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Review Article

Optimizing contrast enhanced mammography: A comprehensive review of artefacts, causes, and remedies

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A R T I C L E I N F O

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A B S T R A C T

Contrast enhanced mammography (CEM) is a promising imaging technique in breast imaging, combining efficiency and cost-effectiveness with the ability to provide structural as well as functional information. However, like all imaging modalities, CEM is prone to artifacts that can occur at various stages of the process, including patient preparation, image acquisition, equipment calibration, and digital subtraction. Recognising and rectifying these artifacts is essential for achieving optimal image quality and accurate diagnosis. The purpose of this article is to familiarise the readers with common artifacts encountered during CEM and minimise their impact on image interpretation, with a focus on strategies for optimising CEM imaging. We have also described a few previously uncharted CEM-specific artifacts observed in our clinical experience. Additionally, this review highlights major pitfalls encountered during CEM reporting and measures to improve diagnostic accuracy.

Introduction

Contrast-enhanced mammography (CEM) is an advanced technique in breast imaging that integrates anatomical information of full-field digital mammography (FFDM) with intravenous contrast administration to provide functional insight into tumour vascularity. CEM has demonstrated higher sensitivity and increased cancer detection rates compared to FFDM, especially in dense breasts.[1,2] It is being increasingly used for various indications, including screening of high-risk patients (>20% lifetime risk) who cannot undergo magnetic resonance imaging (MRI), for diagnostic evaluation, as a problem-solving tool, local staging of breast cancer, pre-surgical planning, as well as for assessing response to neo-adjuvant chemotherapy.[3,6]

CEM utilises dual energy emission to acquire sequential images at different energies, and creates subtracted (recombined) images, which depict the areas of contrast uptake. It is based on the principle of neovascularity, due to which malignancies show enhanced contrast uptake, leading to higher attenuation of X-rays and differential image contrast. In CEM, two similar images are taken at high energy (HE) and low energy (LE) following the injection of a low osmolar iodinated contrast agent at a dose of 1.5 ml/kg body weight and a rate of 3 ml/second. The HE (45-49 kVp) images, with energy close to the K-edge of iodine, show attenuation of all soft tissue except the contrast. The LE (27-29 kVp) images use rays similar to those in FFDM, and in these images the area of contrast uptake is obscured as the kVp is below the K-edge of iodine. These two images are subtracted to create a recombined image (RC) that highlights the enhancing areas. Thereafter, LE and RC images are utilised in image interpretation. The time gap between LE and HE image acquisition is merely seconds, thereby reducing compression time and also minimising the risk of motion artifacts.[1-4]

However, like any other imaging modality, CEM is also susceptible to various artifacts that can lead to false positive or false negative results. The images have to be optimised for accurate evaluation and diagnosis. It is crucial for technologists, radiologists, and physicists to have a deep understanding of these artifacts and their rectification methods to provide optimal imaging, improve diagnostic accuracy, and avoid misinterpretation.[3,4] These artifacts are both inherent to FFDM as well as specific to contrast enhanced mammography.[2] In this review, we will be addressing the CEM specific artifacts, related physics, and the impact they may have on image interpretation. Methods suggesting rectification will also be addressed. As CEM is still an upcoming novel modality, very few articles are available in the literature describing these artifacts

Abbreviations: FFDM, Full-field digital mammography; MRI, Magnetic resonance imaging; CEM, Contrast enhanced mammography; kVp, kilovoltage peak; BI-RADS, Breast imaging reporting & data system; CEDM, Contrast enhanced digital mammography; LE, Low energy; HE, High energy; RC, Recombined; MLO, Mediolateral oblique view; CC, Craniocaudal view.

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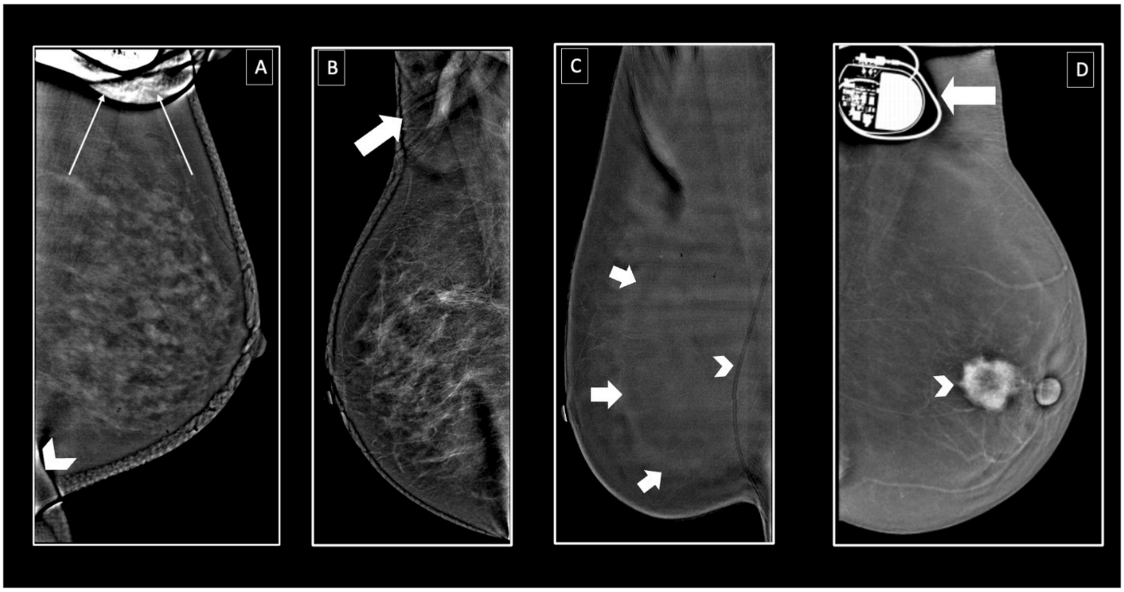

Fig. 1. Overlay artifact; contrast enhanced mammography images in different patients. **A** Mediolateral oblique view, recombined image of the left breast in a 56-year-old woman shows a radiopaque structure obscuring the upper axilla due to overlay of the patient's chin (white arrows). The abdomen is also seen overlying the inferior and posterior breast (white arrowhead). **B**, Mediolateral oblique view, recombined image of the right breast of a 64-year-old woman show curvilinear lines over the axilla (white arrow), consistent with a hair artifact. **C,** Mediolateral oblique view, recombined image of the right breast in a 48-year-old woman show a tubular structure along the posterior breast, consistent with a ventriculoperitoneal shunt (white arrowhead). Additionally, a "breast within breast" artifact is also noted (white arrows). **D,** Mediolateral oblique view, recombined image of the left breast in a 67-year-old woman shows a radiopaque pacemaker overlying the left axilla with a surrounding black halo on the recombined image consistent with overlay and high attenuation artifacts. In addition, a high density irregular mass showing heterogeneous enhancement on the recombined image is seen in the retroareolar location (arrowhead) with associated nipple retraction. On histopathological examination (HPE) and immunohistochemistry, the mass was Luminal B infiltrating ductal carcinoma, non-specific type, Grade II.

and measures for their resolution.

Imaging artifacts

Artifacts in CEM can be broadly classified based on their origin into the following categories: patient-related artifacts, acquisition-related artifacts, equipment-related artifacts, contrast enhancement-related artifacts, and quality control artifacts. In this discussion, we address each type of artifact, highlighting its key imaging features, identifying the root causes, and offering rectification methods to enhance image quality. In our institute, CEDM is acquired in Hologic Selenia Dimensions 1.9.2. All the images in the article were obtained in this system.

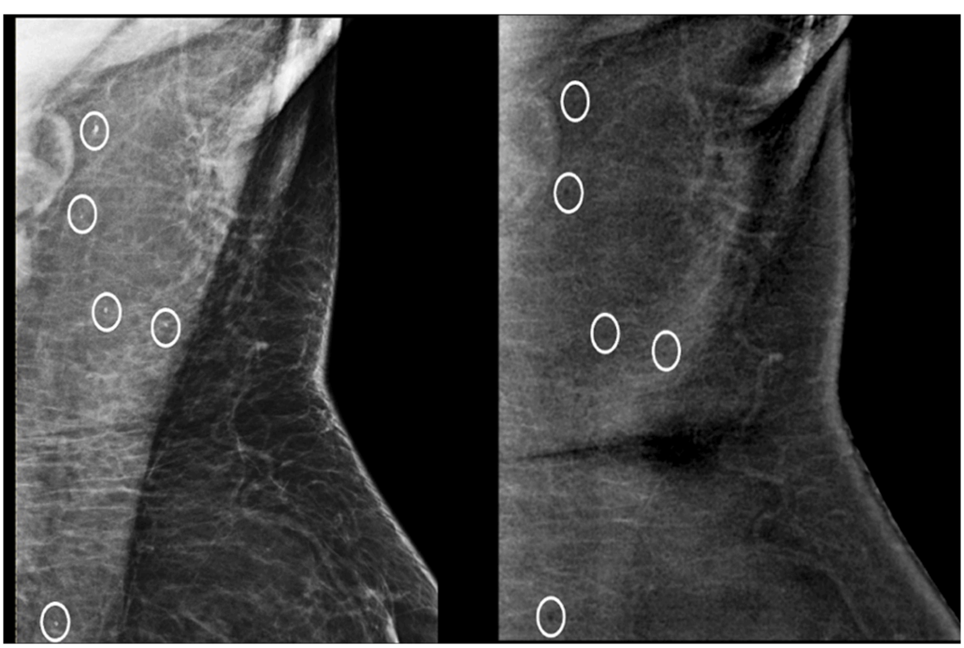

Fig. 2. Antiperspirant artifact; contrast enhanced mammography images in a 58-year-old woman with invasive ductal carcinoma. Low energy image (left) of the left axilla (zoomed-in) showing hyperdense punctate foci due to antiperspirant; recombined image (right) of the left axilla (zoomed-in) shows the antiperspirant as small black dots (white circles).

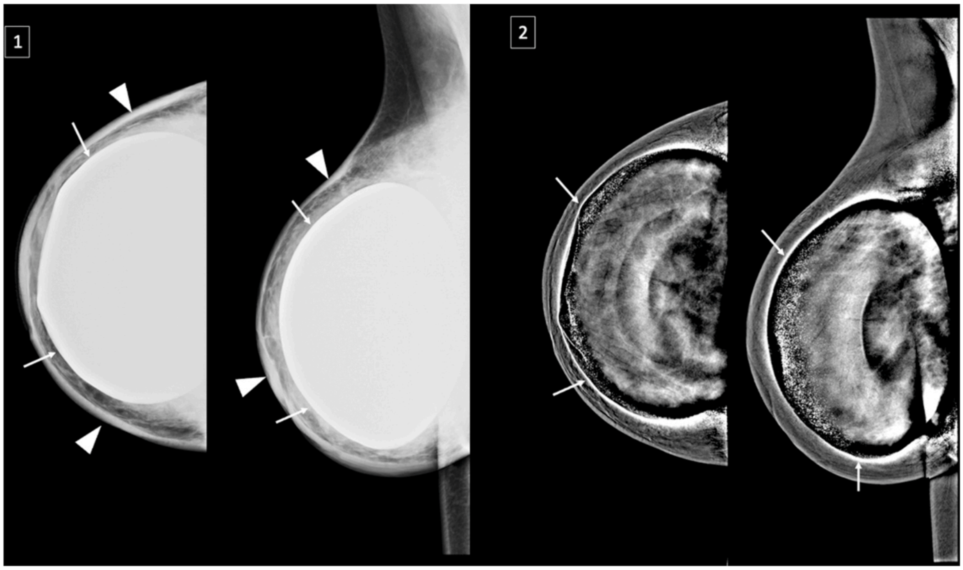

Fig. 3. Breast implant artifact; contrast enhanced mammography performed for new onset swelling in the right breast in a 49-year-old woman with an implant. **1,** Craniocaudal and mediolateral oblique views, low energy images show a breast implant in situ (white arrows) with diffuse thickening of the skin (arrowheads). **2,** Craniocaudal and mediolateral oblique views, recombined images show postprocessing artifact as a bright white band adjacent to the implant.

