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Prediction of Pulmonary Fibrosis Progression using CNN and Regression

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***Abstract*—The term idiopathic is used to refer to disease caused by unknown causes. Idiopathic pulmonary fibrosis is a chronic, progressive disease which affects the lungs and causes scar tissues to develop within them. This prevents the patient's lungs to transport oxygen into the bloodstream effectively. The daily routine of the patient is affected as the ease of breathing continues to decline. Early medical intervention and proper diagnosis can help keep the disease under control. The severity of the disease is measured used Forced Vital Capacity (FVC) values. In this paper we design an easy-to-use web application which collects the patient's CT scans, characteristic data and the initial FVC measurement. We predict the FVC values for up to a period of 2.5-3.0 years which effectively provides the Pulmonologist the rate of decline upon which suitable medications can be provided to stall the decline. We use Regression Techniques and CNN architectures to predict FVC values.**

I. Introduction

"Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive interstitial lung disease (ILD) of unknown cause in which patients experience worsening lung function resulting from progressive fibrosis" [1].Fibrosis is a term which refers to the development of excess fibrotic tissues. IPF has no known cure available, only the progression of the disease can be controlled using timely medication.

IPF makes the lives of the patients difficult to lead. Routine activities like running, walking and, lifting weights are found to be physically taxing. If IPF is treated at a time when the disease is in it's nascent stage then the patient can live longer than the mean survival period of 4 years.

The common symptoms that patients face when diagnosed with IPF are, Shortness of breath, fatigue, shallow breathing etc. These symptoms are shared with most of the other lung related diseases.

IPF is generally diagnosed with High Resolution Computed Tomography (HRCT) scans. Patterns of Usual Interstitial Pneumonia (UIP) is generally found. The progression of the disease is monitored along standard parameters, HRCT scans are used to find patterns of UIP, the Forced Vital Capacity (FVC) values are measured to check lung function. A threshold of 50-55% in FVC values is said to separate the mild-to-moderate patients from the severe ones.[3]. If the prediction of FVC values over a period of time is accurate then the patient's severity of disease can estimated and proper medication can be provided. Several patients lose out on time due to irregular clinic visits, lackadaisical attitude towards the disease, and underestimation of disease's prognosis. We try to tackle this problem by predicting the FVC values over a period of 145 weeks. That includes 12 weeks before the actual date of CT scan test, and 133 weeks from the CT scan test.

IPF does not progress in a linear pattern and using baseline physiological parameters, such as FVC, alone probably oversimplifies the tracking of progression [3]. To tackle this novel staging methods are being developed.[4] developed a scoring system which included factors like Age, recent respiratory hospitalizations and change in FVC values over a period of 24 weeks, and Baseline CT scans.

We propose a novel method of evaluating the progression of IPF by predicting the FVC values over a period of 2.5 - 3 years by considering Baseline CT scans, initial FVC measurement, Age, Gender and Smoking Status.

This paper is divided into 9 sections, section 1 gives an

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overview of idiopathic Pulmonary Fibrosis (IPF) and it's challenges. Section 2 gives an explanation of all the terms and methods used in the paper for better understanding, section 3 is about the related work done in the field of IPF and it's diagnosis. Section 4 explains the Data used for the paper. Section 5 is about the Methodology used in the paper. Section 6 is dedicated to explaining our website and it's functions. Section 7 and 8 is dedicated to explaining the Experimental Setup and the Results and Metrics used in the paper, finally in Section 9 we draw the conclusions and discuss the future scope of the research.

II. Preliminaries

A. Convolutional Neural Networks and Image Recognition

Due to the advent of Convolutional Neural Networks (CNN), image processing has taken a huge leap forward. Convolutional Networks can be effectively used to classify images. Convolutional Neural Networks are a special type of artificial neural networks which can recognize images by assigning weights and biases to the pixels in the image. The advantage of CNN's are that they have very few parameters and the filters are common. The concept of CNN's are derived from the connectivity of neurons within the brain where individual neurons respond to a particular stimulus. Unlike other image recognition techniques where the weights have to manually coded CNN's can efficiently learn these weights. The LeNet architecture was the first proposed architecture which could recognize the handwritten digits using a 5 layer deep CNN. This architecture provided excellent results com- pared to the other methods.

