A deep-learning algorithm to localize basal cell carcinoma foci on Mohs surgery frozen sections

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LETTER TO THE EDITOR

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Dear Editor,

Previous studies applied deep learning to Mohs micrographic surgery (MMS) by developing algorithms able to classify digitized histopathology slides as BCC positive or negative.[1–3] Because the histological location of residual tumour is necessary to guide subsequent excision, we aimed to develop and evaluate an algorithm using convolutional neural networks (CNNs) that would automatically localize and point out BCC tumour islands in digitized MMS histology slides. In this retrospective study (IRB protocol 22.01.16), a total of 246 haematoxylin and eosin-stained frozen section histology slides from 106 different patients were obtained from our Mohs

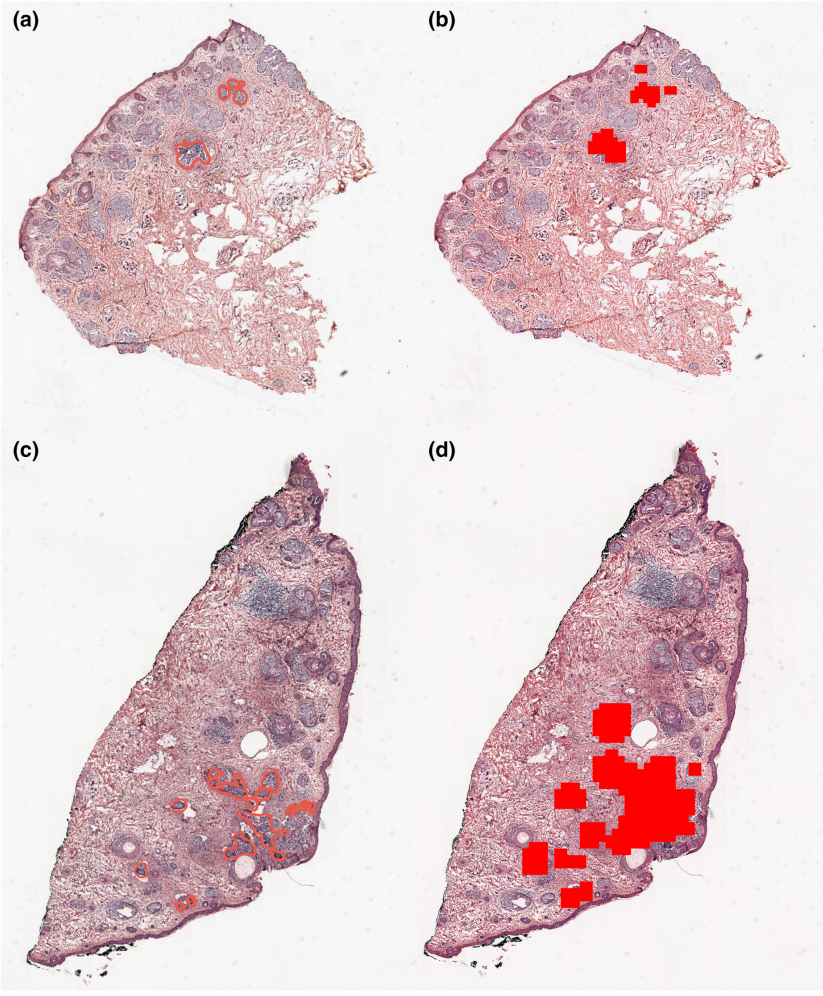

FIGURE 1 Two examples of automatic localization of basal cell carcinoma tumour foci by the deep-learning algorithm (right panel, b, d) compared with corresponding ground-truth data set annotations (left panel, a, c) in frozen digitized slides from Mohs surgery.

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Skin Center. Time-altered slides were excluded from the study. Slides containing artefacts inherent to the technique (tissue folds, shattering, bubbles) were not excluded. The selected slides were representative of all histological BCC variants. 140 slides from 91 different patients were digitized in whole slide images (WSIs) using iScan Coreo Roche digital slide scanner at a 20× magnification. 125 WSIs (from 76 patients), consisting in the training and validation subsets, were exhaustively annotated by a trained pathologist by outlining the BCC tumour islands in a WSI viewer (QuPath software). WSIs were cut into 256×256 pixels patches (n = 204,576) to train a CNN based on pretrained EfficientNet B5 to differentiate BCC from normal tissue. At the slide level, the patches classified as positive by a homemade algorithm were automatically underlined in the WSI. A testing subset consisting of 44 frozen sections (28 BCC positive and 16 BCC negative) from 15 patients was used to evaluate how well the model performs on unseen data. Results were compared to the pathologist's annotation (gold standard). In the test data set, our algorithm correctly classified 29,588/30773 patches (sensitivity 0.732, specificity 0.975, positive predictive value 0.631, negative predictive value 0.984, area under the receiver operating characteristic curve 0.9913). A BCC focus was defined as an annotated continuous part of BCC surrounded by normal tissue. At a slide level, results were considered as True Positive (TP: i.e. tumour focus correctly localized) if the algorithm marked at less one patch into the focus annotated. They were considered False Negative (FN) if no predicted patch matched the annotated focus, and False Positive (FP) if predicted patch(es) did not match any annotated foci. The algorithm correctly localized 843/877 BCC foci (sensitivity 0.961, positive predictive value 0.894) (Figure 1). When analysing the algorithm tumour foci misclassifications, the 100 FP findings (77 in the 10 BCC-positive slides and 23 in the 5 BCC-negative slides) were cutaneous annexes (n = 38), dense inflammatory infiltrates or vessels (n = 27) and artefacts and folds (n = 21). Of note, 14 FP findings were in fact real BCC tumour foci, which were not correctly annotated manually. 34 FN findings were present in 5/10 BCC-positive slides. They were explained by non-optimal staining contrast and some missed foci composed of few tumoral cells and were always close to TP. In the present study, we used a classification model at a patch level that could better fit the need for quick analysis imposed by Mohs surgery.[4] The average time needed for the algorithm to evaluate one WSI containing 3 tissue sections was 13±3 min with a NVIDIA P100 16GB graphic processing unit (GPU). This time could be reduced to less than 5 min by using a multi-GPU system. We evaluated, to the best of our knowledge for the first time, the number of BCC foci correctly localized in a WSI. The algorithm has the ability to localize 96% of BCC foci. It points out automatically its predictions on the WSI (i.e. on all sections of the digitized slide) and could guide the next round of targeted tissue removal. Such decision support system could assist the Mohs surgeon to spot quickly the histological regions of interest. Prospective studies are needed to assess the practicality of integrating such framework in clinical practice and how it affects outcomes.

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None.

CONFLICT OF INTEREST
All authors have disclosed that they have no conflicts of interest to report.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author.

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