



A Fuzzy Rule-based Expert System for the Prognosis of the Risk of Development of the Breast Cancer

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ABSTRACT

Soft computing techniques play an important role for decision-making applications with imprecise and uncertain knowledge. The application of fuzzy soft computing applications is rapidly emerging in the medical diagnosis and prognosis. A fuzzy expert system models knowledge as a set of explicit linguistic rules and performs reasoning with words. Although there are several technology-oriented studies reported for breast cancer diagnosis, few studies have been reported for the breast cancer prognosis. However, prognosis of breast cancer suffers from uncertainty and imprecision associated to imprecise input measures and incompleteness of knowledge as well as diagnosis. This research presents a fuzzy expert system for breast cancer prognosis. This approach is capable enough to capture ambiguity and imprecision prevalent in the characterization of the breast cancer. For this, the paper utilizes a Mamdani fuzzy inference model, which is more intuitive and has high interpretability for interacting with human experts during prognosis process. The main advantage of this work compared to other related studies, mostly presented for assessing the risk of the cancer development stage, is using unbiased input variables in the prognosis process; i.e., this model has the potential to predict the risk of developing breast cancer even in healthy females. Furthermore, the fuzzy expert system was evaluated on real dataset and the results of system were compared to an obstetrician decisions. The performance results on real dataset reveals superiority of the fuzzy expert system in the prognosis process with an average accuracy of 95%, compared to other related works. This approach is optimistic for prediction of breast cancer risk and early diagnosis of the cancer and can consequently improve survival rate.

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1. INTRODUCTION

Breast cancer is one of the most common cancers in the female population [1]. Breast cancer is a malignant tumor that develops from uncontrolled growth of cells in the breast. However, in general, earlier diagnosis and treatment can increase the survival rate, the disease is much more easier to control if it does not spread to other parts of the body. The prognosis process aims at predicting the risk of get affected by breast cancer in females who are referred to the medical centre for the

screening purpose. Prognosis is the principal factor in determining the risk of developing cancer, which may result in early diagnosis of the disease. As the result of the breast cancer prognosis, people with high risk of breast cancer are identified and are suggested for further medical assessments.

Early diagnosis of breast cancer and the right treatment at early stages of the disease can save more lives. The early detection of breast cancer (within 5 years after the first cell division of cancer) can increase the survival rate from 56% to over 86%. This fact clears the need for an accurate and reliable process for prognosis of breast cancer [2].

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For this purpose, recognizing all of the effective variables and their amount of effectiveness in a risk assessment is very important. It is well known that most of breast cancer assessment characterization processes are entirely based on physician's intuition and experience. One of the main challenges in the studies proposed for predicting the risk of the breast cancer is how to manage these sources of uncertainties associated to the decision making process. Generally, the primary stage of investigation of diseases is unclear and uncertain, mainly medical experts follow the way of diagnosis through the interaction with patients and using the history of the patient.

Old age, illness family history, alcohol consumption and smoking, the first menstrual period before age 12 or menopause after age 55, pregnant or not pregnant, overweight or obesity after menopause, sedentary lifestyle and physical activity are the main factors that affect the risk of breast cancer [3].

In the recent decades, computer diagnostic tools are used to help the physicians a second reader. Computer-aided detection tools [4-6] aimed at facilitating and speeding up the healing process have been developed for the diagnosis of various diseases such as diagnosis of cancer types, including breast and lung cancer. Although, there are various studies reported for computer aided detection and diagnosis, there are few technologies presented for computer-aided prognosis.

Between various studies reported for detection of breast cancer, fuzzy rule-based expert system is one of the successful applications with the potential to manage uncertainty and imprecision in the prognosis process. This paper presents a fuzzy expert system for the breast cancer prognosis.

The rest of the paper is organized as follows: first a review of related works for breast cancer diagnosis and prognosis is presented in Section 2. Then a brief introduction to fuzzy inference system (FIS) as the method applied in this study for designing an expert system is explained in Section 3. The fuzzy expert system for breast cancer prognosis is presented and explained in details in Section 4 and the performance evaluation on real patients dataset and comparison results are presented in Section 5. Finally, the paper is concluded in Section 6.