B. CNN in Medical Imaging

Convolutional Neural Networks has become a go-to tool for medical imaging. Pulmonary Tuberculosis is a respiratory disease which can be detected using CNN's by using CT scans for classification [12]. Convolutional Neural Networks can be used in areas of medical imaging which involves the use of CT scans and Chest Radiography. [13] studies the current state of the art in Deep Learning with respect to CT scans and Chest Radiography.

C. Transfer Learning

"Transfer learning, in which a network is trained on one task and re-purposed on another, is often used to produce neural network classifiers when data is scarce or full-scale training is too costly". Yosinski et al. [14] proved that transfer learning can be used on models which have a small training dataset. The idea was to use an already trained network which would have learned certain key features on an another dataset. These features prove to be helpful and the validation accuracies attest to that. This approach could be exploited in our case where we use the ImageNet dataset and an ImageNet architecture for training the model up to the last layer. We freeze the weights learned by these layers, and then we replace the softmax layer.

D. ResNet

The ResNet architecture was developed by He et al. in 2015. This paper showed that deep residual networks can be trained to provide as good an accuracy as shallow networks of small depth. [15] The ResNet architecture comes with several variants. ResNet-18, ResNet-34, ResNet-50, ResNet-101, ResNet-152 etc. We will be using ResNet-50 for our model.

E. EfficientNet

EffiecientNet [16] was proposed by Mingxing Tan, Quoc V, they developed a new idea of scaling up CNN's by scaling all the dimensions of a CNN, ie. depth/width/resolution. They achieve State of the Art results on CIFAR-100 datasets while being comparatively faster and smaller than it's competitors. There are seven version in EfficientNet. We choose B3 for our model.

III. Related Work

Marios Anthimopoulos et al. [4], designed a novel network architecture that captures the low-level textural features of the lung tissue. The relatively slow training and slight fluctuations are the drawbacks of this Deep Learning Approach.

Trusculescu et al. [5], highlight the challenges, but also the implementation options that would lead to daily practice.Give description of various Architectures used in ILDs and their success and drawbacks. Provides an overview of parameter tuning.

Nalysnyk et al. [6], provide a statistical survey of the occurrence and widespread of IPF over USA, Japan and European countries has been presented.The authors concluded that diagnostic capabilities dominate over ecological or environmental factors.

Paras Lakhani and Bhaskaran Sundaram [7], analysed the efficiency of deep CNNs (DCNNs) for detecting tuberculosis (TB).Two DCNNs, AlexNet and GoogleNet, were used to classify images as having TB or healthy.

Sang Min Lee.,et al. [8], gave insights about the various applications of Deep learning and CNNs pertaining to chest related diseases.Deep learning technology particularly CNNs has the potential to automatically detect abnormalities or assist radiologists in reading chest radiographs.

Chenshuo Wang and XianXiang Chen [9], designed a FVC prediction model based on Support Vector Regression is developed which can obtain acceptable FVC values.The main drawback is that authors did not compare the performance of different machine learning techniques in predicting FVC values.

Sampurna Mandal et al. [10], used the OSIC dataset to predict FVC values. They used Multiple Regression techniques to predict FVC values, they also used a Laplace Log Likelihood for Confidence Score prediction. They used ElasticNet Regression, Quantile Regression. The drawback is that they don't give relative percentage values for each week.

Simon Walsh et al [11], investigated the use of a deep learning algorithm for provision of automated classification of

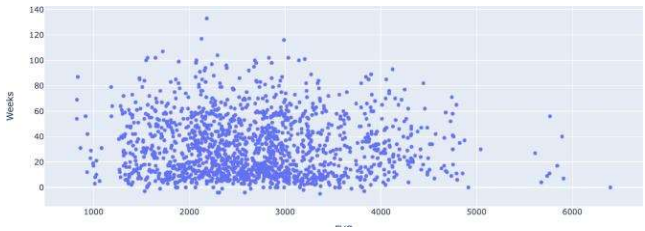


Fig. 1. A Graph representing the decline of FVC with respect to Weeks.

