

## **Cover Page**

**Project Title:** Analysing Density of Tumour Cell from Histopathological images for Breast Cancer Detection.

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**Module Code:** CIS3161

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## **Project Background:**

The preparation procedure preserves the underlying tissue architecture, histopathology images provide clear and thorough perspective of disorders and its effectiveness on tissues. As a result, Metlin., (2010), refers to some disease characteristics, such as lymphocytic infiltration of cancer may only be determined by looking at a histopathological scan. Furthermore, diagnosis from a histopathological image is still "gold standard" for diagnosing wide range of illnesses which is adding practically all kinds of cancer is refers to Rubin., (2007). While the extra structure in these images provide a range of information, it additionally introduces a new batch of obstacles for automated image interpretation. From a diagnostic standpoint, it is believed that correct use of this spatial info will permit for more particular characterizations of picture. The approaches used to assess cytology imaging have typically been applied to histopathology imagery analysis. Certain features of nuclei are indicators of malignant situations. Thus, quantitative measurements for malignant nuclei were devised and evaluated on cytology imagery to suitably include the general observations of an expert pathologist. If histology structures like cell nuclei, glands, and lymphocytes are properly segregated, these same metrics can be utilised to analyse histopathology images. The structure of spatial study of histopathological photography may be viewed in Wiend et al., (1998), Bartels., (1992), and Hamilton., (1994), but it is highly disregarded. The histopathological images can be used to analyse any kind cancer. Additionally, the study Lusine., (2011), illustrates that the stage of the cancer depends on the density of the tumour. So, this project involves in both, where we find the density of tumour by analysing the Histopathological images.

## **Aim:**

The aim of this project is to find the density of tumour cells in a histopathological image data for detecting Breast Cancer using pre-trained Deep Neural Network model (Transfer Learning approach).

## **Objective:**

- Find the density of tumour cells from the histopathological image dataset by dividing the total number of tumour cell present in a single image divide by the total number of other cells.
- Generate data on the fly refers to Afshine., (2018).
- Due to high consumption of images in Deep Learning, Data augmentation is required with Random Rotation, Random Flip, Random Translation, and Random Contrast to enhance the accuracy of the AI model and to prevent the model from overfitting and underfitting.
- Its mandatory to pre-process the data before inputting the image data to the network. This is because of the variation in the shape, size, dimension, colour mode, label, of the images and to prepare the data for some other additional functions like splitting and validating.
- Want to build the sequential model using pre-trained weights and architecture of Efficient net B0 refers to Mingxing., (2019), and Resnet 50 refers to Kaiming., (2015), for comparison with Mean Squared Error loss function and Adam optimizer.
- Ensure that the model performs well with the test data and validation data where the expected range of MSE should be decreased as much as possible and need to be evaluated with appropriate metrics tool and visualizations.

## **Methods:**

The problem will be approached with the use of Deep Neural Networks. In a simple term, a bunch of images will be collected along with the ground truth. then it will be transmitted to the deep learning model with the pre-trained weights of Efficientnet and Resnet. Subsequently, both the models will be compared and evaluated. Then the best performed model will be selected for prediction of tumour density.

### Finding Tumour Density:

- The NuCLS dataset refers to Mohamed., (2021), will be used in this project where the tumour density information is not available. So, we must do a simple manipulation of reading the data and want to divide the total cell information by total tumour cell present in each image. This density information will be collected for every image present in the train image folder and appended as a list or a NumPy Array for training as a train label and for testing as test label along with the corresponding images.

$$\text{Density of tumour} = \text{Total no. of tumour cell} / \text{Total no. of other cells}$$

### Generate Data on the Fly:

- This is a state-of-art method refers to Afshine., (2018), where it saves memory consumption by setting the images in batches. In this project, the batch size is set to 8, where the 8 set of images will be processed at once. This will make the processing faster and smoother. This set of batches will be used in an order for augmenting the data, processing the data and so on.

### Data Augmentation:

- The Deep Convolutional Neural Network requires numerous amounts of data. So, it's essential to augment the image to enhance the accuracy of tumour density prediction. The Data augmentation can be achieved with the keras API which offers significant and different functions such as Random Rotation, Random Flip, Random Translation, and Random Contrast to make the image vary and to give more information to the model to learn. This will be carried out with the concept called "Train data on the fly".

