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A Survey of Breast Cancer Screening Techniques: Thermography and Electrical Impedance Tomography

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ABSTRACT

Breast cancer is a disease that threat many women's life, thus, the early and accurate detection play a key role in reducing the risk in patient's life. Mammography stands as the reference technique for breast cancer screening, nevertheless many countries still lack access to mammograms due to economic, social and cultural issues. Last advances in computational tools, infrared cameras and devices for bio-impedance quantification, have given the chance to emerge other reference techniques like, thermography, infrared thermography and electrical impedance tomography, these being faster, reliable and cheaper. In the last decades, these have been considered as parallel procedures for breast cancer diagnosis, as well many authors concluded that false positives and false negatives rates are greatly reduce. This work aims to review the last breakthroughs about the three above-mentioned techniques and to describe the benefits of mixing several computational skills to obtain a better global performance. In addition, we provide a comparison between several machine learning technique going from logistic regression, decision trees and random forest to artificial, deep and convolutional neural networks. Finally, recommendations and contemporary advances in breast cancer diagnosis approaches are made, such as 3D breast simulations, pre-processing techniques, devices in the research field, prediction of tumor location and size.

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KEYWORDS

Breast Cancer; Thermography; Electrical Impedance Tomography; Machine Learning Techniques; Computer Aided diagnosis

1. Introduction

The cancer is a major public health disease that affects many people across the world. The early detection of cancer is mandatory in order to save the patient's life [1–3].

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Emerging economies are prone to higher risk of cancer, therefore the socioeconomic factor [4,5], aging, unhealthy lifestyle [5–8], growth of the population, may perhaps lead to a higher chance of developing cancer, in addition, the Human Development Index (HDI) is highly correlated with the presence of cancer. In fact, the breast cancer was the first leading cause of cancer-linked death among women in 2018, reaching approximately 15% of the total number of registered cancer deaths [9]. Mammography, ultrasound and magnetic resonance imaging, stand as the main techniques for breast cancer screening, however, limitations like x-rays, expensiveness, accuracy, misinterpretation, and so forth, have let to grow in popularity alternative techniques as thermography and electrical impedance tomography (EIT).

The Globocan’s 2018 fact sheet from the International Agency for Research on Cancer - World Health Organization (WHO), shows the number of new cases and deaths in 2018 from cancer; only in 2018 the male number of cancer’s new cases reach more than nine million, and more than eight million of new females where registered as well. Globocan and other authors [4,9] have predicted a rising in the number of death and prevalence in breast cancer. Indeed, the proportion of breast cancer deceases may vary depending each world’s region and the above-mentioned risks. Specifically, studies have uncovered that the breast cancer mortality-to incidence ratio in developed countries is 0.20, where in less developed countries is almost twice, thus 0.37 [4,7].

In fact, many studies have found that, early-detection of breast cancer could increase the survivability rate up to 90% of all cases within a five-year window, thus, the needed of an easy-access, cheap and trustable screening breast cancer method still latent in most of underdeveloped countries [4,7]. In the other hand, some countries keep multiple barriers for develop an effective breast cancer screening system, e.g., organizational, psychological, structural, sociocultural and religious [10]. To exemplify, the Kaiser Family Foundation in late 2018 have reported that 11% from the total amount of women in USA have not any kind of social insurance, which represents more than 10 million women [11]. Differently, a few countries have religious rules where the woman cannot expose the breast, therefore, the commonly and available methods on the medical field are non-viable for an accurate and prior detection of breast cancer. In contrast, devices and techniques that would not need physicians’ direct contact like thermograms or bio-impedance images will make a considerable impact.

Presently, several techniques are available in the medical field for breast cancer screening and diagnosis, despite the variety, the main differences lie on cost, method, specificity, sensitivity and patient’s discomfort during test, among others. The table 1 show a comparison of the main techniques for breast cancer diagnosis and screening described by Kandlikar et al. [12]. The Mammography is an x-ray technique used as a breast cancer screening and diagnosis method, when an abnormality is in early-stage the mortality index is reduced between 15 to 25% [13,14]. In spite of the mammograms’ benefits, the over-diagnosis (false positives), painful procedure, high number of false negatives (usually when the person who evaluate the results, make erroneous assumptions, or in dense breast) and use of x-rays have been making it a method which need to be renovated [15] or even replaced by new techniques like thermography and EIT, however, it still being the main breast cancer diagnosis technique. Under those circumstances, no matter the individual risk of breast cancer, either, genetically (family) or unhealthy lifestyle the current guidelines suggest breast checks every 1 or 2 years starting at age of 40 or 50 years [13].

In general, more information about, guidelines, health benefits, recommended gap time between tests, type of breast cancer and so forth, are in [13,16,17]. Truthfully, the European Commission has published a document regarding the breast cancer

screening and diagnosis guidelines, summarizing that an accurate system is made of screening, diagnosis, communication to the patient, training, interventions to reduce inequalities, monitoring and evaluation of screening and diagnosis.

”Insert table 1 here (the table must be in landscape mode, therefore, it should be let on appendices)”

A wider explanation in breast cancer techniques for diagnosis is in Warner, E. report [18]. The need for cheap, effective and without side effects, breast cancer diagnostic and screening techniques have led the development of several new techniques like thermography and EIT, henceforth, this article will review the their last breakthroughs.

Given these considerations, thermography, infrared imaging and electrical impedance tomography have emerged as new, accurate and cheap approaches that are describe in the following Sections. Firstly, the thermography is the measurement of the skin’s temperature. Initially, if an infrared camera (IR) is use, the category is infrared imaging, in the other side, if the method employs either, sensors attached to the region of interest (ROI) or liquid crystal the method is simply thermography, producing a temperature matrix. Consequently, many researchers have found a huge correlation between the increase of heat and blood perfusion rates in tissue surrounded by a tumor, indeed, higher than normal tissues. Secondly, EIT is an imaging technique, which evaluate the inner electrical conductivity or impedance (resistance) distribution of a body; the signals are collect with electrodes in contact with skin’s ROI [19,20]. To clarify, similar to the increase in the temperature of cancerous tissue’s surrounds, the malignant tissue has more than twice times higher impedance than the normal one, even the majority of characteristics possess differences [21,22], in addition, many authors have presented several EIT systems for breast cancer diagnosis [12,19–23].

The so called Computer Aided Diagnosis (CAD) system, are computational algorithms capable of identify patterns in almost whichever type of data, now, several research teams are struggling to add the CAD systems in the diagnosis phase in order to increase the global accuracy in detecting breast cancer. Patricio, M., et al give insights in this type of systems, where a human expert and a CAD system play a specific role [24]. Normally, a CAD environment is made of a five-step pipeline, including identification, data preprocessing, feature extraction, prediction or classification, and post-processing.

The paper is organized as follows. Section 2 conveys the last breakthroughs regarding thermography such as main protocols, 3D simulation of the breast and machine learning approaches for thermal databases. Similarly, Section 3 gives similar details but, about electrical impedance tomography. Section 4 covers the promising progress in two-steps systems, mixing EIT and thermography for boost the performance. Finally, Section 5 and 6 formulate the discussion, conclusion and comments about future works.