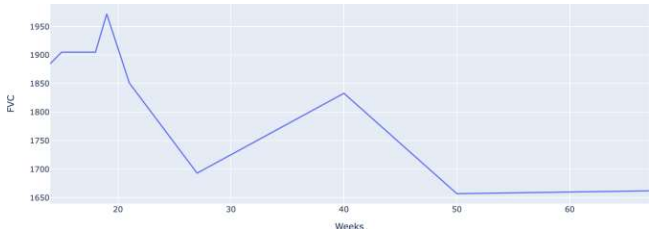


Fig. 2. A Graph representing the decline of FVC with respect to Weeks for a particular patient

fibrotic lung disease on high-resolution CT. In this case-cohort study, for algorithm development and testing, a database of 1157 anonymised high-resolution CT scans showing evidence of diffuse fibrotic lung disease was generated from two institutions. They separated the scans into three non-overlapping cohorts (training set, n=929; validation set, n=89; and test set A, n=139) and classified them using 2011 ATS/ERS/JRS/ALAT idiopathic pulmonary fibrosis diagnostic guidelines. For each scan, the lungs were segmented and resampled to create a maximum of 500 unique four slice combinations, which we converted into image montages. x

IV. Data

We used the Open Source Imaging Consortium (OSIC) dataset available on their website as well as the Kaggle challenge on the Dataset. Their are two components to the dataset: Tabular and Image. The tabular data contains the descriptive features of the Patient, this includes the Patient-ID, Age, Gender, Smoking Status, Week of FVC measurement and the FVC value for that week. There are several measurements for each patient, a unique row for each week. There are 1549 rows out of which 176 Patient-IDs are unique. The Image dataset consists of CT scans of the patient taken over the course of subsequent visits. There are 176 folders, a folder for each patient. On an average, there are 187 images per patient.

We perform basic Exploratory Analysis to understand the data better, and find interesting and insightful patterns from them.

We find the trends between the FVC and the other descriptive features of the Tabular Columns. We find the highest correlation between the Weeks and the FVC values. The correlation is negative indicating that as weeks progress the FVC values decrease.

In Fig. 1 we see an interesting trend, the higher FVC values tend to be concentrated near the earlier weeks, this could be of two reasons, one that there aren't many high FVC value counts within the dataset, two that the high FVC values tend to decrease over the period of time. Both of the reasons are true. We then find the trend of FVC values and Weeks with respect to one patient.

In Fig. 2. we see that the there is a general trend of decreasing FVC as the Weeks progress. The peaks in the graph show that the decrease in FVC is not continuous in nature. But a patient diagnosed with IPF will generally see a downward Trend.

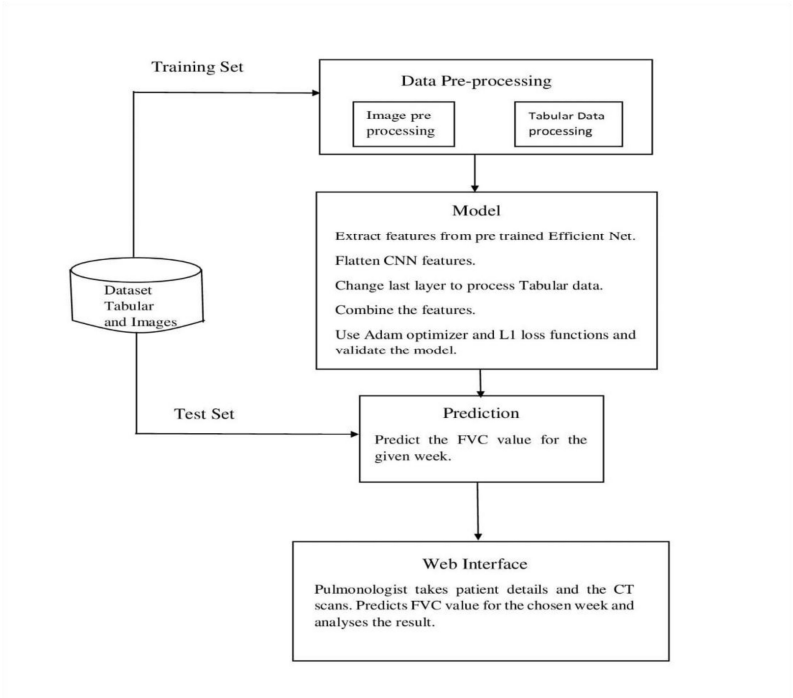


Fig. 3. Complete Architecture

V. Methodology

In this section we describe the entire methodology, from the preprocessing of the Image and Tabular data to the use of CNN and Dense Layers in the final FVC prediction.

In Fig. 3 we give an overview of the steps taken to take in the data and predict the FVC value for a given week.

