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Fine Needle Aspiration Cytology Evaluation for Classifying Breast Cancer Using Artificial Neural Network

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Abstract: Thirteen cytology of fine needle aspiration image (i.e. cellularity, background information, cohesiveness, significant stromal component, clump thickness, nuclear membrane, bare nuclei, normal nuclei, mitosis, nucleus stain, uniformity of cell, fragility and number of cells in cluster) are evaluated their possibility to be used as input data for artificial neural network in order to classify the breast pre-cancerous cases into four stages, namely malignant, fibroadenoma, fibrocystic disease, and other benign diseases. A total of 1300 reported breast pre-cancerous cases which was collected from Penang General Hospital and Hospital Universiti Sains Malaysia, Kelantan, Malaysia was used to train and test the artificial neural networks. The diagnosis system which was developed using the Hybrid Multilayered Perceptron and trained using Modified Recursive Prediction Error produced excellent diagnosis performance with 100% accuracy, 100% sensitivity and 100% specificity.

Keywords: Artificial neural network, breast cancer, fine needle aspiration, Hybrid Multilayered Perceptron, Modified Recursive Prediction Error.

INTRODUCTION

Breast cancer occurs mostly in women, but does occur rarely in men. In Malaysia, the National Cancer Registry reports that the crude rate of mortality in the year 2002 was 148.4 per 100,000 populations for females, with the breast cancer being the number one killer [1]. Breast cancer accounted 30.4% of the newly diagnosed cancer cases in Malaysian women, with the probability of 1 of every 19 woman in Malaysia has the risk to develop breast cancer [1].

Mortality rate due to breast cancer could be reduced through early detection. The most common early screening test is mammography. Mammography as a mass screening tool is convenient, inexpensive and has become the modality choice for an early detection of breast cancers due to its sensitivity in recognizing breast masses. However, the overall 'false negative' rate for screening mammography is about 10% lesions may not show up in a mammogram. Mammography also has 'false positive' findings which may lead to unnecessary biopsies that turn out to be negative or benign. Laine *et al.* [2] suggests that mammograms display only 3% of the total information detected.

From literature review, many researchers have carried out intelligent diagnostic systems specifically to provide 'second opinion' for pathologists in making diagnosis [3,4,5]. Artificial neural network (ANN) was employed to classify between benign and malignant cases. Those approaches require breast features taken from mammogram images, as the input data for the ANN. It has been shown in [6][7][8] that in general, feedforward ANNs can produce the breast pre-cancerous diagnosis result almost favorably comparable with those from human experts. The applicability of ANNs combined with image processing techniques to predict the stages of breast pre-cancerous has also been carried out in [9,10,11]. The system proposed in [9] managed to achieve 92% of sensitivity out of 272 cases. In [11], the diagnostic system managed to achieve accuracy of 88.9% out of the 58 cases tested.

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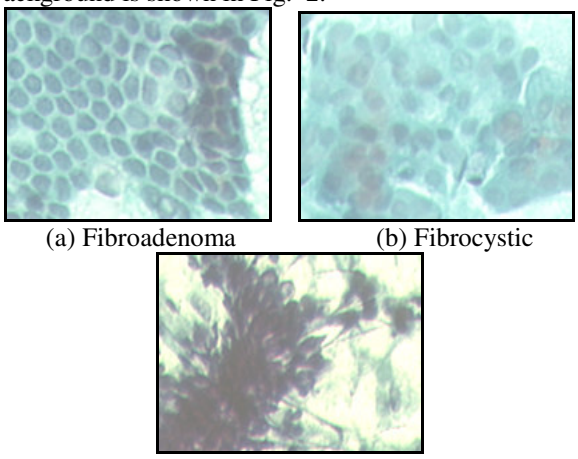
Nowadays, an alternative breast cancer screening test called fine needle aspiration (FNA) cytology is commonly used to diagnose palpable growth in the breast and also to confirm the non-palpable positive results from the mammogram screening. FNA is done by using a very thin needle connected to a syringe to extract the lesions from the breast. The sample from the biopsy is sent to a pathologist for analysis and to confirm the diagnosis. Based on the successful of aforementioned intelligent breast cancer diagnostic systems, this paper demonstrates an intelligent diagnostic system for breast pre-cancerous. This paper will propose and evaluate the capability of thirteen cytology of FNA (i.e. cellularity, background information, cohesiveness, significant stromal component, clump thickness, nuclear membrane, bare nuclei, normal nuclei, mitosis, nucleus stain, uniformity of cell, fragility and number of cells in cluster) to be used as input data for ANN in order to classify the breast cancer cases into four stages, namely malignant, fibroadenoma, fibrocystic disease, and other benign diseases. Hybrid Multilayered Perceptron (HMLP) network is proposed to predict the breast pre-cancerous stage. We empirically assess the capability of the proposed diagnostic system using 1300 reported cases from Penang General Hospital and Hospital Universiti Sains Malaysia, Kelantan, Malaysia.

