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Recognition and prediction of leukemia with Artificial Neural Network (ANN)

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Abstract

Background: Leukemia is one of the mostcommon cancers in children, comprising more than a third of all childhood cancers. Newly affected patients in USA are estimated as 10100cases, and if these cases are diagnosed late or proper treatment is not applied, then it can be mortal. Because rapid and proper diagnosis of leukemia based on clinical or medicinal findings (without biopsy) is impossible, we decided to apply artificial neural network for rapid leukemia diagnosis. For this aim we used clinical and medical parameters taken from 131 patients of Sina hospital of Hamadan.

Methods: We carried out independent sample T-test with SPSS software for 38 parameters. With regard to the results of this analysis we selected 8 parameters that had lowest sig for ANN analysis (among parameters, whose sig were less than 0.05).

Selected parameters of 131 patients were applied for training network with Levenberg-Marquardt learning algorithm, with learning rate of 0.1.

Results: Performance of learning was 0.094. The Relationship between the output of trained network for test data and real results of test data was high and the area under ROC curve was 0.967.

Conclusions: With these results we can conclude that training process was done successfully and accurately. Therefore we can use artificial neural network for rapid and reliable leukemia recognition.

Keywords*:* ANN, artificial neural network, cancer, leukemia, prediction.

Introduction

Leukemia is the general term for four different types of blood cancers that each begin in a cell type in the bone marrow. The rate at which leukemia progresses, how the Leukemia cells replace the normal blood and bone marrow cells, and the treatment needed are different with each type of leukemia. Chronic leukemia usually progress slowly and account for slightly more new cases each year compared with acute leukemia [1,2].

The four major types of leukemia are: Acute Lymphoblastic Leukemia (ALL); Acute Myeloid Leukemia (AML); Chronic Lymphocytic Leukemia (CLL); Chronic Myeloid Leukemia (CML). The incidence of all leukemias is approximately 13 per 100000 people per year. Childhood leukemia has remained an important field of extensive etiologic, diagnostic, and therapeutic research since its diagnosis as a clinical entity over last century. It is one of the most common cancers in children, comprising more than one third of all childhood cancers. Studies from various countries have found an

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increasing incidence of childhood leukemia in recent decades [3-6].

When the bone marrow fails to produce enough normal blood elements, various symptoms arise. Because leukemic patients have very few normal white blood cells to fend off infections, they tend to get repeated infections and fever. Leukemia sufferers also have fewer numbers of normal red blood cells, which means there are not enough red blood cells to carry oxygen to the cells of tissues throughout the body. This condition is called anemia and causes patients to look pale as well as to feel weak and fatigued. Leukemia can also result in decrease platelets, which are responsible for blood clotting. This makes patients bruise and bleed easily, often in the form of nasal and gum bleedings and purple skin blotches. Routine blood tests, such as a complete blood count (CBC), often are the first laboratory finding in patients who has leukemia. Leukemia usually presents with too many white blood cells (WBC) in peripheral blood, too few red blood cells (RBC) and too few platelets. In addition, very immature white blood cells called blasts are observed in peripheral blood samples when examined under a microscope. Blasts are not normally found in circulating blood, and they do not work in the way that mature cells do. Their presence alone is strong enough evidence to diagnose leukemia. Bone marrow aspiration or a bone marrow biopsy is almost always done to confirm a diagnosis of leukemia [7-9].

In summary reliable diagnosis of leukemia needs many laboratories and clinical evidences along with typical features in bone marrow aspiration and biopsy. Since it takes more time to resolve many complications; hence for proper and rapid diagnosis of leukemia we used artificial neural network technique (ANN) which represented a machine learning tool that has turned out to be useful for complex pattern recognition problem [9-18, 21].

Methods

41 clinical and laboratory parameters of 131 patients (63 of them were cancerous and others non-cancerous) who had pathological results were selected from patients' documents from Sina hospital of Hamadan.

These are: age, gender, vomiting, nausea, hematocrit, W.B.C, ESR, infection, weight loss, M.C.H, M.C.H.C, Na^+, MCV, RDW, PT, SGOT, SGBT, creatinine, uric acid, bilirubin D, bilirubin T, LDH, fever, hemorrhage, lymphadenopathy, hepato and splenomegaly, hemoglobin, platelet and so forth.

Feature analysis: After primary statistical analysis, the two tailed student t-test was used to determine the statistical significance for the difference between the two groups of patients with and without Leukemia. Eight of 41 features which showed more significant difference between cancerous and noncancerous group were used as inputs for ANN analysis (statistical analysis was completed by SPSS-15 software)

These features were: gender, fever, hemorrhage, lymphadenopathy, massive liver and spleen, hematocrit, hemoglobin, and platelet.

Artificial Neural Network (ANN): Assembling and training of ANN was done by Matlab software r2007b. In order to train neural network, selected features were normalized; this normalization was necessary to prevent non-uniform learning, in which the weight associated with some features converge faster than others.

After normalization a randomly chosen sample was divided into training (80%), cross validation (10%) and testing datasets (10%). The training data set was presented to the network for learning. Cross-validation data set was used to measure the training performance during training or stop training if necessary. The testing data set was not used in any way during training and hence, provided an independent measure of training performance.

