Research on Recognition of Medical Image Detection Based on Neural Network

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ABSTRACT Bowel cancer, which is easily affected by diet and drugs, has some restrictive factors such as the fecal occult blood test (FOBT) in the routine detection and the high cost and inconvenience of microscopy. In order to break through these restrictive factors, a possible alternative method of FOBT is sought. In this paper, error back propagation neural network (BPNN) algorithm is used, and expression spectrum is used as an auxiliary method to detect medical images, and a colorectal cancer (CRC) diagnosis model based on neural network is constructed. The results show that the accuracy of the model on the training set and the test set are 0.943 and 0.935, respectively, the AUC reaches more than 0.95. Therefore, the CRC diagnosis model based on neural network provides a possible alternative method of FOBT. Experimental results show that the proposed algorithm have high robustness and accuracy, which meets the current clinical needs.

INDEX TERMS Neural network, fecal occult blood detection, error back propagation neural network, medical image.

I. INTRODUCTION

CRC is a collective term of colon and rectal adenocarcinoma which has a high incidence worldwide, and whose mortality rate is the main cause of tumor death, CRC has higher heterogeneity compared with other tumors, and it can be divided into subtypes with different characteristics based on clinical or molecular characteristics [1]. The cause of CRC is more complicated, but it shows specific characteristics at the molecular level whether it is primary CRC (∼70%) or hereditary CRC (10-25%), including the genome Chromosomal instability (CIN) [2], loss of heterozygosity, and copy number variation. Now it has been shown that Epigenetic changes, such as island methylation, can drive adenomas to cancer in a sporadic and genetic form of CRC [3].

As the CRC develops slowly in precancerous lesions, it is usually in the middle and late stages of CRC when patients are aware of it, and this has a great impact on the prognosis of CRC, so early detection can reduce the incidence and mortality of CRC [4]. Considering the high diagnostic performance, the optical colonoscopy (OC) is the gold standard study for early detection of CRC [5]. It can be performed concurrently with biopsy specimens for a clear diagnosis, and at the same time as a therapeutic polypectomy, thus preventing long-term CRC death [6]. However, patients with tumor-related stenosis, older patients and those with comorbidities are more likely to have incomplete or difficult optical colonoscopy [7]. Haan et al. [8] found that CTC was comparable to colonoscopy in detecting larger colon polyps. Two meta-analytical studies have shown that carbon tetrachloride has an 87.9° high sensitivity (100%) for detecting colon cancer which is less than 10 mm for adenomas. Despite such encouraging data, there is currently no cross-continental consensus on whether CTC should be used as a screening method for asymptomatic patients. Detection based on genomic mutations [9], [10], although it provides great help for accurate diagnosis and targeted therapy of CRC, the high heterogeneity of CRC limits the use of this method. MRI [11] is the recommended method for initial stage, because its definition of localization determines the overall expansion of the tumor and its relationship with the peritoneal reflex as high accuracy. Dorudi et al. [12] growth
of cancer at home and abroad, and a complete theoretical system has not yet been formed. Now we will give a brief introduction of our achievements.

Prof. Cui et al. used syntactic pattern recognition to diagnose pancreatic cancer against the X-ray image of the pancreas [27]. Specifically, this method aims to diagnose pancreatic cancer (PC) and chronic pancreatitis (CP) [28]. The analysis of X-ray images based on endoscopic retrograde cholangiopancreatography uses pancreas morphological changes for identification. The pancreas with pancreatic cancer will expand or become narrowed appropriately, and cysts or spongy projections of the pancreaticobiliary ducts develop in the lateral branches [29], [30]. The pancreas with chronic pancreatitis is characterized by abnormal lateral branching of the catheter. Use attribute context-free grammar, enable rapid detection of pathological shape changes, and use syntactic pattern methods for identification and diagnosis. Based on pancreas MRI images, Jennifer A. Flexman obtained indexes of blood vessel size and blood volume fraction, which are used to evaluate the changes of tumor blood vessels in tumor staging. Specifically, the blood vessel size image and blood volume fraction metric in this model of human pancreatic cancer are used to represent the cross-sectional area of the tumor, and it is feasible to monitor the changes of blood vessels to determine the tumor stage [31], [32].

