# Deep Learning for Cancer Cell Detection and Segmentation: A Survey

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# *Deep Learning for Cancer Cell Detection and Segmentation: A Survey*


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***Abstract*-The early stage cancer detection is required to provide proper treatment to the patient and reduce the risk of death due to cancer as detection of these cancer cells at later stages lead to more suffering and increases chances of death. Researchers have been working on and developing various deep learning solutions to produce encouraging results. In this paper, we explore the various techniques and technologies that are already in practice to detect the cancer cells in their early stages and works presently going on in the industry.**



***Keywords-Breast Cancer, Deep learning, Convolutional Neural Networks, Ultrasound, Prostate Cancer, Image Segmentation, Artificial Neural Networks.***


## I. INTRODUCTION

Various research activities on deep convolutional neural networks, image-processing, ultrasound-based cancer detection has been done in the past years. A lot of progress has been made in image processing and recognition, mainly due to the availability of large annotated datasets and deep convolutional neural networks (CNN). There is a lack of raw, latest and updated data for image processing in deep learning which seems to be the major challenge for data scientists for transferring the recent developments in the machine and deep learning to the medical domain. A strong prediction model is needed to assess the possible outcomes and thereby formulate procedures that can be carried out to curtail the possibility of cancer in patients.

Gliomas is a common type of brain tumor and researchers have conducted various image segmentation experiments on a set of 65 patients. The results showed that different algorithms worked best for different regions of the brain but there was no single model that could be classified as the 'one and only' solution to the problem.

Various machine learning and deep learning models are trained and tested for various different types of diseases and the results have shown that prediction and analysis sensitivity has improved multi-fold. Machine learning has seen a tremendous explosion of interest in the modern medical domain. The goal of this paper is to acquaint the reader with various modern technologies that have been employed in the deep learning field to solve medical issues like cancer cell detection and also to illustrate have these technologies can be used in medical imaging to improvise the analysis and diagnosis of medical conditions.

The following sections have been set as follows- the section (II) of the paper describes and summarises the various methods and technologies that have been tested and employed in the medical domain to detect the cancer cells using deep learning techniques, the section (III) is focussed on comparative study of deep learning technologies that have been employed in breast cancer and other general types of diseases and tumours and the section (IV) concludes and discusses the future works that can be performed in the deep learning domain to come up with a more refined and unique solution to predict and diagnose cancer among patients.

## II. METHODS

The below table summarises the various deep learning techniques that have been researched upon in the past and the various studies that are currently undergoing.

**Table 1**. The summary of various deep learning techniques employed in relation to cancer cell detection and segmentation.

| Problem Areas | Technology used |
|---|---|
| Brain Tumour | Brain Tumour Image Segmentation [3] |
| Cancer cell and tumor detection | CNN Architectures, Dataset Characteristics and Transfer Learning [4] |
| Prostate cancer detection | Targeted Contrast-Enhanced Ultrasound based detection [6] |
| Breast cancer | Deep learning from crowdsourcing [5] |
| To detect morphologic changes in chromatin arrangement | A decision support system [7] |
| Breast cancer evaluation | Her2Net: A deep framework for semantic segmentation |

| | |
|---|---|
| | and classification [8] |
| Prostate cancer recurrence | Convolutional Neural Networks (CNN) [2] |
| Colon cancer histology images | Locality Sensitive Deep Learning [1] |

*A. The Multimodal, Brain Tumour Image Segmentation Benchmark (BRATS).*

BRATS stand for Brain Tumour Image Segmentation Benchmark. It was organized with MICCAI conference in 2012 and 2013. The researchers applied 20 tumor segmentation algorithms to sixty-five MRI scans of low and high-grade gliomas patients. Gliomas is the most frequent primary brain tumors in adults. The results showed that different algorithms worked best for different parts and regions of the brain, but no single algorithm stood out the best from the rest. Benchmarking means to compare different machine learning algorithms against a particular solution. The first benchmark was organized on October 1, 2012, in Nice, France, in a workshop held as part of the MICCAI 2012 Conference [3]. The second benchmark was organized on September 22, 2013, in Nagoya, Japan in conjunction with MICCAI 2013.

