

A Narrative Review: Classification of Pap Smear Cell Image for Cervical Cancer Diagnosis

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Abstract: Cervical cancer develops as cells transformation in the cervix of a female that connects the uterus to the vagina. This cancer may impact the columnal epithelial cells of the cervix and therefore can be expanded to the lymphatic and circulatory system (metastasize), sometimes the kidneys, liver, prostate, vagina, and rectum. Many of the cervical cancer patients survived by taking early prevention by undergoing a Pap Smear Test. However, the result of the test usually takes a few weeks which is extremely time-consuming especially at the government hospital. The purpose of this research was to study the detection and classification method of the Pap Smear image to resolve the time-consuming issues and support better system performance to prevent low precision result of the Human Papilloma Virus (HPV) stages. A few studies were considered which features the cell image databases to classify cervical cancer according to its type. Besides, the classification system and the performance of the preceding papers that had been considered include a few features found in the cell images. Those features were the size of the cells, the shape of the cells, the colour, Region of Interest (ROI) and overlapped cell nuclei. The other existing design methods being considered were the Deep Convolutional Neural Network (CNN) and the Artificial Neural Network (ANN). These findings technique showed the highest percentage of the system accuracy, precision, and specificity that might be excellent for further analysis. The research limitation was the method of how the numerous image databases needed to be processed and classified one at a time. None of these articles stated whether they had found the way to compute more images at once. The aim of the study was to review the previous paper in order to define the feature datasets that needed to be considered. The features were important in designing a new classification method and increasing the performance of the systems. The features included the nucleus shape, diameter and surface areas, colour and luminosity of the cell datasets, the region of the nucleus, design and image resolution. In this paper, an extensive analysis was studied for cervical cancer classification techniques. As expected from the outcome, the study of the feature database, the classification method and the system performance were reviewed deeper for further assessments.

Keywords: Image; cervical; cancer; review

1 Introduction

Cervical cancer is a type of cancer that originates in the cervix which is a part of female reproductive systems. This form of disease typically results in a Human Papilloma Virus (HPV) inspection regarded as being one of the commonest cancers among women [1,2]. Cervical cancer is one of the biggest prevalent and curable cancers among women which is a common chronic disease cancer [3]. Four decades ago,



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cervical cancer was rated as the second most prevalent cancer among women in the global community [4]. The yearly number of incidents has risen, cervical cancer has decreased in its relative importance, becoming the second most prevalent female cancer in 1975 [5]. Interestingly, it became the most prevalent cancer among women in 42 low-resource countries [6]. However, there are certain disorders that might resemble cervical cancer that should be aware of. The condition that physicians often face in pelvic examinations for irregular bleeding that may be associated with cervical cancer is prolapsed uterine fibroids. For this case, a broad mass is observed on the pelvic test originating from the cervix. The Pap Smear Test is a technique to diagnose the cervical cancer cell through the screening method. This screening test checks the existence of cancerous or precancerous cells in the cervix. The poor sensitivity associated with the smear test is a concern and includes possible scenarios such as the time required by the medical expert to diagnose the cervical cell, particularly at the initial stage of the epithelial cells involved (Grade 1), the poor visibility of the sample image, and the risk of imprecise microscopic analysis (although various precautions are integrated to attempt the process of preventing the inaccuracies). Awareness regarding the chronic disease of cancer-causing Human Papilloma Virus (HPV) forms the strongest reason for cervical cancer growth and development of novel avenues for prevention and treatment [7]. The use of the technique for prevention measures can contribute to preventing cervical cancer, therefore mortality is largely preventable. The preventive techniques used are the computerized imaging techniques from the Pap Smear to support the artificial diagnosis of cell irregularities or cancers in cytopathology that provide reliable and precise assessment of nuclear morphology [8].

The main purpose of this study is to develop an understanding of the type of cervical cancer cell and its features that can be detected and classified in the image processing technique. This paper reviews the research conduct on the cell features based on its types and the existing classification technique proposed by the researchers to observe the best solution in identifying the cervical cancer cell classification. The Papanicolaou Smear (Pap) is an innovative screening test for cervical cancer, which incorporates a microscopic analysis of the cervical cells, properly extracted, and scattered, and particularly stained. The Pap Test was conducted to assess the diagnosis of this condition. The characterization features need to be observed from the following nucleus and cytoplasm. This characteristic is needed to identify whether the cells are infected or under analysis [9]. By reviewing the past papers, the aim of the findings are to determine the typical feature of the datasets that need to be considered, the method of the classification, and the system's performance. These features include the shape of the nucleus, the diameter and the area of nucleus and cytoplasm, the colour and the brightness of cell datasets, the nucleus region, the pattern, and the resolution of the images.

A Human Papilloma Virus (HPV) check can be performed together with and also as a distinctive Pap test. The HPV Test is done with a small brush to fetch the specimens from the cervix, just like a Pap test. HPV tests are not tested for all dissimilar HPV types. The medical experts test the HPV strains that are at the greatest possible risk of causing cervical cancer. The literature that has been used to show the Pap Smear detection of HPV are the articles that commence with a systematic review and the experimental result of the Pap Smear test. Approximately sixty articles related to Cervical Cancer have been found in a search throughout the dataset devoted to evaluating all of the actual relevant data written worldwide around 2001 to 2020. Consequently, some of the articles chosen were between 2016 and 2020. Fifty articles were chosen and reviewed for their medical significance and future studies consequences. The aim or the basis of choosing this article is based on the result analysis and review of the Pap Smear classification techniques and a few of detection methods with feature considerations. The difference between journal publication, conference publication, and book chapter based on personal understanding, the conference procedures are generally predicted and are of significance in several fields of engineering. The distinctions within each category of publication are definitely as big as the distinctions among them. For example, while book sections may generally require a lot of time to publish, there are some journal articles that have already spent much more period throughout the pipeline than books.

