Subtyping of Breast Cancer from Histopathological Images using Interpretable Convolutional Neural Networks

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Table of Content

1. Objectives

01

Classify the 8 prominent breast cancer subtypes.

- Previous studies that worked on BreakHis performed binary classification of **benign** & **malignant** categories <u>only</u>.
- Subtype-specific classification is important for precision medicine and effective treatment since different subtypes are proven to have **distinct molecular characteristics**.

02

Use squeeze-and-excitation attention mechanism to improve subtype classification.

- Compare classification accuracies of the following combinations:
  - **Subtype classification**: ResNet50 with attention & ResNet50 without attention.
  - **Subtype classification**: EfficientNetB0 with attention & EfficientNetB0 without attention.
  - **Binary classification**: ResNet50 & EfficientNet50

03

Determine the most important regions for diagnosis.

- Model interpretability is very important for the use of deep learning in medicine due to the **black box problem.**
- Being able to interpret the models is useful **to draw insights** and to **trust the diagnosis** of the model.

2. Dataset Overview

- The BreaKHis (Breast Cancer Histopathological Image Classification) dataset.
- **Important Features:**
  - High magnification
  - Big data (7,909 images)
  - Annotations
  - Different variants

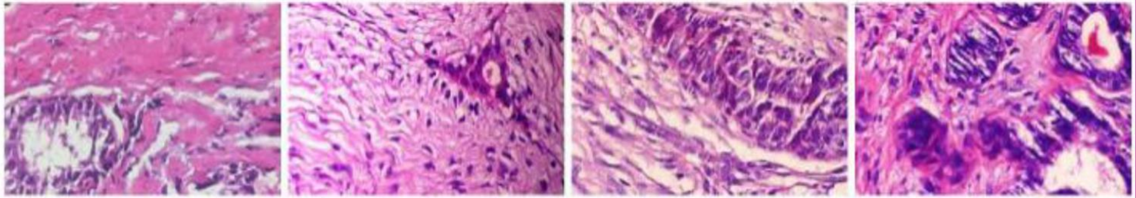


Figure 1. Benign Sub-Classes [43]

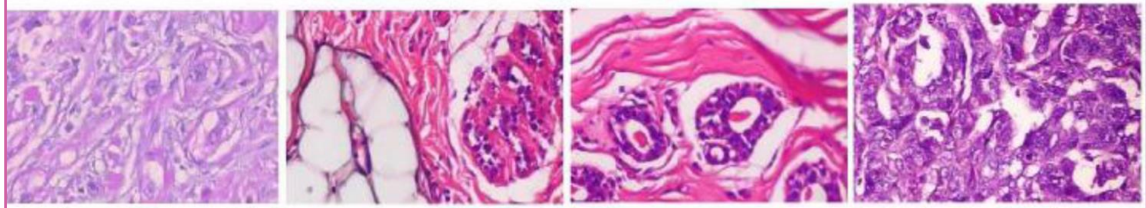


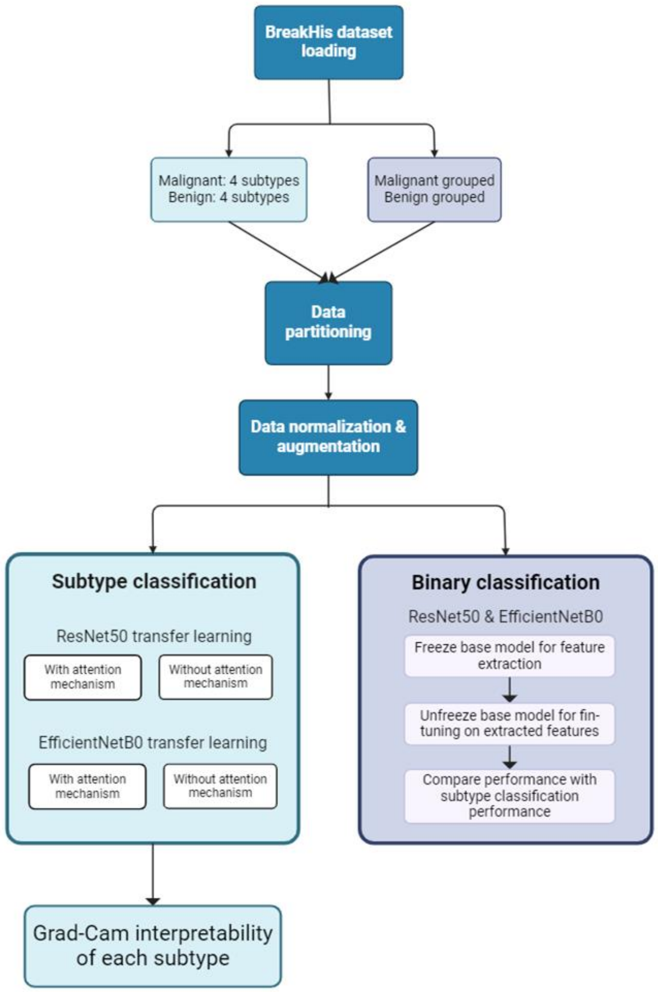
Figure 2. Malignant Sub-Classes [43]

