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Deep learning recognition of diseased and normal cell representation

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Abstract

Cell classification refers to detecting normal and diseased cells from small amount of data. Sometimes, classification of cells becomes difficult because some cells fall into more than one categories/classes. Current state-of-the-art cell classification methods have been developed on the bases of tumor cell classification but these methods cannot classify diseased or normal cells. This study investigated the performance of two classification methods traditional machine learning and deep learning (normal and diseased cell classification) to categorize normal and diseased cells. Millions of normal cells undergo controlled growth and uncontrolled growth may be involved in disease causation but their clinical applications remain limited due to difficulties in distinguishing normal and diseased cells. Previous studies are limited to identify, systematically, the normal and diseased cells. This study collected information about diseased or normal cells to check the networks for correct cell detection and then eliminated false-positive cells. We used machine learning methods along with logistic regression, support vector machine, and CNN (convolutional neural network). We found that our proposed method classified better the normal and diseased cells. With the help of two types of images: normal and diseased cells, we trained a CNN that identified diseased cells with 98% accuracy and enabled the discovery of normal and diseased cells. As a result, it will advance the clinical utility of human diseased cells.

1 | INTRODUCTION

Classification of diseased and normal cell is a complex process, which has been mainly applied to identify and differentiate tumor and numerous types of diseased cells while diagnosing and investigating medical diseases. Living organisms

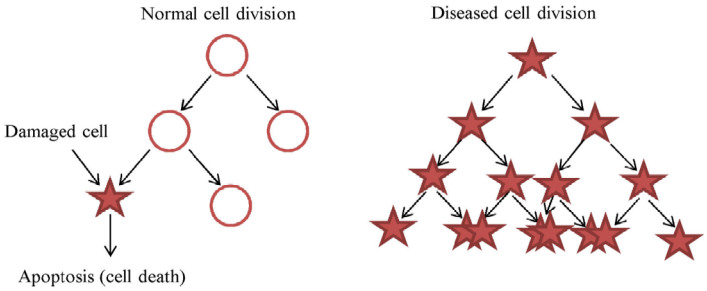

FIGURE 1 Normal and diseased cell division

are made up of cells with specific lifespan. Some cells such as liver cells live for a number of days (300-500 days) and can be replaced by new cells. When healthy cells are injured or damaged, they are removed and replaced with new healthy cells. Normally, healthy cells grow in a controlled manner, but sometimes they may grow in an uncontrolled way and turn into diseased cells (tumor cells) (Figure 1). Investigations of cellular dynamics of normal and diseased cells require cell classification. Some cell classification methods are blood image segmentation, blood smear segmentation using deep learning,[1] overview of medical image and deep learning,[2] leukocyte segmentation,[3] and red blood image segmentation.[4] The Watershed algorithm[5] is a growing method which is often used for fluorescence microscopy images and cell segmentation.[6-10] The efficacy of the segmentation method depends on the determination of a single seed point within each segmented cell. An error can be manually corrected otherwise the segmentation gives an error. However, this manual image correction can be time-consuming. Current machine learning approaches of image detection such as logistic regression (LR), SVM (support vector machine), and LR + SVM[11,12] use hand-made characteristics such as shape, pixel density, texture, and off-shelf classification. Cell image features are classified on the bases of analysis of histopathological image features[13] and HEp-2 cell IIF images,[14] detection of cancer cells by SVM and random forest tree,[15] and classification of apical echocardiograms.[16] Deep learning method is used to investigate medical injury.[17] This method is also used in different other fields like IoT, and its performance is better than traditional techniques.[18-21]

Traditional methods have been used to classify simple cells, but none of these methods are applied to classify normal and diseases cells. Non-deep-learning methods are mainly limited due to their dependence on the extraction phase of the feature. This dependence makes it challenging to identify and extract images with features that are suitable for a specific medical-image recognition problem. In the samples where images lack effective features, to obtain satisfactory results becomes difficult due to the off-shelf classifier. The use of deep learning, with method clinical applications, especially in medical diagnosis, has become popular.[22-29] Convolutional neural network (CNN) was primarily used for image data.[27,29-35] In past, different methods have been used, however, some of them are time consuming and can only be used as a manual collection method (eg, heart contour tracking). In high-dimensional problems such as image recognition, deep learning has outperformed among other methods used in past.[16,36-38] Up till now, no reliable study is available to classify diseased and normal cells. Only a few studies have classified cells without differentiating diseased and normal cells,[1-4,27-29] normal cell and drug treated cell,[28,29] mitochondrial cell movement,[27] and blood image segmentation.[1-4] In this study, we described methods that differ diseased cells from ordinary cells and thus, it becomes a specific contribution in the efficient classification of diseases and normal cells. Five different methods were implemented: LR, SVM, LR + SVM, and deep learning (ResNet-50, ResNet-152). Deep learning has been much better than conventional machine learning methods. We tested CNN ability to identify, automatically (without the need for manual harvesting), common diseases and normal cells. The proposed model achieved an overall accuracy of 98% based on the image. The main objective of this study was to classify, through cells imaging by using traditional machine learning vs deep learning normal or diseased cells.

2 | METHOD

2.1 | Dataset

Images of normal and diseased cells were captured by confocal microscopy. Nine pictures of normal cells images are shown in Figure 2. Pictures from 1 to 6 show minor variations in normal cells position. Figures 1 and 2 show normal cells

