Performance Analysis of Artificial Neural Networks and Statistical Methods in Classification of Oral and Breast Cancer Stages

R.HariKumar, N.S.Vasanthi, M.Balasubramani

Abstract: Cancer staging can be divided into clinical and pathologic stage. In TNM (Tumor, Node, Metasis), prognostic tool have been identified and new methods for prognostic factors have been developed. This paper compares the classification accuracy of the TNM staging system along with that of Chi-Square Test, and Neural Networks. In this investigation, one hundred patients with breast cancer and One hundred twenty five oral cancer patients were studied. The data set using TNM variables (tumor size, number of positive regional nodes, distance metastasis, history of breast feeding, menstrual cycle, hereditary etc) of patients were used as input variables for both the classifications. When TNM classification and Chi-Square methods were compared, it was observed that Chi-Square classification closely followed that of clinical investigation. Artificial neural networks (MLP and RBF) are significantly more accurate than the TNM staging system when both use the TNM prognostic factors alone. New prognostic factors can be added to ANN to increase prognostic accuracy further

Index Terms: Oral Cancer stages, Breast Cancer, TNM stages, Chi-square test, neural networks.

I. INTRODUCTION

Oral cancer is one of the ten most frequent cancers worldwide [1]. The incidence of the tongue cancer seems to be increasing in the USA, and in Scotland where cancer in the rest of the mouth is likewise increasing. The clinician's dilemma is differentiating cancerous lesions from a multitude of other ill defined, controversial, and poorly understood lesions that also occur in the oral cavity. Most oral lesions are benign, but many have an appearance that may be easily confused with malignant lesions and some are now considered pre malignant because they have been statistically correlated with subsequently cancerous changes [2]. Conversely, some malignant lesions seen in an early stage may be mistaken for a benign change. Early carcinomas are probably asymptotic and subsequent manifestations are commonly misinterpreted because they mimic many benign lesions and the discomfort is minimal. Professional consultation is thus often delayed, increasing the chance for local spread and regional metastases. Emphasis must be placed on gaining access to high risk individuals for periodic oral examinations and educational efforts to increase the skill of primary health care providers in recognizing this problem. The most common malignant neoplasm of the oral cavity is squamous cell carcinoma, which accounts for 90% of the total number of malignant oral lesions. Therefore, the problem of oral cancer is primarily that of pathogenesis, diagnosis, and management of squamous cell carcinoma originating from oral muscular surface [4].

Oral tumor presenting with nodal metastases would appear to have a less favorable prognosis [3]. The effect of an elective neck dissection when there is no demonstrable disease is equivocal. The aim of this work was to retrospectively evaluate the clinical features, diagnosis, and treatment of oral cancer patients in Tamilnadu.

A. Statistics of Breast cancer

Cancer is a class of diseases in which a group of cells display uncontrolled growth and invasion and sometimes metastasis. Breast cancer is a type of cancer that starts in breast, usually in the inner lining of the milk ducts or lobules (Cancer Research, 1970; Abeloff et al., 2008;). The main indication of breast cancer is change in breast size or shape, swelling of lymph node and nipple discharge, pain in the nipple etc.(Merck manual of diagnosis and therapy, February-2003). Breast cancer includes several types like ductal carcinoma, lobular carcinoma, invasive ductal carcinoma, invasive lobular carcinoma, and inflammatory breast carcinoma (www.breastcancer.org; Devilee, 2003)[17]. There are four tumor classification values T1, T2, T3 or T4) which depend on the presence or absence of invasive cancer, the dimensions of the invasive cancer, and the presence or absence of invasion outside of the breast. The primary risk factors of breast cancer have been identified as sex, age, hormone, high fat diet, alcohol intake, environmental factor, and genetic abnormality (WHO-Cancer Research, December, 2007).

Breast cancer is second dominant cancer a many Indian women. Recent epidemiological survey indicates breast cancer patient of Tamil Nadu average is higher than the National average and Erode is even higher and every year one million cases are added to the list of cancer patients. According to WHO estimate, 85,000 women were affected by breast cancer in India during 2007 and over 86,500 women in 2008 (THE HINDU-20th March, 2009).

