Biomedical & Pharmacology Journal, September 2018. Vol. **11**(3), p. 1649-1658

Recent Trends in Medical Imaging Modalities and Challenges For Diagnosing Breast Cancer

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http://dx.doi.org/10.13005/bpj/1533

(Received: 20 July 2018; accepted: 10 September 2018)

Breast cancer is the leading deadly cancer and most commonly diagnosed in women. New technologies in supplement to existing imaging modalities improve breast cancer screening. This article contributes to identify the high potential device that suggested high accuracy and reliable tool for breast screening and also to examine new screening modalities. An improved imaging system which ensures early detection, non-invasive and radiation free is expected in diagnosis. Numerous imaging modalities like positron emission tomography/computed tomography (PET/CT) imaging, ultrasound, magnetic resonance imaging (MRI), thermography, electrical impedance tomography and few others with recent developments show great potential for diagnosis. Some of the techniques aim for lesion detection and characterization with increased specificity and accuracy. In this paper, the capabilities of traditional and emerging breast imaging modalities used in breast cancer screening are summarized and their advantages and disadvantages are discussed.

Keywords: Breast Cancer, Thermography, Early Detection, Mammography, Medical Imaging Systems.

The most common type of cancer in women and one of the leading causes of cancer death are breast cancer. According to Information collected from National Cancer Registry Program reports[1], the burden of breast cancer in Indian population is high in 30-60 years age group. It is a rapidly raising rate in younger ages. Risk factors include mainly decreased breast-feeding and physical activity[2,3]. Infection may not be felt or detected by existing imaging modality unless a lump becomes sizeable. By the time a lump grows in noticeable size, it usually reaches a minimum of stage 2 cancers[4]. So, performing early cancer screening is commendable. Survival rate of the patient will be high if the cancer is detected in the earlier stage[5,6]. The early screening protocols include breast awareness, annual screening and clinical breast examination[7]. The motive of the article is to identify most economical and effective imaging modality that performs early detection with high accuracy among existing breast screening modalities.

This paper presents a review on recent trends in Medical imaging and challenges. A special

attention is given to the study on anatomy of breast and factors that affect breast cancer, since it is the most serious breast pathology[8]. Suggesting a best imaging modality in cancer detection is the aim of this review.

This survey is organized as follow. Section 1 gives a brief structure on anatomy of breast and regional lymph nodes which forms vulnerable areas that could be affected by breast cancer. Breast cancer imaging modalities and their potential for diagnosis are discussed in section 2. That includes some pre-screening examinations followed by traditional imaging techniques and emerging trends. Current status in breast cancer imaging is discussed in section 3. Finally, the conclusions of this work are summarized in section 4. The reviewed papers are presented in the bibliography to allow a better understanding in each section.

Breast anatomy

Breast cancer is malignant tumor that develops in breast cells like milk ducts (ductal carcinoma) or in milk supplying lobules (lobular carcinoma) and spreads into other parts[9]. The risk of breast cancer has been associated with mutations in inherited high penetrance genes, age, a family or personal history of breast cancer, reproductive and hormonal factors, hormone replacement therapy (HRT), obesity, alcohol consumption, physical inactivity and exposure to ionizing radiation[10,11]. This section briefly describes the anatomy of breast, factors affecting breast cancer and signs, symptoms and efforts for possible treatment for breast cancer.

A woman's breasts are made up of milk-producing glands. Breast tissue is made up of network of sacs that produce milk termed as lobules and ducts canals[12]. Fat covers the lobes and shapes the breast. The female reproductive hormones like oestrogens, progesterone, and prolactin, have a major impact on breast cancer.

Regional Lymph Nodes for Breast

Fig 2 describes regional lymph nodes for Breast. Breasts rests on pectoralis major muscle and attached to the chest wall by ligaments[13]. Axillary lymph nodes armpit lymph nodes are located in the underarm to the collarbone above the level of the navel. It includes three clinical classes [14]. Class I include underneath the lower edge of the pectoralis minor muscle. Class II includes under the pectoralis minor muscle. Class III is directly above the pectoralis minor muscle. Supraclavicular lymph nodes are present above the collarbone[15,16]. The internal mammary nodes located near the breast bone.