2. Thermography

Thermography is the measurement of the temperature based on infrared radiation, in contrast to other modalities; it is a non-invasive, non-intrusive, passive and radiation-free technique. In medicine, the skin’s surface temperature exposes many features because, the radiance from human skin generally, is an exponential function of the surface temperature, in other words, is influenced by the level of blood perfusion in

the skin [25]. In fact, Krawczyk B., et al. summarize "Thermal imaging is hence well suited to pick up changes in blood perfusion which might occur due to inflammation, angiogenesis or other causes" [26]. As mentioned before, the early detection of breast cancer provides significantly higher chances of survival [3,27]. Thermography, truly has advantages over other techniques, in particular when the tumor is in an early-stage or in dense tissue ¹ [28]. Certainly, many authors² had explain before the high risk for breast cancer when mammographic density is strong [29], also in [30] demonstrated the correlation between body weight, parity, number of births and menopausal status, regarding to breast cancer. The above authors have point out the highly rate of mammograms' false positive cases and the fact that mammography can detect tumors only once they exceed certain size; in brief, thermography could be a solution to these problems. In the medical field, diagnostic of breast cancer using thermography keeps having two different points of view, one side explain that thermography images produce a high number of false positives (the thermal images were not enough for the initial evaluation of symptomatic patients in Kontos research [31]). Similarly, some authors mention low precision and recall [32,33] after the initial evaluation. On the other hand, the thermography stands as a technique capable of overcoming the limitations of mammography.

2.1. Initial years of thermography

The first time ever that was used a thermal/infrared imaging to aid the breast cancer diagnosis was in Montreal in 1956 when the M.D., Lawson, R., recorded the skin's heat energy using a "thermocouple". Known as a device made of two dissimilar metals that allows calculating the electromotive force created by the juncture of two metals [34]. Also he mention that Massopoust, L., and Gardner, W., had used some kind of a system called "Infrared phlebogram" ³ to aid the diagnosis of breast complaints [35] in 1200 cases. Nevertheless, not was before 1958 when Lawson, R., presented one of the first devices capable of create an infrared imaging. He described the process as follows; "At any instant during the scan, the infrared energy radiated from the point on the body at which the scanning mirrors are "looking", is reflected on to a parabolic mirror, thereby focusing the energy from a point on the object on the infrared detecting cell" [36]. The infrared imaging device was called "Thermoscan", in 1965 Lawson's Team obtain a patent where explain the thermography as a diagnostics tool [37].

Afterwards, a team from Texas used a device called Pyroscan for measure the skin temperature, they considered the equipment was expensive but technically was simple, however the false positives were similar compared with mammography [38]. Williams et al. likewise present studies with many common features. In 1960 [39] and in 1964 he was granted with a patent [40], explaining the characteristics of an "Aparatus for measure the skin temperature". On the other hand, Mansfield et al. carry a research, testing different heat-sensing devices in cancer therapy to contrast methodologies [41]. Swearingen in 1965 concluded two main things, first, the true positives rates was greatly increased when mammography and thermography were applied together, second, the thermography was seen as a new technique for diagnostic procedure in mass screening of the breast [42]. During the 20th century, also is conceived a patent to [43] using an infrared radiometer mounted on a carriage guided path; [44] patented the

¹Dense tissue: high index of fibrous or glandular tissue and low of fat

²AACR, American Association for Cancer Research

³(1) A graph indicating the pulsing of the blood within the vein. (2) An X-ray image of a vein that has been injected with a dye that is visible on the image taken, Collins Dictionary

process of diagnosis a disease through thermography. In 1971 Isard, H, et al. cooperate in a ten-thousand-cases study, during the four-year research they determined that 61% of cases were correctly diagnosed with thermography, 83% with mammography and 89% applying both techniques [45], and [46] studied the pathological changes in spatial distribution of temperature over the skin surface.

2.2. Protocols for thermography

The thermography test, may be considerably affected when guidelines are not followed. In the past, many studies had lack standards and protocols when record thermograms; those could be one of the primary reasons for the poor results. Ng [47] and Satish [12] mention several standards to follow, in order to obtain high quality and unbiased results. Firstly, it is recommend that patients should avoid tea or coffee before the test, large meals, alcohol and smoking may affect the physicist's or CAD's judgement. Secondly, the camera needs to run at least 15 min prior the evaluation, keep a resolution of 100mK at 30 °C at the same time the camera should have a 120x120 points temperature matrix. Third, is recommend a room's temperature between 18 and 25 °C, humidity between 40% and 75%, carpeted floor and avoid any source of heat. Also important, the postprocessing phase should be able of identify the type of breast cancer, either, made by a physicians or CAD system. Similarly, Ng et al. in a ninety patients study propose a temperature-controlled room between 20°C and 22°C with and humidity of 60% \pm 5%, the patient rested for 15 minutes[48]. In the other hand, in order to ensure that patients are within the recommended period, they needed to be in the 5th to 12th and 21st day after the onset of menstrual cycle, since at this time the vascularization is at basal level, with least engorgement of blood vessels [49].

2.3. Temperature-based technologies for breast cancer diagnosis

The term "thermography" is not limited to measure the skin's temperature, but also rearrange these values in one "image", like an illustration, creating a heat map of the breast's ROI, where each "pixel" express an equivalent temperature value. Ng et al. mention that the presence of localized or focal areas of approximately 1.0°C or more, including the areola region and significant vascular asymmetry forming "clusters" are features that need to be considered as abnormal [48], they obtained an global accuracy of 59%, and true positive accuracy of 74% using Bayes Net. Arena et al. [50] in 2003 mention the benefits of the digital infrared imaging also called "DII". They tested a weighted algorithm in 109 tissue proven cases of breast cancer, generating positive or negative evaluation result based on six features (threshold, nipple, areola, global, asymmetry and hot spot), they employed an infrared camera with a 320x240 pixels (temperature points), and sensitivity of 0.05 degrees. Comparatively, some researchers not only are not focus on the classification of breast cancer, but also on the localization itself of the tumors. Partridge and Wrobel modeled in 2007 a method using dual reciprocity coupled with genetic algorithms to localize tumors, likewise, the smaller tumors or deeply located, produce only a limited perturbation making impossible the detection [51]; estimation of tumor characteristics can be found in [52]. Kennedy, D., et al. discussed the thermography as breast cancer screening technique, together with the commonest ones, like mammograms and ultrasound. Therefore, are mention the mammography's limitation and problems, in contrast thermograms are early indicators of functional abnormalities that could lead to breast cancer [53].

The infrared cameras used for thermography provide the result in both, a temperature matrix or a heat map image. Rajendra, U., et al. [54] built an algorithm using support vector machines classifier for automatic classification of normal and malignant breast cancer, the selected database is [55,56]. Later, in 2009 Schaefer, G., et al. performed a fuzzy logic classification algorithm having an accuracy of nearly 80%, with a population of 150 cases, they explain that statistical feature analysis is a key source of information in order to achieve a high accuracy, i. e., symmetry (mean) between left and right breast, standard temperature deviation, among others [57]. Araujo, M. presented a symbolic data analysis on 50 patients' thermograms (data: temperature matrices), obtaining four variables, minimum and maximum temperature values from the morphological and thermal matrices, also leave one out cross validation framework was implement [58].

The only public database of breast thermograms are from Marques, R [55] as a master thesis result, where there is a segmentation of the thermal images. Nevertheless, it was not after 2015 when Silva, Da [56] propose a system to diagnostic breast cancer among a population of more than 50 patients. A recent study from Silva, Da et al. present the renovated database, a web-page encompassing all the cases with the corresponding validation technique, mammography or ultrasound [59].

