REVIEW

Comparative Efficacy of Four Imaging Instruments for Breast Cancer Screening

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Abstract

Sensitivity and specificity are the two most important indicators in selection of medical imaging devices for cancer screening. Breast images taken by conventional or digital mammography, ultrasound, MRI and optical mammography were collected from 2,143,852 patients. They were then studied and compared for sensitivity and specificity results. Optical mammography had the highest sensitivity (p<0.001 and p<0.006) except with MRI. Digital mammography had the highest specificity for breast cancer imaging. A comparison of specificity between digital mammography and optical mammography was significant (p<0.021). If two or more breast diagnostic imaging tests are requested the overall sensitivity and specificity will increase. In this literature review study patients at high-risk of breast cancer were studied beside normal or sensitive women. The image modality performance of each breast test was compared for each.

Keywords: Sensitivity - specificity - breast imaging - ultrasound - MRI - digital/optical mammography

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Introduction

Women of various countries with differing ages, genetic, environmental, nutritional, occupational and lifestyle experience different levels of risk for breast cancer. There is an increasing demand for improving breast cancer detection methods that use medical imaging instruments because a successful treatment of breast cancer depends on its correct and early diagnosis. It is essential that we be able to detect tumors early before the primary tumor metastasizes (Siegel et al., 2013). If physicians, oncologists, radiology residents and radiologists have enough knowledge about characteristic, advantages or disadvantages of breast medical tests as well as sensitivity and specificity of breast imaging modalities, it will request to correct imaging processes that give better efficiency for breast disease diagnosis.

The main goal of any cancer screening test is to correctly identify those people who have cancer (called the sensitivity of the test). When sensitivity is high, very few cases are missed. Sensitivity relates to the test's ability to identify a condition correctly. Mathematically, this can be expressed as: patients suspected of breast cancer per patients with pathologically confirmed breast cancer (Zhang et al., 2014). An ideal cancer screening test would also be able to correctly identify all the people who do not have cancer (called the specificity of the test). When specificity is high, there are fewer false positive results, but more cases of true cancer are missed. Specificity relates to the test's ability to exclude a condition correctly. Mathematically, this can also be written as: patients suspected of having benign tumors per patients with pathologically confirmed benign tumors-patients with tumors (benign and malignant) (Zhang et al., 2014).

No screening test has perfect sensitivity and perfect specificity. There is a trade-off between the two for all types of screening tests. That is, when a test gains sensitivity, it loses some specificity (Ting, 2010). Imagine a study evaluating a new test that screens people for a disease. Each person taking the test either has or does not have the disease. The test outcome can be positive (predicting that the person has the disease) or negative (predicting that the person does not have the disease).

This study focuses on introductory mammography (conventional or digital), ultrasound, MRI and optical mammography imaging modalities and their performance, advantages and disadvantages, and finally their sensitivity and specificity in various studies. These studies were classified according to year, imaging test, whether they performed on normal or high risk groups of women, and their region of study. Finally, in the different groups of women sensitivities and specificities of the radiologic imaging test were compared to their reliability in diagnosing breast cancer.

Methodology

MEDLINE, PubMed, EBM Reviews, MEDSEARCH, and SCOPUS databases were accessed and searched for articles dated 2001 to 2014. Articles were collected

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using the following keywords: sensitivity and specificity for conventional and digital mammography, ultrasound, MRI and optical mammography. A total of 31 original and 4 review breast radiologic test papers were retrieved. These articles included six studies on mammograms of conventional or digital mammography and fourteen papers about its on sensitivity and specificity. The sensitivity of ultrasound images yielded ten papers, and MRI images sensitivity yielded 56 results in our studied manuscripts. The sensitivity and specificity of photonic mammograms produced in 45 articles. The distribution of manuscripts included 13 from Asia, 65 from Europe, 48 from America, and two from Australia.

