Title: **Attributes, Performance, and Gaps in current & emerging breast cancer screening technologies**

Authors:

- Hina. M. Ismail (hina.ismail@pg.canterbury.ac.nz) – University of Canterbury, New Zealand
- Christopher G. Pretty (chris.pretty@canterbury.ac.nz) – University of Canterbury, New Zealand
- Matthew K. Signal (Matthew.Signal@tiromedical.com) – Tiro medical limited, New Zealand
- Marcus Haggers (Marcus.Haggers@tiromedical.com) – Tiro medical limited, New Zealand
- J. Geoffrey Chase (geoff.chase@canterbury.ac.nz) – University of Canterbury, New Zealand

Corresponding author:

- Hina Muhammad Ismail (hina.ismail@pg.canterbury.ac.nz) – University of Canterbury, New Zealand
- Mobile #: 0064211266910

The total number of words of the manuscript: 8070 (including references)

The number of words of the abstract: 209

The number of figures: 3

The number of tables: 2

Abstract:

Early detection of breast cancer, combined with effective treatment, can reduce mortality. Millions of women are diagnosed with breast cancer and many die every year globally. Numerous early detection screening tests have been employed. A wide range of current breast cancer screening methods are reviewed based on a series of searchers focused on clinical testing and performance. The key factors evaluated centre around the trade-offs between accuracy (sensitivity and specificity), operator dependence of results, invasiveness, comfort, time required, and cost. All of these factors affect the quality of the screen, access/eligibility, and/or compliance to screening programs by eligible women. This survey article provides an overview of the working principles, benefits, limitations, performance, and cost of current breast cancer detection techniques. It is based on an extensive literature review focusing on published works reporting the main performance, cost, and comfort/compliance metrics considered. Due to limitations and drawbacks of existing breast cancer screening methods there is a need for better screening methods. Emerging, non-invasive methods offer promise to mitigate the issues particularly around comfort/pain and radiation dose, which would improve compliance and enable all ages to be screened regularly. However, these methods must still undergo significant validation testing to prove they can provide realistic screening alternatives to the current accepted standards.

Keywords:

Mammography; Magnetic Resonance Imaging; Ultrasound; Thermography; Microwave Imaging; Elastography

1.0 Introduction

Breast cancer is a leading cause of death among women [1]. In 2012 almost 1.67 million new cases were diagnosed worldwide with approximately 324,000 and 198,000 deaths recorded in less and more developed regions, respectively [2]. Regardless of advances in treatment over the past decades, breast cancer still remains the second leading cause of cancer related death in women [3]. The American Cancer Society estimated the number of new breast cancer cases and at 234,190, with around 40,730 deaths in the United States during 2015 alone [4] . Including of these 10,000 – 12, 000 cases are invasive cancer in women less than 40 years who are not typically screened [5]. With around 3000 deaths in women aged less than 45 [6].

Breast cancer can affect both men and women of any age, but the incidence is much higher in women [7]. Several other factors increase the risk of developing breast cancer, including a family history and radiation exposure [8, 9]. The risk of breast cancer increased for women of all ages in Hiroshima and Nagasaki due to low dose radiation exposure [9]. Nulliparity, early menarche, late menopause also increase women's risk of developing breast cancer. During women's reproductive years the ovary produces steroid hormones that directly affect development and function of the breast.[10, 11].

Cancer treatments are expensive. In the United States breast cancer remains one of the most costly cancers [12]. In 2010, the United States spent approximately $16.5 billion on breast cancer treatment [13]. Reducing the cost of treatments and balancing the patients' needs with available healthcare resources is far from an easy or intuitive task. Using breast cancer related health insurance claims, Ray et al. [14] showed that increased follow up periods for breast cancer patients were associated with reduced mean monthly per patient costs. However, the cumulative costs per patient increased from US$78,882 for a follow up period of <6 months to US$443,062 for a follow up period of >36 months. Early detection of breast cancer screening not only reduces mortality rate, but also decreases overall treatment expenditure [15, 16]. Thus, screening programs for the early detection of breast cancer are key to increasing the chances of successful treatment and reducing costs.

There are several tests and examinations routinely used for the detection of breast cancer [17, 18]. To reduce breast cancer mortality rates, breast screening needs to be successful in producing a desired results [19], low cost, fast, and available without risk to women of all ages. This review provides an overview of current breast cancer detection techniques in light of these requirements. In particular, the novelty of the article is based on around a review of multiple modalities and the use of a range of key features including cost, invasiveness and comfort/compliance metrics, which all play a role in the quality and compliance, and thus efficacy of screening programs.

2.0 Current methods of screening for breast cancer

2.1 Mammography

Over the years, X-ray mammography (XM) has become the primary, non-self-exam screening technique for breast cancer [6, 20]. Mammography forms images of the breast density by passing X-rays through the tissue as shown in Figure 1. However, exposure to this ionising radiation may be harmful and possibly cause cancer itself [21]. Risk is one of the reasons it is not recommended for screening in women under 40 years [22].

Mammography can provide benefit to women aged 40 to 49 years. Mortality rates at these ages can be reduced up to 15% after 14 years of follow up [23]. However, women who started screening every second year at age 50, until 69 years of age, have shown more benefit with less harm [24, 25], and thus this age range and interval are more commonly used in national screening programs. Due to the extensive validation and use, mammography is the most widely used and well-accepted imaging modality for breast screening [26].

However, mammography has also been criticized for a number of reasons. Thornton and colleagues listed physical, emotional, social, financial, or psychological harm caused by mammograms [27]. Additionally, to get the best possible images of breast tissue must be squeezed between two plates as the image is taken [28]. Many women found this compression painful and uncomfortable [29]. Several women experienced enough pain that it affected their decision to attend another examination [30-34] reducing compliance and the likelihood at early detection.

Fig. 1. (a) Mammogram Equipment (National Cancer Institute by Alan Hoofring, 2003)

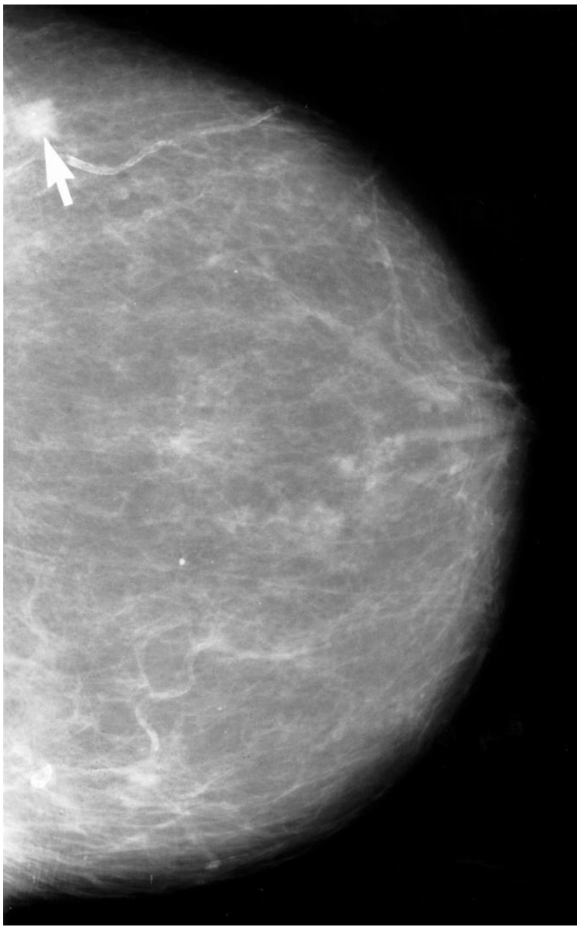

Fig. 1. (b) Mammogram showing a small cancerous lesion as well as calcific deposits in veins (National Cancer Institute, March 1991)

Mammographic breast density is a strong predictor of breast cancer [35-38]. However, younger women naturally have denser breast tissue and it can be difficult to detect cancer with mammography [39], which can lead to misdiagnosis and increased false positive/negative rates [40]. Mammography with adjunctive ultrasonography results in higher rate of cancer detection in young or women with dense breast, but also increases the number of false positive results. The Japan Strategic Anti-cancer Randomized Trial (J-START) investigates sensitivity and specificity with 36,000 women in each group (XM and XM+US) and about 180 cancers per group. Sensitivity rises to 90% with added ultrasound but specificity drops to 87%. Thus, positive predictive value is likely poor given low incidence rates [41].

