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Breast Cancer Risk Assessment by a Hybrid Interval Type-2 Fuzzy Cognitive Map Method

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ABSTRACT: This paper proposes a new method for accessing the breast cancer risk called Hybrid High-order Interval Type-2 Fuzzy Cognitive Map (H-HIT2 FCM). In a simple Fuzzy Cognitive Map (FCM), the weights between nodes and activation functions are constant in each iteration. As an extension in the high order FCM, each node has a different transformation function to make it more flexible. However, using FCM or high order FCM can not make a favorable response in uncertain situations. Applying type-2 Fuzzy Cognitive Map to obtain the weights of FCM, the resulted method will have much better responses in such uncertain situations. An H-HIT2 FCM is proposed in this work, assessing breast cancer risk in three modes of optimistic, realistic, and pessimistic. The proposed method has three levels. In the first level, the patient's profile, family history, and the inherited factors are tested by high order FCM. In the second level, by examining the mass characteristics obtained from the mammograms, the disease risk is achieved by high-order interval type-2 FCM in three modes of optimistic, realistic, and pessimistic. The exact position of the tumor is obtained in the third level. Finally, a Support Vector Machine predicts an overall breast cancer risk. Moreover, compared to the existing methods, the accuracy of the results is desirable. The three-mode assessment will help the patients and their physician run the best treatment. The proposed method is successfully tested on a real radiology dataset, and the corresponding results are reported.

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1- Introduction

Medical diagnosis are such decision problems that usually involve complexity and uncertainty. Applying fuzzy logic to deal with uncertainty and predicting the outcomes has been strongly advocated. For instance, type-1 Fuzzy methods have been developed for classifying medical data [1]. Type-2 Fuzzy Sets (T2 FS) generalize type-1 Fuzzy Sets to effectively deal with the linguistic uncertainty, incorporating uncertainty into the fuzzy sets by membership functions [2-3].

Generally, practical analytical methods are divided into the following two categories: one is based on symbol translation method, namely the computation and processing of language phrase symbols directly; the other is based on the fuzzy interpolation principle. The linguistic variables are calculated and processed according to the membership function. These membership functions need to be redesigned to facilitate the desired lateral distance change [4-5]. T2 FS is a form of traditional fuzzy set where the membership function is a conventional fuzzy set, not a specific real number [6-8]. Thus, T2 FSs can better describe the fuzzy uncertainty [9]. Moreover, the different perceptions of healthcare providers, patients, and their families are given in the decision-making process [10]. The T2 FS principle can solve this problem very well. However, the calculation of T2 Fuzzy Sets is quite complex, which results in high computational costs [11,12]. Moreover, type-1 Fuzzy Sets and T2 FS are unsuitable for datasets with missing data. In [13], a method of generating the embedded type-1 Fuzzy membership functions is introduced, and developing the footprint of the uncertainty of the T2 FS has been presented. In [14], the optimized interval T2 FS design with triangular membership functions is done. The final T2 FS has a better classification rate than the type-1 classifier. In [15], the results demonstrate the advantages of using general T2 Fuzzy inference systems and reducing the computational cost with shadowed sets theory in most cases and less computational resources. In [16], a comparison of Interval T2 FS (IT2 FS) concerning general T2 FS for a set of diagnosis problems is presented.

The Fuzzy Cognitive Map (FCM) is suitable for the cases where incomplete or utterly missing data is available. The main features of FCM are ease of construction, flexibility in system analysis and design, and high-level decision-making. Many studies have found the suitability of FCM in medical decision support systems as an efficient inference engine for modeling complex causal relationships [18]. The nodes and weights in FCM are expressed by graph theory. Signed digraphs are used to express information statements, and the

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term "Cognitive map" describes causality relationships among variables [17]. The method for developing FCM is based on experts who use concepts and the description of the relationships between them. The use of IF-THEN rules justifies their causation suggestions among the ideas, and determines each concept's linguistic weight. Each expert explains its connection with weights. The generalized fuzzy weights suggest the total linguistic weight produced by the center of the area in the defuzzification method. The most critical weaknesses of the FCMs are their dependence on experts and uncontrolled convergence with unwanted governments [18,19].

Breast cancer risk assessment is a decision-making and classification problem which is on the main focus of this work. In [20], the risk level of breast cancer has been determined by considering the genetic profile, family history, and unique medical history. With this assessment, appropriate action is taken to consult, screen, and prevent. It is based on detecting breast cancer using the FCM method to assist professionals in medical care. An interactive risk assessment tool has been developed based on Gail model. This model is based on Dr. Mitchell Gail's model, a research scientist of cancer and genetics epidemiology. The model uses personal information from individuals, reproductive history, and breast cancer history among first-degree relatives (mothers, sisters, and girls). An estimate of the risk of developing breast cancer has been considered in [21]. Gail's model has been tested among many women and has provided accurate estimates of breast cancer risk. The main limitation of this model is that the risk of people with strong family history and other factors related to cancer is not considered [22]. Claus et. al [23] have assessed the risk of this disease based on the family history of the individuals. Although some of the other factors, including cancer data and hormones have been somewhat reviewed, by comparing Gail's model, the Claus model contains more extensive information about family history. The model operates based on first-degree relatives and second-degree relatives in breast cancer, and the age range of individuals aged 29 to 79 years [23]. In [24], the breast cancer risk assessment program calculates the risk based on the BRCA1 and BRCA2 genes, which are highly pervasive breast cancer-sensitive genes [25]. Vasu et. al tested the Gail model on the people of India in 2013. They concluded that this model often does not provide an accurate answer to Asian subjects [26]. Gail's model was tested in Canada, the United States, and other countries [27-30]. The observations and results have shown that for Asian countries, other factors along with the Gail's model should be considered, such as the impact of nutritional elements, consumption of high crops, high sugar intake, spices, and even water intake. In [31], using different artificial intelligence models provides significant advantages considering an early diagnosis. The fuzzy method is used for all the risk factors of the patients. A neuro-fuzzy method in BRCA1 and BRCA2 is the other method that is used in [32] to detect breast cancer risk. In [33], the modified K-means the algorithm is used to create a new training dataset of breast cancer that improves the performance of the Support Vector Machine model.

In this work, the hybrid high order interval T2 FCM (H-HIT2 FCM) is used to have an appropriate response to the decision-making problem. In FCM, weights are crisp, and the function used in each iteration is constant. Using high-order interval T2 FCM (HIT2 FCM), weights are considered as time-variant functions obtained by the IT2 fuzzy system. Three levels of fuzzy are discussed. In L1-HFCM Level, patient profile, family history, and inherited factors are analyzed. High-order FCM is used at this level to have a different sigmoid function in FCM. In L2-HIT2 FCM Level, by examining the characteristics of the mass obtained from the mammograms, the disease's risk is achieved in three modes of optimistic, realistic, and pessimistic by high order T2 FCM. These characteristics in FCM have uncertainties, and this is the primary motivation of using the T2 Fuzzy Cognitive Map (T2 FCM). These are influenced by each other and the overall breast cancer risk over the lifetime of patients. In each mode, the weights of FCM are obtained by the T2 fuzzy system. This method considers uncertainties and mass characteristic variability in the patient treatment time, causing to have desirable answers. The L3-Fuzzy level examines the status of the mass to calculate the risk of disease. The effect of the exact position of the mass is considered to find a risk of cancer at this level. Finally, overall risk of breast cancer is obtained using the Support Vector Machine (SVM) method. Three modes of answer (optimistic, realistic, and pessimistic) have finally stated the risk of the patients. These three modes help doctors and oncologists know about the patients' status and decide about their treatment options.

1- 1- Our Contributions

This work assesses the risk of breast cancer in three modes, namely optimistic, realistic, and pessimistic, by proposing a new method called H-HIT2 FCM applied on a radiology dataset. T2 FCM is applied due to the uncertainty in the collected data, and characteristics of mass are modeled as time-variant functions in the lifetime of patients. The overall cancer risk is finally determined using the Support Vector Machine method.

The main highlights of this paper are summarized as follows:

- T2 FCM is applied due to the uncertainty in the data, considering uncertainties in L2-HIT2 FCM level and using T2 fuzzy in this paper to have an exact robust result. IT2 FCM has less complexity in calculations in comparison to T2 FCM.
- High order T2 FCM is used to have three modes of outputs (optimistic, realistic, pessimistic) applying different weight functions on FCM. These three modes can help oncologists and patients to know better about the status of diseases.
- Characteristics of mass are modeled as a time-variant function in the lifetime of patients. Dependencies of characteristics with each other and the risk grade are considered.
- The exact position of mass is determined to help predict breast cancer risk.

