

SYSTEMIC REVIEW

Evaluation of Different Diagnostic Modalities in Breast Cancer - A Systematic Review

JAVAIRIA RAFIQUE¹, SYED AMIR GILANI², SYEDA KHADIJA-TUL-SUGHRA MURRIUM³, TAUSEEF AHMAD⁴, AIMA GILANI⁵, WALEED JAMEEL⁶

The University of Lahore 1 - KM Defence Road, Lahore Pakistan.

Correspondence to Dr. Syed Amir Gilani, E-mail: profgilani@gmail.com, +92321-4726791

ABSTRACT

Background: Most common cancer in women that is 32 % of all newly diagnosed cancers is breast cancer. Breast cancer develops when cells of your breast multiply and divide uncontrollably, resulting in a lump of tissue known as a tumor. Screening type of mammography has played a key role in reducing breast cancer mortality.

Aim: To evaluate role of three diagnostic modalities in the breast cancer.

Methods: The data bases PubMed and other search engines were searched with the key words: breast cancer, mammography, ultrasound, MRI, sensitivity, specificity, from 1999 to 2020. For inclusion and exclusion of studies we screened the most relevant and irrelevant outcomes. Studies having information of breast cancer, mammography, ultrasound, MRI, sensitivity, specificity was included. Meta-analysis were excluded.

Results: In total 39 studies with breast cancer the overall mean sensitivity of ultrasound, mammography and MRI were 76.81, 74 and 88.18 respectively. Overall mean specificity of ultrasound, mammography and MRI 79.65, 87 and 75.17 respectively. SD of Sensitivity and Specificity of MRI is 10.57 and 16.27. SD of Sensitivity and Specificity of mammography is 20.92 and 16.43. SD of Sensitivity and Specificity of ultrasound is 23.71 and 20.05.

Conclusions: MRI, because of its limitations cannot be used routinely for diagnosing breast cancer. Mammography is readily available screening tool for breast cancer however it has low sensitivity for diagnosis of breast cancer and requires complimentary imaging. Ultrasound can be used as baseline modality as it saves time and safe in all conditions.

Keywords: Breast Cancer, Mammography, Ultrasound, MRI, Sensitivity, Specificity

INTRODUCTION

Breast cancer is a complex disease with an increasing amount of biologic categories. Many factors affect the prognostic and causative significance of this variety, including the observation that variations in clinical outcomes commonly coincide with race¹. Most common cancer in women that is 32% of all newly diagnosed cancers is breast cancer². The emergence of the new breast lumps, pain in bone, chest, abdomen, dyspnea, and frequent headaches are all signs of breast cancer recurrence, according to American Society of Clinical Oncology (ANCO) guidelines for breast cancer follow-up and care³. Despite advancements in detection and treatment of metastatic breast cancer, mortality remains elevated due to growth of the therapy-resistant cancer cells, which limits existing therapies⁴. Invasive ductal carcinoma (50% -75% of patients) is the most frequent breast cancer histology, followed by invasive lobular carcinoma (5%-15% of patients), mixed ductal/lobular carcinomas, and other rarer histologies⁵. DCIS is considered to be a forerunner of invasive ductal carcinoma based on molecular, epidemiological, and pathological studies⁶.

Screening type of mammography played key role in reducing breast cancer mortality. By picking out a subset of cancers diagnosed formerly reach clinical presentation, intervention is more likely to result in long-term survival⁷. Although mammography is most used to detect breast cancer, it is spotted that not all cancers can be seen on mammographic images⁸. USG plays adjunctive role to mammography in aiding classification of breast tumors; however, a breast USG examination is more useful and safer than mammography. Breast USG has mainly been proven beneficial in distinguishing cysts from solid tumors⁹. The breast examination by US started from 1951 with an optimistic opinion that US would replace mammography eventually in detecting breast cancer. However, with more comprehensive studies, it illustrates that US is only valid for the discrimination between cysts and solid masses¹⁰. CT gives incidental finding when scanning for cardiac or respiratory diseases¹¹. At early stage when treatment is easy, MRI is capable of diagnosis. Because MRI is extremely sensitive for the detection of cancer, it is used as a screening method for patients with high risk of development of the breast cancer¹².

Resources material and methodology: Data was searched on PubMed and other search engines with keywords Breast cancer, Mammography, Ultrasound, MRI, sensitivity and specificity. It includes studies from 1999 to 2020. Those studies that contain relevant outcomes were included, all other studies including meta-analysis were excluded. A total of 196 articles was searched. After removing 58 duplicate articles 138 were left. 89 of them were excluded due to irrelevant data and 10 studies were rejected due to insufficient detail. Flow chart summarizes the reviewed flow records. Overall mean of sensitivity and specificity of all three modalities was calculated.

