Classification of different subtypes of idiopathic pulmonary fibrosis (IPF) using UNet through computed tomography (CT) scans

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Abstract

IPF, idiopathic pulmonary fibrosis is a impactful disease across the population. It can be difficult to diagnose due to the less severe display of symptoms, and so commonly IPF is diagnosed at later stages, where treatment is not helpful. MDA5 protein characterizes its severity, and so its vital to differentiate between MDA5 + and -. It is difficult to diagnose for radiologists, therefore tools to help diagnose this disease is required, this is where a convolutional neural network (CNN) in the form of a Unet model is useful. This project used a Unet model to classify the lung CT images and predict the probability of MDA5+ presence in accordance with the lesions present. This model has shown to be very efficient and useful.

Background

Lung function is an important indicator of mortality and morbidity, and it can contribute to multiple different diseases progression.
Age is a big factor in slower cell regeneration, depletion of cells particularly stem cells, and the lungs are unable to maintain a homeostasis in its environment. Due to the aging lung being more fragile, it is more susceptible to environmental exposure induced injury. Physiological and cellular changes are key in the development of a variety of lung diseases, particularly IPF (idiopathic pulmonary fibrosis) (Cho and Stout-Delgado, 2020)
IPF can be a known consequence of aging. Aging leads to higher susceptibility to interstitial lung diseases particularly IPF; it's etiology is unknown but its known that it leads to impaired gas exchange and eventually respiratory failure. Key hallmarks of this disease include epithelial cell injury, fibroblast expansion, ECM remodeling, inflammation and destruction of the lung's features. (Cho and Stout-Delgado, 2020)
IPF is incurable with an average onset being 65 years and a low survival rate of 3-5 years after diagnosis. It's a low likelihood of living 5 years after diagnosis: only about 20-40%. Research suggests it will be a mix of environmental and genetic factors leading to this condition and smoking is a common factor adding to this, around 70% of patients are male, commonly with a smoking history. (Glass et al., 2022)
IPF can be exacerbated by the presence of the MDA5 protein (Melanoma differentiation-association protein-5), this is due to anti-MDA5 antibodies presenting in patients with interstitial lung disease. Expression of MDAS is upregulated in the lungs of patients with MDA5-DM and idiopathic pulmonary fibrosis. MDA5 + diagnosis comes with a poorer prognosis as the disease progresses quicker, MDA5 – is a slower onset. With MDA5+ diagnosis immune pathways can be targeted, which can be very effective.
Early diagnosis is difficult as early symptoms are general such as a cough, this can be recognized as a symptom of many conditions. Histopathological features can appear as usual interstitial pneumonia. Commonly the methods used to diagnose IPF is computer tomography (CT).
Deep learning in medical imaging is soon becoming a mainstay, it helps medical experts carry out screening and diagnosis and reduces the burden, whilst improving accuracy due to the low level of existing experts who can efficiently diagnose IPF. Segmentation of the lung is difficult due to varying changes of the lung as a result of gender, age, neighboring organs. Most segmentation is based on mild defects or healthy lung images, and so to train the ability of segmentation we need complex images. Critiques for deep learning CNN methods can include the fact a large amount of data is required for model training and also the assumption the model cannot be improved after training. (Liu et al., 2022)
The aims of this project are trying to use deep learning techniques to implement a fully functional convolutional neural network, and achieve an output showcasing the probability values of being able to achieve an accurate pinpointing of the lesion.

Fig.1 An IPF patient's lung with IPF, notice there is excessive honeycombing present, this is where there is clusters of cystic airspaces, it is a specific hallmark of IPF. Image from (Hochhegger et al., 2019).

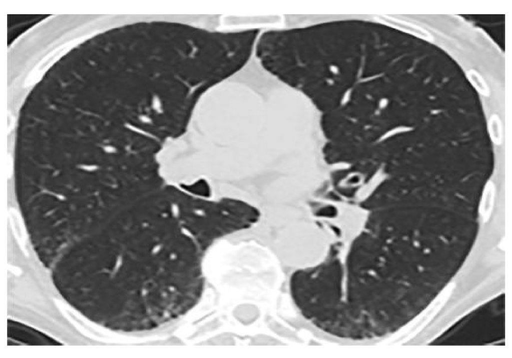

Fig.2 A healthy person's lung, appearance is healthy, minimal fibrosis but not anything indicative of IFP. Image from (Gruden, 2016).