### Data pre-processing:

- Uniform aspect ratio: The first thing is to make sure that all of the images in the dataset are the same size and aspect ratio. The majority of Deep Neural Net models assume a square-shaped input image, which means that each image must be evaluated for squareness and cropped accordingly.
- Image Scaling: The Efficientnet B0 model only accepts the image shape of (224, 224) and Resnet50 is (512, 512). There are many different approaches for up-scaling and down-scaling, and a library function can be used to achieve it.

### Building the model:

- The training of this model will take place using transfer learning techniques with Linear Regression ( $y = \alpha x + \beta$ ) or Polynomial Regression approach refers to Casey., (2020), will be taken which may vary according to the data points. Particularly, Efficient net or Resnet architecture and weights will be used by removing the top layer of that model. Additionally, GlobalAveragePooling, Batch Normalization and dropout layers will be added before the final dense layer. Furthermore, this problem is based on regression, so Adam optimizer will be used with the Mean Squared Error loss function. Finally, the model will be trained for couple of epochs.

### Testing the model:

- The model which has been trained will be used to evaluate and predict the density of tumour for the new image where the tumour density of those images will be unknown. However, the evaluation will take place using the labelled data which are not used in training set. Hence, the number of correct predictions and wrong predictions will be compared to conclude the accuracy of the model. The primary focus of this model is to predict the tumour density with the maximum accuracy as possible.

## Changes in original project proposal:

While compared with the original project proposal, we have made lots of changes in this report. To be more specific, we have added few more methods like “Generating the data in batches”, Gathered more images from other folders of NuCls dataset and updated the task dates (plan of the project) which are specified in the original proposal. Additionally, we have primarily concentrated on EfficientnetB0 in the original report, but the Efficientnet doesn’t perform well with the Histopathological data (Figure 1). So, we have planned to concentrate on Resnet50 which is expected to give better results. Furthermore, In the original report we have specified that, we will be applying `flow_from_directory()` method. Currently, we are not using it. Instead, we are using `DirectoryDataGenerator(keras.utils.Sequence)` class which is published by Afshine., (2018), and data augmentation takes place inside of this class where the same class provides the batches of images. so those batch image will be augmented inside the class and feed to the build function.

```
Epoch 23/25
6/6 - 1s - loss: 0.2278 - mean_absolute_error: 0.3179 - mean_absolute_percentage_error: 86169920.0000
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
```

Figure 1: Best result obtained from Efficientnet at present.

## Progress report against plan:

Initially, requirement of the project has been analysed and fulfilled. Anaconda environment has been created where all the dependencies have been installed appropriately. The NuCLS multi-ratter dataset has downloaded from the official site of the dataset NuCLS Home. Then, the density of the tumour cells is identified for the X train and test labels where it is used for training and validating the Neural Net model.

Subsequently, the train images has been augmented with the use of `DirectoryDataGenerator(keras.utils.Sequence)` class “Generate data in fly” refers to Afshine., (2018), as a batches and it is pre-processed directly with the same batches of image. Then, the data is directed to the model where in this case, it is EfficientnetB0 pre-trained architecture and weights. The model is trained without the top layer of the original model where the top layer is our data then it is trained for couple of epochs with the same configurations as the original model architecture with some slight change because the original paper is based on classification problem whereas ours is regression. Moreover, the trained model is tested with the validation data and evaluated with the predictions made. The performance of the Efficientnet model is low so it needs to be fine-tuned and the MSE of the model will be calculated. Here, the data is trained only with the efficientnet model at the moment and need to be trained with Resnet50 in upcoming days as same as the process carried out for the Efficientnet, and the best performed model will be selected and will be used for prediction.

