Histologic-Detection-and-Grading-of-Cancer-from-Medical-Images

Sathyanarayanan Dhorali

June 20, 2022

I present a deep learning approach for Detecting Invasive ductal carcinoma (IDC) tissue regions from the whole slide images (WSI) of breast cancer (BCa). Deep Learning teaches computers to do what comes naturally to humans. The most common type of all the Breast Cancer type is IDC. IDC starts in your milk ducts and spreads to your surrounding breast tissues. Eventually, it can spread to your lymph nodes and other areas of your body. When its detected early it has the highest percentage of survival rate, The Invasive Ductal Carcinoma has 5 stages. It comprises nearly 80 Percentage out of all of the Breast Cancer Types. IDC is routinely identified by pathologists through visual analysis of tissue slides stained with hematoxylin and eosin (HE). Detecting Invasive breast cancer is challenging task and also the time consuming because it involves a pathologist scanning large swathes of benign regions to ultimately identify the areas of malignancy. Finding Preceicely where the (IDC) Present in WSI plays the crucial part for predicting patient outcome and also finding the estimation of grading tumor aggressiveness.

Stages Of Invasive Ductal Carcinoma:

Stage 0: This is noninvasive cancer. It's only in the ducts and hasn't spread.

Stage IA: The tumor is small and invasive, but it hasn't spread to your lymph nodes).

Stage IB: Cancer has spread to the lymph nodes. It's larger than 0.2 mm but less than 2 mm in size. There's either no sign of a tumor in the breast or there is, but it's 20 mm or smaller.

Stage IIA: Any one of these:

- 1. There's no sign of a tumor in the breast. The cancer has spread to between 1 and 3 underarm lymph nodes, but not to any distant body parts.

 - 3.The tumor is between $20~\mathrm{mm}$ and $50~\mathrm{mm}$ but hasn't spread to nearby nodes .

Stage IIB: Either of these conditions:

- 1. The tumor is between 20 mm and 50 mm and has spread to one to three underarm lymph nodes.
 - 2. The tumor is larger than 50 mm but hasn't spread to underarm lymph nodes

Stage IIIA: Either of these conditions:

- 1. Cancer of any size has spread to four to nine underarm lymph nodes or those under your chest wall. It hasn't spread to other body parts.
 - 2.A tumor larger than 50 mm has spread to one to three nearby lymph nodes.

Stage IIIB: The tumor:

- 1. Has spread to the chest wall.
- 2.Has caused swelling or breast sores.
- 3. Has been diagnosed as inflammatory breast cancer.

4.May or may not have spread to up to nine Lymph nodes under your arm or beneath the chest wall.

5. Hasn't spread to other body parts .

Stage IIIC: A tumor of any size that has spread to 10 or more nearby lymph nodes, breast lymph nodes, and/or lymph nodes under the collarbone. It hasn't spread to other body parts.

Stage IV (metastatic): The tumor can be any size and has spread to other organs, like your bones, lungs, brain, liver, distant lymph nodes, or chest wall. Between 5Percent and 6 Percent of the time, metastatic cancer is discovered upon first diagnosis. Your doctor may call this de novo metastatic breast cancer. More often, it's found after a previous diagnosis of early breast cancer.

The treatments for IDC: The treatments for IDC fall into two main types:

1.Local treatments 2.Systemic treatment

I. Local treatments: Local treatments for IDC target the cancerous tissue of the breast and the surrounding areas, such as the chest and lymph nodes. Options include:

1.Surgery:

Surgery removes the cancerous tumor and determines whether cancer has spread to the lymph nodes. Surgery is typically the doctor's first response when dealing with IDC. Surgical options include:

1.lumpectomy, or removal of the tumor 2.mastectomy, or removal of the breast 3.lymph node dissection and removal

2. Radiation:

Radiation therapy directs powerful radiation beams at the breast, chest, armpit, or collarbone to kill any cells in or near the tumor's location. Radiation therapy takes about 10 minutes to administer daily over the course of 5 to 8 weeks.

Some people treated with radiation may experience swelling or skin changes. Certain symptoms, such as fatigue, may take 6 to 12 weeks or longer to subside.

Different kinds of radiation therapies available for treating IDC include:

1. whole breast radiation, in which external beam radiation beams target the entire breast area.

2.internal partial-breast radiation, in which radioactive materials are placed near the site of a lumpectomy.

3.external partial-breast radiation, in which radiation beams directly target the original cancer site.

II.Systemic treatment: Systemic treatment for IDC are applied throughout the body, targeting any cells that may have traveled and spread from the original tumor. Systemic treatments are effective at reducing the likelihood that the cancer will return after treatment. Options include:

1.chemotherapy 2.hormonal therapy 3.targeted therapy 4.immunotherapy

In Last Decade, deep learning (DL) have gained popularity .Deep Learning methods have been Performed Better Than traditional approaches of most challenging problems Like Image Classification, speech recognition ,Object Tracking and and object detection. These methods are part of Convolutional Neural networks. Convolutional networks were inspired by biological processes in that the connectivity pattern between neurons resembles the organization of the animal visual cortex. Individual cortical neurons respond to stimuli only in a restricted region of the visual field known as the receptive field. The receptive fields of different neurons partially overlap such that they cover the entire visual field. Convolutional neural networks are a specialized type of artificial neural networks that use a mathematical operation called convolution in place of general matrix multiplication in at least one of their layers. They are specifically designed to process pixel data and are used in image recognition and processing.

