Crossref
Similarity Check
Powered by iThenticate

Reason- A Technical Journal
ISSN 2277-1654
Volume XX 2021

TECHNOLOGICAL ADVANCEMENTS IN THE SCREENING AND DETECTION OF BREAST TISSUE MALIGNANCIES

Monalisa Kesh
Amity Institute of Biotechnology, Amity University Uttar Pradesh,
Noida- 201301, Sector-125, India
Email: keshmonalisa@gmail.com

Paper submitted on August 23 2021, Accepted after revision on March 14 2022
DOI:10.21843/reas/2021/62-83/212375

Abstract: Breast tissue malignancy is one among the most common varieties of cancer found worldwide. The number of incidents has been increasing gradually with time. Mammography scanning technique has been found to be one of the trusted methods to detect the lesions in the breast. Although mammography works almost accurately, it is a very invasive and uncomfortable scanning technique the patients have to go through. Young women having very thick breasts are more likely to get a false positive result. To reduce and eradicate all these discrepancies, scientists have been trying to develop and discover certain devices and scanning techniques that would be more accurate and sensitive than the mammograms and will overcome its shortcomings altogether. A number of different scanning techniques and procedures including Sonography, Magnetic Resonance Imaging and others are being used presently for breast cancer screening. This review aims to list and describe all such available technicalities and procedures for imaging along with screening of the breast cancer patients.

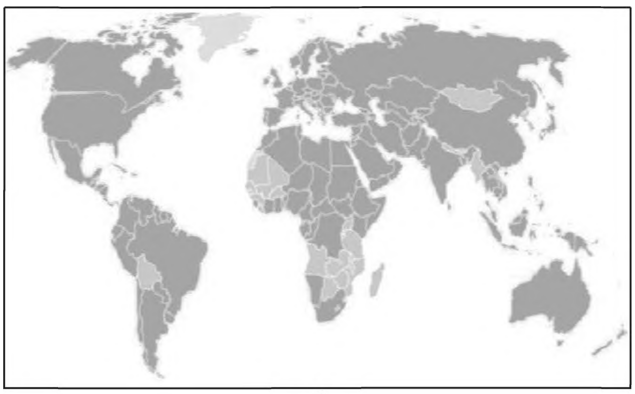
Keywords: Breast Cancer, Imaging, Mammography, Advancement, Technology.

1. INTRODUCTION

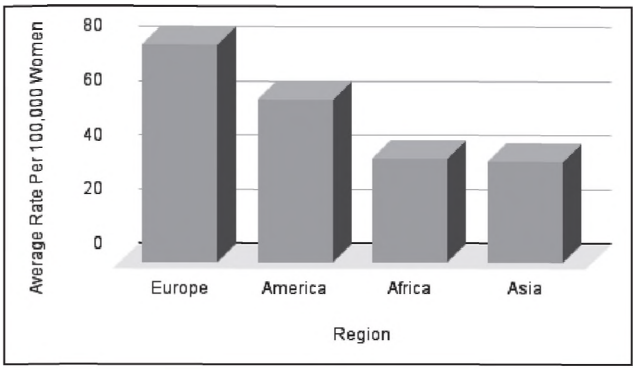
Breast cancer can be considered one of the most common types of cancer terrifying women all over the earth [Fig 1]. It is actually the second most common cancer found worldwide [1] and simultaneously is also the second prime cause of cancer allied death. One in every eight women is suffering from breast cancer. According to the data available, 70% of the patients living in developed countries have been detected with breast cancer in either I or II stage. In only 20-50% of the patients living in the developing countries, breast cancer could be detected at an early stage. It is a type of tissue cancer where the inner layer of milk glands, lobules, and tiny ducts present in the breast get affected. Women between 45 to 55 years of age are at a higher risk of getting breast cancer. Race, iodine deficiency in diet, high hormone level and economic status are also a factor that can result in breast cancer. Breast cancer has many different stages. It has also been reported that viruses play a very significant part in the development and infection of breast cancer [2]. According to a report from The National Cancer Registry Program, in India, the number of people suffering from breast cancer complications have been

found to be higher in the metropolitan cities compared to the ones in the rural areas. About 25 to 32 people out of 100 are patients of breast cancer [3].

Currently there are 23 technologies that have shown potential for breast cancer screening, but out of these the Food and Drug Administration, that is, the FDA has approved only 10 technologies. Out of these 10 technologies, only 3 technologies, firstly, screen-film mammography, followed by digital mammography and lastly, computer-aided detection [CAD], have gained approval for breast cancer screening. Other approved technologies are actually supposed to be used along with mammography or be used for other purposes [4]. Mammography is widely and extensively utilized for screening and diagnosis. It is also used for standard care for women above the age of 40 years. In this technique, firstly the patient's breast is gently pressed by a technician. Then the images of the breast are produced from many different angles. This creates a set of pictures. This set is termed as 'mammograms'. This process is done for each breast. In mammograms, the breast tissue appears to be whitish and opaque while the fatty tissue appears to be darker and pellucid. The cancerous tissue can be identified by observing the white space in the mammograms. This happens due to the x-ray being absorbed by it. This breast compression feels extremely uncomfortable for the females. Some might even feel consistent pain because of mammography. This method is actually very invasive for the patients. A false-positive result is often obtained. At a point when a mammogram indicates an abnormal region that appears to be cancerous, but ends up being normal, this is what is termed as a 'false-positive' test. Some research also shows that extensive mammography can increase the risk of breast cancer in many women with dense breasts [5]. A number of other imaging and scanning techniques can overcome the limitations of mammograms. They vary in their sensitivity and specificity of working. Here by the term 'sensitivity' the author means the proportion of correctly detected tests that indicate the cancerous cells, whereas the term 'specificity' refers to the frequency in which true negative results ('true negative' denotes a result which correctly predicts if a patient does not have breast cancer) are obtained after testing the patients who do not have breast cancer. They are less invasive in nature and can almost accurately monitor and detect breast cancer in the patients. Most of the time the patients of breast cancer would require complete removal of tissue, chemotherapy, radiotherapy and hormone therapy. According to different studies, extraordinary parallels have been noted connecting the normal growth, progression and development of breast malignancy at the molecular degree from which it has been further hypothesized that the mammary cancer stem cells can give rise to breast cancer [6].



A



B

Fig. 1. Breast Cancer Incidences **(A)** Breast Cancer Incidences Found Worldwide **(B)** Graphical Representation of the Average Estimate of Breast Cancer Incidences Observed Every 100,000 Women in Europe, America, Africa and Asia

2. BREAST CANCER GROWTH AND STAGING

There are two ways in which cancer may grow. Firstly, there is 'Carcinoma In-Situ'. When ducts and lobules expand due to replacement of normal epithelial cells by cancerous cells in the passage of breast, it is known as Ductal Carcinoma In-Situ or DCIS. Here the abnormal cells do not grow beyond the area from where they originated. The tumor so formed is benign or non-cancerous. Therefore, this is also considered as non-invasive breast cancer. This type of cancer can convert to invasive cancer but it is not compulsory for it to do so [7]. The growth of this type of breast cancer is so slow that even without treatment it would not affect the health of women. Another type involves the 'Invasive' cancer. Breast cancer is usually invasive. In this type of cancer, the tumor or lesions are malignant. They spread from their site of origin to grow on surrounding tissues of the breast. Staging of breast cancer is done on the basis of TNM (Tumor, Node, Metastasis) staging (Table 1). By thorough analysis of this 'TNM staging', a number of questions can be answered. 'T' of TNM can detect the size of the primary tumor along with the biomarkers involved with the tumor. 'N' can detect if the cancer has any potential or probability to spread among various lymph nodes of the body, and if it does, the nodes that can get affected by it, the size of the tumor and if there's any possibility of more than one tumor to be present in the lymph nodes. Lastly, 'M' can detect the metastasis of cancer, that is, if cancer can stretch to different segments of the body.

