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Survival Time Prediction for Adenocarcinoma Lung Cancer based on Pathological Image Analysis

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요 약

Survival time analysis is one of the main methods used by the pathologist to prognosis for cancer patients. In this paper, we strive to estimate the individual survival time of Adenocarcinoma (ADC) lung cancer patients from pathological images by adopting the convolutional neural network called the SurvPatchV1 model. First, we extracted tissue patches from the whole-slide images (WSI) to deal with extremely large dimensions of WSI. Then the survival time of each patch is estimated through the SurvPatchV1 model. Finally, the individual survival time of each patient is computed. The proposed method is trained and tested on the subset of the NLST dataset for ADC lung cancer. The result demonstrates that our model can obtain all tissue information in lieu of only tumor information in a whole pathological image to estimate the individual survival time.

1. Introduction

Lung cancer is the leading cause of death from cancer, with about half of adenocarcinoma lung cancer cases (ADC). ADC starts in mucus-producing glandular cells of our body. Many organs have these glands, such as the breast, pancreas, lung, prostate, colon and etc. ADC can be more effectively proposed through sophisticated visual inspection of tumor pathology images based on several recognized morphological features such as tumor size or vascular invasion in lung ADC.

Digital pathology images or Whole-slide images (WSI) are often obtained with the extremely large size (e.g., 100000 x 100000 pixels) when compared with a natural image. Hence, they cannot be inputted to a CNN. Additionally, There is a lack of publicly-available databases of localized patch-level images annotated with a large range of Histological Tissue Type (HTT). As a result, computational pathology research is constrained to diagnosing specific diseases or classifying tissues from specific organs, and cannot be readily generalized to handle unexpected diseases and organs. Pixel-wise data annotation for medical images is highly time-consuming and requires domain experts.

Cancer type classification, nuclei detection and segmentation are a fundamental analytical step in virtually all pathology imaging studies and precision medicine [1][2][3][4][5][6]. Multiple CNN architecture such as VGG16, InceptionV3,

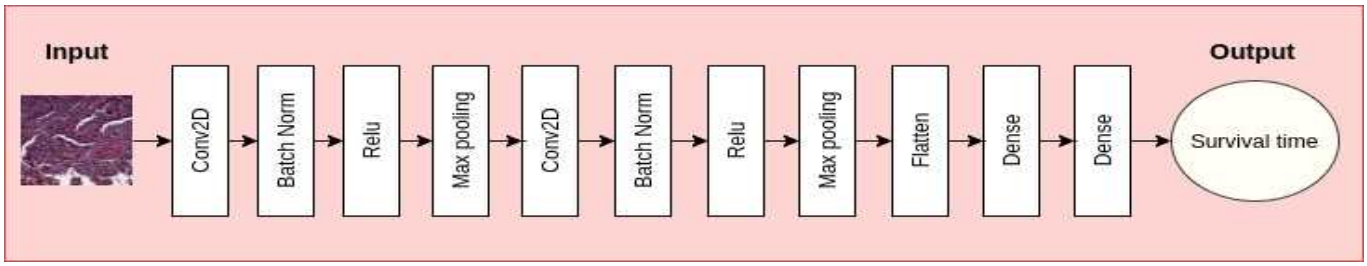

Figure 1 SurvPatchV1 model.

InceptionV2 and InceptionResNetV2 were trained and optimized to classify cancer types [7].

One of the main outcomes in the cancer studies domain is survival time or the time to an interesting event. Additionally, most survival analyses are based on the Cox model, log-rank test and Kaplan-Meier. However, these measurements focus on the survival probabilities for patients in the cancer trial.

In this study, we observed the time from the beginning of a screening period to the death event. This paper aims to introduce the basic concepts of survival time prediction from pathological images, including how to produce the individual survival time of a patient.

2. Method

To address the extremely large dimensions of pathology images, we extracted the whole slide image into smaller patches with size 128 ×128. Due to the noise patches such as the white patches, we sampled all the extracted patches to get the sampled patches. Next, we defined the CNN model to obtain all sampled patches.

Our CNN model called SurvPatchV1 model as in Fig. 1 is composed of 2 convolutional 2D layers followed by Batch Normalization and MaxPooling 2D respectively, and 2 fully connected layers to obtain the final result. Each convolution has kernel size 7 × 7. Each batchnormalization with moentum 0.7. It takes a 128 × 128 patch as an input, and output is the survival time of this patch.

3. Results

We employed the 5-fold cross validation to evaluate the proposed method. We also used 2 metrics: Mean Absolute Error as in (1) and Concordance Index as in (2) as the evaluation metrics. Even though lower MAE value the better performance, the higher CI value the better performance.

- Mean Absolute Error (MAE):

$$MAE = \frac{1}{n}\sum_{i=1}^{n}|x_i - x| \qquad (1)$$

- Concordance Index (CI) [8]:

$$CI = \frac{\sum_{i,j} 1_{T_j < T_i} \cdot 1_{N_j > N_i} \cdot \delta_j}{\sum_{i,j} 1_{T_j < T_i} \delta_j} \qquad (2)$$

Table 1 shows the performance metrics of our method and other methods in comparison. The DeepConvSurv was introduced in [11] for survival analysis with pathology images. However, they used extracted patches from tumor regions annotated under the help of pathologists and obtained the 62.9% CI. Meanwhile, we applied

Table 1. The survival time prediction results of three different methods.