## Updated project plan:

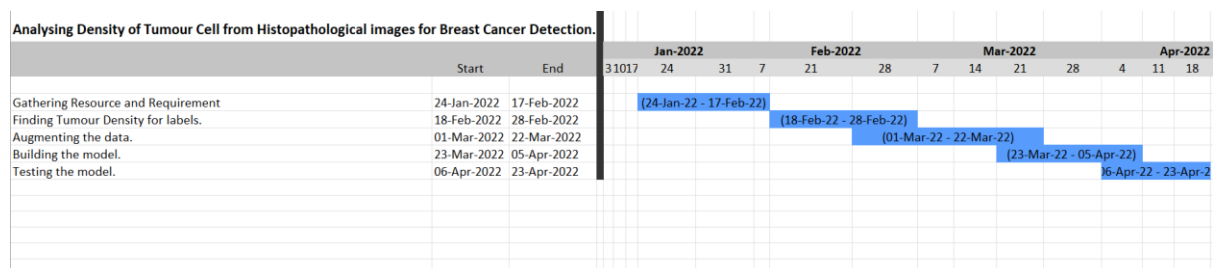


Figure 2: Project Plan, Waterfall Model

<b>Milestones &amp; Sub-topics</b>	<b>Start Date</b>	<b>End Date</b>
Gathering Resource and Requirement, <ul style="list-style-type: none"> <li>• Downloading NuCLS Dataset.</li> <li>• Setting up the Environment.</li> <li>• Revising risk assessment.</li> </ul>	January 24	January 29
Finding Tumour Density for labels, <ul style="list-style-type: none"> <li>• Extracting information from CSV files.</li> <li>• Finding tumour density.</li> <li>• Appending the labels.</li> </ul>	February 01	February 05
Augmenting the data, <ul style="list-style-type: none"> <li>• pre-processing the data.</li> <li>• Analysis of pre-trained models.</li> <li>• Getting familiar with the “Generate data on fly” approach.</li> </ul>	February 06	February 15
Building the Efficientnet model, <ul style="list-style-type: none"> <li>• Coding the sequential network.</li> <li>• Training the images and labels for Efficientnet.</li> </ul>	February 16	February 25
Testing the Efficientnet model, <ul style="list-style-type: none"> <li>• Predicting the test samples.</li> <li>• Calculating the MSE.</li> </ul>	February 26	March 10
Building the Resnet Model, <ul style="list-style-type: none"> <li>• Coding the sequential network.</li> <li>• Training the network with the pre-trained weights of Resnet50.</li> </ul>	March 11	March 18
Testing the Resnet Model, <ul style="list-style-type: none"> <li>• Predicting the test samples.</li> <li>• Calculating the MSE.</li> </ul>	March 19	April 08
Validating, <ul style="list-style-type: none"> <li>• Fine-tuning both the model.</li> <li>• Cross checking the works with supervisor.</li> <li>• Comparing and selecting best model for prediction.</li> </ul>	April 10	April 23

ACTIVITY	START DATE	PLAN START (DAY)	PLAN DURATION (DAYS)	END DATE	PERCENT COMPLETE
Finalize project requirements	Monday, 24 January, 2022	1	1	Monday, 24 January, 2022	100%
Determine what to purchase	Tuesday, 25 January, 2022	2	1	Tuesday, 25 January, 2022	100%
Determine quality, standards, procedures & metrics	Wednesday, 26 January, 2022	3	2	Thursday, 27 January, 2022	100%
Revise the risk assessment	Friday, 28 January, 2022	5	2	Saturday, 29 January, 2022	100%
Setting up the Environment	Sunday, 30 January, 2022	7	5	Thursday, 3 February, 2022	100%
Data collection	Tuesday, 1 February, 2022	8	2	Thursday, 3 February, 2022	100%
Data verification	Thursday, 3 February, 2022	10	2	Saturday, 5 February, 2022	100%
Feature extraction	Saturday, 5 February, 2022	12	6	Friday, 11 February, 2022	100%
Machine resource management	Monday, 7 February, 2022	14	2	Wednesday, 9 February, 2022	100%
Finding tumour density for train labels	Wednesday, 9 February, 2022	16	4	Sunday, 13 February, 2022	100%
Cross verifying the data	Saturday, 12 February, 2022	19	2	Monday, 14 February, 2022	100%
Augmenting the images	Sunday, 13 February, 2022	20	2	Tuesday, 15 February, 2022	100%
Pre-processing the data	Wednesday, 16 February, 2022	23	4	Sunday, 20 February, 2022	100%
Analysis of required pre-trained model	Thursday, 17 February, 2022	24	4	Monday, 21 February, 2022	100%
Building the model (Efficientnet)	Sunday, 20 February, 2022	27	8	Monday, 28 February, 2022	50%
Training the model (Efficientnet)	Sunday, 27 February, 2022	34	3	Tuesday, 1 March, 2022	50%
Testing the model (Efficientnet)	Monday, 28 February, 2022	35	4	Friday, 4 March, 2022	50%
Creating visualizations (Efficientnet)	Thursday, 10 March, 2022	45	2	Saturday, 12 March, 2022	0%
Evaluations (Efficientnet)	Saturday, 12 March, 2022	47	2	Monday, 14 March, 2022	0%
Tuning the model (Efficientnet)	Tuesday, 15 March, 2022	50	3	Friday, 18 March, 2022	0%
Building the model (Resnet)	Monday, 21 March, 2022	56	4	Friday, 25 March, 2022	0%
Training the model (Resnet)	Saturday, 26 March, 2022	61	3	Tuesday, 29 March, 2022	0%
Testing the model (Resnet)	Wednesday, 30 March, 2022	65	4	Monday, 4 April, 2022	0%
Creating visualizations (Resnet)	Tuesday, 5 April, 2022	71	12	Sunday, 17 April, 2022	0%
Comparisons	Monday, 18 April, 2022	83	2	Tuesday, 19 April, 2022	0%
Real-time testing	Wednesday, 20 April, 2022	85	2	Thursday, 21 April, 2022	0%

