

A combined CNN-LSTM and LSTM-QRNN model for prediction of Idiopathic Pulmonary Fibrosis Progression using CT Scans and Clinical Data

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Abstract—Idiopathic Pulmonary Fibrosis (IPF), which causes scarred tissues and lung function damage over time, is a serious progressive lung disease. In addition, this chronic disease is irreversible, with unknown cures and unknown causes, so it is difficult to treat and becomes a challenge faced by doctors and others. Furthermore, Forced Vital Capacity (FVC) can assess the progression of lung function and it can assist to detect the disease in the early stage, so doctors have more time to give appropriate treatment and patients have more opportunities to increase survival time. Thus, the hybrid model convolutional neural network - long short-term memory (CNN-LSTM) and long short-term memory - quantile regression neural network (LSTM-QRNN) have been presented in this paper to predict FVC values by using CT scan images and clinical data. The experiment results show that the model also achieved the better modified Laplace Log Likelihood score in the private leaderboard in Kaggle OSIC¹ dataset.

Index Terms—Idiopathic Pulmonary Fibrosis, Forced Vital Capacity, CNN, LSTM, Quantile Regression Neural Network

I. INTRODUCTION

Idiopathic Pulmonary Fibrosis (IPF) is a chronic lung disease, and it occurs when the scarred or damaged tissues replace the healthy cells [1]. It leads to decreased pulmonary function and death for the patient. In addition, there are unknown cures and unknown causes, and the treatment is also limited. It depends on the progression of lung function decline to have treatment options for the individual patients. Forced Vital Capacity (FVC) can assess pulmonary progression, so it is utilized to analyze the survival of IPF [2] [3]. Thus, the prediction of pulmonary function decrease based on FVC values would help to detect IPF and other respiratory diseases in the early stage and have a chance to enhance the treatment options.

The Kaggle OSIC Pulmonary Fibrosis Progression challenge [4], which provides medical images and clinical data for IPF, has attracted a lot of teams to take part in and tackle the lung function decline issue by predicting FVC values. In addition, there are various approaches to estimating the pulmonary function decline using this dataset in recent years. For instance,

AI Nazi has proposed the Fibro-CoSANet in [5], this model utilized a stacked attention layer for the convolutional neural network to estimate the forced vital capacity (FVC) values throughout weeks. It achieved the high modified Laplace Log-Likelihood (mLLL) score of -6.68 in the public dataset, but the private score has not been reported yet because they could not do some pre-processing steps for a notebook to submit to the competition. In [6], the authors presented the Fibrosis-Net, which is a tailored deep convolutional neural network and machine-driven design. The Fibrosis-Net has achieved -6.8188 mLLL in the private score, which is calculated by the Kaggle system in the private dataset. Moreover, many other studies [7] [8] [9] [10] [11] are also interested in this issue. Quantile Regression and Elastic Net Regression are analyzed in [7] [12] while [9] using honeycombing and deep learning to get the prognosis of the lung disease. The web application using EfficientNet [13] for this issue is presented in [11]. Finally, the top 1st place on private leaderboard [4] (-6.8305) suggested the weighted ensemble between EfficientNetB5 [13] and Multiple quantile regression to forecast the FVC based on CT images and associated clinical metadata.

Inspired by the top 1st rankings approach and long short-term memory (LSTM) architecture [14], we propose the combined convolutional neural network - long short-term memory (CNN-LSTM) and long short-term memory - quantile regression neural network (LSTM-QRNN) to handle the lung function decline crisis based on CT scan and clinical data. Furthermore, the given CT scan is a stack of 2D slices and clinical data is time series, so our target is to take the advantage of LSTM to analyze the sequence data after convolutional neural network and handling time series data.

We summarize our main different contributions as follows:

- The hybrid CNN-LSTM model has used the integration of multiple 2D computed tomography (CT) slices and clinical metadata to predict the decline of pulmonary fibrosis. We utilize the pre-trained model such as EfficientNet [13] and fine-tune the hybrid CNN-LSTM model on the OSIC dataset.
- The uncertainty of forced vital capacity is forecast by the