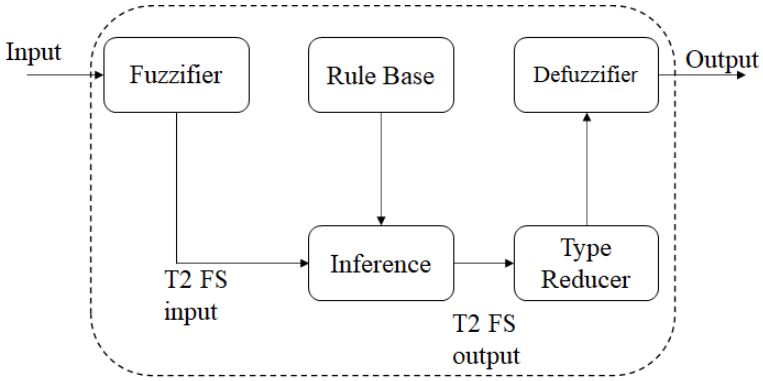


Fig. 1. Structure of Type-2 FS [1].

- The Support Vector Machine is used to find the overall patients' risk as low, moderate, and high risk.
- The proposed method is tested on a real dataset collected from radiology to validate our findings.

The rest of the paper is organized as follows: the next section presents the fundamental concepts. Using T2 fuzzy in FCM is discussed in section 3. Section 4 is devoted to the proposed method and its experimental results. Finally, section 5 concludes the paper and suggests some directions for future research.

2- Fundamental Concepts

2- 1- Interval Type-2 Fuzzy systems

T2 FSs are typically used in the case of uncertainty. In such situations, using precisely specified type-1 Fuzzy Sets membership functions is not suitable. Unlike type-1 fuzzy logic, the T2 fuzzy logic systems use individual fuzzy sets with membership grades that are fuzzy sets. These fuzzy secondary grades provide additional degrees of freedom for modeling with the dynamic input uncertainties [1].

A fuzzy logic system is called a type-1 FSs if it is described using type-1 Fuzzy Sets, while an FS that uses at least one T2 fuzzy set is called T2 FS. T2 FS has more freedom than type-1 FS because it contains more parameters. Therefore, T2 FS has more freedom in dealing with ambiguity than type-1 FS [34]. The structure of an overall T2 FS is shown in Figure 1 [1].

T2 FS is similar to type-1 FS, where the significant difference is using T2 FS rather than type-1 fuzzy sets. Type-1 FS output processor converts a type-1 fuzzy set to a definite number, while T2 FS has two components in the output processor. The first is the type reduction that converts a T2 FS to a type-1 fuzzy set, and the second is defragmentation, which converts the type-1 fuzzy sets to a definite number. T2 FS requires general computational cost and complex execution compared to type-1 FS, which is the specific case of T2 FS. The interval T2 FS has been widely used to reduce computational burden [11, 12].

Type-2 T2 FS is based on the Fuzzy logic system, is shown in three dimensions. A membership degree is a fuzzy set and not fixed. The third dimension is the membership function value at each point of the Footprint of Uncertainty (FOU) that has a two-dimensional domain [35]. Interval T2 FS shows membership degree with an interval instead of FS. Therefore, FOU is used to describe interval T2 FS. Supposing that interval T2 FS consists of $\boldsymbol{M}$ rules and $\boldsymbol{p}$ antecedents in each law, the $\boldsymbol{l}$ th rule is as Equation (1).[3].

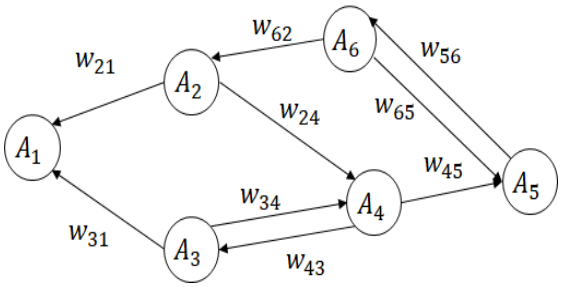
The general structure of the l th rule for an interval T2 FS is $l = 1,..,M$.

$$R^l: If\ x_1\ is\ \tilde{F}_1^l\ and\ ....and\ x_p\ is\ \tilde{F}_p^l, \qquad Then\ y\ is\ \tilde{G}^l \quad (1)$$

Where the interval T2 fuzzy system has p inputs $x_1 \in X_1,\ldots,x_p \in X_p$, and one output $y \in Y$. x_i which is described by Q_i linguistic terms that are mod- eled as interval T2 FS $T_{x_i} = \{\tilde{X}_{ij}\}_{j=1}^{Q_i}$. y is also defined by Q_y linguistic terms that are modeled as interval T2 FS $T_y = \{\tilde{Y}_j\}_{j=1}^{Q_y}$. $\tilde{F}_1^l \in T_{x_1},\ldots,\tilde{F}_p^l \in T_{x_p}$, $\tilde{G}^l \in T_y$ [28].

2- 2- High order Fuzzy Cognitive Map

The FCM contains a set of nodes and edges between the nodes. Figure 2a shows an example of the FCM model. Nodes $A_1, A_2,\ldots,A_n$, show the concepts that are examined to describe the main behavioral characteristics (states and variables) of the system, while edges affect causality between concepts (nodes). In FCM, the node activation levels (sometimes also called node values) are fuzzy and variable with time, measured into the interval $[0,1]$. The bond strength (also called weight) between the A_j node and the A_i node is denoted by w_{ij} , and is measured by the numerical values specified in $[-1,1]$. The absolute amount of the weight corresponds to the relationships between the nodes.



a) FCM model

	A_1	A_2	A_3	A_4	A_5	A_6
A_1	0	w_{21}	w_{31}	0	0	0
A_2	0	0	0	0	0	w_{62}
A_3	0	0	0	w_{43}	0	0
A_4	0	w_{24}	w_{34}	0	0	0
A_5	0	0	0	0	0	w_{65}
A_6	0	0	0	0	w_{56}	0

b) The corresponding relationship matrix

Fig. 2. FCMmodel and its relationship matrix

The FCM can be represented not only as the directed graphs, but also described as an $n \times n$ matrix. The FCM matrix, also called the relationship matrix, stores the full values of the weights of FCM. Figure 2b shows the relationship matrix of the FCM model. The FCM dynamic is generally described as equation (2):

$$A_i^{(t+1)} = f\left(\sum_{\substack{j=1 \\ j\neq i}}^{n} A_j^{(t)} . w_{ji}\right) \qquad (2)$$

of the ith node at iteration $t+1$. f is a continuous nonlinear function such as bivalent (sign), trivalent, hyperbolic tangent, and sigmoid. The sigmoid function is used in this paper and is defined as equations(3).

$$f_{sigmoid} = \frac{1}{1+e^{-x}} \qquad x \in \mathbb{R} \qquad (3)$$

Once all the weights of FCM, w_{ij}, have been determined, the FCM starts from a given initial state through numerical iteration calculations by the equation (2). This may lead to a variety of dynamic behaviors of FCM [36].

The activation level of i th node at the moment $t+1$ in equation (2). only depends on the activation values of all nodes at the moment t, which may diminish the ability of the FCM to describe the dynamic behavior of the complex system. To increase the ability of FCM, equation (4) is used instead of (2).

$$A_i^{(t+1)} = f\left(\sum_{j=1}^{n} w_{ij}^{1}.A_j^{(t)} + w_{ij}^{2}.A_j^{(t-1)} + \cdots + w_{ij}^{k}.A_j^{(t-k+1)} + w_{0j}\right) \qquad (4)$$

where w_{ij}^{l} is the weight from node A_j to node A_i at $t-k+1$th moment, $l = 1,2,\ldots,k$, w_{0j} is the bias related to the j th node, and all the weights in this method are not time-variant and are crisp in each iteration [36].

To enhance FCM flexibility, we enable each FCM node to perform a different transformation function. Accordingly, the sigmoid activation function in equation (3), usually performing as an FCM transformation function, is augmented by a λ_i parameter as the steepness parameter in the i th node in equation (5).

$$f_i(x) = \frac{1}{1+e^{-\lambda_i x}} \qquad x \in \mathbb{R}, \lambda_i \geq 0 \qquad (5)$$

Therefore, by replacing equation (5) into (4), equation (6) is obtained. Equation (6) describes the dynamic of high order FCM [38].

$$A_i^{(t+1)} = f_i\left(\sum_{j=1}^{n} w_{ij}^{1}.A_j^{(t)} + w_{ij}^{2}.A_j^{(t-1)} + \cdots + w_{ij}^{k}.A_j^{(t-k+1)} + w_{0j}\right) \qquad (6)$$

3- Interval Type-2 Fuzzy in FCM

In FCM, when the weights or concepts are not crisp and there are uncertainties, type-1 fuzzy sets are not suitable. Hence, applying IT2 FS in FCM causes in having a desirable answer in decision-making problems. T2 FCM and HIT2 FCM are introduced in this section for an appropriate analysis.