Patient related artifacts

CEM non-specific patient related artifacts

These originate from standard mammographic acquisition and may appear in both low-energy and recombined images of CEM. When not identified correctly, such artifacts may mimic or obscure masses, thereby affecting diagnostic interpretation.

Overlay artifacts. These occur due to unintentional superimposition of external objects or anatomic structures such as hair, chin, shoulder, contralateral breast, or clothes in the field of view. Even internal placements of ventriculoperitoneal shunts and pacemakers may superimpose the breast parenchyma and hinder accurate image interpretation (Fig. 1).

Remedy: Before the examination, ensure that the patient securely ties her hair, and removes all clothing and accessories that might fall within the imaging field. For optimal breast positioning, the patient's breast must be maximally pulled and evenly spread, with the nipple in profile

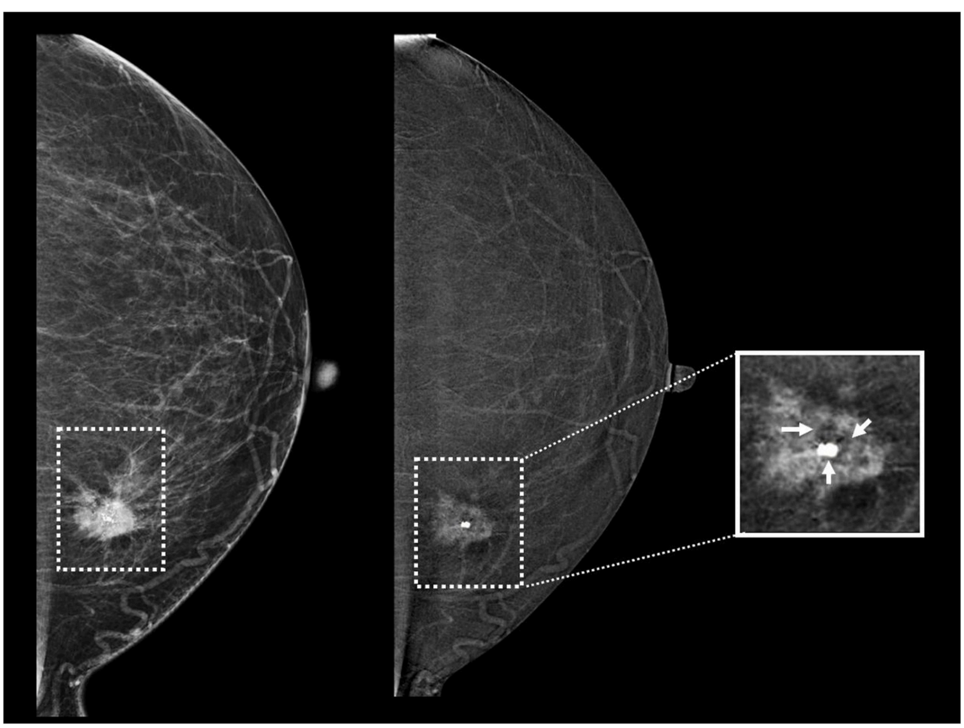

Fig. 4. Artifact due to hyperdense surgical clip/marker; contrast enhanced mammography images from a 54-year-old patient with left invasive breast cancer on chemotherapy. Craniocaudal view, low energy image (left) of left breast showing a high density spiculated mass with fine pleomorphic calcifications and a pre-chemotherapy radio-opaque marker clip placed inside it; Craniocaudal view recombined image (right) showing dark rim surrounding the marker (white arrows) that is inside the heterogeneously enhancing mass.

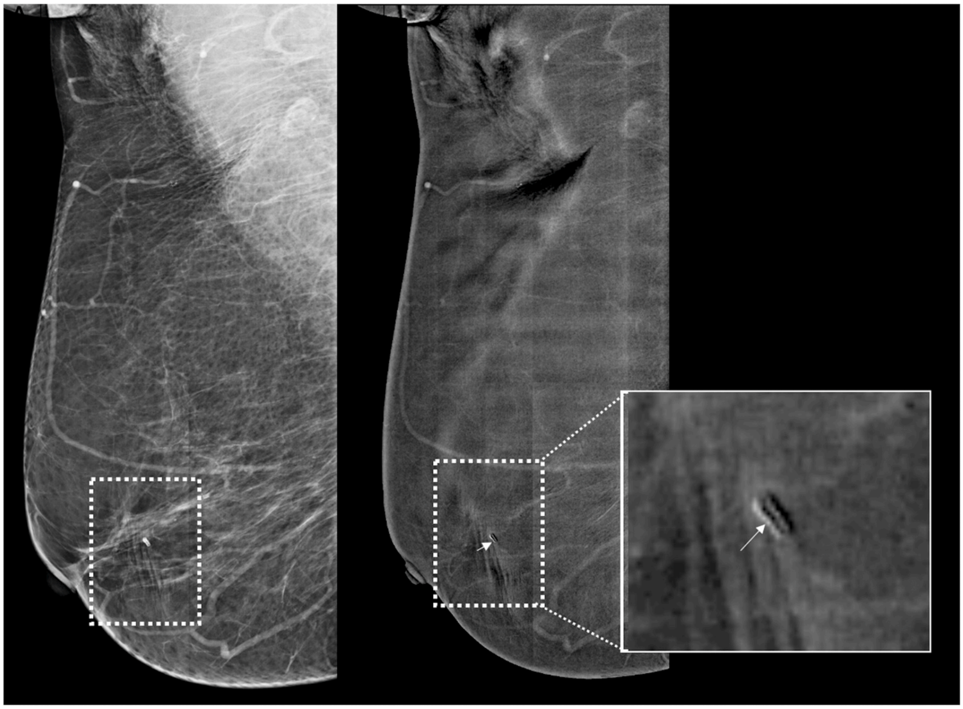

Fig. 5. Misregistration artifact; contrast enhanced images of a 49-year-old woman with papillary neoplasm in the contralateral breast. Mediolateral oblique view of right breast, low energy image (left) shows benign calcification in the retroareolar location and recombined image (right) shows incomplete subtraction with a bright line at the interface of the calcification, giving a 'zebra like' appearance (white arrow).

and aligned along the axis of the image receptor. The technologist should take care that the patient's chin or shoulders fall out of the field of view. Suboptimal positioning by the technologist can be improved with adequate training.[7-10] Also, the technologist should be able to recognise these artifacts and take a new exposure with the superimposed structure out of the field of view.

Antiperspirants induced artifacts. Many antiperspirants contain high atomic number aluminium compounds, which behave similar to calcium with respect to their X-ray attenuation properties. Their residue on the breast surface appears as tiny bright spots on the LE image with corresponding dark spots on the RC image (Fig. 2). These can be mistaken for calcifications if the radiologist is not aware of their imaging appearance.

Remedy: Patients must be advised not to apply antiperspirants or creams to breast on the day of the CEM examination. The breast and axilla must be examined prior to the procedure to check for any such residues and must be thoroughly cleaned.[7-10]

CEM specific patient related artifacts

These are visualised primarily on recombined images and arise from post-processing errors triggered by the presence of specific patient-related factors, such as implants, surgical clips, or chunky calcifications.

Breast implant induced artifacts. The differential attenuation of the X-ray by the silicone and saline breast implants or their capsular calcifications affects postprocessing algorithms and results in inaccurate subtraction. This creates peri-implant white or black bands in RC images that may potentially obscure an underlying pathology.[5-8] (Fig. 3)

Remedy: MRI should be considered for evaluation of the patients with breast implants because it allows detailed visualisation of both the implant and the surrounding tissue. However, if MRI is contraindicated, CEM must be performed using the Eklund technique, which involves careful displacement of the implant out of the field of view, allowing better visualisation of the breast parenchyma, hence avoiding artifacts.[7]

High density artifact caused by surgical clips/markers and dense calcifications. Titanium or zirconium oxide clips or markers are usually used in the breast after biopsy or before starting neo-adjuvant chemotherapy. The sharp contrast between the high attenuating markers/ calcifications and lower attenuation of the surrounding breast, caused by significant X-ray scatter, creates a distinct dark rim surrounding them in RC images.[9] (Fig. 4)

Remedy: These artifacts cannot be completely eliminated and usually do not interfere much with image interpretation.

Errors in acquisition

Motion artifacts

CEDM images are more susceptible to motion artifacts than digital mammography images because dual-energy acquisition requires longer exposure and compression times.[7-11]

Misregistration artifacts - Subtle patient movement between LE and HE images results in misalignment and produces misregistration artifacts on recombined images due to inaccurate subtraction. This manifests as blurring of the margins, particularly around the microcalcifications, markers, and small surgical clips, giving rise to alternate dark and bright lines, referred to as "zebra lines" (Fig. 5). These may obscure microcalcification or small masses and cause interpretation errors. These artifacts are more often encountered in the mediolateral oblique (MLO) projection due to the lack of support to the breast from the bucky tray.[5-7,12]

Remedy: The procedure should be thoroughly explained to the patient, ensuring that she is comfortable, to reduce the likelihood of involuntary movements. It is essential to make sure that the breast is positioned correctly and compressed adequately to minimize movement. Certain studies advocate the application of self-compression to improve patient compliance.[13] Immobilisation devices such as straps or positioning aids can also be utilised. The patient must be instructed to hold still and refrain from heavy breathing during the acquisitions to achieve a high-quality image.[5,7]

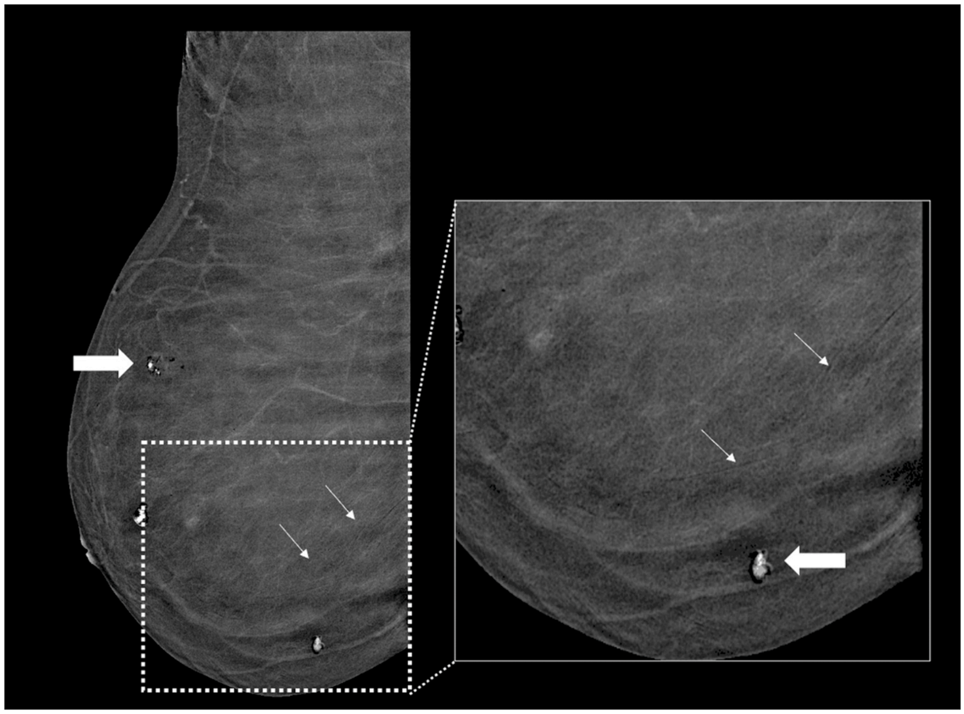

Fig. 6. Ripple artifacts; contrast enhanced mammography in a 44-year-old woman with metaplastic carcinoma in the contralateral breast. Mediolateral oblique view, recombined image of the right breast, showing wavy alternate black lines along inferior and posterior breast (thin white arrows), consistent with ripple artifact. Note is also made of incidental involuted fibroadenomas (block arrows) showing the misregistration artifact.