Table 1: Breast Cancer Staging

Stage of Cancer	Description
Stage 0	In this stage, the cancer cells have formed and are present only at the site of origin. No lymph nodes are affected by the cancerous cells. No other organs are affected by the abnormal cells. At this stage the cancer is non-invasive.
Stage IA	The size of the tumor is up to 2 cm. No nodes are affected by cancerous cells. The cancer has not proliferated outside of the patient's breast.
Stage IB	The tumor size is about less than 2 cm and mini masses of cancerous cells are present in the lymph tissues and nodes which are less than 2 mm in size.
Stage IIA	Here also the mass of the tumor is less than 2 cm. At this stage the cancer cells are present in a maximum of 3 lymph nodes. The diameter of the forming metastasis is more than 2 mm.

Stage IIB	Size of the major tumor is between 2 cm to 5 cm. The cancerous cell masses present in the lymph nodes are between 0.2 mm to 2 mm in size.
Stage IIIA	The primary tumor is less than or almost equal to 5 cm in size. A total of nine lymph tissues and nodes get affected in this stage in the axilla or the cancerous cells have metastasized in the lymph nodes along with the glands but strictly not to the internal organs.
Stage IIIB	Chest and skin have tumor growth on them but have not metastasized to internal organs in this stage.
Stage IIIC	At this stage the primary tumor is invasive. It has spread to more than ten lymph nodes and has metastasized to chest walls or skin.
Stage IV	The cancer at this stage has spread beyond the breast and lymph nodes. Other organs also have cancerous cells. Distant lymph nodes are also affected by the cancer.

3. TECHNOLOGIES INVOLVED IN BREAST MALIGNANCY DETECTION

A number of technologies are involved in breast tissue malignancy detection, monitoring and diagnosis.

Table 2: Short Summary of the Imaging Technologies in a Table form

Sl. No.	Imaging Technique	Sensitivity	Specificity	Advantages	Disadvantages
1	Mammography	About 75–90%	About 90–95%	Cost effective, It also has very high specificity and also possesses good sensitivity that can produce a good result.	In this technique, the sensitivity can decrease with the increase in breast thickness, it also produces very low contrast compared to MRI technique, the accuracy has often been found to be low in young women, it uses ionizing radiation and women with thick breasts often get false-positive results.
2	Magnetic Resonance Imaging	About 75–100%	About 83–98%	MRI technique can be used in the detection of the breast cancer lesions that often escape from the clinical findings and from the Mammograms and ultrasound.	It is very costly, has no ability to differentiate the malignant and the benign lesions in the breast tissues.

3	Dynamic Contrast Enhanced MRI (DCE-MRI)	About 89–99%	About 37–86%	It can very well monitor and also regulate the post treatment results and responses.	False-negative results are often obtained because of the fragments based on bleeding and structure of the breast tumor.
4	Magnetic Resonance Elastography	About 90–100%	About 37–80%	It is non invasive in nature and is also a type of non-ionizing technique.	Inability to detect very small focal breast lesions. It also lacks in spatial resolution, which is only about 25–100 um.
5	Diffusion Weighted Imaging	About 83%	About 84%	This technique is actually a non radioactive type imaging process.	It often fails to detect the high water containing cancer wounds in the breast due to the very high apparent diffusion coefficients.
6	Magnetic Resonance Spectroscopy	About 93%	About 70%	Has the potential to overcome the drawbacks of the mammography technique. It has a very high range of sensitivity and is also radiation free in nature. All imaging planes are possible with the well excelled spatial resolution of this imaging process (spatial resolution of this process can get up to 0.25 cm^3).	Inability to identify or diagnose the earlier malignant lesions. It needs a lot of improvement for its wide uses in clinical trials and other diagnostic procedures.
7	Positron Emission Tomography in integration with Computer aided Tomography Scan as PET-CT Scan	About 90–100%	About 75–90%	This procedure is non invasive in nature. It is also beneficial to the patients since it provides almost twice the medical help required.	Inability to detect the tumors sized less than 8 mm. Also, this process of breast imaging is extremely costly, therefore it can often cannot be afforded.
8	Breast Specific Gamma Imaging	About 90–96%	About 71–80%	Ability to identify lesions smaller than 1 cm in size.	This technique is not suitable for routine screening of breast tumors.

9	Molecular Image Guided Sentinel Node Biopsy	About 90.5%	About 85.7%	Post operative complexities and issues can be well reduced with the use of this technique.	This technique is not useful for the patients who have any inflammatory breast malignancy or any locally type advanced cancer.
10	Ultrasound	About 80–89%	About 34–88%	Cost effective, easy to access, and use, breast lesions can be visualized well with ultrasound.	It can often give out false positive results, and has no such inability to detect the micro calcifications in the breast.
11	Digital Infrared Thermography	About 78%	About 75%	It can be called a very important addition to the ultrasound and mammography technologie, especially in the women who are having very thick parenchyma in their breasts. It is a low radiation breast imaging method.	It is not such an effective process of breast cancer imaging compared to mammography and it can often wrongfully indicate benign tumors as malignant.
12	Thermo-rhythmometry	About 80%	About 70-75%	This technique tries to recognize the anomalies in the breast tissue that can often get missed with tests that just inspect the breasts for only a short time frame.	Often considered a high risk process and sometimes it can also give out unexpected and abnormal results.
13	Electrical Potential Measurement	About 90-95%	About 40-65%	It is non-invasive in nature and is a fast procedure. The test results can be obtained immediately after testing.	This technique is not applied largely to the patients and clinical studies are still conducted to find its broader applications in the imaging of breast cancer.
14	Electrical Impedance Scanning	About 70-85%	About 67-70%	This technique of scanning does not release any kind of radiation, which is a great advantage for the patients. It is also non-invasive in nature and its use can lead to the reduction in the number of biopsies.	Not approved by the FDA as a device for breast cancer screening. It is also not used broadly in clinical trials.
15	Microwave Imaging	About 85-90%	About 85-90%	Tumors as small as 6 mm sized identified. It does not use radiation, It is also a very relaxing process.	Inability to detect microcalcifications in breast tissues, sized less than 6 mm.