2 Review of Study

The primary goal of this literature review is to acquire knowledge of the existing image processing method to classify the cervical cancer cells based on their features. In order to analyze for better solution of the cervical cancer classification, the technique observes are based on research ideology review that includes current understanding and its substantive results, as well as theoretical and methodological contributions to some specific issues.

2.1 Feature of the Data Sets

Based on the previous paper by Eggert et al. [10] and Pau et al. [11], the significant advances in the area of computer vision detection, pattern recognition and system classification have been established by rendering automatic production of medical scenes a viable replacement. Later, Nanni et al. [12] covered a selection of various database colour images identification by observing the characteristics of the feature patterns of nucleus analysis. By relying on this, the image extraction function that comprises the consequential details for a particular diagnostic study project based on the common machine vision systems. This is similar to other study feature databases, which often concentrate mainly on the characteristics of shape, texture and colour [13]. However, cervical dysplasia is classified under the two-tier (standard and non-normal) classification technique used for the treatment of cancer or precancerous lesions in the cervix (Negative for Intraepithelial Lesion or Malignancy), Low-grade Squamous Intraepithelial Lesion or Higher-grade Squamous Intraepithelial Lesion). As a result, extensive studies have shown that the proposed approach can effectively distinguish between Pap fracturing images that work significantly better than other systems in place.

Then, Tsai et al. [14] research appeared which provides different findings of the feature of data sets that preserves the sharpness of the nucleus boundaries. This finding was supported by Chankong et al. [15] also discovered existing single-core thresholding techniques using an edge-based approach and a patch-based fuzzy C-means clustering system to remove cell edges. This study showed surprisingly effective data analysis of potential data processing and classification techniques done on 362 cervical Pap smear images. Fig. 1 shows the ROI extraction and split overlapped cell nuclei. As an image in Fig. 1a showed the original image being processed to turn into grayscale image in Fig. 1b. The grayscale image was then processed to the top-bottom hat transform Fig. 1c and segmented as a mean-shift algorithm in Fig. 1d. The mean-shift algorithm image went through the ROI extraction process Fig. 1e before undergoing the detection of the overlapped nuclei Fig. 1f1 and the single nuclei Fig. 1f2. As the overlapped nuclei and the single nuclei detected, the image then appeared in the final segmented result with the boundary of image extraction as shown in Fig. 1g [16].

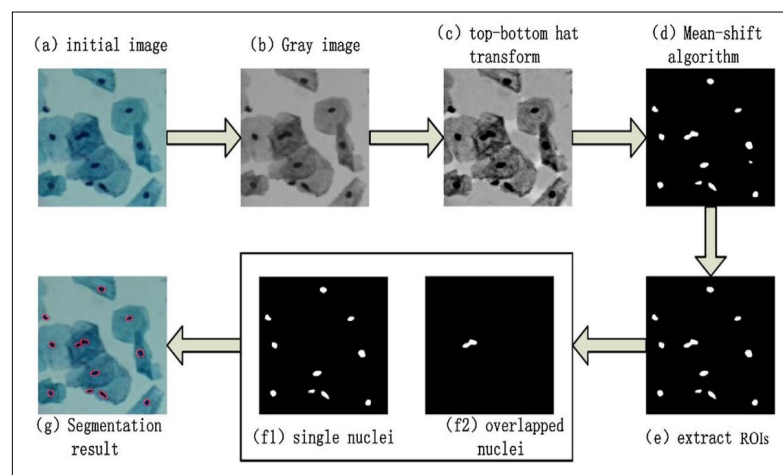


Figure 1: Segmentation process of one cervical image [16]

On the other side, according to the research paper by Alyafeai et al. [17] that identified two different cervigram databases used for testing and assessment and have become the important elements of the proposed deep learning system. Those are the datasets with Intel & Mobile ODT and NCI Guanacaste project. These two different datasets are then trained respectively as 10-fold cross-validation strategy is adopted in the deep learning method. The database parameters considered are batch size, subdivisions, momentum, decay, learning rate, convolutional layers, fully-connected layers, and labels of classes' number. Furthermore, another findings show the database feature and parameters need to be considered in order to identify the effectiveness of the technique to be designed. The features needed in the implementation of classification methods include the colour of datasets to be classified, the size of nucleus, and the sharpness of the nucleus boundaries, the overlapped nucleus study, and the size of the nucleus as well.

