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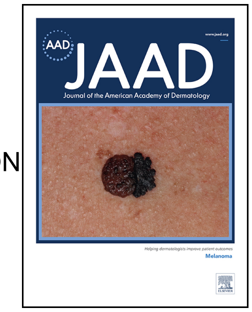

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Gabriele Campanella[1,2], MS; Kishwer S Nehal[3], MD; Erica H Lee[3], MD; Anthony Rossi[3], MD; Brandon Possum[3], HT; Genna Manuel[3], HT; Thomas J Fuchs[1,2], PhD; and Klaus J Busam[2], MD.

Weill Cornell Graduate School of Medical Sciences[1] and Departments of Pathology[2] and Medicine[3], Memorial Sloan Kettering Cancer Center, New York, NY

Corresponding Author:
Klaus J Busam, MD
Dept of Pathology, RmC530
Memorial Sloan Kettering Cancer Center
1275 York Ave, New York, NY 10065
Phone: 212 639 5679
Fax: 212 717 3203
busamk@mskc.org

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Word count: 500
References: 4
Figures: 2

To the Editor:

Advances in digital pathology with rapid slide scanning of whole slide images (WSI) (1,2) and artificial intelligence (AI) offer opportunities for improved accuracy and real time quality assurance of histopathologic interpretations, which could be employed for intraoperative frozen section margin assessment of skin cancer. A recent study explored an AI algorithm for detecting basal cell carcinoma (BCC) in digital images of Mohs slides using a total of 100 cases, 60 for training, 20 for validation and 20 for testing (3). The final model's sensitivity was 70.6%; its specificity was 79.1%.

We also performed a retrospective study (under IRB protocol 18-013) on the feasibility of detecting BCC in Mohs sections, but used a deep-learning system under the multiple instance learning assumption that was trained on thousands of WSI (4).

6,252 WSI were used during the learning phase, 4,699 for training and 1,553 for validation and model selection. Of the entire cohort, 1,154 WSI were positive for BCC.
An additional 200 Mohs sections were used for model finetuning. The final test set consisted of 100 frozen sections from 50 patients. 36 sections had BCC, 64 were benign. The model used was a ResNet34 convolutional neural network (CNN) pre-trained on natural images. We compared the algorithm's performance to that of three Mohs surgeons reading individually the same 100 WSI on a screen.

Our algorithm performed with high sensitivity (Figure 1). It identified correctly all sections with BCC. There were 4 false-positive results (specificity of 94%). The specificity of the surgeons ranged from 91.4% to 100%. Two of three surgeons achieved a specificity of 100% (all margins scored as positive contained BCC). The sensitivity of the surgeons in detecting BCC on the scanned images varied from 90% -97.3% (failure to detect BCC in 1,2 and 4 cases, respectively). The AUC performance of the surgeons compared to the algorithm is illustrated in Figure 2.

When comparing the algorithm to the surgeons one needs to bear in mind that our test conditions don't mirror clinical practice. Scanned images, not slides were used. Furthermore, when a microscopic finding of uncertain significance is encountered in clinical practice, one is not limited to rendering a best guess based on one slide alone. Additional histologic sections can be obtained for further clues. Nonetheless, assistance from a second reader, during Mohs surgery, such as an AI algorithm, could have clinical value. A discordance between the algorithm and a physician could prompt a second look at a particular slide in real time to ensure that no positive margin is missed.

While our findings document clinical grade high sensitivity of our deep learning algorithm, a major limitation of the current study is the binary classification of BCC present versus absent. Further studies are needed to assess how the algorithm performs for the detection of other tumors, such as squamous cell carcinoma. It is possible that different models may be required for various diagnostic problems. Prospective studies are needed to assess the practicality of integrating AI in clinical practice and how it affects outcomes.

Figure Legends

Figure 1:

Performance of the proposed algorithm. Receiver operating characteristics (ROC) curves for the final prediction and individual models trained at different magnifications. AUC: Area under the curve. MPP: Microns per pixel.

Figure 2

Comparison of the performance of the algorithm with that of three dermatologic surgeons. AUC: Area under the curve.