This modality is highly dependent on equipment, operator, radiographer, and as well as breast density. False-negative rates for mammography range from 4% to 34% [42-46]. Table 1 provides a summary of published performance results for mammography. Research has shown that the sensitivity of mammography for detecting multiple malignant foci is often less than 50% [21, 47, 48]. Due to radiation exposure and false positive results, both patients and physicians are concerned about using mammography to screen women below 45 [49]. As a result of these limitations, many unnecessary biopsies have resulted from low specificity of mammography [50].

Finally, mammography has been proven and established in terms of its detection of ductal carcinoma in situ (DCIS) [51].It is also established in terms of potentially differentiating the micro-calcifications that can occur in breast tissue from cancerous lesions. However, as noted, these difficult cases are also a function of operator and radiologist experience and capability, even though the physics of the modality enables their detection and diagnosis.

The financial costs of breast cancer are high. Several studies show breast cancer screening for women aged 50-70 years is cost-effective and costs range between $13,200 and $28,000 per year of life saved [52-56]. In New Zealand, mammogram costs approximately $180 [57]. However, for women below 45 years the number of false positives and cost for extra examinations, unnecessary biopsies, and other effects [58-60], means it is not cost effective. For all these reasons, continuous efforts have been made by researchers to explore alternative imaging modalities for breast cancer screening and diagnosis.

Mammography usually takes only one picture, across the entire breast, in two directions: top to bottom and side to side. Digital breast tomosynthesis is a technique that creates 3-dimensional picture of the breast to improve breast cancer detection especially with dense breast [61, 62]. Digital breast tomosynthesis has improved on the limitations of traditional digital mammography by increasing cancer detection and decreasing false-positive examinations [63]. Additionally, a digital breast tomosynthesis can reduce the pain and displeasure that occur from compressing breast between two plates while taking mammogram. For these reasons digital breast tomosynthesis can replace traditional mammogram in breast cancer screening [64]. The major disadvantage of digital breast tomosynthesis is prolonged time and more radiation exposure at twice that of standard mammography, although it reduces the need for repeat mammographic images and increased dose from those tests. In addition, it leads to increased recommendations for biopsies, increasing detection, but also cost when cancer is not present [65].

However, overall, it is important to note that mammography is still the only proven and accepted wide scale screening modality.

2.2 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) has been progressively integrated into breast imaging and is used to detect lesions [66]. A magnetic field is created to align all the protons in the body in a single direction. Radio waves are sent from a scanner to perturb this alignment. As the protons realign, they emit radio waves which used to determine the molecule type and location. These radio signals are analysed and converted into an image [67]. When applied to soft tissue, MRI can be used to generate highly detailed images of the internal structure of the breast. MRI signal strength, and therefore image contrast, is determined by the density of hydrogen protons within the imaged tissue and their response to rapidly changing radio waves and magnetic fields. The image contrast of MRI systems can be significantly enhanced using a range of chemicals ingested or injected prior to the scan [68]. As show in Figure 2.

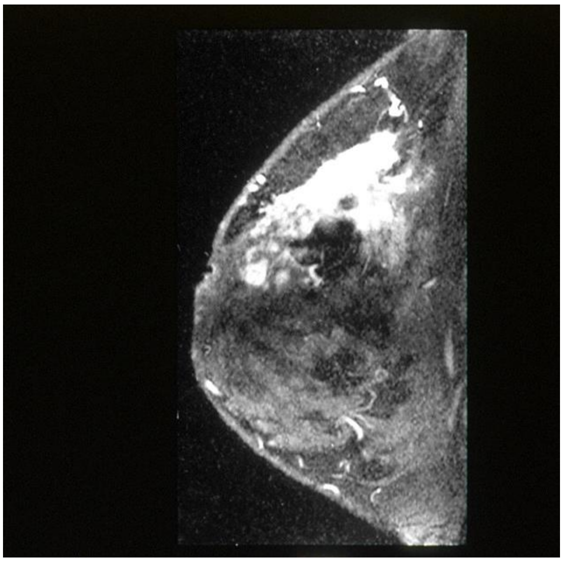

Fig. 2. (a) MRI of individual breast, demonstrating marked enhancement (bright area) which was confirmed to be cancer (National Cancer Institute, February 1994)

MRI can provide superior imaging results and outcomes compared to mammography and other breast screening techniques for women at high risk of breast cancer [69, 70]. MRI is a sophisticated imaging method without the need for ionizing radiation and cannot induce cancers [71]. Women with dense breasts are also considered high risk and for this cohort annual MRI is recommended first for screening with further validation of the outcome [72].

There are many unresolved issues in using MRI for breast cancer screening, including lack of standardised techniques and interpretation criteria [73]. In 2013, Sutcliffe Iii and his colleague published an article which reiterated the issues with MRI and noted that the different levels of training and experience of the radiologist result in significant variation in MRI findings of benign and malignant tumours [74]. Other limitations mentioned in past studies have also suggested that MRI is less reliable in the detection of ductal carcinoma in situ (DCIS) because it is unable to image calcifications, tiny calcium deposits that can indicate breast cancer [10].

The U.S. Food and Drug Administration (FDA) approved MRI in 1991 to help diagnose breast cancer. However, because of its high sensitivity and lower specificity which can lead to false positives, the American Cancer Society does not recommend MRI for all women [75, 76]. The range of specificity varies from 37% to 100% [77-81] and this low specificity leads to more false positives and unnecessary biopsies [82]. These outcomes are summarised in Table 1.

To improve specificity, recommendations for breast MRI state that the dynamic contrast-enhanced (DCE) acquisition should be obtained [83]. The most widely used form of DCE-MRI analysis is the assessment of the type of time-signal intensity curve. The shape of the time-signal intensity curve is an important criterion in differentiating benign and malignant enhancing lesions [84]. To further improve lesion classification, a high-resolution T2 sequence and diffusion-weighted sequences have been added to the state-of-art MRI protocol [83, 85, 86]. However, this makes breast MRI time-consuming, with report investigation times between 20 and 40 min [87].

In addition, the cost of MRI is approximately ten times the cost of mammography [22]. Since the current cost of mammography is one factor leading to limited mammogram prescription and use, this added cost is not sustainable for widescale screening. MRI cost with screening and treatment is estimated at $123 672 per detected breast cancer [88], which is ten times higher than mammography. In addition to the high cost, results take more time to produce [89, 90], and there is a lack of standardization in terms of technique, as well as interpretation guidelines [91].