In contrast, a paper by Riana et al. [18] designed a structure of the Gray-Length Run-Length Matrix (GLRLM) for inflammatory cells and nucleus forms performance. Inflammatory cells and nuclei contain various shapes that may be used to distinguish between them. In order to remove all the elements, it is important to render the first by manually cutting of the inflammatory cells and the nucleus. All feature extractions were examined and chosen by the Decision Tree Classifier (J48). Eleven features were then reduced to eight, namely low gray-level accentuation, gray-level non-uniformity, long-term non-uniformity, long-term low gray-level emphasis, short-term high gray-level emphasis, short-term low gray-level emphasis, long-term high gray-level emphasis, and ran percentage based on the classification rule.

2.2 Classification Method

A previous research study by Shin et al. [19] and Scott et al. [20] developed the classification method of the system where the application of the softmax layer was used as a classification model. Both articles use the same main idea that is deep Convolutional Neural Network (CNN) as the classification method and resulting in high percentage of performance.

Later, another research conducted by Nguyen et al. [21] implemented a new deep neural network architectural design focused on learning algorithms for microscopic picture classification. This proposed method is inspired by the previous study done by references [19,20]. However, what makes it better is the convolutional properties. Then, the two fully connected classifications levels are used for training. Both 2D-Hela and Pap-smear databases (Fig. 2 and Fig. 3) that provide substantial output improvements relative to the neural network framework utilizes mainly features which are derived from a single CNN and many more conventional classification approaches.

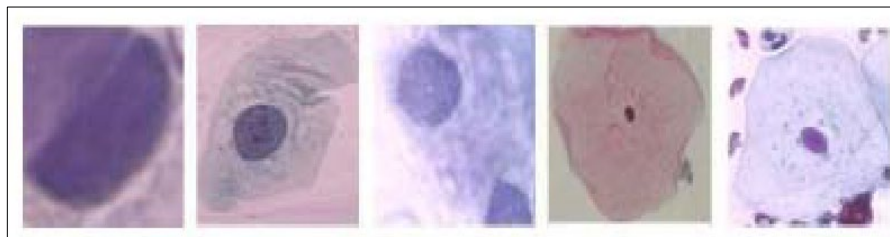


Figure 2: Typical images in Pap-smear datasets [21]

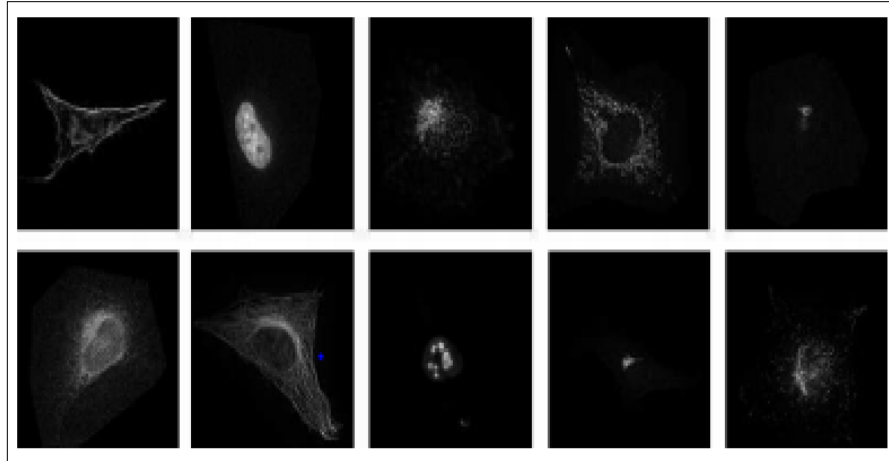


Figure 3: Typical images in 2D-Hela datasets [21]

More recently, new research has emerged that offers contradictory findings on the use of the Unet-based Attribute Segmentation and Classification System by inserting residual blocks, tightly entangled blocks and a completely convoluted structure as a bottleneck between encoder-decoder blocks for Pap Smear images [22]. The researcher has implemented a joint loss feature in the system that resolves certain divisive details of the cell level in clustered nucleus extraction. In order to improve the robustness of the overall structure, the theoretical algorithm is followed by a stacked self-encoder-based type representation training model. DL-based thresholding relies on the identification of artificial and pixel-wise classifications that can be segmented into semantic segmentation [23,24], segmentation features [25,26] and panoptic segmentation [27] that use both semantic and instance segmentation principles to achieve efficiency.

Nevertheless, a number of researchers have sought to establish that it is further based on the fact that the liquid-based Pap test (LBC) is somewhat effective and reliable than conventional techniques because of the simple reality that LBC will generate a smoother and more consistent microstructure analysis slide than the conventional system [28–30]. The LBC method uses centrifugation to remove all heavy molecular substances, such as blood and mucus, throughout the specimen, which gives a smooth slip at the top. LBC related findings provide improved detection of cervical transition zone cell-level components that could also be used for Human Papilloma Virus (HPV) research.

In 2018, according to William et al. [31] based on the methods reviewed from the previous paper, the KNN algorithm was stated to be an outstanding classifier for cervical images, even so integrating KNN algorithms with some algorithms including support vector machines (SVMs), pixel-level classifications and using mathematical shape models will increase efficiency. In addition, the use of multi-level segmentation will boost the efficiency of the classifiers. Besides, all of the formulated classifiers are developed and implemented on precisely pre-processed segmented images that used available commercial segmentation software such as CHAMP digital image software. Consequently, there is not enough evidence that these algorithms work in medical practice.