3- 1- Interval Type-2 Fuzzy Cognitive Map

In FCM, the w_{ij} s are the crisp numbers and are the weights from node j to node i. The weights in equation (2) are not dependent on iteration t. Therefore, in this paper, T2 FCM is used to consider the uncertainties and have suitable results as equation (7). In T2 FCM, the weights are denoted by (W_{ji}).

$$A_i^{(t+1)} = f\left(\sum_{\substack{j=1 \\ j\neq i}}^{n} A_j^{(t)} . W_{ji}\right) \qquad (7)$$

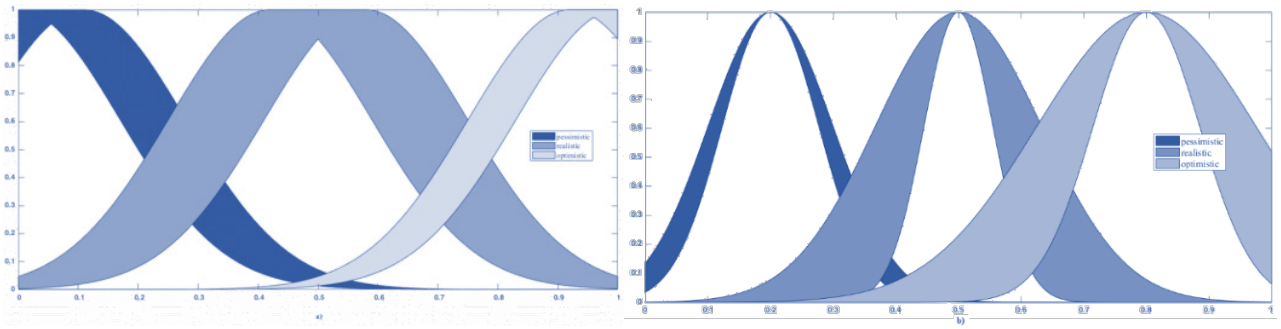


Fig. 3. a) The typical interval T2 FS of three modes of optimistic, realistic, and pessimistic with uncertain mean, b)The typical interval T2 FS of three modes of optimistic, realistic, and pessimistic with an uncertain standard deviation

where W_{ji} has uncertainties and is obtained by T2 Fuzzy logic system.

In T2 fuzzy logic, an interval T2 fuzzy set is denoted $\tilde{F}$ as (8) [30]:

$$\tilde{F} = \left\{\left((x,u),\mu_{\tilde{F}}(x,u)\right)\middle| x \in X, u \in J_x \subseteq [0,1]\right\} \quad (8)$$

where $\mu_{\tilde{F}}(x,u)$ is the membership function of $\tilde{F}$, and the secondary grade is equal to one. In the proposed T2 FCM, the gaussian primary membership function with uncertain mean or uncertain standard deviation is used as (9), respectively

$$\mu_{\tilde{F}}(x) = \frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(x-m)^2}{2\sigma^2}}, m \in [m_1, m_2], \sigma = constant$$

or (9)

$$\mu_{\tilde{F}}(x) = \frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(x-m)^2}{2\sigma^2}}, \sigma \in [\sigma_1, \sigma_2], m = constant$$

where m is the mean and σ is its standard deviation. The Genetic Algorithm (GA) chooses the best membership .function. The detail is discussed in section 3.2

In this paper, the centroid type-reduction is used as equation (10).

$$y_c = \int_{\theta_1 \in J_{y_1}} \cdots \int_{\theta_n \in J_{y_n}} 1 \Big/ \frac{\sum_{l=1}^{n} y_l \theta_l}{\sum_{l=1}^{n} \theta_l} \quad (10)$$

where $\theta_n \in J_{x_n} \subseteq U \in [0,1]$, $\theta_1, \theta_2, \ldots, \theta_n$ belongs to the embedded fuzzy set, the secondary grades of an interval T2 FS are all equal to one, n denotes the number of discretized samples in the output domain of variable y, and y_l is the discretized sample.

3- 2- High Order Interval Type-2 FCM

High order Interval T2 FCM (HIT2 FCM) is used in this part that analyzes the answers in three modes (optimistic, realistic, and pessimistic). The HIT2 FCM dynamic is as (11); thus, the weight function from node j to node i at iteration t is defined as $W_{ji}^{(t)}$. In this paper, $W_{ji}^{(t)}$ is found by T2 fuzzy system.

$$A_i^{(t+1)} = f_i\left(\sum_{\substack{j=1 \\ j\neq i}}^{n} A_j^{(t)} . W_i^{(t)}\right) \quad (11)$$

The typical interval T2 FS of each mode (optimistic, realistic, and pessimistic) is shown in Figure 3. As shown Figure 3a, all fuzzy sets are Gaussian membership functions with an uncertain mean ($m_i \in [m_{i1}, m_{i2}], \sigma = constant$). Moreover, Figure 3b, all fuzzy sets are Gaussian membership functions with uncertain standard deviation ($\sigma_i \in [\sigma_{i1}, \sigma_{i2}], m = constant$), where i=1,2,3 indicate the optimistic, realistic, and pessimistic modes, respectively.

In this part, the main goal to have a suitable answer is finding the best fuzzy set between a primary function with $[\mathbf{m}_{i1}, \mathbf{m}_{i2}], \boldsymbol{\sigma} = \mathbf{constant}$ or $\boldsymbol{\sigma}_i \in [\boldsymbol{\sigma}_{i1}, \boldsymbol{\sigma}_{i2}], \mathbf{m} = \mathbf{constant}$ for each mode ($\mathbf{i} = 1,2,3$) by GA. The cost function is considered as (12):

$$Cost = \frac{1}{(c-2)n} \sum_{t=2}^{c-1} \sum_{i=1}^{n} \left\| \hat{A}_i(t) - A_i(t) \right\|^2 \quad (12)$$

where A_i is the activation level of the i th node at iteration t, $\hat{A}_i$ is obtained by HIT2 FCM, c is the number of input data (observations), and n the number of concepts.

The proposed HIT2 FCM algorithm is as follows:

HIT2 FCM algorithm

Step1: *for* $i, j = 1, \dots, n$

Step2: *for all* N *experts, set credibility weight* $b_t = 1$

Step3: *for* $t = 1, \dots, N$

***Step4*:** finding $[m_{i1}, m_{i2}]$ and σ, or $[\sigma_{i1}, \sigma_{i2}]$ and m for each fuzzy set by GA.

Step5: For each interconnection $(A_i to\ A_j)$, the weights $W_{ji}^{(t)}$ is obtained by T2 FCM.

Step6: If the number of weights with the same sign is less than $\pi \times N$ THEN ask the experts to reassign the weights for this particular interconnection and go to step 5, ELSE take into account the weights of the greater group with the same sign. Then consider that there are no other weights. Penalize the experts who choose "wrong" signed weight with a new credibility weight $b_t = \mu_1 \times b_t$.

Step7: For the weights with the same sign, find their average value $W_{ji}^{(ave)} = 1/N \sum_{t=1}^{N} b_t W_{ji}^{(t)}$

Step8: If $\left|W_{ji}^{(ave)} - W_{ji}^{(t)}\right| \geq W_1$ (W_1 is the weight matrix of the first expert), THEN consider that there is not any change in weight $W_{ji}^{(t)}$, penalize the tth expert $b_t = \mu_2 \times b_t$ and go to step 6

Step9: IF all the $n \times n$ interconnection is not examined, go to step 1, ELSE construct the new weight matrix $W = f_i\left(\sum_1^n W_{ji}^{(t)}\right)$, which has elements the weights $W_{ji}^{(ave)}$.

In most decision problems, finding the best answer is very difficult and sometimes a percentage of probability of victory or failure is requested. Therefore in this method, by finding the responses of three modes, the accuracy of answers is readily discussed. The time-variable weights are the main feature of the HIT2 FCM level. In most problems, the weights of FCM are the time variable

($time = t = 1, \dots, T$,*and* T = numbers of iterations).

4- The Proposed Method and Experimental Results

In this section, the proposed H-HIT2 FCM in three levels namely L1-HFCM, L2-HIT2 FCM, and L3-Fuzzy, are expressed. H-HIT2 FCM obtains an overall breast cancer risk for each patient. As a result, any patient's overall risk is also in three modes of optimistic, realistic, and pessimistic. Eighty cases train the proposed H-HIT2 FCM and this method is later examined for twenty test data.