Fine Needle Aspiration Cytology: In this section, thirteen FNA cytology which are proposed as input data to the developed diagnostic system are presented. The definition will be given in detail and appropriate figures will be included for better understanding. Then, the four stages of breast pre-cancerous cases will be discussed.

Cellularity: The first FNA cytology which is used is cellularity. Cellularity refers to the amount of cells present in a biopsy sample. The fibroadenoma has a very high cellularity yield, while the fibrocystic and malignant cases have variable state of cells which are dependent on different cases and stages of the disease. In this paper, the cellularity is classified into three categories, i.e. scanty, moderate and high. Figure 1 displays the difference in cellularity for each breast cancer category.

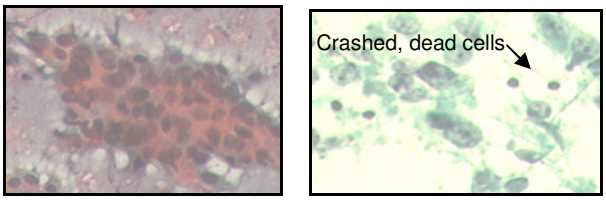
Background Information: Background information describes the cleanliness of the FNA images. In this study, the background of the cells is marked to three criteria (i.e. clean, slightly dirty and very dirty). The dirty background refers to the crashed and dead cells in the background of the smear sample. However, a bloody background does not denote to dirty background. The difference between bloody and dirty background is shown in Fig. 2.



(a) Fibroadenoma (b) Fibrocystic

(c) Malignant

Fig 1: The cellularity of each respected categories of breast diseases



(a) Bloody background (b) Dirty background

Fig 2: The difference between dirty and bloody background.

Cohesiveness: This study describes cell cohesiveness as the state of cohering or sticking together. The cohesiveness of the cell group is also an important characteristic to distinguish between benign and malignant cells, where the benign cells are more cohesive to each other compared to the malignant cells. A sample group of cohesive cells is shown in Fig. 3.

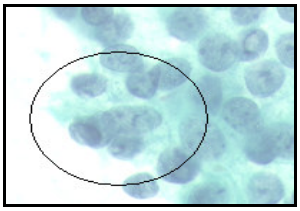


Fig 3: Cell cohesiveness.

Significant Stromal Component: Stroma is important as a connective tissue framework that supports the neoplastic cell population [12]. Thus, this study employs significant stromal components as one of the input data

as the presence presence of stroma is significant in determining the fibroadenoma as shown in Fig. 4.

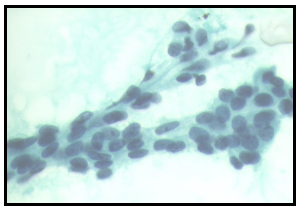
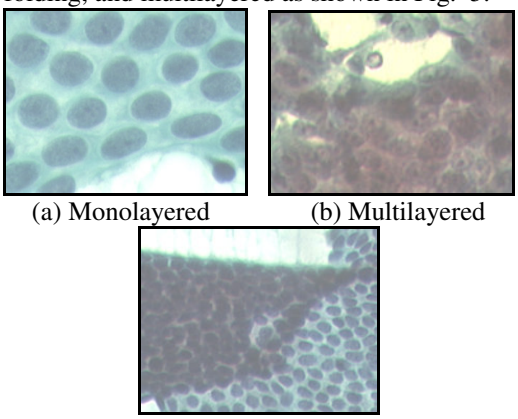


Fig 4: Presence of stromal component in a fibroadenoma cytology.