2. Dataset Overview

TABLE 1. BreaKHis Dataset

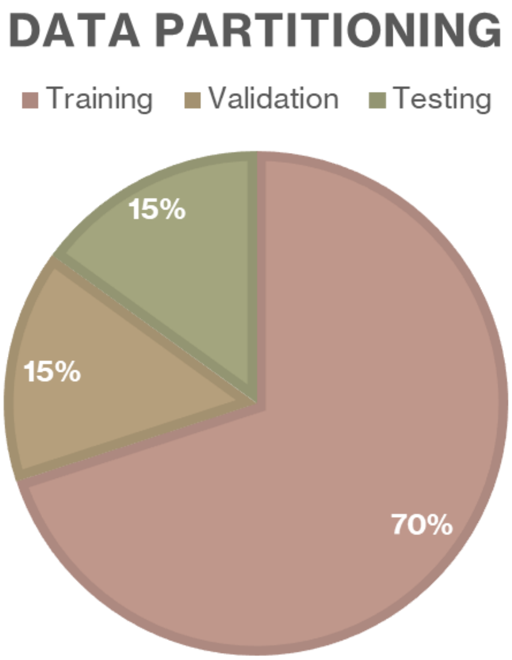
Class	Types	Abb.	40X	100X	200X	400X	
Benign	Adenosis	A	114	113	111	106	444
	Fibro	F	253	260	264	237	1014
	Tubular	TA	109	121	108	115	453
	Phyllodes	PT	149	150	140	130	569
Malignant	Ductal	DC	864	903	896	788	3451
	Lobular	LC	156	170	163	137	626
	Mucinous	MC	205	222	196	169	792
	Papillary	PC	145	142	135	138	560
Total			1995	2081	2013	1820	**7909**

3. Methods



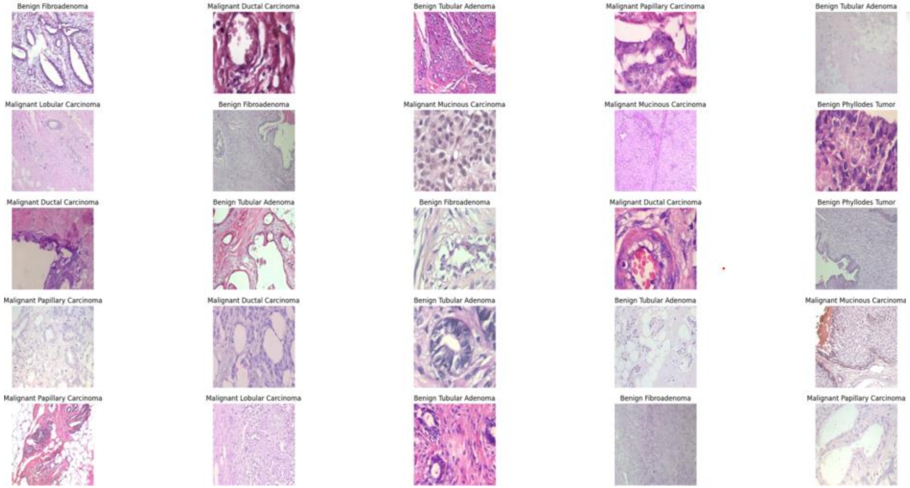
BreakHis dataset loading
Malignant: 4 subtypes
Benign: 4 subtypes
Malignant grouped
Benign grouped
Data partitioning
Data normalization & augmentation
Subtype classification
ResNet50 transfer learning
With attention mechanism
Without attention mechanism
EfficientNetB0 transfer learning
With attention mechanism
Without attention mechanism
Binary classification
ResNet50 & EfficientNetB0
Freeze base model for feature extraction
Unfreeze base model for fin-tuning on extracted features
Compare performance with subtype classification performance
Grad-Cam interpretability of each subtype

Preprocessing

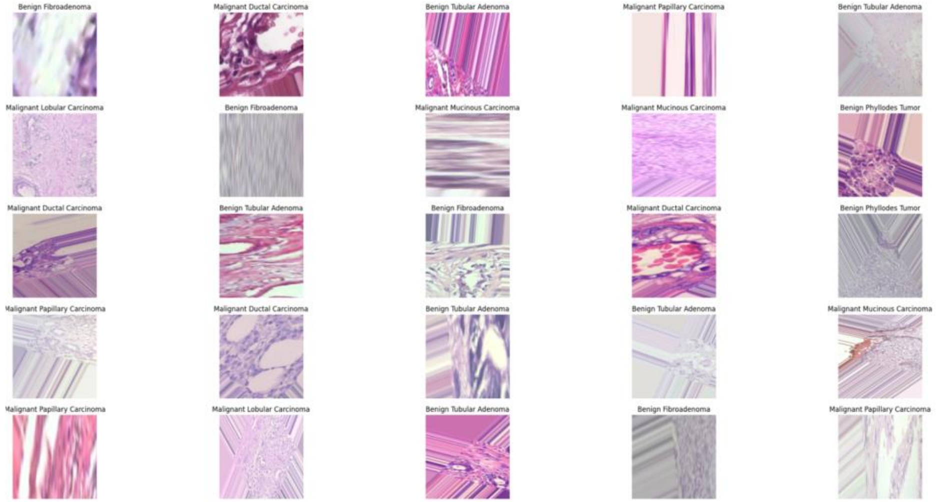


- Scaling *[260*260]*
- Normalization *[/255]*
- One hot encoding *[0, 0, 0, 1, 0, 0, 0, 0]*
- Augmentation
  - *[zoom_range=1.2,*
  - *rotation_range = 90,*
  - *width_shift_range=0.5,*
  - *height_shift_range=0.5,*
  - *horizontal_flip=True,*
  - *vertical_flip=True]*