*B. Deep Convolutional Neural Networks (CNN) for CAD (Computer Aided-Detection).*

Convolutional Neural Networks have come up as the latest trend in the deep learning domain for diagnosis and analysis of cancerous tissues and tumors. For data-driven learning, large-scale well-annotated datasets with representative data distribution characteristics are crucial to learning more accurate or generalizable models [4]. There are basically three methods to implement CNN model- 1) training/building the CNN model from the scratch, 2) the CNN model learns from the data available in a supervised fashion (supervised training) and, 3) the unsupervised training. The researcher Hoo-Chang Shin, Member, IEEE, and his team employed CNN to thoraco-abdominal lymph node (LN) detection (evaluated separately on the mediastinal and abdominal regions) and interstitial lung disease (ILD) detection [4].

The above research under Hoo-Chang Shin found that there is a trade-off between using either good training models or using more of the training data. If less training data is used then it may lead to the poor advancement of the CAD models. Deep CNN architectures with 8, even 22 layers [4] can be useful even for CAD problems where the available training datasets are limited.

*C. A deep learning approach for Ultrasound based Prostate Cancer Detection.*

Prostate Cancer is one the most common types of cancer these days and accounts for more than 30% of cases in America. In the past and even till date, the diagnosis of the cancer is painful and risky in many ways. It involves taking various samples from the prostate using core needles and moreover it carries the risk of infection, sepsis, and bleeding. However, researchers are working on better solutions for the easy and non-invasive diagnosis and treatment of cancer. The contrast-enhanced ultrasound (CEUS) imaging is under study. The CEUS is better suited for visualizing tumor angiogenesis because of its ability to highlight the blood flow in microvasculature [6].

The researchers conducted a number of experiments based on targeted and non-targeted CEUS data on more than 20 subjects. Each group (targeted and non-targeted) contained – the training set, a validation set, and the test set. The training set was used to fit the learning model and the validation set to evaluate the model. The test set was used to measure the accuracy and sensitivity of the model. The deep learning experiments conducted achieved 91% specificity and 90% average accuracy [6].

*D. Deep Learning from crowdsourcing for mitosis detection in breast cancer.*

Crowdsourcing is the new way to develop deep learning models. It is a participative activity wherein an individual, a group or an organization voluntarily undertake a task and the data thereby gained from the activity/survey helps to develop machine learning models. It is widely nowadays in the medical domain by researchers to obtain ground-data. The quality of the crowd is very essential in order to restrict “noisy” annotations. The data is collected from both reliable (expert) and unreliable (crowd) sources and thereby the behavior of the machine learning model developed is unpredictable. Unlike typical supervised methods, which learn a model from ground truth labeled data, learning from crowd annotations is different in the sense that there may be (possibly noisy) multiple labels for the same sample [5].

*E. Her2Net: A deep learning framework for Semantic Segmentation and classification of cell membranes and nuclei in breast cancer evaluation.*

Her2Net is a deep learning framework that classifies and segments the cell membranes and nuclei of stained breast cancer images. Breast cancer is the 2$^{nd}$ most common type of cancer only after lung cancer. About 10% of women in the USA and EU have been diagnosed with breast cancer at some point in their life. Usually, in clinical practice, the doctors analyze and visualize the biopsy tissues slides under a microscope. Such a diagnosis method is error-prone. Also, in many areas where expert pathologists are not available, the HER2 assessment becomes a difficult task.