Methods

The UNEt architecture is a type of convolutional neural network (CNN) originally designed for biomedical image segmentation.
It is known for the U-Shaped structure, where the left side represents the contracting path (encoder) and the right side represents the expansive path (decoder).
We will use the contracting path for feature extraction, followed by a global average pooling and a fully connected layer for classification.
We used a UNet model which has the capability of 1,180,721 trainable parameters. It also has an input tenor with the shape 8, 1, 224, 224 and the output tensor has the shape 8, 1. This UNet model has an encoder which consists of five convolutional layers followed nu ReLU activation functions. The number of filets doubles at each subsequent block, starting from a base number of filters ('n_filters') which is set to 16.
A max pooling operation occurs after each convolutional block to reduce the spatial dimensions by half, capturing the essential features and reducing computational complexity.
Global average pooling is applied to reduce spatial dimensions to 1x1 after the final convolutional block. A single vector for each feature map is produced, leading to a fixed length feature vector.
The output from the global average pooling is flattened and passed through a fully connected layer to produce the final classification output. For binary classification, a sigmoid activation function is applied to produce probabilities between 0 and 1.
We will also finally implement Grad-CAM (Gradient weighted Class Activation Mapping), gradients of target concepts are used, and it flows into the final convolutional layer. A coarse localization map is created which highlights the important regions in the image to predict the concept.

