

# Artificial Intelligence based AFB microscopy for Pulmonary Tuberculosis in North India: A pilot study

Vineeta Khare, M.D.; Ankit Agrawal, BDS; Prashant Gupta, M.D.; Shelley Saxena, B.E., MBA

\* Professor, Department of Microbiology, Era's Lucknow Medical College and hospitals, Lucknow, U.P, India- 226003

\*\* Sevamob Ventures USA Inc, Lucknow, U.P, India

\*\*\* Professor, Department of Microbiology, King George's Medical University, Lucknow, U.P, India-226003

\*\*\*\* Sevamob Ventures USA Inc

DOI: 10.29322/IJSRP.9.12.2019.p9669

<http://dx.doi.org/10.29322/IJSRP.9.12.2019.p9669>

**Abstract- Introduction:** Microscopy is the simplest and the most important step in diagnosis of pulmonary tuberculosis. 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 ZN stained smears of sputum samples from clinically suspected pulmonary tuberculosis cases were included in the study.

**Results:** Out of these 150 smears, 118 were found to be positive and 32 as negative by expert microscopist. These smears were also analyzed by AI system. Out of these only 6 smears were found to be false positive for AFB. Thus, the sensitivity and specificity of AI based microscopy was 81.7% and 80% respectively.

**Conclusion:** This shows that our AI based microscopy system can be very useful to find AFB 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-** Tuberculosis, artificial intelligence, microscope

## I. INTRODUCTION

Microscopy is first and foremost step in the diagnosis of tubercular infections. 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 solutions presented here empower 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 Acid-Fast Bacilli (AFB) in ZN stained sputum smear.[26]

## 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. Sputum samples from 150 clinically suspected pulmonary tuberculosis patients were taken to do this study. 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. The user first prepared Ziehl-Neelsen stained smears from sputum samples of clinically suspected pulmonary tuberculosis patients. 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 AFB bacterium and even marked it on alive camera feed. Detection of AFB 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 AFB and it showed the percentage probability of the detected AFB. 70% was taken as the threshold to be considered as positive by AI. The images were

confirmed by the expert microscopist as AFB positive or negative. 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.

III. RESULTS:

We analyzed 150 smears of sputum samples for AFB from clinically suspected pulmonary tuberculosis cases, as shown in table 1. Out of 150 smears 118 were found to be positive and 32 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 & 3.

Testing output of expert microscopist		Positive	Negative
Sample	Test		
Sputum	AFB smear	118	32

Table 1. Results of AFB smear examined by expert microscopist

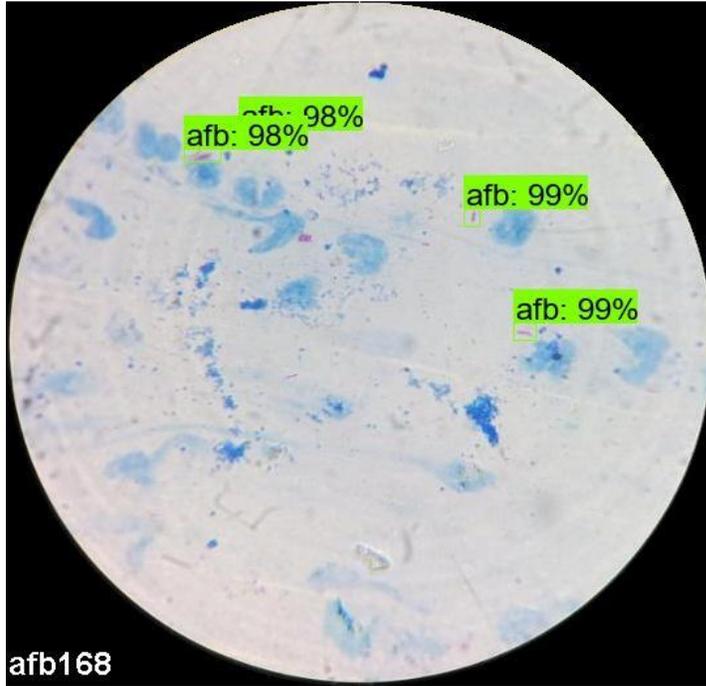
Testing output of AI for AFB smear			
True positive	False negative	True negative	False positive
98	22	24	6