The data as mentioned above is comprised of Tabular and Image Data. We split the Data into training and Testing Data. In the preprocessing stage we separately manipulate the Image and Tabular Data. The Images are transformed to a certain size keeping in mind the model stability.The Tabular data is checked for empty folders for Patient-IDs, these IDs are removed from the Dataset. The tabbular data is then aggregated with respect to each Patient-ID. We then encode the categorical values. We also normalize the numerical values.

In the model phase Fig. 4, We follow a hybrid approach of predicting the FVC values. We first aggregate the Data according to each patient. We then fit a Linear Regression model on the FVC as the dependent variable and the Weeks as the independent variable. We get the slope and the intercept for each Patient's equation. The slope of the equation is the target variable to be predicted. These values are calculated solely based on the tabular features.

To factor in the image features, we use a Convolutional Neural Network (CNN) for extraction of a fixed size feature vector. These vectors capture the semantic features of the image, which can then be used to discriminate between the different CT scans. The process of choosing one CT scan amongst the many CT scans in a folder is random. For the testing set we have used only one CT scan per patient to make the model more robust.

We use EfficientNet-b3 architecture to extract features from the CT scans. We first create a Convolutional Layer to make sure that the number of channels of the input to the Efficient-Net architecture is 3. We then use a pretrained Efficient-Net B3 model to extract 500 length 1-D feature vector. The choice of 500 was a heuristic one. Adam optimiser was used as the optimiser and L1 Loss function was the choice of Loss Function. ReLU was chosen as the activation function.

To extract the features from the Tabular Column we take in an input of 3 features: Age, Gender, Smoking Status. We then pass these features to a Dense Layer which outputs a 500 length feature vector. ReLU activation functions are used. We then finally input this vector to output a 250-length feature vector. The next step is to combine these features(Fig 4.). These features are then used to output a single value, the slope of the Linear Regression Equation for that patient.

The choice of using 250 length vector was to make sure that the number of features from a CT scan are predominant in final vector. Also, the distinctiveness in the tabular features are comparatively less apparent then the features in the CT scans. We hypothesise that subtle features in the CT scans can provide a great deal of discriminatory power to differentiate from the various CT scans. We tried a combination of values, and the best reduction in Loss was obtained with the combination 500,250.

The use of various ImageNet architectures and their results are explained in the Results Section.