4- 1- The Structure of the Proposed Method

Analysis of the risk of breast cancer is done at three levels. In Figure 4, the overall performance diagram of this approach is presented to provide a complete analysis of breast cancer risk. These three levels are expressed as L1-HFCM, L2-HIT2 FCM, and L3-Fuzzy levels. In the L1-HFCM level, patients' Demographic Risk Factors are analyzed, and in the L2-HIT2 FCM Level, characteristics of the mass are obtained from the mammogram image. In this level, investigating the shape of the tumor and properties is done in three modes of optimistic, realistic, and pessimistic. In finding the risk of this level, the effect of mass characteristics is considered as a T2 fuzzy set. In addition to L1-HFCM and L2-HIT2 FCM, in the L3-Fuzzy level, the position of the mass can be examined by mammography images. Thus, by modeling the breast on the coordinate axes (of course, by normalizing the size of the mammograms, the size of the chest is considered the same)

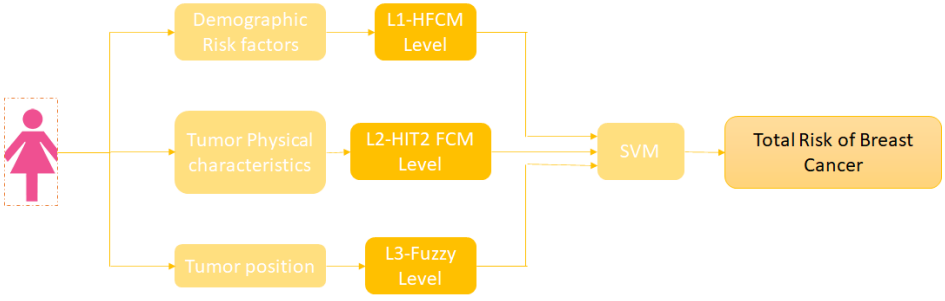


Fig.4. Graphical diagram of the proposed method for obtaining breast cancer risk

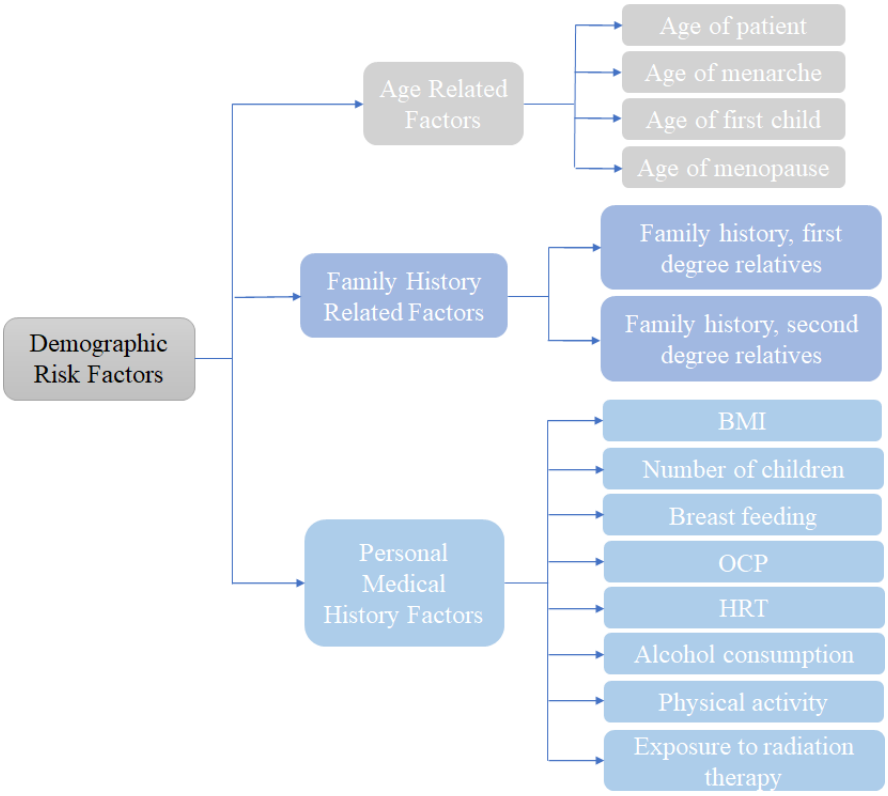


Fig. 5. Familial breast cancer risk factors.

and determining the origin of the coordinates, fuzzy rules are obtained by experts. Due to the patient's condition, the overall risk of cancer, based on each level's risk, is found by the SVM method. Therefore, the overall risk in these three modes is obtained by SVM method, and the answers of these three modes can be a better suggestion for the patient's treatment.

4- 2- L1-HFCM Level

The Demographic Risk Factor (DRF) is analyzed to find a risk of the L1-HFCM level. The construction of an FCM-based system for modeling DRFs and BC risk classification based on these factors requires identifying risk factors and their impact. DRFs are divided into three types, age-related factors, family history related factors, and personal medical history factors shown in Figure 5.

The demographic factors shown in Figure 5 are analyzed in this level for eighty training data. First, all factors are normalized between zero and one $[0,1]$. Normalizing these data is as (13), where X_{min} is the minimum amount of that factor, and X_{max} is the maximum amount.

$$X_{normalized} = \frac{(X - X_{min})}{(X_{max} - X_{min})} \tag{13}$$

Table 1 shows the fuzzy set related to different ranges of DFR [17]. Linguistic values of DRF factors are assigned by experts. As an example:

$$C = [52132443012821600410],$$

for a patient, the normalized factors are as $C = [0.410.630.420.670.750.670.350.330.420.12500410]$. The centroid defuzzification method is implemented to calculate the numerical value of the weight in the range [-1,1].

The risk of eighty training patients in L1-HFCM level is achieved in Figure 6. The risk of L1-HFCM Level can be obtained in three groups: low [0 0.36], moderate [0.36 0.69] and high [0.69 1].

4- 3- L2-HIT2 FCM Level

Here, the second level of risk analysis is evaluated. In the L2-HIT2 FCM Level, the risk is obtained by getting the mass characteristics. Of course the risk of this level risk is calculated by considering the individual's risk in the three modes (optimistic, realistic, and pessimistic). Moreover, by considering the risk of the disease, the treatment of the disease, the risky years, and the surgery time of those areas are diagnosed. Characteristics of mass during the procedure are not crisp and are considered uncertain. Therefore, T2 fuzzy is necessary at this level. In this paper, the fuzzy sets of weights are Gaussian functions that the mean or standard deviation are considered uncertain. A GA selects the best membership function for each mode.

Table 1. Description of Fuzzy values of DRFs [13]

DRFs	Fuzzy values of DRF			
C_1: Age of patient	>60 very high	50- 60 high	35- 50 moderate	<35 low
C_2: Age at menarche	>15 high	12-15 moderate		<12 low
C_3: Age at first child	>30 high	21-30 moderate		<21 low
C_4: Age at menopause	>60 very high	55-60 high	45-55 moderate	<45 low
C_5: Family history of 1st-degree relatives	≥ 2 high	=1 moderate		=0 low
C_6: Family history of 2st -degree relatives	≥ 2 high	=1 moderate		=0 low
C_7: BMI	>28 very high	24-28 high		18-24 moderate
C_8: Number of children	≥ 2 high	=1 moderate		=0 low
C_9: Breastfeeding (months)	>12 high	6-12 moderate		0-6 low
C_{10}: OCP	≥5 high	<5 moderate		=0 low
C_{11}: HRT	=1 Yes			=0 No
C_{12}: Physical exercise	=1 Yes			=0 No
C_{13}: Alcohol intake (drinks/day)	>2 high	1-2 moderate		=0 low
C_{14}: Exposure to chest radiation therapy	> 2high	1-2 moderate		=0 low

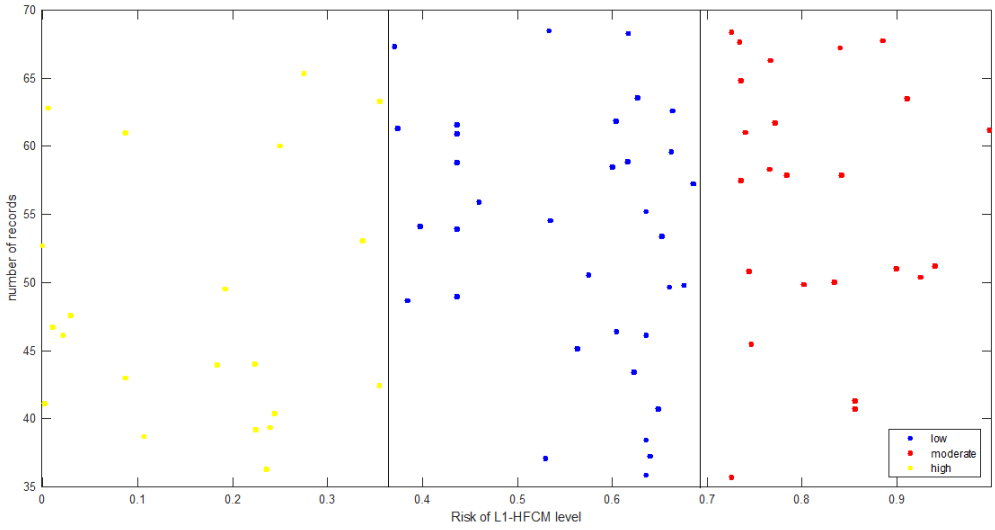


Fig. 6. The risk of patients in L1-HFCM level (low, moderate and high)

At this level, from mammograms of a patient, the masses are detected by image processing. The characteristics of masses are achieved, and the weights between the factors and overall breast cancer risk are obtained. Figure 7 shows the tumor is detected in a mammogram image. The input image is shown in Figure 7a; afterwards, by filtering the image (Figure 7b), the bounding box of the tumor in an image is detected in Figure 7c. After image processing, the tumor is detected in Figure 7f. In Figure 7d, the tumor is shown and the outline of the tumor is illustrated in Figure 7e.

