Machine Learning Algorithm to Analyze Histopathologic Sections of Temporal Artery Biopsy Specimens

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Purpose

To develop a deep residual convolutional network (ResNet) model for image tile/patch classification combined with a whole-slide inferencing mechanism for determining predominant and minor giant cell arteritis (GCA) histologic patterns.

Background

- GCA affects individuals over the age of 50 years with an incidence of 7-29/100,000[1]
- Inflammation in large and medium-sized vessels may lead to vision loss, aortic aneurysm or dissection, and stroke.[2]
- Temporal artery biopsy (TAB) is rapid, safe, and cost-effective, remaining the gold standard in diagnosis
- Ultrasound, computed tomography, and magnetic resonance imaging may be suitable alternatives to TAB, but shortcomings exist, such as cost, expertise, and availability.[3]
- Histopathological TAB evaluation is time consuming due to the many slides generated during tissue processing.
- Deep learning (DL) methods, such as convolution neural or residual networks[4-14], led to breakthroughs in tissue classification tasks (e.g., cancer vs non-cancerous responses)[15]. DL is a machine learning based feature learning paradigm[16], wherein the model iteratively improves upon learned representations of the underlying data with the goal of maximally attaining class separation by taking a more domain agnostic approach, combining feature detection and implementation to discriminate between classes.
- DL network-based approaches are uniquely suited to analyze and learn in an implicit fashion the diversity of image patterns embedded within large datasets, as is the case where pathological responses are localized to sub-locations within the artery in order to expedite the examination, facilitate the diagnosis, or even increase test sensitivity.

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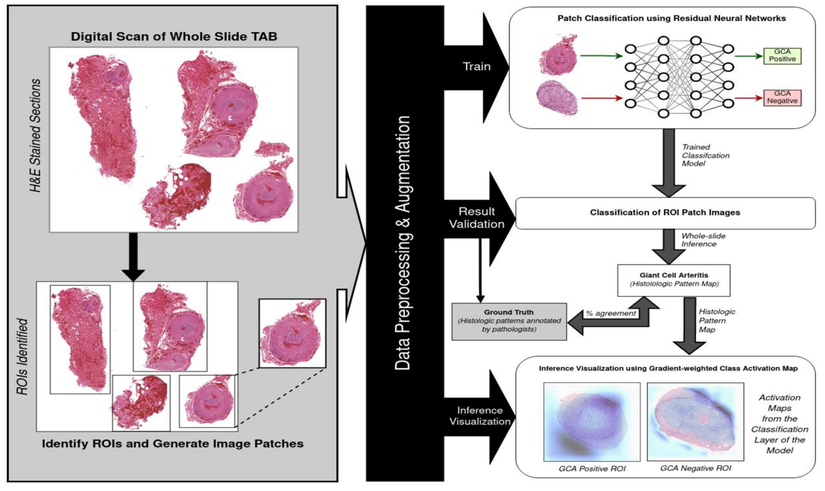
Methods

- Hematoxylin and eosin (H&E) stained, formalin-fixed, paraffin-embedded tissue specimens from 472 patients who underwent temporal artery biopsies (TAB) from January 1, 2000, to December 31, 2019, at the West Virginia University Hospitals were de-identified and digitized using a whole-slide digital scanner at 20x magnification.
- Digital scans of whole slides were chronologically partitioned into two sets, the first 80% samples for model training and the remainder as an independent test set to validate the algorithm.
- Based on identified definitions/characterizations, several image tiles or patches from each scan were identified as regions of interest (ROIs) for GCA detection and manually labeled for training the deep learning model. These tiles were resized into square patches. The developed ResNet classification model takes square patches or tiles as inputs and predicts the probability of GCA presence (Figure below).



Results

- The dataset contained 336 training slides *(positive: 100 slides, 927 ROIs; negative: 236 slides, 2631 ROIs*) and 136 testing slides (*positive: 40 slides, 251 ROIs; negative: 96 slides, 995 ROIs*). We performed training trials after separating ROI image patches from whole slide scans and expanding the ROI image set by augmentation.
- Six transformations were applied to each training image: Rotate 90, Vertical Flip, Horizontal Flip, Rotate Randomly between +10 and -10 degrees, Color Jitter, and Histogram Equalization, to obtain a total of seven images per ROI.
- The model attained 93.19% accuracy and 0.88 AUC on the running validation set.
- The algorithm was tested on unseen data and performed consistently with an accuracy of 91.65% and an AUC of 0.87 at the ROI level. Model prediction and pattern detection were qualitatively validated using a class-activation map visualization method called GradCAM.

Conclusion

Deep neural network learning methods help automate the detection of GCA in TAB digital pathology slides. The findings generated by the model are comparable in performance to an experienced pathologist.

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