Zhijun Chen et al. proposed a subtle anomaly detection method based on CT pancreas images [33]. It is a simple cascade filter detection method. In the first step, the square of the gray level logarithm operation is introduced to improve the edge of the low gray level, and then the gray level is transferred to the deleted blurred area. Numerical operations to enhance the outline of detail [33], [34]. This algorithm has been tested, and the CT images of two tumor pancreas can be selected to indicate small abnormalities.

The international computer-aided diagnosis of pancreatic cancer has only started for more than ten years, and it is not very useful for reference in the exploration stage [35], [36]. Cai Zheyuan began to publish articles on texture extraction and classification of pancreatic endoscopy ultrasound images in 2008. For pancreatic endoscopy ultrasound images, 69 texture features were extracted using image processing-related algorithms, class feature spacing was used for initial feature selection, sequential forward search algorithm was used for further feature optimization, and finally support vector machine classification was used [37]. After testing, this algorithm is feasible and can be applied to the computer-aided diagnosis of pancreatic cancer endoscopic ultrasound images, to identify the presence or absence of pancreatic cancer, and to provide doctors with valuable reference opinions [38].

In theory, the imaging examination of any part of the human body can use computer-aided diagnosis to improve the accuracy of diagnosis. More mature research on computer-aided diagnosis of cancer is breast cancer, lung cancer and liver cancer. Applying computer-aided diagnosis technology to intestinal cancer is a relatively new topic both domestically and internationally, not only because of its concealed location, but also as a narrow and long tubular
TABLE 1. Sample information statistics.

| Platform       | GSE39582 | GSE41258 | GSE44076 | TCGA-COAD | TCGA-READ |
|----------------|----------|----------|----------|-----------|-----------|
| Tumor          | hgu133plus2 | hgu133a | hgu219   | 41        | 9         |
| Mucosa         | 0        | 0        | 50       | 0         | 0         |
| Normal         | 19       | 54       | 98       | 41        | 10        |
| Data Type      | tumor+adjacent | tumor+adjacent | cancer+healthy | tumor+adjacent | tumor+adjacent |

structure, and because of its complicated adjacent relationship and strong adhesion to other organs, which have brought great difficulties to the early diagnosis of intestinal cancer. Currently there is no general digital image processing method [39]. The purpose of this study is to find a universal, rapid and accurate method for the detection of intestinal cancer.

So far, no one has developed a universal and accurate method for intestinal cancer detection based on CT images. Therefore, it is necessary to comprehensively study the more mature liver segmentation and liver tumor detection methods, combined with digital image processing and pattern classification methods, to find a more suitable detection method for intestinal cancer. In general, the steps of bowel cancer detection include: pancreas segmentation, feature extraction and selection, and bowel cancer recognition [40]. A universal and rapid bowel cancer detection method can determine whether there is bowel cancer, and create objective and quantitative diagnostic indicators, which can improve the accuracy of early diagnosis of bowel cancer and improve the overall medical level.

III. ANALYTICAL METHOD

A. DATA SOURCE AND PREPROCESSING
CRC dataset we used was from TCGA (The Cancer Genome Atlas) and GEO (Gene Expression Omnibus). Firstly we use the GDC Data Transfer Tool to download the RNA seq data (read count) of colon adenocarcinoma (COAD) and rectal adenocarcinoma (READ) and the clinical data corresponding to the sample information from the TCGA database (https://portal.gdc.cancer.gov/). According to the COAD and READ information recorded by the TCGA, 41 pairs of COAD normal and tumor samples and 10 pairs of READ normal and tumor samples were obtained.

Then download the CRC gene expression profile data from the GEO database (https://www.ncbi.nlm.nih.gov/geo/), including GSE39582 (19 normal samples, 443 tumor samples), GSE41258 (54 normal samples, 186 tumor samples) and GSE44076 (98 normal samples, 50 mucosa samples, 98 tumor samples). In order to ensure the consistency of the differential expression analysis of different data sets, we downloaded the raw data of GSE39582, GSE41258, and GSE44076, respectively, and used the RMA (robust mean analysis) method for homogenization. The pre-processed sample information is shown in Table 1, and finally contains 1049 CRC samples for subsequent analysis.