Figure 3: Updated Project Plan Table

## References:

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## Appendices:

### Evidence of data augmentation:

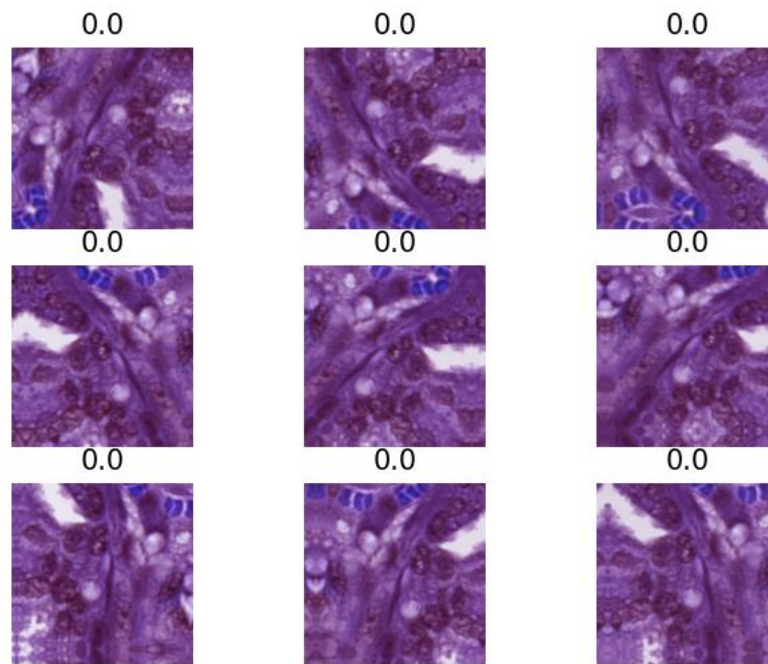


Figure 4: Visualizing augmented images with matplotlib

### Evidence of model building:

block7a_se_reduce (Conv2D)	(None, 1, 1, 48)	55344	block7a_se_reshape[0][0]
block7a_se_expand (Conv2D)	(None, 1, 1, 1152)	56448	block7a_se_reduce[0][0]
block7a_se_excite (Multiply)	(None, 7, 7, 1152)	0	block7a_activation[0][0] block7a_se_expand[0][0]
block7a_project_conv (Conv2D)	(None, 7, 7, 320)	368640	block7a_se_excite[0][0]
block7a_project_bn (BatchNormal	(None, 7, 7, 320)	1280	block7a_project_conv[0][0]
top_conv (Conv2D)	(None, 7, 7, 1280)	409600	block7a_project_bn[0][0]
top_bn (BatchNormalization)	(None, 7, 7, 1280)	5120	top_conv[0][0]
top_activation (Activation)	(None, 7, 7, 1280)	0	top_bn[0][0]
avg_pool (GlobalAveragePooling2	(None, 1280)	0	top_activation[0][0]
batch_normalization (BatchNorma	(None, 1280)	5120	avg_pool[0][0]
top_dropout (Dropout)	(None, 1280)	0	batch_normalization[0][0]
pred (Dense)	(None, 1)	1281	top_dropout[0][0]
=====			
Total params: 4,055,972			
Trainable params: 4,011,389			
Non-trainable params: 44,583			