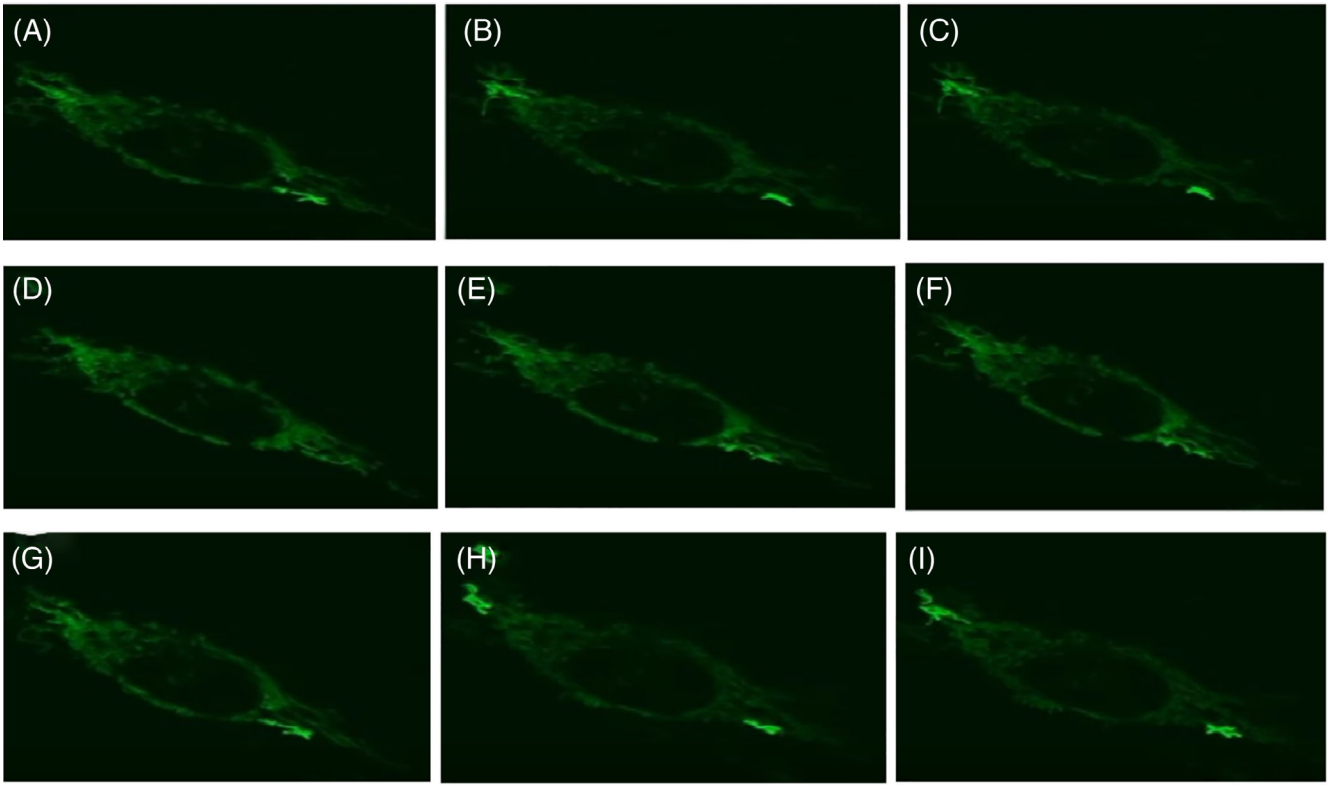

FIGURE 2 Normal cell images

TABLE 1 Diseased and normal cell images

	Data description		
Image types	**Number of images**	**Training**	**Test**
Normal cells	38	30	8
Diseases cells	38	30	8

that got damaged after sometimes, normal cell apoptosis, and renewable cells. Figure 3 shows, nine pictures of diseased cells, no variations, cell growth is continuous without any sign of apoptosis or replacement of old cells by new healthy cells. Table 1 exhibits in detail the dataset used for the experiments. We have used the 60 images for training and 16 test images.

2.2 | Normal and diseased cells classification

Traditional machine learning methods have significantly contributed in the medical imaging of neurodegenerative diseases, breast cancer, and psychiatric diseases.[12,39-41] In the field of medical imaging, deep learning is now common especially in imaging data by using CNN (Convolution Neural Network).[42-47] Deep learning enables the identification of adaptive image features and performance of image classification simultaneously. This has achieved a significant improvement in image recognition. Deep learning has the potential to classify diseased and normal cells. This work is based on traditional machine learning and deep learning methods, the classification of diseased and regular cells. Deep learning used normal or diseased cells images as input and CNN, was used to select the features and map them, and finally classify the results of diseased or normal cell image (see Figure 4).

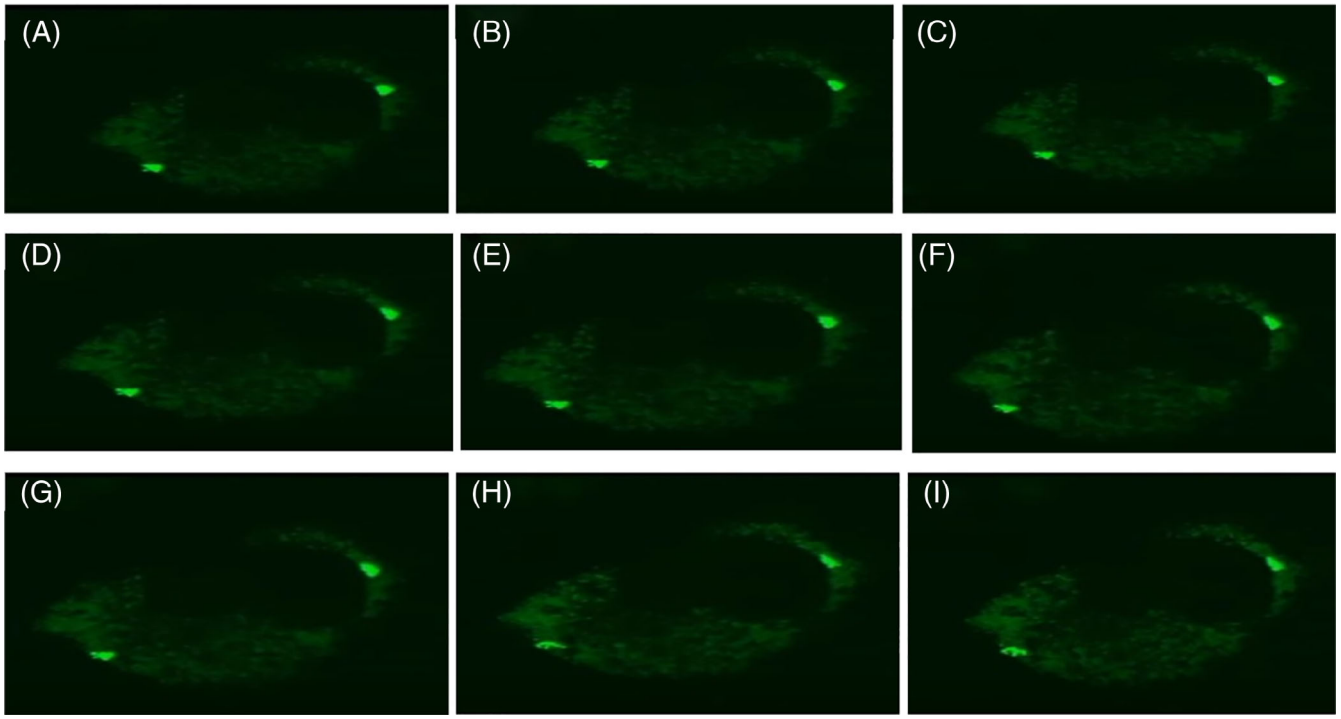

FIGURE 3 Diseases cell images

2.3 | CNN's (neural network) algorithm

The method is developed by using Resnet-50, Resnet-152, the deep neural network architecture with 52, and 152 layers. Caffe DL (deep learning) framework was used to train, test and validate our proposed method. The ResNet-152 is a deep residual pre-trained convolution neural network.[48] RestNet-152 is the deepest network, which presented by ImageNet in 2015 and extremely net depth up to 152 layers.[48] The residual framework allows an easy way to train the network to increase the coverage and accuracy. The main advantages of residual network inputs are speeding up the training of the network, reducing the impact of the gradient problem, increasing the size of the network, and resulting in fewer parameters. The ResNet-152 has residual connections which allow the transferring of important information between layers. The gradient can move layers with the ResNet-152 without losing any information. The gradient moves through the standard neural activation layer of the network which reduces the gradient. In order to avoid this problem, a link inside CNN allows gradients to pass through. This decreases the effect of information loss. In comparison to other methods, ResNet-50 increases accuracy and lowers training time.[48] The authors of residual network have compared their framework with other CNN's methods and have shown that ResNet-152[27] is 8× deeper than visual geometry group nets.[49] We intend to use the residual network (ResNet-50 and ResNet-152) and have pre-trained CNN with diseased and normal cell image dataset[29] for new extracted feature. We used Resnet-50 and Resnet-152 architecture, in Figure 5 and also calculated feature vector for all images. Figure 5 depicts diseased and normal cells as input images, convolutional layers, layer pooling, and classification of normal and diseased cell images.