16	Optical Imaging	About 90%	About 90%	This technique is safe, it can be done fast, it is also a very cost effective one and is non-invasive in nature. Also, no radiation is given to the patients.	This technique is not widely used in clinical trials. Also, it suffers from the problems of low image resolution and poor image reconstruction procedures.
17	Ductal Lavage	About 75-78%	About 90%	This technique is used in patients who can have the tendency of development of breast cancer, even before its occurrence. This process can also be utilized for studying different bio-markers that can be related to cancer in the breasts, along with monitoring of its unusual and abnormal cytology.	This technique has limited clinical use. Though it got FDA approval, it is limited only to clinical trials for determining its appropriate uses in breast cancer determination, and also to detect the specificity as well as the sensitivity of the process.
18	Gene Expression Profiling	About 80%	About 75-79%	This technique can well analyze the tendency of ever developing breast cancer or its recurrence in the patients after analyzing their genetic profile. It can thus help to lower down the number of open breast surgeries along with the number of breast malignant tissue biopsies.	This technique is useless in those patients who have got an aggressive breast malignancy. This technique is also very costly.
19	Gene Testing	About 85%	About 70-75%	By this technique of gene testing, the patients will be able to know if they can have any mutation or any abnormality in a hereditary breast malignant gene. In case of getting a positive output, patients can decide the medications or the therapy types as required.	This technique can often fail to detect breast malignancy in the early stage. It is also a very costly procedure. Sometimes it also can wrongly give out false positive results. This can also take a long time to produce the results of the tests.
20	Serum Proteomic Profiling	About 90%	About 70%	Non-aggressive type of imaging technique. It can reveal if there is a possibility of development of cancer inside the women's body. It is also a very fast procedure.	Only by sole use of this technique, cancer cannot be properly localized, therefore, it should be tied up with any kind of imaging modality to obtain a good result. This process is still in progress for more enhancement.

21	Piezoelectric Finger Sensor	About 80-95%	About 85-90%	PFS can produce certain devices that can detect breast malignant lesions early and very accurately, when compared to other imaging process. Devices which make use of piezoelectricity are much less aggressive in nature and more comfortable.	PFS can often face sensitivity to high temperature and can cause issues in breast cancer screening.

3.1 Mammography

A mammogram is actually an x-ray photograph of the patient's breast which can ease the detection and identification of various cancerous and non-cancerous abnormalities in the breast. A miniature dosage of radiation is applied through the patient's breast after its compression in between two x-ray plates for producing an image. Mammograms are intensively used for both the purposes of screening and diagnosis of breast cancer [8]. Breast cancer screening with mammography points to detect breast cancer at the earliest stage when it is curable [9]. If the tumor growth is found to be heterogeneous or the presumptions regarding the growth of breast tumors appears to be incorrect, screening mammography may not be a sufficient tool for bringing down the loads of breast cancer [10]. The first recombined test of mammography screening was launched in 1963 in New York [11]. If a woman experienced any symptoms relating to breast cancer, for example, a lump in her breast, diagnostic mammography can be used in such detections [12]. A number of anatomical techniques and approaches are based on mammography including the Screen-Film Mammography Technique, Computer Aided Detection Technique, Digital Mammography Technique.

Screen-Film Mammography is done as a standard routine for women aged 40 and over. On a mammogram, the breast tissues come into view as white and smeared while the fatty tissues appear to be darker and pellucid. The cancerous cells appear as white spaces. Mammography of this kind has a

Table 3: Three different Mammography Techniques

Mammography Technique	Screening Type	FDA Approval
Screen-Film Mammography Technique	Routine and clinical screening	Approved in 1969
Computer Aided Detection Technique	Clinical screening	Approved in 1998
Digital Mammography Technique	Clinical screening	Approved in 2000

sensitivity in the range of 71-96% if done yearly. The specificity varies from 90-95%. Age of the patient being tested, natural breast thickness of the women, hormone replacement therapy taken by woman, quality of the radiologist performing the job and the quality of image produced also affect the results of the mammography. This type of mammography is uncomfortable and invasive for many patients. It is often said to be painful as well. One of the drawbacks of this is that it often gives false positives for women with thicker breasts and even in women younger than 40. It has been reported that the chance of encountering a false positive mammogram result for women going through biennial screening in Europe ranging from ages 50 to nearly 70 is about 20% [13] and the chance of undergoing a biopsy because of the false positive test result is about 3% [13]. Still it is one of the three methods that has been approved by the FDA for screening and diagnosis. Studies have calculated that for every 1000 women who have been invited for mammography screening process every other year ranging from ages of 20-50 years, almost 200 will undergo a false positive mammogram result, about 30 of them will experience a biopsy because of this false positive mammogram result and about 3 of them will get identified for having interlude cancer. In recent times, gold-based nanoformulation techniques have significantly eased the contrasting in mammography images [14].

In computer aided detection the computer goes through the mammograms of a patient and spotlight the suspicious areas that indicate cancer. This method uses a laser that converts the mammogram to a digital picture that can be analyzed by the computer or takes input directly from a digital mammogram. A digital mammogram directly provides the computer with digital pictures. It is generally used for cross checking purposes. Radiologists use to check if they have missed a spot on the mammogram while screening it. Depending on its result the radiologist may re-evaluate the mammogram. This method does not increase or decrease the breast cancer rates, but rather increases the proficiency of the radiologist. Using this even a usual radiologist can be as proficient as a specialized one. This does not remove the discomfort of the patients as the mammography is still done. It is also one of the three technologies approved by FDA for screening along with the diagnosis of breast cancer. Then there is the technicalities of digital mammography, which is nearly similar to the screen film mammography, the only difference being that in screen-film the image was taken on a film whereas here the image is digital. It has not been proven that the procedure of digital mammography is better compared to screen film mammography. Although the contrast and the resolution of digital mammography is better at a much lower dose compared to screen film mammography. It is the last one of the three technologies approved by the FDA for the screening and diagnosis of breast cancer malignancy. In the Tomosynthesis method, the x-ray machine is moved around the breast in an arc while taking multiple pictures (usually 12 images). This, just like digital mammography, uses low doses of radiation. The reason behind this is that using multiple images would cover the areas that are being overlapped in normal mammography. This

would reduce the chances of missing a cancer tissue. These pictures that have been taken would be submitted to a computer which would then create a high resolution, cross-sectional, 3-dimensional image of the breast. This technology may improve the detection of breast cancer complications in women with thicker breasts. But currently it takes a long time for the computer to render the image (approximately 2 hours). For this technology to be used the time required for image creation would have to reduce significantly. A study regarding the clinical performance of Digital Mammography along with Digital Breast Tomosynthesis in a number of patients of different age groups and breast density recorded some enhancement in evaluation and rates of cancer detection with Digital Breast Tomosynthesis being greater on the baseline mammograms [15]. But again, women with extremely dense breasts did not have any benefit with the enhanced recall or cancer detection with Digital Breast Tomosynthesis on successive screening series [15].