2.3 Ultrasound

Ultrasound sends high frequency sound energy into the tissue from a hand-held transducer. This sound is reflected by boundaries between tissue where the acoustic impedance changes. Reflected sound is received by the transducer and the depth of reflection can be determined by ‘time of flight’. Depth and detection information is combined into an image of cancerous tissue, as it has different density to surroundings tissue.

Ultrasound is currently used to differentiate breast masses [92], and guide aspirations and biopsies [93]. Studies report ultrasound as a useful adjunct to mammography [94-96], and that in this role it yields improved cancer detection. However, it is not recommended as a screening tool, in part because it is more specifically useful for assessing whether a lump is fluid filled or solid [97].

Current technological advances in ultrasound equipment include very high-frequency 15MHz and multiarray transducers, as well as matrix broadband transducers. These transducers provide high levels of spatial and contrast resolution that allow detection of breast carcinomas as small as a few millimetres. To yield the highest spatial resolution, all modern transducers should be operated at the highest clinically appropriate frequency. However, high resolution ultrasound equipment can be more expensive that traditional machines. In addition, there is a limitation that no high frequency probe can image deeper than 4 cm and this limitation should be kept in mind when evaluating large breasts or lesions, as the operator may have to switch to a lower-frequency probe to achieve better penetration and a wider field of view [98].

Similar to Mammography and MRI, ultrasound also has limitations. It too requires a well-trained, skilled operator and a follow up team that includes radiologists, breast surgeons, pathologists, and expert physician input to interpret images [99]. Screening takes 15min or longer for each breast and it takes additional time for radiologists or physicians to review the images manually, which introduces subjectivity and error based on experience.

Costs for ultrasound screening include review by radiologists, technician time, and communicating results to the doctors. The average cost per patient has been estimated at €127 [100], but may vary by country. Hence, it is almost similar to mammography.

Finally, ultrasound has low spatial resolution, low specificity [101], and is unable to image micro calcifications [99], especially when they are inside fibroglandular breast tissues [102-104]. These factors all increase the rate of false positive results [105, 106]. Table 1 summarizes the reported performance of ultrasound in breast cancer screening. The performance, particularly the percentages range of FPR and FNR are higher than for other modalities, limiting its efficacy in widespread screening or pre-screening.

2.4 Microwave Imaging

Microwave imaging (MI) is based on the dielectric properties of tissues. This imaging technique is applicable to breast cancer detection, due to the differences in dielectric properties between normal and malignant breast tissues [107-110]. There are three types of microwave: passive, hybrid, and active. Passive microwave relies on tumour temperature and detects regions of increased temperature in the breast [111-113]. The key concept of passive microwave is similar to thermography with different range of spectrum [114]. Hybrid methods heat tumours with microwaves and forms images using an ultrasound transducer to detect pressure waves generated by the expansion of heated tissues [115]. Active microwave techniques are classified as radar or tomographic methods. In both approaches, scattered microwave signals are measured after transmitting low-power microwave signals into the breast using an array of 16 antennas are attached in a circular fashion. Each antenna in turn transmits electromagnetic wave in the microwave spectrum and the remaining 15 collect measured data [110, 116].

In the tomographic approach, narrowband signals are used to record a set of scattering parameters of the breast. An inversion algorithm is used to reconstruct a complete map of the dielectric properties of the breast [117, 118]. In contrast, radar methods use wideband or ultra-wide band (UWB) signals to create images that indicate the presence and location of significantly scattering objects [119].

Active microwave imaging techniques are totally dependent on the dielectric properties: permittivity and conductivity. It is reported that dielectric properties for cancerous tissues are three or more times greater than healthy tissues [120]. Radar-based approaches have only involved testing with phantoms [121, 122] and early-stage clinical investigations [123]. There are thus few reports on clinical trials that reflect the significant technical challenges involved in sensor design and implementation, measurement hardware, and the development of patient interfaces [119].

Unlike mammography, this technique is free from ionizing radiation, non-invasive, requires no breast compression, and is less expensive than MRI [124]. The major hurdles limiting patient use are both at the hardware level (challenges in collecting accurate and no corrupted data) and software level (often plagued by unrealistic reconstruction times in the tens of hours). Resolution of the image is also limited to 0.5cm and 1.0 cm in healthy and denser breast, respectively, which limits overall and early detection [110].

2.5 Elastography

Elastography (E) is a medical imaging technique to examine elastic properties of breast tissues, and this technique may be useful to distinguish malignant and benign masses [125]. In elastography, static and dynamic are two methods to examine mechanical properties [126, 127]. Based on viscoelastic behaviour of breast tissues, echo signals are obtained before and after compression from tissues and then converted to displacement distribution images. From measured displacement, elastography is able to provide tissue stiffness information [128].

Elastography is currently most widely method used in clinic. In various organs such as, breast, prostate, and thyroid elastography has proven highly accurate in the evaluation of cancerous tissues [157-159]. Ultrasonography (US) elastography was introduced to overcome limitations of ultrasound and mammography with combine US technology and basic principles of elastography [129, 130]. Unlike mammography, it is non-invasive [160].

The combination of ultrasound elastography and sonography had the best results in detecting cancer with an average 89.7% sensitivity and 95.7% specificity. Due to the lowest false-negative rates elastography is a promising technique and has the potential to reduce unnecessary breast biopsies [131]. The performance of elastography reported by several authors is summarised in Table 1.

Elastography compare to MRI has the lowest cost [132]. Some lesions may contain benign and malignant, elastography can be helpful working with complicated breast lesions. Additionally, elastography reduces unnecessary biopsies costs [133]

The fundamental concept of DIET(digital image elasto tomography) is based on elastography and was first published in 2004 [134]. DIET is non-invasive, portable, inexpensive, comfortable breast cancer screening technique that measures the stiffness of tissue within the breast [135, 136]. The DIET system captures low amplitude surface oscillations in the range 10 – 100 Hz generated by mechanical actuation applied to the breast [136]. Several images are captured during one cycle of a typical frequency, all at different phase angles relative to the input motion. Instead of digital imaging sensors, lasers or other non-contact displacement measurement methods could also be used to detect the actuated surface motion.

The main features are non-invasive, low cost, and fast. Phantom studies have shown the method is capable of detecting stiff inclusions that mimic cancer. Therefore, it could prove suitable for screening at any age. In addition, it is portable and requires no specialist user, reducing variability.

2.6 Summary

Tables 1 and 2 and Fig. 4 provide an overview of all modalities concerning advantages and disadvantages, such as economic, speed, accuracy, operator independency, risk, and comfort. In particular, the diagram of Fig. 4 provides an overview of how each modality interacts in terms of the key features considered. The results summarised here, particularly in Table 1 and Table 2, clearly show the advantages of the current standard, mammography, in performance, but also its disadvantages in regards to its invasive nature, as well as its wide variability in diagnostic performance. Equally, the results show the potential of emerging modalities, such as ultrasound and elastography, assuming they can overcome some specific limitations they face in performance and/or lack of significant clinical data and testing.