2.4. Computer aided techniques in thermography

The majority of studies related with CAD systems and Infrared Imaging Techniques for breast cancer diagnosis, employ the public and web-available database from [55,56,59]. Nevertheless, some authors have created a non-public databases that are used for private purposes only. Ng et al. [48] presented a computerized detection system with bayes net rules on a ninety patients group, the algorithm yield a 59% accuracy, but, they also in 2002 proposed a new system using artificial intelligence. Ng's team [60] employs an artificial neural network (ANN) coupled with a bayes net ruler, obtaining an accuracy of 61.54%, but not was before 2008 when his team create a two-steps algorithm, where a linear regression decided whether to choose a ANN with radial basis function or a back-propagated ANN. This article using the same ninety-person database from Singapore (ML) [61] achieved a greater accuracy of 81%. Mambou et al. [2] article describes a method to use Deep Neural Networks and support vector machines using the mentioned before database. Initially, they pre-process each thermal image for fitting them in a Deep Neural Network (DNN), then, they extract and normalize the features for feeding into a machine learning algorithm. The database is composed of 56 patients where, 37 carried anomalies and 19 were healthy women, the population are from Brazil. The last decade's improvement in microcontrollers and personal computers allowed the development of many software in Machine Learning Techniques (MLT), such as Python, Matlab, Orange3 (based on Python) and WEKA. Nowadays there is four groups of MLT, distributed as follows: supervised, unsupervised, semi-supervised, and reinforcement algorithms. The current breast cancer systems are grouped in supervised and unsupervised MLT. Firstly, we recall the supervised algorithms like linear and logistic regression, linear discriminant analysis (LDA), Gradient Boosted Trees as AdaBoost (AB), Support Vector Machines (SVM) with kernels (like, Radial Base Function - RBF, or Gaussian), Naive Bayesian Networks (NBN), Decision Trees (DT), Random Forest (RF), Artificial Neuronal Networks (ANN) and Deep Neuronal Networks (DNN). Secondly, K-nearest neighborhood (KNN), Principal Component Analysis (PCA), locally-linear Embedding and linear discriminant

analysis stand as unsupervised algorithms. Those techniques usually make part in big intelligent environments alongside several thermography databases. Even though, the number of instances or population size is a key factor to develop a robust MLT. However, in some cases the volume of the database is not a drawback, rather the set's balance. As a result, Krawczyk, B., et al. in 2013 proposed an ensemble algorithm ⁴ for clustering and classification in breast cancer thermal images, likewise they implement a K-fold cross-validation in order to reduce the bias and overfitting of the model, it works as follows, first the database is divided in training and testing set; the training set is split in "K" number of folds, for this research were five folds. Finally, the model is trained five times, where one sub-fold acts as evaluation and the other four ones act as training, the process is rotated over all folds [25].

During, the last 6 year, several reviews ⁵ regarding infrared technologies have emerged and created a well-delimited guide of the current status, main protocols and new directions of breast cancer diagnosis [12,62,63]. The ROI's preprocessing of thermal camera images is another issue to manage in order to boost the global performance of the algorithm. In [64] is mention an optimized method of breast thermography images using extended hidden Markov models (EHMM), Bayes Net and Random Forest in a 140-individuals database from the IUT OPTIC non-public database from Iran. Furthermore, Sathish, D., et al. have explained that the thermal camera's information can be interpreted in three ways. Temperature matrix, gray scale image and pseudo-color image (or heat map), the last one possesses more information than the first two. They concluded that the normalization of thermal images could improve the general algorithm [65], furthermore, the Figure 1 show the three possible variations of thermal images representation.

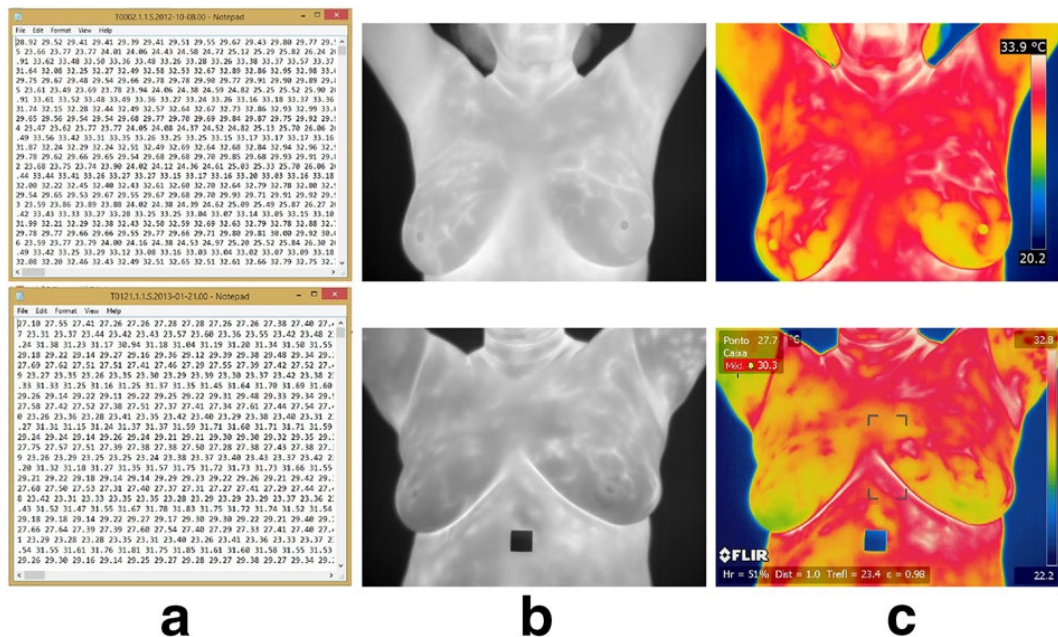


Figure 1. Representation of breast thermograms (a) Temperature matrix (b) Grayscale image (c) Pseudo-color image from [65].

⁴Meta-algorithms that combines several machine learning techniques into just one predictive model decreasing variance, bias and accuracy, the resulted model is better than the other ones separately.

⁵In [62] is mention that 5% of the all articles from January 2012 to January 2017 regarding CAD techniques for diagnosis of breast cancer mention thermography as main method.

Surely, the improvement of the computer, the price reduction of the microcontrollers and the increase of breast cancer among women, have brought more and more research teams interested in non-conventional techniques for detect the indicated disease, like temperature time series with dynamic thermography [66] or [67]. Deep neuronal networks and SVM [2], intelligent textile to measure skin temperature [68], dynamical infrared thermal imaging or "DITI" [67,69].

Table 2 shows references regarding thermography and CAD systems. The first comment the scope of the project and the main methodology implemented. The second column indicates which machine learning technique is used in order to predict the breast's state. The last column exhibits the main achieve results.

Table 2.: Summarized thermography methods. The main parameters of evaluation are: Accuracy (Acc), sensitivity (Sen), specificity (Sp), AUC (area under the curve), ROC (receiver operating characteristic curve) and PPV (positive predictive value).