3.2 Magnetic Resonance Imaging or MRI

Breast MRI is an important technique utilized significantly in breast imaging. Cancer can be successfully detected in the early stage with this screening technique. It is used for the indication of staging of well investigated cancer and screening of it in women suffering from high and elevated risks of breast cancer and monitoring of responses to neoadjuvant chemotherapy procedures [16-18]. It is a type of anatomical imaging, non-invasive in nature, that involves using a vibration in low energized radio frequency response in a very strongly consistent magnetic field [19]. Different tissue types show exceptional reverberation qualities which can be shown with varying difference properties and permit breast injuries to be recognized. Every MRI produces many point by point pictures of the breasts from side to side, front to back and top to bottom [19]. A radiologist then, at that point, deciphers the pictures to distinguish strange districts that might require further examination. Though empirical data on the breast cancer learning curve appears to be lacking, some studies have reported improved performances of the radiologists over time [20]. Breast MRI can often detect malignancies that couldn't be otherwise identified from ultrasound detection or clinical mammograms [21-22]. In this manner, workings of MRI might incorporate appraisal of irregularities that are hazy on a mammogram, similar to that of the assurance of the degree of cancer development after beginning finding, and for assessment of the adequacy of therapies. Other than that, MRI may likewise be valuable in imaging increased breast tissue, thick breast tissue (frequently found in more youthful ladies), and reviewing breast anomalies that can be felt however are not noticeable with customary mammography or ultrasound. During an MRI of the breast, the patient lies on her stomach on the filtering table. Her breasts hang into a downturn or hollow in the table, which contains loops that distinguish the magnetic signals. The table is moved into a cylinder-like machine that contains a really strong magnet. After an underlying series of pictures has been taken, the patient might be given a different specialist intravenously to upgrade the perceivability of tissue attributes. The differentiation specialist is not radioactive in nature and can be utilized to work on

the perceivability of a growth. Extra pictures can be taken subsequent to directing the differentiation specialist. The whole imaging meeting requires around 60 minutes. Breast MRI isn't FDA supported for routine breast malignant growth screening, however clinical preliminaries are being performed to decide whether MRI is important for screening specific ladies, similar to that of the youthful ones experiencing a high danger of breast complications. For breast malignancy screening, the use of atomic MRI was accounted for 40 years prior. [23]. Explicitness of this screening procedure differs from 83-98%, though the affectability lies in the scope of 75-100%. The American College of Radiology has likewise suggested the utilization of Breast MRI for high-hazard populaces. X-ray cannot generally precisely recognize malignant growth and non-harmful breast conditions. While contrast-upgraded MRI is genuinely essentially more precise than mammography for distinguishing multicentric DCIS (Ductal Carcinoma In Situ), it was altogether less explicit than mammography for identifying related obtrusive sickness in one distributed series. X-ray is costly, multiple times the expense of customary mammography and on the grounds that it will produce all the more false positive outcomes, it creates added expenses of extra biopsies and additionally other indicative development.

3.3 Dynamic Contrast Enhanced MRI (DCE-MRI)

DCE-MRI has moderate specificity and extreme sensitivity for diagnosing breast malignancy [38-39]. Sensitivity of this technique varies from 89-99% whereas the specificity differs from 37-86%. It is a non-obtrusive imaging procedure and works by checking the examples of fleeting improvement of a tissue post intravenous infusion of a paramagnetic difference medium. Degrees of tissue vascularization, injury separation and interstitial space organization can be quantitatively dictated by this method [24]. This kind of imaging methodology can be critical in portraying growth angiogenesis with generally speaking events, repeat and endurance of the breast cancer patients. Since this technique is three dimensional in nature, extent of disease condition before morphological alterations of the tissues can be well visualized, moreover it can be used to predict the responses during the early treatment times and even before starting of the therapy. When integrated with a computer aided diagnosis technique (like that of the texture analysis features), DCE-MRI can be useful in detecting some ER+ (estrogen receptor positive) subtypes of breast cancer [25]. As indicated by another report, Triple Negative Breast Cancer (TNBC) has been found to introduce various trademark highlights with significant contrasts from some other breast malignant growth atomic subtypes on DCE-MRI the morphological elements of the sores, similar to the shape and design alongside the examples of their improvement. This can significantly improve the diagnosis of TNBC [26]. There is no limitation of DCE-MRI (unlike that of mammography) due to the density of breast tissue, but the non-specific nature of this technique can create some issues [27].

3.4 Magnetic Resonance Elastography

MRE procedure has effectively arisen as a critical methodology for quantitative imaging of the mechanical properties of delicate tissues in vivo. Other than its utilizations in the analysis of breast malignant growth, lately, MRE has likewise been presented as a clinical device for the assessment of a few entanglements and illnesses remembering intricacies for the mind, heart, skeletal muscles, liver and so forth. [28]. It is a unique flexibility imaging strategy that works by joining MRI methods with exceptionally low recurrence and utilizing mechanical waves for making an elastogram for evaluating the solidness of the tissues. It is a non-invasive and non-ionising method with high sensitivity (90-100%) and moderate specificity (37-80%). Viscoelastic characteristics of breast tissues can be quantitatively measured by MRE technique by the application of external stress and pressure [29]. According to studies, stiffness has been found to be higher in patients with dense breasts, compared to the ones with non-dense breasts. This is a result of the expansion in the quantity of cells, proteoglycans, collagens, and so forth contrasted with the encompassing solid tissue and the non-cancerous tumors present alongside. Though manual palpation is a common technique utilized for the routine screening and studying of breast cancer patients, it lacks sensitivity and specificity. According to some studies, by MRE scanning of the patient's breasts, these restrictions of manual palpations can be overcome. A study on the MRE of breast lesions reported significant gain in diagnostics after analyzing 29 benign and 39 malignant lesions [30]. In breast cancer scanning, MRE is limited by the detection of very small focal lesions along with its spatial resolutions. This is because of overlapping in the tender malignant tumors and elasticity ranges of the stiff benign lesions [31].

3.5 Diffusion Weighted Imaging

DWI or Diffusion Weighted Imaging is a type of unchanged MRI method that utilizes dissemination of water particles for creating contrast in attractive reverberation pictures for tending to a portion of the restrictions looked by ordinary breast MRI procedure. This cycle depends on the recognizable proof of a randomized minute movement of the free water atom which is named as Brownian Movement. When integrated with apparent diffusion of coefficient mapping, DWI can provide information regarding the function of water in the tissues [32]. Sensitivity of this technique varies at 83% whereas the specificity lies at 84%. DWI has been found to possess the ability of enhancing the early monitoring of tumor responses to therapy and monitoring of the residual tumor post therapy procedures. Probable benefits of this technique include enhanced differentiation of non-cancerous and cancerous breast injuries and monitoring and prophecy of their curative efficacies [33]. This method has effectively empowered the location of breast malignant growth, particularly in patients having thicker breasts. Be that as it may, affectability of DWI procedure will in general shift when contrasted with contrast upgraded MRI. The limitation of this technique includes the lack of spatial resolution. Sometimes it is also unable to detect very small focal lesions. Advancement and innovations in DWI are gradually found to be helpful in overcoming

the problems regarding the quality of images produced by this technique. DWI can be considered an accurate, non-radioactive imaging technique that still has not reached its ultimate potential and is improving gradually.

