



Review Article

Radiologic Approach to Screening and Management of Breast Cancer

Srikrishna C Karnatapu^{1*}, Saloni Doke², Theourrn Amalathasan¹, Thebuoshon Amalathasan¹, Brendon Bachan³, Alexander Mair³, Nancy Rodriguez¹, Ali Omeishi¹, Ayesha Khan⁴, Florin Buhas¹, Emmanuel Ogunleye¹, Sanjay Doke⁵, Nyrie Mann⁶, Animisha M. Reddy⁷, Fiyinfoluwa D. Aderibigbe¹, Ebuka Ibuoka¹

¹All Saints University School of Medicine, Hillsborough Street, Roseau, Dominica

²Spartan Health Sciences University, Spartan Drive St. Jude's Highway, Vieux Fort, Saint Lucia

³Richmond Gabriel University, St. Vincent and the Grenadines

⁴Kamineni Institute of Medical Sciences, Narkatpally, Telangana, India

⁵Associate Professor of General Surgery, MGM Institute of Health Sciences, Navi Mumbai, India

⁶Saint James School of Medicine, Anguilla

⁷Apollo Institute of Medical Sciences, Hyderabad, India

*Corresponding author: Srikrishna Chanakya Karnatapu, All Saints University School of Medicine, Hillsborough Street, Roseau, Dominica

Citation: Karnatapu SC, Doke S, Amalathasan T, Amalathasan T, Bachan B, et al. (2022) Radiologic Approach to Screening and Management of Breast Cancer. Ann Case Report. 7: 967. DOI: 10.29011/2574-7754.100967

Received Date: 22 September 2022; Accepted Date: 23 September 2022; Published Date: 27 September 2022

Abstract

Breast cancer screening reduces breast cancer-related mortality. Early detection is necessary for less aggressive treatment. However, current screening techniques are nowhere near perfect owing to high false-positive rates and limited sensitivity. Novel techniques in breast imaging may soon play a vital role in the screening of breast cancer: digital breast tomosynthesis contrast material-enhanced spectral mammography, molecular breast imaging, MRI, and ultrasound. Radiomics and artificial intelligence have the potential to improve screening strategies. Also, non-imaging-based screening tests like liquid biopsy and breathing tests may restore the screening landscape. This article gives an overview of the major controversies in several key areas of breast cancer management. Important studies that have contributed to breast cancer treatment in the field of surgery, breast screening, radiotherapy and chemotherapy are highlighted.

Keywords: Breast cancer management; Breast cancer screening

Introduction

Breast cancer is the most common cancer-affecting women globally. Studies have shown that approximately 2 million women are diagnosed yearly [1]. Breast cancer is the second major

cause of cancer-related mortality in the United States [2]. The prevalence of breast cancer rises at a rate of 0.4% yearly, with over a million cases estimated for diagnosis globally by 2040 [1]. Many observational studies and randomized controlled trials have shown that regular screening mammography can reduce mortality of breast cancer substantially [3, 4].

Early detection and improved treatments have been associated with a drastic reduction in mortality rate of breast cancer [5]. In the last decade, public enlighten and education on the heterogeneous nature of breast cancer via classic histopathological features have been refined by seminal papers using gene-expression profiling techniques [6]. Studies revolving around microarray-based gene-expression studies have shown that there are varying groups of breast cancer with distinct risk factors, molecular features, clinical presentation and response to adjuvant therapies [7, 8]. Advances in chemotherapy, radiotherapy and surgery, as well as the advent of modern screening techniques has allowed for an individualized treatment for patients with breast cancer.

Screening Recommendations

Mammography

Mammography is the mainstay of breast cancer screening. The sensitivity and specificity of mammography is in the range of 77-95% and 94-97% respectively [9]. Mammographic screening is linked to a reduction in breast cancer mortality. An analysis of eight randomized controlled trials (RCTs) beginning in the 1960s showed that the relative risk of breast cancer mortality reduced by 19% [10]. On the other hand, the risk of reduction in mortality varies based on the age of screening. Women in their 40s and 60s have their risk of mortality reduced by 15% and 32% respectively [11].

Screening recommendations vary according to institution and country. In 2009 for instance, the United States Preventive Services Task Force updated its recommendations on mammography to a biannual routine starting at 50 years of age [12]. An American study showed a slight reduction in screening mammography in women aged 40-49 immediately after the publication of the USPSTF guidelines. It is important to note that there was an increase in the screening rate for this group in the following two years [13] and while many European countries and Australia adhere to these recommendations; current guidelines from several American organizations recommend that mammography be done on a yearly basis starting at the age of 40.