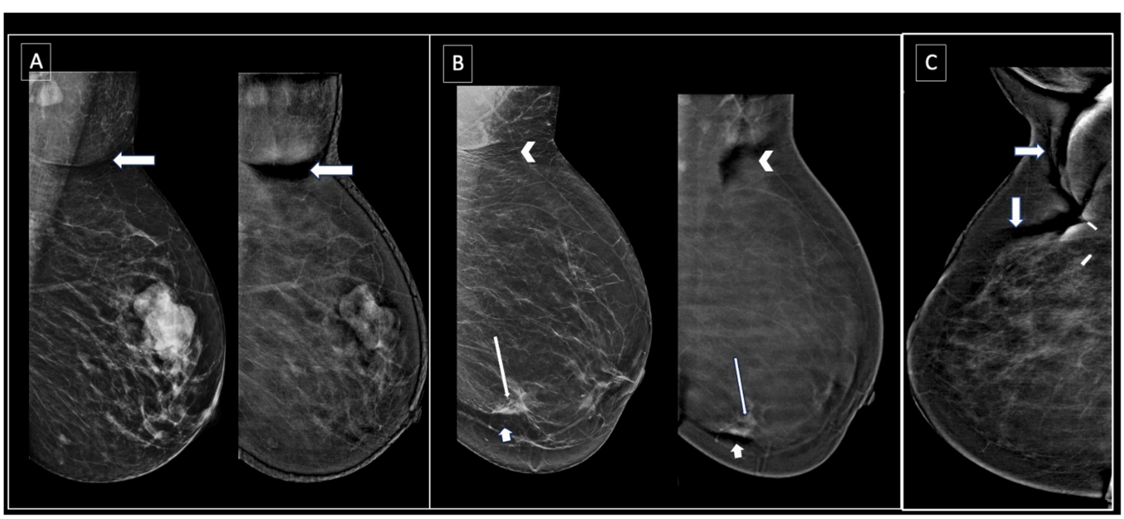

Fig. 7. Air Trapping artifacts; contrast enhanced mammography images in multiple patients. **A,** Mediolateral oblique view low energy (left) and recombined images (right) of the left breast in a 51-year-old patient with prominent axillary fat pad depict a linear low-density in the axillary region secondary to air trapping (white block arrow). **B,** Mediolateral oblique view, low energy (left) and recombined images (right) of the left breast in a 57-year-old woman with invasive ductal carcinoma (long arrow) depicts air-trapping artifact (short block arrow) due to skin retraction adjacent to the heterogeneously enhancing spiculated high density mass (long arrows). Note is also made of air-trapping artifact in the axilla seen as black line (arrowhead). **C**, Mediolateral oblique view, recombined image of right breast of a 46-year-old woman, status post-lumpectomy for previous carcinoma breast depicts air-trapping artifact due to lack of contact between the skin and the detector/ compression paddle leading to air entrapment between scar folds (white arrows).

Ripple artifacts - These are attributed to both fine patient movement during acquisition as well as due to transmitted respiratory motions and cardiac pulsations. They manifest as thin, alternating white and black lines on recombined images (Fig. 6). These artifacts are particularly common in the lower part of MLO views of the left breast due to relatively weak compression and a more pronounced effect of cardiac pulsations.[7-9]

Remedy: Acquire MLO views before craniocaudal (CC) views as the patient is less anxious and not exhausted in the beginning. This will reduce the movement during subsequent image acquisitions, thereby improving overall image quality.[7-12]

Air trapping artifact

Inadequate or inappropriate compression during a mammogram can result in the trapping of air pockets between the breast and compression paddles, or within the skin folds. These air pockets result in weaker

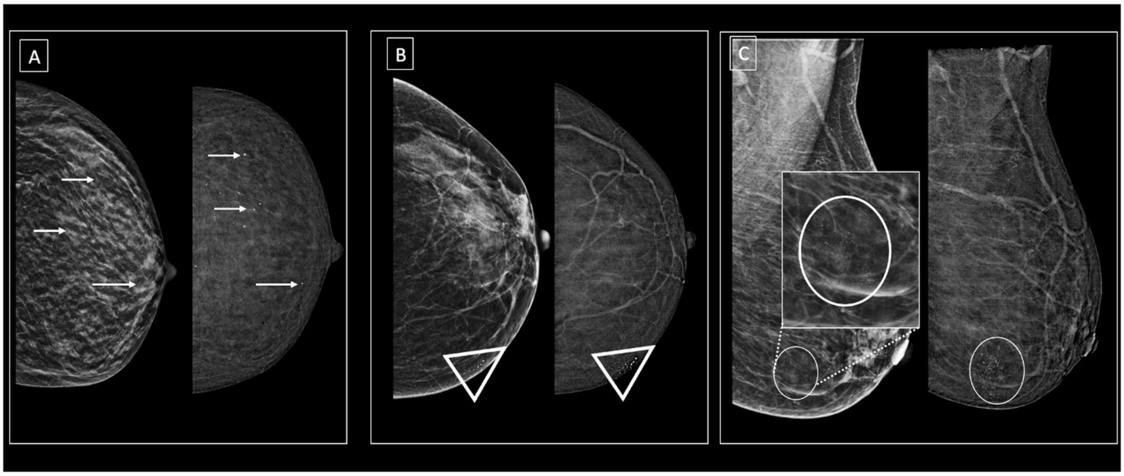

Fig. 8. Contrast Splatter artifact; contrast enhanced mammography images from different patients. **A,** Craniocaudal view, low energy (left) and recombined images (right) of left breast in a 41-year-old woman show multiple high attenuation foci (white arrows) appearing as pseudocalcifications on low energy image (left), which are not subtracted and remain hyperattenuating on the recombined image (right), consistent with contrast splatter artifact. **B,** Craniocaudal view, low energy (left) and recombined (right) images of left breast in a 55- year-old woman shows non-anatomic high attenuating foci on the skin, consistent with contrast splatter artifact. **C,** Mediolateral oblique view, low energy (left) and recombined images (right) of left breast in a 48-year-old woman showing contrast splatter giving dot-dash appearance and mimicking grouped calcifications. It is pertinent to note that contrast splatter appears white on both low energy and recombined images, whereas calcifications appear white on low energy images and black on recombined images.

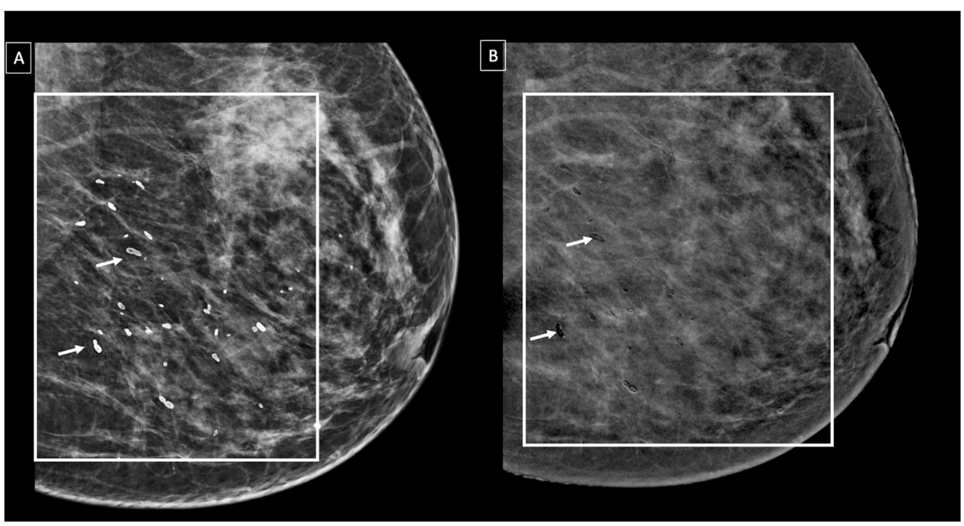

Fig. 9. Contrast enhanced images in a 56-year-old woman, zoomed-in low energy image (left) of left breast depicting benign calcifications in a regional distribution, zoomed-in recombined image (right) showing subtraction of these calcifications (white arrows).

attenuation of X-rays compared to the surrounding breast tissue, creating dark lines, particularly in the axillary and inframammary regions (Fig. 7). This problem is more prevalent in post-lumpectomy and obese patients who have multiple prominent skin folds. These artifacts occur in both low-energy (LE) and recombined (RC) images but are accentuated in RC images during image processing. These can obscure smaller masses and negatively impact image interpretation.[7,9]

Remedy: The technologist should ensure proper breast contact, and also adequate and uniform compression should be applied to the breast to eliminate air pockets.[5-10]

Contrast related artifacts

Certain artifacts can occur due to inadvertent handling of the contrast during acquisition.

Contrast splatter artifact or contamination artifact – These may be caused by contamination of the gloves of the technologist with contrast or by inadvertent spillage of contrast onto the breast surface, compression paddle, or detector. The contrast agent causes greater attenuation of X-rays in comparison to the rest of the breast tissue, resulting in the appearance of bright spots on the RC images. Due to its higher concentration, the surface contrast can also be visible on LE images, whereas, typically, intravenous contrast is primarily visible on RC images. Such areas may mimic pseudocalcifications or appear as abnormal non mass enhancement to the reader (Fig. 8). However, their non-anatomic distribution and morphology are often clues to the diagnosis. Moreover, contrast splatter is bright on both LE and RC images, while calcifications are white on LE images and usually black on RC images (Fig. 9). Also, contrast splatter appears intensely bright on the RC image and resolves on cleaning the surface.[5-10]

Remedy: This can be avoided by thoroughly cleaning the equipment as well as the breast prior to the procedure. Care should be taken to avoid contrast splash while manually injecting the contrast or detaching the pressure injector tubing. The technologist should change gloves after contrast injection to avoid contamination. The technicians must be