3.6 Magnetic Resonance Spectroscopy

MRS or Magnetic Resonance Spectroscopy is used for measuring a chemical spectrum in the area by the use of a high magnetic field strength, ranging from 11-15 T on tissue samples, cell extracts, body fluids, thereby reporting significant information regarding the chemical contents of the areas. It is a sort of biological imaging method that breaks down the particular subatomic parts of a tissue by distinguishing the modifications in the natural chemistry of the tissues and recognizing characteristic properties of breast malignant growth [34-35]. Integration of MRI procedure with the in vivo 1H Magnetic Resonance Spectroscopy protocol can further enhance the total acquisition time period by about 10 min approximately along with the benefits of improvising the diagnostic precision of clinical Breast Magnetic Resonance [36]. Sensitivity of this technique varies at 93% whereas the specificity lies at 70%. MRS can successfully overcome the drawbacks of mammography. Moreover, it is a radiation free imaging technique with excellent spatial resolution. One of the drawbacks of this imaging technique includes its need of larger lesions for detection along with its poor sensitivity in detecting tCho signals, a phosphocholine metabolite which is used as a diagnostic biomarker for detecting elevations in breast cancer [37]. Since the last decade, there has been significant advancements on Breast MRS, simultaneously a number of potential factors have also been identifies which can limit the potentials of MRS including optimization of the assessment methods along with the complexities involved in the acquisition procedures which needs to be taken care of and improved prior including this imaging technique in any clinical environment.

3.7 Positron Emission Tomography (PET) Scan and PET in Integration with Computer-Aided Tomography (CT) Scan as PET-CT Scan

Positron Emission Tomography (PET) is a amalgamation of PET scan and CT scan that can produce highly specific and detailed images of the body. High sensitivity and spatial resolution of the PET scanners used for breast cancer detection (Positron Emission Mammography) are extensively used for the study and detection of primary tumors. It is actually a technical process that observes the blood flow rate, neurotransmitter, rate of metabolism, radiolabeled drugs in the patient and eases the measurement of physiological functions in the body. It is also used for quantitative analysis as a disease process keeps evolving over a time period by monitoring the relative changes because of a specific stimulus [38]. It works by consolidating diverse atomic medication methods and figured tomography, consequently bringing about top notch and specifically detailed pictures. Sensitivity of these techniques varies from 90-100% whereas the specificity differs from 75-90%. It is a non-invasive process and provides the patient with high diagnostic profits compared to individual PET scan or

CT scan. It is a costly process. It fails to detect the tumor whose size is smaller than 8 mm [39]. PET scan with FDG (F-fluorodeoxy-glucose, an analogue of glucose) has been considered an important diagnostic tool for measuring the metabolic activities by evaluating the amounts of accumulation of FDG. FDG has gained popularity for the detection of small tumors, observing and monitoring their treatment responses thereby forecasting the patient's fate having cancer. When the F-fluorodeoxyglucose Positron Emission Tomography radiotracers enter the cells through the glucose transportation channels, the tumor cells take them up in higher quantities compared to the normal cells. Thus PET-CT scans have been considered an important factor for predicting the malignancy status alongside the prognosis of the patients suffering from breast cancer. According to studies, the uptake of F-fluorodeoxyglucose inversely varies with the fate of breast cancer patients. After the initiation of nanoparticle assisted photothermal therapy, it was observed that the tumor cells significantly reduced the uptake of FDG. Thus it was concluded that it can be used as an effective marker for assessing the cancer treatment responses [40].

3.8 Breast Specific Gamma Imaging

BSGI or Breast Specific Gamma Imaging is otherwise called Scintimammography. In this strategy, an innocuous radioactive tracer is inserted inside the patient, which might amass distinctively in the carcinogenic and noncancerous tissue. This molecular breast imaging technique that works by the application of a radiotracer, uses a specialized gamma camera for the identification and image capturing of the breast lesions. This technique got FDA approved in 1999 and is considered an addition to mammography. This technique is successful in the identification of very small lesions (less than 1 cm). Sensitivity of this technique varies from 90-96% whereas the specificity differs from 71-80%. This specialized nuclear medicine imaging technique is very useful in detecting mammographically impenetrable breast cancer with specificity and sensitivity comparable to MRI. Breast density cannot affect BSGI technique. Technetium Tc99m Sestamibi is a radiotracer used in BCGI and works by its infection into the patient's bloodstream, followed by its observations using a specialized camera [41-42]. This process is not suitable for routine tumor screening since a very high dose of radiation is being used and the whole body gets exposed to that huge amount of radiation [43].

3.9 Molecular Image Guided Sentinel Node Biopsy

SLNB or Sentinel Lymph Node Biopsy is a negligibly obtrusive, progressive strategy utilized for the location and recognizable proof of metastasis in the beginning phases of breast malignant growth. It is basically a surgical technique for detection of cancer spread in the lymphatic system. Depending on the status of nodal metastasis, SLNB is conducted to determine the optical therapeutic procedure [44]. This technique is popular for reduced complexities following operative measures which are related with conventional dissections of the axillary lymph

nodes. Sensitivity of this technique varies at 90-90.5% whereas the specificity lies at 85.7%. A review on the significance of the sentinel lymph node micrometastases in human breast malignant growth tracked down that albeit the endurance pace of patients without Micrometastatic Sentinel Lymph Node don't contrast genuinely from those patients experiencing Micrometastatic Sentinel Lymph Node, around 9.3% of the patients (without Micrometastatic SLN) experienced an extra axillary nodal illness following axillary analyzation, though patients with Micrometastatic SLN had a critical decline in their endurance rate when the course of axillary analyzation was precluded [45]. Intense direction of SLNB should check the amount of intrusive methodology required and break down various basin waste through restricted SLN. This can fundamentally work on the exactness of breast malignant growth arranging in ladies experiencing intrusive breast cancer. This procedure isn't prescribed to patients with incendiary breast malignant growth and privately progressed diseases.

3.10 Ultrasound

Ultrasound or Sonography is an imaging strategy that can be utilized for the screening of breast malignant growth in patients with thicker breasts. It can well examine the regions not seen with mammograms. Thus the limitations of mammography technique can be overcome by Sonography technique [46]. Here high frequency sound waves are reflected by the organs in the body, these echoes are different for normal healthy tissues and for cancerous tissues. The image that these reflections form is called a sonogram. It is used as an additive to mammography. Using these technologies together increases the accuracy of detection of cancer. Its capability to detect the difference between fluid filled cysts and solid tumors, as they have different refractive indexes, is the reason why it is used along with mammography. The time range required for it is 15 to 30 minutes. It depends on how difficult it is for the technician to identify the location of the tumor. Sensitivity of this technique varies at 80-89% whereas the specificity lies at 34-88%. Sonography is not used in routine because it cannot detect calcifications in the breast, which is a sign of ductal carcinoma in situ. Currently it is used for image guided biopsy.

3.11 Digital Infrared Thermography

Infrared thermography depends on the rule that chemical along with blood vessel action in both precancerous tissue and the regions encompassing a creating breast malignant growth is regularly higher than in the ordinary breasts. Precancerous and carcinogenic masses have high metabolic rates, and they need a bountiful stockpile of supplements to develop. To do this they increment course to their cells by conveying synthetic signs to continue to exist veins open, enlist dormant vessels, and make new ones (neo-angiogenic). The expanded vascular movement regularly brings about an expansion in surface temperatures of the breast close to the area of growth, which can be imaged through thermographic gadgets. In 1982, the FDA supported the principal breast thermography gadget as an adjunctive breast malignant growth screening

system. From that point forward, a few devices have been endorsed under the FDA's 510(k) comparable device audit. In light of an investigation of breast disease discovery, examination of the viability and accuracy of a non-intrusive advanced infrared warm imaging framework was performed. As per that review, Digital Infrared Thermography can be viewed as an important expansion to mammography and ultrasound in ladies having thicker breast parenchyma [47].

