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RECENT ADVANCES ON ARTIFICIAL INTELLIGENT TECHNIQUES FOR BREAST CANCER DIAGNOSIS

Abstract. One of the most common causes of disease-related death among young women in almost every country in the world is the breast cancer. Valid and timely diagnosis of the breast cancer is vital, as its earlier identification considerably helps any further treatment. There are several methods for breast cancer identification. This paper acknowledges that the gold standard method of breast cancer identification is mammography, which can be further assisted with the adjunctive tool of thermography. For both these techniques there are many research approaches that use computer-aided detection systems to improve the detectability of the breast cancer which are based on these basic methods. The developments are mainly based on the recent progress in the field of machine learning techniques, numerical simulation and statistical methods. They span a broad range of the artificial intelligence (AI) field. The paper elaborates on these recent and future paths of progress in the field of artificial intelligence for breast cancer diagnosis.
Keywords: breast tumor, thermal patterns, thermography, artificial intelligence, Neural Network, Bayesian Networks.

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Аннотация. Одной из наиболее частых причин смерти молодых женщин от болезней почти во всех странах мира является рак груди. Правильная и своевременная диагностика рака молочной железы жизненно важна, так как его раннее выявление значительно помогает при дальнейшем лечении. Есть несколько методов выявления рака груди. В этой статье рассматривается, такие методы диагностирования как маммография и термография. Для обоих методов существует множество исследовательских подходов, в которых используются компьютерные системы обнаружения для улучшения выявляемости рака груди. Большинство разработок основаны на последних достижениях в области методов машинного обучения, численного моделирования и статистических методов. Они охватывают широкий спектр области искусственного интеллекта (ИИ). В статье подробно рас-

сматриваются возможные пути прогресса в области искусственного интеллекта для диагностики рака груди.
Ключевые слова: рак молочной железы, термография, искусственный интеллект, сверточная нейронная сеть, байесовские сети, машинное обучение.

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Түйіндеме. Сүт безі қатерлі ісігі ауруы әлемдегі барлық елдердегі жас әйелдер арасында жиі кездесетін аурулардың бірі болып табылады. Сүт безі қатерлі ісігін дұрыс және уақтылы диагностикалау өте маңызды, өйткені оны ерте анықтау одан әрі емдеуге үлкен көмек береді. Сүт безі қатерлі ісігін анықтаудың бірнеше әдісі бар. Бұл мақалада маммография және термография сияқты диагностикалық әдістер қарастырылады. Екі әдіс үшін де сүт безі қатерлі ісігін анықтауды жақсарту үшін компьютерлік анықтау жүйесін қолданатын көптеген зерттеу тәсілдері бар. Көптеген әзірлемелер машиналық оқыту әдістерінің, сандық модельдеу мен статистикалық әдістердің соңғы жетістіктеріне негізделген. Олар жасанды интеллект (ЖИ) өрісінің кең спектрін қамтиды. Мақалада сүт безі қатерлі ісігін диагностикалауға арналған жасанды интеллект саласындағы прогресстің ықтимал жолдары егжейтегжейлі қарастырылған.
Түйінді сөздер: сүт безі қатерлі ісігі, термография, жасанды интеллект, конволюциялық нейронды желі, байес желілері, машиналық оқыту.

Introduction. One of the most common causes of disease-related death among young women in developing countries is breast cancer [1]. Among the several significant causes, changes in the genome in a cell caused by various factors such as hormonal dysfunctions or external causes can lead to the development of cancerous cells. Genetic predisposition such as BRCA1 and BRCA2 genetic mutations, burdened family history, lack of childbirth, abortions and age are main risk factors that may cause development of tumor. Also, lifestyle with pernicious habits, like smoking, alcohol, obesity, lack of physical activities [3, 4]. As far as the successful treatment is concerned the stage of disease plays an important role in the recovery procedure [2]. In Kazakhstan, the annual rate of mortality per 100,000 women because of breast cancer has increased by 9%, which is 0.39% increment per year [5] since 1990 as seen in Figure 1. Statistics show that the breast cancer accounts for 11.7% of all cancer cases including both genders [6]. In 1991, breast cancer cases were around 10 cases per 100,000 citizens, after 22 years the number of cases has increased 3 folds. On the other hand, number of lung cancer cases is also steadily increasing, which is the main cause of the death among men (Figure 1).