Preprocessing: Extreme augmentation



Before augmentation



After augmentation

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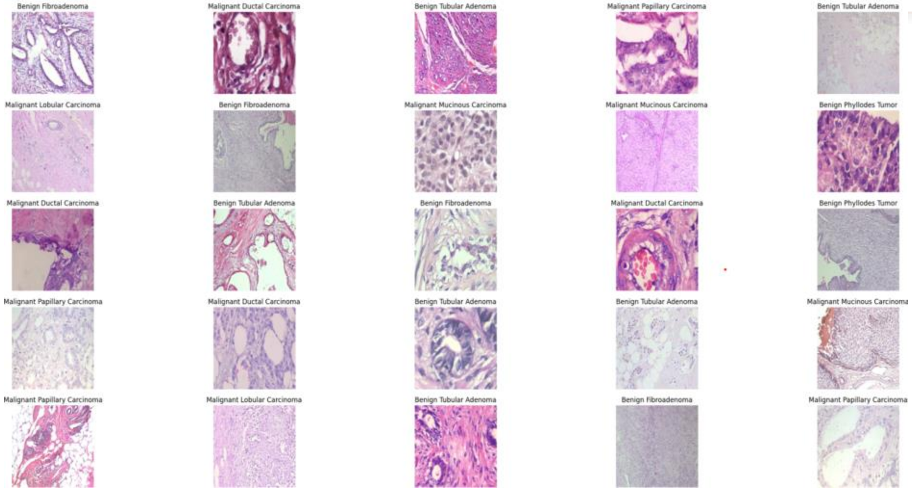
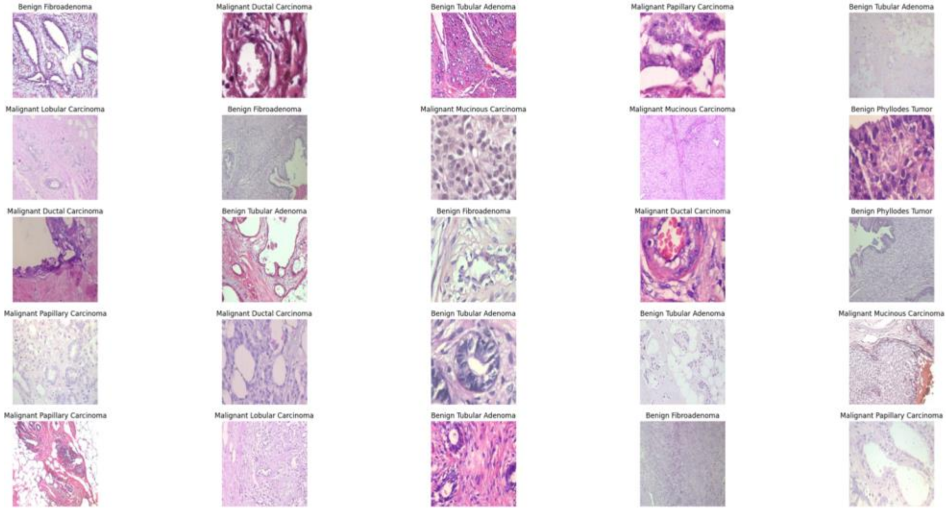
Preprocessing: Suitable augmentation

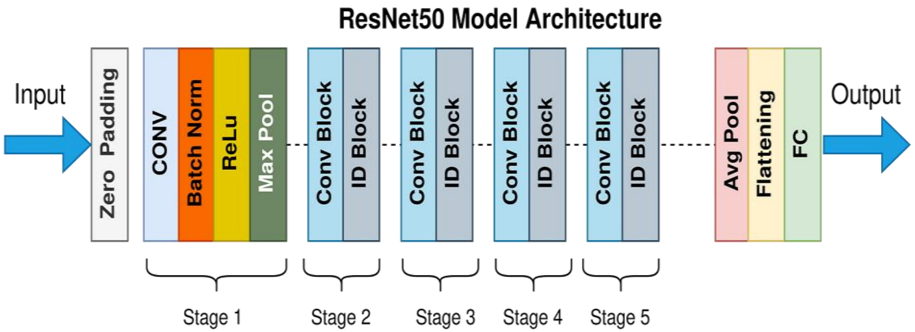


Before augmentation



After augmentation

ResNet50 Model



Model: "functional_1"

Without attention

Layer (type)	Output Shape	Param #
input_layer_1 (InputLayer)	(None, 260, 260, 3)	0
resnet50 (Functional)	(None, 9, 9, 2048)	23,587,712
global_average_pooling2d (GlobalAveragePooling2D)	(None, 2048)	0
dense (Dense)	(None, 8)	16,392

Total params: 23,604,104 (90.04 MB)
Trainable params: 16,392 (64.03 KB)
Non-trainable params: 23,587,712 (89.98 MB)