However, another study was conducted using the BIO-image Classification and Annotation Tool (BIOCAT) [32]. It is able to apply pattern recognition algorithms to bi- and three-dimensional biological sample images and Regions of Interest (ROIs) in individual images for automatic identification and interpretation. Much more research has been done on different facets of computer science, including storage, visualization and analysis of high-dimensional and content-rich biological images [33]. This resulted in projects such as Image J [34], Vaa3D [35], Cell Profiler [36], FARSIGHT [37], Icy [38], OME [39] and BISQUE [40]. In the year 2020, along with the beginning of artificial intelligence in the healthcare sector, a new theory adopted by the decision-making support network will address the problems of experimental bias [41]. The present research investigates six separate deep convolutionary

neural networks-Alexnet, Vggnet (vgg-16 and vgg-19), Resnet (resnet-50 and resnet-101) and Googlenet architectures for multi-class (four-class) detection of potentially cancerous cervical and cancer lesions and their equivalent in-house assessment. The research highlights the introduction of three major deep learning techniques in the Ensemble Classifier to create a high-precision multiclass designation. The six deep models, including the ensemble classifier, were trained and analyzed using traditional and liquid cytology technologies using the Herlev data set from the Pap Smear Hospital Analysis. However, other studies by Ampazis et al. [42], Dewi et al. [43], Ramdhani et al. [44], etc. are more specific and categorized as seven cervical cells. These types of cells are superficial epithelial squamous, medium epithelial squamous, cell columnar epithelium, mild dysplasia, moderate dysplasia, severe dysplasia, and cell nucleus carcinoma. Fig. 4 shows the nine hundred and seventeen data then being classified into two classes. Those are the normal class and abnormal class. The normal class has three types of class (Class 1–Class 3) which includes superficial epithelial squamous, medium epithelial squamous, cell columnar epithelium. While abnormal class has four types of class (Class 4–Class 7). Those are mild dysplasia, moderate dysplasia, severe dysplasia, and cell nucleus carcinoma. These seven classification techniques can be used for further classification study.

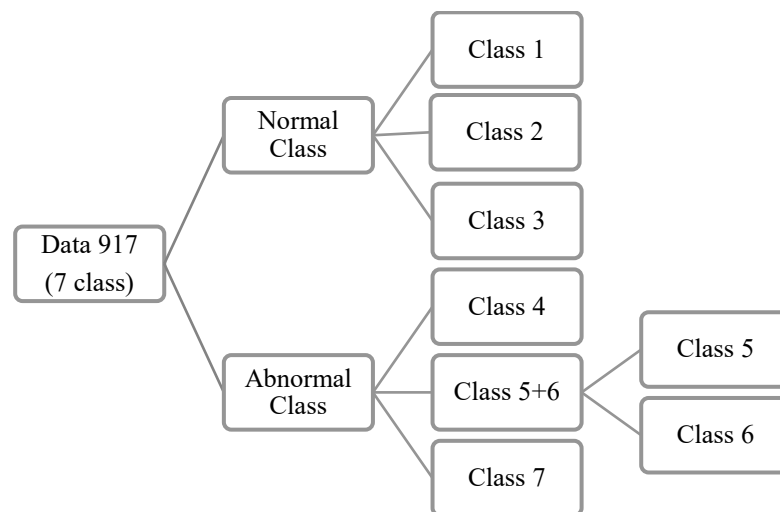


Figure 4: Approach model-based on hierarchical decision [44]

2.3 System Performance

The data performance is the sum of valuable research performed and measured in terms of precision, performance and level of execution of computer algorithm commands. The most interesting finding was that the result of initiative showed that the Random Forest Tree was the strongest classifier on several classification methods to characterize Pap test performance [45]. Tab. 1 displays the average outcome of 30-stage 10-fold cross-validation of the three segmentation techniques. As from the list, Random Forest Tree provides the optimal system based on accuracy, precision, recall and ROC region. Based on the percentage of the average results, Random Forest Tree showed the highest Accuracy, Precision, Recall, and ROC Area followed by Naïve Bayes, and SVM respectively.

Table 1: The average results [45]

| | Accuracy (%) | Precision (%) | Recall (%) | ROC Area (%) |
|--------------------|--------------|---------------|------------|--------------|
| Naïve Bayes | 78.93 | 69.43 | 78.95 | 91.22 |
| SVM | 78.67 | 66.67 | 78.70 | 84.77 |
| Random Forest Tree | 80.18 | 75.96 | 80.18 | 93.39 |

Previous research on data mining classification techniques for cervical cancer is particularly noted by the author, Abdullah et al. [46] that focused on low-sensitivity performance and specificity by improving the Cellular Neural Network (CNN) algorithm and increasing the discovery of results by immediately tracking cancerous cells in the cervix by more than 88 per cent precision. However, another study by Araújo et al. [47] found that the other key point of this research was that it explored the experimental output which indicated to be much more reliable (MAP = 0.936) and smarter (about 4.75 s per image). The researcher discovered that the method of analysis had a small cost of calculation because CNN had only received abnormal segment training and had not drawn high computational characteristics from each region. By analyzing the performance of the system, the researcher observed a false-negative rate, a false-positive rate and a classification error of 0.00 percent, 10.00 percent and 5.00 percent, respectively, as added to the Pap-smear display [48].