3 | RESULTS

3.1 | Heterogeneity between cells

On the basis of normal and diseased cells, we identified subtle differences between normal and the diseased cells (see in Figure 8 histogram shifting). All cells had heterogeneity, we used image J tool to check the diversity of these cells. Figure 8 shows the histogram of cells. It was very difficult to classify the normal and diseased cells, because every cell had different values. In Figure 8 first graph represents the first normal cell histogram and graph third shows second normal

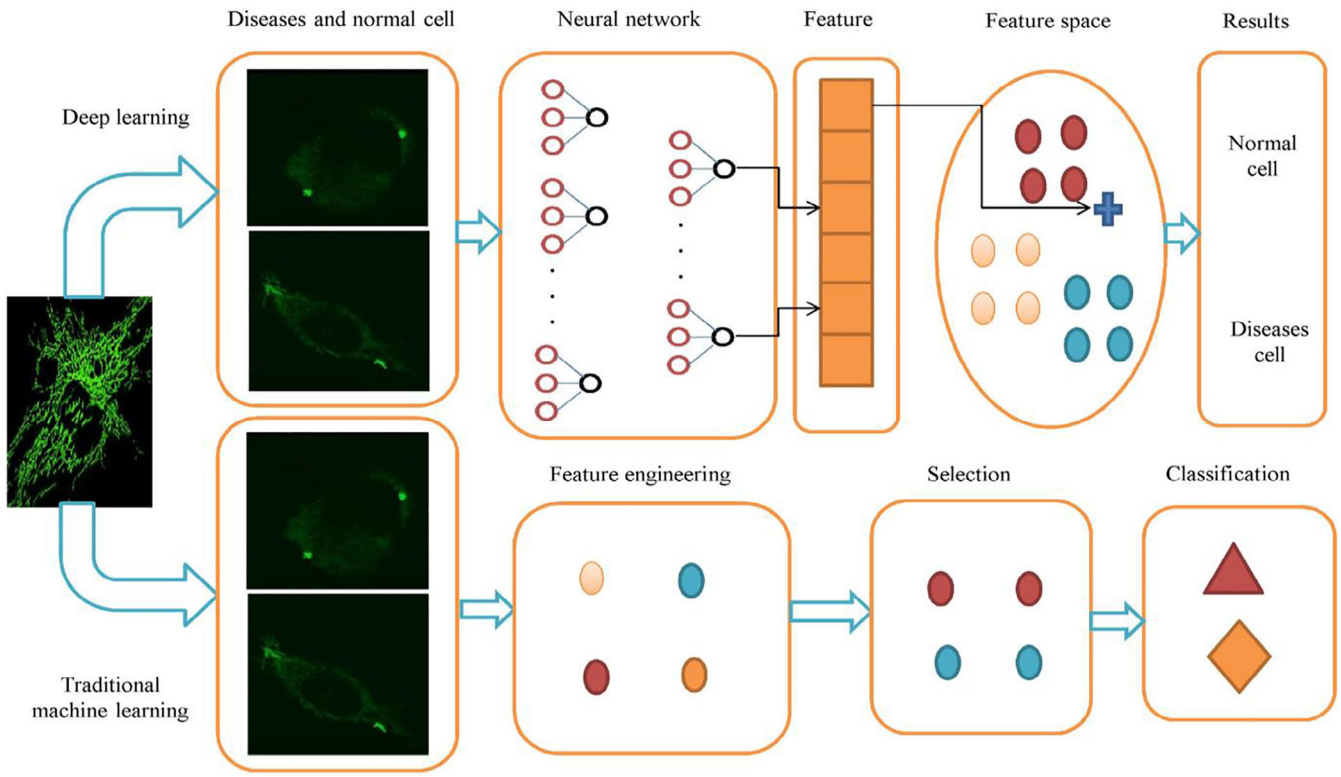

FIGURE 4 A framework of the proposed method NDCC (normal and diseased cell classification), used traditional machine learning and CNN

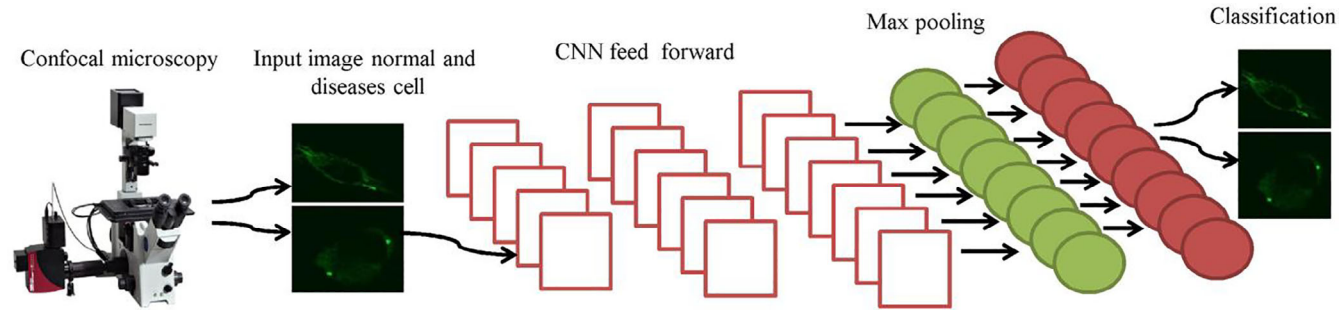

FIGURE 5 CNN for the identification of diseased cells by cross entropy classifier. CNN classifies the normal cell images and detects the part of diseased cells, and is trained to identify the normal cell

cell histogram, so, they have heterogeneity. In Figure 8, graph second and four shows the histogram of diseased first and second cell. Our method clearly classifies the normal and diseased cells.

3.2 | Variation between normal and diseased cells

The SD for normal cell and normal cell proportions is shown in Figure 6A-D. Figure 6A shows the first SD of normal cells and B shows the second SD of normal cell (see Figure 6, graph 1). In Figure 6C,D, these images were taken after 1 hour. Figure 6C highlights first norm difference of the normal cells after a long time (5 minutes) and D shows the second SD of the normal cells after long time (5 minutes) (see Figure 6, graph 2). Figure 7E-H displays the SD of diseased cell and diseased cell probabilities in pixels. Figure 7 figures out the first and second SD of diseased cells in graph 3. Figure 7G,H illustrates images taken after 1 hour. The first and second SDs of the diseased cells after long time (5 minutes)

TABLE 2 Results of various methodologies in which the efficacy of the proposed model is demonstrated by the "NDCC"

	Predicted accuracy of diseased and normal cell images	
Methods	**Data types**	**Accuracy**
Logistic regression (LR)	Normal/diseased cell image	0.85
Support vector machine (SVM)	Normal/diseased cell Image	0.90
LR + SVM	Normal/diseased cell image has a high accuracy	0.93
CNNs (NDCC)	Normal/diseased cell image	**0.98**

Note: The NDCC better categorized the normal and diseased cell.

are displayed in Figure 7G,H and graph 4. The white box plot shows the results for slides containing normal and diseased cells.