¹<https://www.kaggle.com/competitions/osic-pulmonary-fibrosis-progression>

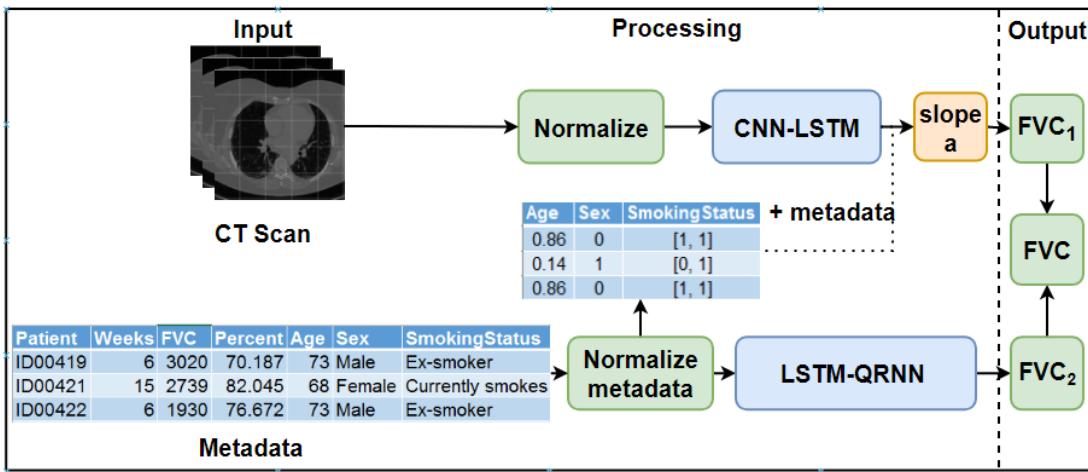


Fig. 1: The overall model for predicting FVC.

combined LSTM-QRNN network using smooth pinball loss [15].

- Enhancing the prediction result with the simple neural network as an ensemble model.
- The model is evaluated on the Kaggle OSIC Pulmonary Fibrosis Progression [4], and it achieves a greater score than the top 1st place on the private leaderboard.

The paper is organized as follows. The description of the methodology is in Section 3. Section 4 has presented our experiment results including data description, data pre-processing, evaluation metric, and comparison results. The conclusion of this work is in the last Section 4.

II. METHODOLOGY

In recent years, CNN has been a powerful tool for analysis of spatial data in computer vision, especially since it has also been applied to tackle a lot of medical image analysis in [16]. The main advantage of CNN is used to extract features from data, however, it has limited in handling the sequence data or time series. In contrast, Recurrent Neural Network (RNN) can tackle the temporal features better, and Long Short Term Memory [14] is an enhancement architecture of RNN. The main pros of LSTM are preventing vanishing and exploding gradients problems [17] by using a memory cell. Thus, combined the CNN-LSTM can get both advantages of these modules, and there are various approaches using hybrid mode in medical image processing such as in [18] [19] [20].

Motivated by the above architecture, the overview of fusion between CNN-LSTM and LSTM-QRNN model has been illustrated in Fig 1. It is a two-stream model: one is used to process CT scans and another is for metadata. After these models have done the process, the simple neural network will be used to fusion both model results. The input data includes a stack of CT slices and clinical information. In addition, the output is the prediction of FVC values throughout weeks in the future. Regarding the first model, the goal is to find out the trend between FVC and Weeks, and its tendency is denoted as slope a . The ground truth of the slope is calculated by clinical

metadata. The general approach formula top 1st [4] [5] [6] [9] is applied to this problem:

$$FVC_i = slope_a * Week_i + FVC_{input}, \quad (1)$$

where i is denoted the i th of the week, FVC_{input} is the first FVC value of the patient, and $slope_a$ is the coefficient of $Week$.

Fig 2 illustrates the structure of the first model. The module will take a stack 2D CT slice as input, then the images will be normalized by spline interpolated zoom (SIZ) [21] with fixed size $32 \times 128 \times 128$ for training and $N \times 128 \times 128$ for testing with N as the number of CT slices for each patient. Then, we will use a pre-trained CNN model such as EfficientNetB5 [13] on ImageNet [22] to extract features and fine-tune it on this dataset. The feature will be 2048 dimensional features, and the CNN model is wrapped in a time-distributed layer, so the output is a sequence of slice features with length N . The CNN performs well in study feature extraction, and the following sequence will be fed into LSTM with 256 hidden units. Following it, the fully connected layer with 1024 units combined the clinical metadata (4 units) to estimate the $slope_a$. Finally, we can calculate the FVC values based on Eq. 1 and the FVC_{input} which is provided in clinical information.