In addition, another founder, Zhang et al. [49] highlighted the findings that their approach had improved previous algorithms in terms of classification accuracy (98.3 percent), curve region (0.99) and, in particular, specificity (98.3 percent) once the Herlev test Pap data set had been implemented and tested with five-fold cross-validation. The images of the experiment are shown in Fig. 5. The example in the Fig. 5a from the Herlev database and Fig. 5b from HEMLBC data sets of normal and abnormal cells show how the result of their maintaining related original scales to better illustrate the various features from the researcher. This pattern of features can be considered for better insight into analysis.

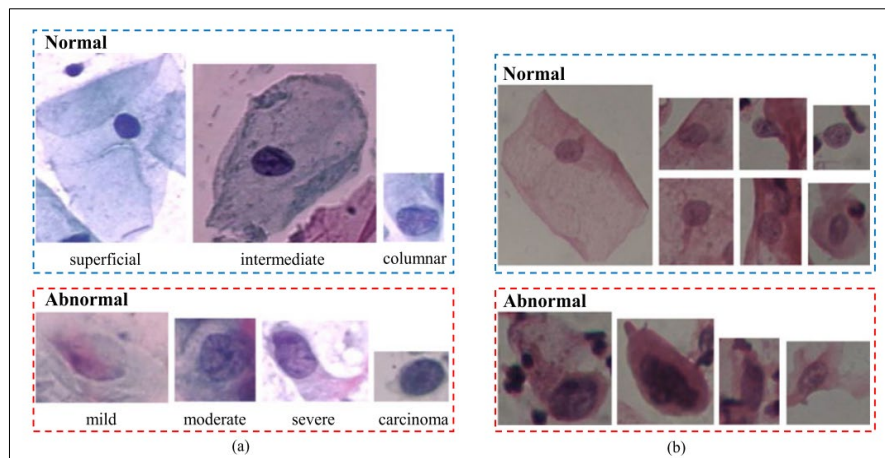


Figure 5: Example images of the (a) Herlev and (b) HEMLBC data set of normal and abnormal cervical cells. All of these examples maintain their related original scales to better illustrate the various features of normal to abnormal cells [49]

Other studies by Ali et al. [50] considered presenting a new hierarchy for the modular architecture in the neural network (HMNNA), composed of three neural networks specially trained in certain essential questions and then arranged the skilled networks in a tree structure created by the hierarchical modular architecture of the modular neural network. The neural network method of Levenberg–Marquardt is equipped for the three advanced nerve networks. Contrary to the usual back propagation algorithm, Levenberg–Marquardt is quick and confident with only one downside, i.e., the Hessian Matrix storage specifications. All 25 algorithms with both databases were better performed by the HMNNA. The Novelty Benchmark data set contained a 95.32 percent accuracy rate, an F -value of 0.949310, an F -value of 88.41 for Herlev, and an F -value of 0.89145.

In 2018, Arya et al. [51] stated that high-order derived statistical techniques were being used in this analysis, and such measures were first-order histograms, GLCM, LBP, Rules, and DWT. ANN and SVM of different kernel values were used to classify a single cell into cancerous and non-cancerous classes. The proposed texture characteristics system achieved 99.50 percent accuracy, 99.00 percent sensitivity and ANN

specificity. By using the SVM quadratic classifier, the precision obtained was 99 percent with a sensitivity of 98.04 percent and a consistency of 98.00 percent for the single-cell image classification (Fig. 6).

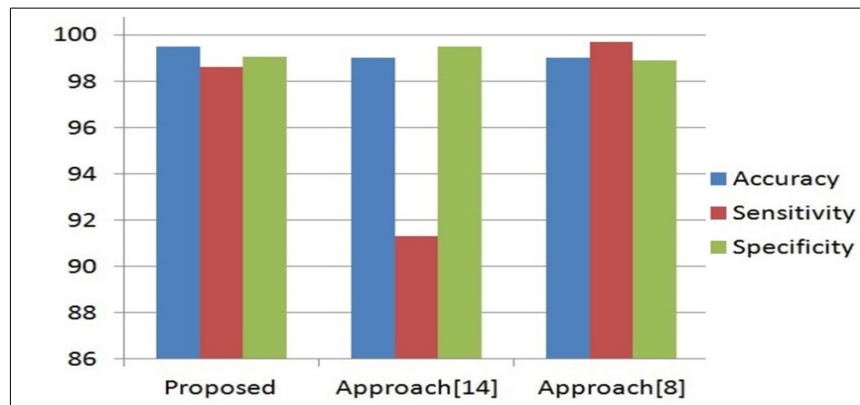


Figure 6: Comparative evaluation with existing approaches [51]

As a summarization, based on the review from the articles, the system performance of the Deep Convolutional Neural Network (CNN) [49] and the Artificial Neural Network (ANN) [51] showed the highest percentage of the system accuracy, precision, and specificity. Thus, the classification technique can be considered for further analysis by using the confusion matrix.