Scope of the project	Machine Learning Technique (MLT)	Evaluation Result	Ref.
Clustering and selection using several MLT in one ensemble unit, 5 folds cross-validation	SVM-RBF	Acc: 90%	[25]
	DT	Sen: 82.6%	
	RF	Sp: 91.9%	
First statistical approach for breast thermograms in a ninety patients study, using a 256x200 IR camera	Bayes Rules	Acc: 59%	[48]
		Sen: 54%	
		Sp: 67%	
		PPV: 74%	
Classifying normal/at risk in confirmed cases of cancer, normal and post operation	No MLT	Acc: 99%	[50]
	Weighted Algorithm	Sen: 99%	
Localization of skin tumors, based on temperature	Genetic algorithm	Acc: 100% ⁶	[51]
Presence, location, size and properties of the tumor	Genetic algorithm	Max Error E:2.6%	[52]
Analysis and comparison of thermography vs breast cancer screening techniques	No MLT	Acc: 83%	[53]
Thermography classifier of breast cancer - Graphical user Interface	SVM	Sen: 83%	[54]
		Acc: 88.1%	
		Sp: 90.48%	
Statistical features from infrared signals and asymmetry from both breasts	Fuzzy Logic classifier	Acc: 79.5%	[57]
		Sen: 79.9%	
		Sp: 79.5%	
Symbolic data analysis for classification as malignant, benign and cyst breasts thermograms from [56,59] database	Linear Discriminant Parzen-window	Acc: 84%	[58]
		Sen: 85.7%	
		Sp: 86.5%	
AI approach for breast cancer diagnosis with thermograms, taking in account the menstrual cycle	ANN, Bayes Rules	Acc: 61.5%	[60]
		Sen: 69%	
		Sp: 40%	
		PPV: 90.91%	

Integrated technique for breast cancer diagnosis using a bio-statistical method as pre-processing technique	ANN, linear regression (RBFN)	Acc: 80.9% Sen: 100% Sp: 71%	[61]
Current status of breast cancer diagnosis with thermography [2,12,63]	Many MLT	–	[62]
Breast thermal images segmentation as a pre-processing method	EHMM	Execution time reduced	[64]
Normalization of breast cancer infrared images improve the global accuracy (min-max approach)	SVM Kernel: Gaussian	Acc: 91% Sen: 87.23% Sp: 94.34%	[65]
Analysis of thermal breast images as time series. First, region of interest (ROI) is segmented and then <i>k-means</i> is implemented	Bayes Net Decision Table RF	Acc: 95.4% Sen: 95.37% Sp: 95.4% ROC: 0.97	[66]
Extensive review in last advances regarding dynamic breast thermography's	Many MLT	–	[67]
Analysis of thermal patches as key features for determine the presence of cancerous tissue in the breast	SVM, DT, AB, RF, KNN, ANN, LDA	Acc: 98% Sen: 98% Sp: 98%	[70]
Thermal breast model in COMSOL®, with tissue properties per layers	–	–	[71]
Tumor localization from skin temperatures in COMSOL®	–	–	[72]
Comparison between Temperature based analysis, intensity based analysis and tumor location matching	SVM	Acc: 83.2% Sen: 85.6% Sp: 73.2%	[73]
Analysis of thermography (DITI) in the diagnosis of breast mass, side diagnostic with Ultrasound and/or MRI as validation techniques	No NLT	Acc: 79.6% Sen: 95.2% Sp: 72.8%	[74]

2.5. Breasts model based on 3D simulation and thermal properties

The temperature emanated from a human breast may vary depending on a range of features, both, static and dynamical. The first are tumor size, depth and location; also, volume of the breast and quadrant of the suspected tumor. On the other hand, the pathophysiological characteristics surely are different from patient to patient, therefore, some authors have implemented DITI, where the breast undergo a thermostimulation reducing her temperature, then letting it reach a steady state temperature, it is measure the response. The review from Zhou and Herman [71] present 3D models of the heat distribution in healthy and non-healthy breasts, the Figure 2 depicts a breast 3D model in COMSOL® for computing the heat distribution when a tumor is present, [72] present similar results. An analysis of thermal patches in the breast could improve many algorithms' accuracy [70], also Gogoi, U et al. propose a method to locate suspicious regions in thermograms matching them with tumor loca-

⁶Tiny tumors cannot be detected with this method [51]

tions in mammograms [73], thus, knowing the ground true, they were able to evaluate the efficiency in 3D model and real thermal images.

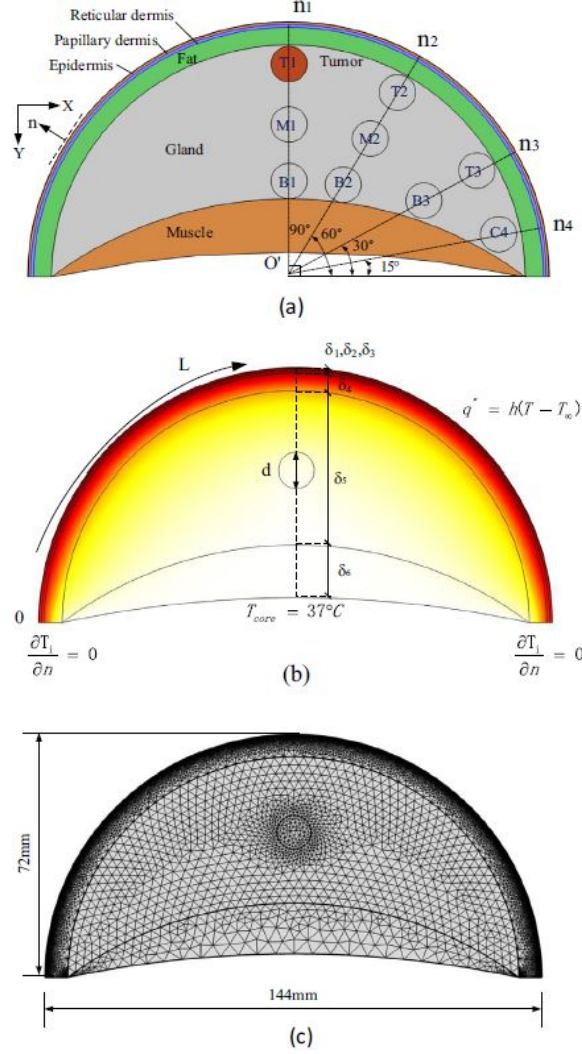


Figure 2. (a) Schematic of the breast tissue layers and the tumor locations in a computational domain; (b) schematic of the breast tissue layers' dimension with boundary conditions for steady state; (c) the computational mesh and breast tissue dimensions, from [71].

Pennes in 1948 [75] proposed the Equation 1 as a heat transfer model of the human tissue:

$$\rho_i c_i \frac{\partial T_i}{\partial t} = k_i \nabla^2 T_i + \rho_b c_b w_{b,i} (T_b - T_i) + Q_i \quad (1)$$

where i represents the breast tissue layers of epidermis, papillary dermis, reticular dermis, fat, gland and muscle respectively. ρ_i , c_i , k_i , T_i , Q_i and $w_{b,i}$; correspond to tissue layer density, specific heat, thermal conductivity, temperature, metabolic heat generation (HG) rate and blood perfusion rate, respectively. Then, ρ_b , c_b and T_b ; stand for blood density, blood specific heat and arterial blood temperature, respectively. also called, a transient heat conduction Bioequation (1), helped [71] research to develop

Table 3. Thermal properties of breast tissue layers (from [71])

Tissue layer	Properties					
	Thickness δ (mm)	Specific heat C (J/Kg K)	Thermal conductivity k(W/m K)	Density ρ (kg/m ³)	Perfusion rate w_b (1/s)	Metabolic HG Q(W/m ³)
Epidermis	0.1	3589	0.235	1200	0	0
Papillary dermis	0.7	3300	0.445	1200	0.00018	368.1
Reticular dermis	0.8	3300	0.445	1200	0.00126	368.1
Fat	5	2674	0.21	930	0.00008	400
Gland	43.4	3770	0.48	1050	0.00054	700
Muscle	15	3800	0.48	1100	0.0027	700
Tumor	d=10	3852	0.48	1050	0.0063	5000

3D models with the properties of the Table 3.

