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https://doi.org/10.1016/j.jaad.2020.06.068

A deep learning algorithm to detect the presence of basal cell carcinoma on Mohs micrographic surgery frozen sections

To the Editor: Nonmelanoma skin cancer represents the most common cancer in the United States with more than 5.4 million cases annually, of which 8 in 10 are basal cell carcinomas (BCCs).[1] Mohs micrographic surgery (MMS) treats BCCs by providing margin control. The process of accurate and complete interpretation of frozen section slides would benefit from the presence of a second reader. We seek to apply deep learning to MMS by developing an algorithm to aid the surgeon in detecting BCC on frozen sections.

We retrospectively selected 75 cases that had positive findings for BCC on MMS and 25 cases that initially had biopsy-proven BCC but had negative findings for tumor on the first stage of MMS among all MMS cases with a biopsy-confirmed diagnosis of BCC and available frozen section slides performed at a single academic center from 2011 to 2018. Digital images of each frozen section were taken at ×2 magnification with a 2-megapixel Olympus (Tokyo, Japan) DP20-5 digital camera. Each ×2 image was independently assigned as positive or negative for BCC. The data were randomly partitioned into 60% training, 20% validation, and 20% test set at the case level. The images were preprocessed via resizing, normalization, and standard data augmentation. A class-balanced data set was fed through the 2-dimensional residual nets (ResNet)[2] pretrained with ImageNet (Stanford Vision Lab, Stanford University, Princeton University). After random hyperparameter search, we arrived at a ResNet-50 with Adam optimizer and learning rate of 0.001 with a dropout of 0.2.

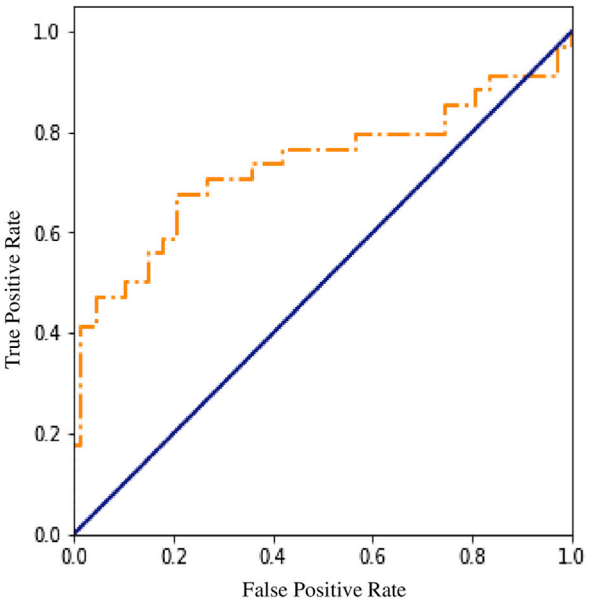

Fig 1. Receiver operating characteristic curve. The curve shows the overall performance of the deep learning algorithm, showing the tradeoff between sensitivity and specificity. The area under the curve is 0.753.

The final model evaluated on the holdout test set achieved an area under the receiver operating characteristic curve of 0.753 (Fig 1). Representative sensitivity/specificity tradeoff values were a sensitivity of 70.6% at specificity of 79.1%. The most common source of false positives was dense aggregates of inflammatory cells, and the most common source of false negatives was small aggregates of tumor cells in relation to the specimen size (Fig 2).

Our algorithm has several key strengths. First, the model consistently analyzes an image through the neural network parameters without emotional bias. Second, it can conduct a detailed image analysis at the pixel level, limited only by the inherent noise of the microscope and camera. The approaches to image analysis by the Mohs surgeon and algorithm differ fundamentally, and consequently, their combined efforts provide increased accuracy of BCC detection, as reflected in the concept of ensemble learning.[3] Finally, the algorithm serves as a safety mechanism to help the surgeon avoid missing residual tumor.

