

A Fuzzy Expert System for Diagnosis of Acute Lymphocytic Leukemia in Children

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ABSTRACT

Fuzzy expert systems are one of the most practical intelligent models with the high potential for managing uncertainty associated to the medical diagnosis. In this paper, a fuzzy inference system (FIS) for diagnosing of acute lymphocytic leukemia in children has been introduced. The fuzzy expert system applies Mamdani reasoning model that has high interpretability to explain system results to experts in a high level. The system has been designed based on the specialist physician's knowledge. The proposed systems, has been implemented in Matlab and evaluated on real patients' dataset. High accuracy of this system (with an accuracy about 96%) revealed its capability for helping experts to early diagnosis of the disease. that the results are promising for more earlier diagnosis and then providing good treatment of patients and consequently saving more children's lives.

Keywords

Fuzzy expert system, acute lymphocytic leukemia, diagnosing of leukemia

1. Introduction

Leukemia is the most common type of childhood cancers in Iran. It includes 30% of the all cancers in the children (according to the Mahak Hospital reports [20]). Diagnosis in the early stages of the leukemia development can increase the chance of treatment to more than 90% chance of improvement. Leukemia is a kind of cancer that starts from blood narrows. Early diagnosis of leukemia especially acute leukemia and in follow-up treatments has an important role in the improvement of the patients which have been assisted by fuzzy expert systems. Because of fuzzy system high interpretability they are near to human's language, easy to interact with human experts. Also, there are patients that do not know their illness. In designing fuzzy expert system for diagnosing acute lymphocytic leukemia in children the following information have been employed: blood test results

for the count of blood cells (C.B.C) and leukemia's symptoms and The output of the fuzzy expert system is diagnosis of acute lymphocytic leukemia, suspected, and healthy) that show in Fig 1 .

During last years, significant advances in medical field has occurred that attempts to incorporation computational techniques and artificial intelligence capabilities in medical diagnosis. Major advances has happened in prevention and detection of illness [1]. Decision making systems in different fields and expert systems as a kind of these systems has played an important role in medical field,[2] such systems are DENDRAL presented in 1965 to describe and explain the molecular structure, [2] [3] and MYCIN was submitted in 1976 to diagnose heart disease[2][4].

The main objective of the proposed fuzzy expert system for diagnosing acute lymphocytic leukemia is to diagnose it in the first stage of illness development. There are uncertainty in real systems, the measured data provided in the blood test experiments and experts knowledge for diagnosis [17]. The main sources of uncertainty associated to diagnosis problems are described in [17]. This study takes advantages of fuzzy expert systems to manage the main sources of uncertainty in the diagnosis of leukemia. The next section explain the acute lymphocytic leukemia in details.

2. Diagnosing of acute lymphocytic leukemia (ALL)

Leukemia is the most common type of childhood cancers in Iran. It includes 30% of the cancers in the children groups. It affects 3 to 5 Iranian children in every 100,000 population of children (according to the Mahak Hospital reports [20]). Diagnosis in the early stages of the leukemia development can increase the chance of treatment to more than 90% chance of improvement. Acute lymphoblastic leukemia (ALL), is one of the most common type of leukemia that most of patients with it are children. It is caused by appearance of too many abnormal white blood cells (WBC) in the child's blood and bone marrow. The ALL can occur in

adults too, but treatment is different for them. It is acute because the WBC grows up very fast. Lymphoblastic refers to the WBC, which are also called lymphocytes. Normally, lymphocytes is an important part of the body's defense system against infections.[?]

2.1. Symptoms

In its early stages, the ALL can look like other sicknesses such as the flu or a cold. The difference between the ALL and flu or a cold, fleeting infection is its persistence, and the fact that the child may begin to bruise easily.

Common symptoms for ALL include: fever, feeling weakness and tired and dizzy, pain, enlarged lymph nodes, bruises, Weight loss.