A last key point to realize is the comparison between steady state and dynamical thermography. While steady state thermography measure the uninfluenced breast temperature, the dynamical one, first reduce the breast temperature with cooling in a desired time (usually between 2 and 6 minutes) on top of the breast and afterwards is measure the surface temperature. Nevertheless, parameters like cooling time, cooling temperature, general protocols and patients age still revision and validation, besides, most of the studies remain in simulation phases [12]. Kandlikar et al. review the main considerations regarding breast tumors simulation, like geometrical parameters, depth, size, and location of malignant or benign tumors [12]. Finally, Lin et al. introduce a new methodology to simulate the early breast tumours using finite element thermal analysis considering parameters like temperature variance, breast contours, deepness of the tumour, and so forth [76]. The next section will review the main techniques for perform electrical impedance tomography and the possible combination of computer aided diagnosis systems, furthermore, the main devices for both, academic and commercial purposes created across the last decades are also shown.

3. Electrical Impedance Tomography

Electrical Impedance Tomography (EIT) or Electrical Impedance Spectroscopy (EIS) is a technique used for evaluate conductivity (also, permittivity) distribution inside the desired object by measuring the voltages between electrodes located in a specific surface. The procedure consists in applying a high frequency and low-current signal through electrodes in the skin. Identically, some electrodes record the voltage response in the skin, therefore, obtaining a "permittivity" factor. The electric conduction in a tissue can vary depending the type of tissue, the separation between electrodes, and significantly in the presence of cancerous tissue or tumor. As a matter of fact, Kubicek, W., et al. employed a four-band electrode (tetra-polar) configuration and EIT techniques to measure the cardiac output [77]. The electrical impedance technique has been used as well for detecting several types of diseases such as cardiac arrest [78]. Equally important, the features of EIT techniques play a key role in the breast cancer early-detection. The impedance of a living tissue is a complex number expressed by

both, magnitude and phase, in fact, certain sub-features may come out after some preprocessing techniques, in order to reduce noise and make them convenient for MLT. Over the last decades, many research teams have disclosure some basic protocols for noise reduction and standardization purposes, as example, frequency, max current and limiting circuit, room temperature, time of analysis, quantity of recorded signals (i. e., tetra-polar), impedance and input stray capacitance. Brown [79] gives a wider explanation on EIT for health care.

3.1. Initial years of electrical impedance tomography

The EIT systems for breast cancer diagnosis use tools to help physicians understand the electro-physical changes in the human body when a tumor or cancerous tissue exists. Kubicek in [77] referenced the initial exploratory research of electrical impedance tomography. In the first place, Jossinet, J., et al. [22,80] explains the main protocols for measure the body's electrical impedance, they use frequencies between 0.488kHz and 1MHz over twelve different points in many tissue samples. On the other hand, the features collected from each sample were impeditivity at zero frequency (I0), phase angle at 500kHz, high-frequency slope of phase's angle, impedance distance between spectral ends (DA), area under the spectrum, area normalized by DA, maximum value of the spectrum, distance between I0 and the real part of the maximum's frequency point and, the length of the spectral curve. Extra information regarding the techniques and features are in [22,80]. Lastly, STATISTICA was the analysis tool, which helped to create a set of rules based on features, thus obtaining an overall classification efficiency of 92%.

In 2003 Zou, Y., and Guo, Z., have reviewed some techniques regarding EIT for breast cancer detection, the main comments suggest that is possible to determine whether is a malignant or benign tumor, thus, the malignant breast tumors have lower electrical impedance than the surrounding normal tissue [81]. Moreover, Zou, Y., cited a research article from 1926 ⁷, where is produce the first recorded ever of the electric capacity of a breast tumors (see [82]). To summarize, the suspension of biological cells or a biological tissue when placed in a conductivity cell, behaves as though it were a pure resistance in parallel with a pure capacity. In short, certain types of malignant tumors, have a rather high capacity in comparison with benign tumors or with inactive tissues of the same or similar character, they concluded [82]. Differently, Cheney, M., et al. have proposed a Noser Algortihm ⁸ approach to solve the EIT reconstruction's problem. It provides a reconstruction with 496 degrees of freedom, by images reconstructed from numerical and experimental data, including statistics from a human chest [83]. In brief, the previously methodology helped other authors to develop better electric models of the breast and tumors. The next section describes the foremost technologies and MLT regarding EIT.

3.2. Computer aided techniques and electrical impedance tomography

In 2007 Stasiak, M., et al. present a PCA analysis method together with neuronal networks for both localization and sizing of breast irregularities with EIT [84]. Recall that PCA is a statistical strategy for dimensionality reduction, used for transform a

⁷The journal of cancer research, AACR. Department of Biophysics, Cleveland Clinic Foundation, Ohio

⁸The inverse conductivity problem is the mathematical problem that must be solved in order for electrical impedance tomography systems to be able to make images [83]

n-dimensional space into a smaller space, taking into consideration the possibility of correlation between variables or features. The main advantage of PCA is the reduction in the quantity of features reducing the overall computational cost, but at the same time decreasing the accuracy. As an illustration, The figure 3 illustrate the sixteen-electrode arrangement on a typical EIT breast's test, where is applied a sinusoidal low current, then is measure the voltage differential between the electrodes. The Figure 3 right's side depict a tumor and the boundary interaction with the low current perturbations. Lastly, the simulated irregularity employs the boundary element method (BEM).

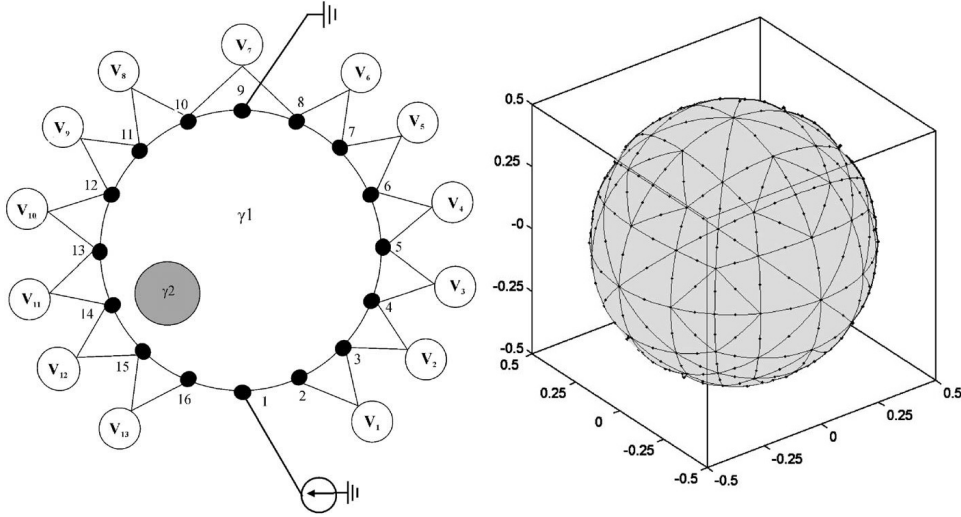


Figure 3. (Left) electrode-to-electrode configuration; (right) discretization of the internal perturbation with isoparametric element in normalized dimensions from [84].

