Contrast-Enhanced Breast Imaging: Better Visualization for Abnormalities

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Objectives

After reading the scientific paper Contrast-Enhanced Breast Imaging: Better Visualization for Abnormalities, the reader will be able to:

1. Understand the history of mammography
2. Differentiate between each of the breast imaging modalities
3. Recognize the benefits with the usage of contrast-enhanced breast imaging
4. Recognize the concerns associated with contrast-enhanced breast imaging

Abstract

Contrast-enhanced breast imaging is a useful diagnostic tool that utilizes various modalities, including mammography, computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US). Contrast-enhanced breast imaging is better at detecting lesions and abnormalities within the breasts than images that do not use contrast. By using contrast, the cancerous tissue absorbs it and provides an easier method to determine cancerous tissue from the normal surrounding tissue. Also, contrast can help determine the difference between a malignant tumor and a benign tumor. In order to evaluate the status of the tumor, the contrast is needed to determine whether the lesion is supplied with blood. If the lesion has an adequate blood supply, it will most likely be considered a malignant tumor. Every modality has its own benefits, but each contributes to the detection of abnormalities within the breasts. Contrast-enhanced breast imaging is one of the many imaging modalities that provides a more accurate diagnosis for the patient.

Contrast-enhanced breast imaging is a relatively new examination procedure that increases the ability to detect abnormal areas in the breasts and the surrounding tissue. It is constantly evolving to improve the quality of the images in order to have an accurate diagnosis. Scientists knew breast health was important and wanted to discover a new method to improve the images; therefore, they introduced contrast-enhanced breast imaging. Mammography has been the key method to image the breasts for over a century and continues to advance due to technological improvements. It started with images that were barely diagnosable and low quality to advanced digital technology and incredible techniques. The images are advanced even more by adding contrast to improve the visualization of breast structures and surround tissues. Scientists wanted to expand contrast-enhanced breast imaging to integrate with existing imaging techniques, so it was not just limited to mammography. Major benefits were realized through combining contrast-enhanced breast imaging with commonplace modalities, such as CT, MRI, and US. While all of these modalities benefit from the use of contrast, they are nuanced enough that they are irreplaceable within radiology. Each one plays a valuable role in diagnosing the patient and accommodating for their needs. Because contrast-enhanced breast imaging is vital in the detection of lesions, it is constantly making advancements in technology, continuing to find ways to utilize each imaging modality, and developing new trials to study methods to improve how breasts are imaged.

History of Mammography

Throughout history, mammography has constantly evolved, which improves the effectiveness of each diagnosis for every patient. Mammography has been a helpful tool for over 100 years. It started in 1913 when Albert Salmon reported his findings of a mastectomy specimen, which demonstrates the spread of tumors to the axillary lymph nodes all guided by radiography.[1] Before it was recognized as mammography, doctors knew the importance of breast imaging even though the images lacked quality. This lack of quality persisted for roughly another three decades due to limited technological advances. Despite this, academics spurred the creation of many novel imaging techniques, albeit most were not useful. In 1930, Stafford Warren discovered a new procedure that helped differentiate malignant from benign tumors. He achieved this through the same fluoroscopic equipment used in other procedures in coordination with stereoscopic viewing techniques. This new method was trialed on 119 patients and determined that 61 growths were benign while the remainder were potentially malignant, with a later proven accuracy of 93%.[2] Just four years after Warren's trial, another technique was introduced by Ira Lockwood, which includes carbon dioxide insufflation of breast tissue and several contrast material injections into the mammary ducts.[2] However, the contrast injections, especially thorotrast, came to a halt due to inflammation and mounting concerns about the effects of radiation.