Breast cancer can be treated effectively with high cure rates if detected at an early stage, but, unfortunately, these patients are usually discovered at a point of advanced disease. Hence,

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there is an urgent need to develop strategies that can diagnose breast cancer at early stage. Most of the currently used strategies include either invasive tests like biopsy of specimens or expensive methodology like micro array. The invasive nature of a biopsy makes it unsuitable for cancer screening in high-risk populations and restricts widespread applicability. This suggests an imperative need for developing new noninvasive diagnostic tools and statistical paradigm that would improve early detection. Hence in the present study, it is proposed to develop a cost effective, simple, noninvasive strategy for detecting breast cancer at early stage using user statistical tools such as Chi square test and RBF neural network classifier.

Section 1 introduces the biological factors and social phenomenon for oral and breast cancer. Section 2, presents methodology for the classification of oral and breast cancer stages through Chi-square test. In section 3, neural network classifiers for (MLP &RBF) cancer is elucidated. In section 4, results from statistical test and Neural network classifiers are analyzed. The paper is concluded in section 5 with a note on research challenges in cancer detection and classification.

II. MATERIALS AND METHODS

The main objective of this research is depicted in the flow chart as in Fig.1. The flow chart shows that the clinical variables (Meta data) are converted into numerical values. Both the numerical values of breast and oral cancer cases are assigned for chi square test. The chi square test values are compared with TNM stages classifications. The classification of breast cancer stages are analyzed by Radial Basis neural network (RBF). Similarly Multi Layer Perceptron Neural network (MLP) is used to perform classification of cancer stages in oral cancer respectively. Both the chi square and neural networks results are compared with TNM clinical classification for more than 80% classification accuracy. If it is not the entire process will be repeated at once to obtain the better results.

This was a retrospective analysis of 125 patients with oral cancer and 100 cases with breast cancer that were referred to the Department of Oncology of GKNM Hospital Coimbatore and histo pathologically diagnosed in 2008. This study was based on the analysis of the hospital charts, referral letters, radiological studies, operative reports, pathological reports, and radiation therapy. The patients were analyzed according to the sex, age, histo pathologically type of tumor, site location, size of tumor, food habits, smoking, chewing of tobacco, and therapeutic approaches. Tumors were staged clinically according to the 1992 classification of the International Union against Cancer (UICC) [3]. Distribution by stage according to the UICC classification was as follows: 24 patients in stage I, 27 patients in Stage II, and 34 patients stage III, 15 patients are stage IV and 25 patients are used as controlled patients for classification validation. This section of the paper explains the classification of oral cancer and Breast cancer using the Chi- Square Test.
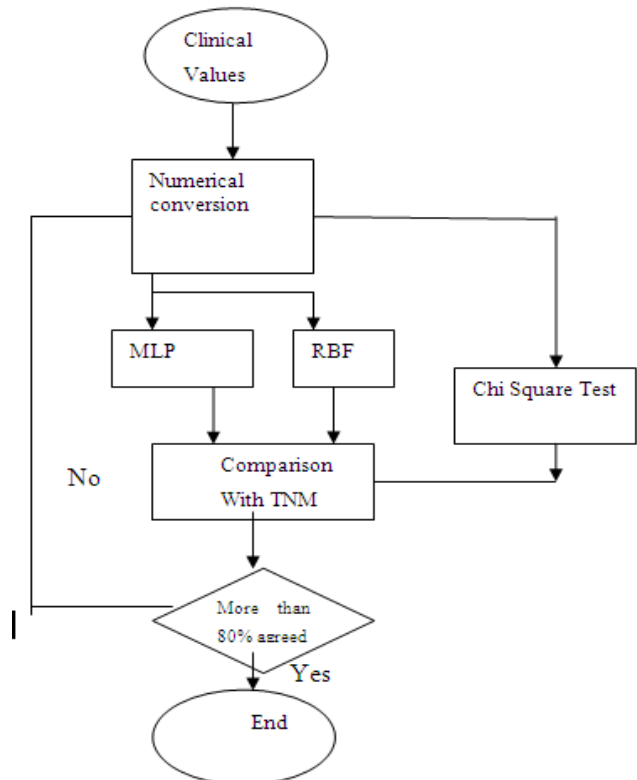
Figure.1 Flow chart for the Cancer stage Classification