Table 2. Results of 150 smear samples by AI system

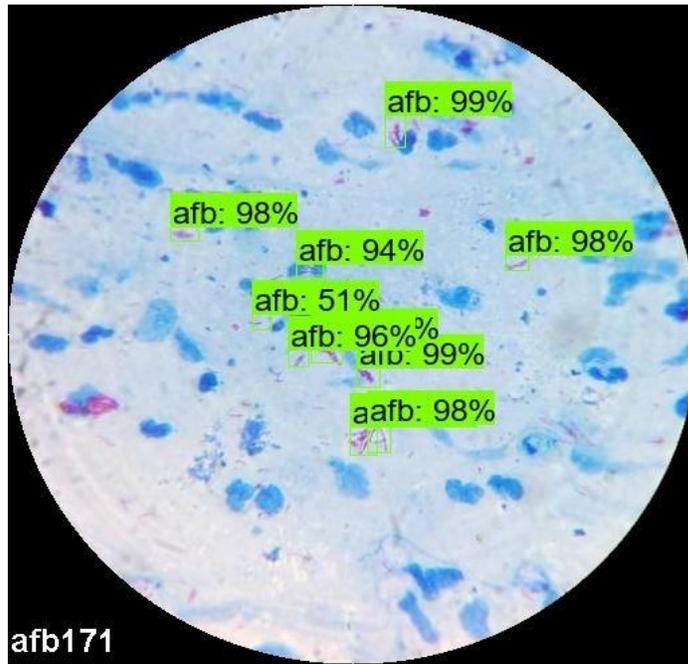
<b>Diagnostic parameters</b>	<b>Value</b>	<b>95% CI</b>
<b>Sensitivity</b>	81.7%	73 % to 88%
<b>Specificity</b>	80 %	61% to 92%
<b>Positive Likelihood Ratio</b>	4.07	1.98 to 8.36
<b>Negative Likelihood Ratio</b>	0.23	0.15 to 0.35
<b>Disease prevalence</b>	79.7 %	72 % to 86 %
<b>Positive Predictive Value</b>	94 %	87 % to 97 %
<b>Negative Predictive Value</b>	52.2 %	42 % to 62 %
<b>Accuracy</b>	81.1%	74 % to 87 %

**Table 3: Diagnostic parameters of AI system**

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



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



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

#### IV. DISCUSSION

In the present pilot study, we have analyzed 150 smears by ZN staining for AFB by AI system. The sensitivity and specificity were found to be good. This shows that this particular AI system may be very useful for AFB smear microscopy 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 sputum smear images, segmentation algorithm is developed to automate the process of detection of TB using digital microscopic images of different subjects. Shape features extraction technique had been implemented to extract eleven shape features and finally for classification the support vector machine was used to be a pattern recognition tool for classify the object in sputum smear images to TB bacillus object and non-TB bacillus object. [28]

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. Costa *et al* in year 2017 developed an automatic microscopy method for identification of AFB, images were based on Red and Green color channels using global adaptive threshold segmentation. [19,28]. They showed that their system was 76.7 % sensitive. Sadaphal P *et al* in year 2018 proposed an automated, multi-stage, color-based Bayesian segmentation system. This system grouped the smears into definite, possible and non-TB by passing photo-micrographic calibration [20, 28]. However, they did not discuss sensitivity and specificity of their system.

Fisher et al, Valen et al, Long et al, Ciresan et al, Ning et al, in their study said that neural network have outperformed the conventional approach in term of accuracy and generalization when we perform cell segmentation in subculture of multiple cell type. [21,25]. 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 [25,27,29-34].