3 Conclusion

This study review possibly provides strategies from the significant findings for researchers equated with the classification method, and the system performance based on the feature of the databases images in implementing the new solution and innovates better algorithm and system design. To come to serve the base first, numerous techniques have been drawn-validated with recruitment and evaluated databases acquired through online cervical image sources of data such as Herlev. In addition, it seems highly appropriate to generate some other image data from hospitals for further validation of the published data. All classifications presented are developed and constructed for feasible thresholding software that is coherently complete, fractured, and contain training data interpretations. In conclusion, the research of the feature database, the classification techniques and the performance of the system have been analysed to provide a better overview of any further assessments. The analysis findings feature the image database needed to be considered including the nucleus shape, diameter and surface areas, colour and luminosity of the cell datasets, the region of the nucleus, design and image resolution. Nevertheless, seven types of classifications of cervical cancer feature patterns can also be revised for further design method. The importance of the feature and the pattern are needed to classify the cell image to increase the system's performance in designing the classification method from the Pap Smear image databases.

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Conflicts of Interest: The authors declare that they have no conflicts of interest to report regarding the present study.

References

1. Lousquy, R., Delpech, Y., Thoury, A., Barranger, E. (2010). Sentinel node biopsy in early-stage cervical cancer in 2009. *Oncologie*, 12(1), 45–48. <https://doi.org/10.1007/s10269-009-1831-9>.
2. Sancho-Garnier, H. (2002). Screening for breast and cervical cancers. *Oncologie*, 4(8), 493–498.

3. Arya, M., Mittal, N., Singh, G. (2016). Cervical cancer detection using segmentation on pap smear images. In *Proceedings of the International Conference on Informatics and Analytics (ICIA-16)*. Association for Computing Machinery, pp. 1–5. New York, NY, USA. <https://doi.org/10.1145/2980258.2980311>.
4. Zaridah, S., Ukm, M. O. G. (2014). A review of cervical cancer research in malaysia. *Med J Malaysia*, 69(Suppl A), 33–41.
5. Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C. et al. (2015). Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *International Journal of Cancer*, 136(5), E359–E386. <https://doi.org/10.1002/ijc.29210>.
6. Arbyn, M., Weiderpass, E., Bruni, L., de Sanjosé, S., Saraiya, M. et al. (2020). Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *The Lancet Global Health*, 8(2), e191–e203. [https://doi.org/10.1016/S2214-109X\(19\)30482-6](https://doi.org/10.1016/S2214-109X(19)30482-6).
7. Arbyn, M., Castellsagué, X., de sanjosé, S., Bruni, L., Saraiya, M. et al. (2011). Worldwide burden of cervical cancer in 2008. *Annals of Oncology*, 22(12), 2675–2686. <https://doi.org/10.1093/annonc/mdr015>.
8. Athinarayanan, S., Srinath, M. V. (2016). Classification of cervical cancer cells in pap smear screening test. *ICTACT Journal on Image and Video Processing*. <https://doi.org/10.21917/ijivp.2016.0179>.
9. Abhinaav, R., Brindha, D. (2019). Abnormality detection and severity classification of cells based on features extracted from papanicolaou smear images using machine learning. In *2019 International Conference on Computer Communication and Informatics*, pp. 1–5. <https://doi.org/10.1109/ICCCI.2019.8822131>.
10. Eggert, U. S., Mitchison, T. J. (2006). Small molecule screening by imaging. *Current Opinion in Chemical Biology*, 10(3), 232–237. <https://doi.org/10.1016/j.cbpa.2006.04.010>.
11. Pau, G., Fuchs, F., Sklyar, O., Boutros, M., Huber, W. (2010). EBImage-an R package for image processing with applications to cellular phenotypes. *Bioinformatics*, 26(7), 979–981. <https://doi.org/10.1093/bioinformatics/btq046>.
12. Nanni, L., Ghidoni, S., Brahnam, S. (2020). Ensemble of convolutional neural networks for bioimage classification. *Applied Computing and Informatics*. <https://doi.org/10.1016/j.aci.2018.06.002>.
13. Das, A. K., Mahanta, L. B., Kundu, M. K., Chowdhury, M., Bora, K. (2016). Automated classification of Pap smear images to detect cervical dysplasia. *Computer Methods and Programs in Biomedicine*, 138, 31–47. <https://doi.org/10.1016/j.cmpb.2016.10.001>.
14. Tsai, M. H., Chan, Y. K., Lin, Z. Z., Yang-Mao, S. F., Huang, P. C. (2008). Nucleus and cytoplasm contour detector of cervical smear image. *Pattern Recognition Letters*, 29(9), 1441–1453. <https://doi.org/10.1016/j.patrec.2008.02.024>.
15. Chankong, T., Theera-Umpon, N., Auephanwiriyakul, S. (2014). Automatic cervical cell segmentation and classification in Pap smears. *Computer Methods and Programs in Biomedicine*, 113(2), 539–556. <https://doi.org/10.1016/j.cmpb.2013.12.012>.
16. Wang, P., Wang, L., Li, Y., Song, Q., Lv, S. et al. (2019). Automatic cell nuclei segmentation and classification of cervical Pap smear images. *Biomedical Signal Processing and Control*, 48, 93–103. <https://doi.org/10.1016/j.bspc.2018.09.008>.
17. Alyafeai, Z., Ghouti, L. (2020). A fully-automated deep learning pipeline for cervical cancer classification. *Expert Systems with Applications*, 141. <https://doi.org/10.1016/j.eswa.2019.112951>.
18. Riana, D., Widiantoro, D. H., Mengko, T. L. (2016). Extraction and classification texture of inflammatory cells and nuclei in normal pap smear images. *Proceedings of 2015 4th International Conference on Instrumentation, Communications, Information Technology and Biomedical Engineering, ICICI-BME 2015*, 65–69. <https://doi.org/10.1109/ICICI-BME.2015.7401336>.
19. Shin, H. C., Roth, H. R., Gao, M., Lu, L., Xu, Z. et al. (2016). Deep convolutional neural networks for computer-aided detection: CNN architectures, dataset characteristics and transfer learning. *IEEE Transactions on Medical Imaging*, 35(5), 1285–1298. <https://doi.org/10.1109/TMI.2016.2528162>.
20. Scott, G. J., Marcum, R. A., Davis, C. H., Nivin, T. W. (2017). Fusion of deep convolutional neural networks for land cover classification of high-resolution imagery. *IEEE Geoscience and Remote Sensing Letters*, 14(9), 1638–1642. <https://doi.org/10.1109/LGRS.2017.2722988>.
21. Nguyen, L. D., Lin, D., Lin, Z., Cao, J. (2018). Deep CNNs for microscopic image classification by exploiting transfer learning and feature concatenation. *Proceedings of IEEE International Symposium on Circuits and*

