Progress in diagnosis of breast cancer: Advances in radiology technology

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ABSTRACT

Breast cancer is the leading cause of cancer in females between the ages of 15 and 54, and the second leading cause of cancer death in women in the United States. Diagnosis begins with detection by breast examination (clinical breast exam or breast self-exam) or by radiologic studies, like mammography. Many advances in the diagnosis of breast cancer have taken place in recent years. This article will review the history of radiologic advances in the diagnosis of breast cancer. Use of technological advancements in digital breast tomosynthesis, magnetic resonance imaging, and ultrasound in breast cancer diagnosis will be presented. Advantages and disadvantages of these diagnostic interventions when compared to older, traditional X-ray films will be discussed. It is important for all nurses, including radiology and oncology nurses, to be well informed about these varied diagnostic modalities, and appreciate the fact that advances in radiologic imaging technologies can yield improved outcomes for breast cancer patients.

Key words: Breast cancer, early detection, breast imaging, mammography, ultrasound, tomosynthesis

Introduction

Breast cancer is the leading cause of cancer in females between the ages of 15 and 54, and the second leading cause of death in United States' women.[1] Although, the death rate from this disease is decreasing in the United States, the worldwide incidence of breast cancer continues to climb.[1] The mortality reduction achieved in the United States and the world can be attributed to several radiologic advances in diagnostic imaging.

Historical perspectives of breast cancer detection

Following the discovery of X-ray and the work of Pierre and Marie Curie to isolate radium from uranium, radiation therapy was first used in the treatment of breast cancer. Treatment consisted of either radium sources or low voltage X-ray.[2] Such treatments augmented surgical techniques, such as the mastectomy, by destroying remaining cancer cells and/or shrinking tumors.

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Several breakthroughs occurred in the decades from 1930 to 1950. This time period ushered advances in chemotherapy. During World War I, researchers discovered that drugs used to fight the effects of mustard gas could also be used to treat certain lymph node cancers. In addition, a staging system classifying breast tumor size, involvement of lymph nodes and metastasis was developed to help determine treatment options and prognosis for breast cancer patients.[3] The 10 years survival rate increased from 10% to approximately 50% during these decades.[2]

In the 1960's, great advances in the use of radiologic techniques to diagnose breast cancer were introduced. In this decade, xeroradiography machines began to be used to diagnose breast cancer. Xeroradiography involved use of an aluminum plate coated with electrically charged selenium. The plate acted as a photoconductor to hold a latent image.

After exposure, the plate was processed using a blue powder. The image formed from the powder was then transferred to a plastic coated paper.[2] Xeroradiography became widely used during this time due to its lower radiation dose and ease of interpretation.

Widespread screening for breast cancer first appeared during the 1960's. However, the patient dose of radiation was high. During the 1970's, manufacturers DuPont and Kodak intervened with faster speed X-ray film to decrease the radiation dose.[4]

In 1973, the Breast Cancer Detection Demonstration Project began and demonstrated that mammography screening along with breast self-exam and clinical breast examination improved outcomes with early diagnosis of cancer.[5] In addition, this 5 years study of over 283,000 women demonstrated that early detection improved long-term survivability.[4,5]

In 1992, Federal legislation known as the Mammography Quality Standards Act (MQSA) was enacted to improve quality initiatives at mammography centers.[6,7] The standards implemented through MQSA sought to ensure that all mammography equipment was capable of rendering images with adequate detail to show subtle breast lesions and proper training was received by medical personnel in each facility. It mandated that mammography labs enact quality control tests on equipment and annual on-site inspections of mammography centers. It also required specific training for technologists, medical physicists and physicians employed in mammography diagnostic centers. Each lab was required to become accredited through the American College of Radiology or four other Food and Drug Administration (FDA) approved state accrediting bodies.[8] Those not following the MQSA standards were subject to significant fines.

The first digital mammography system was approved in the year 2000.[8] The National Institute of Health, in response to the poor sensitivity and specificity of film/screen radiography, supported the research and development behind digital efforts. This has resulted in several advantages. For instance, digital images can be more easily stored and retrieved than film/screen radiographs. Digital images also have superior contrast resolution, meaning they allow the radiologist to distinguish between subtle shades of gray. Computer software programs, known as computer aided diagnosis can be applied to images to help the radiologist be more productive and improve the accuracy of readings. In addition, three-dimensional (3D) image reconstruction as well as dual-energy and contrast subtraction techniques can be applied to images to yield more diagnostic information without additional radiation to the patient. Due to post-processing features to adjust image contrast and density, the radiologist can manipulate and change the appearance of images without additional projections. This in turn, results in lower radiation doses to patients.