2. REVIEW OF RELATED WORKS

Most of the real world problems that we are facing in our daily life are not well-defined. These kinds of problems cannot be solved using the conventional ways of computing. Soft computing techniques are a suitable choice.

Conventionally, breast cancer diagnosis is performed using biopsy with the help of the current

methods. However surgery has the highest accuracy, but it is an invasive procedure, which is time consuming and expensive. Test fine needle aspiration is another method that does not have the disadvantages of previous techniques. Experiments FNA (Fine Needle Aspiration) involving liquid extraction and examination of breast tissue samples under a microscope, which is visually almost verified with no side effects and can be performed with high accuracy [7]. Fuzzy expert systems are used to model human knowledge. The decision making processes are associated with lack of knowledge about the problem specification and imprecision in effective variables. In fact, fuzzy logic appears as an appropriate tool for managing uncertainty issues associated with decision making problems in various real life problems [8-12].

Soft computing and machine learning techniques are recommended as invasive methods for efficient breast cancer prediction and detection. This section briefly reviews current soft computing techniques presented for diagnosis followed by prognosis of the breast cancer.

2. 1. Soft Computing Approaches Applied to Breast Cancer Diagnosis

There are various researches reported for breast cancer diagnosis using soft computing techniques using the well-known anonymous the Wisconsin breast cancer diagnosis (WBCD) database [3]. Neural networks, fuzzy logic and other methods are applied to solve optimization problems and have been used to predict breast cancer using the WBCD with the maximum recognition accuracy of 99.31% [13]. The adaptive neural fuzzy inference system (ANFIS) is used on the database WBCD with an accuracy 95.60% [14]. Another fuzzy logic model can be developed from expert knowledge or from process (patient) input-output data. In the first case, fuzzy model can be extracted from the expert knowledge of the process. The expert knowledge can be expressed in terms of linguistics, which is sometimes faulty and requires the model to be tuned [15]. In another similar study, the combination of fuzzy with genetic algorithm was used in order to detect WBCD. The evaluation results showed its effectiveness in detecting this type of breast cancer with an average accuracy of 97% [16]. In a study reported in the literature[17], a type-2 fuzzy logic (T2FL) in combination with genetic algorithm is proposed for modeling uncertainty along with rule extraction process. This approach has been applied on the WBCD with an average classification accuracy of 96% which is competitive with the best results to date[10]. In another study the genetic algorithm has been used to overcome the problem of over learning and chances of misclassification in feature extraction and representation for the adaptive Neuro-Fuzzy based classifier. The performance of the proposed technique

is satisfactory with 87% classification accuracy [18]. Similar work was reported in the literature[19].

2. 2. Soft Computing Approaches Applied to Breast Cancer Prognosis

Soft-computing approaches including artificial neural networks and fuzzy inference have been used widely to model expert behavior. In one study an adaptive fuzzy inference system (ANFIS) technique has been used in the estimation of survival prediction. A specific form of data pre-processing has to be performed before a standard ANFIS model can be used for prognostic prediction of survival [20].

Another approach proposed a fuzzy logic technique for prediction of most probable risk estimation of breast cancer based on a set of fuzzy rules [21]. This method helps decision making process and choosing suitable treatment for suspected breast cancer patients. In another study, the next generation of multi-level fuzzy systems was presented that allows the use of complex combinations of inputs for the evaluation of breast cancer risk [22]. The accuracy rate according to the ROC analysis is 78.33% for breast cancer. This system uses Mamdani type of fuzzy inference model. Fuzzy risk assessment in other research is quantified by two linguistic variables of high and low. Through fuzzy computations, the multi agent system (MAS) computes the fuzzy probabilities of breast cancer development based on various risk factors and maximum success of average fuzzy-probabilistic MAS method is 88.37% [23].

The fuzzy system defined in other study makes possible the correlation between (stored and evaluated) patient data (like number of invaded axillary nodes, BI-RADS score, age and other case related data) and the prognostic risk of developing breast cancer, emulating the expert thinking and experience with the help of the computer [24]. Other work used fuzzy inference systems (FIS) to evaluate the risk of breast cancer using Mamdani-type and Sugeno-type models and compared their performance [25].