3.3 | Histogram of features and classification of diseased and normal cells

Through histogram pattern, the features are extracted which shows that the pattern varies in with the chambers that make classification easier. However, it was difficult to classify the normal and diseased cells through histogram features. Our method automatically classified the normal and diseased cells with high accuracy, and reduced the mixing between the normal and diseased cells. Figure 8A,B, highlights the histogram of normal and diseased cells. Each normal image had two cells as Figure 6 displays. Similarly, the image of diseased cells also had two diseased cells that Figure 7 pinpoints. The regular cell histogram is shown in Figure 8C,D. Figure 8E,F shows the histogram of the diseased cells.

In this study, deep learning achieved very high-levels of diseased and normal cell classifications, similar type of images, which were obtained through trained CNN Figure 5. Cell imaging is a quantitative measurement of diseased and normal cells that can be identified as potential tumor cells and is based on synthetic biological image data that are useful for medical diagnosis. The most advanced image processing method for diseased cells with advantages closely related to medicine and tumor variability associated with diseased images. The overall objective of the normal and diseased cell image classification normal and diseased cell classification (NDCC) process, is based on ResNet-152, ResNet-50, and some old-style machine learning (ML) methods (LR, SVM, LR + SVM), is to detect normal and affected cells in the centered region. The study focuses on dual goals: first, to select regional features of diseased cells, and second, to classify features with a high probability as Figure 4 elaborate. To test the accuracy of the proposed method (NDCC), we compared machine learning with deep learning using scale-invariant feature transform functions and BoW models. Figures 11 and 2 show the statistical value of this approach. The accuracy differences between ML and DL, are CNN (98%), ResNet-50 (98%), ResNet-152 (66%), LR (85%), SVM (90.5%), and LR + SVM (95%) as depicted in Table 2. The results suggest that deep learning performed better than other machine learning methods. Among non-deep learning, ResNet-50 performed better than other methods, particularly, ResNet-152, which needed more dataset to perform optimally as the dataset was small to yield meaningful results. Figures 2 and 3 figure out total 64 images: 38 images of normal cells and 38 images of affected or diseased cells which were reserved for dual purposes: as input and as data divided for training (diseased, normal), testing (diseased, normal), and forecasting images of the cells. Validation, test and training data were split by in this article, and for training and validation of model, tested data was not used. The model was trained in image grading, with the majority voting on image frames as a video classification. Figure 5 reveals CNNs for diseased cell classifications. The recall and precision of resent-50 is 99.10 and 0.98.11.

3.4 | Distinguishing diseased patches

The image dataset was spilled in training, validation, and testing (see Section 2). The CNN was trained on the training dataset. The training process stopped at the 100 epochs. Figure 9 reveals the training, testing, and losing of CNN along with its overall accuracy test, that is, 98%, and its training accuracy is 98%. The accuracy of diseased cells is 98% (see

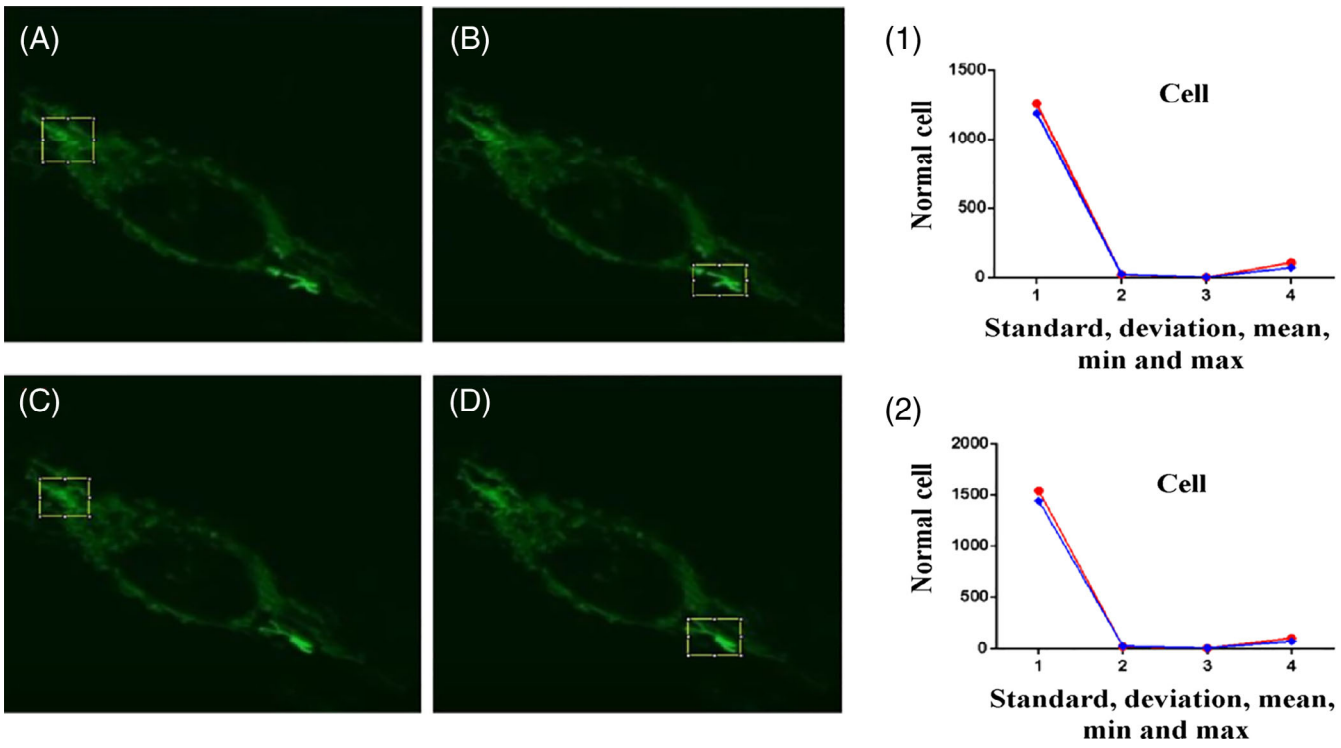

FIGURE 6 Normal cells (A) and (B) (short term monitoring) are shown and their SD and mean are displayed in Graph 1 and normal cells are in (C) and (D) that is, long term monitoring and their SD and mean are shown in Graph 2

