To evaluate AI for Hypochromic Anaemia based on RBC morphology in Leishman stained blood smears: A pilot study

Dr. Rashmi Kushwaha [*], Dr. Ankit Agarwal [**], Shelley Saxena [***]

[*] MD, Professor, Department of Pathology, King George's Medical University, Lucknow, U.P, India- 226003
[**] BDS, Sevamob Ventures Limited, Lucknow, U.P, India
[***] B.E, MBA, Sevamob Ventures USA Inc

DOI: 10.29322/IJSRP.10.04.2020.p10099
http://dx.doi.org/10.29322/IJSRP.10.04.2020.p10099

***Abstract*- Introduction:** Microscopy is the simplest and the most important step in diagnosis of anemia. But the microscopy requires considerable experience and is bound to human errors. Artificial intelligence (AI) based microscopy can be an answer to this problem. AI can be used even where expert microscopists are not available. Sevamob provides artificial intelligence enabled healthcare platform to organizations. It uses deep learning for image recognition, machine learning for triaging and computer vision for object counting. AI models of various medical conditions are first trained in the software from anonymized image data procured from various sources. To determine the accuracy of AI based point-of-care screening solution for sputum, following were used: Android Smartphone / tablet with Sevamob app, tripod and a simple microscope. The system was operated by a nurse or a technician with minimal training.
Methods: 150 Ml Leishman stained smears of blood samples from clinically suspected anemia cases were included in the study.
Results: Out of these 150 smears, 94 were microcytic hypohromic on morphology and remaining 56 smears were normocytic normochromic or macrocytic in morphology when examined by expert microscopist. These smears were also analyzed by AI system. Out of these only 12 smears were found to be false positive for microcytic hypochromic blood picture. Thus, overall accuracy of AI was 81.88%. The sensitivity and specificity of AI based microscopy was 87% and 80% respectively.
Conclusion: This shows that Sevamob's AI based microscopy system can be very useful to find microcytic hypochromic anemia and has potential to replace the requirement of expert microscopist in the coming future. Sensitivity and specificity also depend on the threshold used by our AI system.

***Index Terms*-** Microcytic hypochromic anemia, artificial intelligence, microscopy

I. Introduction

Microscopy is first and foremost step in the diagnosis of microcytic hypohromic anemia. But the microscopy requires considerable experience and is bound to human errors [1]. Also, in remote areas, due to lack of expert microscopist, timely diagnosis at initial level is not possible, which may lead to increased morbidity. Artificial intelligence (AI) based microscopy can be an answer to overcome this problem. AI can be used even in the remotest areas where expert microscopists are not available.[3] The use of artificial intelligence in medicine is currently of great interest.[2,4,5,6] The diagnostic and predictive analysis of medical photos, for instance, photographs of retina[8] and skin lesions, microscopic pathological images[10-12] and radiological images. are

one of the clinical practice fields where artificial intelligence is expected to have a major influence.[7-15].This potential usefulness is largely due to advances in deep learning with artificial deep neural networks (NN),which consist of a stack of multiple layers of artificial neuronal links that loosely simulates the brain's neuronal connections, and methods specialized for analysis of images, such as the convolution neural network, a particular form of deep neural network that conceptually mimics the visual pathway [13,16,18]. Adoption of artificial intelligence tools in clinical practice requires careful, meticulous confirmation of their clinical performance and utility before the adoption.[17] Based on the urgent need for data standardization and interoperability in digital microbiology, we launched a cross-departmental prospective quality improvement project to incorporate artificial intelligence digital microbiology technology and outline the resource requirements for implementation. The solution presented here empowers microbiologists and pathologist to gain an appreciation of and enable the assessment of the appropriateness of the AI system for diagnosis. We have also shown that current AI systems can aid in the timely diagnosis of infections in resource constraint setting of developing countries like India. The use of artificial intelligence-based diagnosis and data regarding the same is scarce to our best knowledge.
Sevamob provides artificial intelligence enabled healthcare platform to organizations. It uses deep learning for image recognition, machine learning for triaging and computer vision for object counting. AI models of various medical conditions are first trained in the software from anonymized image data procured from various sources. The software can then be used to screen for these medical conditions in new samples. The system can work fully off line in last mile, low resource settings. We therefore planned this study with the aim to evaluate AI for identification of microcytic hypochromic anemia based on peripheral smear findings.