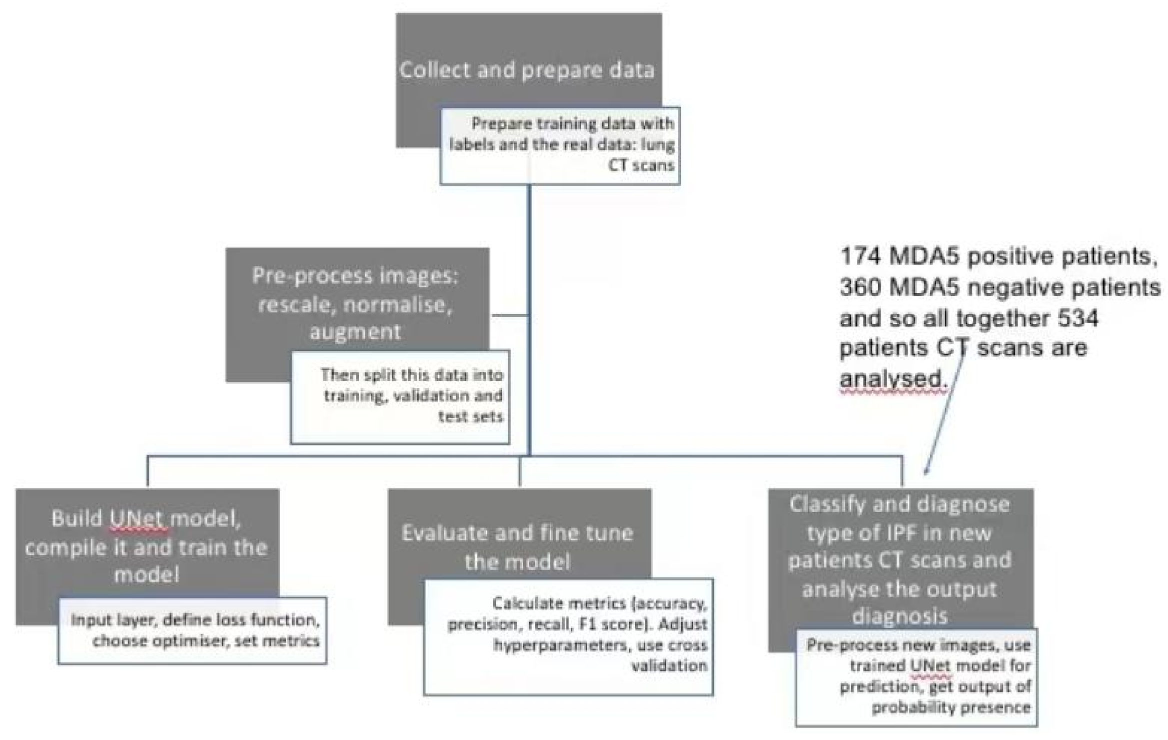

Fig.3 The flow chart of the research

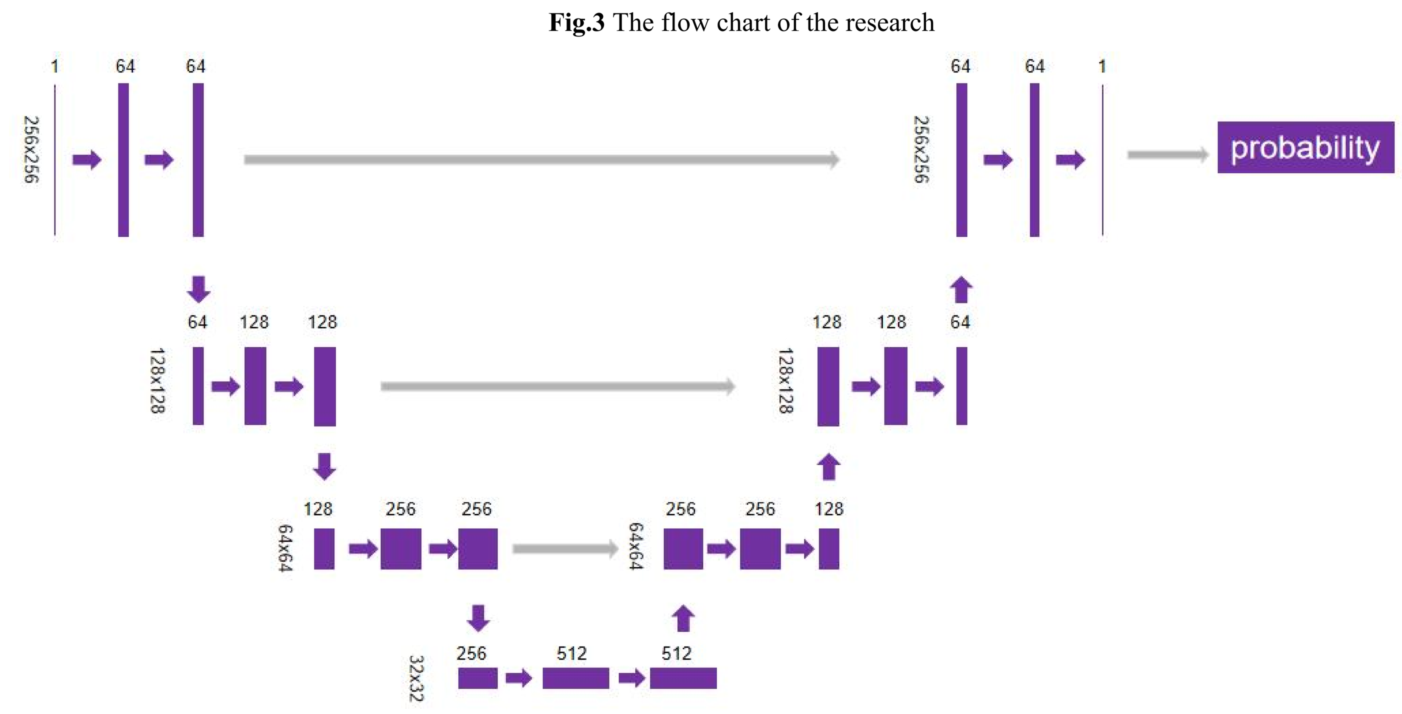

Fig.4 The structure of our UNet

Results

The confusion matrix and ROC curve graph indicates the accuracy and efficiency of this Unet model in predicting which patients are more likely to have MDA5+ present. The confusion matrix shows that the true negative values are 1998, and the true positive values are 1596, this is lower than the false negative and false positive values. We can interpret that this model is under predicting the positive class, as we see high false negative value: 2314. The ROC curve graph shows a weak curve, as indicated by the low area under the curve: 0.52.

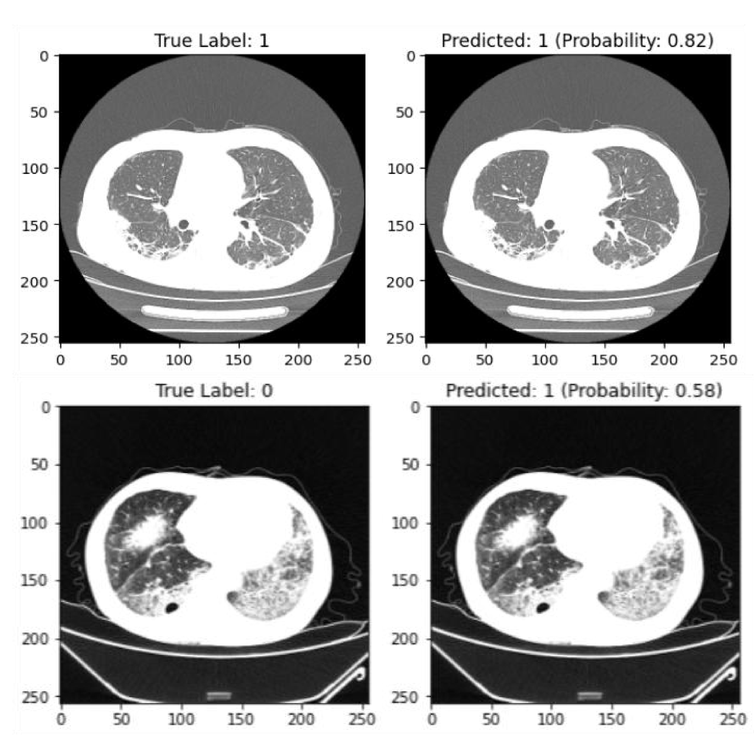

Fig.4 Lung CT scans derived from our Unet model: the model predicts the probability of the lung being classified with MDA5+ IPF. The top two pictures do not have a probability, showing it does not have a chance of being MDA5+, therefore it is MDA5-. Bottom two pictures showcase a 58% probability of being classified as MDA5 with classification of the lung CT scan.