The ANN have been making a huge impact in pattern recognition on several biomedical signals in the last years, thus, Zheng, B., et al. have made a study focused in resonance-frequency electrical impedance spectroscopy (REIS). With an initial set of 140 patients, including 56 who had biopsies, the performance of the overall system is evaluated with ANN and a case-based leave-one-out method [85]. The team makes an equidistance arrangement of a seven electrode-probe on each patient, and then the data goes to a CAD system for interpretation purposes. In addition to ANN for EIT breast cancer prediction, Shetive, et al. in 2012 create a multi-layer perceptron ⁹ (MLP) classifier model who achieved a 96% accuracy [86] on the Jossinet et al. database [22,80].

Similarly, logistic regression, KNN and Naive Bayesian networks were used by Calle-Alonso, F., et al. to classify the EIT data set from [22,80]. Furthermore, the key point in obtaining a global accuracy of 97.5% was transforming the possible six-classes breast tissue (or labels): (1) connective tissue, (2) adipose tissue, (3) glandular tissue, (4) carcinoma, (5) fibroadenoma, and (6) mastopathy, into two classes, (1) Carcinoma and (2) Fib+Mas+Gla . In essence, the table 4: "Acc-1" refers two-classes, "Acc-2" three-classes and "Acc-3" six-classes approach. Given these points, advances in EIT have allowed the construction of different devices able to map and create an Electrical Impedance Map (EIM), in 2015 one team have use the T-Scan 2000ED ¹⁰ on a population of 1.103 women, identifying 29 cancers. Indeed, a multiple logistic regression

⁹A class of feedforward artificial neural network, at least is composed by 3 layers

¹⁰T-Scan 2000ED, from Mirabel Medical Systems, Austin, TX

analysis associate clinical variables and EIS results in [87] study. Subsequently, Haeri, Z., et al. ¹¹., divulge a clinical study using a two different EIT devices, the first setup, is composed by a Covidien electrodes, spectroscop HF2IS and trans-impedance amplifier HF2TA from Zurich Instruments. The second setup, is EIS-Probe similar to the first one, but its electrodes and their location of installation are different, using least absolute deviation (LAD) and least square method (LSM) are implement for data's analysis [88]. Equally important Zarafshani, A., et al. propose a 85 electrodes board to create an Electrical Impedance Mammogram similar to an EIM, likewise, the main device is describe as a wide bandwidth EIM system using novel second generation current conveyor operational amplifiers based on a gyrator (OCCII-GIC) and the input current range from 10kHz to 3MHz [89]. Table 4 describes references regarding electrical impedance technologies.

Table 4. Summarized Electrical Impedance Tomography. The main parameters of evaluation are: Accuracy (Acc), sensitivity (Sen), specificity (Sp), AUC (area under the curve), ROC (receiver operating characteristic curve), correlation coefficient (CC) and mean square error (MSE).

Scope of the project	Machine Learning Technique (MLT)	Evaluation Result	Ref.
Impedance variability on six breast tissue, 9 different features, 1 target	No MLT	Mean (μ) Std. Dev. (σ)	[22]
Classification of breast sample tissues using STATISTICA®, 9 features, 1 target	Statistical analysis	Acc: 92%	[80]
Modeling of EIT distribution in a breast with a tumor, using ANN, PCA amd BEM	ANN	Abs. E: 0.23	[84]
Review of the main advances in EIT for breast cancer diagnosis	No MLT	–	[81]
First test ever of EIT in breast cancerous tissue (1926)	No MLT	–	[82]
REIS system with 7 electrodes, 1 in the center, and 6 concentrically separated. REIS showed high false positive rate	ANN	Acc: 67% Sen: 54% Sp: 90%	[85]
Multi-Layer perceptron algorithm for the EIT data set from [22,80]	ANN - MLP	Acc: 96% MSE: 0.1 CC: 0.99	[86]
CAD system for breast cancer classification in the EIT data set from [22,80]	LR + NBN	Acc-1: 97.5% Acc-2: 89.7% Acc-3: 77.35%	[90]
EIT system for early detection of breast cancer in 1103 women	Multi LR	–	[87]
10 women clinical study, using 2 different setups with a EIT-Probe	LDA, LSE	–	[88]
OCCII-GIC system for make a map of the breast, using 85 electrodes and frequencies from 10kHz to 3MHz	–	–	[89]

The background of the electrical impedance tomography as an early breast cancer diagnosis system, is consider above, nonetheless the EIT devices were not studied, with this intention, the next section, will present the main EIT devices, mostly are not on the market yet.

¹¹Study from: Fraser Health Authority and Jim Pattison Outpatient Care and Surgery Centre (JPOCSC) with study number FHREB2014-065 and 2015s0156, respectively

3.3. Main electrical impedance tomography devices

The EIT devices available on the market and research area are in Table 5. The main remarks towards this type of equipment, physical, is the number of electrodes, where range between 64 and 256, the method of measurement range from but no limited to the one where the patient is lying on the bed, a probe that a human-expert managed or a wearable bra. The electrical part includes the frequency and magnitude of the low-current signal, the electronic components, and the minimum detectable tumor's size. In general, these devices made part of a CAD system compose by an expert and algorithm that give insights of the probability of developing cancer. Likewise, each year more authors explain the advantages of combining CAD systems with human experts, changing the one-step into two-steps diagnosis systems. Nevertheless, a recent study use the bioimpedance analyzer MScan1.0B in 489 patients obtaining parameters as a function of permittivity and conductivity behavior on the breast, the Sn (92.4%), Sp (96.0%) results demonstrated the EIT feasibility and low-cost [91]. Given these points, Feza, H., et al. and Lima, G., et al. present two models of electro-thermal system for medical diagnosis. They have concluded that the improvement on the accuracy is greatly augmented when the techniques are employed the same time, rather than performing the diagnostic separately [92,93]. Likewise, Singh et al. [94] build a prototype of a general purpose EIT device, it use the a multifrequency electrical impedance in medical imaging, then, it is important to realize the main features, like resolution, number of electrodes, size, range of frequency and so forth.

”Insert table 5 here (the table must be in landscape mode, therefore, it should be let on appendices)”

The last advances in MLT and miniaturization have helped to create more accurate and robust system, indeed the Table 5 devices may vary depending on the size, but surely, the proposed by [19] is a huge advance in wearable devices for detect breast cancer. The next chapter reviews the most up to date system mixing both techniques, thermography and EIT.