B. DIFFERENTIALLY EXPRESSED GENE SCREENING
Differentially expressed gene analysis is mainly based on GSE39582 and GSE41258 data, because both are affymetrix platforms and the sample type is tissue. The limma (version 3.8) tool was used to identify differentially expressed genes (DEGs) in normalized and tumor samples of GSE39582 and GSE41258 after homogenization. Genes with fold change more than 2 times and FDR (BH adjusted P-value) < 0.05 were taken as DEGs. TCGA’s COAD and READ data are of the NGS type. The read count value of the transcript was analyzed by DESeq2, and the FDR < 0.05 DEGs threshold was also taken. Before the above differential expression analysis, the similarity of the samples was evaluated on the GEO and TCGA datasets, and the correlation coefficients between the samples were calculated. The results show that the tumor and normal samples from different sources have high internal consistency. Both the heatmap and volcano map expressed by DEGs were constructed using R software.

C. FUNCTIONAL ENRICHMENT ANALYSIS
We use clusterProfiler (version 3.8) package to perform DEA on the biological process (BP) of Gene Ontology (GO), cellular component (CC), molecular function (MF) and KEGG pathway enrichment analysis. Take q value < 0.05 as the threshold for significant enrichment. The dotplot of clusterProfiler displays the enrichment result.

D. PROTEIN INTERACTION ANALYSIS
Using the protein interaction (PPI) information provided by the STRING database (https://string-db.org/), we built a PPI network of DEGs, retaining PPI information with confidence score > 0.9, and using Cytoscape (version 3.7.1) Show PPI network. Hub gene analysis uses Cytoscape’s Network Analyzer plug-in for analysis, calculates the connectivity degree of each gene (node), and ranks genes according to the connectivity degree. For genes, which are significantly up-regulated and significantly down-regulated, construct the above network and take the degree respectively. The largest gene is determined as the hub gene, and finally 2 hub genes are obtained. The PPI network module analysis uses the MCODE tool and the parameters take the default value.
The GO and KEGG analysis of the genes in the module also use the clusterProfiler tool.

E. CONSTRUCTION OF A NEURAL NETWORK-BASED DIAGNOSTIC MODEL

Using the error back propagation neural network (BPNN) algorithm, we constructed a CRC diagnosis model based on hub genes. First, randomly divided the Normal (healthy), Mucosa, and CRC samples of the GSE44076 dataset, set seed = 12345, and divide the 246 samples into a training set and a testing set evenly. The main parameters of the BPNN algorithm are the learning rate, the lambda of the regular term coefficient, the number of hidden layers, and the number of neurons included in the hidden layer. In order to find the optimal parameters, a grid search method is used to evaluate the performance of the model under different parameter combinations. Since our target value is a categorical variable, the accuracy of the model prediction is used as the model’s judgment index. Accuracy is calculated as follows:

\[
\text{Accuracy} = \frac{(TP + TN)}{\text{Total}}
\]  

Finally, the model with the maximum training set and testing set accuracy (training set accuracy + testing set accuracy-1) is the optimal model. The model parameter learning rate = 0.006, lambda = 6e-04, hidden layer = 10 neurons. To avoid biasing the model by random grouping, we used the bootstrap method to calculate the accuracy of the training set and testing set of the model under 100 random samples.

F. STATISTICAL ANALYSIS

Statistical analyses were performed using R (version 3.5.2) software. Student t-test was used to test the significance of differences in gene expression levels of paired samples, and Wilcoxon rank test was used to perform a two-group significance test of gene expression levels of unpaired samples. The Kruskal-Wallis rank test was used for the significance test of two or more groups, and the FDR was calculated using the BH-method. In this study, unless otherwise specified, ** indicates p<1e-5, *** indicates p<0.01, and * indicates p<0.05.

IV. NUMERICAL SIMULATION

A. ANALYSIS PROCESS

In this study, the gene expression profile data of normal and tumor samples provided by the GSE39582 and GSE41258 datasets were first used to calculate the differentially expressed genes (DEGs) of the two using the limma tool. The DEGs common to both were used for subsequent verification. Using the TCGA’s COAD and READ data sets, we verified the identified DEGs to further determine the reliability of our DEGs. We then commented on the possible functions of DEGs, including participating biology processes (BP) and pathways. Analysis of protein interactions allows us to have a deeper understanding of changes in cellular pathways (signaling pathways, metabolic pathways) that may be involved in the transition from normal to tumor.