Table 1 Summary of performance results of every modality

Techniques	Authors	TPR (%)	FNR (%)	TNR (%)	FPR (%)	Patients (#Pos / #Neg)
Mammography	Kuhl et al. [137]	33.0	67.0	93.0	7.0	(9 / 96)
	Dodd [138]	87.2	12.8	85.1	14.9	(3661 / 4051)
	Kolb et al. [139]	77.6	22.4	98.8	1.2	(246 / 27579)
	Manoliu and Ooms [140]	86.6	13.4	80.7	19.3	(279 / 376)
	Ohlinger et al. [141]	100.0	0.0	72.7	27.3	(3 / 11)
	Habib et al.[142]	72.2	27.8	75.0	25.0	(18 / 8)
	Standertskjöld-Nordenstam and Svinhufvud [143]	91.8	8.2	95.6	4.4	NA
	Luczyńska et al. [144]	91.0	9.0	15.0	85.0	(114 / 59)
	Burman et al. [145]	97.8	2.2	83.9	16.1	(47 / 5059)
	Egan and Egan [146]	77.4	22.6	67.4	32.6	(31 / 46)

MRI	Langer et al. [82]	91.6	8.4	70.4	29.6	(36 / 108)
	Spick et al. [147]	100.0	0.0	88.5	11.5	(15 / 96)
	Kuhl et al. [137]	100.0	0.0	95.0	5.0	(9 / 96)
	Heinisch et al. [148]	92.0	8.0	73.3	26.7	(25 / 15)
	Hayashi et al. [149]	43.8	56.2	90.3	9.7	(98 / 166)
	Belli et al. [150]	90.2	9.8	100.0	0.0	(41 / 4)
Ultrasound	Kolb et al.[139]	75.3	24.7	96.8	3.2	(146 / 13,401)
	Egan and Egan [146]	67.7	32.3	93.5	6.5	(31 / 46)
	Satake et al. [151]	89.6	10.4	76.5	23.5	(29 / 17)
	Lumachi et al. [152]	67.5	32.5	80.0	20.0	(37 / 40)
	Stavros et al. [153]	98.4	1.6	67.8	32.2	(125 / 625)
	Ohlinger et al. [141]	100.0	0.0	54.5	45.5	(3 / 11)
	Kuhl et al. [137]	33.0	67.0	80.0	20.0	(9 / 96)
	Habib et al. [142]	94.4	5.6	70.0	30.0	(18 / 10)
	Chang et al. [154]	95.5	4.5	91.4	8.6	(110 / 140)
	Chang et al. [155]	95.5	4.5	77.8	22.2	(110 / 140)
Elastography	Giuseppetti [156]	79	21	89	79	NA
	Thomas [157]	82	18	87	13	(300 / 0)
	Evans [158]	97	3	83	17	(53 / 0)

TPR = True Positive Rate (Sensitivity), TNR = True Negative Rate (Specificity), FNR= False Negative Rate, FPR = False Positive Rate, NA=Not available

Table 2 All modalities in terms of main aspects

Techniques	Economic	Fast	Accurate	Operator Independent	Ionizing Radiation	Comfort
Elastography	✓	✓	✓	✓	✗	✓
X-ray Mammography	✓	✓	✗	✗	✓	✗
MRI	✗	✓	✓	✗	✗	✓
Ultrasound	✓	✓	✗	✗	✗	✓
Microwave Imaging	✓	✗	✓	✗	✗	✓

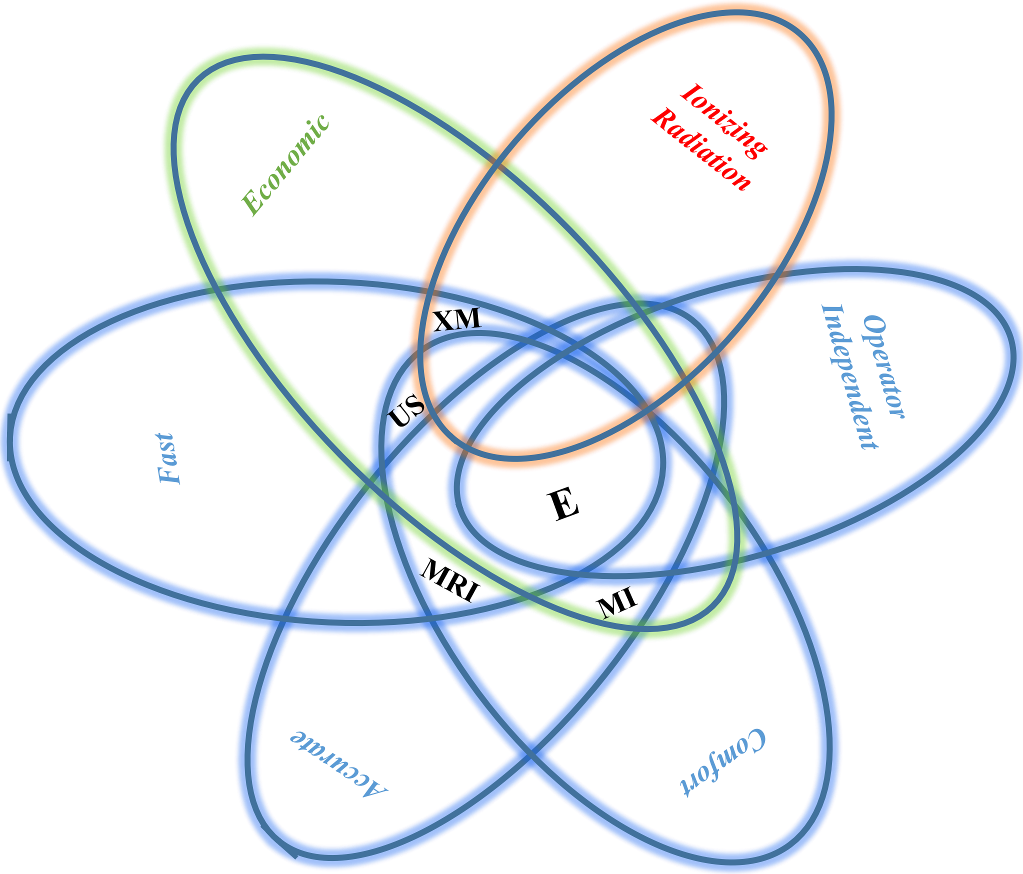

Fig. 4 All modalities in terms of main aspects, where blue (Fast, Operator Independent and Accurate) and green (Economic) are desirable aspects, and red (Invasive) is undesirable. The diagram shows the relative location of all major modalities considered where the goal is to be in all blue and green circles and avoiding the red. The diagram is also captured in Table 2.

3.0 Conclusions

Outside of breast self-exam, mammography is the most widely used and well-accepted technique to detect breast cancer, and is thus an effective gold standard in the field. However, its limitations in exposure to ionizing radiation and comfort due to breast compression, both of which can affect compliance to screening, create a significant need for other less invasive approaches. In addition, its variability in diagnosis based on radiologist experience may be a further limitation to be improved by automated methods, within mammography or via another modality. However, it is important to note that mammography is still the only proven and accepted wide scale screening modality.

In contrast, current and emerging methods using ultrasound, MRI, and Microwave imaging all are non-invasive, but their reported results to date are too variable at this time for use in regular screening. Newer emerging technologies, like DIET and advanced ultrasound systems, can offer non-invasive, all age screening that is low cost. However, these latter emerging technologies still face a long validation process to prove their efficacy in relation to accepted standards before they are accepted as realistic screening alternatives.

Overall, this review thus tries to concisely summarise the overall strengths, weaknesses, and thus gaps in the field, with a strong focus on how newer, emerging technologies can offer novel solutions to broader cohorts.

