Fusion of Digital Mammography with High-Resolution Breast PET: An Application to Breast Imaging

Liliana Reséndiz Sánchez, Luis Martin Torres Treviño, and Gisela Estrada Sánchez

Abstract One of the strategies to reduce mortality from breast cancer is based on screening using digital mammography as an initial evaluation. The detection and diagnosis of breast carcinomas are achieved by interpreting images of different modalities including digital mammograms, magnetic resonance imaging, ultrasound, and thermography; however, the literature shows that multimodal image fusion is highly accurate in representing breast carcinomas. Due to the human complexity in the diagnosis and detection of breast cancer and the implication of using historical patient imaging records, it is important to use processing tools that allow the analysis of breast images for possible improvements of the diagnosis. This chapter proposes the use of diversified data sets composed from different modalities to support the breast cancer diagnosis process and demonstrates that by applying various processing techniques it is possible to support the interpretation of the findings and that they can improve the precision in detecting breast cancer.

Keywords Breast imaging · Medical image fusion · Breast cancer imaging modalities · Diseases-based image fusion · Breast PET positron emission tomography · Fusion mammography with breast PET

L. R. Sánchez (✉)
Facultad de Ingeniería Mecánica y Eléctrica de la Universidad Autónoma de Nuevo León, Ciudad Universitaria, San Nicolás de los Garza, Nuevo León, Mexico
e-mail: liliana.resendizsnch@uanl.edu.mx

L. M. T. Treviño
Centro de Innovación, Investigación y Desarrollo en Ingeniería y Tecnología de la Universidad Autónoma de Nuevo León, Ciudad Apodaca, Mexico
e-mail: luis.torrestrv@uanl.edu.mx

G. E. Sánchez
CT Scanner del Sur, San Ángel, Álvaro Obregón, México
e-mail: dragiselaus@yahoo.com

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1 Introduction

Breast carcinoma could be effectively treated if caught early [3]. Therefore, it is important to have the right tools to notice the presence of signs of breast cancer. There are numerous tests and procedures for the prevention, diagnosis, and treatment, and one of the most important is digital mammography [11]. Clinically, digital mammography (MG) has been used as a standard test to diagnose breast cancer; this corresponds to a general examination and is useful for the detection of breast cancer and the reduction of mortality [6]. However, false positives on digital mammograms lead the second reviews, resulting in increased costs for their health care, as well as unnecessary medical procedures for patients [44]. Diagnostic ultrasound technique is recommended when breast density is reflected [45]. Given that small masses can pass through radiography radiation, the need to resort to other imaging modalities such as high-resolution breast PET could be more effective [16].

During the last two decades, molecular imaging has shown important advancement to integrate their techniques in the evaluation of malignant tumors. Equipment is specifically designed for breast examination and is characterized as a technique that offers greater spatial resolution that allows to detect smaller lesions. It is shown that the fusion of breast PET with mammography (PET/MG) imaging allows for more accurate evaluation by fusing anatomical location with functional imaging. The use of radiotracers in molecular imaging studies allows to detect breast carcinomas before vascularization since the metabolism of cancer cells generally increases before stimulation of the growth of new vessels [42]. The molecular image is obtained from the images from breast positron emission tomography, and it captures enough information to recognize possible oncological lesions at an early stage or not seen in the mammography that can be subject to quantitative evaluations for their detection, characterization, and monitoring.

In interest of improving lesion detection, the goal of this research is the use of diversified data sets of high-resolution breast PET with mammography images in a fused image to support the breast cancer imaging diagnostic process and demonstrate that by applying various processing techniques it is possible to correlate metabolic information to recognize important breast findings. The use of heterogeneous data sets is intended to provide support for a correct clinical diagnosis and can even perform the classification of features that allow the identification of the oncological lesion in malignant and benign groups through the selection, extraction, and classification of characteristics in the fused image.

Several recent studies are summarized in this chapter and indicate that high-resolution breast PET images combined with mammography images give enough evidence to be a useful diagnostic tool, although further evaluation and improvement may be required. So, we present the feasibility to analyze two types of heterogeneous data sets for clinical diagnostic purposes.

The remainder of this chapter is structured as follows: Sect. 2 gives some background of breast cancer screening; breast imaging technologies, mammography, and breast positron emission tomography are examined in Sect. 3. Fusion of mammography and high-resolution breast PET principles are inspected in Sect. 4. Material and methods are described in Sect. 5. Section 6 describes applications of deep learning in cancer detection, and finally, the conclusions are exposed in Sect. 7.