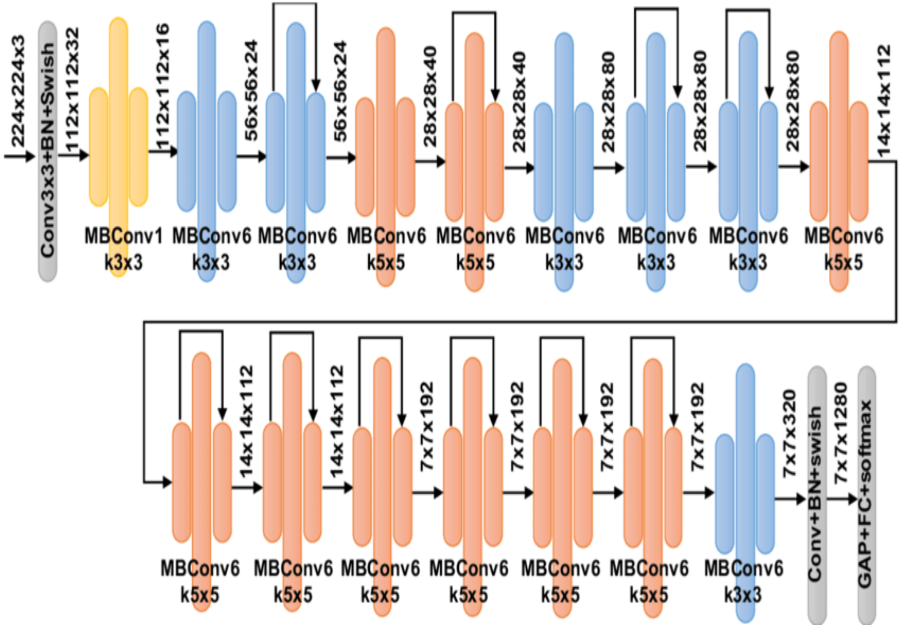
Model: "functional_31"

With attention

Layer (type)	Output Shape	Param #
input_layer_6 (InputLayer)	(None, 260, 260, 3)	0
resnet50 (Functional)	(None, 9, 9, 2048)	23,587,712
squeeze_excite_block_2 (SqueezeExciteBlock)	(None, 9, 9, 2048)	0
global_average_pooling2d_7 (GlobalAveragePooling2D)	(None, 2048)	0
dense_12 (Dense)	(None, 8)	16,392

Total params: 23,604,104 (90.04 MB)
Trainable params: 16,392 (64.03 KB)
Non-trainable params: 23,587,712 (89.98 MB)

EfficientNetB0 Model



Without attention

Model: "functional_1"

Layer (type)	Output Shape	Param #	Connected to
input_layer_2 (InputLayer)	(None, 260, 260, 3)	0	-
efficientnetb0 (Functional)	(None, 9, 9, 1280)	4,049,571	input_layer_2[0]…
global_average_poo… (GlobalAveragePool…	(None, 1280)	0	efficientnetb0[0…
batch_normalization (BatchNormalizatio…	(None, 1280)	5,120	global_average_p…
dense (Dense)	(None, 256)	327,936	batch_normalizat…
flatten (Flatten)	(None, 256)	0	dense[0][0]
concatenate (Concatenate)	(None, 1536)	0	global_average_p… flatten[0][0]
dense_1 (Dense)	(None, 8)	12,296	concatenate[0][0]

Total params: 4,394,923 (16.77 MB)
Trainable params: 342,792 (1.31 MB)
Non-trainable params: 4,052,131 (15.46 MB)