After detecting a tumor from the image, the characteristics are extracted as Table 2. Twelve characteristics of mass are found, and like L1-HFCM, the risk of L2-HIT2 FCM level is determined.

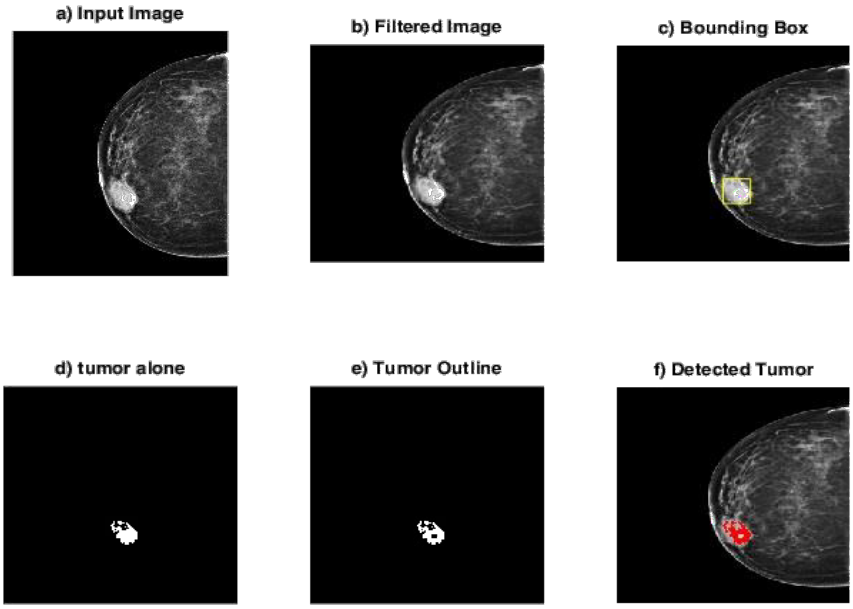


Fig. 7. A view of a mass in the mammography image, the shape of the mass and its range

Table 2. L-2-HIT2 FCM Level Implications for Tumor Grading

Table 2. L-2-HIT2 FCM Level Implications for Tumor Grading

C_1	E (energy)	$E = \sum_{i=1}^{n}\sum_{j=1}^{n} P(i,j)$
C_2	e (entropy)	$e = \sum_{i}\sum_{j} P(i,j)\, log_2\, P\,(i,j)$
C_3	C (contrast)	$C = \sum_{i=1}^{n}\sum_{j=1}^{n} \lvert i-j\rvert^2 \times P(i,j)$
C_4	H (homogeneity)	The momentary inverse difference and the relative smoothness of the area are measured.
C_5	c (correlation)	This concept shows the dependence of the gray line on the mass.
C_6	D (dissimilarity)	Show the similarity or dissimilarity between pixels. $D = \sum_{i,j=0}^{n-1} \lvert i-j\rvert p(i,j)$
C_7	A (area)	The total number of pixels represents the mass.
C_8	P (perimeter)	Determines the total number of pixels around the mass.
C_9	max radius	Measures the maximum distance from the center of the mass.
C_{10}	Eccentricity	$Eccentricity = \sqrt{1-\left(\frac{Min\ Radius}{Max\ Radius}\right)^2}$
C_{11}	Circularity	$A = Area - \pi \times Max\ Radius^2$ $B = \pi \times Max\ Radius^2 - \pi \times Min\ Radius^2$ $Circularity = \sqrt{A^2 - B^2}$
		$\left(\frac{perimeter}{}\right)$

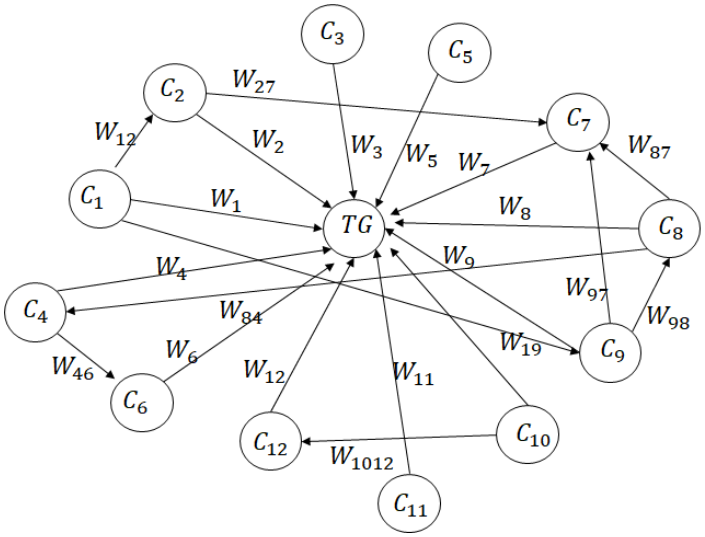


Fig. 8. L2-HIT2 FCM level

The characteristics are derived from the mass, and the relationship between the factors is shown in Figure 8. The weights are considered a transformation function. At this level, the risk is considered in three modes.

In Figure , TG is the tumor grade, $W_{ji}(t)$ has uncertainty and is concluded in three modes optimistic, realistic, and pessimistic. $W_j(t)=W_{ji}(t)(i=j)$, $i,j=1,...,12$, and $t=[1,lifetime]$ and $C_1,C_2,\ldots,C_{12}$ are the mass characteristics. The communication matrix between the factors is as:

	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}	TG
C_1	0	W_{12}	0	0	0	0	0	0	W_{19}	0	0	0	W_1
C_2	0	0	0	0	0	0	W_{27}	0	0	0	0	0	W_2
C_3	0	0	0	0	0	0	0	0	0	0	0	0	W_3
C_4	0	0	0	0	0	W_{46}	0	0	0	0	0	0	W_4
C_5	0	0	0	0	0	0	0	0	0	0	0	0	W_5
C_6	0	0	0	0	0	0	W_{67}	0	0	0	0	0	W_6
C_7	0	0	0	0	0	0	0	0	0	0	0	0	W_7
C_8	0	0	0	W_{87}	0	0	W_{87}	0	0	0	0	0	W_8
C_9	0	0	0	0	0	0	W_{97}	W_{98}	0	0	0	0	W_9
C_{10}	0	0	0	0	0	0	0	0	0	0	0	W_{1012}	W_{10}
C_{11}	0	0	0	0	0	0	0	0	0	0	0	0	W_{11}
C_{12}	0	0	0	0	0	0	0	0	0	0	0	0	W_{12}

(14)

Table 3. A typical W_{ji}

W_{ji}	m_i						σ_i					
	m_{1i}		m_{2i}		m_{3i}		σ_{1i}		σ_{2i}		σ_{3i}	
	m_{11}	m_{12}	m_{21}	m_{22}	m_{31}	m_{32}	σ_{11}	σ_{12}	σ_{21}	σ_{22}	σ_{31}	σ_{32}
W_{12}	0.09	0.151	0.485	0.510	0.872	0.932	0.67		0.9		1.09	
W_{19}	0.011	0.195	0.5	0.5	0.803	0.902	0.75		0.96		1.1	
W_1	0.081	0.115	0.41	0.6	0.805	0.932	0.88		0.98		1	
W_{27}	0.103		0.5		0.899		0.58	1.03	0.78	1.15	0.877	1.324
W_2	0.019	0.195	0.463	0.535	0.863	0.970	0.6		0.95		1.12	
W_3	0.027	0.180	0.495	0.515	0.895	0.910	0.65		0.967		1.1	
W_{46}	0.107		0.497		0.903		0.51	1.11	0.691	1.165	0.870	1.387
W_4	0.097	0.142	0.450	0.55	0.884	0.911	0.66		0.966		1.2	
W_5	0.095	0.165	0.395	0.61	0.866	0.923	0.68		0.899		1.13	
W_{67}	0.009	0.120	0.425	0.525	0.8	0.922	0.70		0.9		1.21	
W_6	0.054	0.142	0.475	0.525	0.855	0.956	0.71		0.935		1.23	
W_7	0.102		0.53		0.9		0.512	1.01	0.711	1.166	0.85	1.356
W_{84}	0.104		0.51		0.894		0.513	1.021	0.702	1.134	0.861	1.34
W_{87}	0.106		0.502		0.902		0.523	1.022	0.730	1.150	0.88	1.375
W_8	0.046	0.148	0.487	0.515	0.870	0.934	0.772		0.94		1.15	

A typical W_{ji} is presented in Table 3. For each W_{ji},, Gaussian membership function is determined by GA.

