CANCER DETECTION IN WHOLE-SLIDE BREAST HISTOLOGY IMAGES AT MULTIPLE RESOLUTIONS

Tony Xu[1, 2], Ozan Ciga[1, 4], Sharon Nofech-Mozes[3], Dina Bassiouny[3], Anne L. Martel[1, 4]

[1] Physical Sciences, Sunnybrook Research Institute, Toronto ON Canada
[2] Faculty of Electrical Engineering, University of British Columbia, Vancouver BC Canada
[3] Laboratory of Medicine and Pathology, University of Toronto, Toronto ON Canada
[4] Department of Medical Biophysics, University of Toronto, Toronto ON Canada

Background

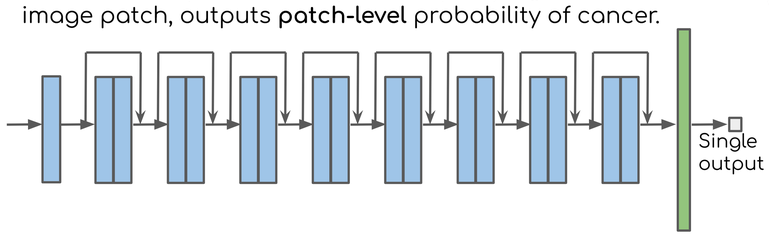
Breast cancer is the most commonly diagnosed cancer for women in Canada, with an incidence rate of around **1 in 8 women**[1]. In order to objectively assess response to treatment and provide guidelines for future treatment, pathologists have developed a **Residual Cancer Burden (RCB) score**[2]. However, obtaining this score is a timely process, which occupies resources that could be spent on other critical tasks. This project proposes the first stage in a pipeline to **automatically assess** the RCB score. Using convolutional neural networks (CNNs), a common method to extract features from images, a **heatmap** is obtained of all cancerous regions in a given whole-slide histology image (WSI) with **90.5% accuracy**.

Purpose

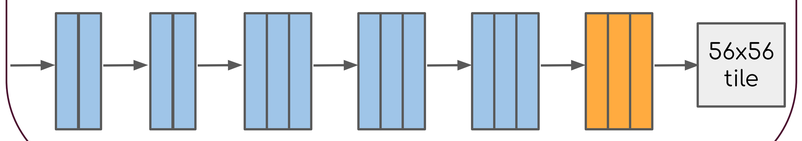
To develop an algorithm that automatically detects cancerous regions in a whole-slide breast histology image.

Models

ResNet18[3] - Inputs a small (224x224 pixel) high resolution image patch, outputs **patch-level** probability of cancer.

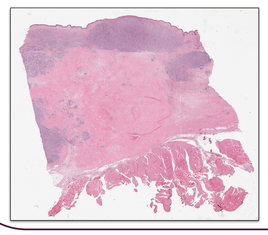


ScanNet[4] - Inputs a large (1792x1792 pixel) low resolution image, outputs a **probability tile** of cancer existing in corresponding group of pixels. Modified from the VGG16 architecture.

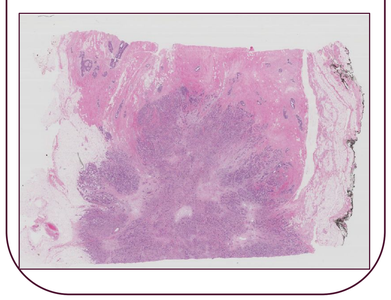


Data

Sunnybrook Dataset: 19 Whole-slide images taken, and sparsely annotated by pathologists here at Sunnybrook. Useful for training but due to sparseness of annotation, not used for validation



BACH Challenge Dataset:[5] 10 fully annotated whole-slide images from an online machine learning challenge.



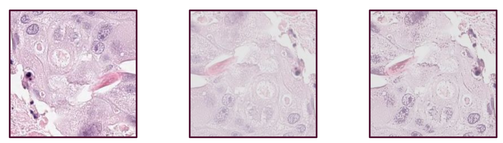
Methodology

Patch-based:
224x224 patches are taken from WSI and passed through the ResNet18 classifier. The output probabilities (~0 for normal, ~1 for cancer) are stitched together to make a pixelated cancer heat-map.

Probability tile:
1792x1792 patches are taken from WSI at 4 times lower resolution and passed through the ScanNet model. The output probability tiles are stitched together to make a cancer heat-map.