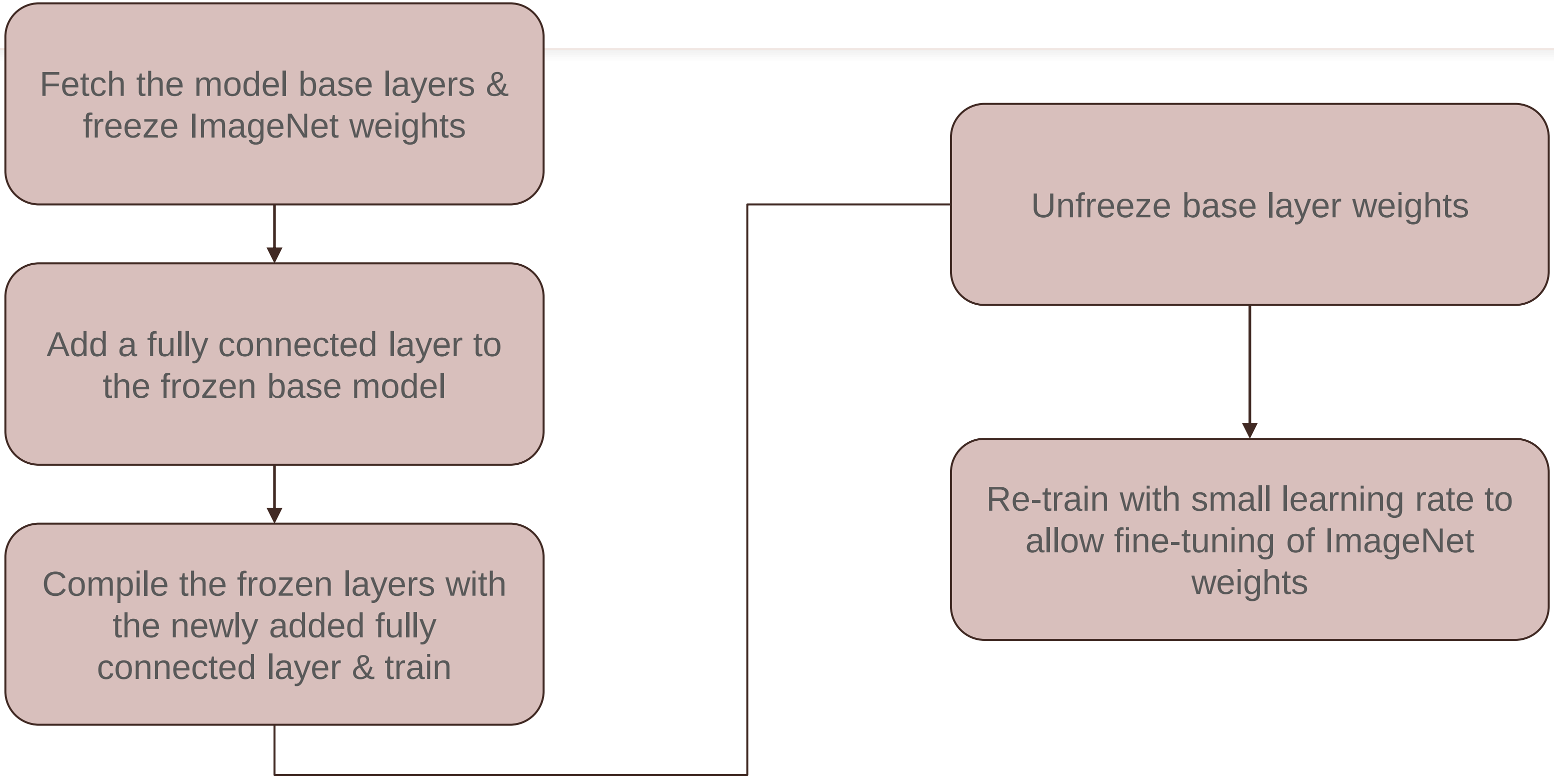
With attention

Model: "functional_27"

Layer (type)	Output Shape	Param #
input_layer_4 (InputLayer)	(None, 260, 260, 3)	0
efficientnetb0 (Functional)	(None, 9, 9, 1280)	4,049,571
squeeze_excite_block_1 (SqueezeExciteBlock)	(None, 9, 9, 1280)	0
global_average_pooling2d_4 (GlobalAveragePooling2D)	(None, 1280)	0
batch_normalization (BatchNormalization)	(None, 1280)	5,120
dense_6 (Dense)	(None, 256)	327,936
dense_7 (Dense)	(None, 8)	2,056

Total params: 4,384,683 (16.73 MB)
Trainable params: 332,552 (1.27 MB)
Non-trainable params: 4,052,131 (15.46 MB)

4. Training Recipe



4. Training: CategoricalCrossEntropy()

- Used when there are two or more label classes.
- Expected labels to be provided in a one_hot representation.

$$L = -\frac{1}{N}\left[\sum_{j=1}^{N}\left[t_j \log(p_j) + (1 - t_j)\log(1 - p_j)\right]\right]$$

$$L(y, \hat{y}) = -\frac{1}{N}\sum_{i}^{N}\sum_{j}^{C} y_{ij} log(\hat{y}_{ij})$$

4. Training: Attention mechanisms for CNNs

To recap, in a convolutional neural network, there are two major components:

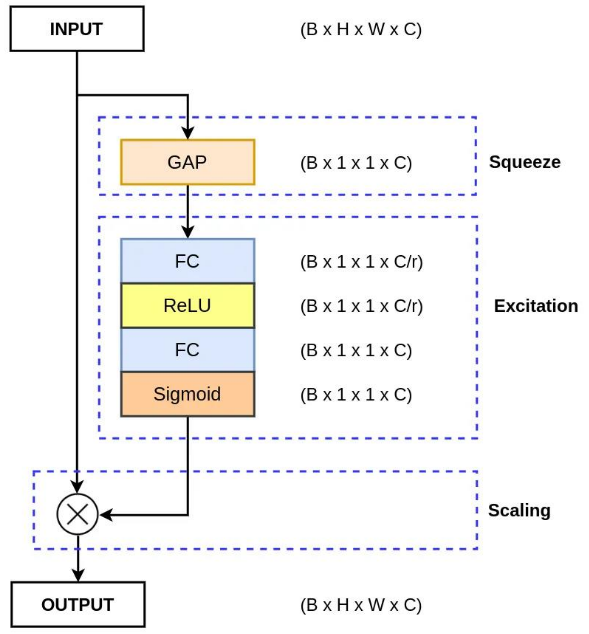
1. The input tensor (usually a four-dimensional tensor) represented by the dimensions (B, C, H, W).
2. The trainable convolutional filters which contain the weights for that layer.

- The convolutional filters are responsible for **constructing the feature maps based on the learned weights within those filters**. These filters (controlled by the **number of channels**) learn **different feature representations of the image**.

- Some filters (feature representations) are more important than others. So, our goal is to weight these channels to give them relative importances. The simplest way to do this is by **scaling the more**

Squeeze-and-Excite Channel Attention

- Introduced in 2018 by Hu et al., Cornell University, and cited more than 30k times.
- **Squeezing: Global Information Embedding**. The main purpose of the Squeeze operation is to extract global information from each of the channels of an image.

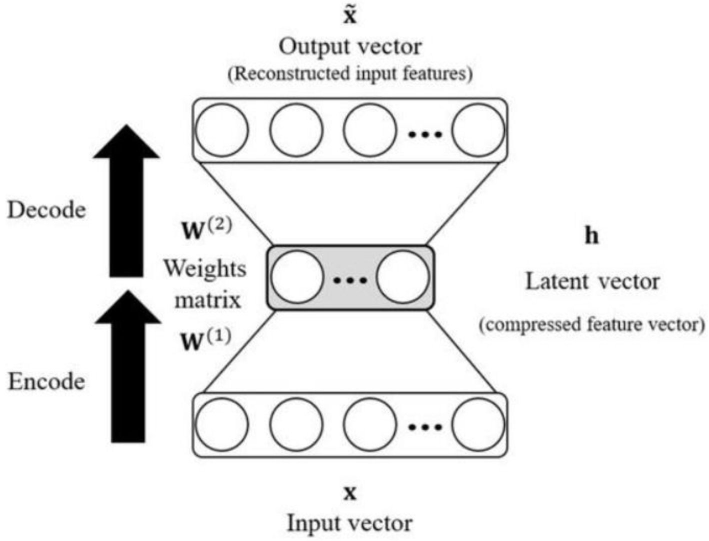


Excitation and Scaling

Activation Function	Top-1 Error Rate	Top-5 Error Rate
ReLU	23.47	6.98
Tanh	23.00	6.38
Sigmoid	**22.28**	**6.03**