- Systems*, 2018-May, 1–5. <https://doi.org/10.1109/ISCAS.2018.8351550>.
22. Hussain, E., Mahanta, L. B., Das, C. R., Choudhury, M., Chowdhury, M. (2020). A shape context fully convolutional neural network for segmentation and classification of cervical nuclei in Pap smear images. *Artificial Intelligence in Medicine*, 107, 101897. <https://doi.org/10.1016/j.artmed.2020.101897>.
 23. Zhang, Y., Qiu, Z., Yao, T., Liu, D., Mei, T. (2018). Fully convolutional adaptation networks for semantic segmentation. *Proceedings of the IEEE Computer Society Conference on Computer Vision and Pattern Recognition*, 6810–6818. <https://doi.org/10.1109/CVPR.2018.00712>.
 24. Ronneberger, O., Fischer, P., Brox, T. (2015). U-net: convolutional networks for biomedical image segmentation. In: N. Navab, J. Hornegger, W. M. Wells, A. F. Frangi (Eds.), *Medical Image Computing and Computer-Assisted Intervention–MICCAI 2015*, pp. 234–241. Cham: Springer International Publishing.
 25. Graham, S., Vu, Q. D., Raza, S. E. A., Azam, A., Tsang, Y. W. et al. (2019). Hover-net: simultaneous segmentation and classification of nuclei in multi-tissue histology images. *Medical Image Analysis*, 58, 101563. <https://doi.org/https://doi.org/10.1016/j.media.2019.101563>.
 26. He, K., Gkioxari, G., Dollár, P., Girshick, R. (2017). Mask R-CNN. In *2017 IEEE International Conference on Computer Vision*, pp. 2980–2988. <https://doi.org/10.1109/ICCV.2017.322>.
 27. Kirillov, A., He, K., Girshick, R., Rother, C., Dollár, P. (2019). Panoptic segmentation. In *2019 IEEE/CVF Conference on Computer Vision and Pattern Recognition*, pp. 9396–9405. <https://doi.org/10.1109/CVPR.2019.00963>.
 28. Cheung, A. N. Y., Szeto, E. F., Leung, B. S. Y., Khoo, U. S., Ng, A. W. Y. (2003). Liquid-based cytology and conventional cervical smears: a comparison study in an Asian screening population. *Cancer*, 99(6), 331–335. <https://doi.org/10.1002/cncr.11786>.
 29. Massad, L. S., Collins, Y. C., Meyer, P. M. (2001). Biopsy correlates of abnormal cervical cytology classified using the Bethesda system. *Gynecologic Oncology*, 82(3), 516–522. <https://doi.org/10.1006/gyno.2001.6323>.
 30. Zhu, J., Norman, I., Elfgren, K., Gaberi, V., Hagmar, B. et al. (2007). A comparison of liquid-based cytology and Pap smear as a screening method for cervical cancer. *Oncology Reports*, 18(1), 157–160. <https://doi.org/10.3892/or.18.1.157>.
 31. William, W., Ware, A., Basaza-ejiri, A. H., Obungoloch, J. (2018). Computer methods and programs in biomedicine a review of image analysis and machine learning techniques for automated cervical cancer screening from pap-smear images. *Computer Methods and Programs in Biomedicine*, 164, 15–22. <https://doi.org/10.1016/j.cmpb.2018.05.034>.
 32. Zhou, J., Lamichhane, S., Sterne, G., Ye, B., Peng, H. (2013). BIOCAT: a pattern recognition platform for customizable biological image classification and annotation. *BMC Bioinformatics*, 14(1). <https://doi.org/10.1186/1471-2105-14-291>.
 33. Eliceiri, K. W., Berthold, M. R., Goldberg, I. G., Ibáñez, L., Manjunath, B. S. et al. (2012). Biological imaging software tools. *Nature Methods*, 9(7), 697–710. <https://doi.org/10.1038/nmeth.2084>.
 34. Schneider, C. A., Rasband, W. S., Eliceiri, K. W. (2012). NIH image to imageJ: 25 years of image analysis. *Nature Methods*, 9(7), 671–675. <https://doi.org/10.1038/nmeth.2089>.
 35. Peng, H., Ruan, Z., Long, F., Simpson, J. H., Myers, E. W. (2010). V3D enables real-time 3D visualization and quantitative analysis of large-scale biological image data sets. *Nature Biotechnology*, 28(4), 348–353. <https://doi.org/10.1038/nbt.1612>.
 36. Carpenter, A. E., Jones, T. R., Lamprecht, M. R., Clarke, C., Kang, I. H. et al. (2006). CellProfiler: image analysis software for identifying and quantifying cell phenotypes. *Genome Biology*, 7(10), R100. <https://doi.org/10.1186/gb-2006-7-10-r100>.
 37. Luisi, J., Narayanaswamy, A., Galbreath, Z., Roysam, B. (2011). The FARSIGHT trace editor: an open source tool for 3-D inspection and efficient pattern analysis aided editing of automated neuronal reconstructions. *Neuroinformatics*, 9(2-3), 305–315. <https://doi.org/10.1007/s12021-011-9115-0>.
 38. de Chaumont, F., Dallongeville, S., Chenouard, N., Hervé, N., Pop, S. et al. (2012). Icy: an open bioimage informatics platform for extended reproducible research. *Nature methods*, 9(7), 690–696. <https://doi.org/10.1038/nmeth.2075>.
 39. Linkert, M., Rueden, C. T., Allan, C., Burel, J. M., Moore, W. et al. (2010). Metadata matters: access to image data in the real world. *The Journal of Cell Biology*, 189(5), 777–782. <https://doi.org/10.1083/jcb.201004104>.