The uncertainty of FVC is also an important value for the prediction of pulmonary function decrease, so inspired by the Quantile Regression Neural Network (QRNN) using smooth pinball loss [15] and the advantages of LSTM in handling time series data. The combined LSTM-QRNN is proposed in the second model in Fig 3. The clinical metadata is the input of the model, and they will be normalized by min-max normalized [23] with range $[0,1]$ for Weeks, FVC, and Age while we use the dummy encoding to normalize the Sex and SmokingStatus pattern. Additionally, the medical data has been collected over the period of 1-2 years, and we have observed that there are some outlier data. Therefore, we have applied the quartile method [24] to detect outlier data, and we remove it when training the model. The normalized data is fed into LSTM layer with 16 units and with rectified linear hidden units (ReLUs) activation. Following the LSTM is a dense layer with 100 units, and the three quantiles (0.2, 0.5,

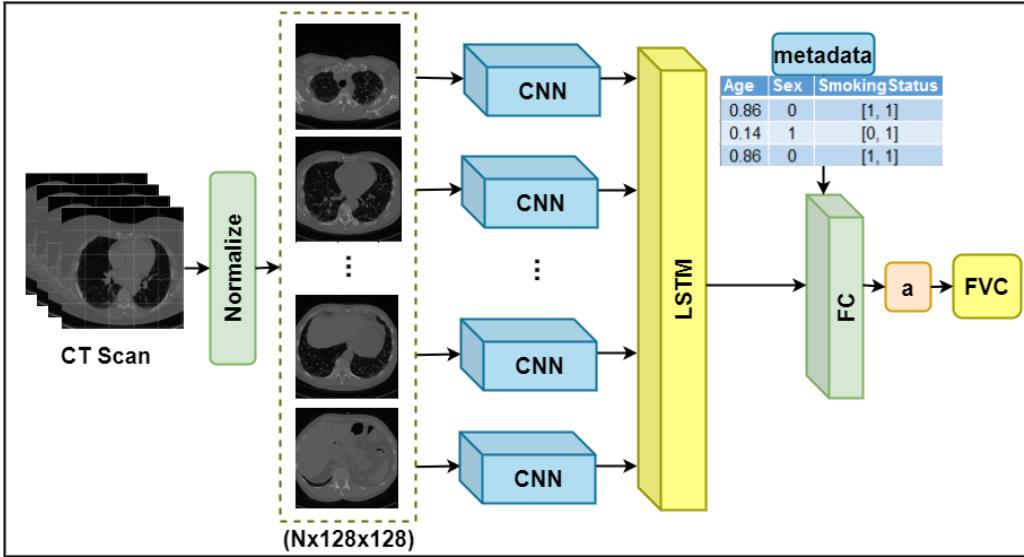


Fig. 2: The structure of CNN-LSTM model.

and 0.8) results will be the output. The main target of this model is to get the advantages of both LSTM and quantile regression, especially using smooth pinball loss function Eq. 2 in [15] [25].

$$S_{\tau,\alpha}(u) = \tau u + \alpha \log \left(1 + \exp \left(\frac{-u}{\alpha} \right) \right), \quad (2)$$

where τ is quantile [0,1] and $\alpha > 0$ is smooth parameter. Thus, the LSTM-QRNN using smooth pinball loss will optimize following this loss function [15] [25].

$$\min_{W,b} \frac{1}{N} \sum_1^N S_{\tau,u} (y_t - q_\tau^t), \quad (3)$$

where N is the training number in the example, y_t is the true value to evaluate the prediction, and $q_\tau^t = WX_t + b$ with W as weight and b is the bias parameter of the model, and X_t is the feature at time t.

Finally, we will use a simple neural network to fusion both models' results. The input dimension of model is two and a dense 200 units follows it with Adam Optimization algorithm [26], then the ensemble result is predicted.

III. EXPERIMENT RESULTS

In this section, the experiment results will be presented as follows: description of the dataset, data preprocessing, evaluation metric, and the comparison of our work in the private dataset. Additionally, our work has been implemented in the Kaggle notebook system.

- Tesla P100-PCIE 16280 MiB GPU.
- Disk Max 73.1 GB.
- Operating system Ubuntu 18.04.5 LTS.