Clump Thickness: The fifth FNA cytology used is clump thickness, which is described as the number of layers of the smear sample. In this study, the clump thickness is categorized to monolayered, monolayered and folding; and multilayered as shown in Fig. 5.

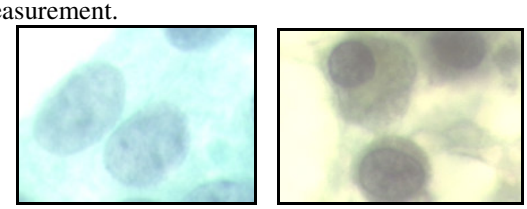


(a) Monolayered (b) Multilayered

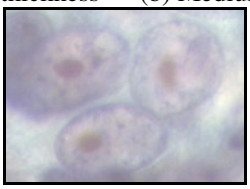
(c) Monolayered and folding

Fig 5: The type of clump thickness in breast cytology.

Nuclear Membrane: The thickness of nuclear membrane is also an important criterion to determine the malignancy of a cell. A normal breast cell has normal membrane thickness, while an abnormal cell has obvious thickened membrane. A benign cell has an even and thin membrane, while a thick and uneven membrane represents the characteristic of a malignant cell. The thickness of the nuclear membrane is categorized as normal thickness (even and thin), medium thickness (slightly thicker and even/uneven) and high thickness (thick and uneven). Figure 6 displays the difference in membrane thickness measurement.



(a) Normal thickness (b) Medium thickness



(c) High thickness

Fig 6: The appearance of various nuclear membrane thicknesses.

Bare Nuclei: In FNA image, the presence of bare nuclei symbolizes the benignity of the cell. In this study, the bare nuclei is described as a group of nucleoli which are not surrounded by their perspective cytoplasts as shown in Fig. 7.

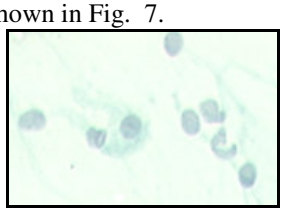


Fig 7: An example of bare nuclei.

Normal Nucleoli: The eighth FNA cytology is normal nucleoli. Normal nucleoli defines a typical characteristic of a cell's nucleolus. In general, a normal cell including benign cells does not have nucleolus or has fine nucleolus in their cells. However, abnormal (malignant) cells have prominent nucleolus and in certain cases have more than one nucleolus. In this study, the normal nucleoli is categorized as no nucleolus, fine nucleolus, prominent nucleolus and multiple nucleoli present.

Mitosis: This study also employs the presence of mitosis as one of the input data to our proposed diagnostic system. Mitosis is the process of nuclear division in cells that produces daughter cells that are genetically identical to each other and to the parent cell. Malignant cells tend to have higher mitotic activities compared to normal and benign cell population.

Nucleus Stain: The tenth cytology is nucleus stain. Generally, the nucleus stain of a malignant cell is coarse while the benign cells display a very fine nucleus.

Uniformity of Cell: In medical field, the uniformity of the cell could be used to differentiate between benign and malignant case. Uniformity of the cell is the measure of the cell shape and type in an extracted lesion. Generally, benign case is usually monomorphisam where a group of cells appear in

different cell shapes and sizes consistently. On the other hand, malignant cells are mostly pleomorphic. Pleomorphism describes a group of different type of cells which appear in variety shapes and sizes.

Fragility: In this study, fragility of a cell is also employed as a measure to distinguish the benign cell from the malignant cell. The nucleus of benign cells are said to be fragile, while the nucleus of malignant cells are sturdy.

Cell in Cluster: The final cytology used is cell in cluster. It is the accumulation of cells in a group regardless of the cohesiveness and cellularity. The larger group of cells determines that the cells are more concentrated and is highly observed in fibroadenoma and some of the severe malignant cases. However, in the cystic category of tumors the cells are more distributed.