3.12 Thermorhythmometry

In spite of the fact that thermorhythmometry depends upon comparable standards as infrared thermography to assist with recognizing breast disease, this method utilizes an alternate methodology. Rather than imaging the breast, tests are set on the breast that screen the skin temperature over a 24-hour time span (known as a circadian rhythm) to distinguish differences which might compare to neo-angiogenesis and malignant growth. This methodology plans to recognize anomalies that could be missed with tests that just inspect the breast for a short timeframe, conceivably missing admonition signs that are just obvious by investigating the day by day temperature patterns of the patients.

3.13 Electrical Potential Measurement

In this strategy, electrodes are set on the breasts which can quantify the modest quantity of regular electric charge at different areas on the breast. The strange development of malignant growth cells might create awkward nature in the ionic inclinations of cells that can hypothetically be identified by the electrodes. The distinction in ionic focus makes an electrical potential that hypothetically could be estimated by anodes put on the breasts. A specialist can go through this noninvasive method in under 20 minutes and test outcomes are accessible for radiologist translation inside five minutes after the methodology. This innovation is presently under clinical examination to accumulate information to submit to the FDA. Starting investigations report an affectability of 90-95% and a particularity of 40-65% percent for substantial injuries. In a study related to the measurements of benign lesions and breast cancer, it was found that on average, the altered electrical potentials monitored and detected via non-invasive measurements of the skin, refeltedc the marked presence of some transformed cells in patients suffering from breast cancer [48].

3.14 Electrical Impedance Scanning

It utilizes the electrical leading properties of the breast tissue to recognize cancers. A limited quantity of current is brought into the body utilizing a handheld test; the breast tissue is then imaged utilizing a professional held device. The device doesn't discharge radiation; rather, a tiny measure of electric flow, like a little battery, is communicated into the body. The current goes through the breast where it is estimated by the filtering test. Spaces of low impedance, which might compare to dangerous growths, appear as dazzling white spots on a PC screen. The scanner sends the picture straightforwardly to a PC, permitting the radiologist to move the test around the breast to get the best perspective on the space being inspected.

The device is planned to diminish the quantity of biopsies expected to decide if a mass is actually cancerous. The FDA endorsed an EIS gadget called the T-Scan 2000, in 1999, as an aide to mammography.

3.15 Microwave Imaging

Microwave signals are utilized to picture the conductivity of the breast. Since the water content of tissue to a great extent decides the conductivity, specialists might have the option to segregate between the low water content of sound cells and high water content in growths to distinguish harmful breast tissue.

3.16 Optical

Infrared light is made to go through the breast tissue distinguishing the spaces of high vascular action that have been displayed to correspond with the quick development of cancers. Since most cancers require a wealth of supplements conveyed through the vasculature of the fine bed for sped up development, the high oxygen content and blood volume has been exhibited to connect with harm. Just gentle bosom pressure is needed for this strategy and the bosom tissue isn't presented to radiation. This technique is leaned toward for its speed, minimal expense, wellbeing, and noninvasiveness; nonetheless, optical imaging has not been approved in huge clinical preliminaries and issues of low picture goal and hardships with picture recreation should be survived.

3.17 Ductal Lavage

This method is not that much utilized in ladies having a high danger of breast malignant growth. It includes the assortment of cells for infinitesimal assessment by washing the breast channels with a saline arrangement. The example is then broken down by a pathologist to distinguish the irregularities. At present, this method is just used in patients with different danger variables of bosom malignant growth improvement with a means to identify disease creating chances even before its event. Ductal Lavage can be used for the examination of different molecular markers associated with breast malignancies and monitoring of abnormal cytology [49]. This technique got FDA approved in 1999 and has overall limited clinical use.

3.18 Gene Expression Profiling

Gene Expression Profiling or Gene Profiling describes the tissue tests dependent on the action of different qualities that assume a part in creating obtrusive breast malignant growth. The overall action of thousands of qualities on a microarray (glass slide with many spots, each exclusively addressing one quality) is investigated by computer calculations to anticipate the conduct of the tissue. By the utilization of this strategy, quality profiles can be utilized to assess the visualization of breast cancer patients, sub-characterizing bosom malignant growths types and foreseeing different treatment reactions. This technique is gradually easing the understanding of the heterogeneous nature of breast malignancy to scientists and researchers, on a genomic scale [50].

3.19 Gene Testing

This method utilizes a blood test to distinguish hereditary changes that have been related with an expanded danger of

creating breast malignant growth. Until this point, the main clinically approved qualities have been BRCA1 and BRCA2. This technique is not FDA approved till date.

3.20 Serum Proteomic Profiling

In this technique, the overall measures of different proteins in the blood are estimated by mass spectrometry. Computer calculations are then used to recognize designs that might be characteristic of the conceivable presence of disease. Notwithstanding, this procedure will just show the presence of cancer. Another methodology should be utilized to picture the tissue and decide the areas of the malignant growth. This technique is still in the experimental phase.

3.21 Piezoelectric Finger Sensor

A piezoelectric finger (PEF) is a piezoelectric cantilever sensor prepared to do all electrical tissue firmness estimation. Estimation of tissue firmness is accomplished by basically setting a PEF on a tissue similar to palpation (electronic palpation) however with a much higher affectability and exactness. It is a nanotechnology based methodology for hindering cell multiplication of breast carcinomas. Biocompatible piezoelectric nanoparticles are utilized to target, alter and invigorate HER2+ bosom disease cells [51]. Piezoelectric has paved the way for development of certain devices that can detect breast cancer lesions earlier and more accurately compared to other techniques and scanning images available at present. The devices using piezoelectric are comparatively less invasive and more comfortable. Piezoelectricity has the potential to replace mammograms in future.

4. CONCLUSIONS AND FUTURE ROADMAP

In this review, the author has distinguished probably the most well-known strategies and systems utilized in the location, checking, determination and treatment of breast malignancies. These methods of breast carcinoma diagnosis and treatment have undergone several changes and improvements over the past few years. The focus has mainly been on controlling and maintaining the disease with maximum patient compliance and decreased patient discomfort along with the reduction in side-effects post treatment and operative measures. It is very important to maintain the integrity of the surrounding normal healthy cells while treating the deceased cancerous cells. Not all imaging techniques can be suitable for a particular patient, it keeps varying from one patient to another depending on their health condition. Some women cannot tolerate excessive aggressive treatment procedures. For some, operation is not an option. Cancer stage is an important aspect in this area, since the scanning techniques often vary according to the patient's stage of cancer. With the use of these scanning techniques one can avail an opportunity of early breast cancer detection, which would save more lives. With the advancement of years along with the emergence of these scanning techniques, new multifunctional imaging modalities can be expected to enter clinical trials in near future for better diagnosis, identification and detection of breast cancer malignancy in patients.