II. Methods

This study is a retrospective observational study and this study was done at three Sevamob pop-up clinics at Lucknow, Jharkhand and Rajasthan, India. Blood samples from 150 clinically suspected iron deficiency anemia patients were taken to do this study. To determine the accuracy of AI based point-of-care screening solution for peripheral blood, following were used: Android Smartphone/tablet with Sevamob app, tripod and a simple microscope. The system was operated by a nurse or a technician with minimal training. The user first prepared peripheral blood smears from blood samples of suspected iron deficiency anemia patients. To perform blood smear microscopy 2ml blood was collected from disinfected site in EDTA vial. First drop of the blood was poured on clean sterile glass slide followed by spreading the drop at 45o angle by the spreader slide to create a monolayer blood smear. Smear was stained by Leishman stain. CBC was done within 2 hours of blood collection. Smear was analyzed by expert microscopist and also by the AI based system.

The user then used the smart phone app to analyze camera feed of microscopic images of various sections of the slide. The app confirmed if the sample had microcytic hypochromic RBC's and even marked it on alive camera feed. Detection of microcytic hypochromic RBC's was done on site by Sevamob AI which worked fully offline on mobile and could be synced on cloud once network was available. AI was trained to detect microcytic hypochromic RBC's and it showed the percentage probability of the detected microcytic hypochromic RBC's. 70% was taken as the threshold to be considered as positive by AI. The images were confirmed by the expert microscopist as microcytic hypochromic RBC's or not. The evaluation of true positive, true negative, false positive and false negative was done based on the result of the comparison between the expert and the AI result.
Inclusion criteria for Blood smear examination: We included 150 patients who came for routine Complete blood count (CBC) evaluation in haematology at our site,Consent was taken from the patient/ patient attendant when they came for routine CBC in hematology lab.

Exclusion criteria: All the patients of Aplastic anaemia, patients on chemotherapy and radiotherapy.

III. Results

We analyzed 150 peripheral blood smears from clinically suspected anemia cases, as shown in table 1.

Out of 150 peripheral smears 94 were found to be microcytic hypochromic and 56 were normocytic or macrocytic as negative by expert microscopist. Based on these findings sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratio of AI based microscopy was calculated. These are depicted in table 1&2.

Table 1. Results of peripheral blood smears examined by expert microscopist and by Artificial Intelligence (AI) method

Model Info		Testing Input		Testing output				Accuracy	
Model Name	**Concept name**	**Positive cases**	**Negative cases**	**Positive Cases Result**		**Negative Cases Result**			
				Correct	**Incorrect**	**Correct**	**Incorrect**		
Blood	Hypochromic RBC(Anemia - Iron deficiency)	94	56	82	12	45	11	**81.88976**	APP
		94	56	89	5	33	23	**77.0492**	Web

Table 2: Results of 150 smear samples by AI-system

Diagnostic parameters	**Value**
Sensitivity	87%
Specificity	80%
Positive Likelihood Ratio	4.35
Negative Likelihood Ratio	0.23
Disease prevalence	
Positive Predictive Value	88%
Negative Predictive Value	78.9%
Accuracy	81.88%

Image 1 and 2 shows the % probability of AFB by AI system. % probability of AI images ranged from 51% to 99% in a microscopicfield.