A. The Chi- Square Test

The Chi- Square Test: A brief account of Chi-Square Test is given below [11]

i)Formulate the null hypothesis

H_0: The clustering procedure is random or inconsistent, select the significant level α.

ii) Compute the χ^2 value by

$$\chi^2 = \sum \frac{(f_0 - f_e)^2}{f_e} \qquad (1)$$

where f_o is the observed frequency and the f_e is the expected frequency.

iii) Look up the χ^2 distribution table. Reject the null hypothesis if $\chi^2 > \chi^2_{\alpha_0}$: df

where $\chi^2_{\alpha_0}$: df is the tabular value of significance level α_0 and degree of freedom df. The number of independent frequencies is the degree of freedom

The Chi square values were derived from the T tests and F tests conducted with the 26 variables on the 100 cases and the results are given in Table 1.

Table 1: Performance of Clinical and Chi-Square Test Classification for Breast Cancer Stages

Breast Cancer Stages	Chi-Square Test		
	Minimal Value	Maximal Value	Average
T1	3.84	19.52	11.7

T2	21.2	32.96	26.9
T3	30.72	40.85	35.5
T4	41.92	90.08	66

The Chi square values were derived from the T tests and F tests conducted with the 26 variables on the 100 cases and the results are given in Table 1. Analysis of chi square values was designed to evaluate various tumor stages of breast cancer in Coimbatore region. The predictive result of T1 stage is 3.84 – 19.52, is a first prognosis stage of Tumor1. It also shows T4 stage values varies from 41.92-90.08, which is an invasive stage of breast cancer. The classification efficiency of Chi-Square test was compared with the clinical data. It was observed that Chi-Square test closely followed the clinical classifications. Therefore, this method can be used as an early procedure for classification of cancer stages. Studies involving the application of artificial neural network, a user friendly bioinformatics tool, for further decision making of tumor stages of breast cancer and oral cancer are explained as below. Table 2 shows the chi-square value for 125 patients with oral cancer with 26 variables.

Table 2: Performance of Clinical and Chi-Square Test Classification for Oral Cancer Stages

Oral Cancer Stages	Chi-Square Test		
	Minimal Value	**Maximal Value**	**Average**
T1	5.62	21.4	13.8
T2	18.5	36.78	28.4
T3	28.2	45.65	34.7
T4	40.2	78.8	72.3

Analysis of chi square values was designed to evaluate various tumor stages of oral cancer in Coimbatore region.From the table 2, it is observed that Cancer stage 3 and 4 are clearly identified by the chi-square values. But there is a significant overlap in the classification region for the stages 1 and 2. A neural network can be used to break the overlap regions into distinguished stages. The role of neural networks for classification of cancer is discussed in the following section of the paper.

III ROLE OF NEURAL NETWORK FOR CLASSIFICATION OF CANCER

Artificial Neural Network (ANN's) is a powerful tool in pattern recognition problems. Specifically, they are useful for automating diagnostic tasks carried out by experts (supervised classification tasks) [12]. The ANN's capability of learning from examples eases this knowledge acquisition problem [16]. On the other hand, the ANN gives opaque knowledge representation. `Guoqiang (2000)[12]and Jonathan lee etal(1990)[14] listed out the advantages of the neural networks in the following theoretical aspects [15],[13].First, neural networks are data driven self-adaptive methods in that they can adjust themselves to the data without any explicit specification of functional or distributional form for the underlying model. Second, they

are universal functional approximators in that neural networks can approximate any function with arbitrary accuracy. Third, neural networks are a nonlinear model, which makes them flexible in modeling real world complex relationships. Finally, neural networks are able to estimate the posterior probabilities, which provide the basis for establishing classification and performance. The MLP & RBF neural networks are discussed in the following section of the paper.