Breast cancer imaging modalities

Breast Imaging - Reporting and Data System (BI-RADS) in 1993 proposed by American College of Radiology has served as guide to standardizing breast imaging reports to improve communication between medical practitioner and patient[17]. Such reporting is primarily used in mammogram reporting [18,19]. Assessment is divided into seven categories[20,21,22].

Diagnosis for breast cancer is a multimodal approach which primarily includes examinations by self and doctor physically and breast screening modalities along with other tests[23]. Each imaging modality has significant benefits along with disadvantages.

Pre-Screening Examinations

Clinical-breast examination (CBE) and self-breast examination (SBE) form prescreening processes. Breast screening is performed prior to screening using imaging modalities[24]. An individual examining for physical or appearance changes in breast is SBE. Presence of lumps, swelling or distortions may lead for cysts, tumors or other abnormalities[25,26]. Detecting breast lesions on regular medical check-up done by a health care provider forms another prescreening procedure in CBE. These two methods hold very less sensitivity. But, they are easy techniques with high specificity.

Traditional Imaging Techniques

Mammography

Mammography assesses the anatomical structures of the breast using low-dose x-rays and identifies any abnormalities. The gold standard for diagnosis of breast cancer is mammography since 1960[29]. However, sensitivity and specificity are influenced by factors such as breast density, age, stage of infection and family history[30,31]. High rate of false –positive mammogram result leads to unnecessary increase in anxiety, worry and increase in stress.

Mammography is not suited for women with dense breasts, fibrocystic breasts and age less than 50. Dense breast tissues and cancer tumor both appear with same property in mammograms, making it difficult to distinguish between two masses[32]. As the density of woman's breast

increases the mammography's ability to detect, abnormalities are reduced. According to American cancer society[33.34], the tissue density of breast was graded into 4 categories. Grade 1 signifies the least dense breast tissue and grade 4 the thickest.

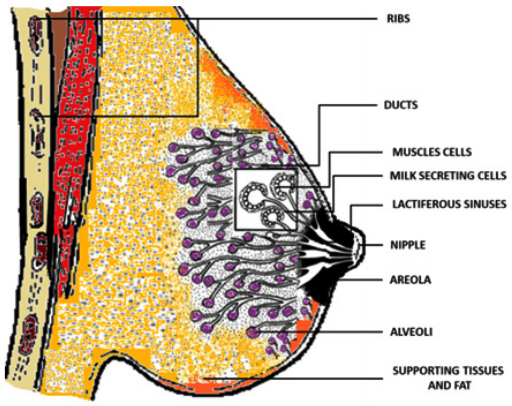

Fig. 1. Anatomy of Human breast as illustrated in [12, Fig. 2]

Mammogram detection rates were observed as 55% for grade 4, 68% for grade 3 and 83% for grade 2.

During screening process the breast tissues are compressed up to a pressure of 42 pounds. This ruptures the encapsulation of a cancerous tumor cell and release malignant cells into the bloodstream. Other threats of mammography include risk due to radiation. Mammography uses Low dose radiation which increases breast cancer risk[35]. Younger women are more susceptible to the effects of radiation than older women because homogeneous cells are more vulnerable to the effects of ionizing radiation. Speculates effect of radiation also leads to BRCA1/2 mutations[36]. Women with a family history of breast cancer or BRCA1/2 gene are not preferred to take up mammography[37].