To address these problems, digitization and quantitative image analysis of IHC slides have become essential. Thus, pathologists these mostly prefer performing quantitative image analysis using computer-aided digital techniques [8]. The main reasons for adopting digital pathology are its reproducibility and simplicity. Additionally, digital imaging technology is a pixel-based technology, which decreases the inter-observer variability and false positivity by improving detection, segmentation accuracy, and other factors [8]. The researchers concluded that Her2Net is reliable and feasible deep learning framework. It can also be integrated into computational

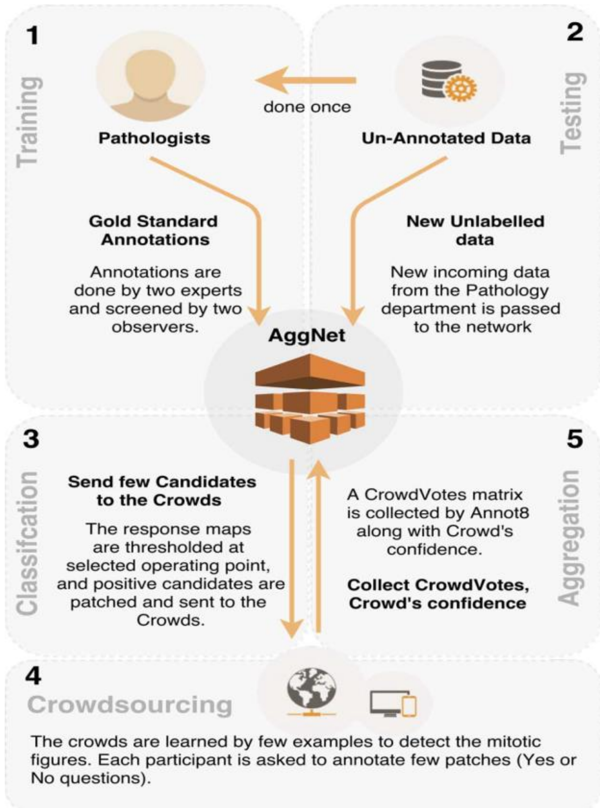


**Fig. 1**. *AggNet* Framework [5].

frameworks. The performance of the framework improves as the training set data is increased.

*F. Convolutional Neural Networks for Prostate Cancer Recurrence Prediction.*

Prostate cancer (PCa) is one of the leading causes of death among American men. In 2017, 161,360 new cases and 26,730 deaths are projected to occur due to PCa. Prostate-specific antigen (PSA) screening and the use of pathological and demographic variables such as the clinical stage, Gleason score, age, race, etc. remains the current gold standard in PCa treatment planning and decision making. PCa recurrence is a prominent cause of concern among the men undergoing curative treatment, especially radical prostatectomy (RP) [2]. The need for precise PCa recurrence prediction stems from the fact that about 16% of the PCa patients who undergo radical prostatectomy experience biochemical recurrence, signified by a rising serum PSA level, within 5 years of the surgery. This uncertainty poses a challenge for the treating physicians who want to minimize unnecessary treatments, and yet save lives.

There have been numerous attempts in the recent past to develop approaches based on quantitative image processing and machine learning to accurately predict PCa recurrence. Accurate prediction of recurrence at the time of initial diagnosis can allow medical practitioners to decide between treatment options such as radical prostatectomy, radiation therapy, chemotherapy, hormone therapy, and active surveillance for more indolent tumors. Accurate prediction of tumor response to treatment can improve long-term treatment outcomes and reduce risks due to unnecessary treatment.

There is an acute need for developing image processing-based recurrence prediction models because previous attempts to do so with clinical, pathological and demographic variables have not been able to accurately stratify the bulk of patients who fall in intermediate cancer grade such as Gleason scores of 3+4 or 4+3, and generally overestimate the recurrence probability for the low-risk patients [2]. It should be noted that in most image analysis-based approaches the available image data from several patients are often split into case-control pairs such that the cases include those patients who experienced biochemical recurrence after specified follow-up time (usually five years) and controls are the patients without recurrence. The case-control pairs are usually matched on the clinical and demographic variables such as age, Gleason score, pathological stage, and race to aid the development of novel biomarkers.

*a. The Approach.*

CNN's are the most popular deep learning models for processing multi-dimensional array data such as color images. A typical CNN consists of multiple convolutional and pooling layers followed by a few fully-connected layers to simultaneously learn a feature hierarchy and classify images. It uses error backpropagation - an efficient form of gradient descent - to update the weights connecting its inputs to the outputs through its multi-layered architecture. Researchers have presented a two-stage approach using two separate CNN. The first CNN detects nuclei in a given tissue image while the second CNN takes patches centered at the detected nuclear centers as input to predict the probability that the patch belongs to a case of PCa recurrence.