40. Kvilekval, K., Fedorov, D., Obara, B., Singh, A., Manjunath, B. (2010). Bisque: a platform for bioimage analysis and management. *Bioinformatics (Oxford, England)*, 26, 544–552. <https://doi.org/10.1093/bioinformatics/btp699>.
41. Hussain, E., Mahanta, L. B., Das, C. R., Talukdar, R. K. (2020). A comprehensive study on the multi-class cervical cancer diagnostic prediction on pap smear images using a fusion-based decision from ensemble deep convolutional neural network. *Tissue and Cell*, 65, 101347. <https://doi.org/10.1016/j.tice.2020.101347>.
42. Ampazis, N., Dounias, G., Jantzen, J. (2004). Pap-smear classification using efficient second order neural network training algorithms. In: G. A. Vouros, T. Panayiotopoulos (Eds.), *Methods and Applications of Artificial Intelligence*, pp. 230–245. Berlin, Heidelberg: Springer Berlin Heidelberg.
43. Dewi, Y. N., Riana, D., Mantoro, T. (2018). Improving Naïve Bayes performance in single image pap smear using weighted principal component analysis (WPCA). In *International Conference on Computing, Engineering, and Design*, pp. 1–5. <https://doi.org/10.1109/CED.2017.8308130>.
44. Ramdhani, Y., Riana, D. (2018). Hierarchical decision approach based on neural network and genetic algorithm method for single image classification of pap smear. In *Proceedings of the 2nd International Conference on Informatics and Computing, ICIC 2017*. <https://doi.org/10.1109/IAC.2017.8280587>.
45. Kurniawati, Y. E., Permanasari, A. E. (2016). Comparative study on data mining classification methods for cervical cancer prediction using pap smear results. *2016 1st International Conference on Biomedical Engineering*. <https://doi.org/10.1109/IBIOMED.2016.7869827>.
46. Abdullah, A. A., Giong, A. F. D., Zahri, N. A. H. (2019). Cervical cancer detection method using an improved cellular neural network (CNN) algorithm. *Indonesian Journal of Electrical Engineering and Computer Science*, 14(1), 210–218. <https://doi.org/10.11591/ijeecs.v14.i1.pp210-218>.
47. Araújo, F. H. D., Silva, R. R. V., Ushizima, D. M., Rezende, M. T., Carneiro, C. M. et al. (2019). Deep learning for cell image segmentation and ranking. *Computerized Medical Imaging and Graphics*, 72, 13–21. <https://doi.org/10.1016/j.compmedimag.2019.01.003>.
48. William, W., Ware, A., Basaza-Ejiri, A. H., Obungoloch, J. (2019). A pap-smear analysis tool (PAT) for detection of cervical cancer from pap-smear images. *BioMedical Engineering Online*, 18(1), 1–22. <https://doi.org/10.1186/s12938-019-0634-5>.
49. Zhang, L., Lu, L., Nogue, I., Summers, R. M., Liu, S. et al. (2017). DeepPap: deep convolutional networks for cervical cell classification. *IEEE Journal of Biomedical and Health Informatics*, 21(6), 1633–1643. <https://doi.org/10.1109/JBHI.2017.2705583>.
50. Ali, M., Sarwar, A., Sharma, V., Suri, J. (2019). Artificial neural network based screening of cervical cancer using a hierarchical modular neural network architecture (HMNNA) and novel benchmark uterine cervix cancer database. *Neural Computing and Applications*, 31(7), 2979–2993. <https://doi.org/10.1007/s00521-017-3246-7>.
51. Arya, M., Mittal, N., Singh, G. (2018). Texture-based feature extraction of smear images for the detection of cervical cancer. *IET Computer Vision*, 12(8), 1049–1059. <https://doi.org/10.1049/iet-cvi.2018.5349>.