4.0 References

[1]. Jemal, A., et al., *Global cancer statistics.* CA: a cancer journal for clinicians, 2011. **61**(2): p. 69-90.

[2]. Globocan. *Estimated Cancer Incidence, Mortality and Prevalence Worldwide.* 2012; Available from: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx.

[3]. Jemal, A., et al., *Cancer statistics, 2007.* CA: a cancer journal for clinicians, 2007. **57**(1): p. 43-66.

[4]. Society, A.C. *Cancer Facts and Figures 2015. Atlanta, Ga: American Cancer Society,.* 2015; Available from: www.cancer.org/acs/groups/content/@editorial/documents/document/acspc-044552.pdf.

[5]. Society, A.C. *Breast Cancer Facts & Figures.* 2004-2014; Available from: http://www.cancer.org/research/cancerfactsstatistics/breast-cancer-facts-figures.

[6]. Zhou, X. and R. Gordon, *Detection of early breast cancer: an overview and future prospects.* Critical reviews in biomedical engineering, 1988. **17**(3): p. 203-255.

[7]. Jemal, A., et al., *Cancer statistics, 2008.* CA: a cancer journal for clinicians, 2008. **58**(2): p. 71-96.

[8]. Tilanus-Linthorst, M.M., et al., *First experiences in screening women at high risk for breast cancer with MR imaging.* Breast cancer research and treatment, 2000. **63**(1): p. 53-60.

[9]. Boice Jr, J.D., et al., *Risk of Breast Cancer Following Low-Dose Radiation Exposure 1.* Radiology, 1979. **131**(3): p. 589-597.

[10]. Cancer, C.G.o.H.F.i.B., *Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies.* The lancet oncology, 2012. **13**(11): p. 1141-1151.

[11]. Opdahl, S., et al., *Joint effects of nulliparity and other breast cancer risk factors.* British journal of cancer, 2011. **105**(5): p. 731.

[12]. Mariotto, A.B., et al., *Projections of the cost of cancer care in the United States: 2010–2020.* Journal of the National Cancer Institute, 2011.

[13]. Sullivan, R., et al., *Delivering affordable cancer care in high-income countries.* The lancet oncology, 2011. **12**(10): p. 933-980.

[14]. Ray, S., et al., *Patterns of treatment, healthcare utilization and costs by lines of therapy in metastatic breast cancer in a large insured US population.* Journal of comparative effectiveness research, 2013. **2**(2): p. 195-206.

[15]. Rosenquist, C.J. and K.K. Lindfors, *Screening mammography in women aged 40-49 years: analysis of cost-effectiveness.* Radiology, 1994. **191**(3): p. 647-650.

[16]. Feig, S.A., *Mammographic screening of women aged 40–49 years. Benefit, risk, and cost considerations.* Cancer, 1995. **76**(S10): p. 2097-2106.

[17]. Sree, S.V., et al., *Breast imaging: a survey.* World journal of clinical oncology, 2011. **2**(4): p. 171.

[18]. Bushra, M. and S. Muhammad, *Automated Detection of Breast Tumor in Different Imaging Modalities: A Review.* Current Medical Imaging Reviews, 2016. **12**: p. 1-19.

[19]. Strickland, R.N., *Image-processing techniques for tumor detection*. 2002: CRC Press.

[20]. Hurley, S.F. and J.M. Kaldor, *The benefits and risks of mammographic screening for breast cancer.* Epidemiologic Reviews, 1992. **14**(1): p. 101-130.

[21]. de González, A.B. and G. Reeves, *Mammographic screening before age 50 years in the UK: comparison of the radiation risks with the mortality benefits.* British journal of cancer, 2005. **93**(5): p. 590-596.

[22]. Elmore, J.G., et al., *Screening for breast cancer.* Jama, 2005. **293**(10): p. 1245-1256.

[23]. Qaseem, A., et al., *Screening mammography for women 40 to 49 years of age: a clinical practice guideline from the American College of Physicians.* Annals of internal medicine, 2007. **146**(7): p. 511-515.

[24]. Mandelblatt, J.S., et al., *Effects of mammography screening under different screening schedules: model estimates of potential benefits and harms.* Annals of internal medicine, 2009. **151**(10): p. 738-747.
[25]. Løberg, M., et al., *Benefits and harms of mammography screening.* Breast Cancer Research, 2015. **17**(1): p. 1-12.
[26]. Andreea, G.I., et al., *The role of imaging techniques in diagnosis of breast cancer.* Curr Health Sci J, 2011. **37**(2): p. 55-61.
[27]. Blanks, R.G., et al., *Women need better information on routine mammography.* British Medical Journal, 2003. **327**: p. 868-868.
[28]. Barnes, G.T., *Mammography equipment: compression, scatter control, and automatic exposure control.* Syllabus: a categorical course in physics, 1993: p. 73-82.
[29]. Robinson, L., P. Hogg, and A. Newton-Hughes, *The power and the pain: Mammographic compression research from the service-users' perspective.* Radiography, 2013. **19**(3): p. 190-195.
[30]. Bai, J., et al., *Correlation of pain experience during mammography with factors of breast density and breast compressed thickness.* Journal of Shanghai Jiaotong University (Medical Science), 2010. **30**(9): p. 1062.
[31]. Feig, S.A., *Adverse effects of screening mammography.* Radiologic Clinics of North America, 2004. **42**(5): p. 807-819.
[32]. Miller, D., V. Livingstone, and P. Herbison, *Interventions for relieving the pain and discomfort of screening mammography.* Cochrane Database Syst Rev, 2008. **1**.
[33]. Kashikar-Zuck, S., et al., *Pain coping and the pain experience during mammography: a preliminary study.* Pain, 1997. **73**(2): p. 165-172.
[34]. Myklebust, A.M., et al., *Level of satisfaction during mammography screening in relation to discomfort, service provided, level of pain and breast compression.* European Journal of Radiography, 2009. **1**(2): p. 66-72.
[35]. Vachon, C.M., et al., *Mammographic breast density as a general marker of breast cancer risk.* Cancer Epidemiology Biomarkers & Prevention, 2007. **16**(1): p. 43-49.
[36]. Harvey, J.A. and V.E. Bovbjerg, *Quantitative assessment of mammographic breast density: relationship with breast cancer risk 1.* Radiology, 2004. **230**(1): p. 29-41.
[37]. Boyd, N.F., et al., *Mammographic density: a hormonally responsive risk factor for breast cancer.* British Menopause Society Journal, 2006. **12**(4): p. 186-193.
[38]. Haiman, C.A., et al., *Genetic determinants of mammographic density.* Breast Cancer Res, 2002. **4**(3): p. R5.
[39]. Joy, J.E., E.E. Penhoet, and D.B. Petitti, *Benefits and Limitations of Mammography.* 2005.
[40]. Saarenmaa, I., et al., *The effect of age and density of the breast on the sensitivity of breast cancer diagnostic by mammography and ultasonography.* Breast cancer research and treatment, 2001. **67**(2): p. 117-123.
[41]. Ohuchi, N., et al., *Sensitivity and specificity of mammography and adjunctive ultrasonography to screen for breast cancer in the Japan Strategic Anti-cancer Randomized Trial (J-START): a randomised controlled trial.* The Lancet, 2015.
[42]. Martin, J.E., M. Moskowitz, and J.R. Milbrath, *Breast cancer missed by mammography.* American Journal of Roentgenology, 1979. **132**(5): p. 737-739.
[43]. Bird, R.E., T.W. Wallace, and B.C. Yankaskas, *Analysis of cancers missed at screening mammography.* Radiology, 1992. **184**(3): p. 613-617.
[44]. Kallsher, L., *Factors influencing false negative rates in xeromammography.* Radiology, 1979. **133**(2): p. 297-301.
[45]. Goergen, S.K., et al., *Characteristics of breast carcinomas missed by screening radiologists.* Radiology, 1997. **204**(1): p. 131-135.
[46]. Holland, R., J. Hendriks, and M. Mravunac, *Mammographically occult breast cancer: a pathologic and radiologic study.* Cancer, 1983. **52**(10): p. 1810-1819.