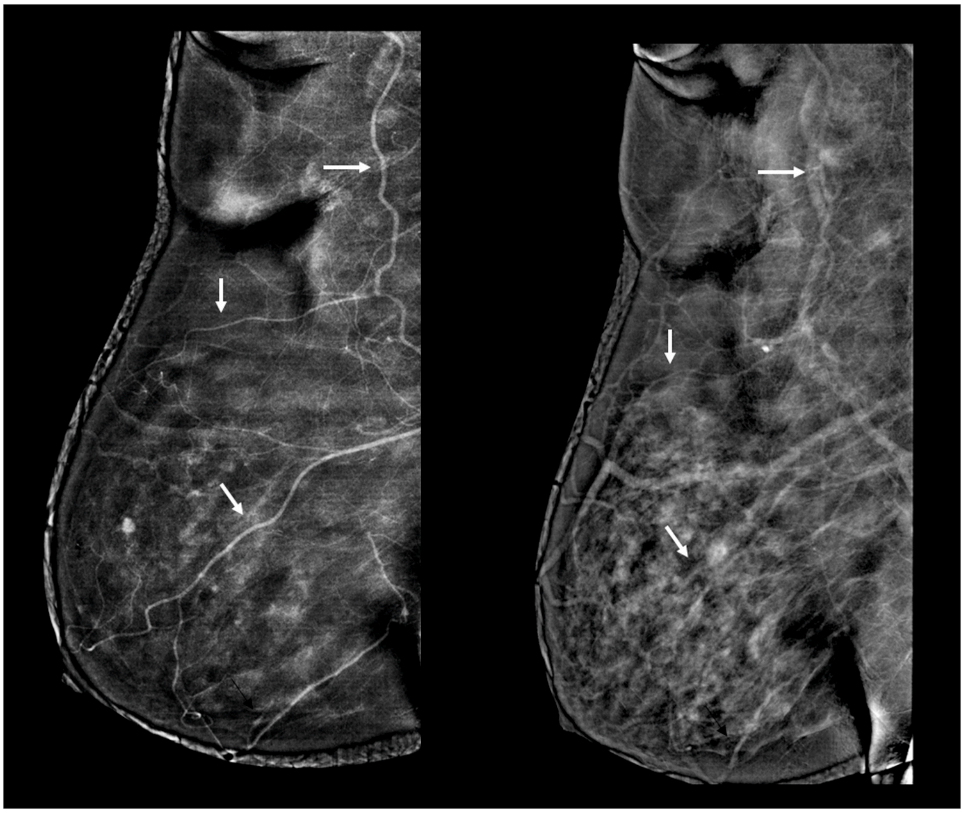

Fig. 10. Transient retention of contrast in the vessels; contrast enhanced mammography images in a 45-year-old woman. Mediolateral oblique view, recombined image (left) showing avid enhancement of the vessels, with contrast retention prior to significant dissipation into the breast parenchyma (white arrows). Subsequent acquisition of recombined image (right) shows contrast uptake in the breast parenchyma with dissipation of contrast from the vessels which appear less dense.

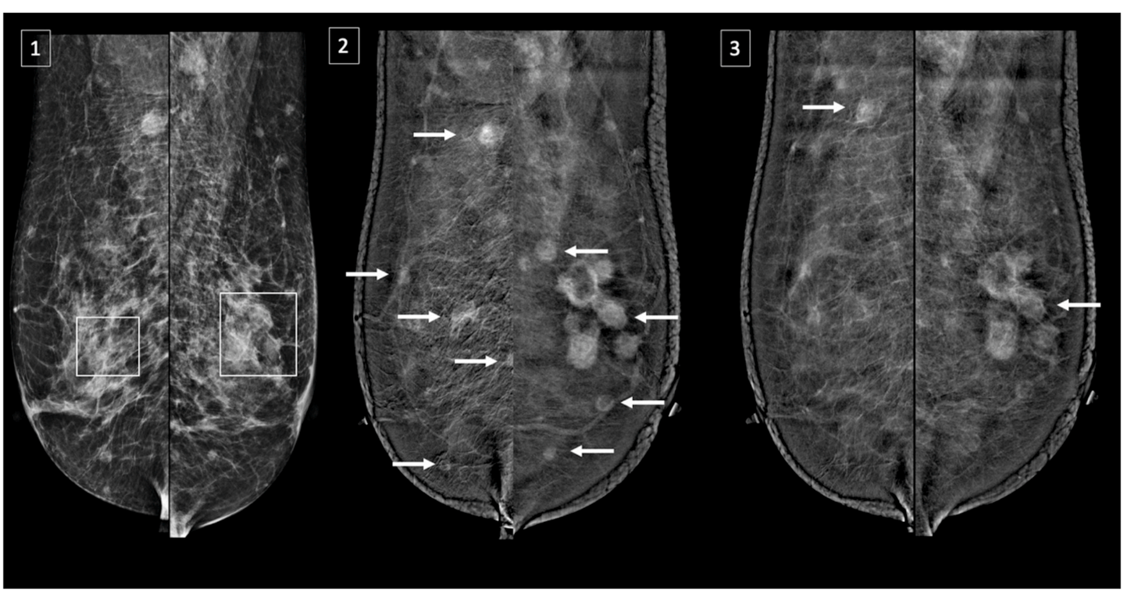

Fig. 11. Injection Synchronization Error; contrast enhanced mammography images of a 61-year-old woman with bilateral breast metastases from papillary thyroid carcinoma. **(1)** Bilateral mediolateral oblique low energy images reveal asymmetric breast parenchyma on comparison of both breasts, along with associated bilateral axillary lymphadenopathy. **(2)** Recombined images at 2 and 3 minutes after contrast injection show multiple enhancing masses in both breasts (white arrows). **(3)** Recombined image at 10 minutes after contrast injection show contrast washout from the previously visible masses, which now appear faint and indistinct. This emphasizes the critical need to capture images within the optimal time window as failure to do so can result in missing significant lesions, leading to an incomplete or misleading assessment of disease extent.

trained to identify these artifacts, and any spillage should be immediately cleaned, and repeat imaging should be done within the stipulated window of the contrast study.

Transient retention of contrast in the veins - This is characterised by retention of the contrast within the venous system in the initial images. Premature compression of the breast parenchyma before the

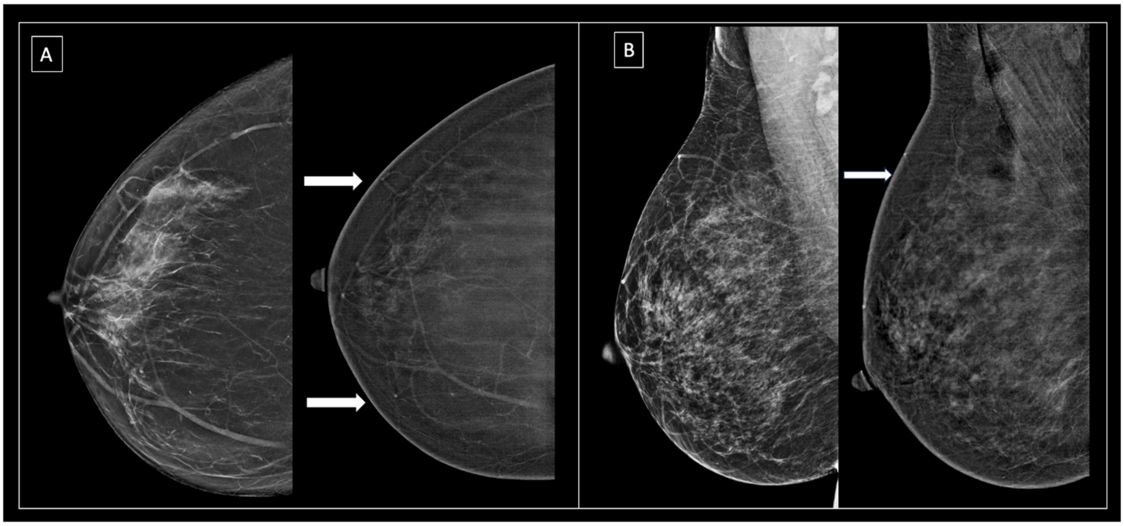

Fig. 12. Skin line enhancement artifact; A, Craniocaudal view, low energy image (left) of right breast in a 43-year-old woman showing normal skin thickness and recombined image (right) showing enhancement along the skin line mimicking skin thickening (block arrow). **B,** Mediolateral oblique view, low energy image (left) of the right breast in a 58-year-old woman showing normal skin thickness, however, there is apparent skin thickening with enhancement (white block arrow) on the recombined image (right).

contrast has sufficient time to reach the breast tissue can restrict contrast distribution into the breast. This artifact is transient and usually disappears in later images (Fig. 10). However, a prolonged presence of the contrast within the vein, even after 10 minutes of injection, may indicate a central venous thrombosis and needs further evaluation and management.[7,9,12]

Remedy: This can be minimised by training the technician to begin the compression only after 2 minutes of initiation of contrast injection, so that the contrast circulates into the breast parenchyma.

Injection Synchronisation Error Artifact - It occurs when there is a mismatch between the timing of contrast injection and image acquisition due to various patient factors or technical reasons. If the imaging is performed outside the stipulated window (typically starting 2 minutes after contrast injection and completing within 8-10 minutes), the contrast may not have adequately perfused or may have dissipated from the breast tissue, resulting in suboptimal enhancement and false negative interpretations.[12] (Fig. 11)

Remedy: Technicians should be trained in protocols to maintain an adequate flow rate as well as precisely time the acquisition in order to obtain high-quality images.

Equipment related and postprocessing technical artifacts

These artifacts result from the interaction of X-rays with tissue, as well as the complexities of postprocessing algorithms. These can vary among various manufacturers.[11] While they are often unavoidable, awareness of these artifacts is crucial for radiologists to prevent potential misinterpretations during image analysis.

Skin line enhancement artifact

This has also been described as a 'skyline artifact' in the literature.[5-10] There is non-uniform scattering of the radiation over the surface of the breast due to variable thickness of the skin, which manifests as a bright skin line or pseudo-enhancement of the skin on the RC images

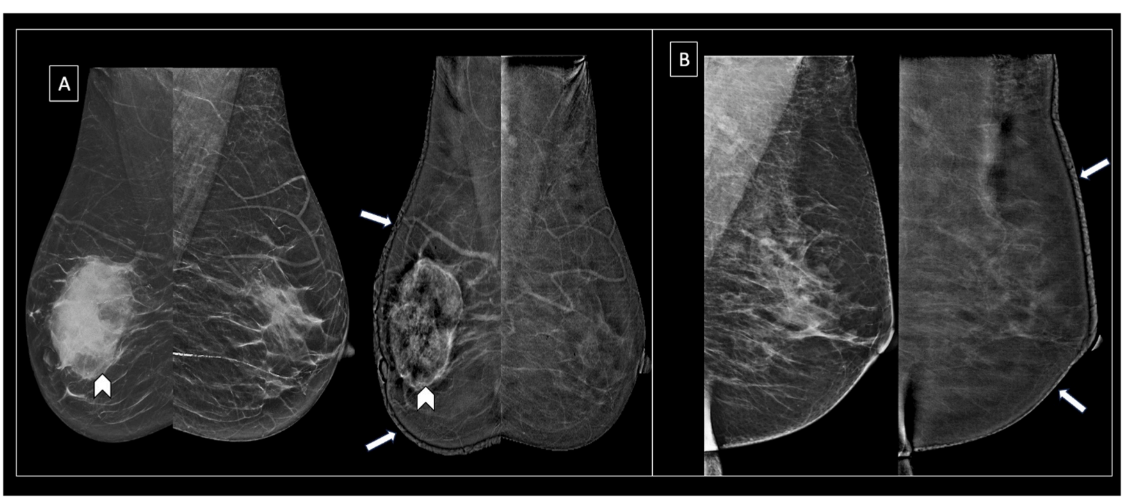

Fig. 13. Tree bark artifact; A, Contrast enhanced mammography images in a woman with histopathologically proven triple negative invasive ductal carcinoma. Mediolateral oblique view, low energy image (left) of right breast shows oval high-density mass (arrowhead) with normal skin thickness of the right breast. Recombined image (right) of right breast shows apparent skin thickening resembling tree bark (white block arrows). Note is made of heterogeneous enhancement of the mass (white arrowheads). **B,** Contrast enhanced images from another patient showing no significant abnormality on low energy image, with fallacious skin thickening on recombined image(white block arrows), Comparison with the low energy images will help in confirming if the skin thickening is artifactual or definite.