A. Dataset

The publicly available dataset OSIC Pulmonary Fibrosis Progression Kaggle [4] is used in this article. The dataset provides a baseline chest CT scan and clinical metadata collected

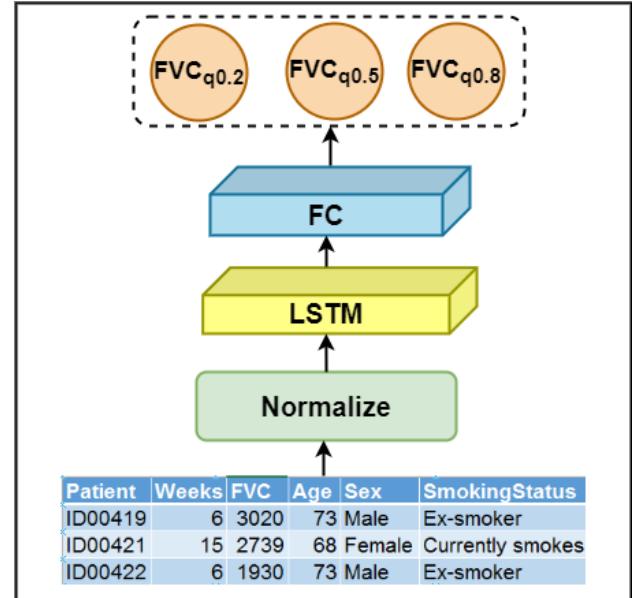


Fig. 3: The structure of LSTM-QRNN model.

from many follow-up visits over the course of around 1-2 years, for approximately 200 patients. The clinical metadata contains 1549 rows with 7 columns Patient, Weeks, FVC, Percent, Age, Sex, and SmokingStatus in the public dataset. There are 176 unique patient IDs in the train set, whilst the test set consists of around 5 patients in public data and approximately 24-28 patients in private data. The instances of CT slice and clinical metadata are presented in Fig 4 and Table I respectively.

B. Data Preprocessing

In this section, we will present how data is reprocessed before it is taken as input to the model. Normalization plays a vital role in the performance model.

TABLE I: The example of clinical metadata for a patient [4].

Patient	Weeks	FVC	Percent	Age	Sex	SmokingStatus
ID00426637202313170790466	0	2925	71.82497	73	Male	Never smoked
ID00426637202313170790466	7	2903	71.28475	73	Male	Never smoked
ID00426637202313170790466	9	2916	71.60397	73	Male	Never smoked
ID00426637202313170790466	11	2976	73.0773	73	Male	Never smoked
ID00426637202313170790466	13	2712	66.59464	73	Male	Never smoked
ID00426637202313170790466	19	2978	73.12641	73	Male	Never smoked
ID00426637202313170790466	31	2908	71.40752	73	Male	Never smoked
ID00426637202313170790466	43	2975	73.05275	73	Male	Never smoked
ID00426637202313170790466	59	2774	68.11708	73	Male	Never smoked

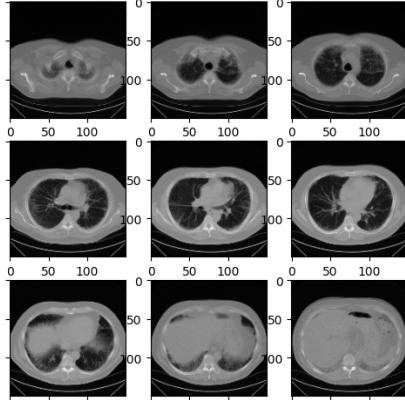


Fig. 4: The example of chest CT scan slices in the dataset [4].

Firstly, we will present how to normalize the CT slices which have formatted DICOM. Therefore, we have converted these to Hounsfield Unit (HU) following the Eq. 4 in [27]

$$HU = RescaleSlope * pixel + RescaleIntercept, \quad (4)$$

where RescaleSlope and RescaleIntercept are metadata in the CT slices.

After converting to the HU, we will normalize these values to the range [-1, 1] in Eq. 5 with the upper bound 1000 and lower bound -1000. The min-max normalization formulation [23]:

$$A' = \frac{A - \min_A}{\max_A - \min_A} * (D - C) + C, \quad (5)$$

where the boundary [D, C], A is original data, and A' is the new value after normalization.

After that, we will apply with or without zero centering for these images as $new_pixel = pixel - mean_pixel$ [28]. Then, the multiple CT slices will be resized to Nx128x128 using spline interpolated zoom (SIZ) [21].

Regarding clinical information, we apply the dummy encoding for the Sex and Smoking Status pattern, and the Min-Max normalization Eq. 5 with range [0, 1] is utilized for FVC, Week, and Age. We have observed that the performance of the model is better when removing the Percent field, so we decided to remove it from all our work.

In addition, we have also used the quartile method [24] to detect and remove the outlier data for the training model. And the example outlier data of FVC is illustrated in Fig. 5

$$lowerfence = q_1 - 1.5IQR, \quad (6)$$

$$upperfence = q_3 + 1.5IQR, \quad (7)$$

where $IQR = q_3 - q_1$ is interquartile range, and q_1 is 25th percentile and q_3 is 75th percentile.