Although there are numerous advantages to digital mammography, a disadvantage was the lack of spatial resolution when compared with film/screen systems. This may hinder the ability to see clustered calcifications or small lesions. In addition, contrast and spatial resolution are lessened when printing films from digital formats.[8]

The 1990's and 2000 decades also demonstrated advancements in the use of ultrasound and magnetic resonance in breast imaging. Both modalities have specific roles that augment traditional mammography in detecting the presence of breast pathology.

Digital and computerized mammography

Traditional film/screen images are composed of intensity and spatial variations that result from radiation exiting the patient and influencing film emulsion. X-ray film suffers from variations related to the selection of technical factors, processing and noise. Digital images allow radiologists to manipulate images without additional projections required to overcome such limitation. Digital images may be obtained in the form of computerized or digital formats.[9]

Computerized mammography

Computerized mammography is accomplished by using a reusable, photostimulable image plate that is less than one (1) millimeter (mm) thick.[2] A phosphor layer, usually consisting of barium fluorohalide crystals or other suitable phosphors, are coated on the plate. The plate is inserted in a protective cassette. When exposed to radiation exiting the breast, the phosphor crystals form an invisible image. After exposure, the plate is placed in an image reader device that scans it with a laser. Light is emitted from the plate in relation to the amount of radiation it received at given spatial locations. The light is then sent to a photomultiplier tube that changes it to an electrical signal. This signal is digitized by the computer and displayed on a computer monitor as a matrix of pixels forming the image. Over-exposure of 500% or under-exposure of as much as 80% can be corrected by the computer, negating the necessity of most repeat exams.[2]

The resulting image has a much higher contrast resolution than typical film/screen images. Contrast resolution is approximately 10 bits per pixel.[2] This allows for up to 1024 variations in contrast per pixel and overcomes the limitation of the human eye, which can only detect about 32 shades of gray.[10] By changing the window level, physicians can change the contrast of the image to detect small contrast variations between pixels with no additional radiation to the patient.

Digital mammography

Digital images in radiology refer to the use of electronic detectors to form an image. The detectors can form an image either indirectly or directly. The indirect method involves the use of a scintillator that emits light when struck by X-ray and a photodiode that changes the light signal to an electronic signal. In this type of system, X-ray strikes a scintillator made of cesium iodide. It gives off light in relation to the amount of X-ray exiting the breast and striking the detector. The light is picked up by a photodiode made of silicon. It changes the light to an electronic signal. The active read-out of the electronic signal by the computer is accomplished through thin-film transistors.[2] They correspond to intensity and spatial locations on the detector that are then displayed on the computer screen as an image.

Direct digital mammography uses a selenium detector device to capture X-ray photons and convert them to an electronic signal in one step. There is no scintillator. This eliminates problems with light spread that can cause image blur and reduction in spatial resolution. However, X-ray photons not hitting this type of detector in a perpendicular line may still result in image blur.[2]

Spatial resolution in computed and digital images is less than with typical film/screen mammography. Spatial resolution is limited by pixel size (picture element size) of the display monitor. Current computed radiography spatial resolution is limited to approximately 100 μm. Micro calcifications that are smaller than this size cannot be detected without reducing pixel size. Smaller pixels yield better spatial resolution, but increases noise (unwanted background information) in the image that degrades image quality.[2]

Digital and computed radiography screening trials

Several studies have been conducted or are in progress regarding the sensitivity and specificity of digital and computed mammography when compared to the older film/screen technology. The only completed, federally funded program, was conducted by researchers funded by the United States Department of Defense.[11,12] In this trial, 4,945 women over age 40 underwent screening mammography. Both film/screen and digital mammography exams were performed for comparison. No statistical difference was noted in sensitivity between the two modalities. Results did show a significantly smaller number of recalls and fewer biopsies were required with digital imaging.

Edward Hendrick conducted a similar study involving 625 women for general electric.[11] In this research, images were interpreted independently using five different radiologists. This study confirmed that recall rates were significantly lower for digital mammography. Specificity and sensitivity were similar to film/screen radiography.[11]

The Digital Mammographic Imaging Screening Trial began in October, 2001.[6] The trial was conducted by The American College of Radiology Imaging Network and funded by the National Cancer Institute. The primary focus of this study was to compare the accuracy of film/screen mammography with digital mammography along with cost factors. All patients received film/screen and digital screening exams for comparison. In 2003, additional patients to the program were closed with a total of 49,528 women at 33 breast centers across the United States enrolled in the trial.[6,13] Data were analyzed and advantages of digital mammography were documented in the results of the trial.