[47]. Kriege, M., et al., *Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition.* New England Journal of Medicine, 2004. **351**(5): p. 427-437.
[48]. Sardanelli, F., et al., *Multicenter Comparative Multimodality Surveillance of Women at Genetic-Familial High Risk for Breast Cancer (HIBCRIT Study): Interim Results 1.* Radiology, 2007. **242**(3): p. 698-715.
[49]. Jesneck, J.L., J.Y. Lo, and J.A. Baker, *Breast Mass Lesions: Computer-aided Diagnosis Models with Mammographic and Sonographic Descriptors 1.* Radiology, 2007. **244**(2): p. 390-398.
[50]. Seely, J.M., *Management of breast magnetic resonance imaging-detected lesions.* Canadian Association of Radiologists Journal, 2012. **63**(3): p. 192-206.
[51]. Ernster, V.L., et al., *Detection of ductal carcinoma in situ in women undergoing screening mammography.* Journal of the National Cancer Institute, 2002. **94**(20): p. 1546-1554.
[52]. Skrabanek, P., *The cost-effectiveness of breast cancer screening.* International journal of technology assessment in health care, 1991. **7**(04): p. 633-635.
[53]. Brown, M.L., *Economic considerations in breast cancer screening of older women.* Journal of gerontology, 1992. **47**: p. 51-58.
[54]. Elixhauser, A., *Costs of breast cancer and the cost-effectiveness of breast cancer screening.* International journal of technology assessment in health care, 1991. **7**(04): p. 604-615.
[55]. Mushlin, A.I. and L. Fintor, *Is screening for breast cancer cost-effective?* Cancer, 1992. **69**(S7): p. 1957-1962.
[56]. Okubo, I., et al., *Cost-effectiveness analysis of mass screening for breast cancer in Japan.* Cancer, 1991. **67**(8): p. 2021-2029.
[57]. Foundation, T.N.Z.B.C.; Available from: http://nzbcf.org.nz/BREASTCANCER/Mammograms/WhatShouldIDo.aspx.
[58]. Miller, A., *The costs and benefits of breast cancer screening.* American journal of preventive medicine, 1992. **9**(3): p. 175-180.
[59]. Van Der Maas, P.J., et al., *The cost-effectiveness of breast cancer screening.* International Journal of Cancer, 1989. **43**(6): p. 1055-1060.
[60]. de Koning, H.J., et al., *Breast cancer screening and cost-effectiveness; policy alternatives, quality of life considerations and the possible impact of uncertain factors.* International Journal of Cancer, 1991. **49**(4): p. 531-537.
[61]. Houssami, N. and D.L. Miglioretti, *Digital breast tomosynthesis: a brave new world of mammography screening.* JAMA oncology, 2016. **2**(6): p. 725-727.
[62]. Houssami, N. and P. Skaane, *Overview of the evidence on digital breast tomosynthesis in breast cancer detection.* The Breast, 2013. **22**(2): p. 101-108.
[63]. Friedewald, S.M., *Breast Tomosynthesis: Practical Considerations.* Radiologic Clinics of North America, 2017.
[64]. van Schie, G., et al., *Generating synthetic mammograms from reconstructed tomosynthesis volumes.* IEEE transactions on medical imaging, 2013. **32**(12): p. 2322-2331.
[65]. Melnikow, J., et al., *Screening for Breast Cancer With Digital Breast Tomosynthesis.* 2016.
[66]. Imaging, M.R.B. *The Breast Health Resource* Available from: http://imaginis.com/breasthealth/mri.asp.
[67]. Berger, A., *How does it work?: Magnetic resonance imaging.* BMJ: British Medical Journal, 2002. **324**(7328): p. 35.
[68]. Safir, J., et al., *Contrast-enhanced breast mri for cancer detection using a commercially available system—a perspective.* Clinical imaging, 1998. **22**(3): p. 162-179.
[69]. Warner, E., et al., *Comparison of breast magnetic resonance imaging, mammography, and ultrasound for surveillance of women at high risk for hereditary breast cancer.* Journal of Clinical Oncology, 2001. **19**(15): p. 3524-3531.
[70]. Laura, C., et al., *Radiological Screening Programs for Women at High Risk of Developing Breast Cancer.* Current Women`s Health Reviews, 2012. **8**(1): p. 72-85.

[71]. Morris, E.A., *Rethinking breast cancer screening: ultra fast breast magnetic resonance imaging.* Journal of Clinical Oncology, 2014. **32**(22): p. 2281-2283.
[72]. Berg, W.A., *Tailored supplemental screening for breast cancer: what now and what next?* American Journal of Roentgenology, 2009. **192**(2): p. 390-399.
[73]. Kovacs, L., et al., *Comparison between breast volume measurement using 3D surface imaging and classical techniques.* The Breast, 2007. **16**(2): p. 137-145.
[74]. Borchartt, T.B., et al., *Breast thermography from an image processing viewpoint: A survey.* Signal Processing, 2013. **93**(10): p. 2785-2803.
[75]. Harms, S., et al., *MR imaging of the breast with rotating delivery of excitation off resonance: clinical experience with pathologic correlation.* Radiology, 1993. **187**(2): p. 493-501.
[76]. Uma, S., S. Raju, and R.J. Naranamangalam, *Characterization of Breast Lesions by Magnetic Resonance Imaging (MRI) and Spectroscopy (MRS).* Current Medical Imaging Reviews, 2006. **2**(3): p. 329-340.
[77]. Stomper, P.C., et al., *Suspect breast lesions: findings at dynamic gadolinium-enhanced MR imaging correlated with mammographic and pathologic features.* Radiology, 1995. **197**(2): p. 387-395.
[78]. Lehman, C.D., et al., *MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer.* New England Journal of Medicine, 2007. **356**(13): p. 1295-1303.
[79]. Lord, S., et al., *A systematic review of the effectiveness of magnetic resonance imaging (MRI) as an addition to mammography and ultrasound in screening young women at high risk of breast cancer.* European journal of cancer, 2007. **43**(13): p. 1905-1917.
[80]. Choi, B., et al., *New subtraction algorithms for evaluation of lesions on dynamic contrast-enhanced MR mammography.* European radiology, 2002. **12**(12): p. 3018-3022.
[81]. Rim, A., M. Chellman-Jeffers, and A. Fanning, *Trends in breast cancer screening and diagnosis.* Cleveland Clinic journal of medicine, 2008. **75**(1): p. S2.
[82]. Langer, S.A., et al., *Pathologic correlates of false positive breast magnetic resonance imaging findings: which lesions warrant biopsy?* The American journal of surgery, 2005. **190**(4): p. 633-640.
[83]. Mann, R.M., et al., *Breast MRI: guidelines from the European society of breast imaging.* European radiology, 2008. **18**(7): p. 1307-1318.
[84]. Kuhl, C.K., et al., *Dynamic breast mr imaging: Are signal intensity time course data useful for differential diagnosis of enhancing lesions? 1.* Radiology, 1999. **211**(1): p. 101-110.
[85]. Woodhams, R., et al., *Diffusion-weighted imaging of the breast: principles and clinical applications.* Radiographics, 2011. **31**(4): p. 1059-1084.
[86]. Westra, C., et al., *Using T2-weighted sequences to more accurately characterize breast masses seen on MRI.* American Journal of Roentgenology, 2014. **202**(3): p. W183-W190.
[87]. Carpenter, A.P., et al., *Managing magnetic resonance imaging machines: support tools for scheduling and planning.* Health care management science, 2011. **14**(2): p. 158-173.
[88]. Saadatmand, S., et al., *Cost-effectiveness of screening women with familial risk for breast cancer with magnetic resonance imaging.* Journal of the National Cancer Institute, 2013. **105**(17): p. 1314-1321.
[89]. Rankin, S., *MRI of the breast.* The British journal of radiology, 2000. **73**(872): p. 806-818.
[90]. Kuhl, C.K. and H.H. Schild, *Dynamic image interpretation of MRI of the breast.* Journal of Magnetic Resonance Imaging, 2000. **12**(6): p. 965-974.
[91]. Sutcliffe, J.B. and P.M. Otto, *Controversies in breast MRI.* Current problems in diagnostic radiology, 2013. **42**(4): p. 149-163.
[92]. Edell, S. and M. Eisen, *Current imaging modalities for the diagnosis of breast cancer.* Delaware medical journal, 1999. **71**(9): p. 377-382.
[93]. Hardy, J., et al., *How many tests are required in the diagnosis of palpable breast abnormalities?* Clinical Oncology, 1990. **2**(3): p. 148-152.