2.2. Diagnosis

To detect ALL, a doctor needs to look at the child's C.B.C test that the test is the kind of test most children have had at least once by the time they are five years old in a routine physical exam. Then Cells must be counted.

2.3. Causes

The main reason of the ALL, is unknown, but something cause the WBC rapidly grows more than normal. The red blood cells (RBC) needed to carry oxygen to tissues, and platelets that are needed to stop bleeding through clotting. When immature lymphocytes crowd out red blood cell production, a child's body does not receive all the oxygen it needs. As a result, children (he or she) may develop anemia.

And when immature lymphocytes crowd out platelets, the child bleeds and bruises easily.

The cause of ALL is not known. However, some factors may increase a child's chance of developing it. Having an identical twin with ALL, Someone who has an identical twin who develops ALL in the first year of life has an increased risk of getting ALL. Inherited syndromes: such as Down syndrome, Klinefelter syndrome, Fanconi anemia, Bloom syndrome, Ataxia-telangiectasia, Neurofibromatosis [8]. There is no known way to prevent leukemia yet and there are no special tests that can find acute lymphocytic leukemia (ALL) early. The best way to find it early is to report any possible signs or symptoms of leukemia to the doctor right away. The doctor will ask you questions about your health (take a medical history), and do a physical exam. He or she will look for any swollen lymph nodes, any fever or bruising, or signs of infection. If the doctor suspects leukemia, blood tests will done

Most people with ALL have too many WBC, not enough red cells, and not enough platelets. Many of the WBC will grow abnormal, These kind of WBC don't work as usual which means a person has leukemia [9].

3. An overview on related works

In this section, Table 1 provides an overview or comparison between some related works in diagnosing blood cancer using fuzzy expert systems.

It also represents their model, advantage and disadvantages of them.

Table 1: an overview of other related works

System's name	Methodology	Inputs	Outputs	Advantages	Disadvantages
Automated Blood Cancer Detection [10]	Diagnose leukemia with using images and fuzzy system. The method work on four different steps: Pre-Processed Image, Image segmentation, Fuzzy rule based decision System, Result	size, shape and quantity (number of Infected cell) of image.	Diagnosing : ALL, healthy	Being automated and can help the physician as a tool for cancer diagnosis.	Having noisy data Because of using images in diagnosing and needs to device can take photo from blood. And it's quality may be low.
Clinical decision Support [11]	Diagnose Pneumonia by using fuzzy system(rule-based).	Pneumonia's symptoms	Diagnosing: Having Pneumonia or not	high accuracy, coverage area and less time requirement, managing uncertainty by using fuzzy systems	Systems have to trust to patient's answers.
VP-expert for diagnosing blood cancer [7]	Diagnose different types of blood cancer by asking some questions from patients and according to their answers.	Blood test, time of sickness and illness's symptoms.	Diagnosing: (ALL or AML or CLL or CML)	high accuracy, coverage area and less time requirement and can help to making decision.	It doesn't have clinical evaluation and Systems have to trust to patient's answers and can not work lonely yet.
Neuro-Fuzzy system [12]	It used mamdani FIS and by providing leukemia's symptoms in three levels of low, middle and high from patients to diagnose leukemia. It used neural nets to find fuzzy system's parameters	Paleness Shortness of Breath Nose Bleeding Frequent infection Anaemia Epistaxis Bone pain Thrombocytopenia Granulocytopenia Asthenia	With Leukemia, Might be Leukemia and Not Leukemia	By using combined systems (neuro-fuzzy) can manage uncertainty and use training	Not having treatment part.