As the decades continued, people gained more knowledge about the importance of mammograms. In 1960, Robert Egan discovered a standardized direct exposure technique and reported his findings on 1000 cases.[2] Mammograms were established to be helpful in detecting unexpected cancers and reducing the number of unnecessary mastectomies. Egan not only developed a wonderful technique, but also took the patient's positioning into consideration. He created these positioning techniques to allow the nipple to be in profile and avoid folds or overlapping structures. Images were captured using a special generator capable of decreasing the kilovoltage exposure, utilizing a direct-exposure film, and providing little to no compression of the breast. The images did not have adequate contrast levels or technique. However, it required a relatively long exposure time, approximately 5 to 6 seconds. Egan's findings piqued people's interest to continue improving breast imaging.

The next major advancement in radiology was in 1970 when John Wolfe introduced breast imaging in the form of xeroradiography.[2] Xeromammography, which is characterized by its use of dry chemical developers, was documented to have a wide latitude and an increased edge enhancement. This type of mammography did not need a viewbox; it was printed on a piece of paper with blue powder and it was also inverted from the previous direct exposure technique. Unfortunately, xeromammography caused a variety of issues including paper jams, non-uniform toner, and high patient radiation doses.[2] Due to the high patient doses, xeromammography was replaced with screen-film mammography. With the development of screen-film mammograms, the techniques allowed the use of a collimated beam, shorter exposure time, decreased dose, and increased contrast. Also, screen-film mammograms helped doctors realize by compressing the breast, it will result in a more uniform density throughout the image. During a mammogram, an average of 20 pounds of pressure is applied to the breast being imaged. The flatter the breast tissue is the more the density becomes uniform and allows better visualization. The screen-film technique was better than any of the previous techniques, but it still needed improvements to better the image quality.[2] In order to ameliorate the image quality, advancements in technology would need to be made.

It was not until roughly 30 years later that digital mammography was introduced instead of using film. When digital mammography was first established, the breast imaging community was skeptical about the transformation. The community was unsure if the diagnostic quality would improve with the decrease of spatial resolution. Not only was quality a concern, but also the price of new equipment. Due to the many uncertainties about the new digital system, the American College of Radiology compared digital to analog mammograms in 33 different locations across the United States and Canada.[2] During this trial, they discovered digital mammograms were more accurate than film mammograms especially in women 50 or younger, and women with extremely dense breast tissue. However, it was revealed that film mammograms performed better in older women with fatty breast tissue. With the digital screen, the radiologist reported the display makes it easier to read even the fatty tissue. Digital mammography provides quality images and easier reading methods; however, radiologists had to adapt to the new workflow. With digital imaging, there was no longer a shiny or dull side of an image. Now, the hanging protocol could be based on the radiologist's preferences and there was no need for a viewing box. Digital mammography brought many new advancements, such as no more lost films, reduced radiation dose, and the ability to view images anywhere.[2] In the early 2000s, scientists discovered a method to advance the field of mammography by enhancing the images with contrast. Contrast-enhanced mammography uses a contrast agent with an iodine concentration of typically 300 mg/ml to 370 mg/ml.[2] Because contrast-enhanced mammography is continuing to evolve, it has varying potential to reduce the number of unnecessary breast biopsies, decrease the number of both false-positives and false-negatives, and increase the contrast resolution.

Focusing on Breast Health

The most common way to examine the breast is through a mammogram; however, contrast can be used to enhance the image to better demonstrate abnormalities. Contrast-enhanced mammograms are very similar to a standard 2D or 3D mammogram many patients receive today; however, there are some differences. The first major difference is contrast-enhanced mammograms use a standard iodinated intravenous contrast agent similar to the contrast used in CT scans. By injecting patients with contrast, it can detect cancers that may not be visible on a standard mammogram. Contrast-enhanced mammography provides a method of problem solving and can help identify early breast cancers. The United States Food and Drug Administration considers mammogram exams with contrast to be "off label," which is unapproved usage of an approved medicine.[3] The positioning is very similar to a standard mammogram, such as utilizing the same views and compressing the breast. The contrast used is best visualized at the two-minute mark, which coincides with the typical positioning time. However, it is important to finish the images within seven minutes of injection as the contrast loses efficacy.