PET/CT imaging

Positron emission tomography/ computed tomography (PET/CT)[38] is the dual scanners that combine classic radiology (CT) and nuclear medicine (PET) imaging in order to merge anatomical and functional details[39] . This combination increases the accuracy of images

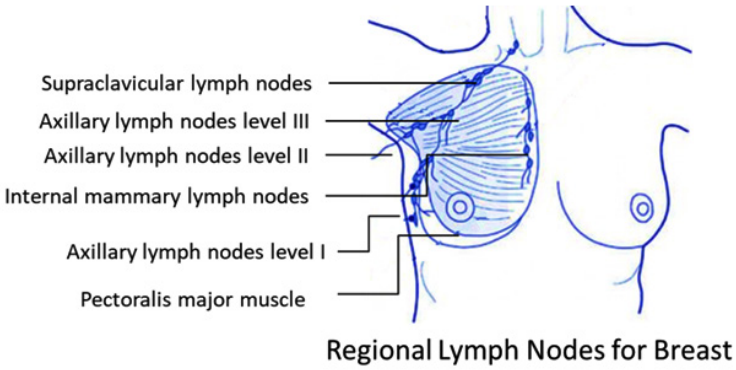

Fig. 2. Regional Lymph Nodes for Breast

Table 1. BI-RADS assessment category is presented in [17, Tab. 2]

BI-RADS Categories	Clinical Assessment
0	Incomplete - no significant abnormality found, Additional imaging modalities required
1	Negative - no significant distortion found. Like no masses, no calcifications, no asymmetry.
2	Benign - no malignant lesion found E.g. Cyst, calcification
3	Probably benign - requires further investigation like biopsy
4	Suspicious abnormality - requires further investigation, ranges from low suspicious to moderate level
5	Highly suggestive of malignancy - requires further investigation, more than 95% malignant
6	Known biopsy-proven malignancy - requires further investigation, breast malignancy already proven

Table 2. Pre-Screening Examinations

Modality	Basic Science in Medical Imaging	Application	Sensitivity	Specificity	Advantage	Disadvantage
SBE-Self-Breast examination [27]	Detecting breast lesions by looking at and feeling each breast for possible lumps and swelling.	Pre-screening	12% to 14%	NA	Increases public awareness Easy technique that can be performed at home	Detect early breast cancer High rates of false positives and over diagnosis
CBE-Clinical breast examination [28]	Detecting breast lesions on regular medical check-up done by a health care provider.	Pre-screening	57.14%	97.1%	Reduced breast cancer mortality. Can detect breast cancer missed by mammography.	Increased false -positive results. High rates of false positives and over diagnosis.

by adding anatomic image registration and localization[40,41]. It offers a precise diagnosis, by measuring metabolism with the use of a radiotracer and identifying changes at the cellular level[42,43].

Ultrasound

Ultrasound is a diagnosing tool helps to differentiate solid mass from fluid filled masses using high-frequency sound waves. Breast ultrasound has been considered a useful tool in describing abnormality detected in mammograms especially in dense breast. Lesions appear as irregular masses, abnormal enlarged ducts or clustered foci of expanded echogenicity with increased Doppler vascularity[44]. Although ultrasound is successfully used to support assessment of abnormalities detected by mammography, it should not be used as a sole modality for screening cancers[45]. However, the sensitivity of ultrasound declines in detecting non-palpable tumors such as microcalifications[46,47].

Magnetic Resonance Imaging (MRI)

MRI is a non-invasive imaging modality which uses a powerful magnetic field and radio frequency pulses to reproduce detailed pictures of organs, soft tissues and bone[48,49]. According to American Cancer Society (ACS) guidelines, MRI is best for diagnosis of breast cancer since it does not involve any harmful radiation for high-risk women with BRCA1 or BRCA2 gene mutation and their first-degree relative[50,51]. MRI is more expensive than other imaging modalities. MRI is sensitive to artifacts leading to high false positive results[52]. It lacks specificity and identifies a potential lesion with enough specificity only when it is used along with other screening technique[53].

Emerging Trends

Thermography

A Noninvasive, painless and radiation free imaging modality that help in early detection and risk assessment[54,55]. Thermography systems uses infrared camera to produce thermogram images that show patterns of heat and blood flow through thermal emissions on the surface of the body[56]. Medical thermography application includes, breast cancer, dentistry, neurology, orthopedics, foot ulcer, pain management, cardiology and veterinary science[57,58]. Significance of thermography for breast cancer screening is discussed in detail in the next section[59]. Breast thermography was approved by FDA in 1982 as an adjunctive diagnostic breast cancer screening procedure[60].