2 Breast Cancer Screening

Despite continued progress in detection and diagnosis, breast cancer is still an alarming global public health problem. Conventional mammography continues to be the cornerstone in the detection of breast carcinoma; however, new technologies provide valuable information on the molecular aspect of the tumor, with the consequent detection of small lesions, at earlier stages, with proper identification and better surgical planning, as well as decreased morbidity and mortality.

The premise of an early detection of breast cancer has a positive effect on the disease through medical intervention [33]. Through an early treatment, the reductions of the morbidity and mortality are still the main goals during significant finding detection.

3 Breast Imaging Technologies

3.1 Mammography

Through the analysis of mammograms, the presence of masses, calcifications, densities, among others, could be evaluated [13]. Several studies show lower sensitivity during the physical examination compared with the analysis of a mammogram [20]. When the goal is to detect calcifications, mammography is more accurate than ultrasound [13]. The diagnosis based on mammography has the ability to identify cancers due their absorption capability of x-rays with respect to the surrounding tissue [7], but there are high false negative and positive rates in patients with a dense breast tissue [46]. Also, mammography presents many drawbacks such as the use of ionizing radiation.

3.2 High-Resolution Breast PET

Historically, in the practice of nuclear medicine, medical specialists visually evaluate images for the detection and monitoring of breast carcinomas [10]. Although the expertise of a physician is considered as the most important factor during diagnosis, there are other aspects that definitely affect the final result, among them, image noise, the ability of visual perception from the physician, deficient image clarity, and inadequate contrast [23].

In 1994, Thompson et al. [50] developed a highly specific technique to detect the increased metabolic rate of breast tumors. The developed technique provides a low-cost, high-spatial-resolution positron imaging system known as high-resolution breast PET.

High-resolution breast PET uses a compression device that allows to detect 1.5 mm lesion [56]. Their technique compression device is solely for minimizing patient motion, is getting a more accurate result, and is also considered as an important tool for monitoring the cancer treatment response. Because cancerous cells present an increased glucose metabolism, the radiotracer molecules are taken up by the cells making suitable the localization of the cancer with high-resolution breast PET. Also in a PET/CT study, the metabolic activity in the tumor can be quantified to assist in assessing the effectiveness of therapy both during and after treatment, allowing for changes in treatment when needed [7].

It was demonstrated the potential to detect breast lesions with a series of special phantom experiments by measuring basic scanner parameters as scatter fraction, as well as sensitivity and major resolution [39]. Also, it was presented clinical results by analyzing images achieving a specificity over 90%, a sensitivity over 86%, and an accuracy of 89% in the diagnostic task that can be categorized as a feasible and accuracy rate [26]. High-resolution breast PET was considered as technique that can assist during the procedure of partial mastectomy to improve negative margins [48]. High-resolution breast PET showed higher accuracy results during the lesion characterization [56]. This imaging procedure is still considered as an emerging imaging technology that produces high-resolution tomographic 12-slice images of 18F-FDG uptake in the breasts [3].

Due to the advances in nuclear breast imaging devices, the interest in high-resolution breast PET has been increasing. Also because of the use of lower doses of radiopharmaceutical and their increased sensitivity, the high-resolution breast PET has been suggested for breast cancer detection and treatment planning [29].

Although, it is still considered a recently introduced nuclear medicine study, which after injecting a radiopharmaceutical called F-18 fluorodeoxyglucose (18-FDG) intravenously to subsequently acquire images of the mammary glands where it is possible to observe the behavior of lesions identified by other diagnostic modalities and their metabolism. Those suspicious breast lesions will have increased metabolism in this study. Silverstain et al. [45] reported that molecular imaging tools such as breast PET have equivalent sensitivity and improved specificity when it is compared with breast MRI so they recommended that breast PET is used when a contraindication is found for MRI in some patients. Specht et al. [47] characterized molecular imaging procedures that offer a better spatial resolution and greater accuracy when it comes to image quantification. Berg et al. [4] found greater specificity at the breast and lesion levels and show the performance when compared to MR imaging. A group of scientists identified the high-resolution breast PET as a useful tool due to the adequate results in early diagnosis of breast carcinoma [23], although further evaluation on improvement may be required. The evolution of positron emission tomography instruments and their requirements to obtain good-quality images are shown in the paper by Eo et al. [14].