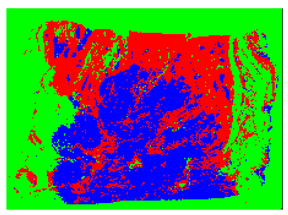
Augmentation:
The following adjustments were performed on both input types to increase robustness and accuracy of the model:

- **Rotation**-images are randomly rotated by a multiple of 90 degrees
- **ColorJitter**-various image properties such as brightness, contrast, saturation and hue are randomly shifted
- **Stain augmentation**[6]-using color deconvolution, images were split into hematoxylin and eosin stains and randomly modified and reformed into an image



Original | Rotate and Colorjitter | Stain augmented

Preprocessing:
A "TissueClassifier" model was applied to determine where noncancerous epithelial cells could be found. This reduces class imbalances and improves model performance. Red refers to stroma, green to fat or background, and blue to useful epithelial cell regions.



Custom Loss Functions:
Loss functions such as Focal Loss[7] and Online Hard Example Mining[8] were used to target training to difficult examples.

Why Lower Resolution?

In manual cancer identification and classification, a pathologist's typical workflow includes a cursory scan over the entire slide in a low resolution and Checking details in high resolution. This network emulates the "scan across" by taking information from lower input resolutions to obtain a better general classification of the WSI.

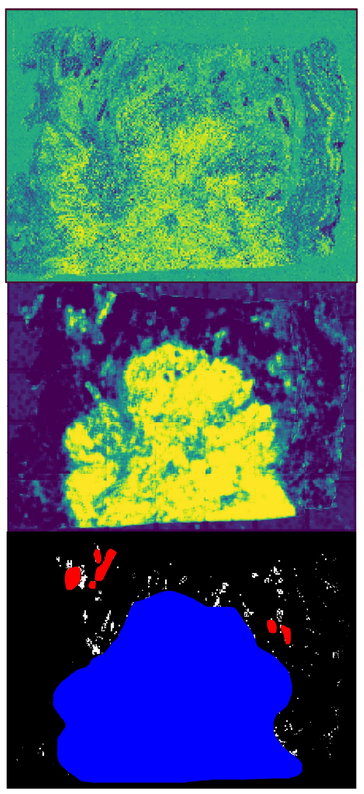
For example, there is no way for the pictured small high-resolution patch to correctly label the inside region of the duct as a part of in situ cancer.

Results

Patch-based:
Obtained **68.4%** Accuracy, regions Require more aggressive thresholding, has trouble grouping regions and properly classifying ducts.

Probability Tile:
Obtained **90.5%** accuracy. Qualitatively, the model filled ductal regions properly more often.

Ground truth:
Pathologist-annotated slide from BACH dataset. White is normal, red is benign (set to be normal) and blue is invasive. Green (not pictured) is in situ.



Conclusions

Due to the importance of **spatial information** for cancerous region classification in a whole-slide breast histology image, a lower resolution patch with a larger field of view should perform better than a high-resolution classifier. In support of this claim, I found that the tile-based ScanNet classifier obtains **90.5% accuracy**, versus the patch-based ResNet classifier's **68.4%**.

Discussion

The next stage of this pipeline involves taking evenly sampled regions defined in this model and extracting high resolution patches. Though low resolution appears more optimal for region definition, high resolution can provide the detail needed to reduce false-positives or reclassify regions properly. This multi-resolution pipeline is currently in development.

References

[1] Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2017. Toronto, ON: Canadian Cancer Society; 2017.
[2] Symmans, W., Wei, C., Gould, R., Yu, X., Zhang, Y., & Liu, M. et al. (2017). Long-Term Prognostic Risk After Neoadjuvant Chemotherapy Associated With Residual Cancer Burden and Breast Cancer Subtype. Journal Of Clinical Oncology, 35(10), 1049-1060. doi: 10.1200/jco.2015.63.1010
[3]He, Kaiming, et al. "Deep Residual Learning for Image Recognition." 2016 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), 2016, doi:10.1109/cvpr.2016.90.
[4] Lin, Huangjing, et al. "Fast ScanNet: Fast and Dense Analysis of Multi-Gigapixel Whole-Slide Images for Cancer Metastasis Detection." IEEE Transactions on Medical Imaging, vol. 38, no. 8, 2019, pp. 1948–1958., doi:10.1109/tmi.2019.2891305.
[5] Aresta, Guilherme, et al. "BACH: Grand Challenge on Breast Cancer Histology Images." Medical Image Analysis, vol. 56, 2019, pp. 122–139., doi:10.1016/j.media.2019.05.010.
[6] Code adapted from Jonathan Mazurski
[7]Lin, Tsung-Yi, et al. "Focal Loss for Dense Object Detection." 2017 IEEE International Conference on Computer Vision (ICCV), 2017, doi:10.1109/iccv.2017.324.
[8] Shrivastava, Abhinav, et al. "Training Region-Based Object Detectors with Online Hard Example Mining." 2016 IEEE Conference on Computer Vision and Pattern Recognition (CVPR), 2016, doi:10.1109/cvpr.2016.89.