary results on breast cancer mortality for women ages 39–49. *Natl Cancer Inst Monogr* 1997;22:53–55.
4. Tabár L, Vitak B,Chen TH, et al. Swedish two-county trial: impact of mammographic screening on breast cancer mortality during 3 decades. *Radiology* 2011;260:658–663.
5. Tabár L, Vitak B, Chen TH, et al. Swedish two-county trial: impact of mammographic screening on breast cancer mortality during 3 decades. *Radiology* 2011;260:658–663.
6. Tabár L, Dean PB, Chen TH, et al. The incidence of fatal breast cancer measures the increased effectiveness of therapy in women participating in mammography screening. *Cancer* 2018. doi: 10.1002/cncr.31840. [Epub ahead of print].
7. "I get no respect." Rodney Dangerfield. https://en.wikipedia.org/wiki/Rodney_Dangerfield. Accessed January 1, 2019.
8. Joe BN, Sickles EA. The evolution of breast imaging: past to present. *Radiology* 2014;273(2 Suppl):S23–S44.
9. Gershon-Cohen J, Ingleby H. Carcinoma of the breast; roentgenographic technic and diagnostic criteria. *Radiology* 1952;60:68–76.
10. Egan R. Experience with mammography in a tumor institution: evaluation of 1000 cases. *Am J Roentgenol* 1960;75:894–900.
11. Shapiro S, Venet W, Strax P, Venet L. *Periodic Screening for Breast Cancer: The Health Insurance Plan Project and its Sequelae, 1963–1986*. Baltimore, MD: The Johns Hopkins University Press, 1988.
12. Duffy SW, Tabar L, Smith RA. The mammographic screening trials: commentary on the recent work by Olsen and Gotzsche. *CA A Cancer J Clin* 2002;52:68–71.
13. Tabar L, Vitak B, Tony HH, Yen MF, Duffy SW, Smith RA. Beyond randomized controlled trials: organized mammographic screening substantially reduces breast carcinoma mortality. *Cancer* 2001;91:1724–1731.
14. Kopans DB. Beyond randomized, controlled trials: organized mammographic screening substantially reduces breast cancer mortality. *Cancer* 2002;94:580–581.
15. Duffy SW, Tabar L, Chen H, et al. The impact of organized mammography service screening on breast carcinoma mortality in seven Swedish counties. *Cancer* 2002;95:458–469.
16. Otto SJ, Fracheboud J, Looman CWN, et al. and the National Evaluation Team for Breast Cancer Screening*. Initiation of population-based mammography screening in Dutch municipalities and effect on breast-cancer mortality: a systematic review. *Lancet* 2003;361:411–417.
17. Swedish Organised Service Screening Evaluation Group. Reduction in breast cancer mortality from organized service screening with mammography: 1. Further confirmation with extended data. *Cancer Epidemiol Biomarkers Prev* 2006;15:45–51.
18. Coldman A, Phillips N, Warren L, Kan L. Breast cancer mortality after screening mammography in British Columbia women. *Int J Cancer* 2007;120(5):1076–1080.
19. Jonsson H, Bordás P, Wallin H, Nyström L, Lenner P. Service screening with mammography in Northern Sweden: effects on breast cancer mortality - an update. *J Med Screen* 2007;14(2):87–93.
20. Paap E, Holland R, den Heeten GJ, et al. A remarkable reduction of breast cancer deaths in screened versus unscreened women: a case-referent study. *Cancer Causes Control* 2010;21:1569–1573.
21. Otto SJ, Fracheboud J, Verbeek ALM, et al. and the National Evaluation Team for Breast Cancer Screening. Mammography screening and risk of breast cancer death: a population-based case–control study. *Cancer Epidemiol Biomarkers Prev* 2011. doi: 10.1158/1055–9965.EPI-11–0476.
22. van Schoor G, Moss SM, Otten JD, et al. Increasingly strong reduction in breast cancer mortality due to screening. *Br J Cancer* 2011. 104(6):910–914.