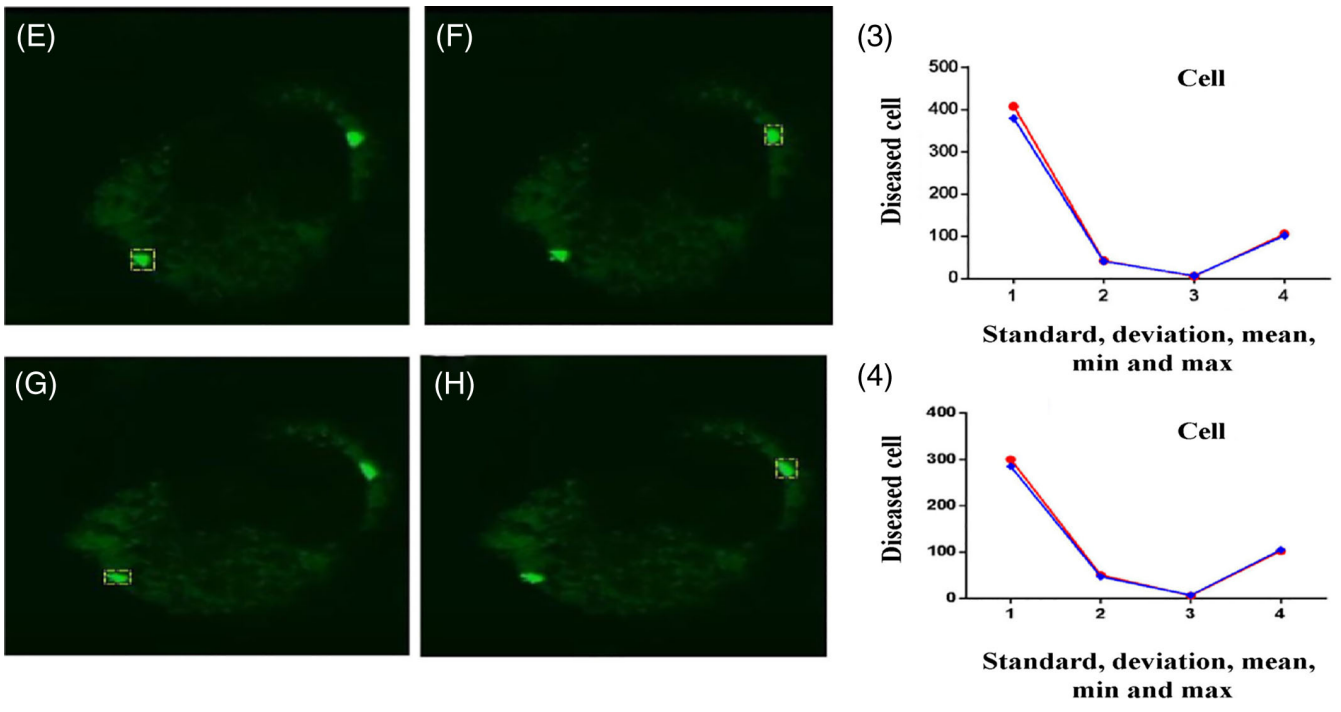

FIGURE 7 Diseases cells (E) and (F) (short term monitoring) are shown and their SD and mean are displayed in Graph 3 and disease cells are in (G) and (H) that is a long term monitoring and their SD and mean are shown in Graph 4

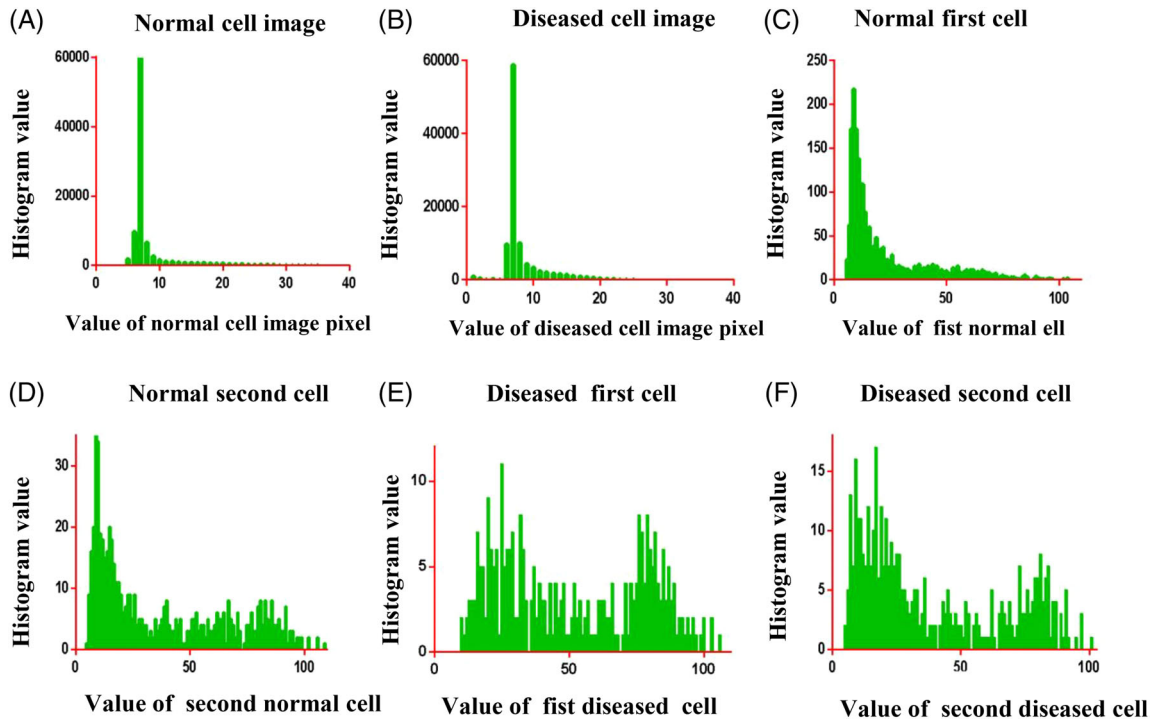

FIGURE 8 Cell view: histogram of normal cell image (A), diseased cell image (B), histogram of normal cell (C and D), and histogram of first diseased cell (E and F)

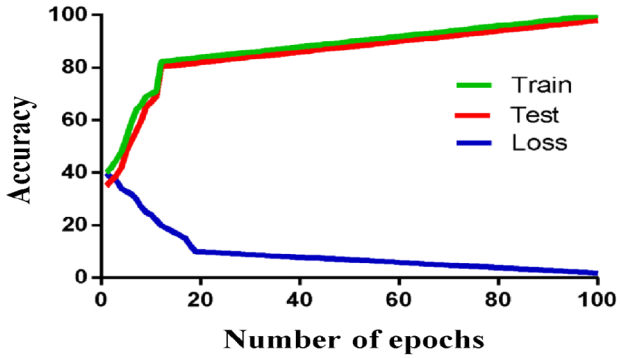

FIGURE 9 Training process are shown, total numbers of epochs are 100 for training, ResNet-50 get good accuracy, 98%

Table 2). Diseased cell region, the image was resized to a 224 × 224 image to speed up the prediction, and cell regions were first identified and only normal or diseased cell regions were predicted (see Figure 7).

