Data Analysis for Risk Prediction of Cervical Cancer Metastasis and Recurrence Based on DCNN-RF

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Abstract. In allusion to the problem of the low survival rate of cervical cancer metastasis and recurrence, combining the advantages of deep learning, a hybrid DCNN-RF method based on patched pathological images was proposed to predict the risk of metastasis and recurrence in cervical cancer patients. In order to improve the generalization ability of the model, according to the features, predicting result could be obtained from random forest, and the integration result was invoked as the result of haematoxylin and eosin pathological whole-slide images (WSI). The experimental results show that the model yielded an accuracy of 90.32% for prediction based on sliding window in cross-validation, and 0.83 AUC in the WSI.

Keywords: Recurrence and metastasis of cervical cancer; H&E pathological images; Convolution neural network; Random forest; Transfer learning.

1. Introduction
Cervical cancer is a high-incidence malignant tumour, the incidence of cancer in women is second only to breast cancer[1]. A large number of studies have shown that the nuclear morphological characteristics of haematoxylin & eosin (H&E) histopathological images are of great significance to the prognosis of various malignant tumours[2-4]. However, due to the complexity of pathological images, there are greater difficulties in manual judgment. With the continuous development of computer technology, the realization of computer-aided diagnosis and prognosis prediction based on H&E pathological images has always been the focus of researchers.

At present, researches based on pathological images at home and abroad are mainly divided into traditional machine learning and deep learning. In the field of traditional machine learning, the realized pathological image research, the main focus is on extracting artificially designed features from images, such as texture, space, and nuclear distribution, and then predicting the extracted features through traditional machine learning algorithms. In the early stage, Jafari-Khouzani et al.[5] acquired second-order texture features from the symbiotic matrix of H&E pathological images to predict prostate cancer recurrence.

This paper uses a DCNN-RF (Deep Convolutional Neural Network- Random Forest) method to predict the risk of metastasis and recurrence of cervical cancer in full-scale pathological images (WSI) of cervical cancer. The risk prediction model of postoperative metastasis and recurrence was constructed by using deep convolution neural network and random forest.

2. Deep Convolution Neural Network

2.1. Deep Convolution Network Model
Deep convolution neural network (MLP) is a multi-layer preceptor (MLP) designed for recognition of 2d or 3D signals and inspired by the visual neural mechanism, which mainly consists of convolution
2. Deep Convolution Network Model

The "extreme" Inception module is the basic module in Xception. As shown in Figure 2(b), it first uses 1×1 convolution to obtain cross-channel correlation, and then each output channel maps spatial correlation separately. Compared with Inception V3, Xception uses deep separable convolution to increase the network width, reduce the amount of parameters, and improve the accuracy.

![Figure 1. (a) Inception Module (b) Xception basic module.](image)

3. Prediction of Risk of Cervical Cancer Metastasis Recurrence

The model in this paper mainly includes three parts: image pre-processing, deep convolution neural network migration learning and random forest classification prediction. The model is shown in Fig 2:

![Figure 2. Model Flowchart.](image)

This paper uses Tensor flow deep learning architecture to fine-tune Xception networks:

1. Input the training image as the cervical cancer H&E image, and re-train all the layers after thawing block3_sepconv1;
2. The Adam optimizer is used to reduce the learning rate from 0.01 to 0.001, so that the weight of the model will not drop too fast. In addition, add early stopping to automatically stop training;
3. Change the default output 1000 classification in Xception to 2 classifications, so that the network only learns two types of output to correspond to the two results: High risk of metastasis and recurrence and low risk of metastasis and recurrence.

Perform transfer learning on the original Xception to obtain a deep convolution neural network that is more sensitive to cervical cancer H&E image features. The network can then be used to extract image features for prediction. The algorithm flow is as follows:

1. The feature vector obtained by Xception network training is used as the input of random forest;
(2) Use Bagging to randomly sample samples to generate n training data sets \( p_1, p_2, \ldots, p_n \);
(3) Establish a classification regression (CART) decision tree for each data set. CART decision tree uses Gini coefficient as its classification attribute. defined as:
(4) Among them, \( p_1, p_{k'} \) is the probability value of two samples randomly selected in the data set Q. Pruning the tree generated by the training set to avoid over-fitting the decision tree that is too complicated. This problem can be solved by pruning. Fix a certain empirical parameter \( \alpha (\alpha \geq 0) \), and perform pruning estimation on the nodes of the divided attributes, that is, judge whether to prune through the loss function of the decision tree. The loss function is as follows:
\[
C_{\alpha} (Q) = \sum_{i=1}^{k} N_i \cdot H(Q_i) + \alpha |Q|
\]
\( N_i \) represents the number of samples of the i category.
(5) Using the voting method, the category with the most output from all decision trees is used as the category of the test data set.

4. Experimental Results and Analysis

4.1. Experimental Data
In this study, the full-size H&E pathological image data set and prognostic tracking data of cervical cancer were downloaded from the TCGA(The Cancer Genome Atlas) public database. 46 cases were followed up as metastasis and recurrence, and 55 cases had good postoperative results. This paper randomly selects 60% as the training sample, 20% as the validation set, and 20% as the test sample.