23. Mandelblatt JS, Cronin KA, Bailey S, et al. Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms. *Ann Intern Med* 2009;151:738–747. Available at: http://cisnet.cancer.gov. Accessed April 16, 2011.
24. Hellquist BN, Duffy SW, Abdsaleh S, et al. Effectiveness of population-based service screening with mammography for women ages 40 to 49 years: evaluation of the Swedish Mammography Screening in Young Women (SCRY) cohort. *Cancer* 2011;117(4):714–722.
25. Broeders M, Moss S, Nyström L, et al. and the EUROSCREEN Working Group. The impact of mammographic screening on breast cancer mortality in Europe: a review of observational studies. *J Med Screen* 2012;19(Suppl 1):14–25. Review.
26. Hofvind S, Ursin G, Tretli S, Sebuødegård S, Møller B. Breast cancer mortality in participants of the Norwegian breast cancer screening program. *Cancer* 2013;119(17):3106–3112.
27. Sigurdsson K, Olafsdóttir EJ. Population-based service mammography screening: the Icelandic experience. *Breast Cancer* 2013;5:17–25.
28. Coldman A, Phillips N, Wilson C, et al. Pan-canadian study of mammography screening and mortality from breast cancer. *J Natl Cancer Inst* 2014;106(11). pii:dju261. doi:10.1093/jnci/dju261.
29. Puliti D, Bucchi L, Mancini S, et al. and the IMPACT COHORT Working Group. Advanced breast cancer rates in the epoch of service screening: the 400,000 women cohort study from Italy. *Eur J Cancer* 2017;75:109–116.
30. Webb ML, Cady B, Michaelson JS et al. A failure analysis of invasive breast cancer: most deaths from disease occur in women not regularly screened. *Cancer* 2014;120(18):2839–2846.
31. Kopans DB. The 2009 US Preventive Services Task Force (USPSTF) guidelines are not supported by science: the scientific support for mammography screening. *Radiol Clin North Am* 48(5):843–857.
32. https://www.washingtonpost.com/archive/lifestyle/wellness/1989/07/04/mammogram-recommendation-draws-fire/65a31f1f-e255-4fff-8747-26d811b560f9/?utm_term=.2db4c53c48e7. Accessed January 19, 2019.
33. Kopans DB, Halpern E, Hulka CA. Statistical power in breast cancer screening trials and mortality reduction among women 40–49 with particular emphasis on the national breast screening study of Canada. *Cancer* 1994;74:1196–1203.
34. Fletcher SW, Black W, Harris R, Rimer BK, Shapiro S. Report of the international workshop on screening for breast cancer. *J Natl Cancer Inst* 1993;85:1644–1656.
35. House Committee on Government Operations. Misused science: the national cancer institutes elimination of mammography guidelines for women in their forties. Union Calendar No. 480. House Report 103–863. October 20, 1994.
36. Kopans DB. The breast cancer screening controversy and the national institutes of health consensus development conference on breast cancer screening for women ages 40–49. *Radiology* 1999;210(1):4–9.
37. Hendrick RE, Smith RA, Rutledge JH, Smart CR. Benefit of screening mammography in women ages 40–49: a new meta-analysis of randomized controlled trials. *Monogr Natl Cancer Inst* 1997;22:87–92.
38. Amir Q, Vincenza S, Katherine S, Mark A, Kevin BW, Douglas KO, for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Screening mammography for women 40 to 49 years of age: a clinical practice guideline from the American college of physicians. *Ann Int Med* 2007;146;511–515.
39. http://www.acpinternist.org/archives/2012/05/policy.htm. Accessed January 19, 2019.
40. US Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2009;151(10):716–726.
41. Siu AL and the U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med* 2016;164(4):279–296.
42. Personal Communication from panel member James Michaelson, PhD. 2019.
43. Oeffinger KC, Fontham ET, Etzioni R, et al. Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. *JAMA* 2015;314(15):1599–1614.