CNNs use relatively little pre-processing compared to other image classification algorithms.

Abstract:

We Need To Classify The Breast Cancer Using CNN .And then set random seeds on a point on the image and traverse along the direction of highest gradient difference (highest gradient magnitude and gradient orientation) Of the random pixel to the ROI (cancer region, in this case) is reached. the traversed paths to contain distinguishing information about that can then be used to perform more effective classification. However, instead of just making use of path length, we would probably be using an RNN with the actual path to learn a bit more about the gradient differences.

Description of dataset:

The dataset comprises digitized Breast Cancer histopathology slides from 162 women diagnosed with IDC at The Cancer Institute of New Jersey and the Hospital of the University of Pennsylvania . All slides were digitized via a whole-slide scanner at 40x magnification (0.25 μ m/pixel resolution). Operating on entire whole-slide histopathology images is intractable due to their extremely large size (on the order of 1010 pixels). In this work, each WSI was downsampled (by a factor of 16:1) to a resolution of 4 μ m/pixel.

Limitations:

Detecting the IDC Breast Cancer By Manual using pathologist is time consuming task and it also challenging task because involves pathologist scanning large swathes of benign regions to ultimately identify the areas of malignancy. Precise delineation of IDC in WSI is crucial to the subsequent estimation of grading tumor aggressiveness and predicting patient outcome.

Step 1:Image Classification Using CNN:

Instead Of Training From The Scratch for the imgae classification We use The Transfer Learning (Vgg16).

Transfer Learning:

Transfer learning (TL) is a research problem in machine learning (ML) that focuses on storing knowledge gained while solving one problem and applying it to a different but related problem. Here we are using vgg16 as the transfer learning

Resize the Image: (50*50*3).

Train Test Split: 75 Percentage for training and 25 Percentage for testing Vgg 16:

The input to the Cov1 layer is of a fixed size image so we resized it, and fed that image as input and then its is passed through the stack of convolutional (conv.) layers, where the filters were used with a very small receptive field: 3×3 (which is the smallest size to capture the notion of left/right, up/down, center). One of the configurations, also utilizes the 1×1 convolution filters, which can be seen as the linear transformation of the input channels. The convolution stride is fixed to the 1 pixel, the spatial padding of the Conv. layer input is such that, the spatial resolution is preserved after the convolution, i.e. the padding is 1-pixel for 3×3 Conv. layers. Spatial pooling is carried out by the five max-pooling layers, which follow some of the Conv. Layers. Max-pooling is performed over the 2×2 pixel window, with stride 2. Three Fully-Connected (FC) layers follow the stack of convolutional layers (which has the different depth in different architectures): the first two have 4096 channels each, the third performs 1000-way ILSVRC classification and thus contains 1000 channels. The final layer is the softmax layer. The configurations of the fully connected layers is the same in all the networks. All hidden layers are equipped with rectification (ReLU) non-linearity. For this Paper we freezed the last five layers and trained only the last five layers with 5 epochs.

Then we plotted the results for the accuracy, loss, auc, precision, fl_s core

Step 2: Computing the Gradient Intensity of random pixel Traverse Untill ROI is Reached and store the directions:

A gradient measures the change in pixel intensity in a given direction. By estimating the direction or orientation along with the magnitude (i.e. how strong the change in direction is.

1. The first step is to simply find and mark the north, south, east and west pixels surrounding the center pixel:

North: I(x, y - 1)South: I(x, y + 1)East: I(x + 1, y)West: I(x - 1, y)

2. Then, We Find Vertical change or the y-change by taking the difference between the south and north pixels:

```
Gy = I(x, y + 1) - I(x, y 1)
```

3. Then, We Find Horizontal change or the x-change by taking the difference between the east and west pixels:

```
Gx = I(x + 1, y) - I(x 1, y)
```

4. After that we need to find the gradient magnitude. The gradient magnitude is used to measure how strong the change in image intensity is. The gradient magnitude is a real-valued number that quantifies the "strength" of the change in intensity.

```
\theta = arctan2(Gy, Gx) * (180/\pi)
```

5. After that we need to find the gradient orientation, The gradient orientation is used to determine in which direction the change in intensity is pointing. As the name suggests, the gradient orientation will give us an angle that we can use to quantify the direction of the change.

$$G = \sqrt{Gx^2 + Gy^2}$$

Now We have computed the Gradient Magnitude and Gradient orientation of the single pixel.But our goal is to traverse the direction from the random to seed to the region of interest.

So We have introduced the sobel filter it will find intensity of the each pixel and its mainly used for the detection of the edges but we gonna specify a random seed and traverse the from the random seed with the highest gradient magnitude and highest gradient orientation to the region of interest and we will store that directed path.

Here we did not have the annotated region of the cancer from the pathologist so we introduced a Mask slic for detecting the region of interest.