3.5 | Model development and validation

We developed predictive model that predict normal and diseased cells. For this, Utilizing cell factures are extracted from diseased and normal cells' images data. The model was tested through CNN (ResNet-50 and resNet-152), and ML approaches (LR, vector support, regression + vector support). Each diseased and normal cell was predicted at high and low ranks, and on the basis of high rank diseased and normal cells features were extracted. Figure 11 shows the predicted accuracy curve (training, testing, and losing). We have defined a means of assessing the accuracy of diseased and normal cells. The evaluation method uses many of the evaluation criteria that are commonly used to assess model success in the classification tasks. The definition and the formula shall be as follows:

When true positive (TPs) are observed, the trend increases and is classified as elevated. If it is determined to be true negative (TNs), the trend decreases, and it is classified as falling. False positives (FPs) are defined as situations where the

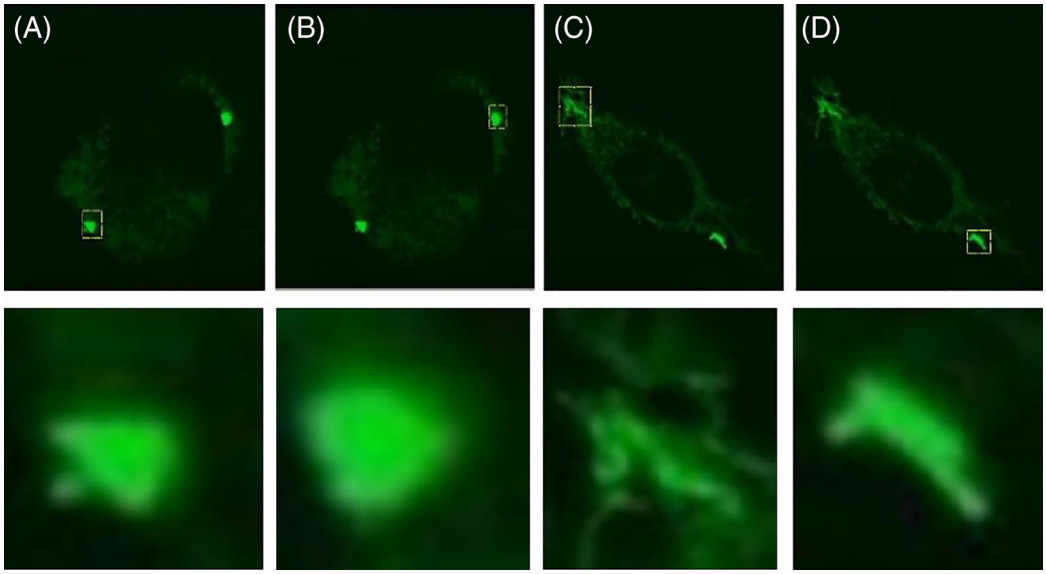

FIGURE 10 Identification of diseased and normal cells shows a typical full-slide picture of diseased cells (A) and (B), normal cells (C) and (D)

trend is declining but classified as rising, and false negative (FNs) are observed when the trend is rising but classified as falling.

$$\text{Accurcy} = \frac{(\text{True Positive (TPs)}) + (\text{True Negative (TNs)})}{(\text{True Positive (TPs)}) + (\text{False positives (FPs)}) + (\text{False Negative (FNs)}) + (\text{True Negative (TNs)})} \quad (1)$$

3.6 | Classification of diseased and normal cell regions

CNN subdivided images into regions consisting of normal and diseased cells. The 98% classification accuracy was compared to the reference standard, and the balanced subset image pixels were computed in the independent test image set. Figure 10 revealed examples of NDCC findings. The classification of cells into normal and diseased cells achieved a good accuracy. Figure 10 shows a representative output. Figure 10A,B demonstrates the probability map of the cells. Figure 10C,D figures out the normal cell slides. Figure 10 reveals diseased (A and B) cells and regular (C and D) cells.

4 | DISCUSSION

The NDCC method was used to classify, automatically, cells in a dataset of normal and diseased cells. First, a region of diseased and normal cells was identified in a whole dataset followed by creation of computer vision classification architecture for normal and diseased cells. To our knowledge, this is the first step in the identification of normal and diseased cells, which we believe can be successfully applied in the field of cell identification. If the exact location of normal and diseased cells is identified, this method can diagnose diseases very accurately, particularly in a number of therapeutic approaches, including heat therapy for tumor cells, and so on. In the past, it has not been possible to localize tumor regions or identify single cells of normal or tumor cells. In normal images, two cells could be observed and classified in both normal (see Figure 2) and diseased cell images (see the Figure 3). We validated the diseased cell classification based on some traditional machine learning and deep learning CNN (see Figure 11). Our results revealed that the CNN performed better than baseline methods. Previous studies classified cancer cells.[27-29,50,51] In this study, we classified diseased cells (damaged cells) and normal cells (Figure 1). Damaged cells were caused all types of diseases like tumors. The method was fully automated, and the accuracy was 98%. The training and testing were obtained through confocal microscopy. Cells were classified on the bases of region (see Figure 10). Figure 9 highlights the means, SD, maximum and minimum values of the normal and diseased cells. After sometimes, normal cells underwent apoptosis/cell death and some variations in the

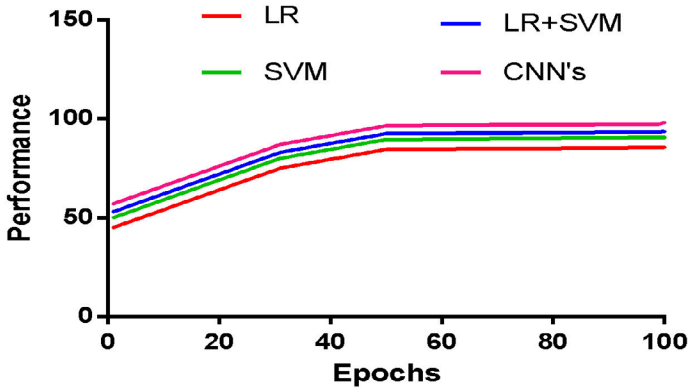

FIGURE 11 Four different machine learning methods including simple ML (LR, SVM, & LR + SVM) and deep learning (NDCC) were implemented. Comparison of these methods revealed 85.2%, 90%, 93%, and 98% accuracy. NDCC performed much better than other methods

mean and SD were observed. However, diseased cells increased frequently and caused more diseases without undergoing cell death/apoptosis. We also figured out the gray level histogram of normal and diseased cells (see Figure 10). We used four methods on archived images, standard machine learning methods (LR, SVM, & LR + SVM) and CNN with good accuracy. However, the CNN method yielded far better results with a very high level of accuracy as Figure 11 shows. In the current literature, studies, that have used deep learning methods to analyze huge amounts of data, have also produced the detailed cell images in which scanty hidden structures can be observed or clearly predicted.[52] This has been the main limitation of computational biology. Kraus et al applied the CNN method and classified a segment of a cell images in an experiment on yeast and mammalian datasets.[53] Esteva 2017 used deep learning to classify skin cancer cells[54] and Xie et al. used CNN to count cells and map cell spatial density across the images by using microscopy.[55] Similarly, Chen et al integrated deep learning and features extraction to classify label-free cells, capture image phases and intensity, and extract the features of a single cell.[56] In the proposed method, diseased and normal cell image classification (DNCC) was based on deep learning. Supervised design methods minimized errors in determination of the diseased cell are. In this study, an attempt has been made to reduce the difference between the projected diseased cell image and the actual diseased cell image. The use of more powerful machine learning technique like DL, therefore, may increase the loss of diseased and normal cells in the calculations. It results in a non-linear relationship between features and provides more accurate results. Cancer is one of the most significant risk factors for wellbeing. In this study, patients were diagnosed with heat therapy, and normal and diseased cell were classified through the unsupervised deep learning method. The deep learning method separated normal and diseased cells. Patients with healthy and diseased could be used as controls. We implemented five methods, non-deep learning (LR, SVM, and LR + SVM), archives good accuracy, but our CNN method (ResNet-50, ResNet-152) yielded a very good accuracy rate as indicated in Figure 11. Figure 12 shows the confusion matrix of ResNet-50 and ResNet-52, which contains the information of diseased and normal cells and predicted cells. Figure 11 revealed two dimensional confusion matrixes, one dimension indexed actual cell and predicted classifier). Therefore, 0 stands for the image of normal cells and 1 for image of diseased cells as Figure 12 reveals.