Table 3. Traditional Imaging Techniques

Modality	Basic Science in Medical Imaging	Application	Sensitivity	Specificity	Advantage	Disadvantage
Mammography [34]	Structural Imaging Using high energy X-rays photon of limited dosage interacts with tissue and gets attenuated. The changes in attenuation is captured and imaged by using reconstruction algorithm	"Gold Standard" Prognostic Diagnostic	68.6% to 83.3%	90% to 95%	High specificity and sensitivity in detecting cancer. Portable device Temporal Response (approximately < 1 minute) Good resolution More accuracy in dense breasts when using digital mammography	False -Positive Prediction cases are high. Poor contrast compared to CT and MRI. Uses ionizing radiation.
PET/CT Imaging [39] [41]	Functional Imaging By annihilation process, High-energy radioactive isotopes create two gamma particles that travel in opposite directions reach towards detectors. Structural Imaging Beam of X-rays attenuate tissues with interaction. 3D Reconstruction of image is possible.	Screening, therapeutic diagnostic prognostic	96%	77%	Image registration and fusion is accurate. Good contrast Functional information. High sensitivity.	Uses Ionizing radiation. Uses radio isotopes. Poor resolution. Non -portable device Expensive device
Ultrasound [46]	Structural imaging Sonoelastography Acoustic impedance difference	Screening, diagnostic therapeutic	Increases from 36% to 95% with Doppler-3'	Decreases from 86% to 79% with Doppler"	High diagnostic utility among women with dense breasts" Portable device	High false -positive rates Poor contrast
MRI [50]	Structural Imaging RF pulse deflects protons along transverse plane of applied magnetic field. T1, T2 and T2* relaxation time gives property of tissues.	Screening, diagnostic prognostic	88.19%	67.7%	Nearly Maximum sensitivity [51] Can detect intra-ductal spread of cancer Good contrast high resolution Nonionizing radiation	Specificity values are less and variable require compatible equipment. Biopsies are difficult. Only the lateral side of the breast can be imaged. Not portable Expensive device.

Table 3. Emerging Trends in Imaging Techniques

Modality	Basic Science in Medical Imaging	Application	Sensitivity	Specificity	Advantage	Disadvantage
Thermography [72]	Functional imaging Identifies vascular and temperature changes on skin surface by using emissivity using thermal camera. [73]	Screening, Diagnostic [74]	80.5%	73.3%	Early Detection Non-invasive Non –radioactive Temporal response Best imaging modality for dense breast.	Easily affected by room temperature. [75] High false positives and false Negatives. Low Specificity [76]
Electrical impedance tomography [77]	Functional and structural Measures local dielectric properties, electrical conductance and capacitance of cancer cells. Scans in approximately	Prognosis Screening Diagnostic	72.2% to 38%.	67% to 95%	Non-invasive Non - radioactive Relatively inexpensive	Poor spatial resolution
Microwave imaging [78]	Functional imaging Employs microwave or millimetre waves to image	Diagnostic			Non-invasive Non -radioactive	Poor resolution at higher depth" Low contrast in Fibro glandular tissues
Optical imaging [79]	Functional imaging Electromagnetic Spectra (650-900nm) use optical fibres. [80] Employs near -infrared light to measure differences in attenuation coefficient and scattering across different tissues.	Screening, diagnostic, prognostic			Non-invasive Non –radioactive Inexpensive and portable Temporal response Good contrast	High scattering decreases contrast. [81] Limited imaging depth Spatial resolution is less

Electrical impedance tomography (EIT)

EIT is one of promising emerging technologies that have unique application in imaging; they are in the phase of gaining challenges in clinical and regulatory acceptance[61]. Conductivity images produced through EIT are mostly cross-sectional hence it is termed as tomography[27a] Here, tissues are reproduced by reactive component rather than conductive[62]. The electrical properties of malignant tissue of the breast differ prominently to both benign and healthy tissue[63]. However, results vary significantly due to different nature of each device and reconstruction approach[64].