A) Application of film-screen and digital mammography

Mammograms from X-ray images of the breast that images can be captured on film or stored directly onto a computer (digital). Film and digital mammography are similar in their ability to detect cancer (Pisano et al., 2005; Skaane, 2009). Most centers now use digital mammography because if they stored on a computer, they can be lightened or darkened, and certain sections can be enlarged and scrutinized more closely. The ability to control images on a computer makes digital mammography a more accurate screening tool for some women. Digital mammography is better at finding cancer in women who fall into one or more of the following groups (Pisano et al., 2008):

Women who are premenopausal or peri-menopausal

Women who are under age 50

Women who have dense breast tissue

Women who are young and those who are pre- or peri-menopausal tend to have dense breast tissue, so these groups overlap (Juliana et al., 2014). But for women who do not fall in one of the above groups, film and digital mammography are similar in their ability to detect breast cancer early.

Ionizing radiation may induce cancer, and this risk is higher for younger women, especially if they are exposed before age 30 (Kayhan et al., 2014). Latency for the disease is more than 10 years, and the increased risk persists for life. Because of this, mammography is not recommended for average-risk women under age 40(Goss and Sierra, 1998; Ronckers et al., 2005).

Table 1. Sensitivity and Specificity of Screening Mammography Examinations Based on BCSC Data

	All Screening Examinations
Sensitivity*	84.90%
True positives	8,774
Cancers‡	10,331
Specificity§	90.30%
True negatives	1,853,216
Non-Cancers#	2,051,360

*Sensitivity = the percentage of cancers that had an abnormal initial interpretation (BI-RADS category 0, 4, 5; Note: 3 with a recommendation for immediate follow-up was recorded as 0). ‡ Cancers = the number of examinations with a tissue diagnosis of cancer within 1 year following the examination. §Specificity = the percentage of non-cancers that had a negative initial interpretation (BI-RADS category 1, 2, or 3 with no recommendation for immediate follow-up). #Non-cancers = the number of examinations without a tissue diagnosis of cancer within 1 year following the examination

Mammogram advantages

Approximately 33% of breast cancers detected by screening mammograms represent over diagnosis (Zahl et al., 2004). Digital mammography produces better image quality than conventional mammography because the artifacts, noise and variability related to film processing are no longer present. In a film-screen mammogram, the images will be in black and white on large sheets of film. With digital mammography, the images are recorded directly into a computer (Bassett, 2004) and images can then be viewed on a computer screen and specific areas of organ can be enlarged or highlighted.

Disadvantages of mammography may cause compression of breast tissue, which gives some discomfort. Additionally, it can be difficult to image dense breast tissue, and the breast must be repositioned for different views. Lastly, a mammogram does not image well around implants.

The mean glandular dose (MGD) of the breast due to exposure to ionizing radiation is important in calculating the breast risk. In spite of the digital advantages presented, this technology leads to a significantly greater MGD to the patient when compared to conventional mammography, especially with fast film-screen mammography and patients with high breast thickness (Riabi et al., 2010; Mehnati and Alizadeh, 2014).

The Sensitivity and Specificity for 2,061,691 Screening Mammography examinations from 2004 - 2008 based on BCSC data through 2009 (2014c) are shown in Table 1.

The summary of sensitivity and specificity of film screen, digital mammography, ultrasound, MRI and optical mammography are shown in Table 2.

Survey of various collected studies for sensitivity and specificity of four imaging tests

Warner and colleagues from Canada studied women aged 26 to 59 years with proven BRCA1 or BRCA2 mutations (or strong family histories of breast or ovarian cancer) underwent mammography, ultrasound, MRI, and clinical breast examination on a single day. Their results showed that higher specificity and sensitivity were for MRI and digital mammography, respectively (Warner et al., 2001).

From Australia Houssami and et al (2003) were sampled from all women consecutively attending a symptomatic breast clinic between 1994 and 1996, ranging in age from 25 to 55 years. They included all 240 women shown to have breast cancer (thus avoiding selection bias) and 240 age-matched women shown not to have cancer. The same specificity for digital mammography and ultrasound naught linearly associated with age in sensitivity and specificity of each test observed. We also looked at a study of Canadian women aged 25 to 65 years with BRCA1 or BRCA2 mutations who underwent 1

Table 2. Summary of Sensitivity and Specificity of Film Screen, Digital Mammography, Ultrasound, MRI and Optical Mammography