A. Multi layer Perceptrons (MLP) Neural Network for classification of Oral Cancer Stages

Multilayer perceptrons (MLPs) are feed forward neural networks trained with the standard back propagation algorithm. They are supervised networks so they required a desired response to be trained [9]. They learn how to transform input data into a desired response, so they are widely used for pattern classification [6]. Most NN applications involve MLPs. They are very powerful pattern classifiers. With one or two hidden layers they can approximate virtually any input-output map. They have been shown to approximate the performance of optimal statistical classifiers in difficult problems. They can efficiently use the information contained in the input data. The advantage of using this network resides in its simplicity and the fact that it is well suited for online implementation [7].

The Levenberg-Marquardt (LM) algorithm is the standard training method for minimization of MSE (Mean Square Error) criteria, due to its rapid convergence properties and robustness. It provides a fast convergence, it is robust and simple to implement, and it is not necessary for the user to initialize any strange design parameters. It out performs simple gradient descent and other conjugate gradient methods in a wide variety of problems. The LM algorithm is first shown to be a blend of vanilla gradient descent and Gaussian Newton iteration. This error back propagation algorithm is used to calculate the weights updates in each layer of the network. The LM update rule is given as [8]

$$\Delta W = \left(J^T J + \mu\right)^{-1} J^T e \qquad (2)$$

Where J is Jacobian matrix of derivatives of each error to each weighted µ is a scalar, and e is error vector. If scalar µ is very large, the above method approximates gradient –descent. While if it is small the above expression becomes Gauss-Newton method. Because the GN method is faster but tends to less accurate near an error minima. The scalar µ is adjusted just like adaptive learning rate used by *trainbpx*. As long as the error gets smaller, µ is made smaller.
Training continues until the error goal is met, the minimum error gradient occurs, the maximum value of µ occurs or the maximum number of epochs has finished [9].

1 Training and Testing Procedures for the Selection of Optimal Architecture

The primary aim of developing an ANN is to generalize the features (there are 24 inputs are given in the input nodes of

the neural networks) of the processed outputs. We have applied different architectures of MLP networks for optimization. The weights between input layer, the hidden layer and output layer network are trained with error back propagation algorithm to minimize the square output error to zero. The simulations were realized by Neural Simulator 4.0 of Matlab v.7.0 [10]. As the number of hidden units is gradually increased from its initial value, the minimum MSE on the testing set begins to decrease. The optimal number of hidden units is that number for which the lowest MSE is achieved. If the number of hidden units is increased beyond this performance does not improve and soon begins to deteriorate as the complexity of the neural network model is increased beyond that which is required for the problem. The training procedure for MLP Neural network is shown in the figure.2.

Neural networks have been touted as having excellent potential for improving classification accuracy in patient specific diagnostic data. However, there have been few studies which have demonstrated these potential using real data sets [5]. The appeal of neural networks as pattern recognition systems is based upon several considerations. First, neural networks appear to perform as well or better than other techniques, and require no assumptions about the explicit parametric nature of distributions of the pattern data to be classified. In this regard they are similar to K-nearest neighbor algorithms. However, neural networks, once trained, are computationally more efficient.
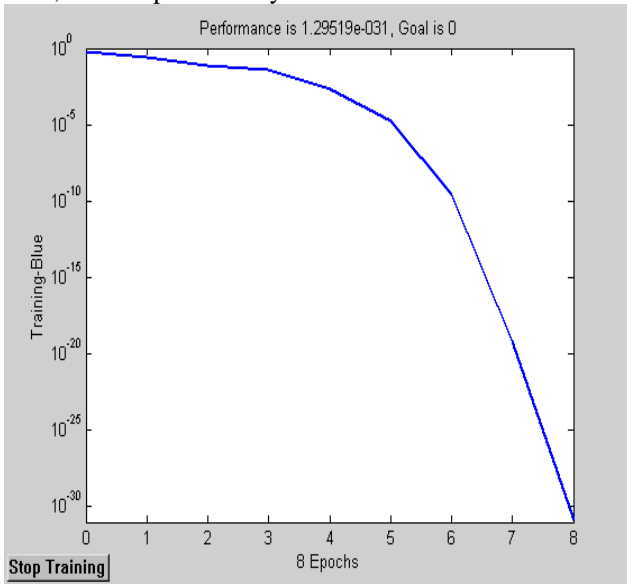
Figure. 2. Training of MLP Feed forward Neural Network (24-12-4)