*G. Locality Sensitive Deep Learning for Detection of Nuclei in Colon Cancer histology images.*

Tumors have generally varying degrees of heterogeneity due to their ability to cause inflammatory response, angiogenesis and tumor necrosis. Researchers have developed various locality sensitive [1] deep learning models to detect and classify nuclei in hematoxylin and eosin (H&E) stained histopathology images of colorectal adenocarcinoma [1]. There are certain existing models like level sets, k-means and graph cuts and the recently proposed method is nucleus detection from H&E histology images.

The proposed deep learning approach is based on two premises: 1) distance from the center of the nucleus must be included into the calculation of probability map for detecting that nucleus, and 2) a weighted factor of local predictions for the class label can yield a more accurate result on a nucleus. The experiment was conducted on 20000 nuclei from different histologic grades. The CNN proved to be a useful tool for understanding the tumor microenvironment in a better way. The existing computing technologies such as parallel computing and graphical processing unit (GPU) [1] are detrimental factors to improvise the prosed framework for whole-slide histology images.

*H. A decision support system to detect changes in the chromatin arrangement in cells.*

There have been various studies on chromatin arrangement and the malignancy-associated changes (MACs) of chromatin arrangement is considered to be an invasive cancer area. MAC analysis and detection is a difficult task as it requires deep knowledge of morphologic features of chromatin network. Researchers are aiming to work on a decision support system (DSS) to automatically and objectively reproduce MAC diagnosis. The researchers took a set of 61 suspected lung cancer patients for clinical diagnosis. A DSS based on an artificial neural network has been set up to learn the relation between 14 morphometric and texture parameters, computed on each nucleus by image processing techniques, with the MAC diagnosis of the expert on each cell [7].

**Table 2.** Neural network classification against MAC morphologic analysis on a set of 20 patients [7].

| Patient | ANN Classification MAC+ cells % | ANN classification on patients | MAC Diagnosis | Follow-up |
|---|---|---|---|---|
| 1 | 0 | Negative | Negative | Negative |
| 2 | 1 | Negative | Negative | Negative |
| 3 | 10 | Negative | Negative | Negative |
| 4 | 8 | Negative | Negative | Positive |
| 5 | 8 | Negative | Negative | Negative |
| 6 | 13 | Negative | Negative | Unknown |
| 7 | 18 | Negative | Negative | Negative |
| 8 | 34 | Negative | Negative | Negative |
| 9 | 24 | Negative | Negative | Negative |
| 10 | 4 | Negative | Negative | Negative |
| 11 | 1 | Negative | Negative | Negative |
| 12 | 13 | Negative | Negative | Negative |
| 13 | 30 | Negative | Negative | Positive |
| 14 | 44 | Positive | Positive | Positive |
| 15 | 43 | Positive | Positive | Positive |
| 16 | 27 | Negative | Positive | Positive |
| 17 | 67 | Positive | Positive | Positive |
| 18 | 85 | Positive | Positive | Positive |
| 19 | 86 | Positive | Positive | Positive |
| 20 | 84 | Positive | Positive | Positive |

The accuracy of the classification model used on patients, compared with MAC morphologic analysis shows satisfactory results. The research concluded that morphometric and texture parameters related to biological -morphologic features, coupled with an ANN algorithm [7] is an efficient method to evaluate the expert assessments.

## III. A COMPARATIVE STUDY OF THE TECHNOLOGIES BEING USED TO DETECT CANCER CELLS

1. *Breast Cancer*

   Breast cancer is one of the most common types of cancer and leads to death if not diagnosed in its early stages. Recent advancements in deep learning have resulted in an early diagnosis of the disease. Researchers are constantly exploring better diagnosis methods so that the process does not become expensive and at the same time the patients don't have to go through painful biopsy procedures. Deep learning and image processing help to not only diagnose early but also predict the disease according to the features, microscopic images, and symptoms. The table summarises a few of them.

