Deep Learning Predicts Breast Cancer HER2 Status

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Outline of talk

- Deep learning has been shown to be useful to identification of breast cancer metastases from analyzing whole sections of whole slide images (WSIs) of sentinel lymph nodes.

- Our study focuses on breast cancer HER2 status using Deep Learning with a small set of image patches from tumor areas.

- Our approach is unique since it provides a very rapid screen before getting IHC result.

Outline of talk (cont'd)

- We obtain excellent predictive results for breast cancer HER2 status in this study, which provide a proof of concept for incorporating automated breast cancer HER2 screen into the digital pathology workflow to potentially augment the pathologists' productivity.

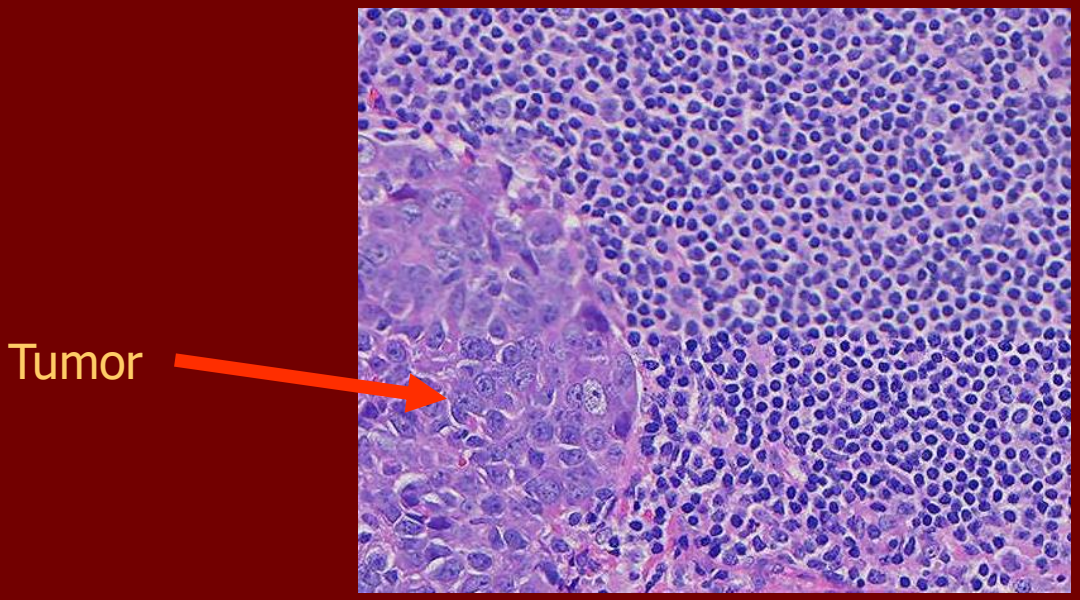
I have no relevant financial relationships with commercial interests to disclose

Introduction

- IHC is often used to also detect proteins expressed on the cell membrane or in the cytoplasm. One of the most widely used examples is HER2, a protein expressed at the cell membrane whose expression can directly guide treatment strategy and prognosis in a number of different tissues
- In breast tissue, guidelines for interpretation of HER2 expression are fairly well established and have undergone multiple modifications by consensus groups, most recently in 2018 with a set of updated CAP guidelines for scoring and interpretation

The Goal of our Study

- We explore how Deep Learning could be used to detect HER2 status for breast cancer screening using image patches from tumor area in whole slide image



Source of Breast Cancer WSIs

TCGA Breast cancer:

Link:

Exploration (cancer.gov)

Project TCGA-BRCA

(Breast Invasive Carcinoma)