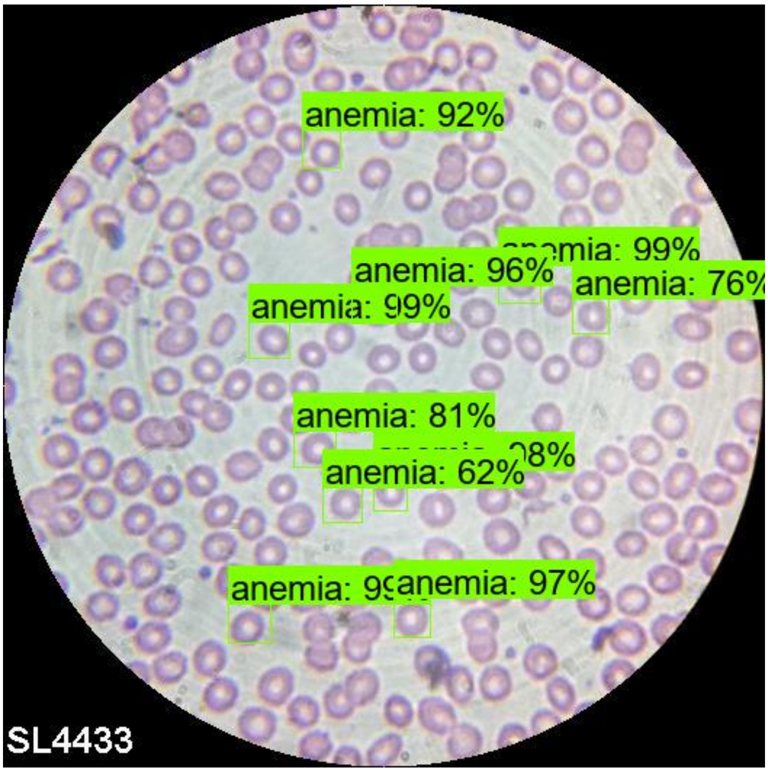

Image 1: Shows the marked area with % probability by the AI based software

ISSN 2250-3153

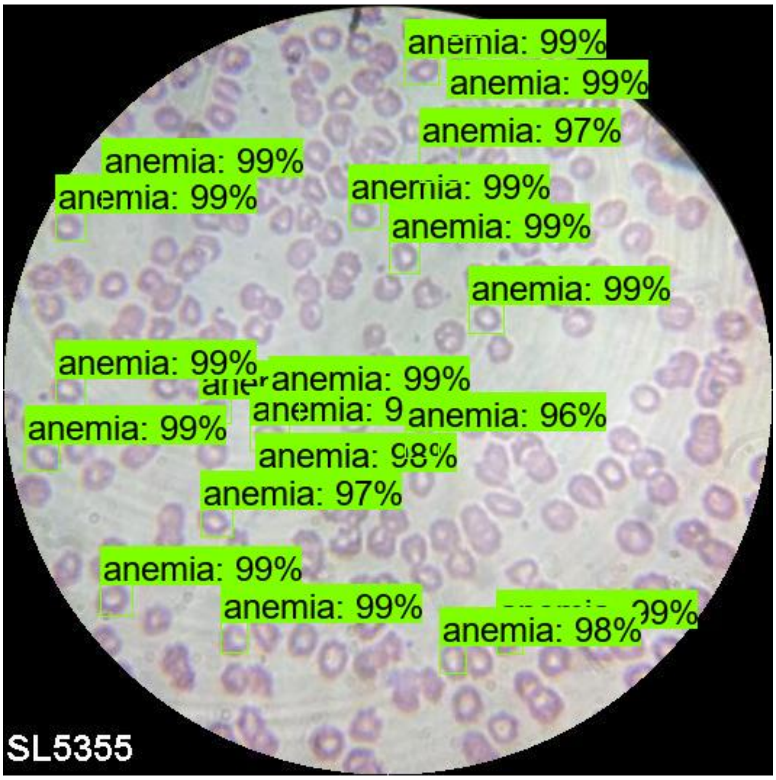

Image 2: Shows the marked area with % probability by the AI based software

IV. Discussion

In the present pilot study, we have analyzed 150 peripheral blood smears by Leishman staining for presence of microcytic hypochromic blood picture and correlated with AI system. The sensitivity and specificity were found to be good. This shows that this particular AI system may be very useful for detection of presence of microcytic hypochromic red blood cells and can replace the requirement of expert microscopist in the coming future. Sensitivity and specificity of AI also depends on the threshold set for the AI system used. In our study this threshold was set at 70% and this was decided after training and internal lab testing of samples at different thresholds of 5% intervals (50%-80%). We found optimal sensitivity and specificity at 70% threshold only. It should be noted that this idea is called as self-adjusting neural networks that adjust themselves to a boundary to that the input data and their outcome must convert. To our understanding the meaning of a self-learning classification system adjusts the "rules" to a given final outcome. At higher threshold, there were too many false negatives. At lower threshold, there were too many false positives. It finds appropriate that the implementation of an automated diagnosis or pre-screening system consists of several modules that should work independently from each other. To start with, this concept a control and evaluation of the objective image quality is necessary so one can easily evaluate between the results of AI and microscopy. The system has used various enhancement techniques, and it has best quality to analyze the microscopic peripheral smear images, segmentation algorithm is developed to automate the process of detection of microcytic hypochromic RBC's using digital microscopic images of different subjects. Shape features extraction technique had been implemented to extract eleven shape features and finally for classification of the support vector machine was used to be a pattern recognition tool to classify the object in peripheral blood smear images to microcytic hypochromic RBC's or other types of RBC's.