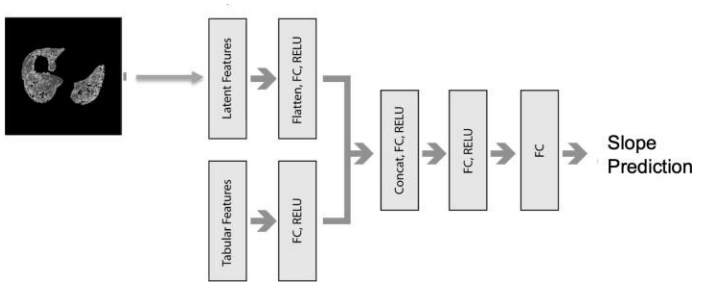


Fig. 4. The architecture used to predict the slope value for each patient

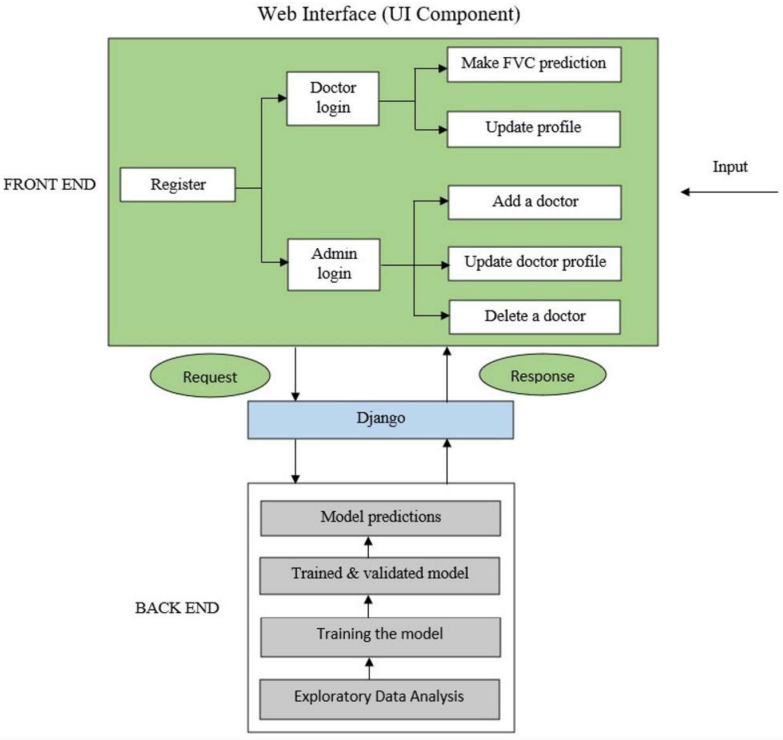


Fig. 5. Web Application Interface

VI. Web Application

In Fig. 5, we provide a pictorial overview of our web application interface. We use Django for our backend operations. The model takes the Image and Tabular Data inputs from the frontend and our model takes these characterstics to predict FVC values from Week -12 to Week 133. We use these ranges to make sure that the model predicts FVC Values effectively for a period of 2.5-3 years. The frontend interface consists of Register Module for Doctors/Pulmonologists and Admins. Admins control the website, and have special privileges. The Doctor can take the descriptive characteristics of a Patient (Fig 6). The input fields are the Gender, Age, baseline FVC, CT scan, Percentage Value and Smoking Status. There is an another input field which takes the week for FVC prediction. We display the FVC value for the chosen week and the percentage of the predicted FVC Value with respect to the ideal FVC Value for a person of similar characteristics (Fig 7).We also a provide a table of values with FVC values from Week -12 to Week 133 (Fig 8).

VII. Experimental Setup

We use the Pytorch library as the deep Learning Library and Google Colab for GPU. The specifications of the computer used for this experiment are as follows • Intel i5 processor • 20 GB RAM • Nvidia 2GB Graphics Card

We measure the mean percentage deviation of the FVC values from the actual FVC values on the Validation Data.

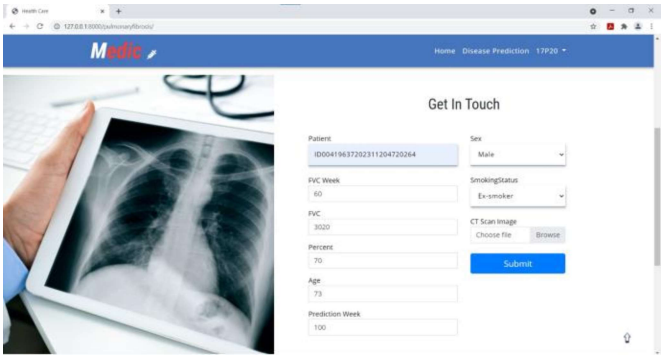


Fig. 6. Input Page

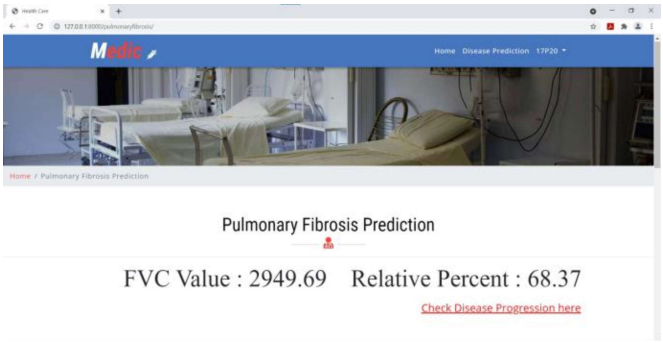
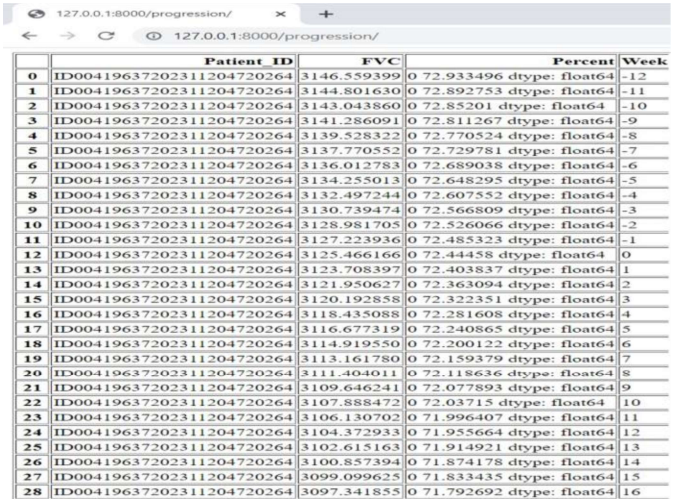