REFERENCES

[1] Momenimovahed, Z. and Salehiniya, H., Epidemiological characteristics of and risk factors for breast cancer in the world, Breast Cancer (Dove Med Press), Vol.11, pp. 151-164, 2019.

[2] Alibek, K., Kakpenova, A., Mussabe-kova, A., Sypabekova, M., Karatayeva, N., Role of viruses in the development of breast cancer, Infect Agents Cancer, Vol. 8, 32, 2013.

[3] Aswathy, M.A., and Jagannath, M., Detection of breast cancer on digital histopathology images: Present status and future possibilities, Informatics in Medicine Unlocked, Vol. 8, pp. 74-79, 2017.

[4] Joy, J. E., Penhoet, E. E., Petitti, D. B. and Institute of Medicine (US) and National Research Council (US) Committee on New Approaches to Early Detection and Diagnosis of Breast Cancer (Eds.), Saving Women's Lives: Strategies for Improving Breast Cancer Detection and Diagnosis, National Academies Press (US), 2005.

[5] Nazari, S.S. and Mukherjee, P., An overview of mammographic density and its association with breast cancer, Breast Cancer, Vol. 25(3), pp. 259-267, 2018.

[6] Feng, Y., Spezia, M., Huang, S., Yuan, C., Zeng, Z., Zhang, L., Ji, X., Liu, W., Huang, B., Luo, W., Liu, B., Lei, Y., Du, S., Vuppalapati, A., Luu, H.H., Haydon, R.C., He, T.C., Ren, G., Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis, Genes & diseases, Vol. 5(2), pp. 77–106, 2018.

[7] Parikh, U., Chhor, C.M., Mercado, C.L., American Journal of Roentgenology, Vol. 210(2), pp. 246-255, 2018.

[8] Bhan, A., Comparative Analysis of Pre-Processing Techniques for Mammo-gram Image Enhancement, Procee-dings of the INCON VIII, International Conference on Ongoing Research in Management and IT, Pune, India, 2013.

[9] Løberg, M., Lousdal, M.L., Bretthauer, M., Kalager, M., Benefits and harms of mammography screening, Breast Cancer Res, Vol. 17(1), 63, 2015.

[10] Esserman, L., Thompson, I.M., Reid, B., Nelson, P., Ransohoff, DF., Welch, HG., Addressing overdiagnosis and overtreatment in cancer: a prescription for change, Lancet Oncol., Vol. 15, pp. 234–242, 2014.

[11] Reynolds, H., The Big Squeeze: A Social and Political History of the Controversial Mammogram, New York: Cornell University Press, 2012.

[12] Sundaram, K.M., Sasikala, D., Rani, P.A., A Study On Preprocessing A Mammogram Image Using Adaptive Median Filter, Int. J. Innov. Res. Sci. Eng. Technol, Vol. 3, pp. 10333–10337, 2018.

[13] Hofvind, S., Ponti, A., Patnick, J., Ascunce, N., Njor, S., Broeders, M., Giordano, L., Frigerio, A., Törnberg, S., Van-Hal, G., Martens, P., Májek, O., Danes, J., Von Euler-Chelpin, M., Aasmaa, A., Anttila, A., Becker, N., Péntek, Z., Budai, A., Mádai, S., Fitzpatrick, P., Mooney, T., Zappa, M., Ventura, L., Scharpantgen, A., Hofvind, S., Seroczynski, P., Morais, A., Rodrigues, V., Bento, M.J., Gomes de Carvalho, J., Natal, C., Prieto, M., Sánchez-Contador-Escudero, C., Zubizarreta Alberti, R., Fernández Llanes, S.B., Ascunce, N., Ederra Sanza, M., Sarriugarte Irigoien, G., Salas Trejo, D., Ibáñez Cabanell, J., Wiege, M., Ohlsson, G., Törnberg, S., Korzeniewska, M., Wolf, C., Fracheboud, J., Patnick, J., Lancucki, L., Ducarroz, S., Suonio, E.J., False-positive results in

mammographic screening for breast cancer in Europe: a literature review and survey of service screening programmes, Med Scree. 19 Suppl, Vol. 1, pp. 57-66, 2012.

[14] Torrisi, L., Restuccia, N., Torrisi, A., Study of gold nanoparticles for mammo-graphy diagnostic and radiotherapy improvements, Rep. Pract. Oncol. Radiother. J. Greater Poland Cancer Cent. Pozn. Pol. Soc. Radiat. Oncol, Vol. 24, pp. 450–457, 2019.

[15] Lowry, K.P., Coley, R.Y., Miglioretti, D.L., Kerlikowske, K., Henderson, L.M., Onega, T., Sprague, B.L., Lee, J.M., Herschorn, S., Tosteson, A.N.A., Rauscher, G., Lee, C., Screening Performance of Digital Breast Tomosyn-thesis vs Digital Mammo-graphy in Community Practice by Patient Age, Screening Round, and Breast Density, JAMA Netw Open, Vol. 3(7), e2011792, 2020.

[16] Mann, R.M., Kuhl, C.K., Kinkel, K., Boetes, C., Breast MRI: Guidelines from the European Society of Breast Imaging. Eur Radiol, Vol. 18(7), pp. 1307–1318, 2008.

[17] Newell, M.S., Giess, C.S., Argus, A.D., ACR practice parameter for the performance of contrast enhanced magnetic resonance imaging (MRI) of the breast, Reston Va: American College of Radiology, 2018.

[18] Sardanelli, F., Boetes, C., Borisch, B., Magnetic resonance imaging of the breast: Recommendations from the EUSOMA working group, Eur J Cancer, Vol. 46(8), pp. 1296–1316, 2010.

[19] Graves, M.J., Zhu, C., Trivedi, R., Saba, L., Suri, J.S., Basic Principles of Magnetic Resonance Imaging In 3D Imaging Technologies in Atheros-clerosis, Eds. Springer, pp. 153–169, 2015.

[20] Warner, E., Causer, P.A., Wong, J.W., Improvement in DCIS detection rates by MRI over time in a high-risk breast screening study, Breast J, Vol. 17(1), pp. 9–17, 2011.

[21] Mann, R.M., Kuhl, C.K., Moy, L., Contrast-enhanced MRI for breast cancer screening, J. Magn. Reson. Imaging, Vol. 50, pp. 377–390, 2019.

[22] Wallyn, J., Anton, N., Akram, S., Vandamme, T.F., Biomedical Imaging: Principles, Technologies, Clinical Aspects, Contrast Agents, Limitations and Future Trends in Nanomedicines, Pharm. Res., Vol. 36(6), pp. 78, 2019.

[23] Goldsmith, M., Koutcher, J.A., Damadian, R., NMR in cancer, XIII: Application of the NMR malignancy index to human mammary tumours, Br. J. Cancer, Vol. 38, pp. 547–554, 1978.

[24] Rahbar, H., Partridge, S.C., Multiparametric MR Imaging of Breast Cancer, Magn. Reson. Imaging Clin. North Am., Vol. 24, pp. 223–238, 2016.