System's name	Methodology	Inputs	Outputs	Advantages	Disadvantages
		Palpitation Digestive Bleeding Enlarge spleen Fatigue			
Designing an Expert System to Diagnose and Propose about Therapy of Leukemia [6]	This is an expert system presented for diagnosis of Leukemia using VP-Expert shell.	Blood test, time of sickness and illness's symptoms	Diagnosing: (ALL or AML or CLL or CML)	It can use as a tool for help to experts to make decision.	It doesn't have clinical evaluation and Systems have to trust to patient's answers.
The Proposed FES	It uses Mamdani FIS and it is a rule based system.	Blood test(C.B.C), ALL's symptoms, time-sickness.	Diagnosing: ALL in children	By using Mamdani FIS, easily to work and understand for each body and fuzzy systems can manage and modeling uncertainty and it's inputs are easily to achieve such as C.B.C and symptoms.	Not suggestion has provided for treatment.

4. The proposed fuzzy expert system

In order to design the fuzzy expert system, first we identified the main sources of information: medical domain knowledge for diagnosis of the disease through physician expert, numerical data. The fuzzy system has been developed through the two following modelling stages:

Stage 1: Surface Structure Identification

- 1) Define the inputs and outputs of systems.
- 2) Choose appropriate type of inference for the FIS.
- 3) Determine input and output variable's linguistic terms and their number according to the domain knowledge.
4. Determine If-then rules of fuzzy system.

Stage 2: Deep Structure Identification

- 1) Determine suitable type of MFs for each linguistic terms.
- 2) Determine parameters of MFs using expert's knowledge or gathered information.
- 3) Refine the parameters of the MFs using regression and optimization techniques [13].

For designing the proposed fuzzy expert system that shown in Fig 5 for diagnosing ALL: before designing, studies have been conducted to search about leukemia illness such as how the leukemia diagnose by doctors for example leukemia's symptoms or blood test and their domain. Then at the first level by using the information that gathered before, determined inputs and outputs of proposed system (C.B.C and ALL's symptoms such as fever, feeling weak and tired and dizzy, pain in bones or joints, enlarged lymph nodes that show in Table 4 and output are ALL, Suspected, healthy). They are presented in Fig 3. The Mamdani FIS has been used in this study because of it is simply in work and understanding and common linguistic terms(low, middle, high) in blood test and r leukemia's symptoms and preparing rules by physician suggested. In second level determined membership functions (MFs) for inputs and outputs fuzzy sets (MFs use for representation of fuzzy sets with their

intensity and fuzzy sets with un-sharp boundaries). The input and output of the FES are provided in Table 2.

Table 2: The input and output of the FES

Inputs	Explain
PLT	Platelets or thrombocytes, are blood cells that stop bleeding in the body.
RBC	Red blood cells or erythrocytes, are the most common type of blood cell that deliver oxygen to the body tissues .
WBC	White blood cells or leukocytes or leucocytes, are the cells of the immune system that protect the body against both infectious disease and foreign invaders.
HCT	The percentage of red blood cells in a blood sample
HB	RBC carry protein in the body and transports and delivers oxygen throughout the body.
Fever	High temperature
Weakness	Feeling weakness
Pain	Feeling pain
Enlarge lymph nodes	The growth in size of the lymph nodes
Time of sickness	The patients suffer from symptoms suddenly and their blood test is sick then child has ALL, if it is a long time that the patent is affected and blood test is abnormal then it is susceptible.

Main components of fuzzy inference system [14] [15]: Fuzzifier, Rule-base and Inference engine, and defuzzifier. They are shown in Fig 1.

In a fuzzy expert system the rule set includes fuzzy If-Then rules. Data base includes the information of MFs and MFs's parameters and at the end inference engine works with fuzzy If-Then rules, details of method proposed in this study is represented in Table 3.