Study	Patient number	Mammography				Ultrasound		MRI		Optical mammography	
		Film		Digit							
		Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)
(Warner et al., 2001)[C]	196			33	99.50	60	93	100	91		
(Houssami et al., 2003)[D]	480			76	88	82	88				
(Warner et al., 2004)[C]	236			36	100	33	96	85	93		
(Sim et al., 2004)[B]	245			54	86	83.30	65.50	93.30	63.60		
(Kriege et al., 2004)[B]	1,909			40	95			71	90		
(Kuhl et al., 2005)[B]	529			33	97	40	90.50	91	97		
(Pisano et al., 2005)[C]	42,760	66N	92N	66NS	92N						
(Leach et al., 2005)[B]	649 (35 cases)			40	93			77	81		
(Hagen et al., 2007)[B]	491 (25 cases)	50	N/A					86	N/A		
(Skaane, 2009)[B]	23,929	62N	98SI	77NS	97SI						
(Fatima et al., 2011)[A]	564			80.50	73.10	87	100				
(Sardanelli et al., 2011)[B]	501			50	99						
(Valente et al., 2012)[C]	224			21	99.50	43.50	96.20	37.10	96.70		
(Akbari et al., 2012)[A]	255	73	45			69	49				
(Michell et al., 2012)[B]	738	39.70	51	58.30	74.20						
(Rafferty et al., 2013)[B]	312 (48 cancer cases)			65.50	84.10						
(Zhang et al., 2014)[A]	312 (51 cancer cases)			62.70	86.20	81.82	93.33			95.45	73.33
(Warner et al., 2008)[B,C]	11 studies (Meta-analyses)			32	99			75	96		
(Granader et al., 2008)[B,C]	8 studies (Meta-analyses)			38	96			97	91		
(Newell et al., 2010)[C]	116							97	80		
(Baltzer et al., 2010)[B]	81							ueMRM # 93 86 ceMRM 96.50 98.30	ueM-RM ## 85.20 ceMRM 92.60		
Park et al.2012 (Park et al., 2012)[A]	34							100	70.40		
(Pinker-Domenig et al., 2012)[D]	150							99	81		
(Marinovich et al., 2013)[A,B,C]	44 studies (2050 patients) (Meta-analyses)							92	60		

Table 2 (cont). Summary of Sensitivity and Specificity of Film Screen, Digital Mammography, Ultrasound, MRI and Optical Mammography

Study	Patient number	Mammography				Ultrasound		MRI		Optical mammography	
		Film		Digit							
		Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)
(Arena et al., 2003)[C]	109									99	N/A
(Chance et al., 2005)[C]	116									96	93
(Athanasiou et al., 2007)[B]	78									73	38
(Leff et al., 2008)[A,B,C]	2000 (Meta-analyses)									96	93
(Arora et al., 2008)[C]	92									97	44
(Busch et al., 2010)[C]	35									89	94
(Wishart et al., 2010)[B]	106									78	75
(Schmitz et al., 2013)[B]	22									85.70	87.50

Sens: sesitivity, Spec: specificity. [A]Asia, [B]Europe, [C]America, [D]Australia, NS = No statistically significant difference in diagnostic accuracy between film mammography and digital mammography. SIG = Statistically significant difference in diagnostic accuracy between film mammography and digital mammography. N/A = Results not available, # observer 1, ## observer 2

to 3 annual screening examinations consisting of MRI, mammography, and ultrasound at a single tertiary care teaching hospital between November 3, 1997 and March 31, 2003 that higher sensitivity and specificity were for MRI and digital mammography, respectively (Warner et al., 2004).

Sim and colegues were sampled from all women consecutively attending a symptomatic breast clinic between 1994 and 2001by mammography, ultrasound, MRI and found same results of above mentioned study (Sim et al., 2004).

A study from Netherland showed that study of screened 1909 eligible women, including 358 carriers of germ-line mutations. Within a median follow-up period of 2.9 years, 51 tumors (44 invasive cancers, six ductal carcinomas in situ, and one lymphoma) and one lobular carcinoma in situ were detected. The sensitivity of clinical MRI for detecting invasive breast cancer was higher than mammography (Kriege et al., 2004).

A study from Germany examined a cohort study of asymptomatic women who, based on their family history and/or mutational analysis, were suspected or proven to carry a breast cancer susceptibility gene (BRCA). Forty-three breast cancers were identified in the total cohort, including 34 invasive and nine ductal carcinoma-in-situ that same specificity in mammography and MRI were reported (Kuhl et al., 2005).