1,092 cases total; 1,062 cases with microscopic slides

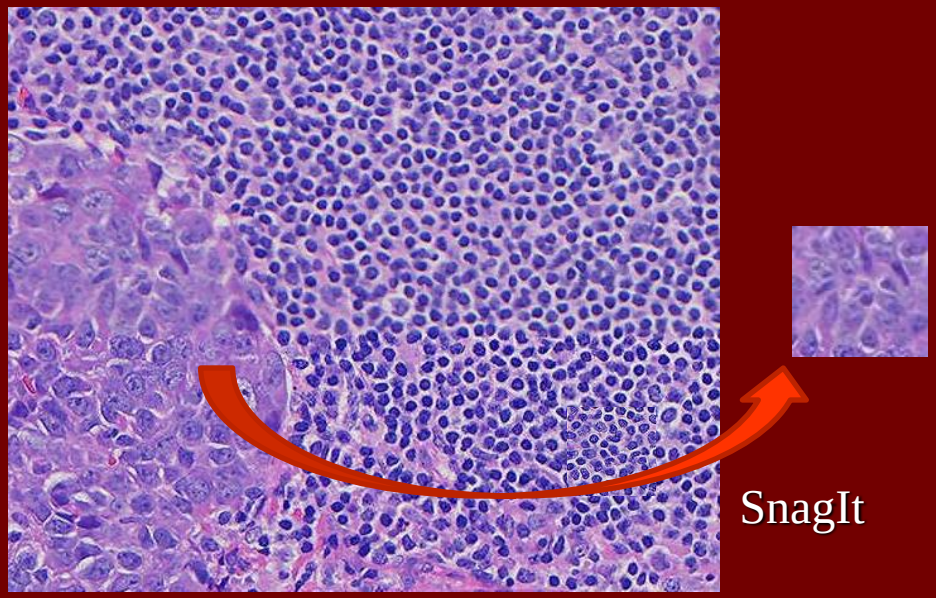
All WSI show tumor cells

Disease Type

- Adenomas and Adenocarcinomas
- Adnexal and Skin Appendage Neoplasms
- Basal Cell Neoplasms
- Complex Epithelial Neoplasms
- Cystic, Mucinous and Serous Neoplasms
- Ductal and Lobular Neoplasms
- Epithelial Neoplasms, NOS
- Fibroepithelial Neoplasms
- Squamous Cell Neoplasms

Digital Images of Breast Cancer WSIs

- SnagIt (TechSmith Corp, Okemos, Michigan, USA) is used to capture and automatically save 80x80 image patch in files with format xxx.jpg