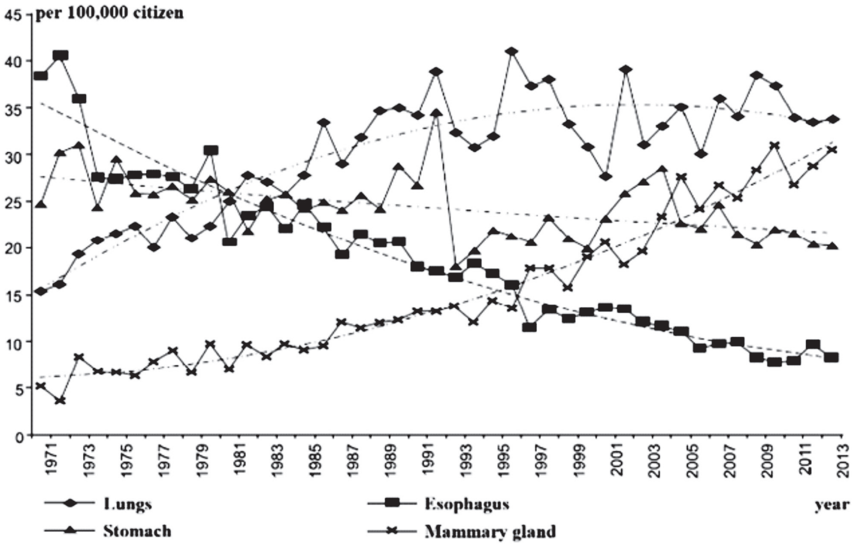

Figure 1 – The dynamics of cancer incidence of various localizations [7]

The last studies conducted by Medical University of Semey in Kazakhstan, revealed that 43.2% of cases are diagnosed at 3rd stage, 40.8% at 2nd stage, 14.2 % at 4th stage, and only 1.8% at 1st stage. According to the stages of cancer development, patients with stages 2 and 3 of the disease were more common (84% in total). This is because stage 1 breast cancer is only determined by mammography, without clinical manifestations. At the 4 stage cancer tumor is fully developed and the patients have sought medical help already. Therefore, these stages 1 and 4 are in the minority.

The diagnosis of cancer at early stages is crucial for treatment and reduction of mortality, when treatment can be started early while tumor size is small and does not have any symptoms. Therefore usage of the latest developments in technique and artificial intelligent can help in breast cancer diagnosing.

Methodology. *1. Bases.* The review paper consists of the scientific papers from such databases as: ScienceDirect, Scopus, PubMed Central, Research Gate, IEEEXplore, etc. In addition, the reference list of the papers were used to find the related papers.

2. Keywords. Different keywords and their combinations were used to find the related papers. The keywords include: “Infrared thermography”, “Deep learning”, “Artificial Intelligence”, “Numerical Simulation”.

3. Elimination and insertion criteria. To find the most relevant articles for the review the following criteria was considered:

Improvement in the performance of the system;

Recent developments in artificial intelligence approaches for breast cancer diagnosis;

Practical relevance of the study.

4. Critical Review and Analysis. The selected papers were reviewed and critically analyzed in terms of their strengths and weaknesses in the research presented and the technologies developed.