As a conclusion, the thirteen aforementioned cytology features are categorized accordingly to the different characteristics of the cells. Table 1 tabulates the proposed FNA cytology as input data for the neural networks. The scoring or marking of the ANN inputs are given based on the discussion with few experienced pathologists from Hospital Universiti Sains Malaysia (HUSM), Kelantan, Malaysia. [13] was used as a reference to score the characteristics of the cytology features.

Stages of Breast Pre-Cancerous Case: In this study, breast disease refers to abnormal growth of inflammation in human breast. They are divided into benign neoplasm and malignant neoplasm. Although the ANN has been applied in a number of researches for breast pre-cancerous diagnosis, from literature review no attempt was carried out to use the ANN to further classify the benign cases into more specific stages (i.e. in [9][14][15]). In this study, the benign cases will be further classified into three stages, namely fibroadenoma, fibrocystic and other benign disease.

Benign tumor is an abnormal and non-cancerous growth of tissue that does not spread to other parts of the body [12][16]. Benign tumor grows slowly and remains locally. It pushes the surrounding normal tissue aside but does not infiltrate the surrounding tissues or spread by blood and lymphatic channels to distant sites.

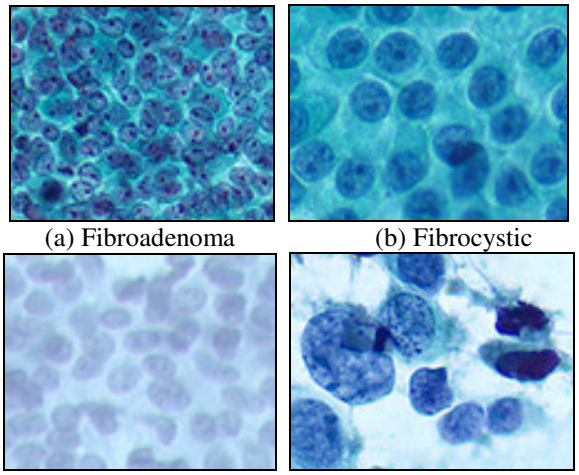
Fibroadenoma is a type of benign solid lump of tissue. It is thought to result from increased sensitivity to the female hormone estrogens. It is normally has a rubbery texture, smooth to the touch and moves easily under the skin.

On the other hand, fibrocystic changes show a variant to the common benign pattern with an additional presence of cyst macrophages and sheets of ductal epithelial cells of oxyphil or apocrine. However, the presence of the typical features of benign pattern such as single bare nuclei and ductular epithelium dominates the smear [17].

A malignant tumor is composed of less well differentiated cells. It grows rapidly and infiltrates the surrounding tissues, unlike benign tumor which grows by expansion. The example for four stages of breast pre-cancerous cases are shown in Fig. 8.

Table 1: Proposed variables for classification.

Input marker	**Categories**
Cellularity	Scanty
	Moderate
	High
Background information	Clean
	Slightly dirty
	Dirty
Cohesiveness	More than 21
	11 – 20
	6 – 10
	Less than 5
Cell in cluster	31 – 50
	11 – 30
	Less than 10
Significant stromal component	Present
	Nor present
Clump thickness	Monolayered
	Monolayered and folding
	Multilayered
Nuclear membrane	Normal
	Medium
	High
Bare nuclei	Present
	Not present
Normal nucleoli	No nucleolus
	Fine nucleolus
	Prominent nucleolus
	More than 1 nucleolus
Mitosis	Not present
	Present normal
	Present abnormal
Nucleus stain	Coarse/hyperchromatin
	Fine/normochromatin
Uniformity of cells	High uniformity
	Medium
	Low/pleomorphism
Fragility	Fragile
	Not fragile