44. Hendrick RE, Helvie MA. USPSTF guidelines on screening mammography recommendations: science ignored. *Am J Roentgenol* 2011;196:W112–W116.

45. DeSantis CE, Fedewa SA, Goding Sauer A, Kramer JL, Smith RA, Jemal A. Breast cancer statistics, 2015: convergence of incidence rates between black and white women. *CA Cancer J Clin* 2016;66(1):31–42.
46. Wolfe JN. Breast patterns as an index of risk for developing breast cancer. *AJR* 1976;126:1130–1139.
47. Baker LH. Breast Cancer Detection Demonstration Project: five-year summary report. *CA Cancer J Clin* 1982;32(4):194–225.
48. Meyer JE, Kopans DB, Stomper PC, Lindfors KK. Occult breast abnormalities: percutaneous preoperative needle localization. *Radiology* 1984;150:335–337.
49. Eddy DM, Hasselblad V, McGivney W, Hendee W. The value of mammography screening in women under age 50 years. *JAMA* 1988;259(10):1512–1519.
50. Moskowitz M. Screening for breast cancer. *JAMA* 1977;238(3):213.
51. Moskowitz M, Gartside P, Gardella L, de Groot I, Guenther D. Special lecture: the breast cancer screening controversy: a perspective. *AJR Am J Roentgenol* 1977;129(3):537–543.
52. Bailar JC. Mammography: a contrary view. *Ann Intern Med* 1976;84:77–84.
53. Feig SA. Assessment of the hypothetical risk from mammography and evaluation of the potential benefit. *Radiol Clin North Am* 1983;21(1):173–191.
54. Feig SA, Shaber GS, Schwartz GF, et al. Thermography, mammography, and clinical examination in breast cancer screening. Review of 16,000 studies. *Radiology* 1977;122(1):123–127.
55. Zhang Q, Qbrukilacchio TJ, Ang L, et al. Coregistered tomographic X-ray and optical breast imaging: initial results. *J Biomed Optics* 2005;10:1–9.
56. Mettler FA, Upton AC, Kelsey CA, Rosenberg RD, Linver MN. Benefits versus risks from mammography: a critical assessment. *Cancer* 1996;77:903–909.
57. Logan WW (ed.) *Breast Carcinoma: The Radiologist's Expanded Role*. New York, NY: Wliey; 1977.
58. Tabar L, Haus AG. Processing of mammographic films: technical and clinical considerations. *Radiology* 1989;173:65–69.
59. Tabar L, Fagerberg G, Duffy S, Day N, Gad A, Grontoft O. Update of the Swedish two-county program of mammographic screening for breast cancer. *Radiol Clin North Am* 1992;30:187–210.
60. Sickles EA, Doi K, Genant HK. Magnification film mammography: image quality and clinical studies. *Radiology* 1977;125:69–76.
61. Sickles EA, Weber WN, Galvin HB, Ominsky SH, Sollitto RA. Baseline screening mammography: one vs. two views per breast. *AJR* 1986;147:1149–1153.
62. Sickles EA. Periodic mammographic follow-up of probably benign lesions: results of 3184 consecutive cases. *Radiology* 1991;179:463–468.
63. Tabár L, Fagerberg CJ, Gad A, et al. Reduction in mortality from breast cancer after mass screening with mammography. Randomised trial from the Breast Cancer Screening Working Group of the Swedish National Board of Health and Welfare. *Lancet* 1985;1(8433):829–832.
64. Kopans DB. The breast cancer screening "Arcade" and the "Whack-A-Mole" efforts to reduce access to screening. *Semin Ultrasound CT MR* 2018;39(1):2–15. doi: 10.1053/j.sult.2017.06.002. Epub June 28, 2017. Review.
65. Chang CHJ, Nesbit DE, Fisher DR, Fritz SL, Dwyer SJ, Templeton AW, Lin F, Jewell WR. Computed tomographic mammography using a conventional body scanner. *AJR* 1982;138:553–558.