The gold standard method and artificial intelligence techniques. Currently, mammography is considered to be the most appropriate method for breast cancer detection. It consists of three stages: detection, analysis and final assessment/management. The first stage includes the breast mammography image segmentation into different types of regions, such as foreground (breast) and background. In the second stage in order to investigate the image in more details the set of ROIs (Regions of Interest) are extracted from it. Finally, the third stage will determine whether the tumor is noncancerous or cancerous. Based on the finding, final decision on the treatment can be made [7]. This traditional screening process is mostly performed manually and qualitatively by specialists. In many cases the findings are laborious and prone to human errors as some breast masses are not considered and these may turn out to be cancerous after biopsies [8]. To overcome this problem, automated mass detection systems using deep learning techniques have been investigated to improve the clinical practice by providing a consistent quantitative analysis and assessment approach with decrease in the dependence on radiologist’s experience. Many of the recent studies have focused on exploring deep learning using breast mammography by replacing or excluding some of the stages in traditional three-stage process. For example, Dynamic Neural Network (DNN) had been applied in breast mass detection and classification of ROIs into one of the determined categories [9-20]. The history of the medical decision support systems (DSSs), as well as clinical decision support systems (CDSSs) started almost 40 years ago. The first works in this field were Shortliffe, 1976, Miller & Masarie, 1989 [21,22]. In the beginning knowledge and inference of CDSSs consisted of the simple rules [21, 23-29]. Further development of the CDSSs lead to the embedding such rules and algorithm as: fuzziness Fuzzy logic, Bayes’ rule, Bayesian belief network, decision trees and artificial neural networks. Furthermore, in order to present temporal and spatial medical knowledge other CDSS comprise structural representations and special knowledge representation schemes [23-29].

Deep learning has demonstrated immense success in next-generation challenges such as object recognition in natural images, machine translation, and automatic speech recognition. This has attracted increased interests to apply deep learning techniques such as Deep Convolutional Networks (DCN) to medical imaging such as mammograms. Convolutional Neural Network (CNN) model is a deep learning technique used for the understanding of the images. The perspective of such networks has been presented by many researchers in the area of mammography. Domingues et al. [10] presented findings on binary classification between cancer and non-cancer breast mass lesions derived from the INBreast database. This was further developed by exploring deep learning methods for mass detection on mammogram images. Several classifiers were tested and special attention was given to Deep Learning methodologies and particularly the Support Vector Machines (SVM) technique. It was shown that these methods may find masses of different sizes in different locations. However, there could be a number of false positive results.

Carneiro et al. [17] presented a new way for identifying of masses from the mammograms by connecting deep learning with the random forest approach. The first stage of the system consists of the combination of the multi-scale deep belief network (m-DBN) [11,15] and Gaussian mixture model classifier for the selection of a set of regions that represent the breast masses. The second stage consists of a cascade of deep convolutional neural networks, which not only can decrease the number of false positive results, but also maintain most of the true positive results. The third stage extracts the texture and morphological features so that these can be further classified by a random forest classifier. Ertosun et al. [12] presented a deep learning-based visual search and localization of masses routine using mammography images. There are two modules. The first is the classification engine and the second is the localization engine. In the classification engine, the system classifies the mammograms to determine whether there is mass or no mass using a deep learning classifier. The next engine then localizes the mass or masses within the mammogram by exploring a regional probabilistic approach as leverage in a deep learning network. The accuracies of the first and second stages were 85%, and 85% respectively with an average of 0.9 false positives per image.

Becker et al. [18] presented the study of a breast imaging CADx system on the bases of the deep neural networks with transfer learning. The work compared previously developed analytically extracted hand-crafted CADx features, pre-trained CNN-extracted features, and an assembly classifier developed using both forms of features. The validation results show that the classifier with both types of feature had the best performance metric. Levy et al. [14] applied end-to-end CNN in order to categories breast tumour as cancer or non-cancer. The study used a combination of transfer learning, careful pre-processing and data-augmentation. The results showed a probability of 0.934 in recall at 0.924 precision. This surpasses human performance recall results which ranges between probability of 0.745 and 0.923. Arevalo et al. [15] presented the grouping of tumour in mammography, which aims to directly learn the content of these images using supervised learning. The framework uses the modern image features such as histogram of oriented gradients (HOG) and histogram of gradient divergence (HGD) descriptors. The assembly of learned and hand-crafted features led to the superlative descriptor for tumour classification.