(a) Fibroadenoma (b) Fibrocystic

(c) Other benign (d) Malignant

Fig 8: Four categories of breast pre-cancerous cases

INTELLIGENT DIAGNOSTIC SYSTEM FOR BREAST PRE-CANCEROUS BASED ON ARTIFICIAL NEURAL NETWORK

From literature review, no attempt was carried out to use the feedforward ANNs to further classify the breast pre-cancerous stages into more than two classes (i.e. benign and malignant cases). Moreover, no attempt was reported of classifying the breast pre-cancerous stages using FNA features. In our previous study [18], the standard multilayered perceptron (MLP) network trained using the gradient descent with momentum and adaptive learning rate, resilient back propagation, Quasi-Newton and Levenberg-Marquardt algorithms produced 69.23%, 73.08%, 72.31% and 80.00% diagnosis accuracy respectively. With additional linear connection between input nodes and output nodes of the standard MLP network, we proposed a hybrid version of standard MLP network called hybrid multilayered perceptron (HMLP) network in order to improve the diagnosis performance. This section is dedicated to explanation on the the hybrid MLP (HMLP) network and the MRPE algorithm.

Hybrid Multilayered Perceptron Network: The standard MLP network is highly nonlinear, therefore modeling a linear system using a nonlinear MLP network is not appreciable. [19] suggested the HMLP network which capable of modeling both linear and nonlinear systems. Nonlinear system is modeled by the standard connections (i.e. represented by line connection in Fig. 9) as of the standard MLP network, and the linear system could be modeled by additional direct connections between input nodes to output nodes (i.e. represented by dotted line connections in Fig. 9). For *m* output nodes, the output of the HMLP network is given by:

$$\hat{y}_k(t) = \sum_{j=1}^{n_h} w_{jk}^2 F\left(\sum_{i=1}^{n_i} w_{ij}^1 x_i^0(t) + b_j^1\right) + \sum_{i=1}^{n_i} w_{ik}^l x_i^0(t) \quad \text{for} \quad 1 \le k \le m \tag{1}$$

where w_{ij}^1, w_{jk}^2 and w_{ik}^l denote the weights of the connection between input and hidden layer, weights of the connection between hidden and output layer, and weights of the linear connection between input and output layer respectively. b_j^1 and x_i denote the thresholds in hidden nodes and inputs that are supplied to the input layer respectively. $F(\bullet)$ is an activation function and is normally be selected as sigmoid function. The detailed HMLP network can be found in [19].

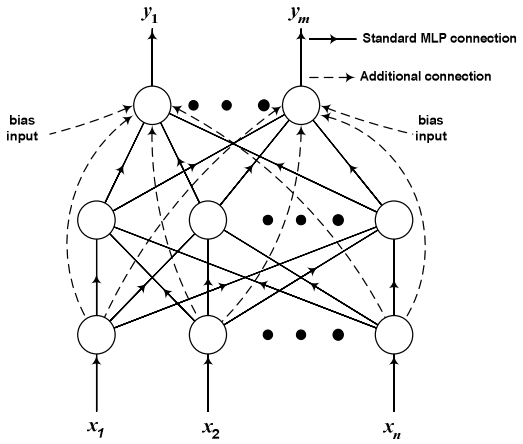


Fig 9: The HMLP network with one hidden layer.

Modified Recursive Prediction Error: Learning algorithm for the HMLP network to determine the values of w_{ij}^1, w_{jk}^2, w_{ik}^l and b_j^1 have been proposed in [19]. To handle the additional linear connections, a modified version of Recursive Prediction Error (RPE) (the detailed RPE algorithm could be found in [20]), namely Modified Recursive Prediction Error (MRPE) is introduced [19]. The MRPE algorithm is able to improve the convergence rate by optimizing the way the momentum and the learning rate are assigned as of in the RPE algorithm. The detailed MRPE algorithm can be found in [19].