Another key difference is contrast-enhanced mammography requires two exposures for each view: one similar to a standard mammogram at low energy and one at a higher energy that gets absorbed by the iodine contrast. Once the images are obtained, subtraction is needed to create an enhanced image with the contrast becoming the focal point. The image is then viewed together with the low-energy image to allow better enhancement. If cancer is present in the breast tissue, it will typically absorb more of the iodine contrast agent than the normal surrounding tissue. In **Figure 1**, there is a noticeable difference between the low-energy images and the contrast-enhanced images.[4] The recombined images are diagnostically proven to be better at identifying cancerous tissue within the breasts. Because the cancerous tissue absorbs the contrast, radiologists can easily determine cancerous tissue from the normal surrounding tissue. However, there are some concerns to consider with contrast-enhanced mammograms. There was a noted small increase in radiation, about 50% more than a standard mammogram, but less than that from tomosynthesis.[3] Even though there is an increase in patient dose, contrast-enhanced mammography produces images that are substantially better than a standard mammogram. With contrast-enhanced mammography technology, it creates a whole new perspective on breast imaging. However, not only mammograms utilize contrast-enhanced breast images, but also other imaging modalities, such as MRI, CT, and US.

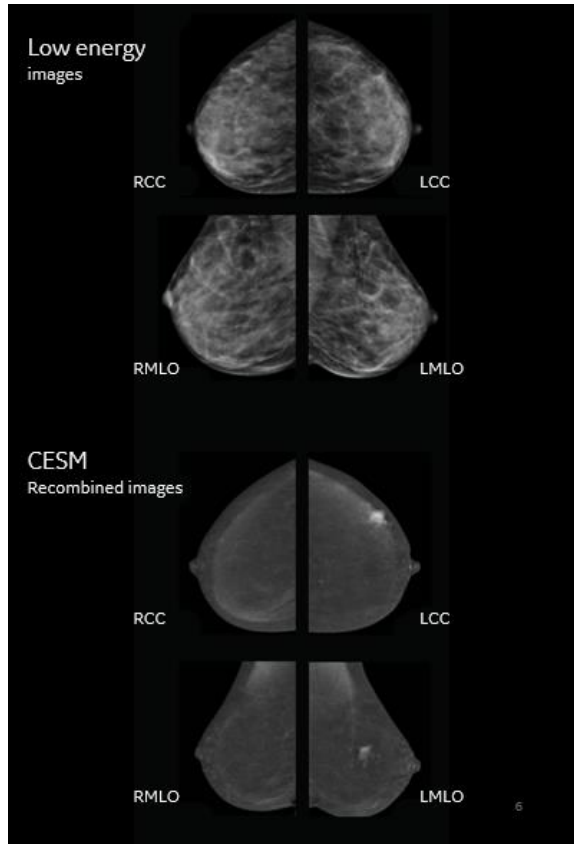

Figure 1: Difference between Low Energy and CESM images

Other Breast Imaging Modalities

Many other imaging modalities offer exams to evaluate the breasts and the surrounding tissues. Breast cancer is found to be the most invasive cancer among women, and the incidents have slightly increased each year. Within 2020, the American Cancer Society indicates there to be an increase in the amount of invasive breast cancer cases estimating to be about 276,480 new cases.[5] If a mammogram reveals a suspicious area, additional images might be required to better evaluate the area, such as CT, MRI, and US.

Computed Tomography

Breast imaging made major advancements when examinations were performed with digital technology. With the improvements in technology today, breast CT was found to be helpful by improving early detection of breast cancer. Although mammography is the current standard for breast imaging, it has the disadvantage of the superimposition effects found in projection images. This effect is where overlaying normal breast tissue can obscure a lesion, therefore, hiding a potential detection. There is also a possibility the overlapping tissue can cause summation artifact and lead to an inaccurate diagnosis, which can lead to additional imaging and unnecessary worry for the patient.[5] Since attenuation is linearly proportional to radiodensity in CT, contrast-enhanced breast CT with a nonionic, iodine-based contrast may be a useful tool for identifying the difference between normal and malignant tissue. Approximately four, 17 second scans are performed only allowing one breast to be imaged at a time before and after the contrast injection. Therefore, the total radiation dose for each breast would equal anywhere between 8 and 32 milligray.[5] On an average breast CT, 100 milliliters of intravenous iodixanol are administered at a rate of 4 milliliters per second with the power injector. During a contrast-enhanced CT, it is common to perform delays with an average delay time of approximately 96 seconds from the start of contrast injection until post-contrast scanning.