The principle of error back propagation neural network is as follows:

Suppose there are a neuron in the input layer, b neurons in the hidden layer, c neurons in the output layer, it is the connection weight of the \( i \)th neuron to the \( j \)th neuron, and the input vector of the input layer is \( I \). The input weighted sum of neurons in the input layer is:

\[
s_i = \sum_{a=1}^{a} X_i W_{ij}, \quad j = 1, 2, \ldots, b
\]  

Then its output is the function, and \( F \) is the excitation function, and then it is transmitted as the input to the hidden layer of the neural network. After the same change, one output of the neural network can be obtained.

Let the expected output vectors of the neural network are, and the actual output vectors. For the input sample, the error signal of the \( I \)th neuron in the output layer is:

\[
e_{ki} = D_{ki} - Y_{ki}
\]  

The total square error of the output layer is:

\[
E = \frac{1}{2} \sum_{j=1}^{c} e_j^2
\]  

In which, \( c \) is the number of neurons in the output layer. If the total number of input vectors is \( n \), the average value of the square error is:

\[
E_{avg} = \frac{1}{2} \cdot \frac{1}{n} \sum_{j=1}^{c} e_j^2 = \frac{1}{2n} \sum_{j=1}^{c} e_j^2
\]
B. (DGES) IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES

Using the limma tool, we analyzed the differentially expressed genes in the normal and tumor grouped samples in the GSE39582 and GSE41258 datasets, and obtained 1691 (up / down: 689/1002) and 414 (up/down: 111/303) differentially expressed genes. After removing genes with inconsistent expression patterns in the two sets of data sets, a total of 270 DEGs (up / down: 90/180) were obtained. The total DEGs accounted for 19.6% and 76.3% of the total DEGs, respectively. The large number of DEGs indicates that the occurrence of CRC involves more molecular-level changes. Further analysis of 270 common DEGs revealed that 90 genes were significantly up-regulated in the tumor group and 270 genes were significantly down-regulated in the tumor group, indicating that the activation and inhibition of certain biological processes may be involved in the transition from normal to tumor state of CRC.

C. DEGS FUNCTIONAL ANALYSIS

In order to further study the functions of these DEGs, we performed GO function annotation on 270 DEGs. Due to the significant difference in up- and down-regulated gene expression patterns, we analyzed the function of up- and down-regulated genes, respectively. We see that genes that are up-regulated in the tumor are mainly involved in biological processes related to the extracellular matrix and extracellular structure, while the genes that are down-regulated are involved in biological processes that are significantly different from up-regulated genes, mainly related to ion detoxification is related to stress response. Analysis of the KEGG pathway found that genes that were significantly up-regulated in the tumor were significantly enriched in the ECM-receptor interaction, focal adhesion, and PI3K-Akt signaling pathway, and these pathways are importantly related to tumor formation and progression. The down-regulated genes were significantly enriched in the pathways such as Fatty acid degradation, Glycolysis / Gluconeogenesis, which indicates that these genes involved in fatty acid and glucose metabolism are inhibited in tumor cells.

Figure 2 is identification of differentially expressed genes. The figure uses the limma tool to analyze the differentially expressed genes of the grouped samples of Tumor and Normal, and obtains 1,691 differentially expressed genes (up / down: 689/1002). Using the limma tool to analyze the differentially expressed genes of the grouped samples of Tumor and Normal, 414 differentially expressed genes (up / down: 111/303) were obtained. After removing genes with inconsistent expression patterns in the two data sets, a total of 270 DEGs were obtained. This shows that 90 genes were significantly up-regulated in the tumor group, and 270 genes were significantly down-regulated in the tumor group. This means that the activation and inhibition of certain biological processes may be involved in the transition from normal to tumor state of CRC.