DISCUSSION

A study performed by Subbhuraam Vinitha Sree et al showed that in women, the breast cancer is 2nd largest reasons of death. When breast's cells begin to grow out of fraction and enter the neighboring tissues and spread the entire physique, it's known as breast cancer. Mammography is one of the most effective and widely utilized screening and detection techniques for breast cancer today. Various imaging modalities have been used to expand accuracy of the breast cancer diagnosis. Breast cancers in high-risk patients have been detected using ultrasound and magnetic resonance imaging. Electrical impedance imaging and nuclear medicine approaches have recently become popular for breast cancer detection and screening¹³. Of 196 high-risk ladies, 6 invasive breast cancers with 1 non-invasive breast cancer were discovered. 5 of invasive tumors were found in the mutation carriers and 6th was found in woman who previously diagnosed with breast cancer. Invasive or noninvasive breast cancer was found to be present in 6.2% of the 96 mutation bearers. MRI detected all 6 invasive tumors, which stood all smaller than 1.0 cm in diameter and node-negative. Just 3 invasive malignancies found using ultrasound, 2 on mammography, and 2 on physical examination. Additional MRI to more widely accessible trinity of mammography, ultrasound and breast examination revealed 2 more invasive breast cancers that might be overlooked otherwise¹⁴.

The breast ultrasonography is a useful tool in conjunction with mammography. The combination of 2 screening tests has 92% sensitivity and a 96% specificity¹⁵. Lei Yang et. Al performed a study in which 23 investigations stood considered, including

Received on 24-07-2021

Accepted on 14-12-2021

twelve studies that used S-US screening following a -ve MAM result with 11 joint screening readings that used together P-MAM and P-US. S-US screening could detect 96% [95% confidential intervals: 82–99%] of the occult breast cancers overlooked by MAM and identify percentage of 93 (9% confidential intervals: 89 to 96%) of healthy females, according to meta-analyses, with CDR of 3.0/1000 (95% confidential intervals: 1.8/1000 to 4.6/1000), RR of 8.8% (95% confidential intervals: 5.0 to 13.4% (95% confidential intervals: 2.7 to 5.4%), ProC of 73.9% (95% confidential intervals: 49 to 93.7%) and ProNNIC of 70.9% (95% CIs: 46.0 to 91.6%). P-US screening resulted in recollection of considerably women with the positive screening findings [1.5% (95% confidential intervals: 0.6 to 2.3%), $P = 0.001$] and the detection of suggestively more invasive malignancies [16.3% (95% CIs: 10.6 to 22.1%), $P = 0.001$]. Other performance measures, such as Sensitivity, Specificity, CDR, BR, and ProNNIC, did not show any significant differences between the two screening methods¹⁶. Huay-Ben Pan in his study explained that ultrasonography (US) is now the standard of care for detection plus characterization of breast lesions, as well as assessment of the breast cancer. However, a few single-center cohort study examining breast US in context of screening have been found. Regardless of the fact that mammography is considered the major approach for screening; it has a unique ability to identify micro calcifications. The study ACRIN 6666 shown that the US is good for detecting mass or lesions, especially in the dense breast populations. Common USG findings in Ductal carcinoma in situ (DCIS) included hypo-echoic lobular area, lesion with ductal extension and dilatation, and hypoechoic nodular mass with dilated lactiferous duct primary to retro areolar area, totally of which stood likely related to cancer's nuclear grade. CAD, ABUS, elastography, and micro bubbles in ultrasound with contrast enhancement are examples of computer programmes that have created and agreed for the use in clinical training. Furthermore, progressing competency of early breast cancer diagnosis requires standardize scanning, increasing computer technology deployment and familiarity with picture of DCIS¹⁷. A study performed by Constance D Lehman et. Al described that the usage of breast MRI is fast raising as this fascinating technology develops and more evidence becomes available to support the tool's effectiveness in specific patient categories. When compared to other imaging modalities, breast MRI is extremely sensitive and has an adequate specificity. MRI has not been researched for its impact on breast cancer recurrence or death, despite the fact that it clearly detects tumors that are undetectable by mammography, ultrasound, or clinical breast exam. It is necessary to do cost-effectiveness analyses of MRI in various patient populations. There is still a lot of effort to be done to improve breast MRI's application and performance. It is necessary to do research to determine the best acquisition procedures¹⁸.