The uses of magnetic resonance imaging and ultrasound in diagnosing breast pathology

Ultrasound

Ultrasound is being used today to supplement traditional mammography when suspicious lesions are noted on mammograms.[14] It can be used to differentiate a cyst from solid mass and can pinpoint solid masses that have characteristics of malignant lesions.

Cysts imaged with ultrasound appear as well defined, echo-free areas in the breast. These areas have well-defined walls and are round or oval in shape. There is normally posterior acoustic enhancement. In addition, Doppler ultrasound can be used to check for vascularity of the lesion. Cysts are always avascular. Peart[2] documented that ultrasound can detect cysts as small as one to two mm with

100% specificity. Cysts that do not demonstrate the above characteristics are biopsied.

Ultrasound images of malignant masses demonstrate breast lesions with internal echoes. They have an irregular shape with poorly defined, spiculated margins. Often times they are connected to ducts in the breast and may contain calcifications.[2]

Ultrasound also has limitations. It is highly operator dependent. Improper gain settings used to control intensity of the sound waves can produce internal echoes in cysts that can lead to false positive results and unnecessary biopsies. Complicated cysts can lead to confusing results. In addition, ultrasound cannot penetrate bone. Ribs can interfere with imaging lesions close to the chest wall. Size of the breast can also limit the value of ultrasound. Large breasts are hard to penetrate and lesions deep in the breast may be missed. Lastly, ultrasound does not detect early calcifications as well as does traditional mammography.[2]

Magnetic resonance imaging

Significant benefits have been realized from the selective use of magnetic resonance imaging (MRI) in breast imaging. The sensitivity of MRI is 96%.[2] As a result, it has been used to reduce the number of false positive mammograms and minimize unnecessary biopsies. Its benefits have also been realized as a screening tool in high-risk patients or patients with dense breasts that are difficult to image with traditional mammography. MRI can also be used to detect reoccurrence or spread of cancer. It can therefore be used as a staging tool when physicians consider different treatment options such as radiation, surgery or chemotherapy.

Magnetic resonance imaging, like ultrasound, does not detect early calcifications.[2] To survive as a replacement for mammograms, it would have to meet all current benefits of mammography and add additional benefits. In addition, the cost of MRI is prohibitive as a stand-alone screening modality. To be used as a screening tool, the cost must decrease and third party payers must be willing to increase reimbursement.

Digital breast tomosynthesis

Digital breast tomosynthesis (DBT) technology began in 1971 in an attempt by researchers to reduce the problem of imaging overlapping structures in the breast.[15] The original research involved obtaining images at different angles that could be used to produce slices of breast tissue.[15] At the time, there were no digital detectors and computer processing speeds were slow by today's standards. This limited further development of DBT until the 1990s when digital detectors became available. The first useable unit was developed in 2000 at Massachusetts General Hospital.[15] Numerous other systems were developed that varied the image capture angles and algorithms used to process the images.

Digital breast tomosynthesis was approved by the United States FDA in 2011 for breast imaging after numerous studies demonstrated its efficacy in distinguishing cancerous from noncancerous lesions. The studies showed increased detection rates as well as improved sensitivity.[16,17]

Tomosynthesis acquires 3D images and is usually combined with 2D digital mammography images.[16] DBT requires the use of a moving X-ray tube and digital detector.[18] The digital detector is an electronic device composed of tiny detector elements. There are two primary types of detectors in use today. One type uses an indirect image capture process. This involves remnant radiation from the patient striking a scintillator on the surface of the detector. The scintillator (usually composed of cesium iodide) gives off light. The light is then captured by the detector elements as an electrical charge that is digitized and displayed with spatial and intensity values on a computer screen. Another common type of detector uses a direct conversion process that directly converts remnant radiation into an electrical signal in each detector element. A minimum of 10 exposures are acquired over an angle range of 10°-50° during tomosynthesis. Image acquisition can be accomplished using a step-and-shoot technique where the X-ray tube stops at various points in its arc around the breast or continuous method where the tube moves in a continuous arc during the acquisition process.[18]

Following acquisition, images are reconstructed using complex mathematical algorithms. Fourier transformation algorithms are used to represent intensity and spatial locations of anatomy on images. This information can then be displayed on a monitor with the use of filtered back projection or iterative technique algorithms. Each method produces some image artifact, but one study concluded that iterative reconstruction provides the best image quality.[15] Structures in the same plane are combined by the images taken at different angles, thereby allowing them to become more apparent.[15] Images from different depths can be reconstructed in different slice thicknesses or combined together without additional exposure to the patient.