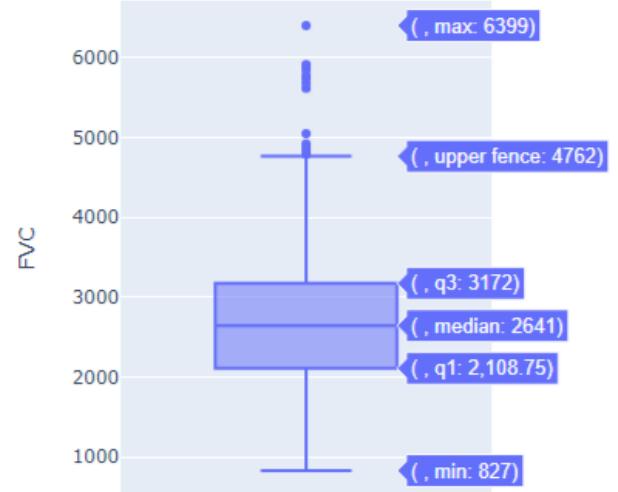


Fig. 5: The example of outlier data of FVC values.

C. Evaluation Metric

The modified Laplace Log-Likelihood (mLLL) is used in the competition OSIC Pulmonary Fibrosis Progression Kaggle [4], so it is also used in this study for evaluating the result of the model.

$$\sigma_{clipped} = \max(\sigma, 70), \quad (8)$$

$$\Delta = \min(|FVC_{true} - FVC_{predicted}|, 1000), \quad (9)$$

$$metric = -\frac{\sqrt{2}\Delta}{\sigma_{clipped}} - \ln(\sqrt{2}\sigma_{clipped}). \quad (10)$$

The threshold of metric is at 1000 ml to prevent adverse penalty results because of large errors. σ is the standard deviation (confidence measure), and the uncertainty of measurement in FVC is reflected by clipping σ at 70 ml. The average of the metric across the last three weeks is the final metric score. In addition, the value of the metric is always negative, so a higher score is better.

D. Training process

The training process of three main models will be presented in this session.

- **CNN-LSTM:** We have trained the model for 30 epochs with early stopping, reduce learning rate method, the batch size is two, the initial learning rate is 0.003, and using Stochastic gradient descent (SGD) optimizer. The main purpose of this model is to predict the trend of FVC value ($slope_a$), and the loss function is mean absolute error (MAE). In our experiences, we have applied two training approaches for it, and Table II has presented the validation score when training with MAE loss, mLLL, and Root mean square error (RMSE) for pre-trained EfficientNetB5.
 - Applying the top 1st training approach without cross-validation (CV).
 - Applying cross-validation (CV) with k-fold is 5.

TABLE II: Validation loss and metric CNN-LSTM

Method	MAE (loss)	mLLL	RMSE
CV	2.97236	-6.7991	196.54
Without CV	2.92029	-6.8053	104.57

- **LSTM-QRNN:** we have used the cross-validation with k-fold is 10, the batch size is 128 and the epoch is 800 to train and evaluate the model with loss function is smooth pinball loss Eq. 2. The final result will be the average result of folds.

TABLE III: Validation loss and metric LSTM-QRNN

Method	Smooth pinball loss	mLLL	RMSE
LSTM-QRNN	65.5741	-6.7094	244.18

- Simple ensemble model: we used the MAE loss with an epoch is 150 and batch size is 32 to train this model.

E. Results

To evaluate the performance of our module, we have used the private dataset in OSIC to get the private mLLL score. The grade will be calculated by the Kaggle system because they have not published the private data yet. Thus, we submitted our work to the competition. There are some scenarios that we used to evaluate the model.

1) Transfer learning and fine-tuning for CNN-LSTM:

Transfer learning (TL): as we mentioned in Section 2, we use the pre-trained model CNN EfficientNetB5 on ImageNet to extract features, and these features are fed into LSTM and concatenate with patient information such as Age, Sex, and Smoking Status to estimate slope a then FVC value.

Fine-tuning (FT): the pre-trained CNN weight is used and we re-train all layers on this dataset as mentioned in III-D. Table IV shows that the fine-tuning gives a significant score higher than if we just used the CNN to extract features, so we applied it for other pre-trained models.

TABLE IV: Comparison of mLLL in the private dataset OSIC [4].