As demonstrated, the effect of each weight is not considered as the crisp coefficients. The effect of each weight is a function of the time variable, and $W_{ji}(t)$ has uncertainty. Additionally, t is the patient's life expectancy ($t = 1, ..., n, and\ n = lifetime$). These time-variable functions are proportional to each factor, and as stated, the effect of these functions is considered as (11).

Moreover, based on these factors, the L2-HIT2 FCM level has been investigated. Finally, by examining the amount of risk obtained from the mass characteristics and their weights, the risk of L2- HIT2 FCM level has been divided into three groups: benign, normal, and malignant in three modes (optimistic, realistic, and pessimistic) as shown in Figure 9.

4- 4- L3-Fuzzy Level

This level is examined by obtaining the position of the mass. By positioning the coordinates at the corner of the mammography image (the right or left side of the breast in the image of the mammography is considered), and determining the position of the mass, the risk of L3-Fuzzy level is obtained in three groups. These groups are as low, moderate, and high.

Using the output of L2-HIT2 FCM level, the precise position of the mass can be calculated relative to the coordinate axis, as shown in Figure 10, and it is possible to obtain the risk of this level from the relevant fuzzy rules (Figure 10 is the same as Figure 7e with coordinate axis). The L3-Fuzzy level risk is achieved at three groups with low [0-0.39], medium [0.39- 0.72], and high [0.72-1]. The results of the L3-Fuzzy level for the 80 training data are as Figure 11.

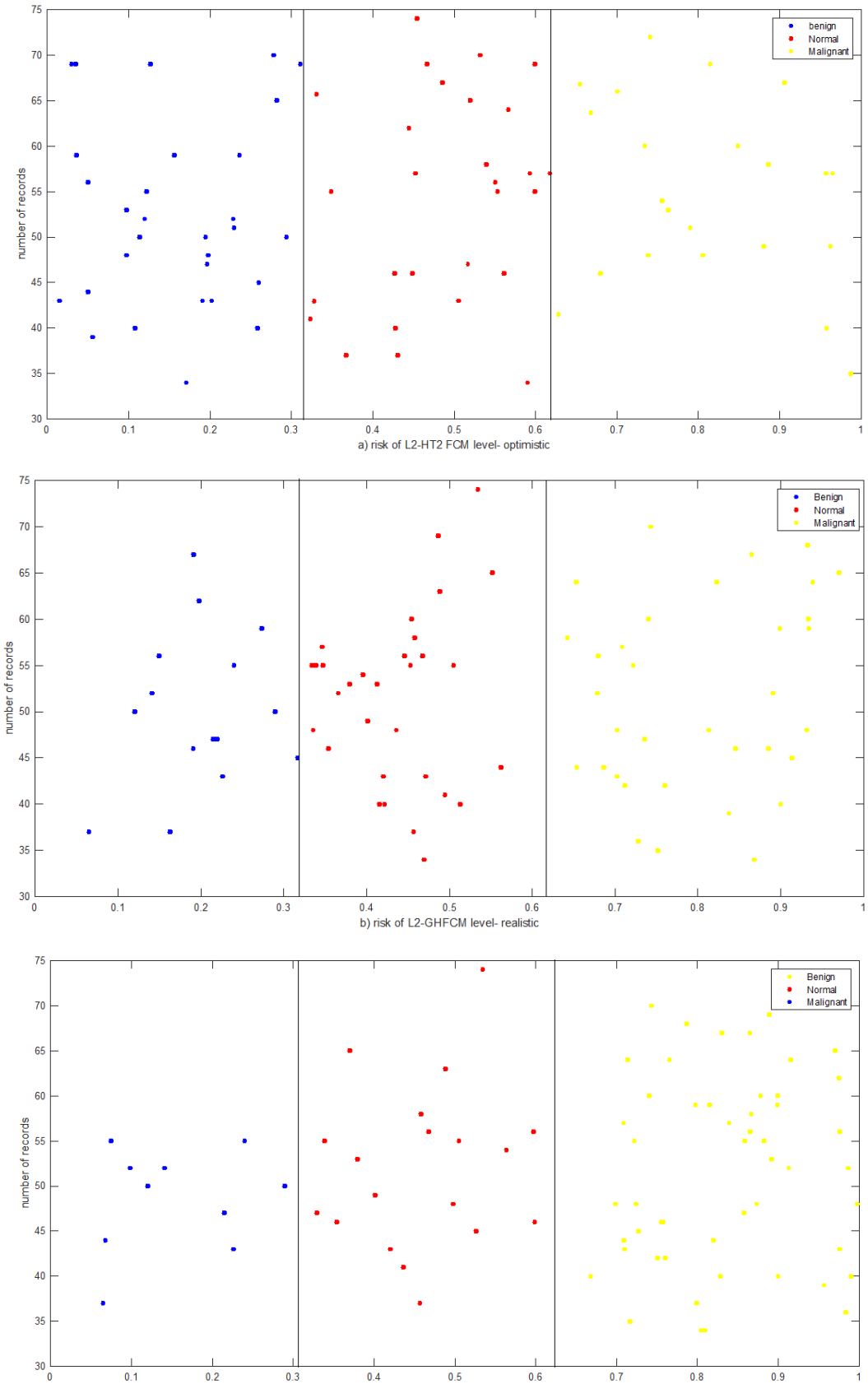


Fig. 9. a) Risk of L2-HIT2 FCM level of patients in optimistic mode (benign [0- 0.32], normal [0.32- 0.62] and malignant [0.61-1]), b) Risk of L2- HIT2 FCM level of patients in realistic mode (benign [0- 0.32], normal [0.32- 0.62] and malignant [0.62-1]), c) Risk of L2- HIT2 FCM level of patients in pessimistic mode (benign [0- 0.31], normal [0.32- 0. 62] and malignant [0.62-1])

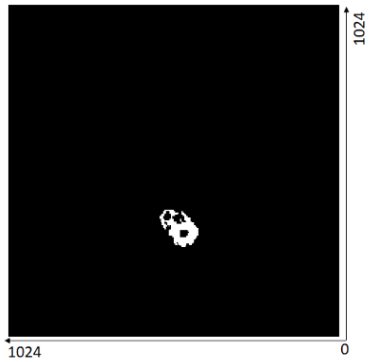


Fig. 10. Diagnosed tumor and its position

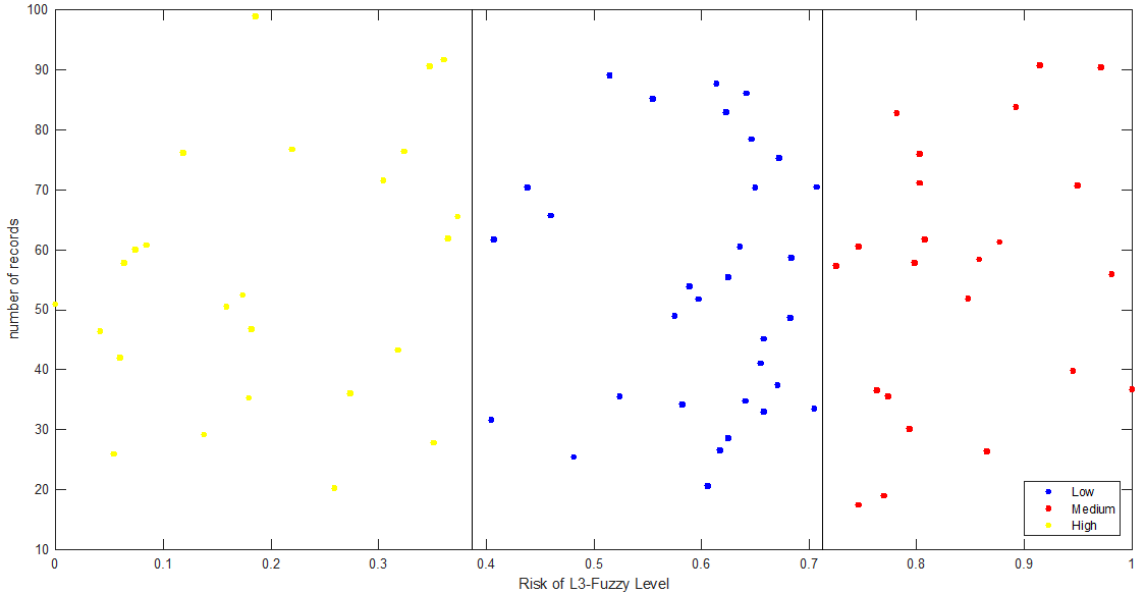


Fig. 11. Risk of patients in L3-Fuzzy level

4- 5- Obtaining Breast Cancer Risk by H-HIT2 FCM

As mentioned earlier, the overall risk of breast cancer in this paper is achieved by the H-HIT2 FCM method. To analyze this method, we use a real datset gathered from Iran radiology, in Tabriz. The overall risk of breast cancer is found by Support Vector Machine (SVM) taking into account the outputs of L1-HFCM, L2-HIT2 FCM, and L3-Fuzzy levels. SVM, a popular way of classification, performs well in various settings and identifies as one of the best out-of-box classifiers. Support Vector Machine s are set to binary ratings, where there are two categories. Extensions of Support Vector Machine s are used for more than two classes. High accuracy, elegant mathematical ability, and direct geometric interpretation are the advantages of SVMs [38-39].