Fig. 7. Prediction Page



	Patient_ID	FVC	Percent	Week
0	ID00419637202311204720264	3146.559399	0 72.933496 dtype: float64	-12
1	ID00419637202311204720264	3144.801630	0 72.892753 dtype: float64	-11
2	ID00419637202311204720264	3143.043860	0 72.85201 dtype: float64	-10
3	ID00419637202311204720264	3141.286091	0 72.811267 dtype: float64	-9
4	ID00419637202311204720264	3139.528322	0 72.770524 dtype: float64	-8
5	ID00419637202311204720264	3137.770552	0 72.729781 dtype: float64	-7
6	ID00419637202311204720264	3136.012783	0 72.689038 dtype: float64	-6
7	ID00419637202311204720264	3134.255013	0 72.648295 dtype: float64	-5
8	ID00419637202311204720264	3132.497244	0 72.607552 dtype: float64	-4
9	ID00419637202311204720264	3130.739474	0 72.566809 dtype: float64	-3
10	ID00419637202311204720264	3128.981705	0 72.526066 dtype: float64	-2
11	ID00419637202311204720264	3127.223936	0 72.485323 dtype: float64	-1
12	ID00419637202311204720264	3125.466166	0 72.44458 dtype: float64	0
13	ID00419637202311204720264	3123.708397	0 72.403837 dtype: float64	1
14	ID00419637202311204720264	3121.950627	0 72.363094 dtype: float64	2
15	ID00419637202311204720264	3120.192858	0 72.322351 dtype: float64	3
16	ID00419637202311204720264	3118.435088	0 72.281608 dtype: float64	4
17	ID00419637202311204720264	3116.677319	0 72.240865 dtype: float64	5
18	ID00419637202311204720264	3114.919550	0 72.200122 dtype: float64	6
19	ID00419637202311204720264	3113.161780	0 72.159379 dtype: float64	7
20	ID00419637202311204720264	3111.404011	0 72.118636 dtype: float64	8
21	ID00419637202311204720264	3109.646241	0 72.077893 dtype: float64	9
22	ID00419637202311204720264	3107.888472	0 72.03715 dtype: float64	10
23	ID00419637202311204720264	3106.130702	0 71.996407 dtype: float64	11
24	ID00419637202311204720264	3104.372933	0 71.955664 dtype: float64	12
25	ID00419637202311204720264	3102.615163	0 71.914921 dtype: float64	13
26	ID00419637202311204720264	3100.857394	0 71.874178 dtype: float64	14
27	ID00419637202311204720264	3099.099625	0 71.833435 dtype: float64	15
28	ID00419637202311204720264	3097.341855	0 71.792692 dtype: float64	16

Fig. 8. Results Page

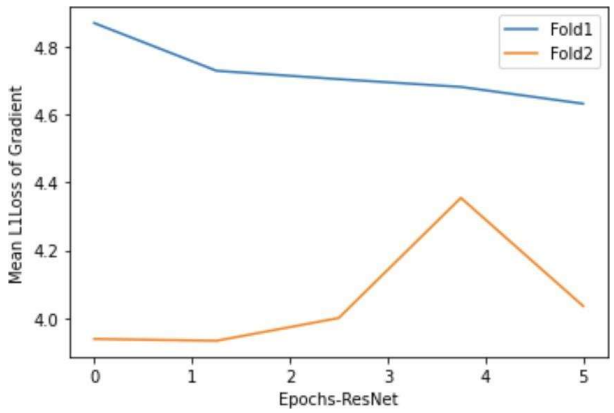


Fig. 9. ResNet-50 Epochs v/s Mean L1 Loss of Gradient

We also measure the L1 Loss of the Actual Slope and the Predicted Slope on the Training Data. The loss function used to optimise the training is the L1 Loss function. We also display the results of the Loss function as the training progresses. We compare the performances of two ImageNet architectures - EfficientNet-B3 and ResNet-50. We also experiment with the number of epochs, and the number of folds. We start from 5 epochs to 20 epochs/Fold. We try 2 folds and 3 folds.We used 2 folds and 5 epochs/Fold for the Web application.