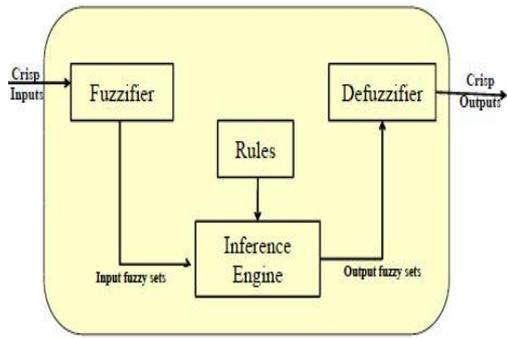


Fig 1. A fuzzy inference system architecture [5]

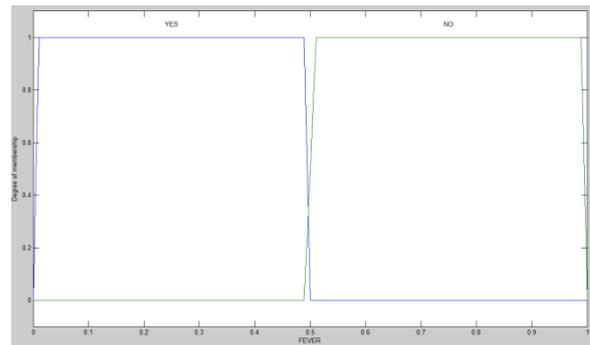


Fig 5: MFs OF fever (input of proposed system)

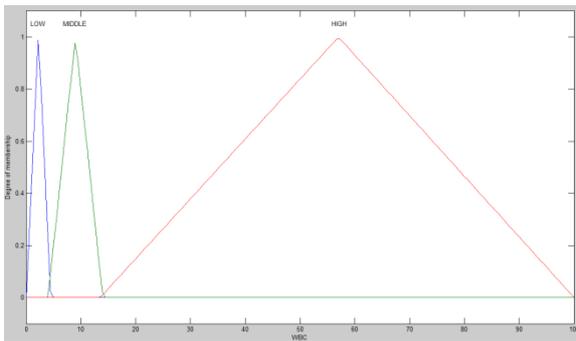


Fig 2: MFs OF WBC(input of proposed system)

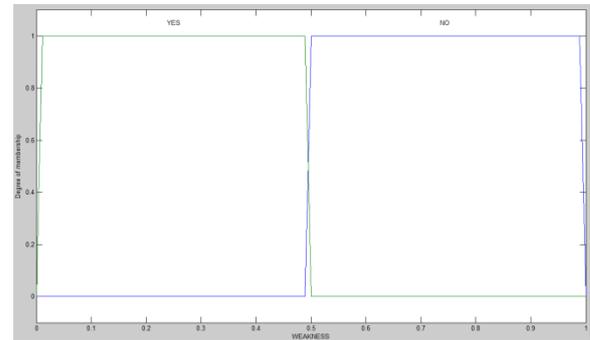


Fig 6: MFs OF weakness (input of proposed system)

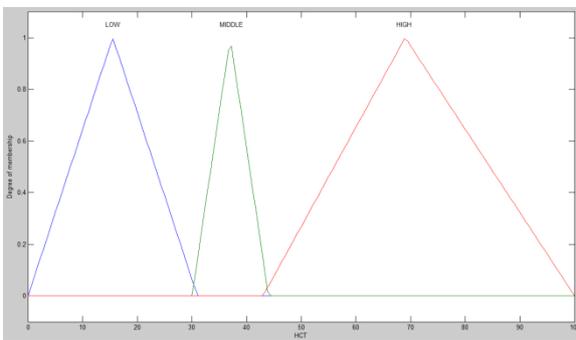


Fig 3: MFs OF HCT(input of proposed system)

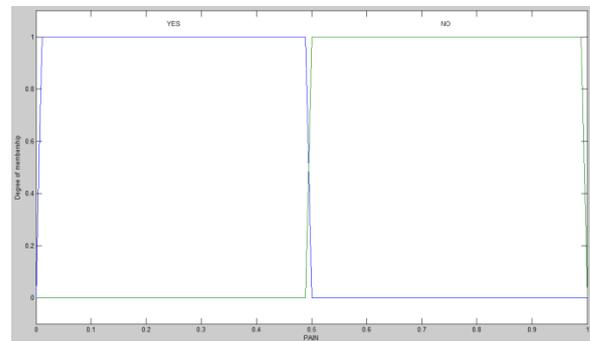


Fig 7: MFs OF pain (input of proposed system)