The women screening mammography study at 33 sites in the United States and Canada (who underwent both digital and film mammography) was available for 86.3 percent of women using only conventional and digital mammography that resulted same sensitivity and specificity (Pisano et al., 2005).

A cohort study in women aged 35-49 years with a strong family history of breast cancer or a high probability of a BRCA1, BRCA2, or TP53 mutation was conducted. We recruited participants from 22 centres in the UK, and offered the women annual screening with Contrast-enhanced MRI (CE MRI) and mammography for 2-7 years. They diagnosed 35 cancers in the 649 women screened with both mammography (higher specificity) and CE MRI (higher sensitivity) (Leach et al., 2005).

The women with truncating mutation in either BRCA1 or BRCA2 genes identified at the counseling genetic section of the Norwegian radium hospital in Oslo were offered breast MRI examinations in addition to a conventional screening program consisting of mammography (XRM) annually. A total of 25 cancers were observed, five (20%) as interval cancers and only sensitivity showed that was higher for MRI (Hagen et al., 2007).

Women who had cancer detected at the baseline screening (2392 cases), interval cancers, and subsequent cancers were arranged according to age group. For the age group 45-49 years, follow-up was 18 months because the program was stopped by the Norwegian government during the study period (Skaane, 2009).

The prospective analysis included two groups of women (median age 40; 11-81 years) who attended a breast care clinic at KIRAN for screening (559) or presented a palpable breast lump (545). Mammography was performed on 564 (51%) women and classified as BIRADS I in 227 (40%), II in 110 (20%), III in 53 (9%), IV in 130 (23%) and as V in 44 (8%). A second group of women were subjected for breast screenings in the ultrasound; among them 408 (76%) were absolutely normal, 97 (18%) revealed benign pathology and 35 (6%) had suspicious findings. Both sensitivity and specificity were higher for sonogram (Fatima et al., 2011).

The study enrolled asymptomatic women aged ≥25: BRCA mutation carriers; first-degree relatives of BRCA mutation carriers, and women with strong family history of breast/ovarian cancer, including those with previous personal breast cancer. A total of 18 centers enrolled 501 women and performed 1592 rounds (3.2 rounds/woman) by digital mammography (Sardanelli et al., 2011).

A retrospective review was performed by Valente and et al on the patients diagnosed with invasive breast carcinoma between 2008 and 2010 who had subsequent histopathologic evaluation of one or more axillary lymph nodes using mammography, sonography and MRI that sonography have shown higher sensitivity (Valente et al., 2012).

The studies of 384 mammography and ultrasonography reports for 255 women were assessed, then divided into benign and malignant groups. The radiologic and pathologic reports were compared, and another comparison was performed based on age group (over and under 50 years old), history of breastfeeding and gravidity (Akbari et al., 2012). Michell and Rafferty in separate studies have shown that addition of digital breast tomosynthesis (DBT) increases the accuracy of mammography compared to FFDM and film-screen mammography combined and film-screen mammography alone in the assessment of screen-detected soft-tissue mammographic (Michell et al., 2012); (Rafferty et al., 2013).

Zhang and et al compared diffuse optical tomography, Ultrasound and mammography in the diagnosis of breast tumors. They showed higher sensitivity and specificity for optical mammography and ultrasound, respectively (Zhang et al., 2014). in BRCA1 and BRCA2 mutation carriers, MRI is more sensitive for detecting breast cancers than mammography, ultrasound, or Clinical breast examination alone (Warner et al., 2008). Also, in women with an increased risk without the BRCA gene, MRI has essential role for cancer detection rate (Granader et al., 2008).

B) Application of MRI

Breast magnetic resonance imaging (MRI) uses magnetic fields to create an image of the breast. There is growing evidence that a breast MRI in combination with mammography (compared to mammography alone) can increase detection of cancer in certain women who are at a higher risk for breast cancer. The American Cancer Society and the National Comprehensive Cancer Network now recommend considering a breast MRI as part of a breast cancer screening plan for women who have one or both of these risk factors (2014a; 2014b):

Drawbacks to breast MRI as a screening tool

A screening breast MRI has some drawbacks compared to mammography (Liu et al., 2014). It is more invasive because a contrast agent is given through an IV before the procedure. Additionally, not all centers that do breast MRIs have radiologists specially trained to read images of the breast. Breast MRIs are also expensive, not always covered by insurance, and have more false positive results than mammography.