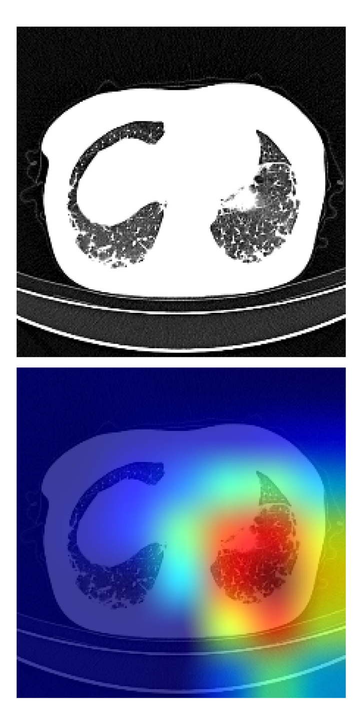

Fig.5 Pictures from grade cam shows the focus of image where model paid attention to. These two pictures are from the same person who has IPF with MDA+.

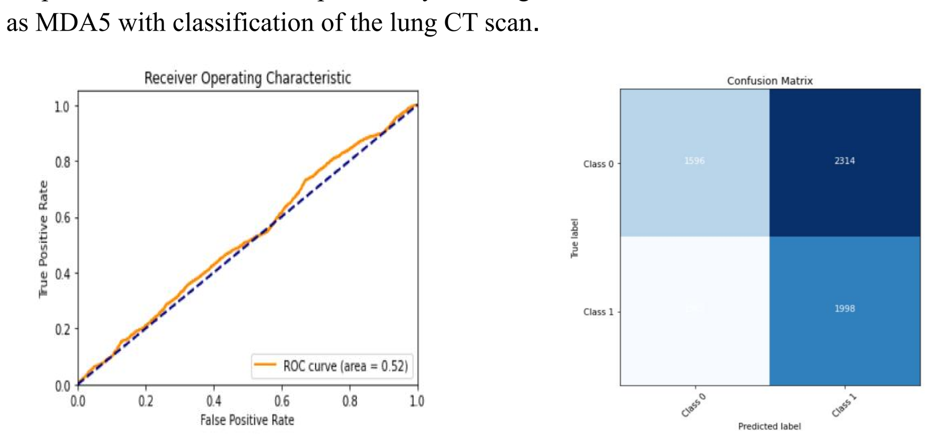

Fig.6 and 7 ROC curve graph and confusion matrix. Receiver operating characteristic (ROC) curve shows the trade off between true positive rate (sensitivity) and false positive rate for different threshold values. The area under the curve (AUC) provides a measure of the model's ability to distinguish between positive and negative classes.Confusion matrix graph displays the performance of the classification model, it shows the counts of true positives, true negatives and false negatives. This evaluates the accuracy, precision, recall, and other metrics of the model.

Discussion

Deep learning methods in AI networks such as UNet is essential for helping radiologists keep up with their clinical workload and increase accuracy rates for X-Rays, CTs, MRIs. UNet is a cornerstone for medical image segmentation, but there are alternatives which can arguably be more effective as Unet models have limitations. It's limitations include the presence of conventional kernels which only allow linear model patterns to be imaged, and so its difficult with non-linear patterns. Furthermore they neglect the importance of interpretability and explainability in the Unet models which restricts clinical decision making and making diagnoses for medical professionals.
This Unet model can be efficient and useful to diagnose patients with IPF and furthermore with the probability function, it is useful as we can differentiate with MDA5+ and MDA5-. However our model, as indicated by the ROC curve graph is not completely accurate. In terms of the confusion matrix graph we can deduce sensitivity is low due to high level of false negatives , and the model is missing a lot of positive cases. This is crucial as mis diagnoses can occur and opportunities for intervention are missed. The decision threshold might be set too high or the model may not be complex enough for the cases presented in the data. In terms of the ROC curve, the AUC value shows there is a limited ability to distinguish between the positive and negative classes. This shows the model is performing poorly. With the limited time for this project it was difficult to troubleshoot the model, with more time we could have run and tested many more times, allowing us to improve the model.Grad-cam is a useful interpretation tool, it can be utilised as a part of optimisation. We can use grad-CAM as a gradient-based visualitsation method which enables us to interpret and produce maps based on the interpretability (Gurbandurdy Dovletov et al., 2022). We can apply to pre trained classifiers if we need to.
One example to rival this is U-KAN which is known as the Kolmogorov-Arnold Networks, the results from this model are known to be advanced and can navigate non linear data. Accuracy is enhanced and theoretical interpretability is strong (Li et al., 2024).

Key References

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