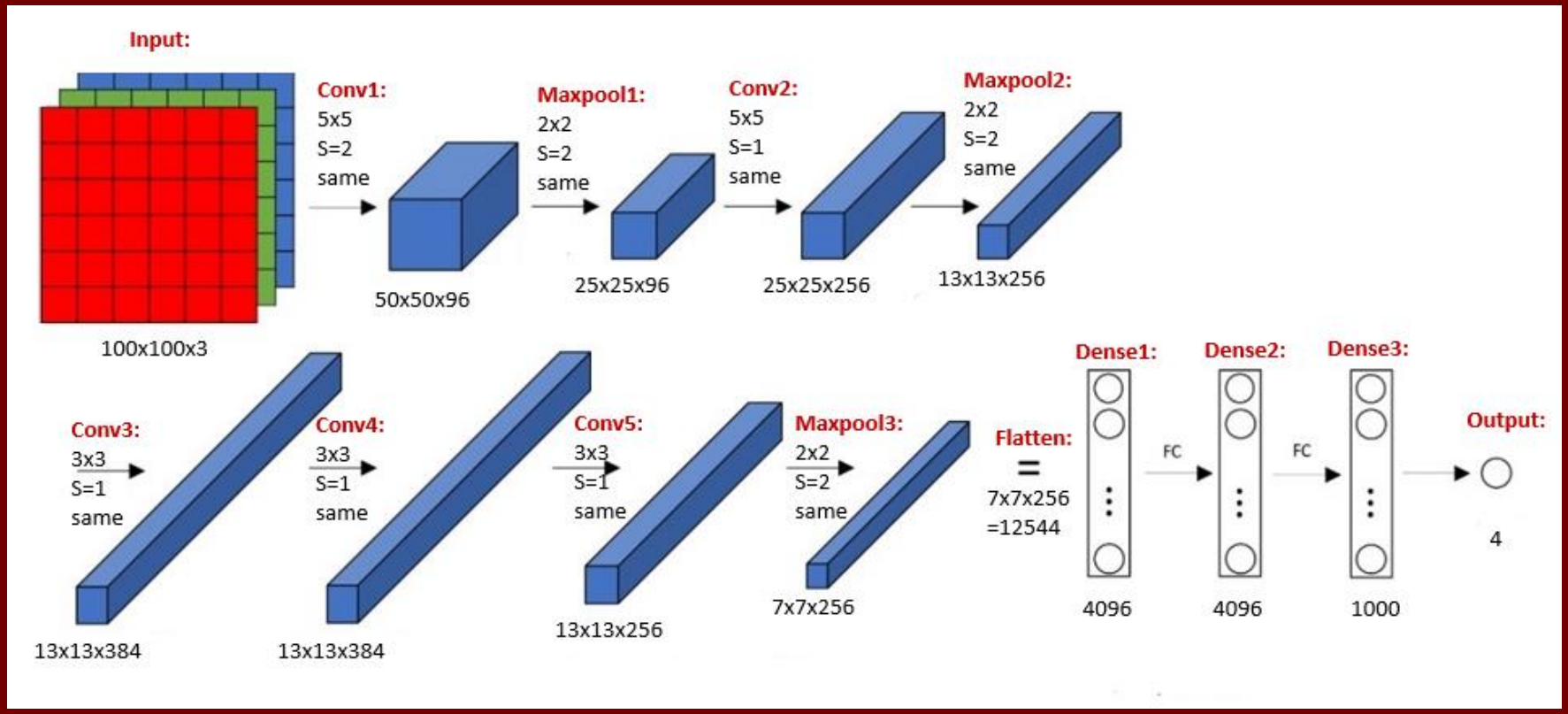
Our Programming Platform

- We design a CNN model in Python language, commonly used in deep learning (together with TensorFlow and Keras libraries);
  Windows 10 Professional 64bit

- Keras allows for parallel computing using graphic processing unit (GPU) with Compute Unified Device Architecture (CUDA)

- Hardware:
  9th Gen Intel® Core™ i7 9700 (8-Core, 12MB Cache, 4.7GHz)
  RAM: 32GB DDR4 at 2666MHz
  GPU: NVIDIA® GeForce RTX™ 2070, 8GB GDDR6
  (2304 CUDA cores)

Schematics of our Deep Learning Model (14 Layers)



Schematics of our Deep Learning Model (14 Layers)

```
Model: "sequential_5"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
conv2d_13 (Conv2D)           (None, 50, 50, 96)        7296
_________________________________________________________________
max_pooling2d_7 (MaxPooling2 (None, 25, 25, 96)        0
_________________________________________________________________
conv2d_14 (Conv2D)           (None, 25, 25, 256)       614656
_________________________________________________________________
max_pooling2d_8 (MaxPooling2 (None, 13, 13, 256)       0
_________________________________________________________________
conv2d_15 (Conv2D)           (None, 13, 13, 384)       885120
_________________________________________________________________
conv2d_16 (Conv2D)           (None, 13, 13, 384)       1327488
_________________________________________________________________
conv2d_17 (Conv2D)           (None, 13, 13, 256)       884992
_________________________________________________________________
max_pooling2d_9 (MaxPooling2 (None, 7, 7, 256)         0
_________________________________________________________________
flatten_3 (Flatten)          (None, 12544)             0
_________________________________________________________________
dense_9 (Dense)              (None, 4096)              51384320
_________________________________________________________________
dense_10 (Dense)             (None, 4096)              16781312
_________________________________________________________________
dense_11 (Dense)             (None, 1000)              4097000
_________________________________________________________________
dense_12 (Dense)             (None, 4)                 4004
=================================================================
Total params: 75,986,188
Trainable params: 75,986,188
Non-trainable params: 0
_________________________________________________________________
```