In another study eight set of fuzzy rules were used, the Mamdani max-min inference mechanism was implemented. Tumor size, number of nodes and the metastasis were used as input parameters and the breast cancer risk was obtained as an output. Coimbatore (North and South) was found to be at highest risk for breast cancer by 20% criteria in comparison with other areas [26]. Another approach has been proposed for assessment of the breast cancer risk by introducing a set of fuzzy rules that can be used to process the relevant data from breast cancer cases in order to assess breast cancer risk prognosis which is qualitative [1]. A fuzzy hybrid model has been considered using fuzzy sets classification of risk factors, breast cancer and crispy rules (constructed by translating physicians' perceptions of hormone-sensitive breast cancer's risk).

The accuracy obtained for the proposed model was 72.1% [27]. Though in this research, the fuzzy procedure still needs to be calibrated and validated with real data and under real conditions (for a large number of patients) prior to its use on a large scale. This procedure can be easily integrated and used in screening programs and automatically assign breast cancer risk factors to females in order to highlight the cases that need prior attention and care. The quality of this approach was reported successful although this approach needs evaluation on real data in order to give a real view of the system performance.

Although, various studies have been reported for diagnosis of the breast cancer using soft computing techniques, there are few studies reported for prognosis of the breast cancer. However, the uncertainty issues are associated to prognosis process as well as the diagnosis. Furthermore, all proposed breast cancer prognosis methods are for assessment of the risk of cancer progress to advanced stages in people diagnosed with breast cancer. Thus, they use biased input variables such as size of tumour and metastasis. Therefore, they are more applicable for diagnostic purpose and stage identification of the cancer rather than prognosis. Furthermore, the majority have not provided overall performance of the fuzzy expert systems on real people dataset. This work just applies parameters corresponding to the clinical history of females referred for screening, which could be applicable even for assessment of the risk of breast cancer development in healthy females.

This study presents a fuzzy inference system for analysis of the risk of breast cancer and evaluates performance of the fuzzy expert system on real dataset including information of people referred to hospital for screening with or without breast cancer developing.

3. A FUZZY EXPERT SYSTEM

Fuzzy set A in universe of discourse X can be defined as a set of ordered pairs of element x in X and the grade of membership of x, $\mu_A(x)$, to fuzzy set A where the two dimensional membership function $\mu_A(x)$ is a crisp value between 0 and 1 for all $x \in X$ [28]. Linguistic terms are modelled using fuzzy sets. One of the parameters in the design of a fuzzy logic is the number of fuzzy sets associated to a linguistic term. Fuzzy inference system as a soft computing method mimics cognitive reasoning of the human mind based on linguistic terms for performing tasks in a natural environments.

Fuzzy inference is the process of formulating the mapping from given input(s) to output(s) using fuzzy logic. This mapping provides a basis from which decisions can be made or patterns discerned.

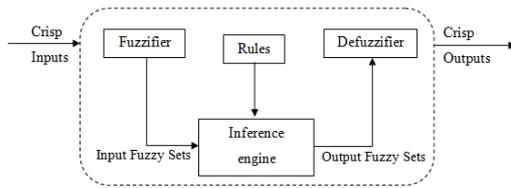


Figure 1. Architecture of a fuzzy inference system

It has found successful applications in a wide variety of fields, such as automatic control, data classification, decision analysis, expert systems, time series prediction, robotics, and pattern recognition. A fuzzy inference system (see Figure 1) with crisp inputs and outputs implements a nonlinear mapping from its inputs space to output space. This mapping is accomplished by a number of fuzzy if-then rules, each of which describes the local behavior of the mapping. In particular, the antecedent of a rule defines a fuzzy region in the input space, while the consequent specifies the output in the fuzzy region. Basically, a fuzzy inference system is composed of five functional blocks as shown in Figure 1. The structure of the fuzzy inference system is described as follows.