66. Kopans DB, Meyer JE. Computed tomography guided localization of clinically occult breast carcinoma--the "N" skin guide. *Radiology* 1982;145(1):211–212.
67. Slanetz PJ, Jain R, Kline JL, et al. CT-guided preoperative needle localization of MR imaging-detected mammographically occult lesions. *AJR Am J Roentgenol* 1999;172:160–162.
68. Niklason LT, Kopans DB, Hamberg LM. Digital breast imaging: tomosynthesis and digital subtraction mammography. *Breast Dis* 1998;10(3–4):151–164.
69. Jong RA, Yaffe MJ, Skarpathiotakis M, et al. Contrast-enhanced digital mammography: initial clinical experience. *Radiology* 2003;228(3):842–850.
70. Lewin JM, Isaacs PK, Vance V, Larke FJ. Dual-energy contrast-enhanced digital subtraction mammography: feasibility. *Radiology* 2003;229:261–268.
71. Dodd GD, Fry, K, Delaney W. Preoperative localization of occult carcinoma of the breast. In: Wende Westinghouse Logan, eds. *Management of the Patient with Cancer*. Philadelphia: Saunders, 1966:88.
72. Frank HA, Hall FM, Steer ML. Preoperative localization of nonpalpable breast lesions demonstrated by mammography. *N Eng J Med* 1976;295:259–260.
73. Kopans DB, Deluca S. A modified needle-hookwire technique to simplify the preoperative localization of occult breast lesions. *Radiology* 1980;134:781.
74. Kopans DB, Meyer JE. The versatile spring-hookwire breast lesion localizer. *AJR* 1982;138:586–587.
75. Kopans DB, Swann CA. Preoperative imaging-guided needle placement and localization of clinically occult breast lesions. *AJR* 1989;152:1–9.
76. Kopans DB, Meyer JE, Lindfors KK, Bucchianeri SS. Breast sonography to guide aspiration of cysts and preoperative localization of occult breast lesions. *AJR* 1984;143:489–492.
77. Gallagher WJ, Cardenosa G, Rubens JR, McCarthy KA, Kopans DB. Minimal-volume excision of nonpalpable breast lesions. *AJR* 1989;153:957–961.
78. Jellins J, Kossoff G, Buddee FW, Reeve TS. Ultrasonic visualization of the breast. *Med J Aust* 1971;1:305–307.
79. Kobayshi T. Ultrasonic diagnosis of breast cancer. *Ultrasound Med Biol* 1975;1:383–391.
80. Fornage BD, Lorigan James G, Andry E. Fibroadenoma of the breast: sonographic appearance. *Radiology* 1989;172:671–675.
81. Kopans DB, Meyer JE, Lindfors KK, Bucchianeri SS. Breast ultrasound to guide aspiration of cysts and preoperative localization of occult breast lesions. *AJR* 1984;143:489–492.
82. Kopans DB, Meyer JE, Steinbock RT. Breast cancer: the appearence as delineated by whole breast water path ultrasound. *J Clin Ultrasound* 1982;10:313–322.
83. Sickles EA, Filly RA, Callen PW. Breast cancer detection with sonography and mammography: comparison using state-of-the-art equipment. *AJR* 1983;140:843–845.
84. Kolb TM, Lichy J, Newhouse JH. Occult cancer in women with dense breasts: detection with screening US - diagnostic yield and tumor characteristics. *Radiology* 1998;207:191–199.
85. Gordon PB, Goldenberg SL, Chan NHL. Solid breast lesions: diagnosis with US-guided fine-needle aspiration biopsy. *Radiology* 1993;189:573–580.
86. Berg WA, Blume JD, Cormack JB, et al. and the ACRIN 6666 Investigators. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. *JAMA* 2008;299(18):2151–2163. doi: 10.1001/jama.299.18.2151. Erratum in: JAMA 2010;303(15):1482.