[94]. Moss, H.A., et al., *How reliable is modern breast imaging in differentiating benign from malignant breast lesions in the symptomatic population?* Clinical radiology, 1999. **54**(10): p. 676-682.
[95]. Skaane, P., K. Engedal, and A. Skjennald, *Interobserver variation in the interpretation of breast imaging: comparison of mammography, ultrasonography, and both combined in the interpretation of palpable noncalcified breast masses.* Acta Radiologica, 1997. **38**(4): p. 497-502.
[96]. Khalkhali, I. and H. Vargas, *Practical use of ultrasound at a dedicated breast center.* The breast journal, 2005. **11**(3): p. 165-166.
[97]. Madjar, H., *Role of breast ultrasound for the detection and differentiation of breast lesions.* Breast Care, 2010. **5**(2): p. 109-114.
[98]. FORNAGE, B.D., *Local and Regional Staging of Invasive Breast Cancer With Sonography: 25 Years of Practice at MD Anderson Cancer Center.* Oncologist, 2014. **19**: p. 5-15.
[99]. Smith, R.A., et al., *American Cancer Society guidelines for breast cancer screening: update 2003.* CA: a cancer journal for clinicians, 2003. **53**(3): p. 141-169.
[100]. Haloua, M., et al., *Ultrasound-guided surgery for palpable breast cancer is cost-saving: Results of a cost-benefit analysis.* The Breast, 2013. **22**(3): p. 238-243.
[101]. Moore, S.K., *Better breast cancer detection.* Spectrum, IEEE, 2001. **38**(5): p. 50-54.
[102]. Kolb, T.M., J. Lichy, and J.H. Newhouse, *Occult cancer in women with dense breasts: detection with screening US--diagnostic yield and tumor characteristics.* Radiology, 1998. **207**(1): p. 191-199.
[103]. Berg, W.A., et al., *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, 2012. **307**(13): p. 1394-1404.
[104]. Soo, M.S., J.A. Baker, and E.L. Rosen, *Sonographic detection and sonographically guided biopsy of breast microcalcifications.* American Journal of Roentgenology, 2003. **180**(4): p. 941-948.
[105]. Buchberger, W., et al., *Incidental findings on sonography of the breast: clinical significance and diagnostic workup.* AJR. American journal of roentgenology, 1999. **173**(4): p. 921-927.
[106]. Sickles, E.A., R.A. Filly, and P.W. Callen, *Breast cancer detection with sonography and mammography: comparison using state-of-the-art equipment.* American Journal of Roentgenology, 1983. **140**(5): p. 843-845.
[107]. Fear, E.C., et al., *Confocal microwave imaging for breast cancer detection: Localization of tumors in three dimensions.* Biomedical Engineering, IEEE Transactions on, 2002. **49**(8): p. 812-822.
[108]. Gabriel, S., R. Lau, and C. Gabriel, *The dielectric properties of biological tissues: II. Measurements in the frequency range 10 Hz to 20 GHz.* Physics in medicine and biology, 1996. **41**(11): p. 2251.
[109]. Schepps, J.L. and K.R. Foster, *The UHF and microwave dielectric properties of normal and tumour tissues: variation in dielectric properties with tissue water content.* Physics in medicine and biology, 1980. **25**(6): p. 1149.
[110]. Grzegorczyk, T.M., et al., *Fast 3-D tomographic microwave imaging for breast cancer detection.* Medical Imaging, IEEE Transactions on, 2012. **31**(8): p. 1584-1592.
[111]. Haslam, N.C., A.R. Gillespie, and C. Haslam, *Aperture synthesis thermography-A new approach to passive microwave temperature measurements in the body.* Microwave Theory and Techniques, IEEE Transactions on, 1984. **32**(8): p. 829-835.
[112]. Barrett, A., P.C. Myers, and N. Sadowsky, *Detection of breast cancer by microwave radiometry.* Radio Science, 1977. **12**(6S): p. 167-171.
[113]. Land, D., *A clinical microwave thermography system.* IEE Proceedings A (Physical Science, Measurement and Instrumentation, Management and Education, Reviews), 1987. **134**(2): p. 193-200.
[114]. Field, S.B. and C. Franconi, *Physics and technology of hyperthermia.* 1987.