A trial was studied by many scientists to quantify contrast-enhanced breast lesions scanned with a dedicated breast CT and compared their conspicuity with that of mammography. In the 46 women that were studied, 54 lesions were identified, and the results indicated contrast-enhanced breast CT performed better than mammography.[6] They found malignant lesions stood out significantly more in a contrast-enhanced breast CT than mammography. It was also discovered benign masses were significantly more conspicuous with the contrast-enhanced breast CT than with mammography. However, benign calcifications were visualized significantly better in mammography than contrast-enhanced breast CT. They realized there were more benefits with contrast-enhanced breast CT rather than standard mammography. Scientists noted breasts with high and low densities favored the contrast-enhanced breast CT over mammography because it was found to be more conspicuous.[6] It was revealed contrast-enhanced breast CT is tremendously useful in the breast imaging community. Scientists are gaining knowledge about how different imaging modalities allow lesions to be visualized better than the current method.

Magnetic Resonance Imaging

Breast MRI continues to become a more noticeable component of imaging to aid in the diagnosis of patients with suspected breast carcinomas. Dynamic contrast-enhanced (DCE) MRI allows the ability to identify lesions from normal tissue because the lesions are connected vascularly, which is enhanced from the contrast.[7] Therefore, DCE MRI has emerged as an imaging modality that is possibly complementary to mammography because MRI provides additional information utilizing three-dimensional spatial and temporal technology. Screening for breast cancer is often performed with standard mammography, which is the basic concept of the detection of cancer before symptoms occur. Standard mammography does not have a high specificity in asymptomatic cases; however, it typically does not detect cancer until significant growth has occurred. Up to 50% of cancers are detected between screening rounds among women with a large relative fraction of dense tissue breast.[8] This is fortunate since a large portion of the population has breast tissue that can be considered dense. Due to dense breast tissue, the imaging characteristics are less specific and may resemble benign lesions. Therefore, the mammographic screening in women with an increased risk has consequently lower performance than in women with less dense breast tissue. For better visualization of dense breast tissue, a mammogram can be replaced with a DCE MRI. During breast MRI, women with an increased risk for developing breast cancer are placed prone to aid in the detection of breast cancer and are screened starting at a younger age. DCE MRI became rapidly tested as a supplementary screening tool after the realization that it has very high sensitivity for the detection of breast cancer. This level of detection is due to the nature of how breast cancer propagates. In order for the tumor to grow larger than 2mm in diameter, it must recruit new blood vessels to ensure more nutrients are available.[8] These hastily formed blood vessels are more permeable than healthy vessels and consequently allow for Gadolinium-based contrasts to accumulate within the tumor mass. The paramagnetic properties of the Gadolinium contrast increase the signal on T1-based sequences, which allows for a quicker MRI scan time. A standard breast MRI protocol is comprised of pre-contrast and post-contrast T1-weighted acquisitions as well as its T2-weighted counterpart, which aid in the detection of a lesion.