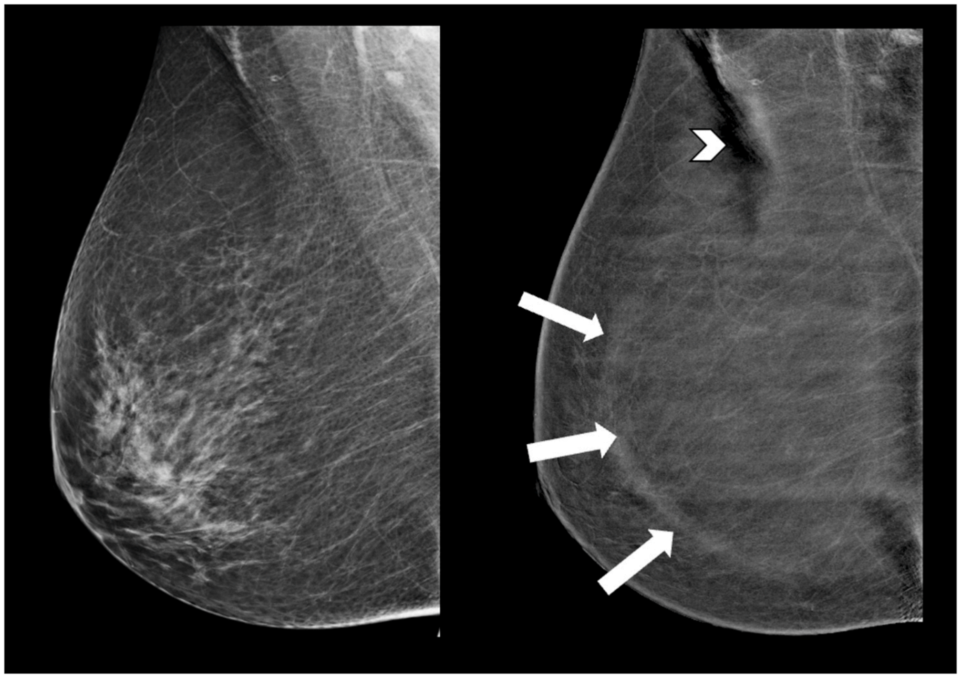

Fig. 14. Halo artifact/ breast-in-breast artifact; contrast enhanced images in a 47-year-old woman. Mediolateral oblique view, low energy image (left) showing normal breast parenchyma and recombined image (right) showing a C-shaped white line creating a rim-like artifact, seen parallel and posterior to the skin line, mimicking a breast-within-breast appearance (white block arrows). Additionally, air trapping artifact (white arrowhead) is also seen in the axilla.

(Fig. 12). This enhancement can be mistakenly interpreted as abnormal skin involvement, potentially leading to an incorrect upstaging of the disease.[7,9,12]

Remedy: The radiologist must carefully review the low-energy (LE) images where the skin will appear normal and uniform in thickness. This helps to identify the enhancement as an artifact rather than a pathological finding.[12,14]

Tree bark artifact /skin thickening artifact

This artifact is the result of detector saturation, likely secondary to overexposure, excessive X-ray scatter at the skin surface, with equalisation of pixel values between the skin and adjacent breast tissue. This process causes the skin line to blur or disappear on LE images and creates a false appearance of skin thickening on RC images, resembling the texture of tree bark.[8,9,15] (Fig. 13)

Remedy: Checking the skin thickness on LE images prevents misdiagnosis.

Halo artifact/breast-within-breast artifact

This is one of the most prevalent artifacts in CEM studies.[14,16] It has also been referred to as a 'Rim/Scatter Radiation' artifact in literature.[7,9,14,16] This appears as a uniform, convex, high-density line parallel to the skin at the boundary between pre-mammary fat and fibroglandular tissue, causing a double contour appearance on RC images (Fig. 14). It is primarily caused by variable scatter of the X-rays due to an abrupt change in thickness of the central and peripheral breast regions, causing the processing algorithm to create a fallacious boundary. Yagil et al., also suggested that this artifact could be the result of differential contrast absorption in the outer breast due to reduced compression and a more abundant blood supply in these regions.[16] This artifact usually doesn't affect the image interpretation.

Remedy: Although there is no definitive solution to eliminate this artifact, newer algorithms are being introduced to reduce it. Gennaro et al., in their study, proposed an algorithm that eliminated this artifact in 84.5% of cases.[12] These evolving recent algorithms hold promise for significantly improving image quality.

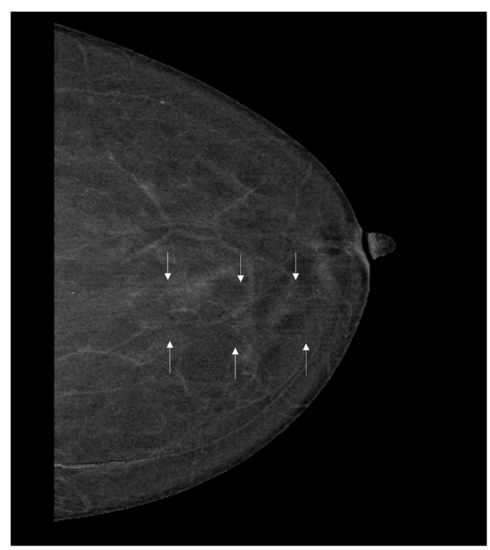

Fig. 15. Vibration artifact; Craniocaudal view, recombined image of left breast in a 41-year-old woman shows horizontal parallel lines extending across the breast (white arrows).

Grid line artifact

Grids are used to reduce the scattered radiation and improve image contrast. A moving grid is utilised in the digital mammography system. If the resolution of the system is comparable or even higher than the grid spacing, this can lead to the formation of the grid artifacts. These are non-specific artifacts seen in digital mammography.[7,14-15]

Remedy: Frequency matching techniques or angling the grid can help reduce these artifacts. Additionally, using noise suppression algorithms specifically designed to target and suppress the frequencies associated with scattered radiation can further minimise grid artifacts. Weekly gain calibration is another effective method for reducing these issues, and newer imaging systems are generally less susceptible to grid artifacts

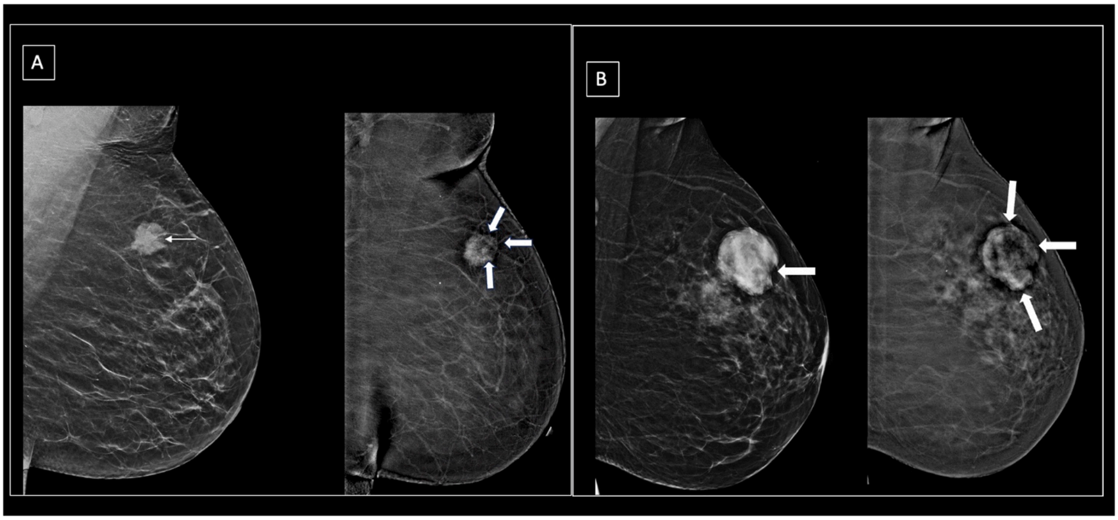

Fig. 16. Negative-rim artifact; A, Contrast enhanced mammography of a 51-year-old woman, mediolateral oblique view, low energy image (left) showing high-density mass with spiculated margin (white arrow) seen in the upper breast. In the recombined image (right) the mass shows heterogenous post contrast enhancement with surrounding negative-rim artifact (white block arrows), seen as black line around the mass. **B, C**ontrast enhanced mammography of a 55-year-old woman, mediolateral oblique view, low energy image (left), of the left breast shows high density mass with circumscribed margins in the upper breast. In the recombined image (right) there is a dark negative-rim artifact surrounding the heterogeneously enhancing mass (white block arrow) due to differential attenuation and scatter at the edges of denser mass.

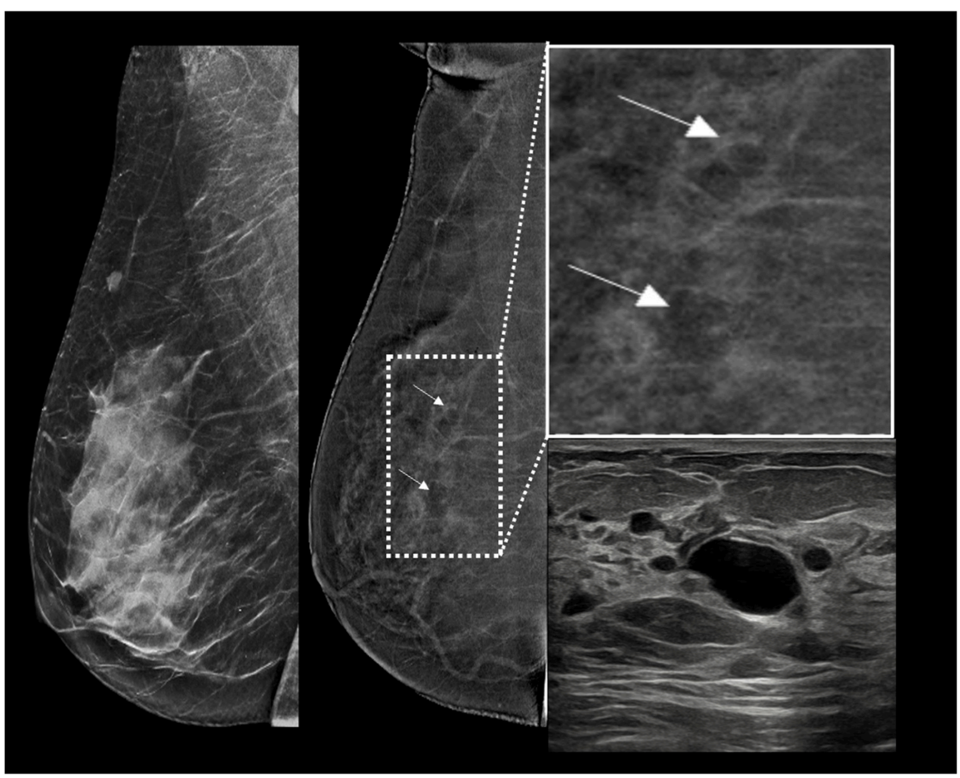

Fig. 17. Negative contrast enhancement/ Eclipse sign; Negative contrast enhancement in cysts, contrast enhanced mammography and ultrasound images in a 42-year-old woman who had presented with mastalgia and had positive family history for breast carcinoma. Mediolateral oblique view, low energy image (left) of the right breast reveals heterogeneously dense breast; recombined image and digitally zoomed image (right) show negative enhancement due to cysts seen as low-density areas (white arrows); correlative ultrasound image (lower right corner) depicting multiple thin-walled anechoic cysts scattered in the breast parenchyma.

due to improved design and technology.[7,15-17]

Vibration artifact

It manifests as horizontal black lines or alternate black and white lines in digital as well as RC images (Fig. 15). This artifact is likely caused by vibrations from the detector’s cooling fans, leading to electrical interference during the data readout process.