We choose a learning rate of 1e-3 to start. Random initialisation of weights for the Neural Network. We use Adam optimiser and ReduceLROnPlateau as the scheduler. A ReduceLROnPlateau scheduler changes the learning rate when a metric plateaus after a certain number of epochs, here we initialise the number of epochs as 20.

VIII. Metrics and Results

A. Metrics

L1 Loss Function is used as the loss function which is used to penalise the predictions of the model. We use L1 Loss function as it's better than L2 loss function. L2 loss functions heavily penalises the outliers. The definition of L1 loss function is :

L1 Loss function is the sum of all the differences between the predicted value and the true value. We take the mean value of the L1 Loss for all the patients within the training dataset. L1 Loss function is defined as :

$$L1LossFunction = \sum_{i=1}^{n} |Y\,true - Y\,pred|$$

B. Results

We used EfficientNet-B3 and ResNet-50 for our experimentation. We see Fig. 9 and Fig. 10 the results for the two architectures. Although, ResNet-50 provides marginally better results compared to EfficientNet-B3, EfficientNet-B3 is faster than ResNet-50, by 1 minute. EfficientNet-B3 takes 2 minutes to complete the training, whereas ResNet-50 takes 3 minutes

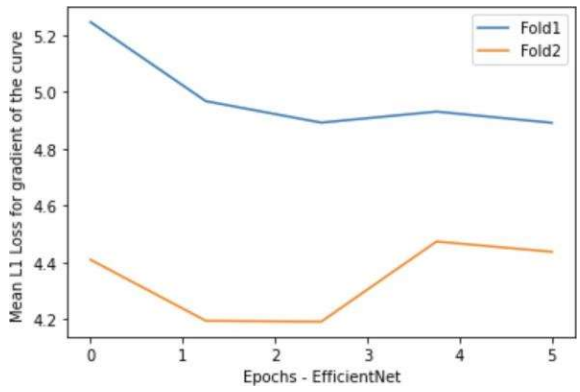


Fig. 10. Efficient Net-B3 Epochs v/s Mean L1 Loss of Gradient

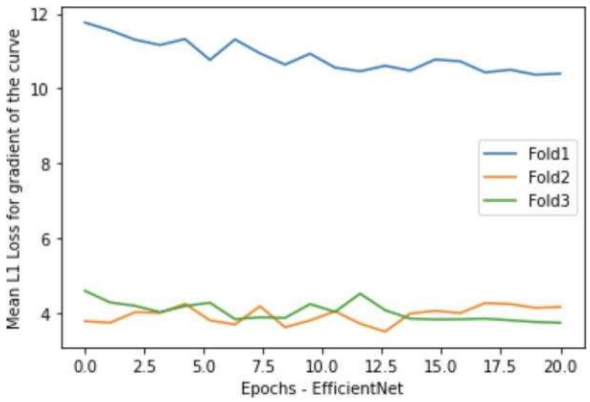


Fig. 12. EfficientNet-B3 Results with 20 epochs and 3 folds.

FOLDS	EPOCHS	LOSS
FOLD 0	1	4.6937647
	2	4.478111
	3	4.5925894
	4	4.6512218
	5	4.558476
FOLD 1	1	4.51825
	2	4.0460496
	3	4.3040376
	4	4.127783
	5	4.113472

Fig. 11. EfficientNet-B3 Results

to complete for 5 epochs and 2 folds. Fig. 11 displays the tabular version of EfficientNets Results.

In Fig 12. we see the graphical results of EfficentNet-B3 with 20 epochs and 3 folds. By taking 20 epochs and 3 folds the lowest loss we get is 3.647. With this model saved we run the model on our validation data consisting of 15 unique patients, we notice a 1% mean percentage difference between the Actual FVC measurement and predicted FVC measurement. With ResNet-50 we notice a 1.23% mean percentage difference between Actual FVC measurement and predicted FVC measurement.

IX. Conclusion

In this paper,we propose a method of combining CT scan images and Tabular Data features to predict the decline in Idiopathic Pulmonary Fibrosis using the Forced Vital Capacity (FVC) as the metric to assess the condition of the lung. We also design a web-based application which not only provides an interface for the Pulmonologist to input the data and get the results, but also provides results both for a chosen week and over a period of 145 weeks. Further scope lies in using much more descriptive features to accurately predict the prognosis and also providing Internet Of Things (IoT) solutions which can alert the patients on weeks when the decline in FVC start to pick up pace.

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