The fuzzification and the defuzzification are the two bounds between the fuzzy logic system and the measured phenomenon data. Fuzzification is used for the transformation of a real value $x \in R$ (acquired from the studied process) in one of the fuzzy values from a fuzzy set for a specific fuzzy variable. Defuzzification is the inverted process that transforms the output fuzzy variable (computed by the set of inference rules between the input variables) in a crisp, real value $x \in R$ (normally sent back to the process as control feedback).

Fuzzy logic models can be developed from expert knowledge or from process (patient) input-output data. In the first case, fuzzy models can be extracted from the expert knowledge of the process. The expert knowledge can be expressed in terms of linguistics, which is sometimes faulty and requires the model to be tuned. Therefore, identifying the processes is a more attractive way which uses the help of expert knowledge. This process requires defining the model

input variables and the determination of the fuzzy model type.

4. A FUZZY EXPERT SYSTEM FOR BREAST CANCER PROGNOSIS

This section explains the breast cancer prognosis input-output features then it presents the specification of the fuzzy expert system and the design of its corresponding components.

4. 1. Breast Cancer Prognosis Feature Specification

The proposed FIS for the evaluation of the risk of the breast cancer consists of six inputs: age, age of first menstrual cycle, age at last menstrual period (LMP), age at first pregnancy, body mass index (BMI), and smoking. These parameters were identified with the help of three experts (one obstetrician and two midwives). However, most of the features are in agreement with other similar studies [22, 23] and complete them.

The output zone reflects the percentage of risk factor for breast cancer in the female under observation. It classifies females in five categories: very low, low, medium, high and very high. Feature specifications and output feature are described in Table 1. The input and output variables are modeled using a Gaussian membership function as follows:

$$\mu(x, m, \sigma) = \exp\left[-\frac{1}{2}\left(\frac{x-m}{\sigma}\right)^2\right] \tag{1}$$

4. 2. Fuzzy Rule-based Expert System Specification

For each linguistic term associated to the features elicited for the prognosis of the risk of breast cancer, a fuzzy set and corresponding membership function were designed. Figure 2 shows the membership function associated to the features explained in Table 1. A fuzzy rule set establishes a relationship between different input fuzzy sets and output sets. The proposed rule base fuzzy expert system consists of a set of fuzzy rules, which are extracted using the knowledge of three medical experts.

TABLE 1. Feature specification of the breast cancer risk assessment

Feature	Description
Age	Age is one of the main factor
Age of first menstrual cycle (FMC)	Risk significantly increases with the age of menarche
Age at last menstrual period (LMP)	The increase in risk may be due to a longer lifetime exposure to the hormones estrogen and progesterone
Age at first pregnancy (FPA)	The women having pregnancy before 20 year of age have low risk of breast cancer in comparison to the women having pregnancy after the age of 20.
Body mass index (BMI)	The BMI factor of women after post menopause age increases the risk of breast cancer
Smoking	Smoking is an effective factor in most cancers including breast cancer

TABLE 2. Rule set of the expert fuzzy system for breast cancer risk prognosis

Rule 1. If (age is very young) and (FMC is normal) and (LMP is normal) and (FPA is normal) and (BMI is low) then (risk factor is very low)
Rule 2. If (age is very young) and (FMC is normal) and (LMP is normal) and (FPA is normal) and (BMI is low) then (risk factor is very low)
Rule 3. If (age is young) and (FMC is late) and (LMP is normal) and (FPA is late) and (BMI is high) and (smoking is medium) then (risk factor is low)
Rule 4. If (age is young) and (FMC is normal) and (LMP is late) and (FPA is normal) and (BMI is high) and (smoking is medium) then (risk factor is medium)
Rule 5. If (age is middle) and (FMC is late) and (LMP is normal) and (FPA is late) and (BMI is high) and (smoking is medium) then (risk factor is medium)
Rule 6. If (age is middle) and (FMC is normal) and (LMP is normal) and (FPA is normal) and (BMI is low) then (risk factor is very low)
Rule 7. If (age is old) and (FMC is late) and (LMP is late) and (FPA is normal) and (BMI is high) and (smoking is high) then (risk factor is very high)
Rule 8. If (age is old) and (FMC is early) and (LMP is normal) and (FPA is late) and (BMI is High) and (smoking is low) then (risk factor is medium)
Rule 9. If (age is very old) and (FMC is late) and (LMP is late) and (FPA is normal) and (BMI is high) and (smoking is low) then (risk factor is high)
Rule 10. If (age is very old) and (FMC is late) and (LMP is normal) and (FPA is normal) and (BMI is normal) then (risk factor is medium)