Materials & Methods

- 10 cases for each of the following:
  HER2 +
  HER2 –

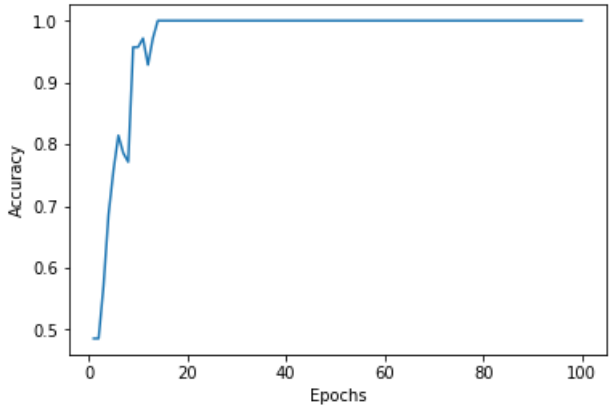
- 5 representative 80x80 images for each of the 20 cases
  -> a total of 5x20=100 images

- 70 images (~70%) were used for training the model, 20 (~20%) for validation, and 10 (~10% or 2 cases) for testing

- Evaluation for
  (a) Image-by-Image, and
  (b) Case-by-case (majority voting ≥3/5)

DISPLAY OF ANALYSIS RESULTS

```
Epoch 99/100
70/70 [==============================] - 1s 9ms/step - loss: 4.8429e-04 - acc: 1.0000 - val_loss: 4.3707 - val_acc: 0.1667
Epoch 100/100
70/70 [==============================] - 1s 9ms/step - loss: 4.8320e-04 - acc: 1.0000 - val_loss: 4.4025 - val_acc: 0.1667
10/10 [==============================] - 0s 2ms/step
Test loss: 0.203584700823
Test accuracy: 0.899999976158
```




```
Actual (rows) Predicted (columns)
--------------------------------------------
col_0  0  1
row_0
0      4  1
1      0  5
--------------------------------------------
RESULT FOR EACH IMAGE:
Observed DX=  0 Predicted DX=  0
Observed DX=  0 Predicted DX=  1
Observed DX=  0 Predicted DX=  0
Observed DX=  1 Predicted DX=  1
Observed DX=  1 Predicted DX=  1
Observed DX=  1 Predicted DX=  1
Observed DX=  1 Predicted DX=  1
Observed DX=  1 Predicted DX=  1
Observed DX=  0 Predicted DX=  0
Observed DX=  0 Predicted DX=  0
--------------------------------------------
```

RESULTS

Accuracy:

(a) Image-by-Image: 90%, and

(b) Case-by-case: 100% (majority voting ≥3/5),

SUMMARY

- Our study focuses on screening of breast cancer HER2 status using Deep Learning with a small set of image patches from tumor area of WSI
- Our approach is unique since it provides a very rapid screen while waiting for IHC result
- We obtain excellent predictive results for HER2 status from this pilot study with 90% accuracy
- Current limitations include:
  (a) the model was only validated on one WSI source (TCGA),
  (b) representative images require preselection of tumor-rich areas
  (c) lack of explicit diagnostic criteria [inherent to DL]
- Our preliminary study provided a proof of concept for incorporating automated breast cancer screen for HER2 using digital microscopic images into the pathology workflow to augment the pathologists' productivity. This could have significant impact on health economics.
- Future studies will need to:

  (a) include more WSIs from different platforms and many more cases for training, and validation,
  (b) automated segmentation of WSIs for tumor-rich areas.


Delicate Arch, Moab National Park, UT
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