High-resolution breast PET provides functional imaging information and is considered as a useful tool as a result of their high sensitivity because it can identify the stage of the breast cancer especially in those patients scheduled for conservative surgery as well as assess recurrence versus postsurgical changes and monitor the neoadjuvant chemotherapeutic response; the aforementioned contributes to improve the treatment planning of the disease [34].

It was concluded that the imaging sensitivity of high-resolution breast PET was higher than whole-body PET [57]. Also, there was found stronger correlations with immunohistochemical information of breast cancer using high-resolution breast PET up against to whole-body PET [32].

The values of specificity and sensitivity for breast PET images were established in different clinical situations by Martins MV et al. [30]. Molecular imaging is still considered as a worthy technique when it is combined with mammography [3, 42].

The effectiveness and characterization of breast images were studied, found a moderate positive predicted value, and considered the information of mammography should be used together to make diagnostic decision to improve the efficacy of studies [8].

The sensitivity and specificity as diagnostic values were evaluated by Farajati J et al. [18]; using the maximum high-resolution breast PET uptake value > 1.9, they concluded a specificity greater than 95% and with a sensitivity of 100%.

4 Fusion of High-Resolution Breast PET with Mammography

Efforts to demonstrate the benefits of using high-resolution breast PET with mammography have been different. Weinberg et al. [55] concluded in a device with biopsy capability combining with a conventional mammography; this allowed to exploit the potential of correlation of high-resolution breast PET with mammography. Thompson et al. [50] provide a low-cost imaging system in which high-resolution breast pet images can be correlated with mammography images.

Thompson [49] considered a group of designs as compatible when combining the high-resolution breast PET image with the mammography image. High diagnostic accuracy for breast lesions was found; when mammography and breast PET images were analyzed, it was found a sensitivity of 91%, a specificity of 93%, and an accuracy of 92%.

Fusion makes it possible to recognize breast cancer since the mammography image provides morphological information and the functional image provides metabolic information [17].

High-resolution breast PET contributed with extra information in patients with implants as well the hormonal status or even density does not affect the diagnose value. Also, breast PET imaging was very helpful to show breast cancer with more characterization, such as multifocal or multicenter disease and, in some cases, intraductal involvement [17].

The images provided by high resolution breast PET are suitable as a complementary study for detecting breast cancer [1].

Breast cancer cells show an increased absorption of the radiopharmaceutical than normal cells [17]. The fusion of breast PET with mammography was considered as an optimum choice due to their capability to provide additional morphological information in findings.

High-resolution breast PET and mammography are studies acquired in different conditions. Bergman et al. [5] proposed a process that makes simple the correlation of both modalities, and this allowed to obtain more accurate results during the registration of mammography image with functional image [5].

5 Material and Methods

The database was retrospectively reviewed for one hundred female patients with a suspicious breast lesion on mammography or clinical background. All breast PET images were reported by a nuclear medicine physician. The characterization of the images included breast density, right, left, or bilateral lesion, multifocality, multicentricity, and extension or intraductal component. Digital imaging and communications in medicine (DICOM) is used as the standard representation, communication, and storage of medical images and related information. A DICOM file format has been used, so we have implemented a tool for medical image registration that allows establishing correspondence between features in two sets of images, by using a rigid transformation model. The utilization of Grassroots DICOM library was chosen as a framework library.

5.1 Image Processing and Analysis

Image fusion combines information of two data sets of a related scenario, and this makes suitable to get additional information in a single scene. Image registration is a processing technique where two images are aligned by overlapping them; this allows to get a third integrated image. Both data sets were acquired with different conditions and devices. This task in which the input images are aligned before getting the fused image is called image registration.

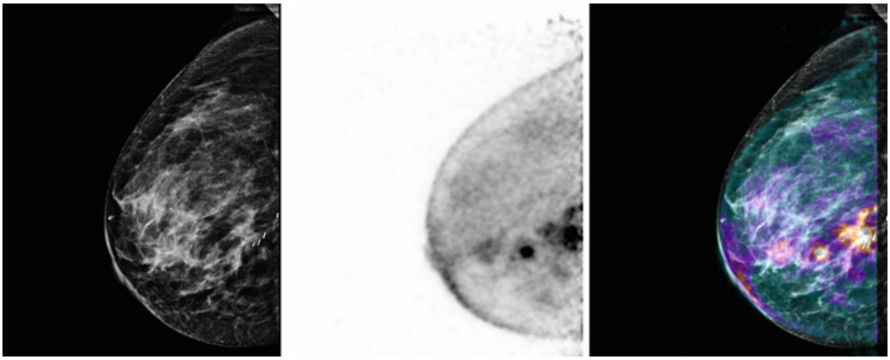

Fig. 1 Standard craniocaudal (CC) view of MG image. BIRADS 3 (left), high-resolution breast PET image (middle), and fused image previously registered (right). Patient with antecedent of ductal infiltrating carcinoma, treated with tumorectomy. Fusion PET/MG shows 18-FDG uptake near to the surgical staples and a multifocal lesion