**Table 3.** Technologies currently in use to detect cancer cells.

| Research/Technology | Description | Results and Conclusion |
|---|---|---|
| Fuzzy method for pre-diagnosis from the Fine Needle Aspirate Analysis [9]. | The method employed is Fuzzy Method. It is based on computational intelligence. Fig 2 gives an appropriate description of the entire process of diagnosis. | This method provides 98.59% sensitivity and hence the diagnosis is more reliable. |
| Application of K-Nearest Neighbours Algorithm on Breast Cancer Diagnosis Problem [10]. | The machine learning classifier employed is the 'K-nearest neighbors' algorithm'. There are various perks of using this method: 1) It is simple to implement, 2) efficient for the small training set and 3) no need to retrain the model if the new training pattern is added to the existing pattern. | This paper analyses the Wisconsin-Madison Breast Cancer diagnosis problem. Though the same algorithm cannot be applied to all problems based on diagnosis. The KNN method has it set of disadvantages like storage issues etc. |
| Microcalcification classification assisted by content-based image retrieval for breast cancer diagnosis [11]. | The researchers worked upon microcalcification classification method assisted by mammogram retrieval for breast cancer detection. | This method proved to be very useful in improving the performance of the classifier by 78%-82% |
| A Multichannel Markov Random Field Framework for Tumour Segmentation with an Application to Classification of Gene Expression-Based Breast Cancer Recurrence Risk [12]. | The aim is to have reliable and accurate segmentation, efforts are to automate the process since the segmentation is tedious and expensive. It is a crucial process for image classification system. | The results showed that improved segmentation can lead to better extract the tumor characterization with applications on predicting the breast cancer. |

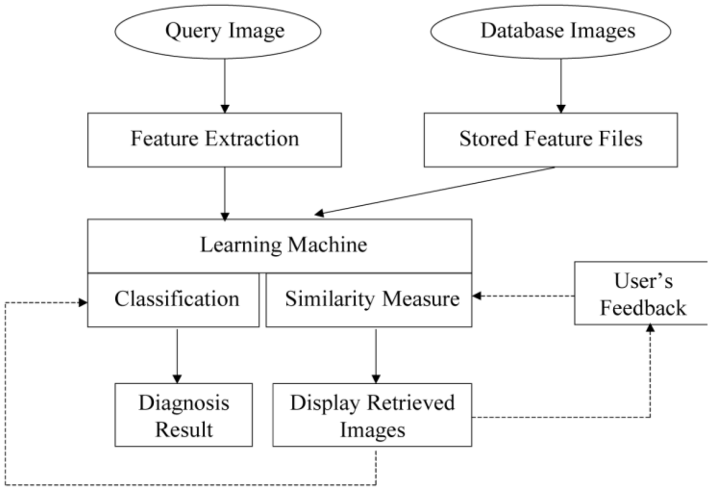


**Fig. 2.** The proposed content-based mammogram retrieval and classification framework [11].

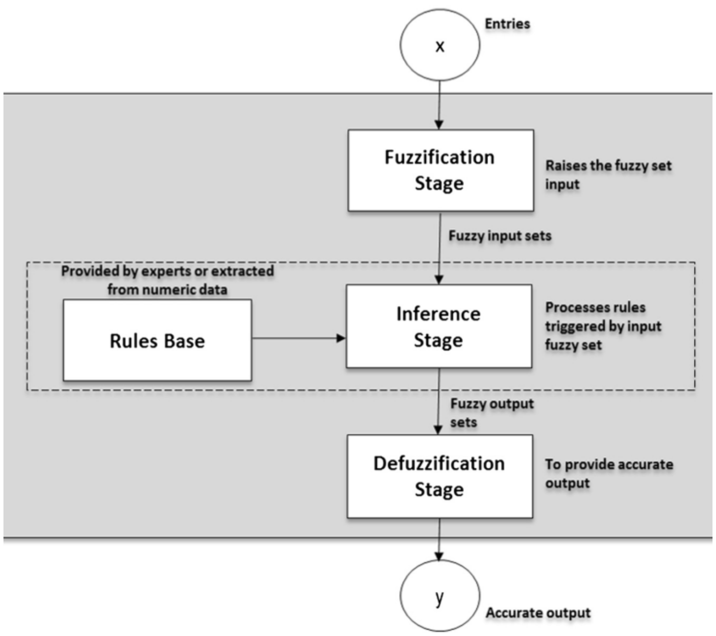


**Fig. 3.** Structure of Fuzzy System Process [9].

2. *General types of cancer and other techniques used in the biomedical and bioinformatics field.*