The rules of the fuzzy expert system for breast cancer prognosis are given in Table 2. The rule set of the fuzzy inference system is represented in Figure 3. This figure illustrates the Mamdani inference model; each row represents one rule in the rule set and columns show input and output variables. The vertical red lines represent the firing strength of fuzzy sets involved in the rules antecedent according to the input given to the FIS.

5. EXPERIMENTAL RESULTS AND PERFORMANCE EVALUATION

The fuzzy expert system has been successfully developed and tested for predicting the risk of developing breast cancer using a dataset including 80 female information who referred to hospital for breast cancer screening with or without breast cancer. The dataset was collected from cancer institute at ImamKhomeini hospital in Tehran. The dataset includes 30% patient with breast cancer and 70% healthy people.

The performance evaluation were conducted using three different methods: (1) comparing the LMSE of the FIS to the real results, (2) comparison of the obstetrician judgment with the FIS on unseen samples, and (3) using statistical hypothesis test. These are explained in the rest of this section.

The fuzzy expert system was implemented in Matlab. For evaluation purpose, the least mean square of the error (LMSE) was calculated which compares the result of the fuzzy expert with the real dataset results. The following results were obtained using the fuzzy expert system for assessment of the risk of breast cancer on the real females dataset. Furthermore, a specialist physician (obstetrician) confirmed the result of fuzzy expert system for all 80 people and 20 other

samples, which were not included in the process of design of the FIS, with an average accuracy of 96%.

In order to compare the results of proposed fuzzy expert system for breast cancer prognosis, the designed fuzzy expert system in this study was compared to the similar works in Table 3. One of the main drawbacks of most of presented approaches is that they have not been evaluated on real datasets. Consequently, their performance on real circumstances is not clear. The comparison results reveal the superiority of the designed method in terms of interpretability and accuracy compared to the other related works with an average accuracy of 95%, which shows the superiority of the system for the prognosis. The efficiency of the proposed method was statistically evaluated using t-test hypothesis testing approach. We performed the right-tailed t-test with the following null hypothesis as:

$$H_0: \mu > 95\% \quad (2)$$

where μ is the mean of the accuracy results obtained on the dataset. The t-test result failed to reject the null hypothesis with significant value $\alpha=0.05$ at $p\text{-value}=0.81$ which confirms the FIS has an average accuracy of 95% on the dataset. The performance result of the fuzzy expert system reveals an average accuracy of 95% with 95% confidence interval [93.8%, 98.2%] for all categories (healthy and unhealthy) in the dataset. The confidence intervals are statistically calculated using the mean and standard deviation values obtained from the value of output membership function using the method explained in the literature [6]. The main advantages of the FIS compared to others similar works are:

- 1) It applies the Mamdani FIS to capture the uncertainty in the knowledge of expert. This allows us to describe the knowledge in more intuitive manner, and explains the expert system reasoning to physicians.

2) Furthermore, it does not need input variables obtained from clinical experiments or surgery, thus it is applicable for prediction of the risk of developing breast cancer even in healthy females.

3) Performance evaluation on real circumstances reveals the superiority of the presented fuzzy expert system in terms of trade off between accuracy and interpretability..