Performance of various training algorithms in 24-12-4 MLP Architecture is shown in table.3. LM method required less amount of training time to achieve the target than its counterpart. Therefore LM training algorithm was selected

Table. 3 Performance of Various Training Algorithms in 24-12-4 MLP Architecture

S.no	Training Algorithm	Training Epochs	Mean Square Error(MSE) Index
1	Levenberg-Marquardt (LM)	**8**	**1.157 E-06**
2	Gradient Descent Back Propagation (GD)	179	1.262 E-06

| 3 | Gradient Descent with Momentum Back Propagation (GDM) | 951 | 3.60E-06 |
| 4 | Gradient Descent with Adaptive learning Rate Back Propagation (GDA) | 200 | 2.53E-06 |

The results of the MLP back propagation neural models trained with the Levenberg-Marquardt (LM) learning algorithm are shown in table 4. The gain or learning rate η (0.3), momentum α (0.5), and training epochs are tabulated for each architecture [8].

Table 4 Estimation of MSE in Various MLP Network Architectures

Architecture	Training Epochs	Mean Square Error (MSE) Index	
		Training	Testing
24-12-4	**38**	**0**	**7.31E-03**
16-3-1	6	0	2.19E-02
8/8/2001	283	0	9.13E-03
8/4/2001	6	0	5.10E-02
4/4/2001	**9**	**0**	**2.83E-08**
4/4/2004	12	0	7.74E-03
2/2/2002	3820	3.00E-08	3.7 E-08
2/4/2002	**8**	**0**	**0**
1/1/2001	4538	1.08E-08	1.20E-08

In the MLP networks testing procedures MSE index and number of epochs used for training are inversely proportional to each other. Therefore a compromise between them was achieved by taking into the consideration of larger training cost will ruin the system even though considerable accuracy is achieved in the targets (epilepsy risk levels). Therefore we had selected (24-12-4), (4-4-1) and (2-4-2) MLP network architectures due to their lesser number of training epochs.

2. Radial Basis Function Neural Networks for Classification of Breast Cancer Stages

The RBF neural network is widely used for function approximation, pattern classification and recognition due to its structural simplicity, universal approximators, and faster learning abilities due to locally tuned neurons. An RBF neural network is generally trained in two steps one after another[5]. In the first step, the centers of hidden layer neurons are selected. Then the weights between the hidden and output layers are estimated. The centers of the hidden layer neurons of an RBF neural network are selected in different ways. Generally, these centers are selected by using some clustering algorithm like, k-means, fuzzy c-means, etc.RBF networks train rapidly, usually orders of magnitude faster than MLP, while exhibiting none of its training pathologies such as paralysis or local minima problems. Such a system consists of three layers (input, hidden, output). The activation of a hidden neuron is determined in two steps: The first is computing the distance (usually by using the Euclidean norm) between the input vector and centre c_i that represents the ith hidden neuron. Second, a function h that is

bell-shaped is applied, using the obtained distance to get the final activation of hidden neuron. In this case the Gaussian function G(x) was used [13].

$$G(x) = \exp(\frac{-x^2}{\sigma^2}) \qquad (3)$$

The parameter σ is called unit width and is determined using the heuristic rule "global first nearest neighbor". The activation of a neuron in the output layer is determined by a linear combination of fixed non linear basis functions, i.e.

$$F^{"}(x) = \sum_{i=1}^{M} w_i \phi_i(x) \qquad (4)$$

Where $\phi_i(x) = G(\|x - c_i\|)$ and w_i are adjustable weights that link the output nodes with the appropriate hidden neurons. The orthogonal least squares (OLS) method has been employed as a forward selection procedure that constructs RBF centers one by one from training data points until satisfactory network is obtained [12]. Table 5 depicts Estimation of MSE in various RBF Network for breast cancer classification stages.