Moreover, a study consisting of multiple trials observing women with a family history of breast cancer and the BRCA1/BRCA2 genetic mutations was performed to determine the viability of MRI when used as a supplemental screening tool. Furthermore, Dutch Magnetic Resonance Imaging Screening Study and British Magnetic Resonance Imaging Screening Study showed that breast MRI had a sensitivity of 71% and 77% respectively.[8] With the sensitivity of 77%, MRI revealed it was almost twice as sensitive as mammography. However, while MRI was shown to be more sensitive, this study concluded that mammography had a higher specificity by a margin of 9%.[8] With improved technique and detailed guidelines, MRI showed a higher efficacy. Within the German EVA Trail and High Breast Cancer Risk Italian 1 Study, they revealed the breast MRI sensitivity to be over 90%.[8] Because the sensitivity is high in breast MRIs, BRCA mutation carriers are unlikely to develop true interval cancers. The cancer in a breast MRI can be detected because of the contrast. If it was not for the contrast, it would be nearly impossible to find some cancers within the breast.

Ultrasound

Recent developments have allowed for the studying of focal lesions with contrast-enhanced ultrasounds. To ensure the best visualization of the breasts, a new US contrast medium called SonoVue was developed to be utilized in B-mode and Doppler ultrasounds. SonoVue was shown to have the ability to demonstrate microcirculation, especially for lesions within the liver.[9] A study was obtained to determine the accuracy of differentiating the diagnosis of malignant and benign breast lesions using contrast-enhanced ultrasound (CEUS). A total of 71 random patients with breast tumors were selected for the trial. US was utilized before and after a large injection of SonoVue contrast with quantification software to determine the physical structure of vessels. With the use of CEUS, the total findings successfully differentiated 45 malignant and 31 benign tumors from all the lesions.[9] Similar to CESM, the timing of CEUS is important. There are three phases to be aware of after injecting SonoVue, such as early (0-1 minute), mid (1-4 minutes), and late (4-6 minutes) phases. Within the early phase, there was a noticeable difference between the enhancement pattern in malignant and benign lesions. Tumors with claw-shaped enhancements were discovered to be malignant 91.1% of the time, while homogenous enhancements were benign 83.9% of the time using CEUS.[9] Compared to a late phase, it was more helpful with detecting the difference in malignant and benign tumors. During a CEUS, malignant tumors showed 88.9% and benign tumors only 9.7% when contrast was present.[9] This study found if the peak intensity and peak time were more uniform in the enhanced ultrasound, it suggested it was benign, while a varying peak intensity and peak time were found to be malignant.[9] CEUS is a reliable tool to differentiate malignant and benign tumors to help accurately diagnose the patient.

By utilizing CEUS, it can help determine the BI-RADS score for each lesion within the breasts. A number between zero and six is assigned to each lesion in the breasts. Each number is categorized based on the risk of the breast lesion shown on the CEUS with 6 being the most severe. In **Figure 2**, CEUS evaluated and scored this lesion a four.[10] With a score of four, it will most likely be benign, but it is still a high enough number to be examined using other methods, such as a biopsy. The lesion in the contrast-enhanced ultrasound (see **Figure 2**) is considered to be homogenous without claw-shaped enhancements. With the identification of the enhancements, the lesion has more characteristics leading to it being benign. With CEUS, it is easier to assign accurate BI-RADS scores because the contrast enhances the tumor to better identify if it is malignant or benign.

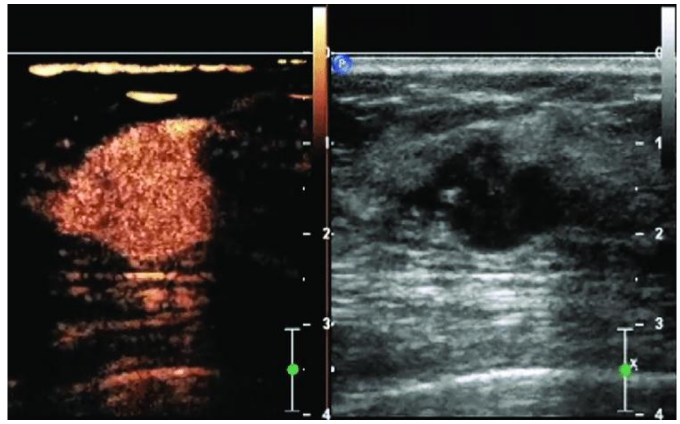

Figure 2: Contrast-enhanced lesion with a score of four

Usage of Contrast-Enhanced Imaging

When contrast-enhanced imaging is used, it plays a key role in detecting cancers and abnormalities within the breasts and the surrounding tissues. Contrast is a crucial aspect of imaging; therefore, many benefits arise when contrast is administered.