Detecting cancer at an early stage has been the focus area in the healthcare domain. Researchers have come up with different deep learning solutions and depending on various factors like data size, architecture (including deep neural networks (DNNs) and recurrent neural networks (RNNs)) and data type different levels of accuracy have been obtained. Deep learning has the potential to achieve good levels of accuracy in the diagnosis of cancers like breast, lung and cardiovascular. The algorithms are built on multiple processing layers of neurons.

**Table 4.** Technologies currently in use to detect cancer cells and help early diagnosis.

| Research/Technology | Description | Results and Conclusion |
|---|---|---|
| A machine learning approach for accurate annotation of noncoding RNA [13]. | The aim of this research is to search the genomes to locate the noncoding RNA genes which are quite important as it is modeled from the structure of a set of sequences from the family. Computing is needed from optimally aligning the sequence. The researchers developed a machine learning approach to efficiently search the genomes from the noncoding RNAs with high accuracy. | The model developed was quite fruitful as it captures the essential features of a ncRNA family. It models a sequence segment with a feature vector and a classifier to distinguish between a genome from ncRNA family and others. |
| Machine learning in Medical Imaging [14]. | The general research has been done on how machine learning algorithms can be used to classify, assess and predict diseases. The 'Support Vector Machines' and nonlinear models like 'The Kernel Trick' has been tested and analyzed. | The researchers compared the CSVM and CHO for the assessment of image quality in cardiac SPECT imaging. |
| Machine learning and biomedical engineering research [15]. | The main focus of this research is not to build classifiers as simply add-on towards a statistical analysis but to a more computational-intensive statistical technique called 'support vector machines (SVMs)'. | The results of this research were much more related to the assessment of the existing models of machine learning. The study did not focus not focus on any particular disease. |
| Detecting cardiovascular disease with deep learning [16]. | It has been noted that coronary artery disease is another major cause of death among women. The Breast Arterial Calcifications (BSCs) detected in mammograms are indicators associated | The results showed that deep learning is useful in efficiently developing an automated system for BAC detection in |

| | | |
|---|---|---|
| | with the disease. The researchers developed a 12-layer CNN to distinguish a BAC from a non-BAC. | mammograms so that the patients are identified and assessed accordingly with the cardiovascular risks. |

## IV. CONCLUSION AND FUTURE RESEARCH DIRECTIONS

This paper summarises the various technological advancements and deep learning models that are currently under study and also in use to detect and segment the cancer cells and tumors. Image analysis and Convolutional Neural Networks (CNN) has resulted in early and quick diagnosis of the cancer cells so that the treatment is done timely and the patient does not have to suffer at a later stage. There is a vast scope of improvement in the deep learning models. Future work on deep learning models can increase the sensitivity and accuracy of the predictive model.

The focus is also to create a more unique model can fit the needs of various diagnosis issues. Currently, there is no single algorithm that can resolve various predictive problems at once. There is also a lack of ground-truth data that can be processed to formulate a 'perfect' model and this sometimes leads to 'over-fitting' or 'under-fitting' of the model. Active research is going on to come up with an all-round deep learning solution to cancer problems.