As per our best knowledge such AI based pilot study has never been done before in India or elsewhere in the world. Few automated microscopy systems have been used in the past, but they were not based on artificial intelligence. MM Alam et al in their study used "you only look once" (YOLO) object detection and classification algorithm. YOLO framework has been trained with a modified configuration BCCD Dataset of blood smear images to automatically identify and count red blood cells, white blood cells, and platelets. Moreover, this study with other convolutional neural network architectures considering architecture complexity, reported accuracy, and running time with this framework and compare the accuracy of the models for blood cells detection. (19). Acharya V et al in their study proposed an image-processing technique for counting the number of red blood cells. It aimed to examine and process the blood smear image, in order to support the counting of red blood cells and identify the number of normal and abnormal cells in the image automatically. K-medoids algorithm which is robust to external noise was used to extract the WBCs from the image. Granulometric analysis was used to separate the red blood cells from the white blood cells. The red blood cells obtained were counted using the labeling algorithm and circular Hough transform. The radius range for the circle-drawing algorithm is estimated by computing the distance of the pixels from the boundary which automates the entire algorithm. A comparison is done between the counts obtained using the labeling algorithm and circular Hough transform. Results of the work showed that circular Hough transform was more accurate in counting the red blood cells than the labeling algorithm as it was successful in identifying even the overlapping cells. [20].

In case of histopathology examination AI have been successfully used to segment the colon gland, breast tissue, as well as the nuclei as reported by different authors in their study [26-33].

The limitation of our study is the small sample size. A larger sample size study is further required to validate our system.

V. Conclusion

In this pilot study automated AI based software for identification of microcytic hypochromic RBC's has been done. This AI based software method reduces fatigue and screening time by providing images on the screen and avoiding visual inspection of microscopic. The system has an acceptable degree of accuracy, specificity and sensitivity.

References

[1] Cruz D., Jennifer C., Valiente L.C., et al. : 'Determination of blood components (WBCs, RBCs, and platelets) count in microscopic images using image processing and analysis'. Proc. Int. Conf. on Humanoid, Nanotechnology, Information Technology, Communication and Control, Environment and Management (HNICEM), December 2017.

[2] Chen JH, Asch SM. Machine learning and prediction in medicine: beyond the peakofinflated expectations. N Engl J Med 2017; 376 (26):2507–2509.

[3] Seong Ho Park , Kyunghwa Han. Methodologic Guide for Evaluating Clinical Performance and Effect of Artificial Intelligence Technology for Medical Diagnosis and Prediction. RSNA. Radiology 2018; 286 (3): 800-809.

[4] Cabitza F, Rasoini R, Gensini GF. Unintended consequences of machine learninginmedicine. JAMA2017;318(6):517–518.

[5] Lee J-G, Jun S, Cho Y-W, et al. Deep learning in medical imaging: general overview. Korean J Radiol. 2017; 18(4):570–584.

[6] Kohli M, Prevedello LM, Filice RW, Geis JR. Implementing machine learning in radiology practice and research. AJR Am J Roentgenol2017;208(4):754–760.

[7] Zhou SK, Greenspan H, Shen D. Deep learning for medical image analysis. San Diego, California. Elsevier Inc., 2017. 430 p.

[8] Gulshan V, Peng L, Coram M, et al. Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photograph. JAMA2016; 316 (22): 2402–2410.

[9] Esteva A, Kuprel B, Novoa RA, et al. Dermatologist-level classification of skin cancer with deep neural networks. Nature2017;542(7639):115–118.