Remedy: Recalibrating the imaging system and detector service is required.

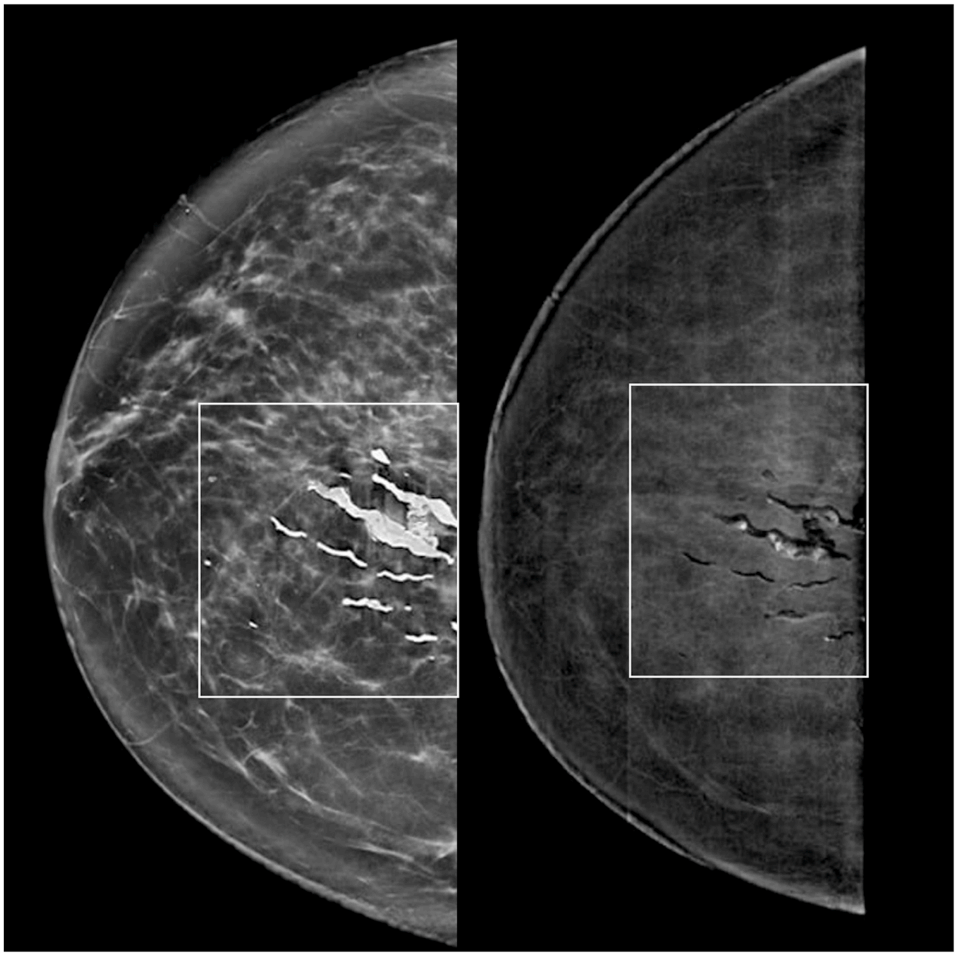

Fig. 18. Negative contrast enhancement in coarse calcification; contrast enhanced images in a 72-year-old woman, craniocaudal view, low energy image (left) of the right breast depicts extensive dystrophic calcification in the posterior third of the breast and recombined image (right) showing subsequent subtraction of the dystrophic calcification appearing dark, with some misregistration artifacts (bright areas at interface).

Recombined image enhancement related artifacts

Negative-rim artifact

This artifact presents as a dark rim around enhancing masses on recombined images. It is likely caused by differential attenuation and pronounced scatter at the edges of denser structures, in addition to post-processing effects that exaggerate the contrast at the interface (Fig. 16). This phenomenon is particularly evident around irregular or lobulated masses. Notably, this artifact has not been documented in prior studies. This artifact may obscure subtle details surrounding the mass.

Remedy: Refinement of post-processing algorithms may help minimise the artifact.

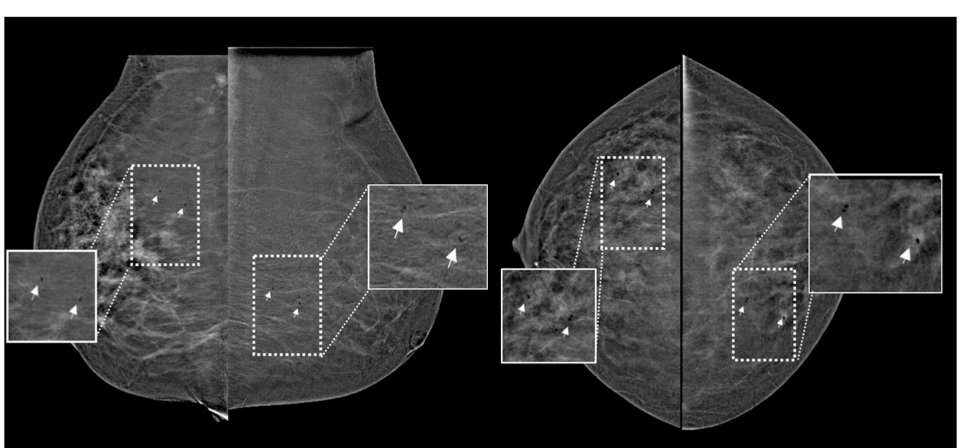

Fig. 19. Defective pixel artifact; Recombined images in two different patients (left and right), showing black dots (arrows) having identical morphology seen at corresponding matching locations, consistent with defective pixels. The artifact was corrected after detector recalibration.

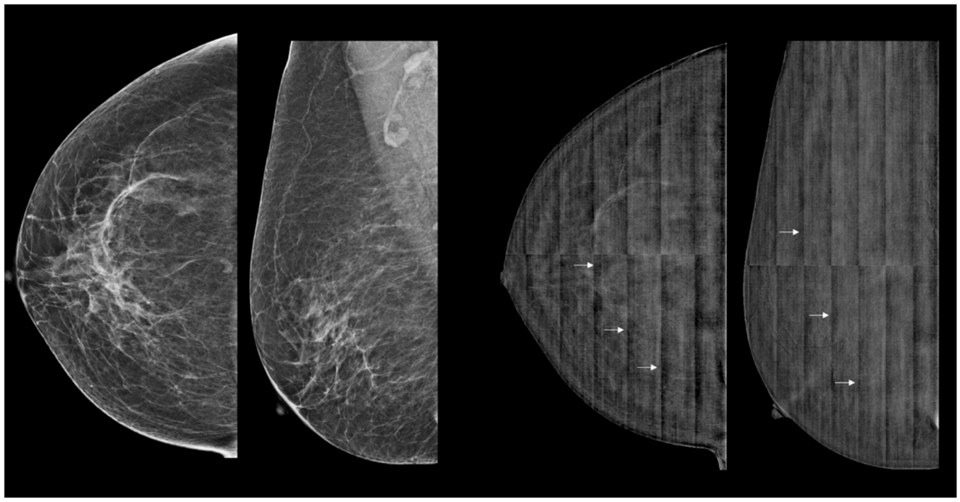

Fig. 20. CEM gain calibration artifact; Craniocaudal and mediolateral oblique views, low energy (left) and recombined images (right) of the right breast in a 44-year-old woman show no artifact in low energy images, however, multiple vertical lines (white arrows) are present along the entire breast parenchyma in the recombined images due to incomplete CEM gain calibration prior to acquisition in the contrast enhanced mode.

Negative contrast enhancement/Eclipse sign/Crescent sign

This is caused by cysts, hematomas, coarse calcifications, and certain non-enhancing masses. These get completely subtracted in the recombined images and appear as darker low-density areas within the breast parenchyma in comparison to the surrounding enhancing fibroglandular tissue (Fig.s 17,18). This cannot be considered a true artifact and does not compromise the quality of the study.[7] An important point to note is that malignant lesions showing negative contrast enhancement have a thick, nodular, or irregular rim, whereas benign cysts may show an absent or smooth-enhancing rim.

Quality control artifacts

It is crucial to follow vendor-specific quality control processes, understand potential artifacts that may arise, and have the knowledge to correct them to ensure the best image quality. Proper training of

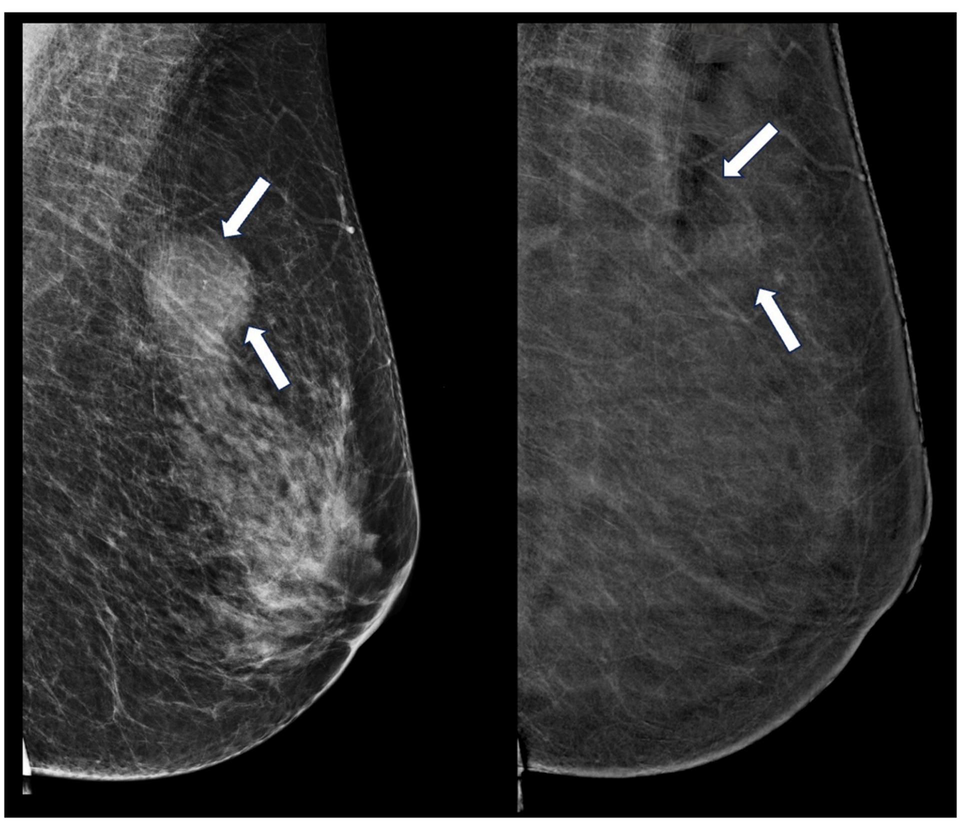

Fig. 21. Pitfalls in interpretation of contrast enhanced mammography, False negative interpretation; contrast enhanced mammography images in a 54-year-old woman with histopathologically proven mucinous carcinoma. Mediolateral oblique view, low energy image (left) of the left breast showing equal density round mass in upper breast with punctate calcification within (white arrows) and the recombined image (right) showing no enhancement of the malignant mass (white arrows).