5 | CONCLUSION

In this article, we suggest use of DNCC in the classification of diseased and normal cell images DNCC method allows end-to-end training and can also be applied in microscopy imaging for cell identification and cell counting. Our model also demonstrated that DNCC can be successfully adapted to various datasets including mammalian cells and yeast cells. Our findings show that the systemic and natural cell classification has been successful to classify millions of cells of unknown significance that currently restrict the understanding of clinical genomes. The accuracy of both diseased and normal cells in our deep learning network (DNCC) is 98%, accuracy which is very good. These results support the assertion that DNCC may be a very good method for classifying diseased cells that are largely penetrant benign tumors.

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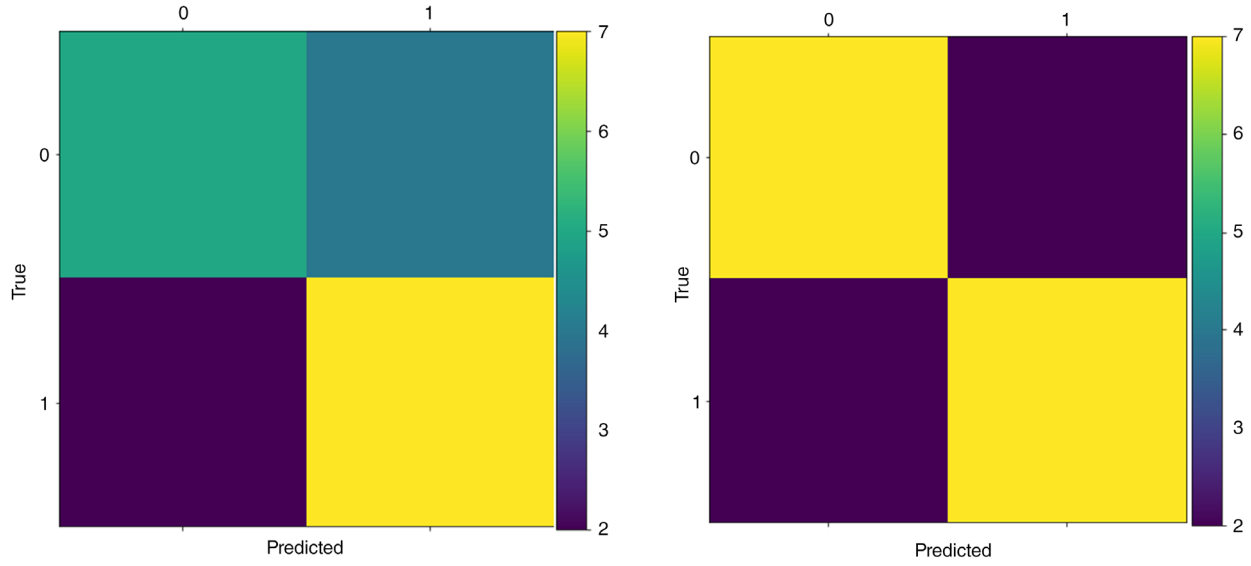

FIGURE 12 The 2 × 2 CM (confusion matrix) of normal, diseased cells, and predicted cells. The first CM shows the ResNet-152 and the second CM shows the ResNet-50

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REFERENCES

1. Imran-Razzak M, Naz S. Microscopic blood smear segmentation and classification using deep contour aware CNN and extreme machine learning. Paper presented at: Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition Workshops; 2017.
2. Imran-Razzak M, Naz S, Zaib A. Deep learning for medical image processing: overview, challenges and the future. *Classification in BioApps*. Cham: Springer; 2018:323-350.
3. Shirazi SH, Umar AI, Naz S, Razzak MI. Efficient leukocyte segmentation and recognition in peripheral blood image. *Technol Health Care*. 2016;24(3):335-347.
4. Shirazi SH, Umar AI, Haq NU, Naz S, Razzak MI. Accurate microscopic red blood cell image enhancement and segmentation. Paper presented at: Proceedings of the International Conference on Bioinformatics and Biomedical Engineering; 2015; Springer, Cham.
5. Beucher S. The watershed transformation applied to image segmentation. *Scann Microscopy-Suppl*. 1992;299:1–26.
6. Aigouy B, Farhadifar R, Staple DB, et al. Cell flow reorients the axis of planar polarity in the wing epithelium of drosophila. *Cell*. 2010;142(5):773-786.
7. Fernandez-Gonzalez R. & Zallen, J. A Oscillatory behaviors and hierarchical assembly of contractile structures in intercalating cells. *Phys Biol*. 8(4):045005(2011).
8. Leung CY, Fernandez-Gonzalez R. Quantitative image analysis of cell behavior and molecular dynamics during tissue morphogenesis. *Tissue Morphogenesis*. 2015;1189:99-113.
9. Mashburn DN, Lynch HE, Ma X, Hutson MS. Enabling user guided segmentation and tracking of surface labeled cells in time lapse image sets of living tissues. *Cytometry A*. 2012;81(5):409-418.
10. Mosaliganti KR, Noche RR, Xiong F, Swinburne IA, Megason SG. ACME: automated cell morphology extractor for comprehensive reconstruction of cell membranes. *PLoS Comput Biol*. 2012;8(12):e1002780.
11. Erickson BJ, Korfiatis P, Akkus Z, Kline TL. Machine learning for medical imaging. *Radiographics*. 2017;37(2):505-515.
12. Orru G, Pettersson-Yeo W, Marquand AF, Sartori G, Mechelli A. Using support vector machine to identify imaging biomarkers of neurological and psychiatric disease: a critical review. *Neurosci Biobehav Rev*. 2012;36(4):1140-1152.
13. Wang P, Xu S, Li Y, Wang L, Song Q. Feature-based analysis of cell nuclei structure for classification of histopathological images. *Dig Signal Process*. 2018;78:152-162.
14. Cascio D, Taormina V, Cipolla M, Bruno S, Fauci F, Raso G. A multi-process system for HEp-2 cells classification based on SVM. *Pattern Recogn Lett*. 2016;82:56-63.
15. Hasan MR, Hassan N, Khan R, Kim YT, Iqbal SM. Classification of cancer cells using computational analysis of dynamic morphology. *Comput Methods Progr Biomed*. 2018;156:105-112.