Table 5. Estimation of MSE in Various RBF Network Architectures for Breast Cancer

Architecture	Train MSE Index	Test MSE Index
1-16-1	4E-12	0.0001
2-8-2	9.47118E-05	1.50987E-07
4-4-4	0	0.001873
8-2-8	1.6E-11	1.67205E-05
28-1-1	0.000676636	5.53126E-08

Figure 3 shows the analysis of spread constant in RBF (28-1-1) neural network with Mean Square Error (MSE) under testing condition. As the spread constant increases the Average MSE is reached the very minimal level. Therefore the spread constant of 9 is taken for our RBF neural network. The results are discussed in the following section of the paper.
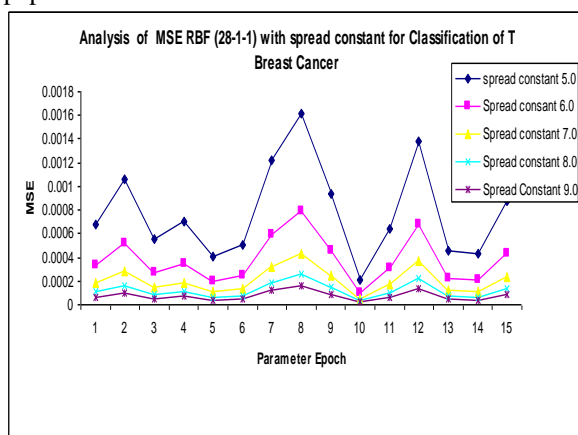
Figure 3 Analysis of spread constant in RBF (28-1-1) neural network with Mean Square Error (MSE) under testing condition.

IV. RESULTS AND DISCUSSION

Oral cancer is commonest cancer in India accounting for 50-70% of total cancer mortality. High proportion of cases among males may be due to high prevalence of tobacco consumption habits among males. Moreover tobacco is consumed in both chewing and smoking form in males. Due to poor oral hygiene further increasing the risk of oral cancer in tobacco chewers. Though, oral cancer occur at site which is accessible for clinical examination and amendable to diagnosis by current diagnostic tools, the crux of the problem is that majority of the cases report late to the health care facility as evident from the findings of present study. The classification efficiency of both the clinical standard and neural network are compared. Neural network closely follows the clinical classifications. Therefore, this method can also be used as an early procedure for classification of cancer stages.

Table.6 Performance of Clinical and MLP neural network Classification of Oral Cancer Stage

SSl.no	Oral Cancer Stage	% of Classification By Clinical Procedure	% of Classification by MLP
1	T1	98	92
2	T2	100	89
3	T3	97	87
4	T4	100	90

The table 6 it is observed that the MLP neural network classification is working perfectly in T1 classification and more than 85% accuracy in other three stages of oral cancer classification.

From the table 7 it is observed that the RBF neural network classification is working perfectly in T1 and T2 classification and more than 90% accuracy in other three stages of breast cancer classification

Table.7 Performance of Clinical and RBF neural network Classification for breast Cancer stage

S. no	Breast Cancer Stage	% of Classification By Clinical Procedure	% of Classification by RBF
1	T1	98	95
2	T2	100	91
3	T3	97	92
4	T4	100	93

V. CONCLUSION

Application of Neural networks to the medical field offers an immense potential to clinical medicine. It makes the diagnostic procedure, better, quicker and error free. The novel method proposed is a boon to practicing oncologist.

They only have to go through the input pattern with a defined the clinical parameters and the network tell about the classification of oral cancer stages.

This approach is very desirable because it minimizes observer bias facilitates comparison of results across individuals and different methodologies. Training a network may be time consuming, but once trained, they show reliable results. This reduces the cost of cancer classification and thus making the facility access able for a larger number of patients.

In this paper a generic classification of the oral and Breast cancer stages from clinical parameters using MLP &RBF neural network was considered. MLP &RBF neural networks were chosen to optimize the cancer stage classification by incorporating the low false alarm and near nil missed classifications. In the present study, majority of the cases of carcinoma alveolus may be correlated with tobacco chewing habit. Smokeless spit tobacco contains over 1000 chemicals; some of them are directly related for causing cancer. The tobacco consumption is well established risk factor for development of oral cancer. It is related to dose and during of tobacco consuming habits as noticed in this study. Thus on the basis of findings of present study, health education of the community regarding hazards of tobacco consumption in terms of development of oral cancer; complete durability of cancer in earlier stages and education about risk of oral cancer is recommended. Further research is in the direction to compare the MLP and RBF neural network with Support Vector Machine (SVM) model to solve this open end problem.

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