The two groups were compared in a study performed by Georgia Tsina et al on basis of many factors. Objective of the study was to decide if use of MRI in breast cancer screening changes early therapeutic decision. In 18% of patients, MRI showed multifocal or a multi-centric breast cancer of one side, tumor in both breasts, or larger cancer than primarily diagnosed. Most of the patients undergo second look breast ultrasound, with or without added biopsy. On basis of many parameters, the two groups were compared. The study's goal was to see if using MRI for the breast cancer screening affects initial therapeutic decision. MRI indicated a multifocal or multi-centric one-sided breast cancer, both sides tumor, one bigger disease than first diagnosed in 18% patients. The majority of the patients had second look breast ultrasonography, which may or may not have included a biopsy. An MRI exam had no effect on the number of mastectomies performed. When an MRI was conducted, the utilization of neoadjuvant chemotherapy increased and the percentage of reoperations reduced¹⁹.

Mammography is gold standard in breast cancer screening and diagnosis. It has a specificity of 94% and a sensibility of 40–73%, both of which are significantly reliant on breast density²⁰.

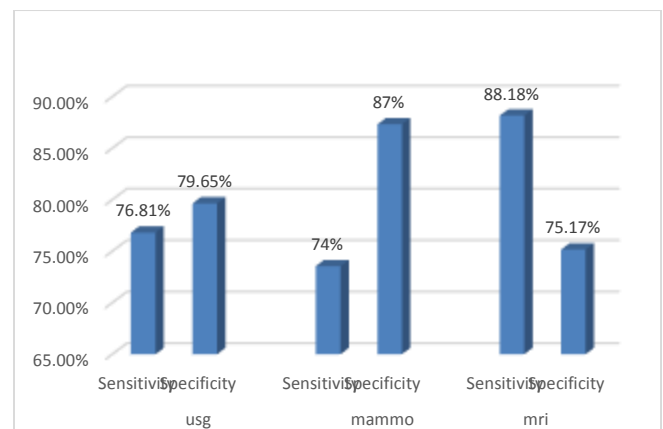
Total 2662 women received 7473 mammograms and screening ultrasound, with 110 of them having 111 breast cancer trials: 33 on mammography alone, 32 on ultrasound alone, 26 on both, and 9 on MRI after mammography and ultrasound 11 were not discovered by either imaging screens. 75 females were diagnosed of cancer out of 4814 incidence screens in 2nd and 3rd years combined. Incidence of screening ultrasound found 3.7 malignancies per 1000 screens as a supplement (95% confidence interval, 2.1 5.8; $P = .001$). Mammography with ultrasound had a sensitivity of 0.76 (95% of confidence interval: 0.65-0.85), specificity with 0.84 (95% confidence interval: 0.83-0.85), and PPV3 of 0.16. (95% CI, 0.12 0.21). 16 women (2.6%) had breast cancer, according to the MRI scans. The MRI supplementary yield was 14.7 per 1000 (95% of confidence interval: 3.5-25.9; $P = .004$). MRI and mammography plus ultrasound had a sensitivity of 1.00 (95% confidence interval: 0.79-1.00), specificity of 0.65 (95% of confidence interval: 0.61-0.69), PPV3 of 0.19 (9% of confidence interval: 0.11-0.29). Sensitivity, was 0.44 (9% CI, 0.20- 0.70, $P = .004$), Specificity was 0.84 (95% confidence interval, 0.81-0.87, $P = .001$), and PPV3 was 0.18 (95% CI, 0.08 to 0.34, $P = .98$) for mammography and ultrasonography. After negative mammography and ultrasound results, number of screens needed to detect one cancer was 127 (95% CI 99 to 167) for mammography, 234 (95% CI, 173-345) for supplemental ultrasound, and 68 (95% CI, 39-286) for MRI²¹.

CONCLUSION

Ultrasound can be used as baseline modality as it saves time and safe in all conditions.

Mammography is readily available screening device for breast cancer however because of its low sensitivity for breast cancer diagnosis it requires complimentary imaging.

MRI cannot be used as a baseline modality for diagnosing breast cancer because of its limitations. It is rarely recommended when some suspicion could not be picked up on mammography or ultrasound.



Limitations:

Ultrasound: Many cancers and calcifications are not visible on ultrasound which may be only sign of cancer in early disease.

Mammography: Mammography contains x-rays which are not safe in many conditions.