Although screening by mammography has increased the detection of early invasive cancers and ductal carcinoma in situ (DCIS), there has been no dramatic changes in the rates of advanced cancer within the last three decades. Data analysis from the Surveillance, Epidemiology and End results (SEER) program conducted by the National Cancer Institute for Breast Cancer Screening between 1979 and 2008 showed a disturbing increase of 122 early breast cancers per 100,000 women. On the other hand, there was an 8% decrease in late-stage cancers within that period [14]. This discovery supports the theory that mammography screening detects certain cancers that would not progress to an invasive form.

Breast Ultrasound

Breast screening ultrasonography is mainly indicated for women who possess dense fibro glandular tissue with lower mammographic detection rates. Mammography is usually less sensitive in dense breasts, sometimes reducing as low as 30-48% [15, 16]. Dense breasts usually have at least 50% glandular tissue in mammography (American College of Radiology [ACR] category 3 & 4).

Breast ultrasonography is also recommended by the ACR, alongside mammography in women with a high risk of developing breast cancer who cannot withstand an MRI. Women considered high risk are those with a mutation in the BRCA gene or women who are related to a BRCA carrier, women who have undergone a chest irradiation between the ages of 10 and 30, and women who have at least a 20% lifetime risk of breast cancer [17].

According to multicenter research (ACRIN 6666 trial) which evaluated ultrasound in women at very high risk of breast cancer, screening ultrasound was able to detect 3.7 more cancers per 1000 screens in this group [18]. Six studies were done between 1995 and 2004 to evaluate screening ultrasonography in women with an average risk of breast cancer. These six studies had 42,838 examinations, and 150 additional cancers were detected on breast ultrasound only in 126 women. 90% of these women had heterogeneously dense or dense parenchyma [19]. This supports the view that breast ultrasonography screening is beneficial in women with dense breast.

The Role of MRI

No randomized trial has been conducted to determine the role of MRI in reducing breast cancer mortality [20]. Mammography screening combined with MRI has a higher sensitivity (90-100%) in high-risk patients compared with mammography alone (25-59%). However, a lower specificity exists with the combined method (73-93%) [21]. Based on nine trial results, in 2007, the ACS recommended annual screening MRI to supplement annual screening mammography for women who have a high risk of breast cancer [22].

The Society of Breast Imaging and the American College of Radiology in 2010 recommended a yearly MRI and mammography in BRCA ½ carriers beginning at 30 years of age. A similar recommendation applies for in women with 20% or a high lifetime risk of breast cancer. Women who have had a chest irradiation in the past should begin annual MRI screening and mammography at least 8 years after receiving treatment but not before 25 years of age. For women who have a history of breast cancer, biopsy-proven lobular neoplasia, or ovarian cancer, MRI and annual mammography should be considered from the time of diagnosis [23].

Breast CT

Contrast-enhanced computed tomography (CE-CT) is a very sensitive imaging modality that supplements ultrasonography and mammography. Medical researchers have evaluated the ability of computed tomography to distinguish malignant tumors from benign tumors. However, due to its relatively low specificity and high spatial resolution, contrast-enhanced computed tomography is adequate for evaluating extension of tumor within the breast and for detecting lesions that are not detected by other methods. Helical CT technology reduces exposure to x-ray compared to conventional CT and promotes rapid scans without gaps [24]. The multi detector-row CT, which enables high spatial resolution with faster scanning than helical CT, will widen CT role in breast cancer management.

Presently, women with early-stage breast cancer can choose between mastectomy, local therapy, or breast conserving treatment (BCT). To select candidate eligible for BCT, it is essential to conduct a preoperative assessment of tumor extension. This will include extensive intraductal component, multicentricity, and daughter lesions in the breast [25].

Resection margins without tumors are associated with highly effective local control for patients opting for BCT [26]. Multiple resections and the anxiety that accompany it could be minimized if there were better methods of defining the extent of tumor prior to surgery. Micro calcifications on mammography [27] and dilated ducts on ultrasound [28] are typically discovered on EIC, but ultrasound and mammography do not have much value in cases without these findings. The sensitivity of mammography for EIC detection is reported to be 41%-81%. Mammography often does not detect multicentricity [27, 28]. This information may be provided by CE-CT.