16. Khamis H, Zurakhov G, Azar V, Raz A, Friedman Z, Adam D. Automatic apical view classification of echocardiograms using a discriminative learning dictionary. *Med Image Anal*. 2017;36:15-21.
17. Yu H. Research and optimization of sports injury medical system under the background of Internet of Things. *Trans Emerg Telecommun Technol*. 2020.e3929:1–14.
18. Zhang C, Wang X, Li F, He Q, Huang M. Deep learning–based network application classification for SDN. *Trans Emerg Telecommun Technol*. 2018;29(5):e3302.
19. Memon ML, Maheshwari MK, Shin DR, Roy A, Saxena N. Deep-DRX: a framework for deep learning–based discontinuous reception in 5G wireless networks. *Trans Emerg Telecommun Technol*. 2019;30(3):e3579.
20. Zhao J, Qu H, Zhao J, Jiang D. Spatiotemporal traffic matrix prediction: a deep learning approach with wavelet multiscale analysis. *Trans Emerg Telecommun Technol*. 2019;30(12):e3640.
21. Kumar S, Asthana R, Upadhyay S, Upreti N, Akbar M. Fake news detection using deep learning models: a novel approach. *Trans Emerg Telecommun Technol*. 2019;e3767:1–23.
22. Forsberg D, Sjöblom E, Sunshine JL. Detection and labeling of vertebrae in MR images using deep learning with clinical annotations as training data. *J Dig Imag*. 2017;30(4):406-412.
23. Gao XW, Hui R, Tian Z. Classification of CT brain images based on deep learning networks. *Comput Methods Progr Biomed*. 2017;138(1):49-56.
24. Lee H, Tajmir S, Lee J, et al. Fully automated deep learning system for bone age assessment. *J Dig Imag*. 2017;30(4):427-441.
25. Shen D, Kooi T, Bejnordi BE, et al. Deep learning in medical image analysis. *Ann Rev Biomed Eng*. 2017;19:221-248.
26. Wang J, Ding H, Bidgoli FA, et al. Detecting cardiovascular disease from mammograms with deep learning. *IEEE Trans Med Imag*. 2017;36(5):1172-1181.
27. Iqbal MS, Luo B, Mehmood R, Alrige MA, Alharbey R. Mitochondrial organelle movement classification (fission and fusion) via convolutional neural network approach. *IEEE Access*. 2019;7:86570-86577.
28. Iqbal MS, Khan T, Hussain S, et al. Cell recognition of microscopy images of TPEF (two photon excited florescence) probes. *Proc Comput Sci*. 2019;147:77-83.
29. Iqbal MS, el-Ashram S, Hussain S, et al. Efficient cell classification of mitochondrial images by using deep learning. *J Opt*. 2019;48(1):113-122.
30. Anthimopoulos M, Christodoulidis S, Ebner L, Christe A, Mougiakakou S. Lung pattern classification for interstitial lung diseases using a deep convolutional neural network. *IEEE Trans Med Imag*. 2016;35(5):1207-1216.
31. Cha KH, Hadjiiski L, Samala RK, Chan HP, Caoili EM, Cohan RH. Urinary bladder segmentation in CT urography using deep learning convolutional neural network and level sets. *Med Phys*. 2016;43(4):1882-1896.
32. Ghafoorian M, Karssemeijer N, Heskes T, et al. Deep multi-scale location-aware 3D convolutional neural networks for automated detection of lacunes of presumed vascular origin. *NeuroImage Clin*. 2017;14:391-399.
33. Lekadir K, Galimzianova A, Betriu À, et al. A convolutional neural network for automatic characterization of plaque composition in carotid ultrasound. *IEEE J Biomed Health Inform*. 2017;21(1):48-55.
34. Rajkomar A, Lingam S, Taylor AG, Blum M, Mongan J. High-throughput classification of radiographs using deep convolutional neural networks. *J Digit Imag*. 2017;30(1):95-101.
35. Samala RK, Chan HP, Hadjiiski L, Helvie MA, Wei J, Cha K. Mass detection in digital breast tomosynthesis: deep convolutional neural network with transfer learning from mammography. *Med Phys*. 2016;43(12):6654-6666.
36. Guan Y, Plötz T. Ensembles of deep lstm learners for activity recognition using wearables. *Proc ACM Interact Mob Wearable Ubiquit Technol*. 2017;1(2):11.
37. Madani A, Arnaout R, Mofrad M, Arnaout R. Fast and accurate view classification of echocardiograms using deep learning. *NPJ Dig Med*. 2018;1(1):6.
38. Ordóñez FJ, Roggen D. Deep convolutional and lstm recurrent neural networks for multimodal wearable activity recognition. *Sensors*. 2016;16(1):115.
39. Cruz JA, Wishart DS. Applications of machine learning in cancer prediction and prognosis. *Cancer Inform*. 2006;2:59-78.117693510600200030.
40. Doyle S, Hwang M, Shah K, Madabhushi A, Feldman M, Tomaszeweski J. Automated grading of prostate cancer using architectural and textural image features. Paper presented at: Proceedings of the 4th IEEE International Symposium on 2007 Biomedical Imaging: from Nano to Macro. ISBI 2007; April 12, 2007:1284-1287; IEEE.
41. Salvatore C, Battista P, Castiglioni I. Frontiers for the early diagnosis of AD by means of MRI brain imaging and support vector machines. *Curr Alzheimer Res*. 2016;13(5):509-533.
42. Bejnordi BE, Mullooly M, Pfeiffer RM, et al. Using deep convolutional neural networks to identify and classify tumor-associated stroma in diagnostic breast biopsies. *Mod Pathol*. 2018;13:1.
43. Hussein A, Elyan E, Gaber MM, Jayne C. Deep imitation learning for 3D navigation tasks. *Neural Comput Appl*. 2018;29(7):389-404.
44. Hu Y, Modat M, Gibson E, et al. Weakly-supervised convolutional neural networks for multimodal image registration. *Med Image Anal*. 2018;49:1-3.
45. Kiskin I, Zilli D, Li Y, Sinka M, Willis K, Roberts S. Bioacoustic detection with wavelet-conditioned convolutional neural networks. *Neural Comput Appl*. 2018;32:1-3.
46. Mahmood F, Durr NJ. Deep learning and conditional random fields-based depth estimation and topographical reconstruction from conventional endoscopy. *Med Image Anal*. 2018.48:230–243.

47. Wang X, Yang W, Weinreb J, et al. Searching for prostate cancer by fully automated magnetic resonance imaging classification: deep learning versus non-deep learning. *Sci Rep*. 2017;7(1):15415.
48. He K Zhang X, Ren S, Sun J. Deep residual learning for image recognition. Paper presented at: Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition; 2016:770–778.
49. Simonyan K. & Zisserman, A. Very deep convolutional networks for large-scale image recognition; 2014. arXiv preprint arXiv:1409.1556.
50. He Y, Wang W, Wang H, et al. Ghost imaging based on deep learning. *Sci Rep*. 2018;8:1–7.
51. Liu J. Cheng, Y., Wang, X., Zhang, L., & Wang, Z. J. Cancer characteristic gene selection via sample learning based on deep sparse filtering. *Sci Rep* 8(1):8270(2018).
52. Angermueller C. Pärnamaa, T., Parts, L., & Stegle, O. Deep learning for computational biology. *Molec Syst Biol*. 12(7):878 (2016).
53. Kraus OZ, Ba JL, Frey BJ. Classifying and segmenting microscopy images with deep multiple instance learning. *Bioinformatics*. 2016;32(12):i52.
54. Esteva A, Kuprel B, Novoa RA, et al. Dermatologist-level classification of skin cancer with deep neural networks. *Nature*. 2017;542(7639):115-118.
55. Xie W, Noble JA, Zisserman A. Microscopy cell counting and detection with fully convolutional regression networks. *Comput Methods Biomech Biomed Eng Imag Visualiz*. 2018;6(3):283-292.
56. Chen CL, Mahjoubfar A, Tai LC, et al. Deep learning in label-free cell classification. *Sci Rep*. 2016;6:21471.

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