Microwave imaging

Microwave excitation was applied to evidence breast cancer[65]. Laser infrared thermography with Microwave sources of energy for heating of biological tissues is a part of active dynamic thermal (ADT) imaging[66,67]. Unfortunately, due to poor control of microwave energy dissipation, it has limited application. Microwave irradiation generates heat inside a specimen proportional to its dielectric or mechanical properties[68].

Optical imaging

Optical imaging based on geometric optics but is limited to superficial tissue surfaces[69]. Optical parameters are quantified at several wavelengths and blood oxygen saturation of tumor and surrounding tissues are estimated[70]. Accurate quantification of size and optical properties of breast is a critical requirement for the use of optical imaging[71].

Current status in breast cancer imaging and discussion

Health care providers recommend mammogram, clinical breast exam, magnetic resonance imaging in women with a high risk of breast cancer. Other screening tests include clinical trials like thermography and tissue sampling

At present, mammography is considered as golden tool of measurement for breast cancer screening. However, mammography does not ensure sufficient screening accuracy with high mammary gland density. Ultrasonography attains better accuracy in breast cancer detection even in dense breasts. Still, the terms for ultrasound equipment and image reading effectiveness have not been standardized. It is commonly used for follow-ups of an abnormality. The role of magnetic resonance imaging (MRI) for breast cancer screening is emerging to simplify features of potential lesion.

Table 4. Recommendations on breast cancer screening

Recommendations	Based on	Screening modality	Study Design
Level A	Consistent scientific evidence	clinical breast examination	Beyond screening mammography, For women aged 25-39 years, for every 1-3 years CBE is considered. Whereas, women aged 40 years and older annual CBE is recommended.
		mammography Initiation age	Initiate at ages 40-49, Strongly recommended no later than 50 years
		mammography screening interval	Annual or biennial
		mammography stop age	Until age 75
Level B	Inconsistent scientific evidence	mammography, ultrasound, MRI and Thermography	Health care providers periodically assess patient's history.
Level C	Expert opinion	self-breast examination, clinical breast examination , mammography and clinical trials like thermography and tissue sampling	• Council average-risk women about breast self-awareness and encouraged to notify their health care provider if they experience a change. • Breast self-awareness is defined as a woman's awareness of the normal appearance and feel of her breasts.

Even there is a massive development in the field of screening breast cancer still, clinical breast examination and mammography is recommended with consistent scientific evidences. According to practice bulletin published in July 2017 by American College of Obstetricians and Gynecologists[82], the screening recommendations in precautionary grounds are as given in table 4,

Cancer screening helps in proper medication if cancer is identified at earlier stages. A combined approach to breast cancer screening increases chances of identifying breast cancer at early treatable stage. But the screening modalities with non-invasive, non-radioactive, inexpensive, portable, with temporal response and good contrast are recommended.

CONCLUSION

Although Mammography still remains the gold standard for detecting breast cancer, it is still criticized for its effectiveness. There is a need for an imaging modality such that it is free from radiation risk, pain and anxiety, false alarm and non-invasive. Early detection of breast cancer thus necessitates so that treatments are more effective. Ultrasound, Breast MRI and other imaging modalities diagnosis muscle density, fluids and masses. Whereas breast thermography evaluates aberrant thermal emissions on the surface of the body due to increased blood vessel circulation and metabolic changes associated with infection. Since the temperature of cancerous tissues is generally higher than that of healthy tissues, thermograms have been considered a promising screening method for early detection of breast cancer by generating thermograms. PET-CT also plays an important role in staging breast cancer and monitoring treatment response but using ionizing radiations. These imaging modalities used in adjuncts to mammography enhance the ability to detect cancer and assess treatment planning and staging. There is a need for an imaging modality such that it is free from radiation risk, pain and anxiety, false alarm and non-invasive. Early detection of breast cancer thus necessitates so that treatments are more effective and decrease mortality rate.

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