[10] Ehteshami Bejnordi B, Veta M, Johannes van Diest P, et al. Diagnostic assessment of deep learning algorithms for detection of lymph node metastases in women with breast cancer. JAMA 2017;318(22):2199–2210.
[11] Vandenberghe ME, Scott ML, Scorer PW, Söderberg M, Balcerzak D, BarkerC. Relevance of deep learning to facilitate the diagnosis of HER2 status in breast cancer. Sci Rep2017;7: 45938.
[12] Yu KH, Zhang C, Berry GJ, et al. Predicting non–small cell lung cancer prognosisbyfully automated microscopic pathology image features. Nat Commun 2016; 7: 12474.
[13] Lakhani P, Sundaram B. Deep learning at chest radiography: automated classificationof pulmonary tuberculosis by using convolutional neural networks. Radiology 2017; 284(2):574–582.
[14] Prevedello LM, Erdal BS, Ryu JL, et al. Automated critical test findings identification and online notification system using artificial intelligence in imaging. Radiology. 2017; 285(3):923–931.
[15] Yasaka K, Akai H, Abe O, Kiryu S. Deep learning with convolutional neural net work for differentiation of liver masses at dynamic contrast-enhanced CT: a preliminary study. Radiology doi: 10.1148/radiol.2017170706. Published online October27, 2017.
[16] An intuitive explanation of convolutional neural networks. The data science blog. https://ujjwalkarn.me/2016/08/11/intuitiveexplanation-convnets. AccessedAugust11, 2017.
[17] Herrmann D , Clunie A et al. Implementing the DICOM Standard for Digital Pathology; Nov 2, 2018, IP: 4.16.85.218]m http://www.jpathinformatics.org
[18] Goodfellow I, Bengio Y, Courville A. Deep learning. Cambridge, Mass: MIT Press, 2016.
[19] Alam MM, Islam MT. Machine learning approach of automatic identification and counting of blood cells. Healthc Technol Lett. 2019 Aug; 6(4): 103–108.
[20] Acharya V, Kumar P. Identification and red blood cell automated counting from blood smear images using computer-aided system. Med Biol Eng Comput. 2018 Mar;56(3):483-489. doi: 10.1007/s11517-017-1708-9. Epub 2017 Aug 17
[21] Ronneberger O, Fischer P, Brox T. U-net: convolutional networks for biomedical image segmentation. In Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics). https://arxiv.org/abs/1505.04597v1
[22] Van Valen, D.A., Kudo, T., Lane, K.M., Macklin, D.N., Quach, N.T., De Felice, M.M., et al. (2016) Deep learning automates the quantitative analysisof individual cells in live-cell imaging experiments. PLoS Comput. Biol. 2015; (12):1–24.
[23] Long, J., Shelhamer, E. and Darrell, T. Fully convolutional networks for semantic segmentation. Proc. IEEE Comput. Soc. Conf. Comput. Vis.Pattern Recognit. 2015; 3431–3440.
[24] Ciresan D.C., Giusti A., Gambardella L.M., Schmidhuber, J. Deep neural networks segment neuronal membranes in electron microscopy images. NIPS Proceedings. 2012; 1–9.
[25] Ning F, Delhomme D, Le Cun Y, Piano F, Bottou L, Barbano P.E. et al. Toward automatic phenotyping of developing embryos from videos. IEEE Trans. Image Process. 2015; 14, 1360–1371.
[26] Kainz, P., Pfeiffer, M. and Urschler, M. Semantic segmentation of colon glands with deep convolutional neural networks and total variation segmentation. Peer J , 2017; e3874
[27] Bentaieb A, Hamarneh G. Topology aware fully convolutional networks for histology gland segmentation. Int. Conf. Med. Imag Comput. Comput. Interv. 2016; 460–468.
[28] Chen H., Qi X, Yu L, Heng PA. DCAN: deep contour-aware networks for accurate gland segmentation. Proc. IEEE Conf. Comput Vis Pattern Recognit. 2016; 2487–2496.
[29] Li, W., Manivannan, S., Akbar, S., Zhang, J., Trucco, E. and McKenna, S.J. Gland segmentation in colon histology images using hand-crafted features and convolutional neural networks. Proc. Int. Symp. Biomed. Imaging. 2016: 1405–1408.
[30] Xu Y, Li Y, Liu M, Wang Y, Lai M, Chang E.I.C. Gland instance segmentation by deep multichannel side supervision. Lect. Notes Comput. Sci. (including Subser. Lect. Notes Artif. Intell. Lect. Notes Bioinformatics), LNCS. 2016; 496–504
[31] Xu J, Luo X, Wang G, Gilmore H, Madabhushi A, Reserve CW. A deep convolutional neural network for segmenting and classifying epithelial regions in histopathological images. Neurocomputing 2017; 191: 214–223.
[32] Litjens G, Sánchez C.I, Timofeeva N, Hermsen M, Nagtegaal I, Kovacs, I et al. Deep learning as a tool for increased accuracy and efficiencyofhistopathological diagnosis. Sci. Rep. 2016; 6: 1–11.
[33] Naylor P, Laé M, Reyal F, Walter T. (2019) Segmentation of nuclei in histopathology images by deep regression of the distance Map. IEEE Trans Med. Imaging. 2019; 38: 448–459.

AUTHORS

First Author – Dr. Rashmi Kushwaha, MD, Professor, Department of Pathology, King George's Medical University, Lucknow, U.P, India- 226003, Email ID: docrashmi27@yahoo.co.in
Second Author – Dr. Ankit Agarwal, BDS, Sevamob Ventures Limited, Lucknow, U.P, India, Phone: +91-7408417918 Email ID: dr.ankitagarwal06@sevamob.com
Third Author – Shelley Saxena, B.E, MBA, Sevamob Ventures USA Inc, Email ID: saxenas@sevamob.com