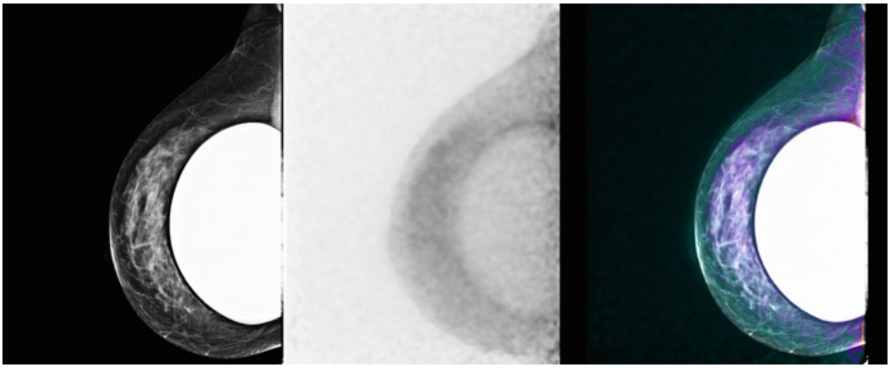

Fig. 2 Standard craniocaudal (CC) view of MG image (left), breast PET image (middle), and fused image previously registered (right), in a patient with breast implants

5.1.1 Image Registration

By finding the optimum geometrical transformation to correlate anatomical region between both images, valuable information is extracted and used to interpret and diagnose clinical findings that are considered as very complex tasks. One of the challenges of image registration is the aligning a series of two-dimensional images (Breast PET image) on a two dimensional image (MG image), due to different imaging condition in which different sensors are used to acquired to make a multimodal analysis as well low-quality and noise were present. The main goal is to integrate the information obtained from Breast PET device with a digital mammography image to get detailed scene representation. See Figs. 1, 2, 3, 4, and 5.

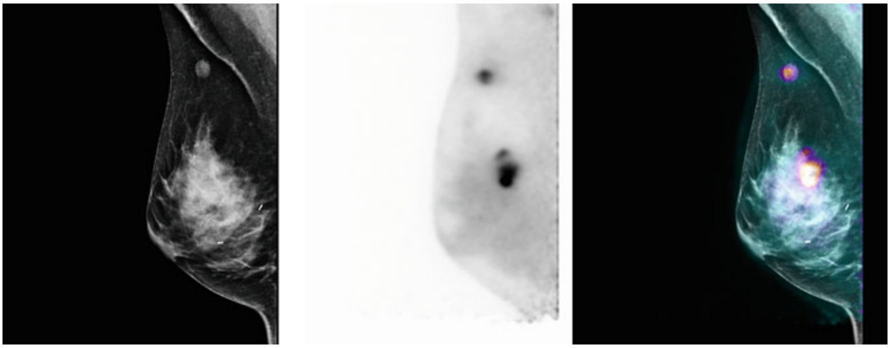

Fig. 3 The medio lateral oblique (MLO) view of MG image with density category: d (left), breast PET image (middle), and fused image previously registered (right). Patient with antecedent of a growing lymph node in the axilla, with two negative biopsies (surgical staples). Fusion PET/MG shows 18-FDG uptake in the upper quadrants, not suspected in the mammography

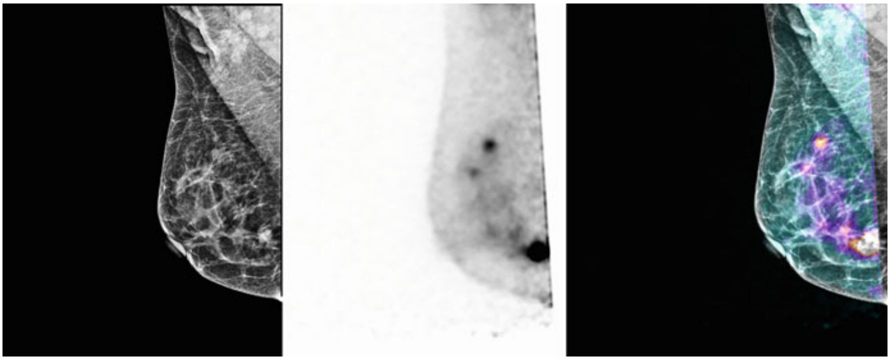

Fig. 4 The medio lateral oblique (MLO) view of MG image with one lesion in the inferior quadrant (left). High-resolution PET (middle) and fused PET/MG image (right) that show 18-FDG uptake in the same lesion shown in the mammography plus two other lesions in the upper quadrants (multicentric lesions)