Figure 3 is GO and KEGG annotation of differentially expressed genes (show top 10 categories). The figure shows that genes up-regulated in the tumor are mainly involved in biological processes related to extracellular matrix and extracellular structure. The biological processes involved in the down-regulated genes are significantly different from the up-regulated genes, mainly related to ion’s detoxification and stress response. KEGG pathway analysis found that genes that were significantly up-regulated in tumor were significantly enriched in ECM-receptor interaction, focal adhesion and PI3K-Akt signaling pathway. These pathways are important for tumor formation and progression. The down-regulated genes will be significantly enriched in fatty acid degradation, Glycolysis / Gluconeogenesis and other pathways. This indicates that these genes involved in fatty acid and glucose metabolism are inhibited in tumor cells.
D. DEGS INTERACTION NETWORK AND HUB GENE ANALYSIS

The 90 DEGs up and 180 DEGs down get 715 and 1089 PPI network edges, respectively. These edges have a confidence score > 0.9. Hub gene analysis found that the CCND1 and FOS genes had the highest degree of up-regulation and down-regulation in the DEGs network and were significantly higher than other genes (43/54). The module analysis can significantly divide the up-regulated DEGs network into 3 subclusters, which contain 25, 12, and 5 genes, respectively. Among them, subcluster1 is closely related to cancer occurrence, and the functions of subcluster2 and subcluster3 are unknown. The down-regulated DEGs network can be significantly divided into 5 sub-networks, among which subcluster1 is related to glycolysis / gluconeogenesis metabolism, subcluster2 is related to ion metabolism, subcluster3 is related to bile secretion, and subcluster4 is related to nitric biosynthesis process.

Figure 4 is analysis of Differentially Expressed Gene Interaction. The figure shows that the 90 DEGs upwardly adjusted and the 180 DEGs downwardly obtained 715 and 1089 PPI network edges respectively, and the confidence score of these edges is >0.9. Hub gene analysis found that the two genes CCND1 and FOS had the highest degree in the up and down-regulation DEGs network and were significantly higher than other genes (43/54). Module analysis can significantly divide the up-regulated DEGs network into three subnetworks (subcluster), which contain 25, 12, and 5 genes, of which subcluster1 is closely related to cancer occurrence, and the functions of subcluster2 and subcluster3 are unknown. The down-regulation of DEGs network can be divided into 5 sub-networks. Subcluster1 is related to glycolysis/glucconeogenesis metabolism, subcluster2 is related to ion metabolism, subcluster3 is related to bile secretion, and subcluster4 is related to nitric biosynthesis process.

E. DEGS EXPRESSION ANALYSIS IN INDEPENDENT VALIDATION SET

Using expression data of intestinal cancer (colon and rectal adenocarcinoma) provided by TCGA, we verified the expression of the 270 DEGs. Since TCGA’s CRC expression data is of RNA type, we used the read count values corresponding to these DEGs to compare the overall expression of up- and down-regulated genes on normal and tumor. It is significantly higher than normal, and the down-regulated genes are also significantly lower than normal on the tumor. These are highly consistent with our results based on the GEO chip expression data. Further testing the expression levels of each of the up- and down-regulated genes in tumor and normal, it was found that in COAD and READ samples, 99% (261/263) and 93% (244/263) of the gene expression were significant. The difference (FDR < 0.05, which further shows the reliability of the DEGs we identified.

Figure 5 is the expression of differentially expressed genes on the TCGA CRC dataset. The figure shows that in the COAD sample, the expression of up-regulated genes on the tumor is significantly higher than normal, and the down-regulated genes on the tumor are also significantly lower than normal. In the READ sample, the expression of...
up-regulated genes on the tumor is significantly higher than normal, while the down-regulated genes on the tumor are also significantly lower than normal. In the significance test, 99% (261/263) of gene expressions on COAD samples were significantly different. In the significance test, 93% (244/263) of the READ samples were significantly different in gene expression.

F. CONSTRUCTING A NEURAL NETWORK-BASED DIAGNOSTIC MODEL

The neural network model constructed based on the expression values of FOS and CCND1 of the two hub genes has an accuracy of > 0.9 on both the training set and the testing set, and the median accuracy of 100 random samples reached 0.943 and 0.927, respectively, indicating random grouping has less impact on our model. On the whole, the AUC predicted by the model for Normal (healthy), Mucosa, and CRC samples also exceeded 0.97, indicating that the prediction model based on the FOS and CCND1 genes has good performance. Furthermore, we compared the expression levels of the two genes in all samples, and there was no strong correlation between the expression levels of the two genes (cor = 0.16, p = 0.013). The expression levels of these two genes in Mucosa samples were significantly lower than those in Normal (healthy) and CRC samples (p < 1e-5), while the FOS gene expression in Normal (healthy) samples was significantly higher than that in CRC samples, and the expression characteristics of CCND1 gene were opposite. It is significantly higher than Normal on CRC.