4. Electrical impedance tomography and thermography combined systems

During the last decade, several authors present different works on electro-thermal architectures for breast cancer diagnosis. The electro-thermal word refers to systems made of both techniques EIT and thermography, usually, it is injected a low-current into the breast, in order to measure changes in the temperature's behavior of the breast. Feza et al. suggest that a hybrid system is need in order to improve the performance of breast carcinoma diagnosis, since each technique has weaknesses that are highly reduce in electro-thermal systems. Indeed, the method provides a better contrast resolution, in other words, tumors between 3mm and 9mm were saw with this CAD technique. In general, the method still being theoretical, nonetheless, it works as follows, first a low current is injected on the breast, afterwards an IR camera takes a snapshot of the breast. Under those circumstances, what will be the difference? In detail, the cancerous tissue has almost five to ten-times larger electrical conductivity factor than normal tissue, for that reason, the breast heat map will change and show other insights on the final image, in addition, the current's frequency may change the results, for that reason in [92], different parameters are tested. The Feza et al. system works

as presented in Figure 4, firstly, an electrical current goes through surface of the breast, controlling both, voltage and current. Secondly, an IR camera capture the breast surface temperature, afterward, a CAD system could provide a result using the mapped information.

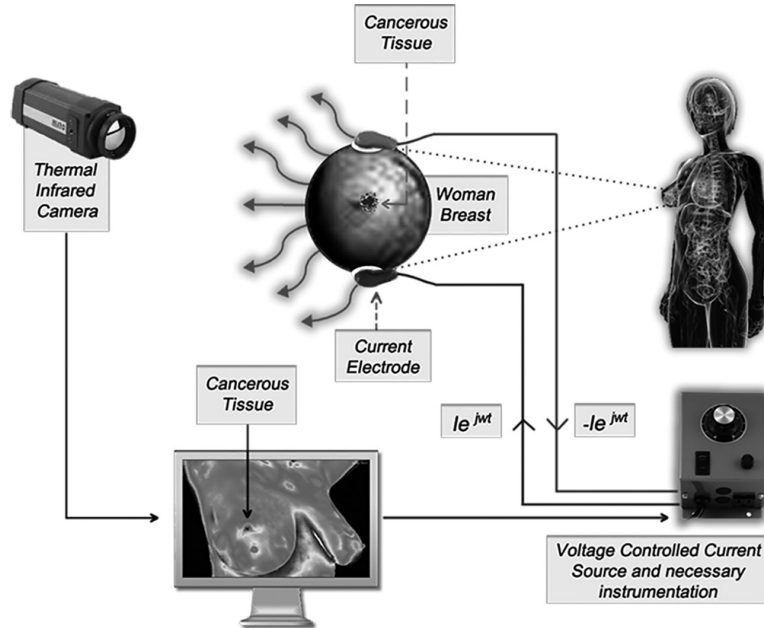


Figure 4. Block diagram of Feza et al. Electro-Thermal Imaging System, CAD and EIT system with IR camera [92].

A recent study from 2019 (Menegaz and Guimaraes) explain that some natural or unnatural (others diseases) processes in the human body, can lead to notably temperature gradients, as a result the thermography evaluation could give erroneous outcomes. The impedance was the ratio between the variations of the structure’s surface temperature and the external modulated heat flux. On the other hand, they validate the method with silicone phantom samples using hyperplastic materials with simple geometry. A damage metrics or “cancerous tissues” with different thickness measure the global performance in [93]. Nonetheless, is known that phantom tissue is commonly used for test new bio-electrical-based devices, but surely, real patients surely provide better insights. To finish, the next chapter discuss the overall review’s conclusions.

5. Discussion

The early-detection of BC plays a key role in reducing the mortality rate; nevertheless, many authors explain the limitations when only humans take part in the breast cancer judgement, occasionally with non-permissible false positive and false negative cases, consequently, the integration of CAD systems into the current BC screening methods, surely will boost the global performance. In addition, higher the confident rate higher the technique cost (as showed Table 1), therefore, many researchers have been working in develop new easy-to-use, intelligent and inexpensive systems for detecting BC. Indeed, these objectives allowed the inclusion of MLT in the pipeline for BC detection; Yassin et al. [62] review the MLT in medical imaging for BC, explaining that the biomedical information like image, signals or stacked data, are a complex

set of information that describe a person health. To emphasize, in many cases for a physician is hard to be completely sure in the diagnostic, likewise, many features are hidden to “human eyes”, even among experts. Under those circumstances, intelligent systems are capable of “see” these out of sight features that may perhaps increase the performance.

The increase in breast cancer deaths and prevalence (5-years window) have let rise new diagnosis techniques like thermography and electrical impedance tomography. Identically, the arguing in reducing the FN and FP cases, have been allowing the integration of CAD systems into the whole method or pipeline for BC diagnosis. A diagnosis system is made of a measurement phase, typically thermography, EIT, mammography, etc., afterwards a CAD system will pre-process, find hidden patterns, post-process and diagnose (the process may change depending on the measurement technique). Finally, a patient will get a result based on both, physician and the CAD system.

On the other hand, the data itself lies as main drawback in many ML pipelines, for example, Sathish et al. [65] have an accuracy increase of almost 20% in BC thermography diagnosis when feature engineering is applied (min-max normalization of thermal images). The feature engineering tries to pre-process the input data in a way that the computer can distinguish easier the target disease, for example, normalization, ROI segmentation, filters, polynomial features and dataset expansion, data augmentation, and so forth. In contrast, the cost, accuracy and wearability of the system are crucial factors to address, under those circumstances two questions arise. Firstly, is it the system suitable for high, middle or low-income communities? Secondly, it is sufficiently autonomous and robust the CAD system to accurately detect BC? Consequently, the Table 1 gives insights to assess those questions. This chapter deals with two significant points.

Firstly, the thermography has grown the last years as an important technique for BC diagnosis; in particular, the majority of studies have been targeting the only freely available database on the web [54,55] for thermal images. Unfortunately, opposed to other types of bio-medical databases (e.g., mammography, cancer cell images, ultrasound, MRI) there is not databases for thermography, aside the one above-mentioned. The best results across the reviewed MLT are ANN, DNN [2,65,72] up to 98%, SVM [2,53,68,70,72] up to 91% and RF [65] equal to 95% in accuracy, (see Table 2). It is important to realize that ANN models like CNN or DNN are more robust than a typical LR, SVM or RF. Artificial Neural Networks have the ability to identify hidden patterns that others models cannot. To point out, a CNN is made of units called “neurons”, layers and connection between layers, hence, higher the quantity of layer, higher the model’s deepness. Nonetheless, all the MLT have to deal with problems regarding underfitting, overfitting, hyper-parameters selection, architecture, banishing and exploding gradients, and so forth [62,63]. Finally, Borchardt et al. argue that the importance of feature extraction and interpretation are vital steps to achieve the desired performance, also they characterize the main public and private database and exhort the community to create additional ones, in order to support research teams [63].

Secondly, EIT is also a technique capable of detect BC however, fewer studies exist due the lack of public databases [22,80]. A part of the researchers are focusing in developing 3D models with diverse electrical tissue properties [84], another part in portable and non-portable devices [19,91–93,95,96] as shown in Table 6. Furthermore, the phenomenon and performance with CAD systems are reviewed [77,80–83,85–90,97], and finally, two teams suggest a considerable reduction in FP and FN rates in electro-

thermal CAD systems [23,98]. To put it differently, the miniaturization of electronic devices and the hyper-connection of a globalized world suggest that in the short-term future, many new wearable and portable devices will track our health day-to-day. Consequently, wireless and wearable devices will track breast health constantly, reducing the BC mortality rates. Nevertheless, still a debate about whether the data's structure could influence the performance, in detail, some EIT + CAD systems map the breast's bio-impedance creating an "image" [19,93,95], on the other hand, several systems prefer to obtain frequency-based parameters [22,23,80,91], like resistivity, phase angle, and so forth (see Chapter 3). Finally, some questions still unanswered, which EIT approach is better, image-centered or parameter-centered? Will be in the near future a standard protocol for EIT BC detection?