[115]. Fear, E.C., *Microwave imaging of the breast.* Technology in Cancer Research & Treatment, 2005. **4**(1): p. 69-82.
[116]. Li, X., et al., *An overview of ultra-wideband microwave imaging via space-time beamforming for early-stage breast-cancer detection.* Antennas and Propagation Magazine, IEEE, 2005. **47**(1): p. 19-34.
[117]. Fhager, A., M. Gustafsson, and S. Nordebo, *Image reconstruction in microwave tomography using a dielectric Debye model.* Biomedical Engineering, IEEE Transactions on, 2012. **59**(1): p. 156-166.
[118]. Stang, J.P., *A Three-dimensional Active Microwave Imaging System for Breast Cancer Screening*. 2008: ProQuest.
[119]. Bourqui, J., J.M. Sill, and E.C. Fear, *A prototype system for measuring microwave frequency reflections from the breast.* Journal of Biomedical Imaging, 2012. **2012**: p. 9.
[120]. Chaudhary, S., et al., *Dielectric properties of normal & malignant human breast tissues at radiowave & microwave frequencies.* Indian journal of biochemistry & biophysics, 1984. **21**(1): p. 76.
[121]. Sill, J.M. and E.C. Fear, *Tissue sensing adaptive radar for breast cancer detection - experimental investigation of simple tumor models.* Microwave Theory and Techniques, IEEE Transactions on, 2005. **53**(11): p. 3312-3319.
[122]. Klemm, M., et al., *Microwave radar-based breast cancer detection: Imaging in inhomogeneous breast phantoms.* Antennas and Wireless Propagation Letters, IEEE, 2009. **8**: p. 1349-1352.
[123]. Klemm, M., et al. *Experimental and clinical results of breast cancer detection using UWB microwave radar*. in *Antennas and Propagation Society International Symposium, 2008. AP-S 2008. IEEE*. 2008. IEEE.
[124]. Fear, E.C., P.M. Meaney, and M. Stuchly, *Microwaves for breast cancer detection?* Potentials, IEEE, 2003. **22**(1): p. 12-18.
[125]. Garra, B.S., et al., *Elastography of breast lesions: initial clinical results.* Radiology, 1997. **202**(1): p. 79-86.
[126]. Gennisson, J.L., et al., *Ultrasound elastography: Principles and techniques.* Diagnostic and Interventional Imaging, 2013. **94**(5): p. 487-495.
[127]. Goddi, A., M. Bonardi, and S. Alessi, *Breast elastography: a literature review.* Journal of ultrasound, 2012. **15**(3): p. 192-198.
[128]. Cho, N., et al., *Nonpalpable breast masses: evaluation by US elastography.* Korean journal of radiology, 2008. **9**(2): p. 111-118.
[129]. Ophir, J., et al., *Elastography: a quantitative method for imaging the elasticity of biological tissues.* Ultrasonic imaging, 1991. **13**(2): p. 111-134.
[130]. Claire, P.-B., et al., *Ultrasonic Elasticity Imaging as a Tool for Breast Cancer Diagnosis and Research.* Current Medical Imaging Reviews, 2006. **2**(1): p. 157-164.
[131]. Zhi, H., et al., *Comparison of ultrasound elastography, mammography, and sonography in the diagnosis of solid breast lesions.* Journal of ultrasound in medicine, 2007. **26**(6): p. 807-815.
[132]. Gheonea, I.A., Z. Stoica, and S. Bondari, *Differential diagnosis of breast lesions using ultrasound elastography.* Indian Journal of Radiology and Imaging, 2011. **21**(4): p. 301.
[133]. Grajo, J.R. and R.G. Barr, *Compression elasticity imaging of the breast: An overview.* Applied Radiology, 2012. **41**(10): p. 18.
[134]. Peters, A., et al., *Digital image-based elasto-tomography: proof of concept studies for surface based mechanical property reconstruction.* JSME International Journal Series C Mechanical Systems, Machine Elements and Manufacturing, 2004. **47**(4): p. 1117-1123.
[135]. Kashif, A.S., et al., *Separate modal analysis for tumor detection with a digital image elasto tomography (DIET) breast cancer screening system.* Medical physics, 2013. **40**(11): p. 113503.
[136]. Van Houten, E.E., A. Peters, and J.G. Chase, *Phantom elasticity reconstruction with Digital Image Elasto-Tomography.* Journal of the mechanical behavior of biomedical materials, 2011. **4**(8): p. 1741-1754.

[137]. Kuhl, C.K., et al., *Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results 1.* Radiology, 2000. **215**(1): p. 267-279.
[138]. Dodd, G.D., *Present status of thermography, ultrasound and mammography in breast cancer detection.* Cancer, 1977. **39**(6): p. 2796-2805.
[139]. Kolb, T.M., J. Lichy, and J.H. Newhouse, *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 1.* Radiology, 2002. **225**(1): p. 165-175.
[140]. Manoliu, R. and G. Ooms, *The accuracy of mammography: an analysis of 655 histologically verified cases.* Radiologia clinica, 1976. **46**(6): p. 422-429.
[141]. Ohlinger, R., et al., *Non-palpable breast lesions in asymptomatic women: diagnostic value of initial ultrasonography and comparison with mammography.* Anticancer research, 2006. **26**(5B): p. 3943-3955.
[142]. Habib, S., et al., *Diagnostic accuracy of Tc-99m-MIBI for breast carcinoma in correlation with mammography and sonography.* J Coll Physicians Surg Pak, 2009. **19**(10): p. 622-6.
[143]. Standertskjöld-Nordenstam, C. and U. Svinhufvud. *Mammography of symptomatic breasts. A report on 1119 consecutive patients*. in *Annales chirurgiae et gynaecologiae*. 1979.
[144]. Luczyńska, E., et al., *Contrast-enhanced spectral mammography: comparison with conventional mammography and histopathology in 152 women.* Korean Journal of Radiology, 2014. **15**(6): p. 689-696.
[145]. Burman, M.L., et al., *Effect of false-positive mammograms on interval breast cancer screening in a health maintenance organization.* Annals of internal medicine, 1999. **131**(1): p. 1-6.
[146]. Egan, R. and K. Egan, *Detection of breast carcinoma: comparison of automated water-path whole-breast sonography, mammography, and physical examination.* American journal of roentgenology, 1984. **143**(3): p. 493-497.
[147]. Spick, C., et al., *Breast MRI used as a problem-solving tool reliably excludes malignancy.* European journal of radiology, 2015. **84**(1): p. 61-64.
[148]. Heinisch, M., et al., *Comparison of FDG-PET and dynamic contrast-enhanced MRI in the evaluation of suggestive breast lesions.* The breast, 2003. **12**(1): p. 17-22.
[149]. Hayashi, Y., et al., *Analysis of complete response by MRI following neoadjuvant chemotherapy predicts pathological tumor responses differently for molecular subtypes of breast cancer.* Oncology letters, 2013. **5**(1): p. 83-89.
[150]. Belli, P., et al., *MRI accuracy in residual disease evaluation in breast cancer patients treated with neoadjuvant chemotherapy.* Clinical radiology, 2006. **61**(11): p. 946-953.
[151]. Satake, H., et al., *Role of ultrasonography in the detection of intraductal spread of breast cancer: correlation with pathologic findings, mammography and MR imaging.* European radiology, 2000. **10**(11): p. 1726-1732.
[152]. Lumachi, F., et al., *Accuracy of ultrasonography and 99m Tc-sestamibi scintimammography for assessing axillary lymph node status in breast cancer patients. A prospective study.* European Journal of Surgical Oncology (EJSO), 2006. **32**(9): p. 933-936.
[153]. Stavros, A.T., et al., *Solid breast nodules: use of sonography to distinguish between benign and malignant lesions.* Radiology, 1995. **196**(1): p. 123-134.
[154]. Chang, R.-F., et al., *Improvement in breast tumor discrimination by support vector machines and speckle-emphasis texture analysis.* Ultrasound in medicine & biology, 2003. **29**(5): p. 679-686.
[155]. Chang, R.-F., et al., *Support vector machines for diagnosis of breast tumors on US images.* Academic radiology, 2003. **10**(2): p. 189-197.
[156]. Giuseppetti, G.M., et al., *Elastosonography in the diagnosis of the nodular breast lesions: preliminary report.* La Radiologia medica, 2004. **110**(1-2): p. 69-76.

[157]. Thomas, A., et al., *Real-time sonoelastography performed in addition to B-mode ultrasound and mammography: improved differentiation of breast lesions?* Academic radiology, 2006. **13**(12): p. 1496-1504.

[158]. Evans, A., et al., *Quantitative shear wave ultrasound elastography: initial experience in solid breast masses.* Breast Cancer Res, 2010. **12**(6): p. R104.