Radiation dose to the patient is somewhat higher with DBT compared to digital mammography. However, dose estimation varies and is dependent on a number of variables that include imaging protocols used as well as the thickness and density of the breast. In addition, dose can vary based on reader preference related to image noise. Increased dose improves image quality by decreasing noise. The amount of acceptable noise is often determined by the interpreting radiologist and therefore varies by institution. Dose with a combined 2D and tomosynthesis exam is estimated to be about three times higher than with a standard screening mammogram consisting of craniocaudal (CC) and mediolateral oblique (MLO) projections.[16] Emory University School of Medicine completed a study using breast phantoms constructed of oil and water. Both average and dense breast representations were tested. The study indicated an approximate 8% increase on average breast density and an 83% increase with dense breast phantom exposures using DBT.[19] Another study conducted by Olgar *et al*.[20] concluded that DBT dose was 34% higher. Although the radiation dose is higher, it is still under the dose limit prescribed by the MQSA.[15]

Digital breast tomosynthesis has several advantages over digital mammography. It minimizes the impact of tissue overlap that can make interpretation of dense breast images difficult. By obtaining images from multiple angles and combining them together in a 3D image, overlapping dense tissue is better separated and delineated from fibrous tissue. In addition, lesion margins are better visualized with DBT than digital mammography. Many studies have shown that DBT has a higher sensitivity and specificity than digital mammography alone.[15,21-23] As a result, it can rule out many false-positives and reduce the high number of recall rates and associated patient anxiety. Even though the overall dose rate is higher when compared with a two view screening mammogram, DBT can reduce the need for some additional exposures when suspicious areas are found on screening exams.[15]

Standard use of DBT imaging protocols do not exist at this time. Numerous studies have been conducted comparing the sensitivity and specificity of 2D screening mammograms only compared with a combination of 2D plus 3D DBT or 2D plus 3D MLO only protocols. The studies included radiologists with varying years of experience and training. The results concluded that 2D (CC and MLO) plus 3D projections (CC and MLO) provided the best overall sensitivity and specificity.[15] In addition, DBT has been used in conjunction with diffuse optical tomography that uses near-infrared laser to overlay oxygen saturation information on DBT images. Since saturation is higher in cancerous areas versus cysts, this protocol could add additional information to DBT images.

Advantages of DBT have been highlighted recently in the national news and media to encourage women to ask the health care provider for this new technology in addition to mammography.[24] However, DBT is not available in the hospital radiology departments and breast imaging centers in many rural areas. DBT imaging requires new equipment to be purchased by the hospital or clinic. As with any new technology, start-up costs are very expensive. For smaller hospitals and breast centers, the purchase of DBT equipment is cost-prohibitive at the present time. In rural areas, there may not be enough patient volume to pay for this new technology. In addition, reimbursement from third party payers is lagging behind the costs of new technology [Table 1].

Conclusion

During the past 50 years, great advances in the use of radiologic techniques and modalities in the diagnosis of breast cancer have reduced mortality and increased life expectancies for breast cancer patients. Technologic advancements include digital radiography, MRI, ultrasound

Table 1: Breast imaging technologies — indications, benefits, disadvantages

Imaging technology	Indications	Benefits	Disadvantages
Mammography	Breast cancer screening	Widely available Current standard for breast cancer screening	Limited spatial resolution; further testing needed to differentiate types of lesions, masses, cysts
Ultrasound	Supplement mammography when a suspicious lesion is found on mammogram	Widely available Use to differentiate cystic lesions from solid masses	Skill of operator is a variable in the quality of imaging. Large breasts and deep lesions may limit the imaging quality
MRI	May be used in patients at high-risk for breast cancer, patients with dense breast tissue, or in breast cancer staging	Widely available Can follow mammography to view breast lesions, and minimize unnecessary biopsies	Costly Higher doses of radiation necessary
DBT	Latest 3D imaging technology May follow traditional mammography to better visualize dense breast tissue, fibrous and overlapping tissue	Better visualization of breast tissues; better 3D image quality; increased specificity to distinguish masses that demonstrate characteristics of malignancy; less need for breast biopsy; less patient anxiety	Costly Not widely available, especially in rural areas Higher radiation dose to the patient

MRI = Magnetic resonance imaging, 3D = Three-dimensional, DBT = Digital breast tomosynthesis and tomosynthesis in breast cancer detection. It is important for nurses to be well informed about these varied diagnostic modalities, and appreciate the fact that advances in radiologic imaging technologies can yield improved outcomes for breast cancer patients.

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