Breast MRI as a screening tool in combination with mammography for women at average risk of breast cancer may offer some benefits to women at higher risk of breast cancer. However, this combination is not recommended for a routine breast cancer screening for women at average risk.

Benefits of MRI

MRI is non-invasive

MRI does not involve radiation

MRI's contrasting agent is less likely to produce an allergic reaction that may occur when iodine-based substances are used for X-rays and CT scans

MRI gives extremely clear, detailed images of soft-tissue structures that other imaging techniques cannot achieve

MRI can easily create hundreds of images from almost any direction and in any orientation

Unlike techniques that examine small parts of the body (i.e. ultrasound or mammography), MRI exams can cover large portions of the body

MRI can determine if a cancer has spread, and help determine the best treatment

Disadvantages of MRI

MRI is expensive

MRI will not be able to detect all cancers (i.e. breast cancers indicated by micro calcifications)

MRI cannot always distinguish between malignant tumors or benign disease (such as breast fibro adenomas), which could lead to false positive results

MRI is not painful, but the patient must remain still in an enclosed machine, which may be a problem for claustrophobic patients

An undetected metal implant in a patient's body may be affected by the strong magnet of the MRI

There is a small chance that a patient could develop an allergic reaction to the contrasting agent, or that a skin infection could develop at the site of injection

If a patient chooses to be sedated for the scanning, there is a slight risk associated with using the sedation medication

Newell and at all studied breast MRI to differentiate between malignant and benign lesions using computer-aided, they showed high sensitivity of MRI for differentiation (Newell et al., 2010).

This study was performed to assess for malignant and benign mass lesions of a diagnostic approach combining DWI with T2-weighted images (unenhanced MR mammography, ueMRM) and compare the results with contrast-enhanced MR mammography (ceMRM). They showed higher sensitivity and specificity for ceMRM (Baltzer et al., 2010).

Thirty-four women with 34 invasive breast cancers underwent Diffuse Weighted Imaging (DWI) and PET/CT before and after chemotherapy and before surgery. They showed DWI breast MR and PET/CT show similar accuracy for predicting pathological response. Also, the combined use of DWI and PET/CT can potentially improve specificity (Park et al., 2012).

A study in 150 patients underwent breast MR imaging at 3 T. Lesion size, morphology and enhancement kinetics were assessed according to the BI-RADS classification. Using 3 Tesla breast MRI allows an accurate diagnosis of breast cancer (Pinker-Domenig et al., 2012).

Stusy of Meta-Analysis of Magnetic Resonance Imaging in Detecting Residual Breast Cancer showed that after Neoadjuvant Therapy, MRI is more accurate than mammography but No difference in MRI and ultrasound accuracy was found (Marinovich et al., 2013).

C) Application of ultrasound

Breast ultrasound is a technique that uses high frequency sound waves, usually between 5 and 15 MHz, to produce images via the backscattering of mechanical energy from boundaries between tissues. Ultrasound breast imaging has high special resolution in the order of 1-0.1 mm. The patient is usually in supine position to get real-time images, and a benefit of ultrasound is that it is free of ionizing radiation (Liu et al., 2014). It is primarily used either to complement other screening or diagnostic tests such as X-ray mammography, or to guide breast biopsy. However, its specificity in breast cancer characterization is low. This is because the acoustic characteristics of benign and malignant lesions are overlapping. Similar to X-ray mammography and breast MRI, only morphologic information is obtained, which usually is not enough to find all cancerous lesions (Egorov and Sarvazyan, 2008).

Breast ultrasound suffers relatively low soft-tissue contrast compared with X-ray mammography and contrast-enhanced MRI. In detecting breast disease, a ultrasound is able to tell whether a lump is a solid mass or is a fluid-filled cyst, but a significant number of breast cancers are difficult to see using ultrasound because they are echoic with the fat of the breast tissue (Kopans, 2007). The beneficial points of breast sonogram for breast disease include tumor differentiation, preoperative staging, and follow-up after cancer treatment and interventional diagnosis. High-resolution and quality-controlled ultrasound can further improve early cancer detection. Therefore, technological improvements in image quality have allowed doctors to expand the possibilities for the use of breast ultrasound. Breast sonogram is useful in high-risk patients and women with dense breasts who are mammographically problematic (Madjar, 2001).