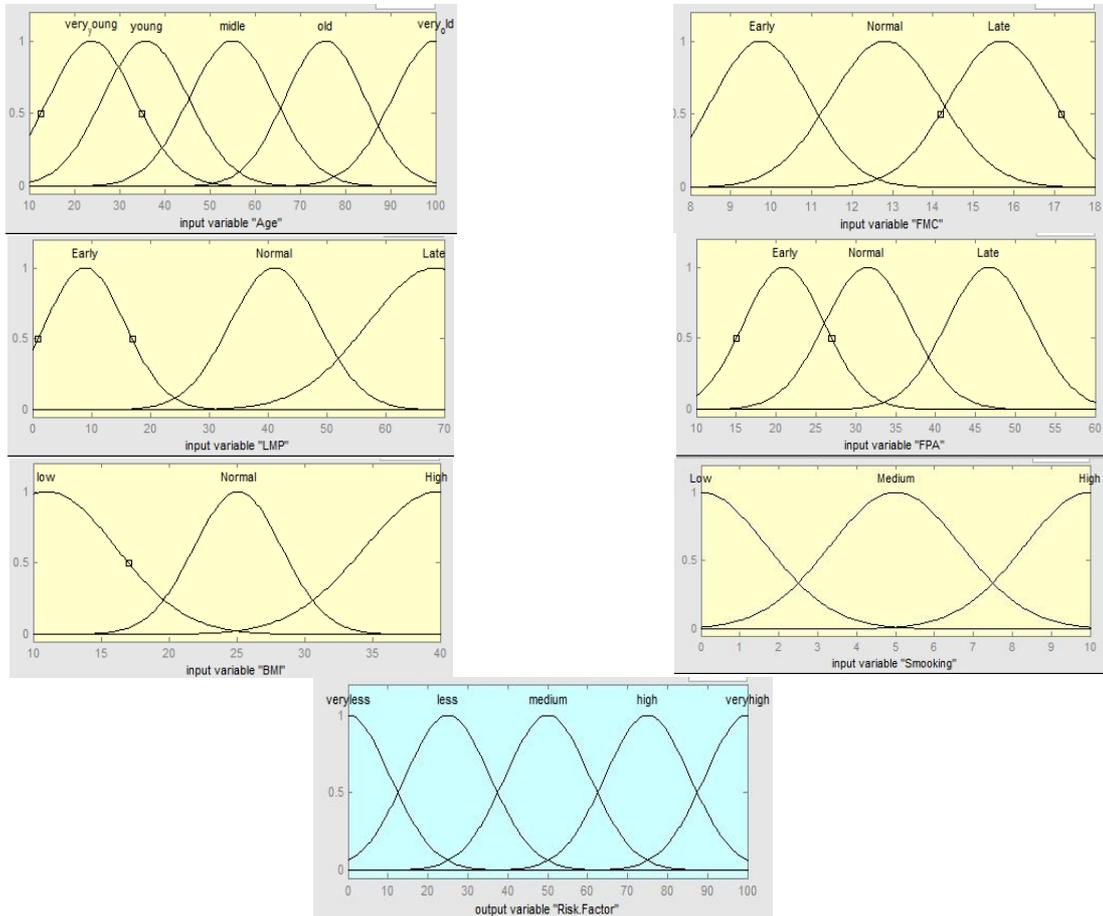


Figure 2. Membership functions associated to the breast cancer prognosis input-output features