Our model has several notable limitations. Most importantly, our pilot algorithm is limited by the small sample size. A larger, more diverse data set is needed to achieve higher area under the curve and

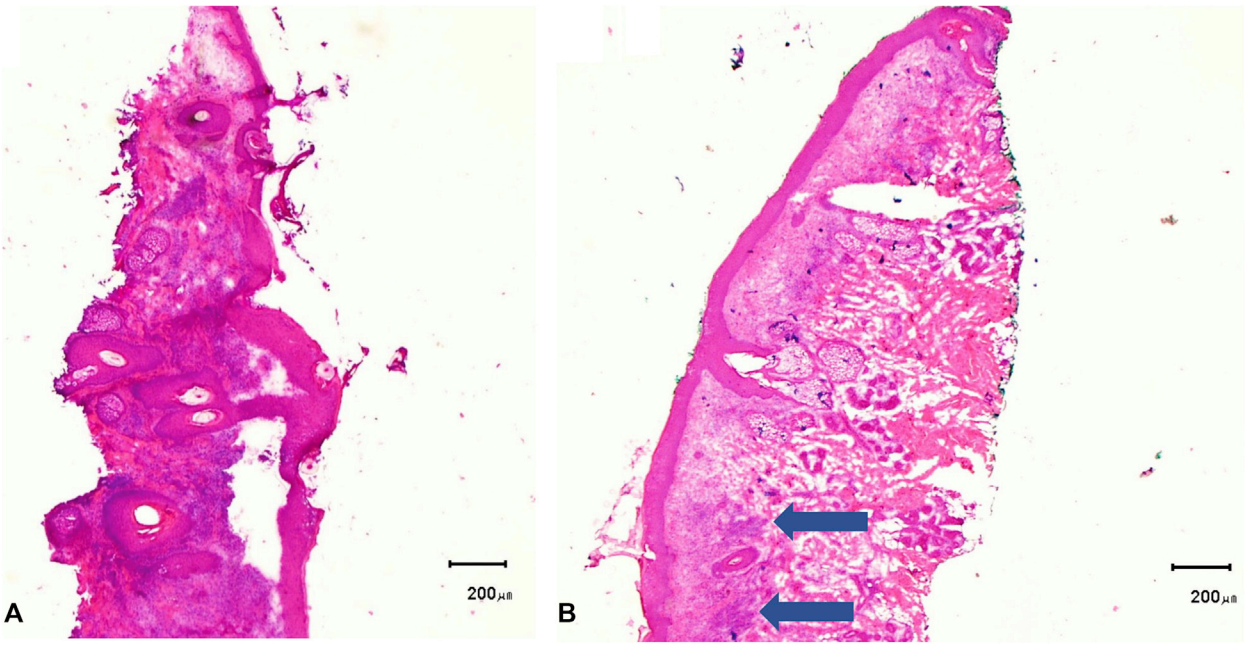

Fig 2. Error analyses. Examples of images confidently predicted by the algorithm as (**A**) positive for tumor and incorrect (false positive) and (**B**) negative for tumor and incorrect (false negative). Arrows indicate areas involved by basal cell carcinoma. Of note, these images were taken of deeper cuts, where sections are thicker and have missing tissue due to block exhaustion.

potential incorporation into clinical use. Also, the algorithm does not assess image quality and must commit to a positive or negative finding for tumor; however, given our envisioned application of the model as a safety mechanism, not a fully autonomous reader, image quality control is left to the surgeon.

We developed a proof-of-concept algorithm that may assist in detection of BCC on MMS frozen sections. Future studies with larger, multicenter data sets can further refine the model.

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Funding sources: Dr J.H. Sohn was supported by a National Institutes of Health T32 training grant (5T32EB001631-15).

Conflicts of interest: None disclosed.

IRB approval status: Reviewed and approved by the University of California—San Diego IRB (190196CX).

Reprints not available from the authors.

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https://doi.org/10.1016/j.jaad.2020.06.080