Benefits

Contrast is a vital addition to each imaging modality and without it, cancerous tissues or tumor can be missed. It helps the radiologist determine the difference between normal and abnormal tissues within the breast. There are many beneficial uses for all types of contrast media in every breast imaging modality. The key reason contrast is used, whether it is iodine-based or gadolinium, its absorption by the cancerous tissues and better visualization for a more accurate diagnosis. Contrast also has the potential to differentiate between malignant and benign tumors, which helps determine the treatment needed for the findings. This technology can be life changing by allowing the patient to know the status of their cancer without having more studies performed. As a medical professional, the technologist wants what is best for the patient and by providing multiple modalities, there are multiple options for breast imaging. Each modality is slightly different and can accommodate for the patient's needs. It is also beneficial that not all the modalities use radiation such as MRI and US. This is very helpful if someone is radiation sensitive or may be pregnant. Each exam may have their own specialties, but they all rely on contrast to enhance the image for better visualization.

Concerns

With every procedure, there are always concerns to consider before performing the exam. The biggest concern with injecting contrast is the possibility of an allergic reaction. Even though it is not common in many people, it is still a factor that needs to be considered before scheduling an examination. However, if a patient is allergic to the iodine-based contrast, they could receive an MRI with gadolinium contrast as an alternative. Because there is such a wide variety of imaging modalities, a patient is not limited to one exam. For example, if a patient was claustrophobic and could not handle an MRI, there are at least three other imaging options available for them. Another important factor to be aware of is the patient's kidney function. It is crucial the patient's creatine and GFR is within acceptable ranges. If they are not within normal range, the patient may have to reschedule and wait until their labs are acceptable in order for their kidneys to filter out the contrast properly without damage. However, ultrasound uses a contrast that is safe for the kidneys and the function does not have to be checked before administering the contrast. Because the contrast is not excreted by the kidneys, it does not affect the renal function of the patient.[11] Since there are so many imaging modalities that utilize contrast, it allows a variety of opportunities for the patient to receive a contrast-enhanced imaging examination. When using contrast-enhanced imaging, the benefits outweigh the risks and are overall more beneficial for the patients.

Conclusion

Contrast-enhanced breast imaging has grown in popularity as multiple modalities have made it possible to more accurately diagnose lesions within the breasts and the surrounding tissue. As technology advances, the world of breast imaging will continue to evolve and metamorphosize to provide cutting edge treatment to those in need. Mammograms are the most common method to image the breasts that can make use of contrast; however, there are various other modalities that offer contrast-enhanced imaging such as computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US). While all of these modalities benefit from the use of contrast, they each have their respective strengths and weaknesses. Contrast-enhanced breast imaging is a critical method in differentiating normal and abnormal tissue and between malignant and benign tumors. The contrast allows tumors to be visualized by absorbing the solution to make it appear more vibrant on the image. There are many benefits to using contrast-enhancement techniques with breast imaging, such as improved diagnostic accuracy, decreased false-negatives, and increased overall quality. Studies showed a higher sensitivity as well as a higher specificity when used to aid in the diagnosis of cancers when compared with the more traditional methods of mammography. Despite the upsides to modern contrast-enhanced breast imaging, there are issues that need to be noted. The use of chemical components will always present more of a risk than simple physical exams given the immune system's potentially damaging overreaction to foreign bodies. Another point of contention is the larger dose of radiation needed for CT or 3D mammography and its effect on the body for prolonged or repeated exposures. As medical advances are made, the prominence of contrast-enhanced breast imaging to identify lesions will continue to increase. Therefore, more patients will be able to receive an accurate diagnosis.

Resources

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