For each mode of optimistic, realistic, and pessimistic, the SVM is performed on the three values obtained from three levels. The output of running SVM will also belong to three classes of low, moderate, and high, and since this is more than two, SVM for k-class case (k>2) is used. One-versus-one (OVO) and one-versus-all (OVA) are two common approaches for the case k>2. OVO is applied in this work where $\binom{k}{2}$ pairwise SVM should be implemented, and finally, the prediction would be the class that wins the most pairwise competitions; for more detail, the interested reader is referred to [39].

Furthurmore, before running SVM, we apply Principal Components Analysis (PCA) on the outputs of three levels to have a better result. PCA is a powerful technique for extracting structure from the high-dimensional dataset. Estimating the principal components is performed by solving the eigenvalue problem or using iterative algorithms. The new dataset values that are obtained in PCA algorithms are called principal components. The number of principal components is either the same number or less than the present original

Table 4. Average and standard deviations of the three levels- optimistic mode

.verage and standard deviations of the three levels- optim

	C_1	C_2	C_3
Prompt center	0.5581	0.5631	0.6881

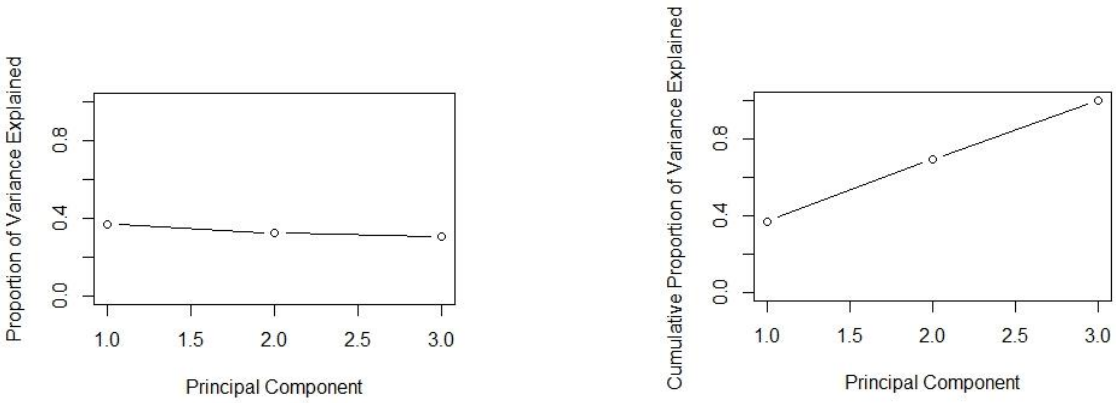


Fig. 12. a) The variance ratio of main components; b) The cumulative ratio of variance in main variables

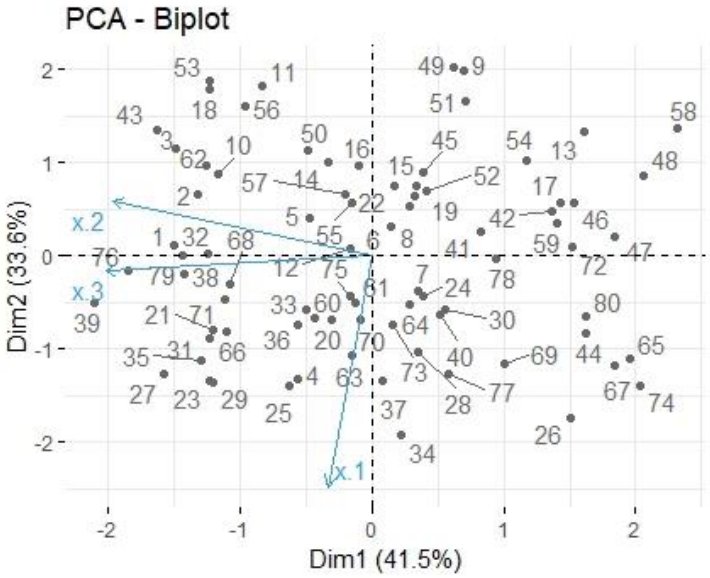


Fig. 13. Dual charts of individuals and variables

variables. In PCA, the most substantial possible variance is in the first component. The following components with the highest variance refer to the components being orthogonal to the previous components [39]. Here after, we will present all the results for the optmistic mode; however, same analysis can be implemented for the realistic and pessimistic mode.

The PCA of three levels is shown in Table 4. C_1,C_2, and C_3 are the outputs of three levels in optimistic mode.

The centrality and scale of the components proportional to the standard mean and standard deviations in optimistic mode are shown in Table 4. Figure 12 shows the variance ratio of each of the main components in the data, as well as the cumulative ratio of the variance of them in optimistic mode.

Figure 13, illustrates the information for both sample and data matrix variables. Thus, three principal components would be enough as presented in Table 5 for the optimistic mode, calculated by software R.

Table 5. The principal components of three levels

Table 5. The principal components of three levels

	PCA_1	PCA_2	PCA_3
$C_1(X.1)$	0.6083413	0.4383690	0.6616294
$C_2(X.2)$	0.6378010	-0.2261309	0.7362572

Table 6. SVM with different kernels

Table 6. SVM with different kernels

SVM	Table prediction				K-fold CV									
linear		1	2	3	K	1	2	3	4	5	6	7	8	9	10
	1	12	0	0											
	2	0	22	0	Accuracy%	0	78.5	79	77.5	93	82.5	87.5	96	90	93.5
	3	0	0	46											
radial		1	2	3	K	1	2	3	4	5	6	7	8	9	10
	1	14	0	0											
	2	0	22	1	Accuracy%	0	65.5	76.5	83	85	78.5	78.5	87	87.5	90
	3	0	2	41											
sigmoid		1	2	3	K	1	2	3	4	5	6	7	8	9	10
	1	14	0	0											
	2	0	18	0	Accuracy%	0	64.5	78.5	79	82.5	85.5	87.5	88.5	90	87.5
	3	0	3	45											
ynomial		1	2	3	K	1	2	3	4	5	6	7	8	9	10
	1	12	0	0											
	2	0	19	0	Accuracy%	0	65	65	62.5	67	68.5	67.5	64.5	67	69

The first component of the set of features is a linear combination of the features $X_1,...,X_p$ as(15):

$$z_1 = \phi_{11}X_1 + \phi_{21}X_2 + \ldots + \phi_{p1}X_p \quad (15)$$

This component has the most considerable variance, and by normalizing the factors the equation $\sum_{j=1}^{p}\phi_{j1}^2 = 1$ is valid for all elements. After finding the other two components similarly, the overall risk of patients is determined using the SVM. The eighty training patients belong into three groups as 1,2, and 3, where 1=low, 2=moderate, and 3=high. The overall risk with different SVM methods and Cross-Validations (CV) are obtained in Table 6 for the optimistic mode.

The results of the SVM models are depicted in Figure 14, where X-axis is PCA1. Y-axis is PCA2 in Figure 14a,b and PCA3 in Figure 14c,d. According to Table 6, the linear SVM with CV=8 is selected due to high accuracy.

By choosing linear SVM and $CV = 8$, the overall risk of breast cancer is obtained for eighty train data. The patient's risk is found in optimistic mode by using SVM applied on outputs of three levels (L1-HFCM level, L2-HIT2 FCM level in optimistic mode, and L3-Fuzzy level). Ten random results of breast cancer risk are presented in Table 7.

The difference between H-HIT2 FCM outputs and real-world results is shown in Figure 15 which shows that the responses are very close with real ones in training patients.