Method	Private score (mLLL)
Transfer learning CNN-LSTM (B5) + LSTM-QRNN	-6.8308
Fine-tuning CNN-LSTM (B5) + LSTM-QRNN	-6.8098

2) *With and without cross-validation when training for CNN-LSTM:* From Table V, the training with CV has achieved greater scores without CV except for EfficientNetB5 and EfficientNetB1.

TABLE V: Comparison of with and without cross-validation when training CNN-LSTM.

Method	mLLL	mLLL(with CV)
FT CNN-LSTM (B5) + LSTM-QRNN	-6.8098	-6.8177
FT CNN-LSTM (B1) + LSTM-QRNN	-6.8156	-6.8163
FT CNN-LSTM (ResNet50) + LSTM-QRNN	-6.8226	-6.8215
FT CNN-LSTM (VGG16) + LSTM-QRNN	-6.8314	-6.8232
FT CNN-LSTM (B0) + LSTM-QRNN	-6.8628	-6.833

3) *CNN-LSTM, LSTM-QRNN, and fusion between CNN-LSTM and LSTM-QRNN:* We will evaluate three models separately to observe how their performances perform in the private dataset. Because the fine-tuning gives a better score, so we will use it for other experiments. Moreover, the result is summarized in the table below. From Table VI, we have

TABLE VI: Comparison of mLL scores CNN-LSTM, LSTM-QRNN and fusion both [4].

Method	Private score (mLLL)
CNN-LSTM Efficient-NetB5	-6.8209
LSTM-QRNN	-6.8658
CNN-LSTM + LSTM-QRNN	-6.8098

observed that the CNN-LSTM achieved a significantly higher score than LSTM-CNN, however, the score is enhanced when we combined the two models.

4) *With and Without Zero Center Normalization:* Table VII has shown that the model can achieve a better score when the CT scan images have been normalized with zero-center. Therefore, normalization plays an important role in enhancing the performance of the model.

TABLE VII: Comparison of with and without zero center normalization

Method	Private score (mLLL)
CNN-LSTM with zero center + LSTM-QRNN	-6.8098
CNN-LSTM without zero center + LSTM-QRNN	-6.8176

5) *Comparison of modified Laplace Log-Likelihood scores with other studies:* After evaluating our work on the above scenario, we will compare it with other studies. Because we have evaluated the model performance in the private dataset OSIC, and the result is depicted in Table VIII. We have observed that the proposed model exceeded the top 1st OSIC [4] and Fibrosis-Net [6] by 0.0207 and 0.009 respectively.

IV. CONCLUSION

In this paper, the fusion between hybrid models CNN-LSTM and LSTM-QRNN is presented to address the pulmonary function decline problem, and it achieved a better score in private score in Kaggle OSIC [4]. From our experience with this model, it has been observed that the combined model CNN-LSTM has achieved a higher score

TABLE VIII: Comparison of modified Laplace Log-Likelihood scores in the private dataset OSIC [4].

Method	Private score (mLLL)
Top 3rd place OSIC [4]	-6.8336
Top 2nd place OSIC [4]	-6.8311
Ours transfer learning CNN-LSTM + LSTM-QRNN	-6.8308
Top 1st place OSIC [4]	-6.8305
Ours fine-tuning CNN-LSTM	-6.8209
Fibrosis-Net [6]	-6.8188
Ours fine-tuning CNN-LSTM(B1) + LSTM-QRNN	-6.8156
Ours fine-tuning CNN-LSTM(B5) + LSTM-QRNN	-6.8098

when combining the clinical metadata of patients such as Sex, Smoking Status, and Age. Additionally, pulmonary fibrosis often occurs in elderly people from 50 years old [1], and it is also related to Smoking Status and Sex such as the number of male patients is greater than females. Therefore, when working on a medical crisis, we also investigated and collected the information, and analyzed the dataset carefully to have a suitable approach. From the experiment results, the model has got the greater mLLL score when CT slices have been applied to zero-center, so normalization is an important part. Moreover, the transfer learning and fine-tuning technical from pre-trained CNN models in ImageNet also helps to enhance the performance of models in the small dataset, especially medical data. Furthermore, when we utilized multiple CT slices to train the model, we can prevent missing temporal information among slices. The score of CNN-LSTM is significantly higher than LSTM-QRNN, and the fusion model CNN-LSTM and LSTM-QRNN has improved the result. Finally, machine learning plays an important role in healthcare, and it has supported both clinicians and patients to give predictions for the progression of this disease.

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