In the last decade, several registration methods have considerably grown. One of the main contributions to image registration was described by Pluim et al. [36]. There are several applications of fusion between modalities such as computed tomography (CT) with positron emission tomography (PET), as well as magnetic resonance (MR) among others [24, 40, 41, 43, 54]. The image registration task is still facing new challenges and developments that will surely continue to position it as a very active area within image analysis and processing. Currently, there is a big initiative in the development of automatic and efficient registration techniques.

The images captured by breast PET are three-dimensional, and mammography images are considered a 2D imaging modality. The complexity is visible because there is no positional information between both modalities, which represents a challenge during the registration process. For the purpose of depicting fused image,

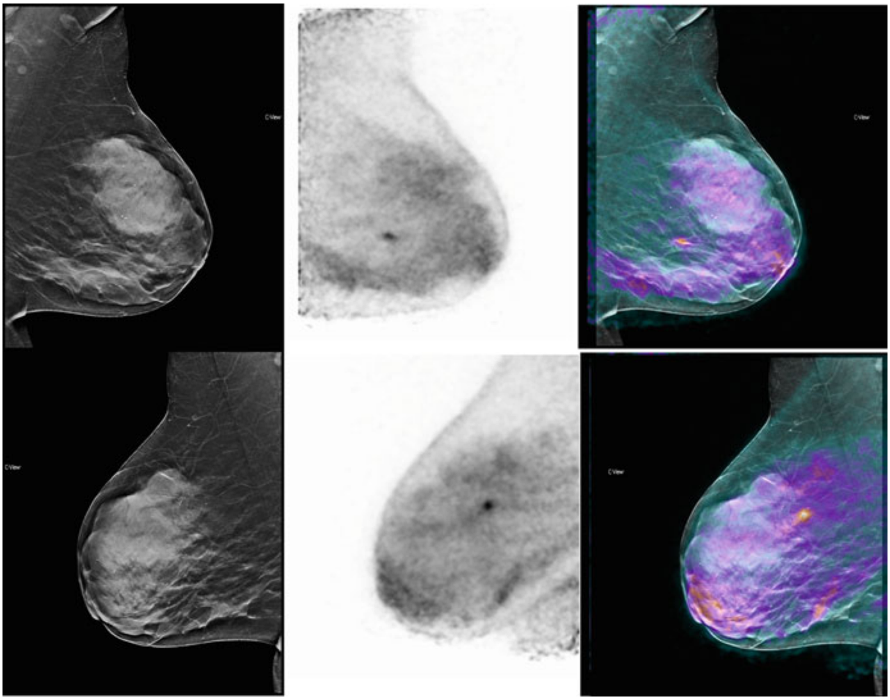

Fig. 5 The mediolateral oblique (MLO) view of MG image (left), high-resolution breast PET image (middle), and fused image previously registered (right). Left breast (upper images). Right breast (inferior images). Patient with mother and sister with breast cancer, BIRADS 3. Fusion PET/MG shows focal 18-FDG uptake in both breast. Bilaterality

we studied the registration methodologies based on intensity and their features. The methodologies included the common geometrical transformations and professional assessment techniques realized by physicians.

6 Applications of Deep Learning in Breast Cancer Detection

In the last two decades, there have been substantial advances in methods to detect breast cancer with artificial intelligence techniques. The complexity of each particular task makes the workflow meaningful. But with the development of new machine learning methods and their application in the clinical area, the need for precision is crucial to a major contribution to classification, diagnosis, and planning treatment [15]. Litjens et al. [28] evidence the existence of demand in the application of machine learning models for the purposes of prediction and prognosis of cancer due to a prominent need for personalized treatments.

Currently, there are applications assisted by Artificial Intelligence techniques that are already in use, and their constant evaluation of their performance is tracked to refine the ways of communicating to the patient that risk information, as well as to the doctor who provides the primary care [15].