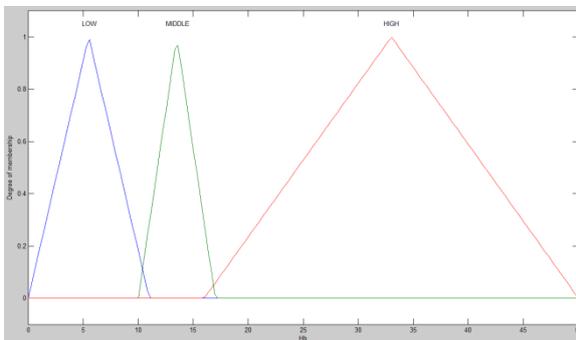


Fig 4: MFs OF Hb (input of proposed system)

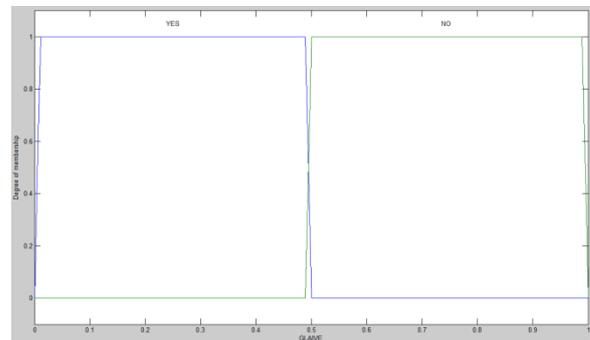


Fig 8: MFs OF enlarge lymph nodes (input of proposed system)

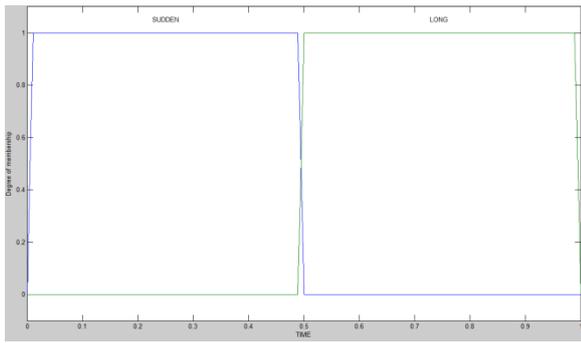


Fig 9: MFs OF time-sickness (input of proposed system)

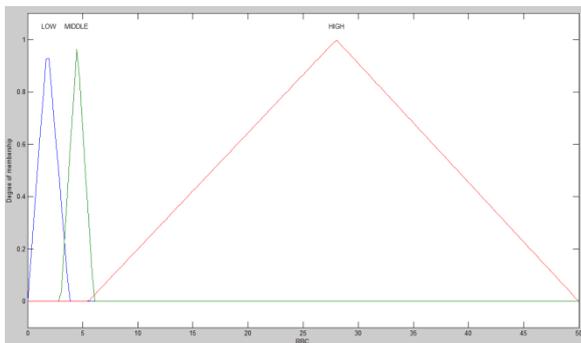


Fig 10: MFs OF RBC (input of proposed system)

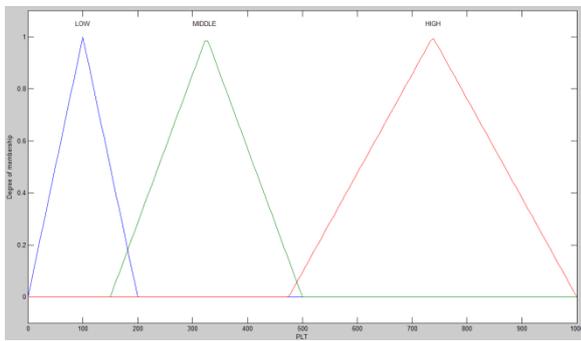


Fig 11: MFs OF PLT (input of proposed system)

