Using deep neural networks to count Ki-67 positive cells in neuroendocrine tumors

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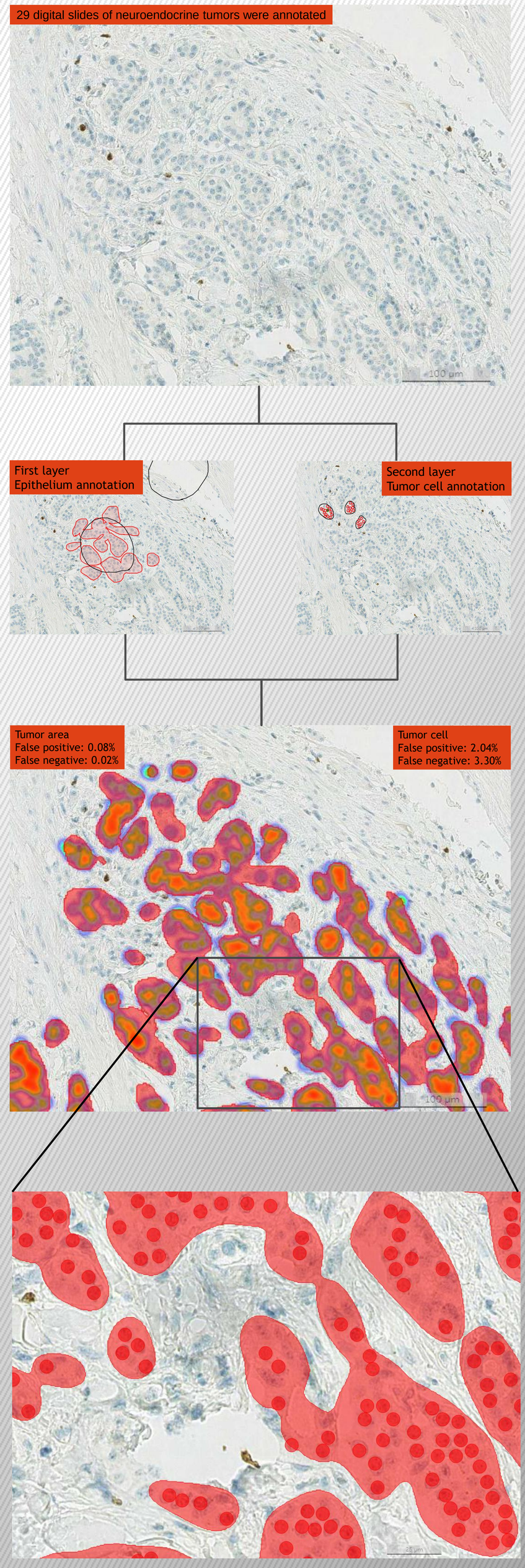
Background & Objective: The Ki-67 proliferation index has prognostic importance in neuroendocrine tumors. However, its manual evaluation is subjective and time consuming. We intend to train Aiforia™, a cloud based machine-learning platform, to detect Ki-67 positive cancer cells in gastrointestinal neuroendocrine tumors.

Methods: 43 random neuroendocrine tumor cases from 2015-2016 were chosen from the archive of Haukeland hospital. The scanned slides were investigated. Some cases were removed from the study due to processing artifacts. Finally, scanned slides of the 29 remaining cases were uploaded to Aiforia™ and used for training the algorithm. The designed algorithm consisted of two layers. The first layer detected the epithelium regions and the second layer segmented the individual positive and negative tumor cells within the first layer. To train the algorithm, the researcher manually annotated 6072 epithelium regions and 13030 positive and negative tumor cells.

The training data for the first layer was digitally augmented for 20% size scaling, 10% aspect ratio change, 10% shear angle, 20% brightness, 10% contrast change, and 1% white balance change. The data were flipped both vertically and horizontally. The augmentation parameters for the second layer were the same except for the white balance change of 1%.

Result: The algorithm was trained for 51 hours. In result, the first layer of the algorithm performed relatively well, but also falsely detected crypt epithelium in mucosa. To overcome this issue, we introduced several more annotations in mucosa to familiarize the algorithm with all the possible variation of epithelium as the target, and mucosa as background.
In the second layer of the algorithm, cell segmentation was an intricate task. Since tumor cells have great variety in their appearance, it was hard to define a category, not too general and not too specific, to include all target cells. Also, inhomogeneous staining was another issue that complicated the cells segmentation task.

Conclusion: The present study shows the attempt of automated Ki-67 positive tumor cells detection in neuroendocrine tumors. Automation and implementation of this project can greatly improve routine workflow of pathologists. The chosen platform, Aiforia™, offers a user friendly interface and great technical support. Next step, we are going to validate these results against the ground truth, which is pathologists' manual counting.



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