Mordang et al. [16] dedicated his study on the detection of macro calcification candidates by using convolutional neural network. The findings indicated that CNN had a significantly higher mean sensitivity compared to the state-of-the-art method cascade classifier: 0.6914¥0.0041 (mean¥stdev) versus 0.6381¥0.0038 ($p<0.001$). The work concluded that CNN outperformed the cascade classifier in terms of sensitivity for the whole specificity range. The above review shows that there are a number of ongoing works in this field. Almost all these works are based on mammograms with very little emphasis on the preliminary mass screening stage. Currently the use of thermograms has not been fully investigated. There are long-term prospects to apply the techniques to thermograms. An integrated system for the early detection of breast tumor incorporating thermograms with cancer risk markers will complement the existing work with mammograms.

Thermography and artificial intelligence methods. It is well-known, that the probabilities for effective treatments of breast cancer are reliant on the stage of malignant tumors. The likelihoods are clearly higher as soon as the tumors are detected in the initial stages of growth. To improve the chances for effective treatment, the accuracy of early detection of malignant tumor is life-threatening. The first step of the process will involve the detection of tumor development. Thermograms will be suitable for this preliminary screening stage. The technique is based on the phenomenon of higher metabolic rates of growing tumors compared with surrounding tissues. This leads to hyperthermia, i.e. elevated temperature in surrounding regions of the breast. As such, thermal imaging can be used to identify and classify the growing tumor inside the breast. It is known, that each breast has a unique thermal pattern that should not vary with time, much like a fingerprint. With the development of a growing tumor in one of the breast, the thermal patterns of this breast will deviate from the baseline pattern. As the tumor grows, the deviation should increase. By continuous monitoring and comparing the thermal patterns of the left and right breasts over a period of time, abnormalities such as tumor growth can be detected. Any significant changes between the left and right breasts could define abnormal development inside one of the breasts and warrants an investigation. In the last two years we have been developing the intelligent system to identify the tumor position and size [29-36], which is based on patient specific data and inverse thermal modeling using design optimization techniques. This approach is simple and it provides the continuous personalized monitoring quantitatively without complex and expensive medical facilities. It is relative inexpensive and noninvasive with great potential for mass screening applications.

In real life medical problems, it is common practice to apply different Artificial Intelligence (AI) tools in order to provide practical and successful solutions. Artificial Neural Network (ANN) is a widely used analytical tool, which assists the physicians in diagnosis of patients with breast tumors. Ng and Kee [37] employed both ANN and bio-statistical methods to identify malignant tumors using thermograms. There were 82 patients thermograms analyzed, which consisted of 30 asymptomatic, 48 benign and 4 malignant. The inputs of the ANN were identified by the use of a regression analysis. The authors achieved 80.95% in accuracy in tumor diagnosing, whereas the accuracy of the radial basis function of neural network was 75% in unhealthy population, and 90% in healthy population. Mital and Pidarati [37] used several methods, such as ANN, genetic algorithm (GA) and thermal simulations together in order to bond temperature of skin surface with the locations of tumors in terms of tumor depths and sizes. The ANN was trained with tumor features in order to characterize surface temperature distribution. In addition, GA was employed to find suitable features of the tumors, based on a layered semi-spherical breast. Numerical simulation was used to find correlation between surface temperature distribution and simulated temperature distribution. The errors were within 5 and 2 mm in terms of the tumor depth and size, respectively.

The study in [38] investigated the application of ANN with thermography for the early diagnosis of breast cancer. It was concluded that without large population of data it was impossible to train reliable ANN. Therefore numerical simulation, as well as thermograms, were used for ANN training. Thus using numerical inputs can greatly improve the training, since changing tumor parameters in a numerical breast model produces new training data and the number of available cases becomes unlimited by the amount of clinical data. On the other hand to produce precise surface temperatures the numerical model applied must be well validated by clinical data. Saniei et al [39] trained a dynamic neural network to estimate the location and metabolic heat generation of the tumor in the breast based on the surface temperature distribution. Results of the research demonstrated that the estimation error of depth was higher than the estimation error of size. The deep-seated tumors had also larger errors than other cases. The findings matched actual parameters and offered the possibility of determination of necessary parameters from a group of surface temperature data.

