Transferrable Deep Learning Algorithms for Identifying Area At Risk in Acute Myocardial Infarction

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Introduction: Objective analysis of complex histopathology devoid of observer bias is critical to many areas of biological research and medical diagnosis. Current automated methods for imaging, processing, and statistical analysis of tissue sections can be sensitive to variability in tissue images, such as color and brightness variations, blur, dust, and tissue folds that create excessive noise and degrade the analyses of microscopic specimens.

Deep learning presents an opportunity for a one-click solution that is insensitive to such noise and adaptable to different tissue types via transfer learning. Here we apply these objective methods to sections of heart tissues that have undergone myocardial infarction in order to delineate the areas at risk of infarction and the normal regions in a fully automated and objective procedure.

Materials and Methods: Eight C57BL6 mice underwent coronary artery ligation for 90 min, followed by reperfusion for 24 hours. Just prior to heart excision at 24 hours, the coronary artery was reoccluded; lectin-488 (a vascular endothelial marker) was injected to label cardiac vessels located exclusively in the nonischemic region. The eight resulting microscopy images were hand-segmented by expert annotation to obtain "ground truth" for the normal, infarct, and AAR regions, and were then divided into 512x512 tiles.

The raw fluorescence tiles were trained against their corresponding ground truth segmentation tiles in a deep learning convolutional neural network based on the U-net encoder-decoder architecture. The specific architecture features four down-sampling components of increasing kernel size, their four corresponding residual up-sampling components of diminishing kernel size, a latent feature convolution at the median with a maximum kernel size of 256x256, and interpretive convolutions at the final decode step.

The 2679 sample 512x512 tiles and their matching ground truth segmentations were split using a 60/20/20 ratio into 1607 training samples, 536 validation samples, and 536 test samples. Training samples determine loss and change the model parameters; validation samples allow for a running tally of metrics to find a stopping point and/or determine if the model is overfitting; test samples are used to evaluate the final efficacy of the model. The Adadelta optimizer (λ=1.0, ρ=0.95) was used for gradient descent, and binary crossentropy used as the loss function. Weight changes were truncated using a gradient normal clipping of 1.0 to prevent an exploding gradient.

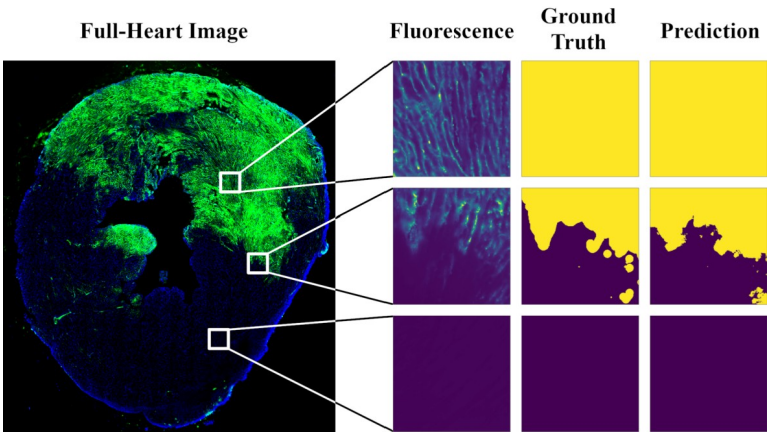

Figure 1: Segmentation of normal and AAR regions. Left: Stained heart section. Lectin stain (green) identifies normally perfused vessels; blue identifies cardiomyocyte nuclei. Right: Yellow color specifies the normal region for ground truth and predictions.

Results and Discussion: Results were obtained using a single fluorescence stain (lectin-488), thereby segmenting two classes: "normal" tissue, and "none" (anything physically outside the normal region).

After stopping at 113 epochs (patience = 30), the model achieved an accuracy (the proportion of pixels segmented correctly) of 0.9718 and a Dice coefficient (the proportion of overlap with the ground truth segmentation) of 0.9881 on the test set.

These results show that encoder-decoder convolutional neural networks are effective at segmenting tissue regions where microscopy images have discontinuities and variability.

Conclusion: Current work sets a foundation to implement segmentation of additional tissue classes using multiple fluorescence inputs as molecular probes, to identify and quantify the presence of myriad physiological and pathological features of histological specimens in a fully automated and objective process.