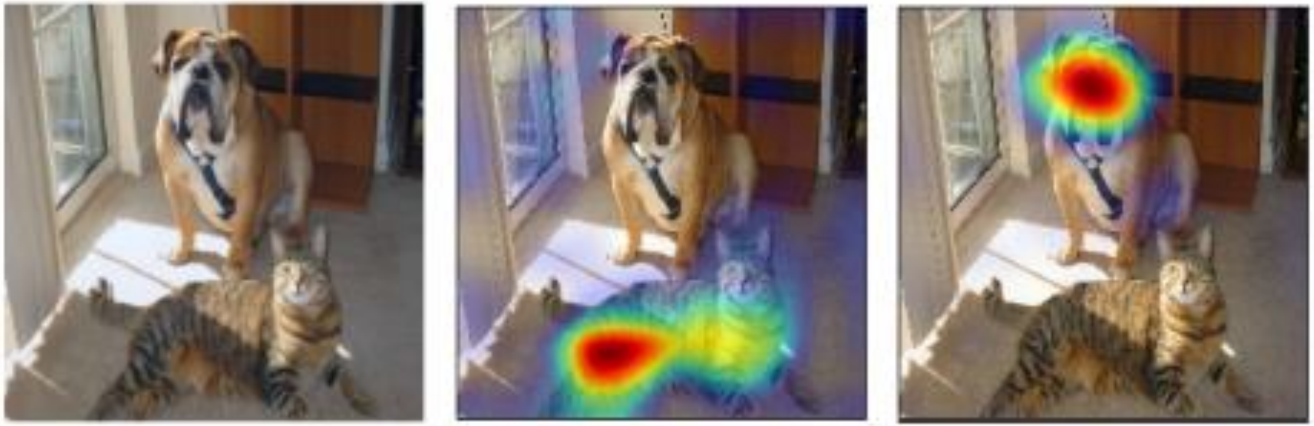
- **Excitation:** Then, we generate a set of weights for each channel. This is done by a ReLU activation followed by a sigmoid activation function scaling the values between 0 and 1.

- **Scaling**: The 1 x 1 x C sigmoid-scaled vector is applied directly to the input by an element-wise multiplication, which scales each channel in the input tensor with its corresponding learned weight from Excitation module.



4. Training: GradCam

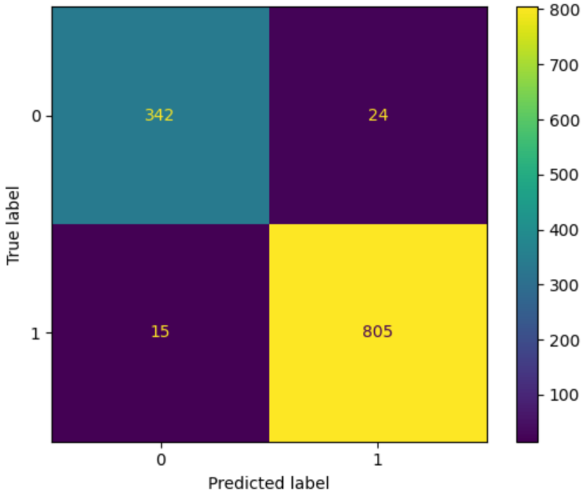
- Short for Gradient-weighted Class Activation Mapping, it is a technique used in deep learning to visually explain the decisions of convolutional neural networks (CNNs). That is, *to identify which regions of the image were important* for classification.



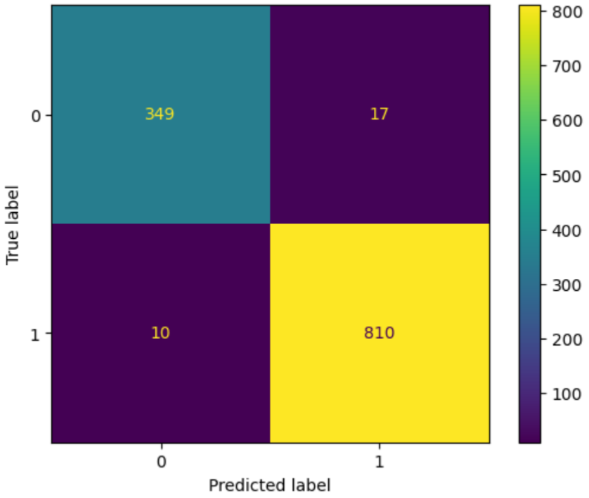
Original Image | Grad-CAM 'Cat' | Grad-CAM 'Dog'

5. Results: Binary Classification

	Test Accuracy
ResNet50 binary classification	96.71%
EfficientNetB0 binary classification	97.72%