Wahab et al [40] suggested to use multiple features retrieved from a range of numerical simulations carried out by the use of different tissue compositions of breast models which were fed into an optimized ANN system of 6-8-1 network architecture with a momentum constant value of 0.3, iteration rate of 20000, and a learning rate of 0.2. The total accuracy of 96.33% and 92.89% for testing and validation respectively was achieved. Pramanik et al [41] developed an automatic method of breast thermographic analysis. There are three main steps in the analysis: segmentation of breast regions from the original images, extraction of features, and classification and performance analysis by the use of the ANN. The first step was based on the Otsu's thresholding approach followed by a reconstruction method. The third stage based on the feed-forward ANN with gradient descent training classification of the thermograms were executed. The disadvantage of the study is the limited number of the thermograms, namely 306 thermograms of 102 breast cancer patients were employed. The accuracy, sensitivity and specificity obtained in the proposed system were 90.48%, 87.6%, and 89.73%, respectively. Raghavendra et al. [42], developed an preliminary screening computer-aided diagnostics system based on the histogram oriented gradients, which further uses kernel locality preserving projection (KLPP) to extract descriptors. The generated KLPP features are ranked and classified. To validate the developed system various machine learning techniques was used. The obtained results showed their effectiveness, where the accuracy was equal to 98%, sensitivity was 96.66%, specificity was 100% and area under the curve was 0.98.

Etehadtavakol et al. [43], conducted a study investigating lazy snapping method for the segmentation the region of interest. The study concluded that lazy snapping is one the most appropriate and effective methods for the segmentation, as it took short time to differentiate the hottest or coldest region of interest, in addition it produces results in the real time. Ragvahendra et. al. [44], presented the comprehensive revision of computer-aided diagnostics system for breast tumor screening using thermograms. The paper focuses on the advantages and disadvantages of the CAD systems, as well as suggesting further improvement of the system. The work can be used as a basis of further development of the CAD systems, that explore machine learning methods for the tumor detection. Thus, the reviewed articles showed high accuracy of the ANN used in combination with other approaches to diagnose the breast tumor. The results of the studies agreed with the actual parameters and the technology thereby has the potential to identify the required parameters from breast surface temperature data. Therefore, ANN, CNN can be further developed and integrated with other physics-based simulation methods for intelligent systems for the breast cancer identification. Another future research direction for AI in thermography is to use CNN as an AI-based diagnostic tool for breast cancer diagnosis as it has been applied successfully in using mammography due to its efficiency in handling images compared to ANN, but no research has been carried out to evaluate its capability in using thermography for diagnosis. Furthermore, it can be a potentially powerful patient specific diagnostic tool by combining it with physics-based reverse thermal modeling methods [31] as a front end fast screening tool.

Bayesian networks for medical diagnosis. Knowledge representation and decision-making are important tasks, in the field of medicine where many parameters are involved and interrelated to make a decision. Thus, several Artificial Intelligence (AI) methodologies and techniques have been applied to represent medical knowledge: production rules, semantic nets, Bayesian networks (BNs), frameworks, scripts, statements, logic, causal networks, etc. Perhaps one of the most successful tool for medical diagnosis is the Bayesian probability theory [45] based on representation of knowledge and approximation of reasoning with uncertainty [46-48]. Bayesian Networks (BNs) [46] proved to be effective in the decision support tasks emerging from a significant number of applications in the medical field [49] Bayesian Networks and Neural networks are very strong machine learning tools, but at the same time they are conceptually different. Modern Neural networks in the last ten years surprised all researchers with their incomparable ability to recognize patterns. Their applicability to real life AI problems attract the interest of many investors and companies. However, the way that they find solutions is a black box. Bayesian Networks on the other hand are very useful for medical like problems where one can build an expert model for diagnosis or for industrial problems of reliability and troubleshooting. Bayesian networks are conceptually different in the sense that they encapsulate the knowledge from data in variables that can be concepts of a domain expert. Furthermore, this is the only framework that can provide causal reasoning that explores causes and effects.