## REFERENCES


1. Sirinukunwattana, K., Raza, S. E. A., Tsang, Y. W., Snead, D. R., Cree, I. A., & Rajpoot, N. M. (2016). Locality sensitive deep learning for detection and classification of nuclei in routine colon cancer histology images. *IEEE transactions on medical imaging*, *35*(5), 1196-1206.
2. Kumar, N., Verma, R., Arora, A., Kumar, A., Gupta, S., Sethi, A., & Gann, P. H. (2017, March). Convolutional neural networks for prostate cancer recurrence prediction. In *Medical Imaging 2017: Digital Pathology* (Vol. 10140, p. 101400H). International Society for Optics and Photonics.
3. Menze, B. H., Jakab, A., Bauer, S., Kalpathy-Cramer, J., Farahani, K., Kirby, J., ... & Lanczi, L. (2015). The multimodal brain tumor image segmentation benchmark (BRATS). *IEEE transactions on medical imaging*, *34*(10), 1993.
4. Hoo-Chang, S., Roth, H. R., Gao, M., Lu, L., Xu, Z., Nogues, I., ... & Summers, R. M. (2016). Deep convolutional neural networks for computer-aided detection: CNN architectures, dataset characteristics and transfer learning. *IEEE transactions on medical imaging*, *35*(5), 1285.
5. Albarqouni, S., Baur, C., Achilles, F., Belagiannis, V., Demirci, S., & Navab, N. (2016). Aggnet: deep learning from crowds for mitosis detection in breast cancer histology images. *IEEE transactions on medical imaging*, *35*(5), 1313-1321.
6. Feng, Y., Yang, F., Zhou, X., Guo, Y., Tang, F., Ren, F., ... & Ji, S. (2018). A Deep Learning Approach for Targeted Contrast-Enhanced Ultrasound Based Prostate Cancer Detection. *IEEE/ACM Transactions on Computational Biology and Bioinformatics*.
7. Sacile, R., Montaldo, E., Ruggiero, C., Nieburgs, H. E., & Nicolò, G. (2003). A decision support system to detect morphologic changes of chromatin arrangement in normal-appearing cells. *IEEE transactions on nanobioscience*, *2*(2), 118-123.
8. Saha, M., & Chakraborty, C. (2018). Her2net: A deep framework for semantic segmentation and classification of cell membranes and nuclei in breast cancer evaluation. *IEEE Transactions on Image Processing*, *27*(5), 2189-2200.
9. Sizilio, G. R., Leite, C. R., Guerreiro, A. M., & Neto, A. D. D. (2012). Fuzzy method for pre-diagnosis of breast cancer from the Fine Needle Aspirate analysis. *Biomedical engineering online*, *11*(1), 83.
10. Sarkar, M., & Leong, T. Y. (2000). Application of K-nearest neighbors algorithm on breast cancer diagnosis problem. In *Proceedings of the AMIA Symposium* (p. 759). American Medical Informatics Association.
11. Wei, L., Yang, Y., & Nishikawa, R. M. (2009). Microcalcification classification assisted by content-based image retrieval for breast cancer diagnosis. *Pattern recognition*, *42*(6), 1126-1132.
12. Ashraf, A. B., Gavenonis, S. C., Daye, D., Mies, C., Rosen, M. A., & Kontos, D. (2013). A multichannel markov random field framework for tumor segmentation with an application to classification of gene expression-based breast cancer recurrence risk. *IEEE transactions on medical imaging*, *32*(4), 637-648.
13. Song, Y., Liu, C., & Wang, Z. (2015). A machine learning approach for accurate annotation of noncoding RNAs. *IEEE/ACM Transactions on Computational Biology and Bioinformatics (TCBB)*, *12*(3), 551-559.
14. Wernick, M. N., Yang, Y., Brankov, J. G., Yourganov, G., & Strother, S. C. (2010). Machine learning in medical imaging. *IEEE signal processing magazine*, *27*(4), 25-38.
15. Foster, K. R., Koprowski, R., & Skufca, J. D. (2014). Machine learning, medical diagnosis, and biomedical engineering research-commentary. *Biomedical engineering online*, *13*(1), 94.
16. Wang, J., Ding, H., Bidgoli, F. A., Zhou, B., Iribarren, C., Molloi, S., & Baldi, P. (2017). Detecting Cardiovascular Disease from Mammograms With Deep Learning. *IEEE Trans. Med. Imaging*, *36*(5), 1172-1181.