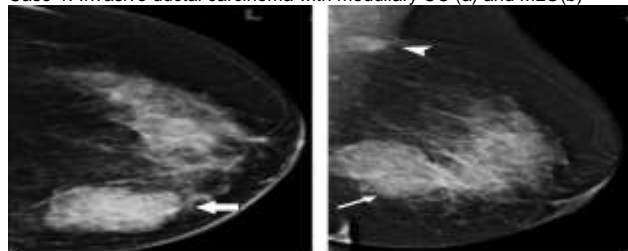
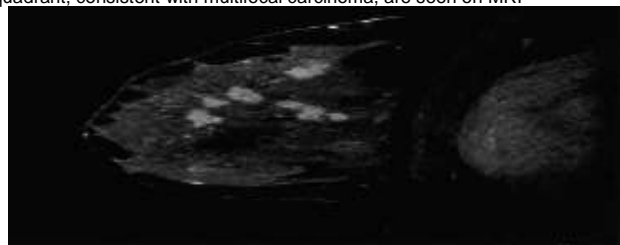
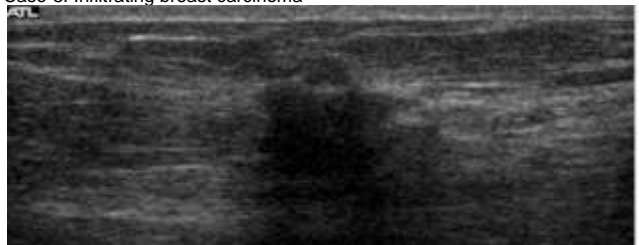
Mammography cannot be performed on underage females as it is recommended for the females of 40 or more than 40 years.

Mammography is not advised for pregnant females.

Mammography cannot be performed on lactating mothers.

MRI cannot be used as baseline modality for early diagnosis of breast cancer as it is expensive as well as time taking. MRI is not readily available modality.

Modality	Sensitivity	Specificity
Ultrasound	76.81	79.65
Mammography	74	87
MRI	88.18	75.17

Case-1: Invasive ductal carcinoma with medullary CC (a) and MLO(b)²²Case-2: Multiple heterogeneously enhancing abnormal masses in one quadrant, consistent with multifocal carcinoma, are seen on MRI²³Case-3: Infiltrating breast carcinoma²⁴

Acknowledgments: All praises to **Almighty Allah** the one Who is most deserving of thanks. He is the most glorified and exalted. I humbly bow my head before **HIM**. All respects and love for **His Holy Prophet ﷺ** Who is cleansed of all imperfection, who is the beacon of light and Knowledge. I wish to extend sincere and special thanks to my honorable supervisor and Dean Faculty of Allied Health Sciences [FAHS] Professor **Dr. Syed Amir Gilani**. I do also much appreciation to my co-supervisor **Prof. Syeda Khadija Tul Sughra** for exemplary support and encouragement. Special thanks to Mr. Tauseef Ahmad for his excellent support step by step during the data analysis.

Funding sources: There is no funding source.