Bayesian networks (BNs) are probabilistic models that can encode any type of certain or uncertain knowledge. Thus, they provide a mathematically adequate way to set up a knowledge representation scheme. Furthermore, it is the only mathematically consistent way to make decisions. BNs can be associated with supervised or unsupervised learning techniques in order to utilize historic data and make intelligent predictions. With the help of BNs we can also discover causal connections. Given *n* variables $X_1, X_2, \ldots X_n$, a BN is a graphical factorization of the joint probability distribution of the n dimensional variable X with components X_i. A BN is defined by a directed acyclic graph “G” determining the conditional independencies among the variables of and a set of local probability distributions. There are also directed arcs from a variable X_i to another variable X_j, (*parent* of X_i). Let us name all the parents that variable X_i has as $Pa(G)_i$. This graph structure results in a factorization of the joint probability distribution for X:

$$p(X) = \prod_{i=1}^{n} p(X_i \mid pa(g)_i)$$

BNs have already been used in a variety of different engineering fields, yet only a few works utilize BNs for predictive maintenance. Among a large variety of machine-learning algorithms, those based on Bayesian Networks attract particular interest for handling diagnosis and troubleshooting. As the name suggests, BN are based on the Bayes’ rule, given by the following expression:

$$p(A \mid B) = \frac{p(B \mid A)\, p(A)}{p(B)}$$

where *p(A)* is the *prior* probability of an event *A* and *p(B)* is the normalizing constant. The prior probability *p(A)* can be viewed as an initial belief about event *A* before any information about event *B* is considered. The conditional probability *p(A|B)*, also called the *posterior* probability, represents the probability of *A* occurring given *B* has already occurred. Similarly, *p(B|A)*, also called the *likelihood*, is the conditional probability of *B* occurring given *A* has already occurred. Bayes' rule can be used to update the prior probabilities based on new evidence; this process is called the Bayesian inference. Given the effectiveness of BNs in causal reasoning in the engineering and medical fields, we hypothesize that they would have great potentials in applications in intelligent patient-specific breast cancer diagnosis.

Future development and directions. It is expected that patient specific diagnosis for breast cancer will be a major trend in future development in breast cancer research, which is based on technology advancements in medical imaging and scanning, AI and physics-based inverse simulation. For a successful identification of the tumor being cancerous, the thermograms must be integrated with risk markers such as age, medical conditions, lifestyles, dietary habits, genetics, etc. The thermograms need to be quantified and classified based on the associated parameters. Then they should be stored in correctly designed database, in which data mining and deep learning techniques can be applied to predict the development of cancerous tumors. The methodology known as risk markers for cancer existence on thermograms is still an open area of research. Another development is to combine data-driven machine learning with physics-driven inverse thermal simulation [31] for more patient specific and quantitative diagnosis of breast cancer. It is envisaged that the findings could further be exploited to assist in the quidance and teletraining of surgeons for cancerous breast operation procedures. Furthermore, computer-aided-diagnostics like the one under discussion can help medical experts from different countries to collaborate and discuss the treatment of complex cases.

Conclusion. Computer-aided diagnostics in healthcare have already confirmed its efficiency and accuracy. In particular, recent development and expansion in the field of thermography also show its effectiveness. The study presents a comprehensive review of the methods and techniques that can be used to identify the breast cancer at its earlier stages, which is very important for further treatment. In addition, it is shown that numerical simulation can be helpful in producing additional inputs for the artificial neural network or bayesian network. Therefore combining the physics-driven simulation, data-driven AI and thermography will likely lead to the development of revolutionary diagnostic systems for breast cancer.

Such a development of computer-aided diagnostics can further scale the real-time decisions resulting to a reliable expert model.

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