The consideration of hundreds and sometimes thousands of clinical cases allows artificial intelligence techniques to recognize the subtle patterns of breast tissue that are considered precursors of breast carcinomas. The techniques allow learning by taking advantage of all information directly from the data by creating models that are significantly more accurate in various populations. The use of applications based on artificial intelligence techniques allows additional assistance, thus achieving a double diagnosis that discards errors on a larger scale [35].

Deep learning applications in healthcare have grown in importance in recent years [52], and the performance of the different techniques in object detection and classification tasks has been key for its use and application with medical images. Automatic feature extraction still presents a constant and ongoing challenge to find the features that accurately describe the output versus input data. The reproducible capacity of deep learning techniques and their non-discriminatory approach to characteristics makes the implementation feasible [38].

Dreyer and Allen [12] show the importance of using platforms to handle large amounts of information derived from image-based medical records, as well as emphasize effective analysis of results [12].

Deep learning techniques are useful when applied to various fields of research using diversified data sets collected from different sources [53], enhancing the diagnostic process in the medical area, which helps to spread the hypothesis through the application of various techniques that they allow to predict the acceleration of the multiple repetitive tasks of doctors [31].

An analysis of different studies that exploit deep architectures was carried out and is presented in the paper by Hamidinekoo et al. [19]. In this analysis, it has been identified the convolutional neural network as the most common architecture.

Arevalo et al. [2] tested several conventional neural network architectures and compared them with two descriptors during the manual diagnosis of injuries. Their experimentation was carried out with the BCDR-FM data set, and it was not tested with pre-trained networks.

The use of mammography images with a combination of pre-trained convolutional neural network is shown in the work realized by Carneiro et al. [9]; they found these models useful in medical applications and showed that it is not necessary a pre-registration of the input images in a multiview classification. Additionally, the risk of breast cancer is established according to BIRADS. As a result, the pre-trained models show better performance against the randomized ones. Huynh et al. [21] used the pre-trained AlexNet to address mass diagnosis by analyzing the performance of support vector machines (SVM) as a classifier. A scheme in which a convolutional neural network that has been pre-trained was adjusted in a subset of the DDSM database is presented by Jiao et al. [22]. The features that represent the masses were extracted from the layers of the model using different scales that correspond to high and medium levels, and then the use of support vector machine was used as a classifier merging their predictions in each case. Levy and Jain [27] adopt AlexNet and GoogleNet architecture to classify findings in mammography images. They explore transferred learning and compare against one made from scratch.

Ting et al. [51] proposed a deep classification algorithm using mammography images of MIAS database and built an architecture including 28 convolutional layers. Rampun et al. [37] adapted AlexNet architecture by modifying to get a new pre-trained version, then adjust with curated breast imaging subset of DDSM (CBIS-DDSM), and made their predictions based on three models. Lehman et al. [25] developed an algorithm and trained a deep convolutional neural network based on ResNet-18 architecture, to measure the amount of fibrous and glandular tissue. There is a major risk of breast cancer in women with dense breast as the tumors can be masked.

In summary, the technology can improve user practice through the use of artificial intelligence algorithms as an aid in the management of data science, tools, and knowledge in medicine to incorporate them into patient care. The literature review shows substantial efforts in the area of artificial intelligence applied to medicine and has addressed the improvement of algorithms as well as their accuracy, execution, and propagation in volumes of data as well as in the application in electronic records of the health. It is important to emphasize the veracity of the information that is used during the training phase as well as in the test phase to obtain greater accuracy in any diagnostic result.

7 Conclusions

Although there are several imaging options capable of identifying and defining breast cancer, the fusion of breast PET combined with mammography can provide additional information for the detection of the primary lesion since breast PET measures metabolism, mammography images offer anatomical reference through different views of each breast that can be evaluated together by the interpreting physicians, and merging both techniques allows the anatomical localization related to the functional image. The fused image can be obtained through the application of conventional image analysis and processing techniques as well as artificial intelligence techniques. Breast PET and MG are synergistic and when combined in a single image, allow to detect minor findings specially in patients with dense breast. The literature review shows the fusion of breast PET findings with mammography (PET/MG) allowing to identify the primary lesion in dense breast, multifocal disease, multicentric disease, bilaterality or ductal involvement. Integrating information between these images could increase the specificity, sensitivity, accuracy, and the positive predictive value of MG in diagnostic work-up of breast cancer.

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