Benefits of Ultrasound (Choi et al., 2014)

ultrasound is non-invasive

ultrasound does not involve radiation

ultrasound is lighter than other breast test instrument and portable

tumor differentiation

tumor preoperative staging

usefulness in high-risk patients

usefulness in women with dense breasts

Disadvantages of Ultrasound

Ultrasound characteristics of benign and malignant lesions are overlapping

Sonogram specificity in breast cancer is low

D) Application of optical mammography

The history of optical transillumination images of the breast began as early as 1929 by Max Culter (Cutler, 1929), who undertook the first exploration of the application of light for breast cancer imaging. The development of optical techniques in both methodology and instrumentation brought more attention to its breast imaging application in recent decades. But near-infrared (NIR) at wavelength range (650-1000 nm) in optical mammography operates provides the structural and functional information of the breast. The image contrast is created by the absorption of hemoglobin and other dominant tissue chromospheres in the NIR wavelength range, such as water and lipid. The functional information is obtained by using spectroscopic methods, which can detect concentrations of tissue chromospheres, further determine the oxygen saturation and therefore study breast tissue metabolism (Fang et al., 2009).

Advantages of optical mammography

Lack of ionizing radiation

Non-invasiveness

Relatively compact instrumentation

Cost-effectiveness

More importantly, it has the potential to distinguish malignant tumors from benign lesions or normal tissue non-invasively. The primary limitation of optical breast imaging is the relatively poor spatial resolution compared with conventional techniques such as X-ray mammography. Another challenge is how to exploit its potential for quantitative and absolute measurements of oxygenation. Also, It was not enough manufactured and available in every country.

The study performed by Parisky with 875 biopsied lesions showed that there were 187 malignant and 688 benign findings. Lesions that were considered to be a false negative by infrared had microcalcification. Additional evaluation was done among 589 women with 479 biopsied lesions and 110 malignancies. Performance analysis of infrared imaging in all 875 biopsied lesions revealed that the specificity improved statistically in dense breast tissue compared to fatty breast tissue. This study concluded that infrared imaging is a safe noninvasive technique which can be used as a complementary technology along with traditional mammography in determining benign or malignant tumors with high sensitivity (Parisky et al., 2003).

The digital infrared imaging (DII) was examined in a study of 109 tissue proven cases of breast cancer. Its sensitivity has been successfully demonstrated in lesions as small as 4 mm (Arena et al., 2003).

In another study, a 3-wavelength LED and 8 detectors with 4 cm separation between source and detectors were placed on the subject's breast. The wavelengths were at 760 and 850 nm. From two nations 116 subjects (44 were cancer-verified by biopsy and histopathology) were reviewed. They reported valuable sensitivity and specificity for optical mammography (Chance et al., 2005).

Between 2004 and 2005, women between the ages of 41_72 participated in study by Alexander from France. All of them presented non-palpable BIRADS 4-5 mammographic and/or ultrasonographic findings. But their study showed lower sensitivity for optical mammography (Athanasiou et al., 2007). In a Meta-analyzed study, it was suggested that distinguishing between benign and malignant lesions is possible by optical mammography since malignant tissues show higher levels of absorption and scattering compared to healthy tissues. They proved that the optical mammography technique is able to distinguish cancer from non-cancerous tissues by high sensitivity and specificity (Leff et al., 2008). Arora and et al performed a prospective clinical trial for patients whom a breast biopsy was recommended based on a prior mammogram or ultrasound underwent DITI. DITI identified 58 of 60 malignancies (Arora et al., 2008).. The diffuse Optical Tomography Computer Aided Detection (DOT CAD) is capable of producing tomographs that distinguish healthy tissues from malignant with high specificity (Busch et al., 2010). Wishart and et al showed that sensitivity and specificity using a No Touch Breast Scan is higher in women under 50 but sensitivity altogether was lower than other studies (Wishart et al., 2010). They recruited patients who had a high probability of a breast lesion and who were scheduled for needle biopsy. In the analysis, 14 patients had a malignant lesion and 7 patients had benign lesions. They presented average sensitivity and specificity for optical mammography (Schmitz et al., 2013).