Multilayer perception model of the ANN was used. The network consists of an input layer, a hidden layer and an output layer. The input layer contained 8 neurons corresponding to eight input features; the hidden

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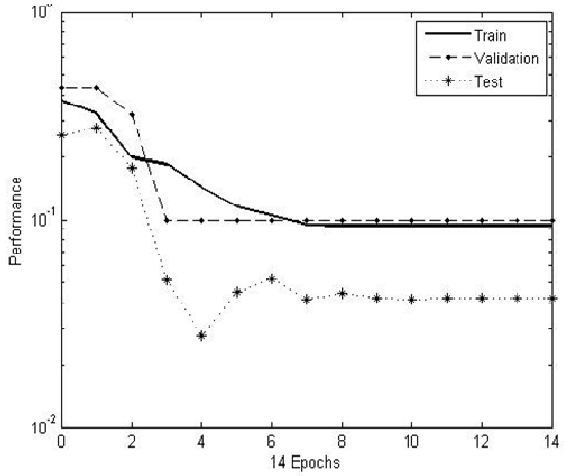


Fig. 1 - training plots of the assembled ANN
(The training error was minimized at around 14 epochs)

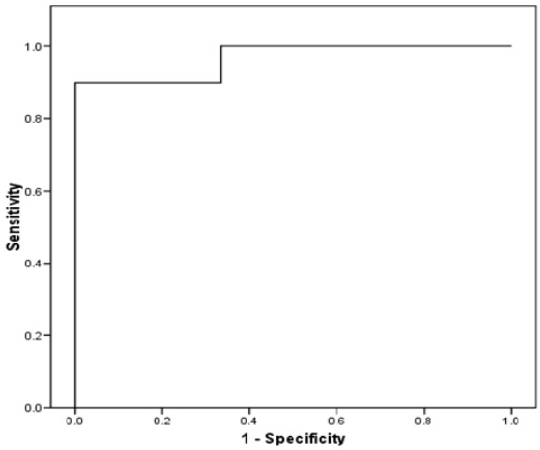


Fig. 2. Plot of sensitivity against (1-specificity).
(The area under ROC curve used to measure the accuracy of trained ANN results)

layer contained eight neurons transforming the input features from input layer to hidden layer. Finally, the output layer had only one neuron, representing two possible diagnosis states cancerous or noncancerous. Then the neural network was trained with the data on hand; learning function was LM (Levenberg-Marquardt back-propagation) and learning rate was 0.1.

Training neural network is essentially a non-linear least squares problem, and thus can be solved by a class of non-linear least squares algorithms. Among them, the Levenberg-Marquardt is a trust region based method with hyper-spherical trust region. This method works extremely well in practice, and is considered the most efficient algorithm for training median sized artificial neural networks.

Like Quasi-Newton methods, the Levenberg-Marquardt algorithm was designed to approach second order training speed without having to compute Hessian matrix. When the performance function has the form of a sum of squares then the Hessian matrix can be approximated as:

$$H = J^T J \qquad (1)$$

and the gradient can be computed as:

$$G = J^T e \qquad (2)$$

The Levenberg-Marquardt algorithm uses this approximation to the Hessian matrix in the following Newton-like update:

$$W_{K+1} = W_K - [J^T J + \mu I]^{-1} J^T e \qquad (3)$$

Results

The training process of the created neural network was performed with LM algorithm, the training process finished at around 14 epochs as seen in Fig. 1.

In order to evaluate the test outputs, the ROC (receiver operating characteristic) and regression analysis between real results and outputs of the trained neural network was performed. The ROC plot is merely the graph of points defined by sensitivity and (1 – specificity). Customarily, sensitivity takes the y axis and (1-specificity) takes the x axis. The sensitivity is how good the test is at picking out patients with sepsis. It is simply the True Positive Fraction (TPF). In other words, sensitivity gives us the proportion of cases picked out by the test, relative to all cases that actually have the disease. Specificity is the ability of the test to pick out patients who do not have the disease. It is simply the True Negative Fraction.

After plotting the ROC curve (Fig. 2) the area under ROC curve was measured to estimate the diagnostic performance; and area under roc curve for this analysis was 0.967.

We analysed relation between target value and output of trained neural network for test dataset statistically (Table 1); Phi coefficient

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Table 1. target value * Output of trained ANN cross-tabulation

		target value		Total
		Non-cancerous	cancerous	
Output of trained ANN	Non-cancerous	2	0	2
	cancerous	1	10	11
Total		3	10	13

(This table show the Relation between target value and output of trained neural network for test dataset)

value was 0.778 and its P value was 0.005.

Discussion

Recently ANNs have become popular in medical diagnosis. Although ANN architectures and training algorithms vary, they share one basic function: all networks accept a set of inputs and generate corresponding outputs. ANNs are particularly attractive for diagnostic problems without a linear solution.

Usually physicians analyze clinical and laboratory symptoms of blood cancer qualitatively and finally use bone marrow biopsies as a better procedure for assessing the nature of disease. Then accurate and reliable detection of cancer need more paraclinical tests and costs and take much time. In this research we apply simple and early clinical and assessment for proper detection of leukemia.

Therefore by using trained ANN we can predict cancer with least clinical and laboratory tests and without requirement of much time. Accuracy of the detection of cancer by the assembled artificial neural network was analyzed by roc and regression analysis. Outputs of trained ANN for testing data were used to plot ROC curve, area under ROC curve was 0.967. These results demonstrate high performance of ANN training. Phi coefficient between known results of testing data set and output of trained ANN was 0.778 with P value = 0.005. This coefficient illustrates a good relation between trained ANN output and real target for test data set including high performance of training of ANN also. In summery area under the ROC curve, performance of training and regression coefficient value, were all demonstrated the good learning process of ANN and accurate diagnosis of cancer.

In a similar research for stomach cancer, we noticed the same results (that was printed in WSEAS conference eBook).

Conclusion

In order to improve the performance of training process we must use large sample size (more patients). Finally we used the weight and bias matrix value of trained network and assembled ANN structure to program the software for quick and accurate detection of cancer quantitatively.

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