Thirdly, the BC might affect whomever woman, but specific considerations, like gene expression, nutrition habits, hereditary issues, dense breast and so forth, may increase the chances of BC. Indeed, new techniques like DNA (deoxyribonucleic acid) gene expression are tested for cancer diagnosis like breast, bladder [99], leukemia [100], human colorectal carcinoma [101], prostate [102], breast [103], and so forth. Even though, these techniques remain highly expensive for the middle and low-income patients.

Although the above paragraphs express the author's opinion, many questions still pending, e.g. is it abundantly and well balance the available databases? Is it necessary to follow a protocol prior to an EIT or thermal test? Is it enough the FP and FN rate or the current models still lack performance? Those questions may bring new insights in the future work that researchers will take. Lastly, the main purpose of this review is give insights to the readers about the current advances in thermography and EIT, for early-BC detection. Equally important, one aim was explain the importance of machine learning techniques as CAD systems key source. On the contrary, the lack of public databases is a huge problem that has been limiting the research outcomes in the two-discussed techniques for BC detection.

6. Conclusion

Thermography and EIT are not contemporary techniques for breast cancer screening, nevertheless, until the last years, the price of implementation, complexity and accurateness compared with similar techniques, diminished the chance of proliferation as a BC diagnosis technique. With this in mind, it is important to know about the last breakthroughs in techniques for BC detection prior to start a project, even the initial knowledge may change the outcomes and this review aims from assist new researchers' ideas about BC to deploy low-cost and affordable models using MLT. The state-of-the-art involve but not limited to the technique, background, application for CAD + MLT systems and last advances related with the three above-mentioned techniques are presented. The review explains the most popular MLTs, nevertheless, each year new methods, techniques and architectures become known, consequently it is difficult to compare the performance between several studies, likewise the available computational power increase each year, and the price's decreasing may affect the final pipeline. Despite the advantages of CAD systems, clinically, some countries present problem with the high rate of FP and FN, even when MLT are applied, thus, many systems need revision and rearrangement in how is implemented.

As mentioned through this review, there is global scarcity in public clinical databases. Furthermore, it is important to mention the benefits of publicity and standardization regarding clinical databases, where those could help research teams in

finding resources, create reliable links and develop new and robust models. We advise that future systems should be made up of two or more different databases, for example electro-thermal, electro-thermal-mammography system, where a patient's information "not directly related" with breast cancer support the global system. New ANN techniques like RNN and self-normalizing networks, auto-encoders, gradient boosting machines, or optimization methods like particle swarm, Parzen Tree, evolutionary algorithms, artificial bee colony and so forth, surely will increase the model performance giving the CAD systems the needed reliability for a wide implementation either, in hospital or new wearable devices. Therefore, the portable and wearable devices are promising trends that appeared in the last years, thus, developing reliable devices and machine learning libraries capable of measure the chance of having cancer, without the need of qualified personal and low-cost, will influence widely the research community and the global population. At the same time, is important to have in mind that the key goal is not to remove the physicians from the diagnosis part but strengthen the current ones. Finally, new programming libraries for machine learning developing, like Scikit-Learn [104] and TensorFlow [105] have been growing not just in quantity of MLT but also in optimization and robustness making them feasible as CAD systems.

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The authors have no conflict of interest to declare.

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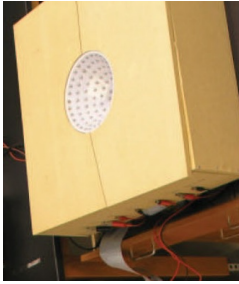


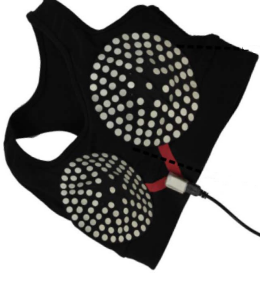
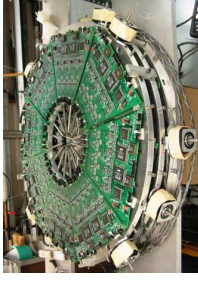
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Table 1. Comparison of breast cancer screening and diagnosis techniques, structured from [12].

Characteristics								
Technique	Mechanism of operation	Sensitivity	Specificity	Cost	Method	Wearable	Cause of discomfort	Recommend for
Mammography	Low energy X-rays	90%	>94%	Moderate	Compressed the breast	No	Pain in the breast	Screening and diagnostic
Magnetic Resonance Imaging (MRI)	Magnetic field and pulsating radio waves	90%	50%	High	Contrast substance injected and dynamic images obtained	No	Claustrophobia, reaction to contrast agent, renal insufficiency patients	Screening in women at high risk for breast cancer
Positron Emission Tomography (PET)	Gamma rays emitted by tracer substance	90%	86%	High	Small amount of radioactive tracer injected in the body	No	No	Determine if cancer has spread to other part of the body
Ultrasound	High frequency sound waves	82%	84%	Low	Hand-held or automated ultrasound device	No	No	Screening in dense breast
Tomosynthesis (3D Mammography)	Low energy X-rays	84%	92%	Low	Compressed the breast	No	Pain in the breast	Screening and diagnostic
Electronic Palpation Imaging (EPI)	Pressure changes	84%	82%	Low	Hand-held electronic, tactile sensor	Possible	Pain in the breast	Follow-up after abnormal findings
Thermography	Surface Temperature measurement	>90%	>90%	Low	Temperature sensors attached to the skin's surface	Yes	No	Screening
Electrical Impedance Tomography (EIT)	Electrical Impedance in the tissue	87%	82%	Low	Electrodes attached to the skin's surface	Yes	Tickling for current variation	Screening
Biomarkers from Blood Sample Test	Blood samples biomarker	82% 88%	- 90%	Low	Blood results and interpretation	No, test in situ	No	Screening

Table 5. Electrical Impedance Tomography devices and properties.

Reference	USA [23]	Russia [98]	Germany [95]	Korea [19]	USA [96]
Device					
Year	2008	2012	2001	2014	2007
Location	Bed	Hand-held device +ref. electrode	Probe + ref. Probe	BRA (wearable)	Bed
Dimension	11.7 cm height 19.1 cm diameter	16x18x10 cm	7.2x7.2 cm	30x25x5 cm	60 cm diameter
Weight	N/A	2 Kg	N/A	72g	N/A
Img. device	Computer	Computer	Computer	Mobile device	Computer
Dimension	2D slices	2D slices	2D	3D	3D
# electrodes	128 (7 layers)	256 (planar)	256 (planar)	92 (flexible)	64 (4 layers)
Frequency	10kHz	10 - 50 kHz	58 Hz - 5kHz	100 Hz - 100kHz	10kHz - 10MHz
Amplitude	1mA	0.5mA	1V - 2.5V	10 μ A - 400 μ A	N/A
SNR (dB)	77dB	N/A	N/A	90dB	94dB
Minimum detectable size	12mm	N/A	N/A	5mm	N/A