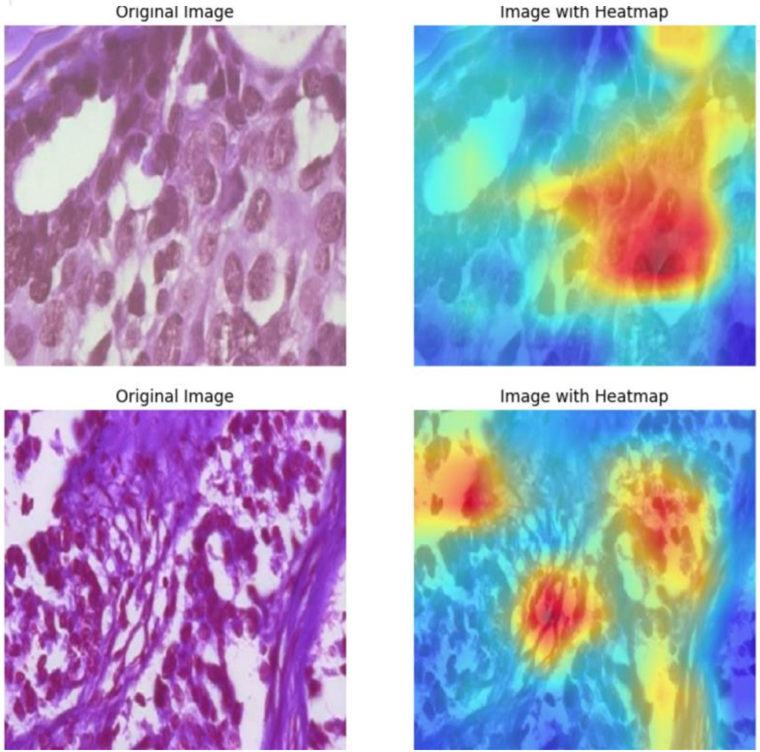


ResNet50

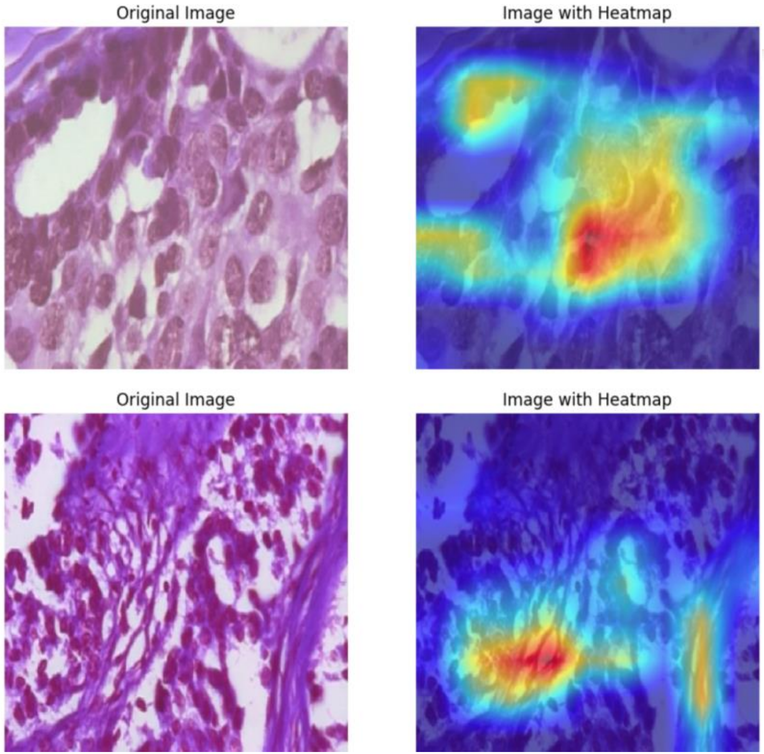


EfficientNetB0

5. Results: Binary Classification (GradCam)



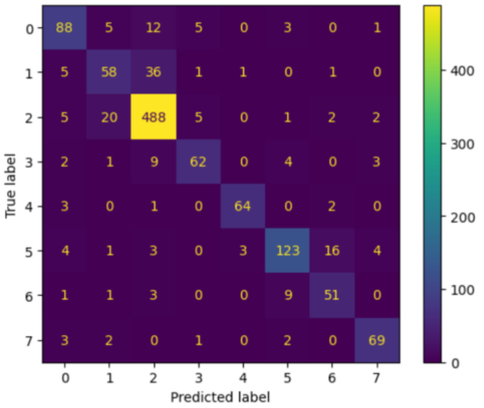
ResNet50



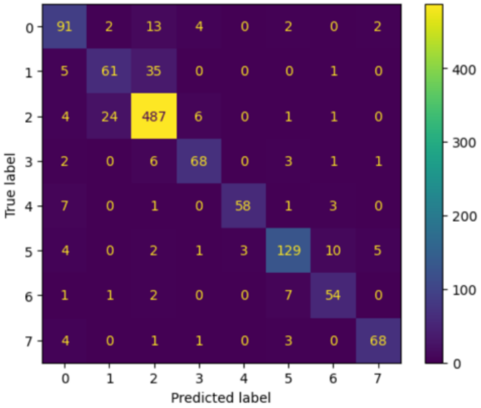
EfficientNetB0

5. Results: Subtype Classification

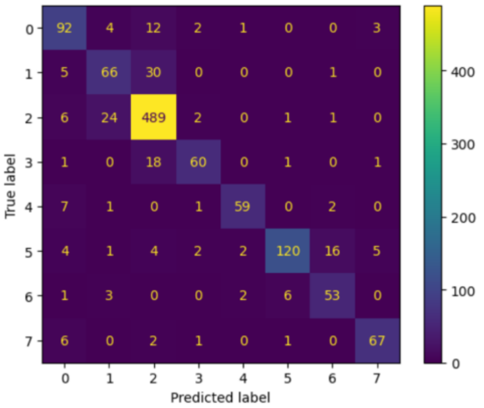
	Test Accuracy
ResNet50 subtype classification without attention	84.57%
ResNet50 subtype classification with attention	85.67%
EfficientNetB0 subtype classification without attention	84.82%
EfficientNetB0 subtype classification with attention	85.75%