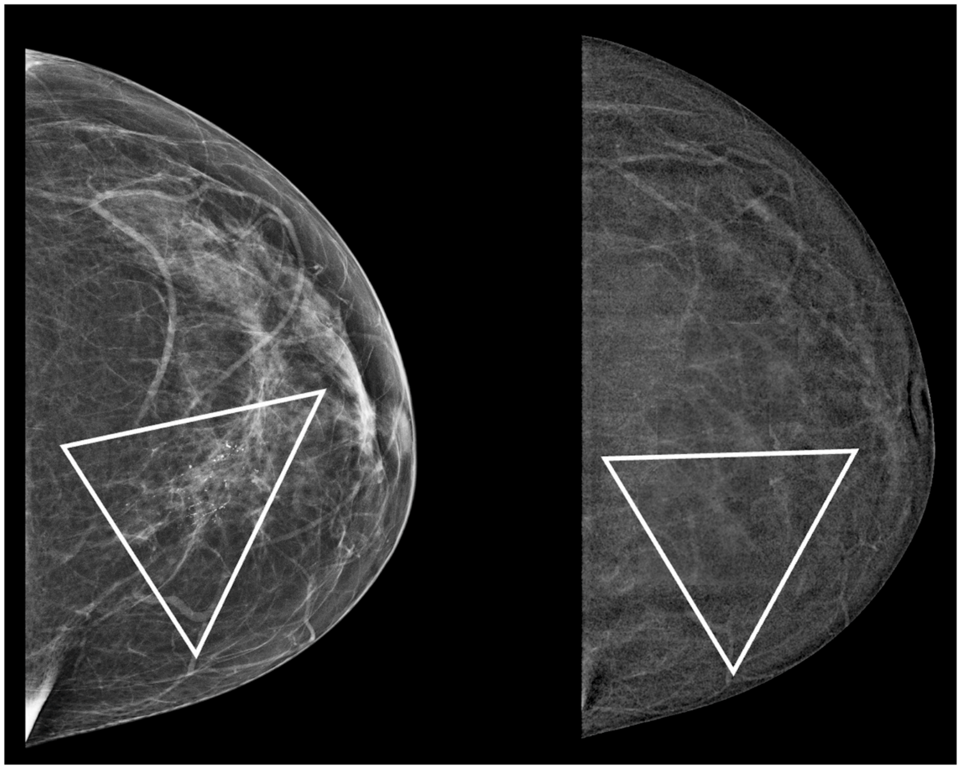

Fig. 22. Pitfalls in interpretation of contrast enhanced mammography, False negative interpretation; contrast enhanced mammography images in a 56-year-old woman. Craniocaudal view, low energy image (left) of the left breast shows fine pleomorphic calcifications in segmental distribution with no discernible mass and the recombined image (right) shows no enhancement, with subtraction of the suspicious calcifications seen on low energy image. Stereotactic vacuum assisted biopsy was done from the suspicious calcifications which revealed ductal carcinoma in situ (DCIS).

technologists and scheduling of daily and weekly quality control tasks are important for maintaining consistency. Weekly quality controls should be done either at the end of the week or before the first patient at the start of the week.

Defective pixel artifact

Digital mammography detectors are composed of an array of pixels that convert X-ray signals into electrical signals, which are then processed to form an image. Defective pixel artifacts occur when individual pixels or groups of pixels in the detector array malfunction, leading to dark or bright spots in the low energy image. These are accentuated on the recombined images during the processing, appearing as persistent dark spots in the images (Fig. 19). The cause is usually prolonged usage, wear and tear resulting in pixel degradation or electronic failure.[18,19]

Remedy: Detector calibration, which automatically detects and compensates for the defective pixels by interpolating the data from the neighbouring pixels.

Gain calibration artifact

Failed contrast-mode gain calibration prior to a CEM procedure can lead to significant artifact on RC images that severely compromise the image (Fig. 20).

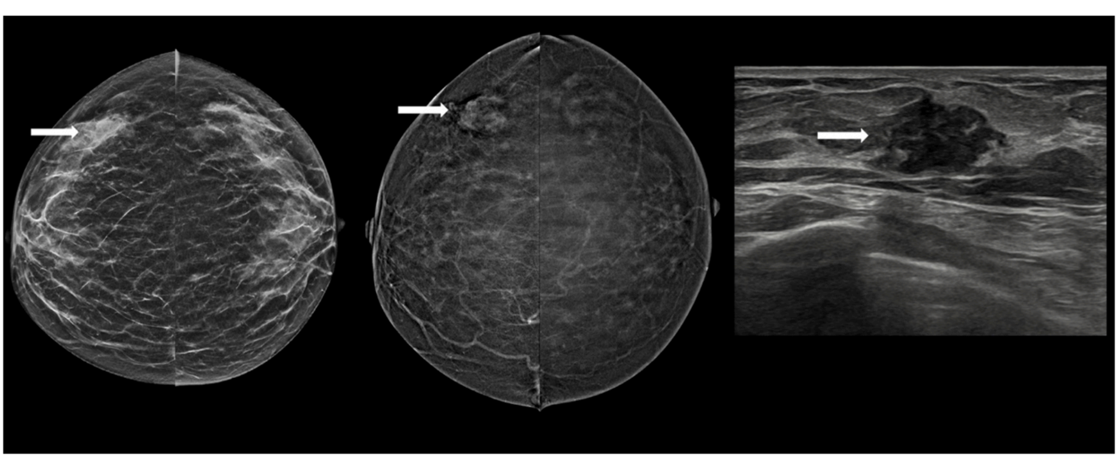

Fig. 23. False positive interpretation; contrast enhanced mammography images of a 46-year-old woman. Craniocaudal view, low energy image (left) of the right breast shows a subtle asymmetry (white arrow) in the outer right breast; recombined image (middle) shows heterogeneous enhancement within the mass (white arrow) and the correlative ultrasound image (right) shows an irregular hypoechoic mass whose margins are not circumscribed. Ultrasound guided vacuum assisted biopsy using 9-gauge needle revealed sclerosing adenosis with no in-situ component or invasive malignancy.

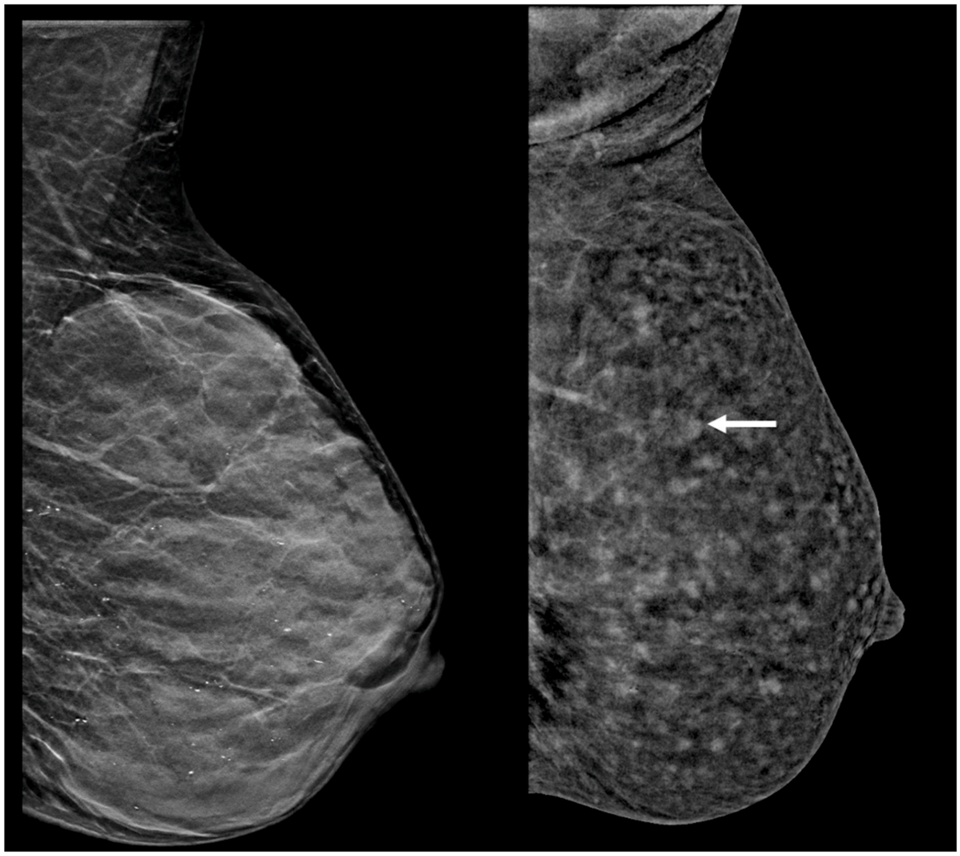

Fig. 24. False negative interpretation due to marked background parenchymal enhancement; contrast enhanced mammography images in a 38-year-old woman with bilateral breast pain and history of breast cancer in mother. Mediolateral oblique view, low energy image (left) of the left breast depicts extremely dense breast with diffuse round and punctate calcifications. Recombined image (right) shows marked background parenchymal enhancement which is potentially obscuring an oval circumscribed homogeneously enhancing mass in the upper breast, which was first detected on ultrasound and retrospectively located on the recombined image. The mass was biopsied under ultrasound guidance using 14-gauge needle, and histopathology revealed a fibroadenoma.

Remedy: Adequate daily CEM recalibration of the system prior to beginning the acquisition. To avoid this, it's important to test the system on a phantom after any quality control step and before conducting a contrast enhanced imaging procedure.[19]

Ghosting artifact

It occurs when latent image from a prior exposure gets superimposed on a subsequent image due to rapid acquisitions, leading to a "ghost" effect. This artifact can affect image clarity and accuracy.[7-10,18-19]

Remedy: This artifact is rarely encountered, and recalibration of the imaging system to remove the memory of the previous image as well as keeping a check that serial exposures are not acquired in rapid succession are sufficient to eliminate the unwanted overlay.[9]

Challenges and considerations in image interpretation with CEM

CEM requires meticulous interpretation of both LE and RC images and may present several diagnostic limitations if a systematic approach is not followed. All factors, including patient preparation, positioning, contrast administration, adequate equipment calibration, and the functional characteristics of the pathology, collectively influence the quality of RC images and subsequent diagnosis.[2,8,18] Artifacts from patient motion, breast implants, surgical clips, and post-processing algorithms can degrade image quality and hinder accurate evaluation. Contrast splatter or surface residues can mimic suspicious lesions and calcifications. Restricted field of view (FOV) is another challenge, particularly in the evaluation of posterior and lateral breast lesions, including the axilla and those close to the chest wall, thereby compromising comprehensive local staging of malignancies. Multimodality imaging is often necessary to compensate for these limitations. Certain malignancies, such as invasive lobular carcinoma, mucinous carcinoma, and ductal carcinoma in situ (DCIS), may not exhibit enhancement on RC images due to their variable neoangiogenesis.[2,8] (Fig.s 21, 22) Certain benign pathologies, such as fibroadenomas, sclerosing adenosis, papilloma, fat necrosis, post-surgical inflammation, and intramammary lymph nodes, may enhance in post-contrast images, potentially leading to false-positive interpretations and unnecessary biopsies (Fig. 23). Marked background parenchymal enhancement (BPE) can obscure underlying lesions, leading to false-negative results (Fig. 24). Intradermal lesions, like nevi and the presence of out-of-profile nipples, may also falsely mimic malignant masses (Fig.s 25, 26). Relying solely on RC images can result in false negatives, making it essential to base intervention decisions on the most suspicious findings across both RC and LE images. Correlating LE images to identify potential artifacts and utilising ultrasound where appropriate can enhance the specificity.