4.2. Lab Environment
Experimental platform hardware configuration: Intel(R) Xeon(R) E5-2640 v4 @ 2.40GHz 10-core CPU, 64G DIMM 2400MHz memory, Matrox G200eR2 discrete graphics card, 64-bit Linux operating system. Software: anaconda3 as the development platform, and Google’s deep learning open source framework Tensor flow as the program framework.

4.3. Evaluation Index
In order to evaluate the prediction results of the model, this paper records recurrence and metastasis as positive samples, and non-recurrence and metastasis as negative samples. Use precision, recall, accuracy and AUC (Area under Curve) to evaluate the test set. Index definitions are shown in Table 1. The precision rate (the precision rate) represents the probability that the sample predicted to be a positive sample is a true positive sample, and is defined as follows:
\[
P = \frac{TP}{TP + FP}
\]
The recall rate (Recall) is also called recall rate, which represents the positive probability of being correctly predicted in the sample, which is defined as:
\[
R = \frac{TP}{TP + FN}
\]
Accuracy is the probability of being judged to be correct, defined as:
\[
acc = \frac{TP + TN}{TP + FN + FP + TN}
\]

| reality         | forecast result                  |
|-----------------|----------------------------------|
| Positive example| TP (True Positive example)        |
| Counter example | FP (False Positive example)       |
| Positive example| FN (False Negative example)       |
| Counter example | TN (True Negative example)        |

Table 1. Evaluation indicator definitions.
AUC (Area under Curve) represents the probability that a positive example is ranked in front of a negative example, and is used to evaluate the quality of the classifier. The larger the AUC value is, the more likely the current classification algorithm will rank the positive examples in front of the negative examples, that is, the better the classification effect. The formula is:

\[ AUC = \frac{\sum_{i=1}^{N} rank_i \times N + M}{M + N} \]

In that, \( i \) is the number of samples predicted to be positive, \( N \) is the number of negative samples, and \( M \) is the number of positive samples.

4.4. Experimental Results and Comparison

During training, for CNN (Convolutional Neural Network) feature extraction, the Xception network trains for 30 epochs, and the loss value no longer drops after 10 epochs and automatically stops training. For the random forest classifier, the CART algorithm is selected to construct the decision tree, and the grid search is used for parameter selection. In the test, the large image is randomly selected, and the trained model is input after pre-processing to obtain the probability of each image block, and then the majority voting algorithm is used to determine the category of the large image according to the probability.

For the image block-based DCNN-RF model, after 10-fold cross-validation, the accuracy rate is 90.32%, the precision rate is 89.42%, the recall rate is 86.45%, and the confusion matrix is shown in Table 2.

### Table 2. Confusion matrix.

| reality                  | Forecast results | Total |
|--------------------------|------------------|-------|
|                          | Recurrence and metastasis |       |
| Recurrence and metastasis| 2453             | 185   |
| No recurrence and metastasis| 245              | 1563  |
| Total                    | 2698             | 1748  |

In order to enhance the contrast of the experiment, other methods are selected for comparison under the same image block to test the performance of the model. The ROC (Receiver-Operating Characteristic) curve can compare the performance of different models. The vertical axis is "True Positive Rate", and the horizontal axis is "False Positive Rate". It is shown as in Figure 3.

It also uses RF as a classifier, and the Xception network with deep separable convolution has a higher AUC than the Inception v3 network. Using the same Xception model to extract features, RF has the best classification effect, and the accuracy is shown in Table 3. Compared with the ACC (Accuracy) of the SVM (Support Vector Machine) classifier which is 88.83%, the ACC of the RF classifier can reach 90.32%, and the ACC of the softmax is lower than the former two. Similarly, compared with the ACC of the Inception v3 network, the models that use the Xception network to extract features have a higher ACC. In summary, Xception+RF can get better results.

Use an independent test set for testing, randomly pick blocks of full-size H&E images, and integrate by majority voting algorithm to obtain an AUC of 0.96. The results show that the H&E pathological image analysis based on DCNN-RF can effectively predict the risk of cervical cancer metastasis and recurrence, and the results are better than other algorithms.
Table 3. Accuracy of different models.

| model                  | ACC     |
|------------------------|---------|
| Inception V3+RF        | 73.06%  |
| Xception               | 80.12%  |
| Xception+ SVM          | 88.83%  |
| Methods in this paper  | 90.32%  |

Figure 3. ROC curves of the model.

5. Conclusions
This paper proposes a DCNN-RF method to predict the risk of metastasis and recurrence of cervical cancer patients. This method combines the advantages of DCNN's automatic feature extraction and random forest. It automatically extracts the features of high-resolution cervical cancer pathological images through the convolution neural network based on Xception. Experimental results show that extracting the characteristics of cervical cancer pathological images can objectively and repeatable predict the risk of metastasis and recurrence of cervical cancer patients, and provide effective guidance for postoperative adjuvant treatment.

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