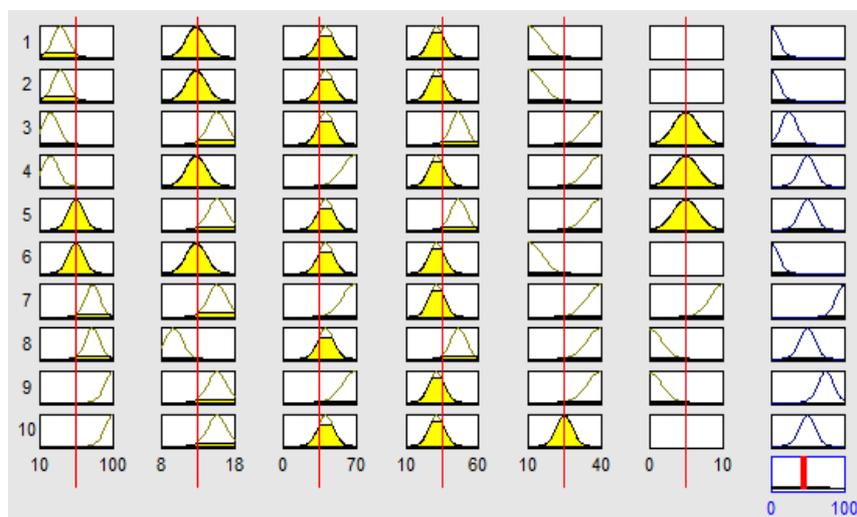


Figure 3. A representation of fuzzy inference system for breast cancer prognosis

TABLE 3. Comparison to similar works

Approach	Input variable number	Output variable type	Accuracy
Fuzzy logic system [21]	4	Fuzzy	Not reported
Fuzzy inference system [25]	2	Fuzzy -Crisp	Not reported
Fuzzy expert system [26]	3	Fuzzy	Not reported
Fuzzy-probabilistic multi agent system[23]	7	Crisp	88.37%
Fuzzy inference system [22]	8	Fuzzy	78.33%
Fuzzy expert system [1]	3	Fuzzy	Not reported
Adaptive neuro-fuzzy inference system [20]	2	Crisp	Not reported
Fuzzy logic system [24]	4	Fuzzy	Not reported
Fuzzy logic system [27]	5	Fuzzy	72.1%
Fuzzy expert system[This work]	6	Fuzzy	95%

6. CONCLUSIONS

This study presented a fuzzy rule-based expert system for prognosis of the breast cancer in healthy and unhealthy females. The proposed FIS predicts the risk of the breast cancer developing using features related to clinical history of females.

The fuzzy expert system was successfully developed and tested for assessing the risk of breast cancer in 80 female dataset with or without breast cancer who referred to hospital for breast cancer screening. The performance results reveal an average accuracy of 95% for all categories in the dataset (healthy and unhealthy).

This approach provides wide spread of information to help the physician in reaching a more logical conclusion for a more accurate prediction of the breast cancer risk. Furthermore, it can identify females with high risk of developing breast cancer. This approach is beneficial for early diagnosis of the breast cancer and right treatment at early stages of the developing breast cancer, which can improve the survival rate.

Our future work is to learn the FIS using soft computing technique such as ANFIS (Adaptive Neural Network Fuzzy Inference System) and GA(Genetic Algorithm) and verify the FIS results on more real datasets.

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Prognosis

تکنیکهای محاسبات نرم نقش مهمی در سیستمهای تصمیم مبتنی بر عدم قطعیت ایفا می کنند. از جمله کاربردهای محاسبات نرم فازی استفاده آن در پیش بینی و تشخیص پزشکی است. یک سیستم خبره فازی دانش موجود در سیستم را با قوانین زبانی مدل می کند و با کلمات عمل استدلال را انجام می دهد. هرچند مطالعات متعددی برای تشخیص سرطان سینه گزارش شده، اما تنها اندکی از مطالعات برای پیش بینی سرطان سینه گزارش شده اند. این درحالی است که پیش بینی سرطان سینه نیز از عدم قطعیت توأم با داده های ورودی نادقیق و کامل نبودن علم پزشکی و دانش مورد نیاز رنج می برد. این تحقیق یک سیستم خبره فازی برای پیش بینی سرطان سینه را نشان می دهد. برای این منظور از مدل استنتاج فازی ممدانی استفاده شده که مناسب تر و از قابلیت انعطاف بالایی برای تفسیر کردن دانش فرد خبره در طول فرآیند پیش بینی برخوردار است. مزیت اصلی این روش در مقایسه با مطالعات دیگر توانایی این روش در تعیین ریسک سرطان سینه در زنان سالم می باشد. در نهایت سیستم خبره فازی بر روی پایگاه داده حقیقی و نتایج حاصله از سیستم ارزیابی و این ارزیابی را با تصمیمات موجود مقایسه می کند. کارایی بدست آمده از سیستم بر روی پایگاه داده حقیقی در جریان پیش بینی سرطان سینه، میانگین ۹۵٪ را نشان می دهد. این روش، روشی خوشبینانه برای پیش بینی کردن میزان ریسک سرطان سینه می باشد و باعث تشخیص زود هنگام سرطان و جلوگیری از مرگ و میر افراد می گردد.

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