The standard RPE algorithm proposed in [20] minimizes the following cost function:

$$J\left(\hat{\Theta}\right)=\frac{1}{2N}\sum\varepsilon^{T}\left(t,\hat{\Theta}\right)\Lambda^{-1}\varepsilon\left(t,\hat{\Theta}\right) \quad (2)$$

by updating the estimated parameter vector, $\hat{\Theta}$ (consists of *w*'s and *b*'s), recursively using the Gauss-Newton algorithm:

$$\hat{\Theta}(t)=\hat{\Theta}(t-1)+\mathrm{P}(t)\Delta(t) \quad (3)$$

and

$$\Delta(t)=\alpha_m(t)\Delta(t-1)+\alpha_g(t)\psi(t)\varepsilon(t) \quad (4)$$

where $\varepsilon(t)$ and Λ are the prediction error and a $m\times m$ symmetric positive definite matrix respectively, and *m* is the number of output nodes; $\alpha_m(t)$ and $\alpha_g(t)$ are the momentum and the learning rate respectively. $\alpha_m(t)$ and $\alpha_g(t)$ can be arbitrarily assigned to some values between 0 and 1, and the typical values of $\alpha_m(t)$ and $\alpha_g(t)$ are closed to 1 and 0 respectively. In [19], $\alpha_m(t)$ and $\alpha_g(t)$ are varied to further improve the convergence rate of the RPE algorithm according to:

$$\alpha_m(t)=\alpha_m(t-1)+a \quad (5)$$

and

$$\alpha_g(t)=\alpha_m(t)\left(1-\alpha_m(t)\right) \quad (6)$$

where *a* is a small constant (typically $a=0.01$); $\psi(t)$ represents the gradient of the one-step-ahead predicted output, $\hat{y}$ with respect to the network parameters:

$$\psi(t,\Theta)=\left[\frac{d\,\hat{y}(t,\Theta)}{d\Theta}\right] \quad (7)$$

P(t) in equation (3) is updated recursively according to:

$$P(t)=\frac{1}{\lambda(t)}\left[P(t-1)-P(t-1)\psi(t)\left(\lambda(t)I+\psi^{T}(t)P(t-1)\psi(t)\right)^{-1}\psi^{T}(t)P(t-1)\right] \quad (8)$$

where $\lambda(t)$ is the forgetting factor, $0<\lambda(t)<1$, and has been updated using the following scheme:

$$\lambda(t)=\lambda_0\lambda(t-1)+(1-\lambda_0) \quad (9)$$

where λ_0 and the initial forgetting factor, $\lambda(0)$ are the design values. The initial value of the *P(t)* matrix, *P(0)* is set to αI where *I* is the identity matrix and α is a constant, typically between 100 and 10000.

The gradient matrix, $\psi(t)$ can be modified to accommodate the extra linear connections for a one-hidden-layer HMLP network model by differentiating equation (1) with respect to the parameters, θ_c, to yield:

$$\psi_k(k)=\frac{dy_k(t)}{d\theta_c}=\begin{cases}u_j\\ x_i\\ u_j(1-u_j)w_{jk}^2\\ u_j(1-u_j)w_{jk}^2x_i\\ 0\end{cases}$$

$$\begin{aligned}
&if \quad && \theta_c=w_{jk}^2 && 1\le j \le n_h\\
&if \quad && \theta_c=w_{ik}^l && 0\le i \le n_i\\
&if \quad && \theta_c=b_j^1 && 1\le j \le n_h\\
&if \quad && \theta_c=w_{ij}^1 && 1\le j \le n_h, 1\le i\le n_i\\
&otherwise
\end{aligned} \quad (10)$$

The MRPE algorithm to determine the output $y_k(t)$ for a one-hidden-layer HMLP network can be implemented as follows [19]:

1. Initialize weights, thresholds, *P(0)*, *a*, *b*, $\alpha_m(0)$, λ_0 and $\lambda(0)$. (*b* is a design parameter that has a typical value between 0.8 and 0.9).
2. Present inputs to the network and compute the network outputs according to equation (1).
3. Calculate the prediction error according to:

$$\varepsilon_k(t)=y_k(t)-\hat{y}_k(t) \quad (11)$$

where $y_k(t)$ is the actual output.

4. Compute matrix $\psi(t)$ according to equation (10). Note that, elements of $\psi(t)$ should be calculated from the output layer down to the hidden layer.
5. Compute matrix *P(t)* and $\lambda(t)$ according to equations (8) and (9) respectively.
6. If $\alpha_m(t)<b$, update $\alpha_m(t)$ according to equation (5).
7. Update $\alpha_g(t)$ and $\Delta(t)$ according to equations (6) and (4) respectively.
8. Update parameter vector $\hat{\Theta}(t)$ according to equation (3).