Is digital breast tomosynthesis a replacement for abnormal mammography?

Digital breast tomosynthesis (DBT) is a modern technology that produces three-dimensional images with reconstruction into slices, ultimately minimizing the effect of overlapping mammary glands, especially in women with breast dense parenchyma. DBT makes significant improvement to accuracy, mainly attributed to the reduction of false-positive interpretations [29, 30].

According to a recent systematic review involving 2475 female subjects from 11 studies, an analysis of tomosynthesis for breast cancer screening and diagnosis showed that the specificity and sensitivity of tomosynthesis ranged from 54% to 100% and 69% to 100% respectively. The researchers also found that a one-view tomosynthesis was not necessarily superior to two-view digital mammography and that there was inconclusive evidence for superiority of two-view tomosynthesis [31].

Advances in Radiotherapy

Radiotherapy has improved the overall survival of breast cancer patients after breast cancer surgery [32]. One course of whole breast radiotherapy consists 50-50.4 Gy. This course is delivered in 25 fractions after which a 10-16 Gy is given to boost the tumor bed. Treatment is administered 5 days per week, for 5-7 weeks.

Within the last decade, many alternative radiotherapy techniques have been developed to minimize the number of fractions and normal breast tissue exposed to radiotherapy. One of these techniques is called hypo fractionation. In hypo fractionation, a large radiation dose is delivered over a short period compared to the standard radiotherapy. To date, three randomized controlled trials (UK and Canada) have shown similar cosmetic outcomes between standard regimens and hypo fractionation [33]. Fractionation, doses, and patient selection criteria are not uniform among these trials, which has precluded hypo fractionation as a first line practice.

High dose of radiation is delivered by accelerated partial breast irradiation (APBI) to the postsurgical cavity, saving healthy breast tissue from radiation. Accelerated partial breast irradiation can be delivered as brachytherapy, external beam conformal therapy and intraoperative radiotherapy.

Conclusion

Breast cancer screening within the next decade will progress beyond the conventional familiar tools such as MRI, ultrasound, and mammography. There will be enhancement of various new imaging options, combined with neural networks and/or artificial intelligence by the integration of modern screening protocols targeted at precision and more personalized medicine. Supplemental and primary screening tools will progress beyond screening mammography and MRI or ultrasound for women with dense breast tissues and elevated risk of breast cancer. There is need for new screening benchmarks as well as development of cancer registries to enhance tracking efficacy of screening tools and treatments.

References

1. Cancer Tomorrow. International Agency for Research on Cancer.
2. Breast Cancer Statistics. Centers for Disease Control and Prevention.
3. Simon S (2019) Facts & Figures 2019: US Cancer Death Rate Has Dropped 27% in 25 Years. American Cancer Society.
4. Tabár L, Dean PB, Chen TH, Yen AM, Chen SL, et al. (2018) The incidence of fatal breast cancer measures the increased effectiveness of therapy in women participating in mammography screening. *Cancer*, 125: 515-523.

5. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, et al. (2005) Effect of screening and adjuvant therapy on mortality from breast cancer. *The New England journal of medicine*, 353: 1784-1792.
6. Prat A, Perou CM (2011) Deconstructing the molecular portraits of breast cancer. *Molecular oncology*, 5: 5-23.
7. Sotiropoulos C, Pusztai L (2009) Gene-expression signatures in breast cancer. *The New England journal of medicine*, 360: 790-800.
8. Weigelt B, Baehner FL, Reis-Filho JS (2010) The contribution of gene expression profiling to breast cancer classification, prognostication and prediction: a retrospective of the last decade. *The Journal of pathology*, 220: 263-280.
9. Humphrey LL, Helfand M, Chan BK, Woolf SH (2002) Breast cancer screening: a summary of the evidence for the U.S. Preventive Services Task Force. *Annals of internal medicine*, 137: 347-360.
10. Gøtzsche PC, Jørgensen KJ (2013) Screening for breast cancer with mammography. *The Cochrane database of systematic reviews*, 6: CD001877.
11. Pace LE, Keating NL (2014) A systematic assessment of benefits and risks to guide breast cancer screening decisions. *JAMA*, 311: 1327-1335.
12. US Preventive Services Task Force (2009) Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Annals of internal medicine*, 151: 716-236.
13. Wang AT, Fan J, Van Houten, HK, Tilburdt JC, Stout NK, et al. (2014) Impact of the 2009 US Preventive Services Task Force guidelines on screening mammography rates on women in their 40s. *PloS one*, 9: e91399.
14. Bleyer A, Welch HG (2012) Effect of three decades of screening mammography on breast-cancer incidence. *The New England journal of medicine*, 367: 1998-2005.
15. Mandelson MT, Oestreich N, Porter PL, White D, Finder CA, et al. (2000) Breast density as a predictor of mammographic detection: comparison of interval- and screen-detected cancers. *Journal of the National Cancer Institute*, 92: 1081-1087.
16. Kolb TM, Lichy J, Newhouse JH (2002) Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. *Radiology*, 225: 165-175.
17. Mainiero MB, Lourenco A, Mahoney MC, Newell MS, Bailey L, (2013) ACR Appropriateness Criteria Breast Cancer Screening. *Journal of the American College of Radiology: JACR*, 10: 11-14.
18. Berg WA, Zhang Z, Lehrer D, Jong RA, Pisano ED, et al. (2012) Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. *JAMA*, 307: 1394-1404.
19. Berg WA (2004) Supplemental screening sonography in dense breasts. *Radiologic clinics of North America*, 42: 845-51.
20. Feig S (2010) Cost-effectiveness of mammography, MRI, and ultrasonography for breast cancer screening. *Radiologic clinics of North America*, 48: 879-891.
21. Warner E, Messersmith H, Causer P, Eisen A, Shumak R, et al. (2008) Systematic review: using magnetic resonance imaging to screen women at high risk for breast cancer. *Annals of internal medicine*, 148: 671-679.
22. Saslow D, Boetes C, Burke W, Harms S, Leach MO, Lehman, et al, (2007) American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA: a cancer journal for clinicians*, 57: 75-89.
23. Lee CH, Dershaw DD, Kopans D, Evans P, Monsees B, et al. (2010) Breast cancer screening with imaging: recommendations from the Society of Breast Imaging and the ACR on the use of mammography, breast MRI, breast ultrasound, and other technologies for the detection of clinically occult breast cancer. *Journal of the American College of Radiology: JACR*, 7: 18-27.
24. Muramatsu Y, Akiyama N, Hanai K (1995). Medical exposure in lung cancer screening by helical computed tomography. *Jpn J Radiol Technol*. 152: 1-8.
25. Schnitt SJ, Connolly JL, Khettry U, Mazoujian G, Brenner M, et al. (1987) Pathologic findings on re-excision of the primary site in breast cancer patients considered for treatment by primary radiation therapy. *Cancer*, 59: 675-681.
26. Gage I, Schnitt SJ, Nixon AJ, Silver B, Recht A, et al. (1996) Pathologic margin involvement and the risk of recurrence in patients treated with breast-conserving therapy. *Cancer*, 78: 1921-1928.
27. Healey EA, Osteen RT, Schnitt SJ, Gelman R, Stomper PC, et al. (1989) Can the clinical and mammographic findings at presentation predict the presence of an extensive intraductal component in early stage breast cancer?. *International journal of radiation oncology, biology, physics*, 17: 1217-1221.
28. Tsunoda-Shimizu H, Ueno E, Tohno E, et al (1996) Ultrasonographic evaluation for breast conservative therapy. *Jpn J Breast Cancer*, 11:649- 655.
29. Bernardi D, Ciatto S, Pellegrini M, Tuttobene P, Fanto' C, et al. (2012). Prospective study of breast tomosynthesis as a triage to assessment in screening. *Breast cancer research and treatment*, 133: 267-271.
30. Michell MJ, Iqbal A, Wasan RK, Evans DR, Peacock C, et al. (2012). A comparison of the accuracy of film-screen mammography, full-field digital mammography, and digital breast tomosynthesis. *Clinical radiology*, 67: 976-981.
31. García-León FJ, Llanos-Méndez A, Isabel-Gómez, R (2015) Digital tomosynthesis in breast cancer: A systematic review. *Radiologia*, 57: 333-343.
32. Darby S, McGale P, Correa C, Taylor C, Arriagada R, et al. (2011). Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet (London, England)*, 378: 1707-1716.
33. START Trialists' Group, SM Agrawal RK, Aird EG, Barrett JM, Barrett-Lee PJ, et al. (2008). The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial. *The Lancet. Oncology*, 9: 331-341.