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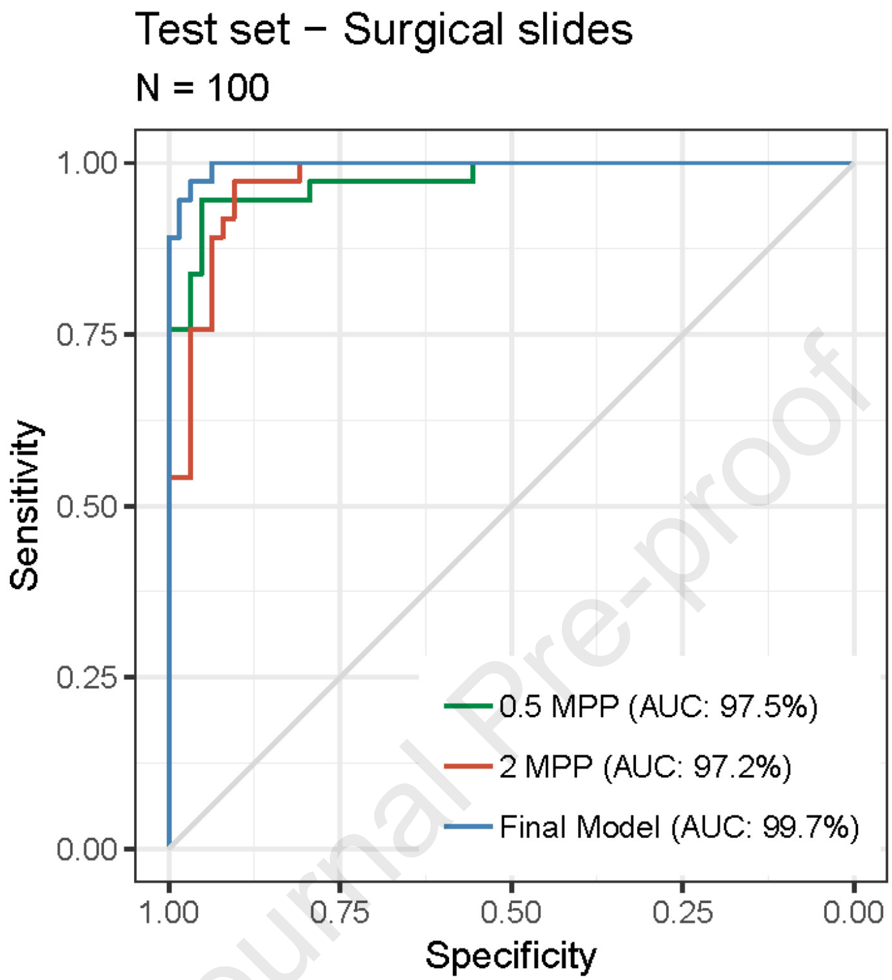
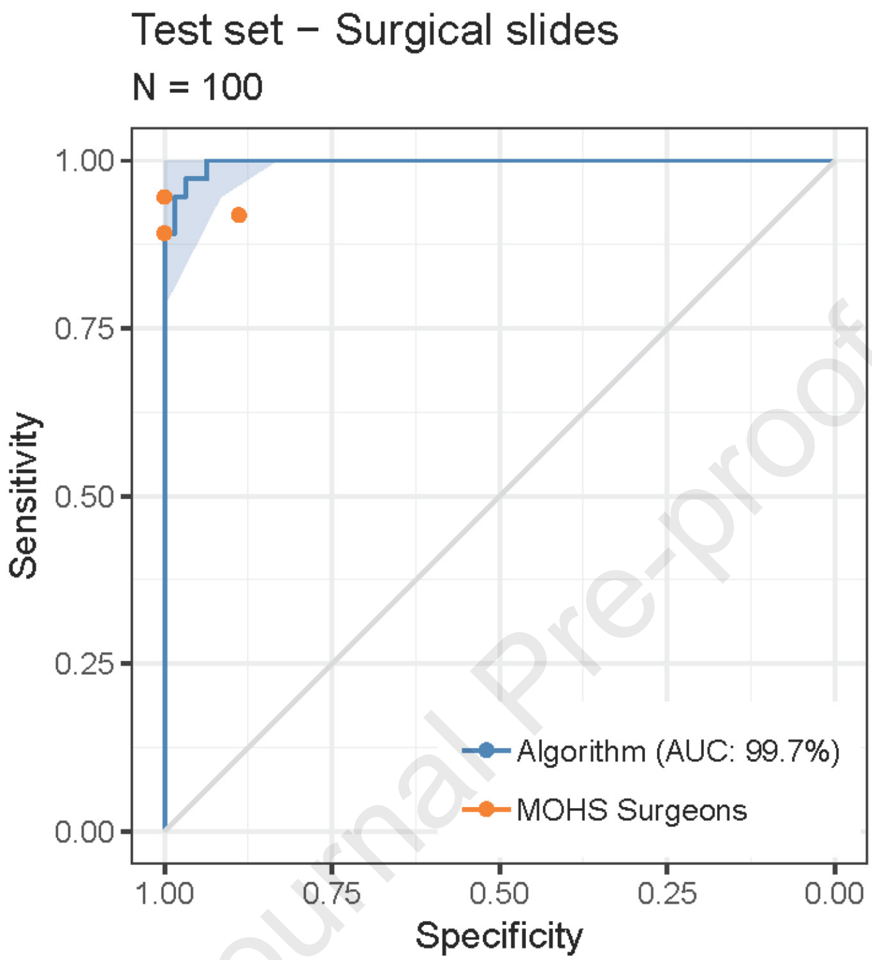

Test set − Surgical slides
N = 100
1.00
0.75
0.50
0.25
0.00
Sensitivity
1.00
0.75
0.50
0.25
0.00
Specificity
0.5 MPP (AUC: 97.5%)
2 MPP (AUC: 97.2%)
Final Model (AUC: 99.7%)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