[25] Wang, H., Hu, Y., Li, H., Xie, Y., Wang, X., Wan, W., Preliminary study on identification of estrogen receptor-positive breast cancer subtypes based on dynamic contrast-enhanced mag-netic resonance imaging (DCE-MRI) texture analysis, Gland Surg., Vol. 9, pp. 622–628, 2020.

[26] Azzam, H., Kamal, R., El-Assaly, H., Metwally, L.I.A., The value of dynamic contrast-enhanced MRI in differentia-ting triple-negative breast cancer from other subtypes, Egypt J Radiol Nucl Med 50, 106, 2019.

[27] Amornsiripanitch, N., Bickelhaupt, S., Shin, H.J., Dang, M., Rahbar, H., Pinker, K., Partridge, S.C., Diffusion-weighted MRI for Unenhanced Breast Cancer Screening, Radiology, Vol. 293, pp. 504–520, 2019.

[28] Glaser, K.J., Manduca, A., Ehman, R.L., Review of MR elastography applications and recent developments, J. Magn. Reson. Imaging, Vol. 36, pp. 757–774, 2012.

[29] Patel, B.K., Samreen, N., Zhou, Y., Chen, J., Brandt, K., Ehman, R., Pepin, K., MR Elastography of the Breast: Evolution of Technique, Case Exam-ples and Future Directions, Clin. Breast Cancer, Vol. 21, 102–111, 2020.

[30] Sinkus, R., Siegmann, K., Xydeas, T., Tanter, M., Claussen, C., Fink, M., MR elastography of breast lesions: understanding the solid/liquid duality can improve the specificity of contrast-enhanced MR mammography, Magn Reson Med, Vol. 58(6), pp. 1135-1144, 2007.

[31] Lorenzen, J., Sinkus, R., Lorenzen, M., Dargatz, M., Leussler, C., Röschmann, P., Adam, G., MR elastography of the breast: preliminary clinical results, Rofo Fortschr. Geb. Röntgenstrahlen Nukl, Vol. 174, pp. 830–834, 2002.

[32] Malayeri, A.A., El Khouli, R.H., Zaheer, A., Jacobs, M.A., Corona-Villalobos, C.P., Kamel, I.R., Macura, K.J., Principles and applications of diffusion-weighted imaging in cancer detection, staging and treatment follow-up, Radiographics, Vol. 31(6), pp. 1773-1791, 2011.

[33] Durur-Subasi, I., DW-MRI of the breast: A pictorial review, Insights Into Imaging, Vol. 10, 61, 2019.

[34] Bolan, P.J., Meisamy, S., Baker, E.H., Lin, J., Emory, T., Nelson, M., Everson, L.I., Yee, D., Garwood, M., In vivo quantification of choline compounds in the breast with 1H MR spectroscopy, Magn. Reson. Med., Vol. 50, pp. 1134–1143, 2003.

[35] Jagannathan, N.R., Kumar, M., Seenu, V., Coshic, O., Dwivedi, S.N., Julka, P.K., Srivastava, A., Rath, G.K., Evaluation of total choline from in-vivo volume localized proton MR spectros-copy and its response to neoadjuvant chemotherapy in locally advanced breast cancer, Br. J. Cancer, Vol. 84, pp. 1016–1022, 2003.

[36] Stanwell, P., Mountford, C., In Vivo Proton MR Spectroscopy of the Breast, Radio Graphics, Vol. 27, pp. 253–266, 2007.

[27] Flavell, R.R., Naeger, D.M., Mari Aparici, C., Hawkins, R.A., Pampaloni, M.H., Behr, S.C., Malignancies with Low Fluorodeoxyglucose Uptake at PET/CT: Pitfalls and Prognostic Importance: Resident and Fellow Education Feature, RadioGraphics, Vol. 36, pp. 293–294, 2016.

[38] Berger, A., How does it work? Positron emission tomography, BMJ, Vol. 326 (7404), 1449, 2003.

[39] Narayanan, D., Berg, W.A., Dedicated Breast Gamma Camera Imaging and Breast PET: Current Status and Future Directions, PET Clin. Vol. 13(3), pp. 363-381, 2018

[40] Jørgensen, J.T., Norregaard, K., Simón Martín, M., Oddershede, LB., Kjaer, A., Non-invasive Early Response Monitoring of Nanoparticle-assisted Photothermal Cancer Therapy Using 18F-FDG, 18F-FLT and 18F-FET PET/CT Imaging, Nanotheranostics, Vol. 2(3), pp. 201-210, 2018.

[41] Shaikh, K., Krishnan, S., Thanki, R., Breast Cancer Detection and Diagnosis Using AI In Artificial Intelligence in Breast Cancer Early Detection and Diagnosis, Springer International Publishing: Cham, Switzerland, pp. 79–92, 2021.

[42] Gong, Z., Williams, M.B., Comparison of breast specific gamma imaging and molecular breast tomosynthesis in breast cancer detection: Evaluation in phantoms, Med. Phys, Vol. 42, pp. 4250–4259, 2015.

[43] Urbano, N., Scimeca, M., Tancredi, V., Bonanno, E., Schillaci, O., 99mTC-Sestamibi breast imaging: Current status,

new ideas and future perspectives, Semin. Cancer Biol, 2020.

[44] Lyman, G.H., Somerfield, M.R., Bosserman, L.D., Perkins, C.L., Weaver, D.L., Giuliano, A.E., Sentinel Lymph Node Biopsy for Patients With Early-Stage Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update, J. Clin. Oncol., Vol. 35, pp. 561–564, 2016.

[45] Cox, C.E., Kiluk, J.V., Riker, A.I., Cox, J.M., Allred, N., Ramos, D.C., Dupont, E.L., Vrcel, V., Diaz, N., Boulware, D., Significance of sentinel lymph node micrometastases in human breast cancer, J Am Coll Surg., Vol. 206(2), pp. 261-268.

[46] Candelaria, R., Fornage, B.D., Second-look US examination of MR-detected breast lesions, J. Clin. Ultrasound, Vol. 39, pp. 115–121, 2011.

[47] Arora, N., Martins, D., Ruggerio, D., Tousimis, E., Swistel, A.J., Osborne, M.P., Simmons, R.M., Effectiveness of a noninvasive digital infrared thermal imaging system in the detection of breast cancer, The American Journal of Surgery, Vol. 196(4), pp. 523-526, 2008.

[48] Marmo, A.A., Morris, D.M., Schwalke, M.A., Iliev, I.G., Rogers, S., Electrical Potential Measurements in Human Breast Cancer and Benign Lesions, Tumor Biol, Vol.15, pp. 147-152, 1994.

[49] Domchek, S.M., The utility of ductal lavage in breast cancer detection and risk assessment, Breast Cancer Res.,Vol. 4(2), pp. 51-53, 2002.

[50] Bao, T., Davidson, N.E., Gene expression profiling of breast cancer, Adv Surg, Vol. 42, pp. 249-260, 2008.

[51] Marino, A., Battaglini, M., De Pasquale, D., Degl'Innocenti, A., Ciofani, G., Ultrasound-Activated Piezoelectric Nanoparticles Inhibit Proliferation of Breast Cancer Cells, Sci Rep, Vol. 8, 6257, 2018.