Conflict of interest: There is no conflict of interest

REFERENCES

- Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D, Conway K, Karaca G, Troester MA, Tse CK, Edmiston S, Deming SL. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. *Jama*. 2006 Jun 7;295(21):2492-502.
- Kelsey JL, Bernstein L. Epidemiology and prevention of breast cancer. *Annual review of public health*. 1996 May;17(1):47-67.
- Scully OJ, Bay BH, Yip G, Yu Y. Breast cancer metastasis. *Cancer Genomics-Proteomics*. 2012 Sep 1;9(5):311-20.
- Al-Hajj M, Wicha MS, Benito-Hernandez A, Morrison SJ, Clarke MF. Prospective identification of tumorigenic breast cancer cells. *Proceedings of the National Academy of Sciences*. 2003 Apr 1;100(7):3983-8.
- Waks AG, Winer EP. Breast cancer treatment: a review. *Jama*. 2019 Jan 22;321(3):288-300.
- Polyak K. Breast cancer: origins and evolution. *The Journal of clinical investigation*. 2007 Nov 1;117(11):3155-63.
- Friedewald SM, Rafferty EA, Rose SL, Durand MA, Plecha DM, Greenberg JS, Hayes MK, Copit DS, Carlson KL, Cink TM, Barke LD. Breast cancer screening using tomosynthesis in combination with digital mammography. *Jama*. 2014 Jun 25;311(24):2499-507.
- Ma L, Fishell E, Wright B, Hanna W, Allan S, Boyd NF. Case-control study of factors associated with failure to detect breast cancer by mammography. *JNCI: Journal of the National Cancer Institute*. 1992 May 20;84(10):781-5.
- Chen DR, Hsiao YH. Computer-aided diagnosis in breast ultrasound. *Journal of Medical Ultrasound*. 2008 Jan 1;16(1):46-56.
- Kuhl CK, Schrading S, Leutner CC, Morakkabati-Spitz N, Wardelmann E, Fimmers R, Kuhn W, Schild HH. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. *Journal of clinical oncology*. 2005 Nov 20;23(33):8469-76.
- Shan J, Alam SK, Garra B, Zhang Y, Ahmed T. Computer-aided diagnosis for breast ultrasound using computerized BI-RADS features and machine learning methods. *Ultrasound in medicine & biology*. 2016 Apr 1;42(4):980-8.
- Schacht DV, Yamaguchi K, Lai J, Kulkarni K, Sennett CA, Abe H. Importance of a personal history of breast cancer as a risk factor for the development of subsequent breast cancer: results from screening breast MRI. *American Journal of Roentgenology*. 2014 Feb;202(2):289-92.
- SubbhuraamVinithaSree, Eddie Yin-Kwee Ng, Rajendra U Acharya, Oliver Faust. Breast imaging: A survey. *World J ClinOncol* 2011 April 10; 2(4): 171-178.
- Comparison of Breast Magnetic Resonance Imaging, Mammography, and Ultrasound for Surveillance of Women at High Risk for Hereditary Breast Cancer By E. Warner, D.B. Plewes, R.S. Shumak, G.C. Catzavelos, L.S. Di Prospero, M.J. Yaffe, V. Goel, E. Ramsay, P.L. Chart, D.E.C. Cole, G.A. Taylor, M. Cutrara, T.H. Samuels, J.P. Murphy, J.M. Murphy, and S.A. Narod. *Journal of Clinical Oncology*, Vol 19, No 15 (August 1), 2001: pp 3524-3531.
- B. T. A. Tejerina, B. T. Antonio, D. R. Francisco, and G. A. de Lara, "Breast imaging: how we manage diagnostic technology atmultidis," *Journal of Oncology In press*.
- Lei Yang, Shengfeng Wang, Liwen Zhang, Chao Sheng, Fengju Song, Ping Wang, and Yubei Huang. Performance of ultrasonography screening for breast cancer: a systematic review and meta-analysis. (2020) 20:499.
- Huay-Ben Pan, The Role of Breast Ultrasound in Early Cancer Detection, *Journal of Medical Ultrasound* (2016) 24, 138-141.
- Constance D Lehman and Mitchell D Schnall, Imaging in breast cancer: Magnetic resonance imaging. *Breast Cancer Research* 2005, 7:215-219.
- Georgia Tsina and Philippe Simon, Breast Magnetic Resonance Imaging and Its Impact on the Surgical Treatment of Breast Cancer, Hindawi Publishing Corporation Obstetrics and Gynecology International Volume 2014, Article ID 632074, 5 pages.
- R. A. Smith, "The evolving role of MRI in the detection and evaluation of breast cancer," *The New England Journal of Medicine* vol. 356, no. 13, pp. 1362–1364, 2007.
- Wendie A. Berg, MD, PhD, Zheng Zhang, PhD, Daniel Lehrer, MD, Roberta A. Jong, MD, Etta D. Pisano, MD, Richard G. Barr, MD, PhD, Marcela Bo`hm-Ve`lez, MD, Mary C. Mahoney, MD, W. Phil Evans III, MD, Linda H. Larsen, MD, Marilyn J. Morton, DO Ellen B. Mendelson, MD, Dione M. Farria, MD, Jean B. Cormack, PhD, Helga S. Marques, MS Amanda Adams, MPH, Nolin M. Yeh, MS Glenna Gabrielli, BS 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*, April 4, 2012—Vol 307, No. 13.
- Michelle V. Lee, MD. Venkata S. Katabathina, MD. Michyla L. Bowerson, MD. Marina I. Mityul, MD. Anup S. Shetty, MD. Khaled M. Elsayes, MD. Aparna Balachandran, MD. Priya R. Bhosale, MD. Ann E. McCullough, MD. Christine O. Menias, MD. BRCA-associated Cancers: Role of imaging in screening, diagnosis, and management. *radiographics* 2017; 37:1005–1023.
- Elizabeth A. Morris, MD. Breast cancer imaging with MRI. *RadiolClin N Am* 40 (2002) 443 – 466.
- Chandra M. Sehgal & Susan P. Weinstein & Peter H. Arger& Emily F. Conant. A Review of Breast Ultrasound. *J Mammary Gland Biol Neoplasia* (2006) 11: 113–123.