9. Repeat steps (2) to (8) for each training data sample.

EXPERIMENTS AND RESULTS

The applicability of the proposed breast pre-cancerous diagnostic system using the HMLP network based on FNA features has been evaluated using 1300 reported cases from Penang General Hospital and HUSM, Kelantan, Malaysia. The data distribution of training and testing phases for the system is tabulated in Table 2. Five models of the standard MLP networks with various training algorithms and one model of the standard RBF network were used to compare the diagnosis performance. The first MLP network model was trained using the gradient descent with momentum and adaptive algorithm, which based on [21][22]. The resilient back propagation algorithm for the second MLP network is based on [23]. The third, forth and fifth MLP networks were trained using Quasi-Newton, Levenberg Marquardt and Recursive Prediction Error (RPE) respectively. The details for the Quasi-Newton and Levenberg Marquardt can be found in [23], while the RPE algorithm can be found in [20][24]. The RBF network was implemented based on [25] and [26]. The adjustable weights of the network were estimated using linear least square algorithm. The performance comparison was done using accuracy, sensitivity, specificity, false negative and false positive. The definition and procedure of those analyses in [27] was closely followed.

Intelligent Breast Cancer Diagnostic Performance: Table 3 depicts the percentage of accuracy, specificity, sensitivity, false negative and false positive for the diagnostic performance results. The HMLP network outperformed the five MLP models and the RBF network in term of the percentage of accuracy by more than 14%. A trend is similar to that for specificity, sensitivity, false negative and false positive. Based on Table 3, in general, the four MLP network models (i.e. the MLP networks trained using Quasi Newton, gradient descent with momentum and adaptive learning rate, resilient back propagation and Levenberg-Marquardt learning algorithms) and the RBF network successfully classified the malignant case (i.e. produced 100% of sensitivity), but all these neural networks were not capable to further classify the benign case into fibroadenoma, fibrocystic and other benign disease. The specificity produced is between 63% and 66%, which led to high false positive rate (i.e. between 34% and 36%). Only the standard MLP network trained using RPE algorithm produced good diagnostic performance with 91.89%, 97.47% and 89.07% of accuracy, sensitivity and specificity respectively. With additional linear connection between input nodes and output nodes, the result demonstrates that the HMLP network trained using MRPE algorithm improved the diagnostic accuracy produced by the standard MLP network up to 100.00%. The HMLP network successfully determine all malignant cases (i.e. produced 100% sensitivity) and is capable to further classify the benign cases into fibroadenoma, fibrocystic and other benign cases (i.e. produced 100% specificity).

Dominant Input Features Analysis: The dominant input analysis is simulated using the thirteen input features extracted from the FNA images. The objective of the analysis is to identify the features that highly contribute to the classification of breast pre-cancerous stage. The HMLP network with MRPE algorithm was selected to do this analysis as it produced the best diagnostic performance. The respective features were fed into the system one by one and the simulation result was measured. Table 4 summarizes the results.

Table 2: Data distribution for training and testing phases

Category of breast pre-cancerous stage	Number of training data	Number of testing data
Fibroadenoma	240	150
Fibrocystic	240	150
Other benign disease	50	30
Malignant	270	170
Total	800	500

Table 3: Diagnostic performance comparison between the six MLP network models, the RBF and the HMLP networks

Type of Neural Networks	Accuracy	Sensitivity	Specificity	False Negative	False Positive
MLP with QN	75.38	100.00	65.22	0.00	34.78
MLP with GDX	76.00	100.00	65.71	0.00	34.29
MLP with RPROP	75.38	100.00	63.97	0.00	36.03
MLP with LM	74.62	100.00	64.13	0.00	35.87
MLP with RPE	91.89	97.47	89.07	2.59	10.93
RBF	81.82	100.00	79.87	0.00	20.13
HMLP	100.00	100.00	100.00	0.00	0.00

Note: QN, Quasi-Newton algorithm, GDX - gradient descent with momentum and adaptive algorithm, RPROP resilient back propagation algorithm, LM – Levenberg Marquardt, RPE- Recursive Prediction Error algorithm.