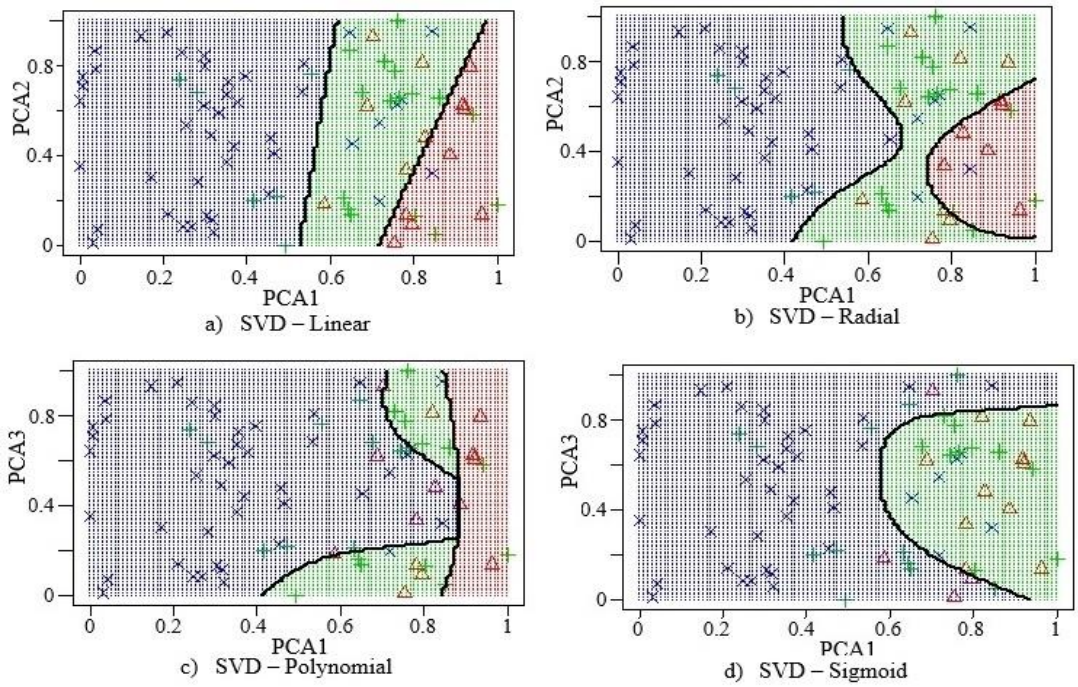


Fig. 14. The SVM results a) linear, b) radial, c) polynomial, and d) sigmoid- training data

Table 7. The results obtained through the proposed H-HIT2 FCM method- training data

	L1-HFCM	L2-HIT2 FCM	L3-Fuzzy	The proposed H-HIT2 FCM method		
	Level	Level	Level	Optimistic	Realistic	Pessimistic
1	0.5347	0.8075	0.9605	Moderate	High	High
					3(high)	
2	0.2444	0.7256	0.9559	Moderate	High	High
					3(High)	
3	0.3499	0.8583	0.9995	Moderate	High	High
					3(High)	
4	0.3546	0.3238	0.5901	Low	Moderate	High
					2(Moderate)	
5	0.8441	0.3732	0.9979	Moderate	High	High
					3(High)	
6	0.3145	0.1183	0.2798	Low	Moderate	Moderate
					2(Moderate)	
7	0.4907	0.2333	0.1173	Low	Low	Moderate
					1(Low)	
8	0.3474	0.6845	0.9907	Moderate	High	High
					3(High)	
9	0.507	0.7074	0.9325	Moderate	High	High
					3(High)	
10	0.2791	0.4827	0.7861	Moderate	Moderate	High
					2(Moderate)	

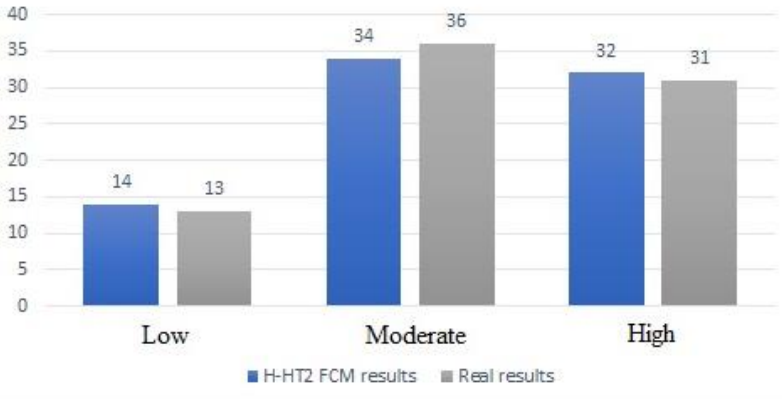


Fig. 15. The comparison of the H-HIT2 FCM results and real results

Table 8. Accuracies of different methods for 20 test patients

Methods	Accuracy
Fuzzy	70%
FCM	95%
SVM	90%
H-HIT2 FCM	95%

4- 6- Comparing the Results of the Proposed H-HIT2 FCM Method with Other Existing Methods

In the proposed method, the obtained results have three responses for each three optimistic, realistic, and pessimistic modes. However, these three responses are expressed as High, Moderate, and Low risk. Compared to the other existing methods, this method has an exact response with the least error. Three responses show the patient situation in three modes. These modes can help patients and oncologists to have a better suggestions for treatments.

The comparison of the accuracies of the existing method for 20 test data with H-HIT2 FCM is shown in Table . **Error**! Not a valid bookmark self-reference. Table 9 shows the comparison of the eight results of the test dataset in various methods. The responses are slightly different in other methods, but in the H-HIT2 FCM, almost all the esponses are the same as reality with no error.

The comparison between the H-HIT2 FCM results and other methods for the twenty trains is shown in Figure 16. The responses of the H-HIT2 FCM are very close to the real results.

5- Conclusion

This paper presents a new method for medical data classification considering uncertainty in the dataset. The method, called H-HIT2 FCM, is based on the integration of high-order FCM and type 2 FCM in a three-level structure. The L1-HFCM level has modeled a demographic risk profile based on the domain experts' fourteen breast cancer personal risk factors. The second level, L2-HIT2 FCM, has determined the features (twelve features) of the screening mammogram for normal, benign, and malignant cases in three optimistic, realistic, and pessimistic modes. These results are assumed the variability of mass characteristics in the patient's lifetime. At the L3-Fuzzy level, the exact position of the mass is obtained. Finally, the SVM method is modified to predict the overall risk of breast cancer by taking into account the outputs of three levels (i.e., L1-HFCM, L2-HIT2 FCM, and L3-Fuzzy). The proposed method H-HIT2 FCM has been applied to a radiology dataset that appropriately detects the overall risk.

The accuracy of the proposed method is 97%, which is much better in comparison to the similar methods in the literature. The results show that the integrated risk assessment method considering the medical guidelines is a decision tool that can be proposed to clinical oncologists. These methods help them improve the breast cancer risk assessment analysis. Reliable predictions are expressed throughout the patient's survival, attributed to the patient's longevity in optimistic, realistic, and pessimistic modes.

Future research can consider the type of nutrition diet of the patient and the amount of vitamin D in her body related to breast cancer risk. Evaluation of the method on a larger number of patients is also suggested to have a much precise risk assessment.

Table 9. Comparison of the results through the H-HIT2 FCM method and other methods

	Fuzzy	SVM	FCM	H-HIT2 FCM		
				optimistic	realistic	pessimistic
1	2.1 (High)	3.5 (High)	High	High	High	High
					3 (High)	
2	1.2 (Low)	2.9 (High)	High	Moderate	High	High
					3 (High)	
3	0.7 (Low)	1.7 (Low)	Moderate	Low	Moderate	Moderate
					2(Moderate)	
4	1.6 (High)	3.9 (High)	High	High	High	High
					3(High)	
5	0.6 (Low)	0.7 (Low)	Low	Low	Low	Low
					1(Low)	
6	1.9 (High)	4.4 (High)	High	High	High	High
					3(High)	
7	0.5 (Low)	1.8 (High)	Moderate	Low	Moderate	Moderate
					2(Moderate)	
8	1 (Low)	1.9 (High)	Moderate	Moderate	Moderate	High
					3(High)	

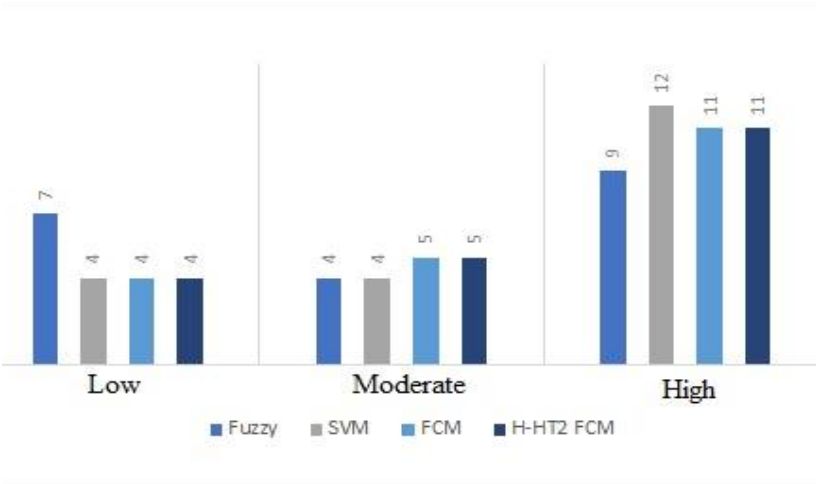


Fig. 16. The comparison of the H-HIT2 FCM results and other methods results

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