E) Combination using all modalities?

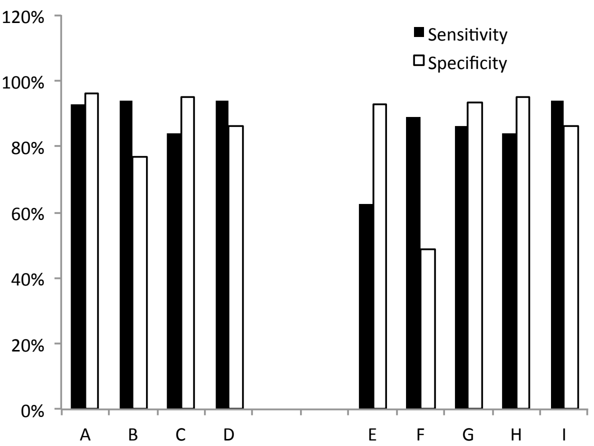

Figure 1. Summary of combined sensitivity and specificity of breast MRI and mammography in women from A to D, A: Kuhl et al., B: Leach et al., C: Warner et al., D: Granader et al. and combined use of breast ultrasound and mammography from E to I: E: Sim et al., F: Kuhl et al., G: Zhang et al., H: Warner et al, I: Granader et al

According to the results of the collected papers, no single device of four above-mentioned instruments is perfect. No screening test has perfect sensitivity and perfect specificity. There is a trade-off between the two for all types of screening tests. That is, when a test gains sensitivity, it loses some specificity but if we have the facility to combine breast-imaging devices, we will improve the sensitivity and specificity. It will help in the diagnosis and treatment of patients. Sensitivity and specificity of combined breast imaging devices are summarized in Figure 1.

The study by Zhang et al. on the combined use of breast imaging showed an increase in sensitivity and specificity. When mammography added to ultrasound and optical mammography help to improve sensitivity and specificity to 95.5% and 93.3%, respectively (Zhang et al., 2014).

A study of the average sensitivity and specificity of collected articles showed that maximum sensitivity is found using optical mammography, where there is a calculated difference between it and other, MRI is coming close to it. However, the maximum specificity was recorded for digital mammography, with the ultrasound is coming close to it. However, it means in imaging centers with limited facility these devices according to patient conditions perhaps can used instead of each other.

Conclusion

Medical imaging devices are the third eye of a physician and help to obtain the correct diagnosis of disease, especially in breast cancer. The review of the selected articles was used to determine whether mammography (conventional or digital), ultrasound, MRI or optical mammography is a more accurate imaging test for the diagnosis of breast cancer, based upon sensitivity and specificity. Results showed that no imaging method has perfect sensitivity and perfect specificity for the diagnosis of breast cancer but a study of 35 published original and review manuscripts (as well as a calculation of mean sensitivities and specificities) determined that optical mammography has the highest sensitivity (91.7 ± 8.49) and digital mammography has highest specificity (91.68±8.3). Many pieces of evidence expressed that some interventional factors contribute to the sensitivity of medical imaging and diagnosis which is not related to the device, but is rather dependent on the patient's condition, especially family history and genetic characteristics (Kriege et al., 2004; Sardanelli et al., 2011). Sensitivity varied significantly with age and breast density (Devolli-Disha et al., 2009) This review of accuracy of mammograms and sonograms in relation to age in women with breast symptoms articles showed that the greater sensitivity of mammography in women 50 years or older relative to younger women has been shown in other studies that have considered mammography only and greater extent, in women 51–55 years. However, from a biologic perspective, the 45 is age as the decision basis makes sense because it correlates with the transition of hormonal (menopausal) status. Specificity is not influenced by age for either mammogram or sonogram. This fact may explain the different findings in published studies, with some reporting a greater specificity for ultrasound than for mammography.

Also, women who, based on their family history and/or mutational analysis, were suspected or proven to carry a breast cancer susceptibility gene, especially BRCA (Kuhl et al., 2005) have effective factors on the efficiency of imaging devices because they depend upon each patient. Doctors' knowledge about imaging modality and image parameters will help she/he in the selection of the most correct and safe diagnostic method. Early detection of breast cancer in early stages provides a relatively high treatment rate. In women with elevated breast cancer risk, ultrasound may detect small, node-negative breast cancers not seen on mammography (Zhang et al., 2014), while MRI and photonic mammography may depict additional breast cancers beyond mammography and ultrasound. Another important point is evaluating and comparing medical imaging devices with respect to their diagnostic performance in differentiating benign and malignant breast tumors.