Table 4: Results for dominant input features analysis

Input Marker	Performance Marker	Percentage (%)
Cellularity	Accuracy	74.3
	Sensitivity	50.00
	Specificity	85.19
	False Negative	50.00
	False Positive	14.81
Background information	Accuracy	79.49
	Sensitivity	81.67
	Specificity	78.51
	False Negative	18.33
	False Positive	21.49
Cohesiveness	Accuracy	58.97
	Sensitivity	0.00
	Specificity	85.18
	False Negative	100.00
	False Positive	14.82
Cell in clusters	Accuracy	58.97
	Sensitivity	0.00
	Specificity	85.18
	False Negative	100.00
	False Positive	14.82
Significant stromal component	Accuracy	58.97
	Sensitivity	0.00
	Specificity	85.18
	False Negative	100.00
	False Positive	14.82
Clump thickness	Accuracy	58.97
	Sensitivity	0.00
	Specificity	85.18
	False Negative	100.00
	False Positive	14.82
Nuclear membrane	Accuracy	82.57
	Sensitivity	78.33
	Specificity	84.44
	False Negative	21.67
	False Positive	15.56
Bare nuclei	Accuracy	65.13
	Sensitivity	76.67
	Specificity	60.00
	False Negative	23.33
	False Positive	40.00
Normal nucleoli	Accuracy	76.41
	Sensitivity	71.67
	Specificity	78.52
	False Negative	28.33
	False Positive	21.48
Mitosis	Accuracy	62.05
	Sensitivity	10.00
	Specificity	85.19
	False Negative	90.00
	False Positive	14.81

Nucleus stain	Accuracy	80.00
	Sensitivity	83.33
	Specificity	78.52
	False Negative	16.67
	False Positive	21.48
Uniformity of cells	Accuracy	75.38
	Sensitivity	55.00
	Specificity	84.44
	False Negative	45.00
	False Positive	15.56
Fragility	Accuracy	63.07
	Sensitivity	16.67
	Specificity	83.70
	False Negative	83.33
	False Positive	16.30

From Table 4, it is shown that cellularity, cohesiveness, cell in clusters, significant stromal component, clump thickness, nuclear membrane, mitosis, uniformity in cells and fragility cytology features highly contribute to the specificity performance (i.e. more than 83%). The finding demonstrates that these features carry the strong weight for the HMLP network to determine the benign cells from the malignant cells. On the other hand, background information and nucleus stain produce high percentage of sensitivity (81.67% and 83.33% respectively). The result suggests that these features are highly significant to be used as input data for the HMLP network to determine the malignant cells. The results also proved that each cytology feature is significantly important in determining either benign or malignant case. Thus, combination of all cytology features is capable of producing up to 100% of accuracy, sensitivity and specificity as proven in Section 4.1.

CONCLUSION

In this paper, an intelligent diagnostic system based on the HMLP network to determine the four stages of breast pre-cancerous, namely malignant, fibroadenoma, fibrocystic disease, and other benign diseases was proposed. The effectiveness of the proposed diagnostic system has been demonstrated empirically using 1300 reported cases. The HMLP network outperformed the five MLP network models (i.e. the MLP networks trained using Quasi Newton, gradient descent with momentum and adaptive learning rate, resilient back propagation, Levenberg-Marquardt and recursive prediction error algorithms) and the RBF network trained using linear least square algorithm.

This project has also successfully demonstrated that the combination of all thirteen cytology of fine needle aspiration image (i.e. cellularity, background information, cohesiveness, significant stromal component, clump thickness, nuclear membrane, bare nuclei, normal nuclei, mitosis, nucleus stain, uniformity of cell, fragility and number of cells in cluster) has high capability to be used as input data for the HMLP in order to classify the breast pre-cancerous cases and is capable of producing up to 100% of accuracy, sensitivity and specificity without any case of false negative and false positive.

Although the results obtained so far are encouraging, more investigations on both theoretical and practical aspects are needed to further vindicate the applicability of the proposed diagnostic system to screen for breast pre-cancerous stages based on FNA cytology features.

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