Conclusion

CEM represents a transformative leap in breast imaging, combining efficiency and cost-effectiveness with the ability to provide structural as well as functional diagnostic information. Through meticulous patient preparation, expert application of imaging techniques, and relentless focus on training, these artifacts can be minimised, ensuring high quality CEM scans. Radiologists must remain vigilant of the technical and diagnostic challenges associated with CEM, particularly keeping in mind the false positives and negatives while interpreting the images. As

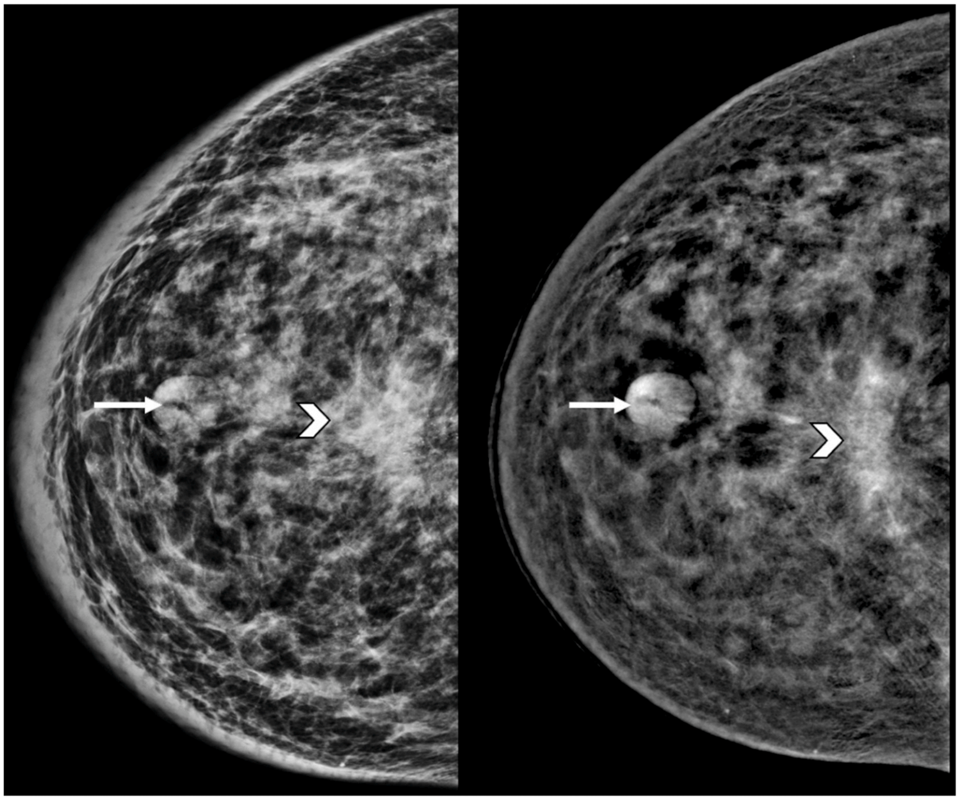

Fig. 25. False positive interpretation due to distorted enhancing nipple; contrast enhanced images in a 59-year-old woman with right breast swelling and palpable lump. Craniocaudal view, low energy (left) and recombined images (right) depicting enhancing irregular spiculated mass (white arrowhead) in the posterior third of right breast, with enhancement of the nipple mimicking as another enhancing mass in the central breast, creating potential pitfall in image interpretation.

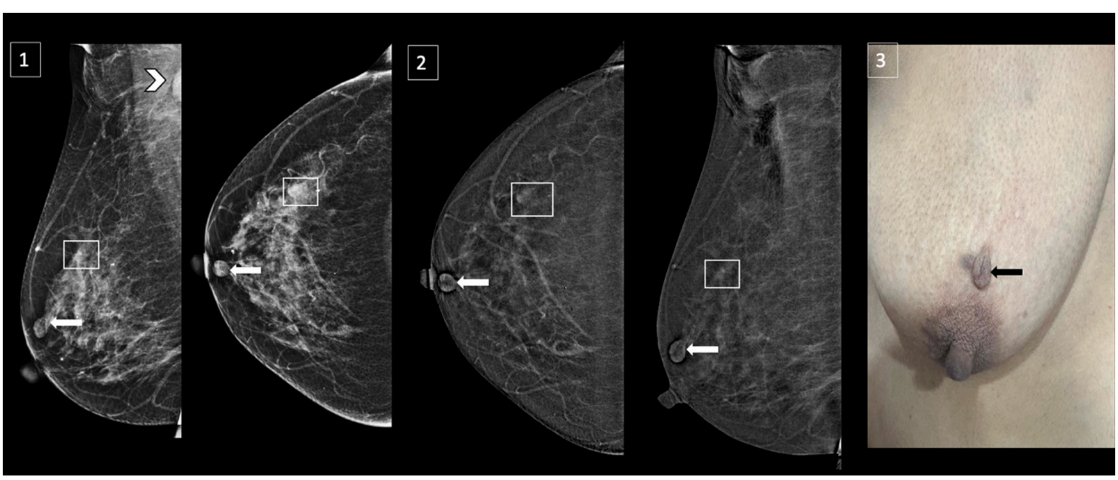

Fig. 26. False positive interpretation due to enhancing skin lesion; contrast enhanced mammography in a 60-year-old woman who came with right axillary lymphadenopathy which was proven as metastatic on fine needle aspiration cytology (FNAC).

1: Mediolateral oblique and craniocaudal views, low energy images, show an oval circumscribed equal density mass (white arrow) in the retroareolar location with partially visualised enlarged right axillary lymph node (white arrowhead). Additionally, another mass with indistinct margins is seen in upper-outer quadrant of the breast, which is better appreciated on the craniocaudal view (white rectangle).

2: Mediolateral oblique and craniocaudal views, recombined images demonstrate a relative homogeneous enhancement within the retroareolar mass (white arrow) and heterogeneous enhancement in the other mass present in the upper-outer quadrant (white rectangle).

3: Evaluation of the patient's breast in the region above the nipple-areola complex confirmed the presence of a skin tag potentially mimicking a retroareolar mass on mammography (white arrow). The histopathology from the mass in the upper-outer quadrant was suggestive of invasive ductal carcinoma.

technology evolves, continued advancements and proper training will further solidify CEM's role as a cornerstone in breast cancer detection and care.

Table 1

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Table 1
Summary of contrast enhanced mammography related artifacts, causes and remedies.

			Artifact	Imaging findings	Cause	Remedy
Patient Related Artifacts	CEM Non-Specific	1	Overlay artifact	Radiopacity in the field of view	Superimposition of clothes, hair, chin, shoulder, or other anatomical structures	Careful breast positioning to keep superimposed objects out of the field of view
		2	Artifact due to antiperspirants	Bright spots on LE images that appear as dark spots on RC images	Due to use of antiperspirants on the breast	Examination of the breast prior to the procedure. Proper cleaning of the detector, breast, and axilla prior to the procedure
	CEM Specific	3	Breast implant induced artifacts	Peri-implant white or black bands in RC images	Differential attenuation of the X-ray by the silicone and saline breast implants or their capsular calcifications	Eklund technique for positioning, preferable evaluation with MRI
		4	High density artifact due to surgical clips, markers, and chunky calcifications	Distinct dark rim surrounding titanium or zirconium oxide clips/ markers.	Sharp contrast between high attenuating markers and lower attenuation of the surrounding breast, caused by significant X-ray scatter	Cannot be completely eliminated and usually do not interfere much with image interpretation.
Artifacts Related to Errors in Acquisition	5		Misregistration artifact	Alternate dark and bright lines on calcifications and clips on recombined images, giving “zebra artifact.”	Slight movement between acquisition of LE and HE images	Reduce patient movement by breath holding, and maximising compression.
	6		Ripple artifacts	Alternate undulating wavy dark and bright lines (ripples) in RC images; more frequent in MLO view	Caused due to patient movement between LE and HE acquisitions, respiration, and transmission of cardiac pulsations	Acquire mediolateral oblique view before craniocaudal view to reduce patient movement.
	7		Air-trapping artifact	Dark lines in both LE and recombined images, but more apparent on RC images	Inadequate/inappropriate compression of the breast during acquisition leading to air getting trapped between skin and breast	Ensure adequate compression and appropriate patient positioning.
Contrast Related Artifacts	8		Contrast splatter artifact/Contamination artifact	High density lines or dots seen in both the LE and RC images	Due to an inadvertent splash of contrast onto the breast parenchyma, detector, or compression paddle	Examination of breast prior to the procedure. Proper cleaning of detector and breast prior to the procedure.
	9		Transient retention of contrast in veins	Retention of contrast within veins without dissipation to breast parenchyma	Due to premature compression of breast parenchyma before the contrast reaches breast	Proper training of technicians to ensure adequate timing of compression
	10		Injection Synchronization	Suboptimal enhancement of mass on RC image and false negative interpretations	Mismatch between the timing of contrast injection and image acquisition outside the stipulated window of 2 to 8 minutes	Strict protocols to maintain adequate flow rate as well as precisely time the acquisition (typically starting 2 minutes after contrast injection and completing within 8-10 minutes)
Equipment Related and Post-processing Technical Artifacts	11		Skin line enhancement/ Skyline artifact	Thin white line along the skin in RC images mimicking skin enhancement	Image filtration applied to RC images to equalize breast thickness	Confirming skin thickness on the LE images
	12		Tree bark artifact	Abnormal tree bark like thickening along the skin in RC image	Excessive X-ray scatter along the skin line	Confirming skin thickness on the LE images
	13		Halo/ Breast-in- Breast artifact/Scatter radiation/Rim artifact	High density line posterior and parallel to the skin in RC image	Non uniform thickness of breast parenchyma causing abnormal X-ray scatter	Seen in older systems
	14		Grid line artifact	Vertical grids in the LE and RC images	Due to the comparable resolution of the CEM with that of the grid.	Using moving grids
	15		Vibration Artifact	Horizontal alternate black and white lines	Electrical interference in readout process	Recalibration and detector service
Recombined Image Enhancement Related Artifacts	16		Negative rim enhancement	Rim of negative enhancement surrounding enhancing masses in RC images	Caused due to abnormalities in subtraction and scatter at the edges of denser structures	Cannot be removed
	17		Negative contrast enhancement/Eclipse artifact	Complete subtraction of cysts, benign masses, and calcifications in RC images	Due to the inherent nature of CEM.	Cannot be removed
Quality Control Artifacts	18		Defective Pixel artifact	Dark spots on recombined images	Due to defective/malfunctioning detector pixels owing to prolonged usage, or wear and tear, resulting in pixel degradation or electronic failure	Recalibration and detector service
	19		Gain calibration artifact	Vertical bars on image	Failed calibration prior to CEM procedure	System recalibration and ensuring proper quality control tests on phantom prior to procedure
	20		Ghosting artifact	Radiopacity on the image	Superimposition of prior exposure on a new image	Recalibrating the imaging system and acquiring the image again to eliminate the unwanted overlay.

Declaration of competing interest

The authors declare that they have no competing financial interests.

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None.

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