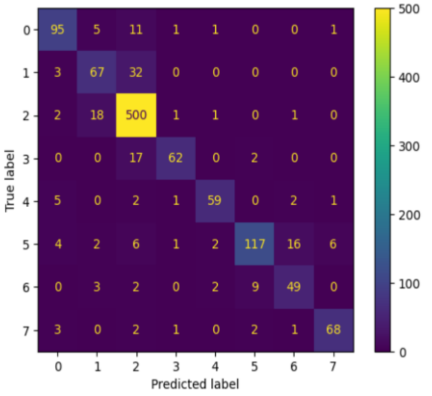
ResNet50 w/o attention



ResNet50 w/ attention

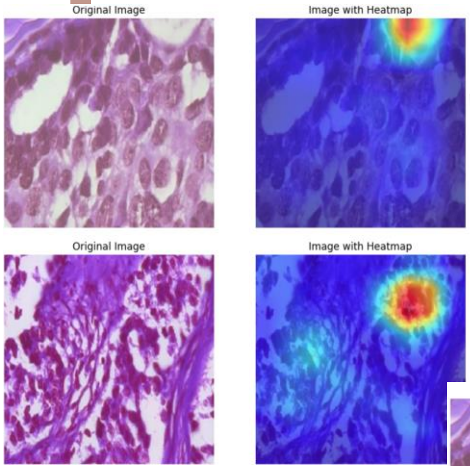


EfficientNetB0 w/o attention



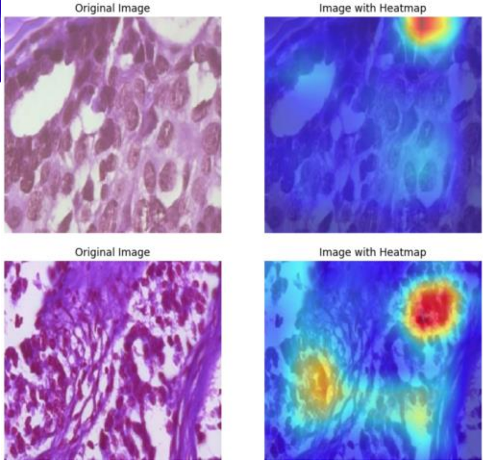
EfficientNetB0 w/ attention

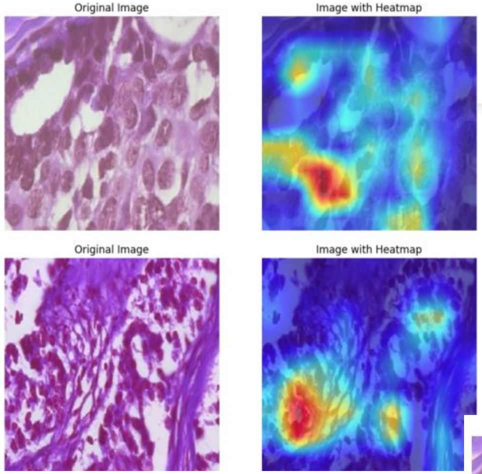
5. Results: Subtype Classification (GradCam)



ResNet50 w/o attention

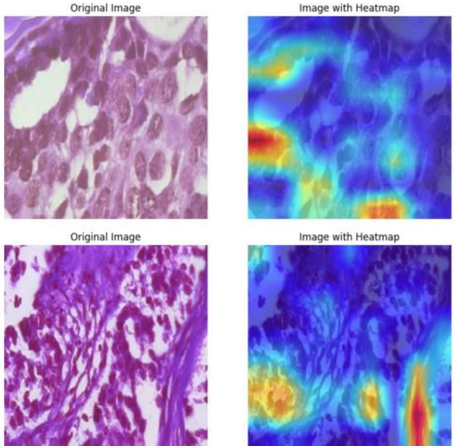
ResNet50 w/ attention





EfficientNetB0 w/o attention

EfficientNetB0 w/ attention



6. Conclusion

- Used advanced CNN architectures such as **ResNet50 and EfficientNetB0**, as well as innovative feature extraction methods such as the **squeeze-and-excitation attention** mechanism, combined with **Grad-CAM**.
- We achieved an **85% accuracy for subtype classification** with high interpretability of these models.
- The findings show an improvement in subtype classification accuracy when attention mechanisms are applied.
- In addition, for binary classification, we achieved **a maximal classification accuracy of 97.7%** by EfficientNetB0.
- These findings highlight that AI-based models can revolutionize diagnostic procedures by providing accurate, efficient, and interpretable insights from histopathological images.

7. Contribution

- Ahmed Hesham: Attention mechanism, Grad-Cam
- Aly Farag: Data loading & preprocessing, Training recipe
- Ereeny Adel: Binary classification
- Lydia Sidarous: Subtype classification

All members contributed equally to draft composition and presentation prep.

References

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[2]	Y. Zheng *et al.*, "Application of transfer learning and ensemble learning in image-level classification for breast histopathology," *Intell. Med.*, vol. 3, no. 2, pp. 115–128, 2023.
[3]	P. Agarwal, A. Yadav, and P. Mathur, "Breast cancer prediction on BreakHis dataset using deep CNN and transfer learning model," in *Data Engineering for Smart Systems*, Singapore: Springer Singapore, 2022, pp. 77–88.
[4]	S. H. Kassani, P. H. Kassani, M. Wesolowski, K. A. Schneider, and R. Deters, "Classification of histopathological biopsy images using ensemble of deep learning networks," *Conference of the Centre for Advanced Studies on Collaborative Research*, 2019.