Figure 5: Summary of the Efficientnet B0 model



### Evidence of model training:

```
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
Epoch 17/25
6/6 - 2s - loss: 0.2858 - mean_absolute_error: 0.3781 - mean_absolute_percentage_error: 41666784.0000
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
Epoch 18/25
6/6 - 2s - loss: 0.2375 - mean_absolute_error: 0.3297 - mean_absolute_percentage_error: 598.0383
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
Epoch 19/25
6/6 - 2s - loss: 0.2608 - mean_absolute_error: 0.3531 - mean_absolute_percentage_error: 20833632.0000
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
Epoch 20/25
6/6 - 2s - loss: 0.2867 - mean_absolute_error: 0.3791 - mean_absolute_percentage_error: 41666788.0000
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
Epoch 21/25
6/6 - 3s - loss: 0.3460 - mean_absolute_error: 0.4383 - mean_absolute_percentage_error: 83333448.0000
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
Epoch 22/25
6/6 - 2s - loss: 0.3415 - mean_absolute_error: 0.4338 - mean_absolute_percentage_error: 62498284.0000
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
Epoch 23/25
6/6 - 2s - loss: 0.2976 - mean_absolute_error: 0.3899 - mean_absolute_percentage_error: 41666808.0000
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
Epoch 24/25
6/6 - 2s - loss: 0.3212 - mean_absolute_error: 0.4136 - mean_absolute_percentage_error: 41666808.0000
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
Epoch 25/25
6/6 - 2s - loss: 0.3243 - mean_absolute_error: 0.4188 - mean_absolute_percentage_error: 62500100.0000
WARNING:tensorflow:Can save best model only with val_loss available, skipping.
```

Figure 6: Results obtained by training the Efficientnet model

### Literature review:

Breast cancer is one of the deadliest diseases in the world which has reached over 2.26 million cases in 2020. It tremendously harms women's health and life. Breast cancer's history is a tangled web of attempts to comprehend the elusive nature of this hormone-responsive malignancy and physicians' determination to defeat it through physical removal (surgery), cell annihilation (chemo-radiotherapy), or targeted therapy to cell receptors (biomodulation) refers to Ritu., (2014). Since the location of the organ allowed for easy identification, written accounts, and pictures of breast cancer date back to antiquity. The Edwin smith surgical papyrus, which dates from 3,000–2,500 B.C. and is thought to have been written by Imhotep (an Egyptian physician-architect), contains accurate tales of breast cancer. If the cancer was "cold to the touch, bulging, and spread all over the breast," the condition was considered incurable. As demonstrated by votive offerings in the shape of breasts in Greek temples that housed Asclepius, the god of medicine, a divinity was exhorted to grant cure from breast diseases in ancient Greece. In the medical language, the terms carcinoma (carcinoma), scirrhus (hard, Greek Skyros), and cacoethes (malignant disease, Greek cacoethes) all derive from Hellenistic texts. Hippocrates' notion of humour imbalance as a cause of disease (about 400 B.C.) and his classic descriptions of the progressive stages of breast cancer, represent early hypotheses on the cause of cancer. In the first century A.D., Leonidas of Alexandria, following Greek traditions, courageously and deftly outlined his approach of incision and cautery. His requirement that a large margin of excision be left and that only small tumours be removed foreshadows the biomedical principles of modern surgical treatment. Galen determined that breast cancer in A.D. 200 was a systemic disease after attributing it to the formation of black bile in the blood. The end of menstruation, according to these ancient physicians, was somehow known to cause cancer; in actuality, it was most likely due to the association of cancer with old age. Galen permitted surgical injuries to flow freely to get rid of the black bile and frowned on the use of ligatures in accordance with this notion. He invented the term "crab" for cancer to describe the dilated veins emanating from the tumour.

### **A feasibility study:**

As per the data suggests, a cross-sectional analysis for 546 women has been conducted to find relationships between breast size and tumour density, status of lymph nodes, invasion of vascular or lymphatic, p53, histologic, and nuclear grade, tumour differentiation, index of mitotic, tumour necrosis, bcl-2, proliferation of ki-67, oestrogen, and progesterone receptor, p27, cyclin e, and c-erb-b2. For the cancer-free breast, breast size was classified as fatty or dense. All tumour markers were assessed by a single pathologist. Erin., (2005), has been analysed whether interval cancer or cancer discovered on a screen influenced the connections. Women with tumours greater than 1.0 cm were more likely than women with tumours smaller than 1.0 cm to have thick breasts. In screen-detected malignancies, breast density was connected to tumour density, status of lymph node, and invasion of vascular or lymphatic. In lady detected with interval cancer, breast density was inversely related to histologic grade and mitotic index. However, these findings suggest that breast size is connected to tumour density, lymph node status, and lymphatic or vascular invasion in screen-diagnosed cancers. Similarly, the connections between subsequent breast cancer and breast density based on tumour traits have generated unclear results, according to a few additional research. The study Lusine., (2011), added 1042 postmenopausal ladies who had been detected with breast cancer. According to the findings, maximum mammographic density is connected to highly aggressive tumour characteristics as well as in situ malignancies. So it is feasible to detect breast cancer with the density of tumour cells.