Figure 6 is CRC diagnostic model based on FOS and CCND1 genes. The figure shows that the accuracy of the neural network model based on the expression values of the two hub genes FOS and CCND1 on the training set and testing set are both > 0.9, and the median accuracy of 100 random samples has reached 0.943 and 0.927, respectively. In other words, random grouping has less impact on our model. The AUC of the model training for Normal (healthy), Mucosa and CRC samples all exceeded 0.97. The model’s AUC for Normal (healthy), Mucosa and CRC samples also exceeded 0.97. The figure compares the expression levels of the two genes on all samples, and there is no strong correlation from the expression levels of the two (cor = 0.16, p = 0.013). The expression levels of these two genes in Mucosa samples are significantly lower than those of Normal (healthy) and CRC samples (p < 1e-5), while the expression of FOS genes in Normal (healthy) samples is significantly higher than that of CRC samples, and the expression characteristics of CCND1 genes are opposite. The CRC is significantly higher than Normal.

V. IN CONCLUSION

This study used the GSE39582 and GSE41258 data sets from GEO to identify a group of differentially expressed genes between normal and CRC. A total of 270 DEGs were obtained in two sets of data sets from different sources, 90 of which were in CRC samples. There are medium up-regulated genes and 180 down-regulated genes in CRC samples.

TCGA database’s CRC (colon adenocarcinoma + rectal adenocarcinoma) independent data set was used to verify 270 DEGs. Among them, more than 90% of the genes showed differential expression in normal and tumor samples. And the expression patterns of up- and down-regulated were also consistent. This shows that our DEGs filtered based on the GEO dataset are reliable.

The functional annotation of differentially expressed genes found that genes that are up-regulated in the tumor are mainly involved in biological processes related to the extracellular matrix and extracellular structure, while down-regulated genes are mainly related to the detoxification and stress response of ion. Pathway enrichment analysis shows that the pathways involved in up-regulated genes are mainly related to tumor formation and development, while the pathways involved in down-regulated genes are mainly related to fatty acid and sugar metabolism.

Analysis of the protein interaction network based on DEGs shows that the hub genes with a degree significantly higher than other genes: FOS and CCND1, where the FOS gene is the hub gene that down-regulates the DEGs network, and CCND1 is the hub gene that up-regulates the DEGs network. The module analysis of the interaction network divides the up- and down-regulated DEGs networks into 3 and 5 sub-networks, respectively. The functions of the sub-clusters are significantly different.

Using two hub genes: FOS and CCND1, we constructed a CRC diagnostic model based on the neural network algorithm. The accuracy of the model on the training set and the test set was 0.943 and 0.935, respectively, and the AUC reached above 0.95, reflecting our model has better performance.

FIGURE 6. CRC diagnostic model based on FOS and CCND1 genes. A: 100 times random training and test set accuracy distributions; B: Model ROC and AUC values of training set; C: Model ROC and AUC values of testing set; D: FOS and CCND1 genes were distributed on Normal (healthy), Mucosa and CRC samples.
[38] W. W, X. Xia, M. Wozniak, X. Fan, R. Damasevicius, and Y. Li, “Multi-sink distributed power control algorithm for cyber-physical-systems in coal mine tunnels,” *Comput. Netw.*, vol. 161, no. 1, pp. 210–219, Oct. 2019.
[39] R. Ma, L. Zhang, G. Li, D. Jiang, S. Xu, and D. Chen, “Grasping force prediction based on sEMG signals,” *Alexandria Eng. J.*, vol. 59, no. 3, pp. 1173–1185, 2020, doi: 10.1016/j.aej.2020.01.007.
[40] W. Wei, X. Fan, H. Song, X. Fan, and J. Yang, “Imperfect information dynamic stackelberg game based resource allocation using hidden Markov for cloud computing,” *IEEE Trans. Services Comput.*, vol. 11, no. 1, pp. 78–89, Jan. 2018.

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