Mask Slic:

Supervoxel methods such as Simple Linear IterativeClustering (SLIC) are an effective technique for partitioning an image or volume into locally similar regions, and are a common building block for the development of detection, segmentation and analysis methods. MaskSLIC an extension of SLIC to create supervoxels within regions-of-interest.

Here We have got The Region Of Interest the cancer by using the method maskslic.and we will provide the cancer region pixels along with the random seed to the sobels filter . it will generate the path directions from the random seed to the region of interest . Then We feed an input through the BiLstm for the further classification.

Step 3: Train The Direction Path with bidirectional Lstm:

Bidirectional LSTM (BiLSTM) is a recurrent neural network used primarily on natural language processing. Unlike standard LSTM, the input flows in both directions, and it's capable of utilizing information from both sides. It's also a powerful tool for modeling the sequential dependencies between words and phrases in both directions of the sequence.

In summary, BiLSTM adds one more LSTM layer, which reverses the direction of information flow. Briefly, it means that the input sequence flows backward in the additional LSTM layer. Then we combine the outputs from both LSTM layers in several ways, such as average, sum, multiplication, or concatenation.

We provide the Directional input(N;S;W;E) to the BiLstm , The BiLstm would able to classify the benign or Malignant. Then we combine Cnn and Rnn to classify the breast regions.

References:

- [1] C. DeSantis, R. Siegel, P. Bandi, and A. Jemal, "Breast cancer statistics, 2011," CA: A Cancer Journal for Clinicians, vol. 61, pp. 408–418, 2011, [doi:10.3322/caac.20134].
- [2] C. Elston and I. Ellis, "Pathological prognostic factors in breast cancer. i. the value of histological grade in breast cancer: experience from a large study with long-term follow-up," Histopathology, vol. 5, pp. 403–410, 1991, [doi:10.1046/j.1365-2559.2002.14691.x].
- [3] C. Genestie, B. Zafrani, B. Asselain, A. Fourquet, S. Rozan, P. Validire, A. Vincent-Salomon, and X. Sastre-Garau, "Comparison of the prognostic value of scarff-bloom-richardson and notting-ham histological grades in a series of 825 cases of breast cancer: major importance of the mitotic count as a component of both grading systems." Anticancer Res, vol. 18, pp. 571–576, 1998.
- [4] S. Naik, S. Doyle, S. Agner, A. Madabhushi, M. Feldman, and J. Tomaszewski, "Automated gland and nuclei segmentation for grading of prostate and breast cancer histopathology," 2008 5th IEEE International Symposium on Biomedical Imaging: From Nano to Macro, pp. 284–287, 2008, [doi:10.1109/ISBI.2008.4540988].
- [5] S. Doyle, S. Agner, A. Madabhushi, M. Feldman, and J. Tomaszewski, "Automated grading of breast cancer histopathology using spectral clustering with textural and architectural image features," 2008 5th IEEE International Symposium on Biomedical Imaging: From Nano to Macro, pp. 496–499, 2008, [doi:10.1109/ISBI.2008.4541041].
- [6] M. Balazsi, P. Blanco, P. Zoroquiain, M. Levine, and M. J. Burnier, "Invasive ductal breast carcinoma detector that is robust to image magnification in whole digital slides," Journal of Medical Imaging, vol. 3, p. 027501, 2016, [doi:10.1117/1.JMI.3.2.027501] pp. 571–576, 1998.
- [7] A. Muhamed Ali, H. Zhuang, A. Ibrahim, O. Rehman, M. Huang, and A. Wu, "A machine learning approach for the classification of kidney cancer subtypes using mirna genome data," Applied Sciences, vol. 8, no. 12, p. 2422, 2018.
- [8] A. Krizhevsky, I. Sutskever, and G. Hinton, "Imagenet classification with deep convolutional neural networks," International Conference on Neural Information Processing Systems, vol. 1, 2012, [doi:10.1145/3065386].
- [9] C. Wong, A. Gatt, V. Stamatescu, and M. McDonnell, "Understanding data augmentation for classification: when to warp?" Conference: 2016 International Conference on Digital Image Computing: Techniques and Applications, 2016, [doi:10.1109/DICTA.2016.7797091].
- [10] K. Jarrett, K. Kavukcuoglu, M. Ranzato, and Y. LeCun, "What is the best multi-stage architecture for object recognition?" 2009 IEEE 12th International Conference on Computer Vision, 2009, [doi:10.1109/ICCV.2009.5459469].
- [11] B. Bejnordi, G. Zuidhof, M. Balkenhol, M. Hermsen, P. Bult, B. Ginneken, N. Karssemeijer, G. Litjens, and J. Laak, "Context-aware stacked convolutional neural networks for classification of breast carcinomas in whole-slide histopathology images," Journal of Medical Imaging, vol. 4, p. 044504, 2017, [doi:10.1117/1.JMI.4.4.044504].
- [12] H. Rezaeilouyeh, A. Mollahosseini, and M. Mahoor, "Microscopic medical image classification framework via deep learning and shearlet transform," Journal of Medical Imaging, vol. 3, p. 044501, 2016, [doi:10.1117/1.JMI.3.4.044501].