The most positive point of this study is its usefulness for all clinical groups associated with medical imaging for breast cancer detection, physicians, residents, radiologists and medical physics experts in diagnostic and therapeutic equipment whose field of expertise is breast disease. Their consciousness about sensitivity and specificity of breast imaging devices will help in management and design permanent treatment of patients accompany with physician and to have practical strategies in breast disease to reduce errors and technical problems of medical equipments diagnosis.

In this study, four common and important devices used in the diagnosis of breast cancer were selected, and in order to study their sensitivity and specificity, large numbers of the original (31) and review (4) articles from 2001-2014 were assembled and investigated. The results of the study of sensitivity for conventional mammography (68353 patients) resulted in a range from 39.7% to 73%, and for digital mammography (73272 patients) we found a range from 21% to 76%. These are both popular diagnostic methods put into practical use in the diagnosis of breast cancer. Sonogram (2875 patients) uses available medical equipment and easily seen as a placeholder, with a sensitivity ranging from 67% to 88%.

MRI and optical mammography are advanced diagnostic equipment that have less availability in breast cancer diagnosis in comparison to mammography and ultrasound. The sensitivity for MRI (4860 patients) ranged from 37.1% to 100%, and for optical mammography (11963 patient), from 73% to 99%. There was a large standard deviation from 8.3 to 30.03 in these results. The high standard deviation perhaps indicates that there was a lot of variability, including the population study of four continents, patient family and mutation history, diagnostic device characteristics and others factors in the studied articles' results. Also, some studies repeated in our collected tables related to four devices, because in a few references, two or more devices were separately studied in the same population.

Comparative studies of the combination of four imaging devices, shows that in most cases, increased sensitivity and specificity can be achieved when using both or more devices, as shown in Figure 1. In this study, the increase of sensitivity and specificity for mammography and MRI was higher than for mammography and ultrasound (10.3%).

Mammography alone, or even mammography combined with a breast ultrasound, seems insufficient for early diagnosis of breast cancer in women who are at increased familial risk with or without documented BRCA mutation. If MRI is used for surveillance, a diagnosis of intraductal and invasive familial or hereditary cancer is achieved with a significantly higher sensitivity and at a more favorable stage (Kuhl et al., 2005) that was in agreement by presented data in Figure 1.

New findings in the study of medical imaging devices are in differentiating benign and malignant breast tumors. The requisite of this dissociation is the ability of medical imaging test to provide structural and functional information of breast tissue metabolism. Leff et al. showed that distinguishing between benign and malignant lesions is possible using optical mammography, since malignant tissues show a higher level of absorption and scattering compared to healthy tissues. The optical mammography technique is able to discriminate cancerous from non-cancerous tissue with 96% sensitivity and 93% specificity (Leff et al., 2008).

Furthermore, diffuse optical tomography (DOT) and Ultrasound elastography (UE) were superior to conventional mammography in terms of both specificity and accuracy. DOT and UE improve the specificity and accuracy of breast cancer diagnosis, and combining the two modalities improves the diagnostic value(Zhang et al., 2014).

The addition of a screening ultrasound or MRI to mammography in women with increased risk of breast cancer resulted in a higher cancer detection yield, but also an increase in false positive findings (Berg et al., 2012). Also, imaging analysis methods show that a 3D-Automated Breast Ultrasound (ABUS) is a computer-based system for evaluating the whole breast.

Finally, sensitivity and specificity were used as statistical measures of the performance of a binary classification test for breast imaging devices. A study of the average sensitivity and specificity of collected articles showed that the maximum sensitivity is for optical mammography and MRI is second one. The maximum specificity was recorded for digital mammography and ultrasound is second one but using two or more diagnosis devices together induce higher sensitivity and specificity, especially in high risk women. A comparison of sensitivity between optical mammography and others was significant ($p<0.001$, $p< 0.006$) exception MRI. The digital mammography has the highest specificity for breast cancer imaging. A comparison of specificity of between digital mammography and optical mammography was significant ($p<0.021$).

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