87. Schmidt RA. Stereotactic breast biopsy. *CA Cancer J Clin* 1994;44(3):172–191.
88. Parker SH, Lovin JD, Jobe WE, Burke BJ, Hopper KD, Yakes WF. Nonpalpable breast lesions: stereotactic automated large-core biopsies. *Radiology* 1991;180:403–407.
89. Kopans DB, Meyer JE, Sadowsky N. Breast imaging. *N Engl J Med* 1984;310(15):960–967.
90. Sickles EA. Quality assurance: how to audit your own mammography practice. *Radiol Clin North Am* 1992;30:265–275.
91. Kopans DB. *Breast Imaging*. Philadelphia: J.B. Lippincott Co; 1989.
92. Kopans DB. Standardized mammography reporting. In *Breast Imaging*. Philadelphia: The Radiologic Clinics of North America; 30;1992:257–264.
93. El Yousef SJ, Duchesneau RH. Magnetic resonance imaging of the human breast: a phase I trial. *Radiol Clin North Am* 1984;22:859–868.
94. Slanetz PJ, Edminster WB, Yeh ED, Talele AC, Kopans DB. Occult contralateral breast carcinoma incidentally detected by breast magnetic resonance imaging. *Breast J* 2002;8:145–148.
95. Thurfjell EL, Lernevall KA, Taube AAS. Benefit of independent double reading in a population-based mammography screening program. *Radiology* 1994;191:241–244.

96. Chan H, Doi K, Vyborny CJ, Lam K, Schmidt RA. Computer-aided detection of microcalcifications in mammograms: methodology and preliminary clinical study. *Invest Radiol* 1988;23:664–671.
97. Birdwell RL, Ikeda DM, O'Shaughnessy KF, Sickles EA. Mammographic characteristics of 115 missed cancers later detected with screening mammography and the potential utility of computer-aided detection. *Radiology* 2001;219:192–202.
98. Warren Burhenne LJ, Wood SA, D'Orsi CJ, et al. Potential contribution of computer-aided detection to the sensitivity of screening mammography. *Radiology* 2000;215:554–562.
99. Miller ER, McCurry EM, Hruska B. An infinite number of laminograms from a finite number of radiographs. *Radiology* 1971;98:249–255.
100. Kopans DB. Digital breast tomosynthesis from concept to clinical care. *AJR Am J Roentgenol* 2014;202(2):299–308.
101. Rafferty EA, Georgian-Smith D, Kopans DB, Wu T, Moore R. Eliminating the fake out: comparison of full-field digital tomosynthesis in distinguishing mammographic abnormalities from superimposition of normal breast structures. Presented at the Radiological Society of North America 88th Scientific Assembly, November 2003.
102. Rafferty EA, Kopans DB, Georgian-Smith D, et al. Comparison of full-field digital tomosynthesis and conventional two view film screen mammography in lesion detection and assessment of lesion conspicuity [abstract]. In: Abstracts of the 103rd Annual Meeting of the American Roentgen Ray Society. San Diego, CA, May 4–9, 2003.
103. Rafferty EA, Georgian-Smith D, Kopans DB, et al. Evaluation of the call-back rate for screening mammography using full-field digital tomosynthesis versus conventional film-screen mammography. ARRS annual meeting, 2003.
104. Wu T, Stewart A, Stanton M, et al. Tomographic mammography using a limited number of low-dose cone-beam projection images. *Med Phys* 2003;30:365–380.
105. Friedewald SM, Rafferty EA, Rose SL, et al. Breast cancer screening using tomosynthesis in combination with digital mammography. *JAMA* 2014;311(24):2499–2507.
106. Kuhl CK, Schrading S, Strobel K, Schild HH, Hilgers RD, Bieling HB. Abbreviated breast magnetic resonance imaging (MRI): first postcontrast subtracted images and maximum-intensity projection-a novel approach to breast cancer screening with MRI. *J Clin Oncol* 2014;32(22):2304–2310.