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 tuberculosis bacilli identification had 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] TB Microscopy Network Accreditation: An assessment tool. October 2013.
- [2] Chen JH, Asch SM. Machine learning and prediction in medicine: beyond the peak of inflated 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 learning in medicine. *JAMA* 2017; 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 Roentgenol* 2017; 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. *JAMA* 2016; 316 (22): 2402–2410.
- [9] Esteva A, Kuprel B, Novoa RA, et al. Dermatologist-level classification of skin cancer with deep neural networks. *Nature* 2017; 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, Barker C. Relevance of deep learning to facilitate the diagnosis of HER2 status in breast cancer. *Sci Rep* 2017; 7: 45938.
- [12] Yu KH, Zhang C, Berry GJ, et al. Predicting non-small cell lung cancer prognosis by fully automated microscopic pathology image features. *Nat Commun* 2016; 7: 12474.
- [13] Lakhani P, Sundaram B. Deep learning at chest radiography: automated classification of 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 network for differentiation of liver masses at dynamic contrast-enhanced CT: a preliminary study. *Radiology* doi: 10.1148/radiol.2017170706. Published online October 27, 2017.
- [16] An intuitive explanation of convolutional neural networks. The data science blog. <https://ujjwalkarn.me/2016/08/11/intuitive-explanation-convnets/>. Accessed August 11, 2017.
- [17] Herrmann D, Clunie A et al. Implementing the DICOM Standard for Digital Pathology; Nov 2, 2018, IP: 4.16.85.218jm <http://www.jpathinformatics.org>
- [18] Goodfellow I, Bengio Y, Courville A. Deep learning. Cambridge, Mass: MIT Press, 2016.
- [19] Costa M, Costa F, Sena, J F, Salen J, Lima M.O. Automatic identification of mycobacterium tuberculosis with conventional light microscopy. Proceedings of the 30th Annual International Conference of the IEEE EMBS, (2008), pp. 382- 385, Vancouver, British Columbia, Canada.
- [20] Sadaphal, P, Rao, J., Comstock, G.W. & Beg, M.F., Image processing techniques for identifying Mycobacterium tuberculosis in Ziehl-Neelsen stains. *International Journal of Tuberculosis Lung Disease*. 2008; (12); 579-582. ISSN 1027-3719.

- [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 analysis of 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] Cattamanchi A, Davis J et al. Sensitivity and Specificity of Fluorescence Microscopy for Diagnosing Pulmonary Tuberculosis in a High HIV Prevalence Setting; *Int J Tuberc Lung Dis.* 2009 Sep; 13(9): 1130–1136.
- [27] 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
- [28] Raj kumar. M. Tuberculosis Disease Detection Using Image Processing. 2018 IJSRCSEIT | Volume 3 | Issue 3 | ISSN : 2456-3307.
- [29] Bentaieb A, Hamarneh G. Topology aware fully convolutional networks for histology gland segmentation. *Int. Conf. Med. Imag Comput. Comput. Interv.* 2016; 460–468.
- [30] 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.
- [31] 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.
- [32] 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
- [33] 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.
- [34] Litjens G, Sánchez C.I, Timofeeva N, Hermsen M, Nagtegaal I, Kovacs, I et al. Deep learning as a tool for increased accuracy and efficiency of histopathological diagnosis. *Sci. Rep.* 2016; 6: 1–11.
- [35] Naylor P, Laé M, Reyat 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. Vineeta Khare, MD, Professor, Department of Microbiology, Era’s Lucknow Medical College and hospitals, Lucknow, U.P, India- 226003, Email ID: [vinitakhare@yahoo.com](mailto:vinitakhare@yahoo.com)

**Second Author** – Dr. Ankit Agarwal, BDS, Sevamob Ventures USA Inc, Lucknow, U.P, India, Phone: +91-7408417918 Email ID: [dr.ankitagarwal06@gmail.com](mailto:dr.ankitagarwal06@gmail.com)

**Third Author** – Dr. Prashant Gupta, MD, Professor, Department of Microbiology, King George’s Medical University, Lucknow U.P, India-226003, Email ID: [prashantgupta46@hotmail.com](mailto:prashantgupta46@hotmail.com)

**Fourth Author** – Shelly Saxena, B.E, MBA, Sevamob Ventures USA Inc