Method	SurvPatchV1 (Ours)		InceptionV2		DeepConvSurv [9]	
Fold	MAE	C-Index	MAE	C-Index	MAE	C-Index
1	495.69	0.57	571.87	0.56	507.03	0.54
2	597.39	0.55	911.29	0.50	566.78	0.45
3	526.45	0.64	554.36	0.50	547.17	0.61
4	338.55	0.67	394.61	0.51	419.69	0.65
5	567.62	0.60	907.12	0.51	567.94	0.57
Mean	**505.14**	**0.65**	667.85	0.52	521.72	0.56

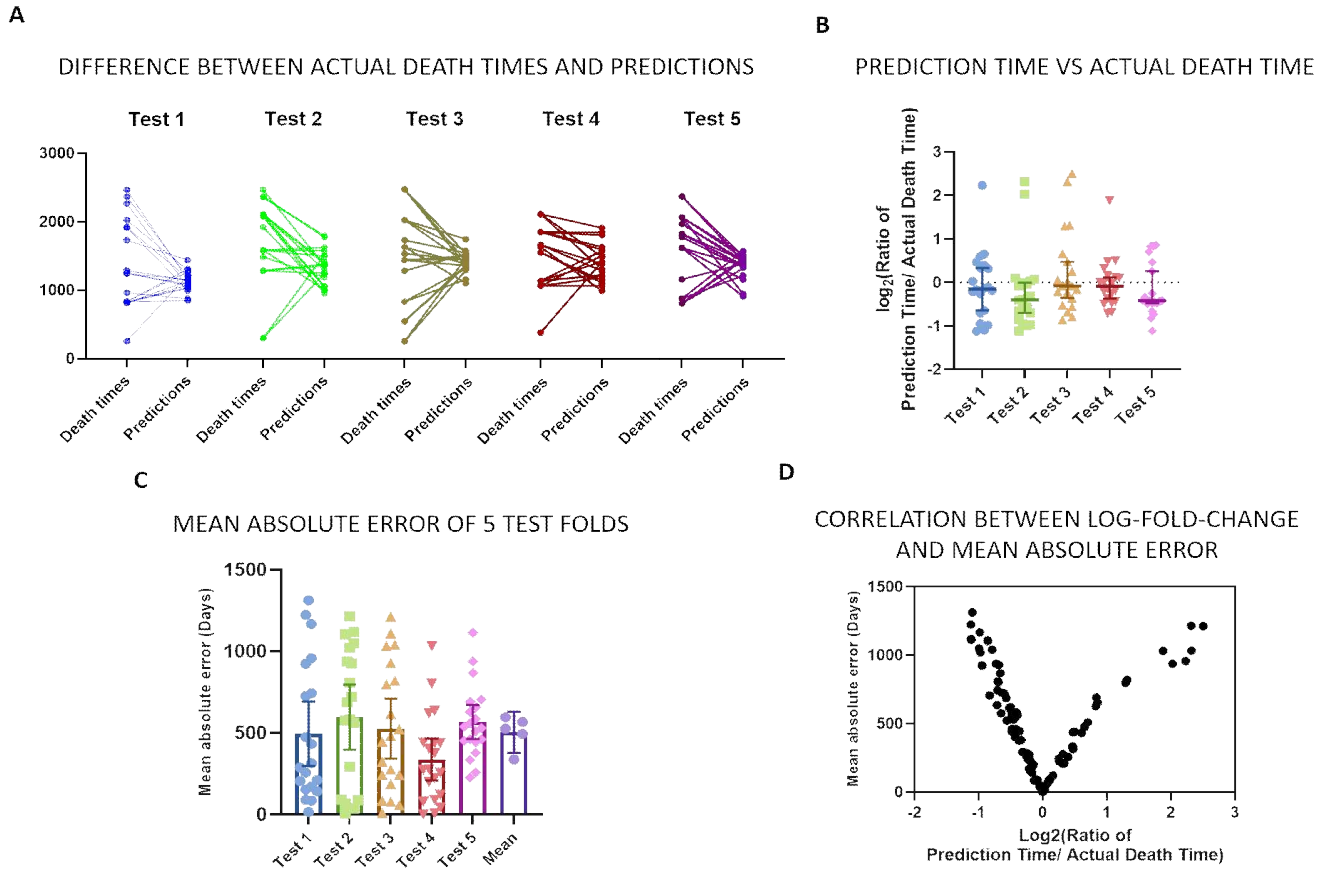

Figure 2. The result visualization of interdependencies of prediction time and actual time via the 5 test folds.

tumorous patches and non-tumorous patches into deep learning model and achieved 60.51%CI. In other words, our methods had significant performance in survival analysis. Besides that, we also attempted to apply the DeepConvSurv and InceptionV2 architecture to investigate the performance with the same input. Of the compared methods, our method (SurvPatchV1 model) produced best result (MAE = 505.14 and CI(%) = 60.51).

Fig. 2A showing the difference between the prediction time and actual death time of each patient in five independence tests. In more detail, Scatter plot (Fig. 2B) displaying the log-fold-change distribution of predicted values with true values. The patient with negative log fold change has a lower prediction time than their actual death time, and the patient with positive log fold change indicates that the predicted time is higher than the actual death time. Almost all the samples show the estimated value are lower than the actual value. In addition, the mean absolute error distribution of 5 test folds is visualized in Fig. 2C. We can also observe that our model is relatively stable with different test set. Fig. 2D showing the correlation between log-fold-change and mean absolute error of all test sets.

4. Conclusion

In this paper, we introduced the method for survival time prediction from ADC lung cancer pathological images. Our proposed method applied the entire tissue information on a pathological image instead of the only cancer tissue information. Besides that, we estimated the individual survival time based on the pathological image of a patient. In the future, we expect to improve the performance and extend our method on combining pathological images with clinical

data or CT images.

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