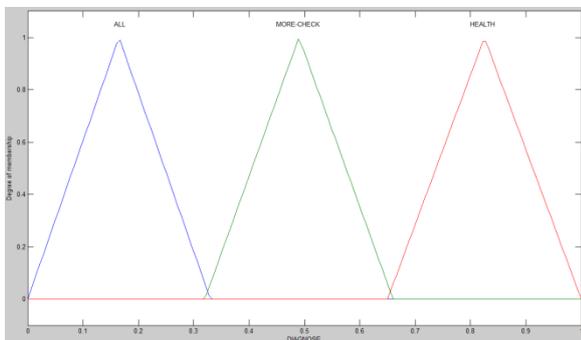


Fig 12: MFs OF diagnose (output of proposed system)

Table 3: The proposed FES Rule-set

1) IF (PLT is LOW) and (RBC is LOW) and) WBC is HIGH) and (HCT is LOW) and (HB is LOW) and (FEVER is YES) and (WEAKNESS is YES) and (PAIN is YES) and)enlarge lymph nodes is YES) and) Time of sickness is SUDDENLY) then) DIAGNOSE is ALL)
2) IF (PLT is LOW) or) RBC is LOW) or) WBC is HIGH) or (HCT is LOW) or (HB is LOW) then) DIAGNOSE is MORE-CHECK)
3) IF (FEVER is YES) or (WEAKNESS is YES) or (PAIN is YES) or) enlarge is lymph nodes YES) or) Time of sickness is SUDDENLY) then) DIAGNOSE is MORE-CHECK)
4) IF (FEVER is YES) or (WEAKNESS is YES) or (PAIN is YES) or) enlarge lymph nodes is YES) or) Time of sickness is LONG) then) DIAGNOSE is ALL)
5) IF (PLT is MIDDLE) and) RBC is MIDDLE) and) WBC is MIDDLE) and (HCT is MIDDLE) and (HB is MIDDLE) and (FEVER is NO) and (WEAKNESS is NO) and (PAIN is NO) and) enlarge lymph nodes is NO (then) DIAGNOSE is HEALTH)
6) IF (PLT is HIGH) or) RBC is HIGH) and) WBC is LOW) and (HCT is HIGH) and (HB is HIGH) then) DIAGNOSE is MORE-CHECK)
7) If(PLT is LOW) or) RBC is LOW) or) WBC is HIGH) or (HCT is LOW) or (HB is LOW) or (FEVER is YES) or (WEAKNESS is YES) or (PAIN is YES) or) enlarge lymph nodes is YES) or) Time of sickness is LONG) then) DIAGNOSE is ALL)

5. Experimental Results and Performance Evaluation of the proposed Fuzzy Expert System

ANDMETHOD: MIN
 OR METHOD: MAX
 IMPLICATION: MIN
 AGGREGATION: MAX
 DEFUZZIFICATION CENTROID

The proposed FES were designed in MATLAB software. Figures 2-12 represents the MFs defined for input and output variables. The parameter of the FIS are as follows:

Blood test input domain information in children have been provided from Khatamol-Anbia hospital as, show in table 2.

The FES were evaluated with a dataset including 100 patients dataset of children with leukemia. In the dataset 30 samples were sickness and 32 samples were health and 38 samples were susceptible that gathered from physician and laboratory results. For performance evaluation, the FES results have been compared to the real results and the mean square error (MSE) measure was measured which was in data set 0.4 error. The main advantage of this work compared to other related works is in evaluation process using real patients' dataset. In some of the studies it has just been mentioned the method provides a high accuracy. The comparison of some method's accuracy are show in Table 4.

Table 4: comparison of accuracy

Method's names	Accuracy
Neuro-Fuzzy system [12]	Not reported
Model of experts for decision support in the diagnosis of leukemia patients [18]	Not reported
Designing an Expert System to Diagnose and Propose about Therapy of Leukemia [6]	Not reported
Implementation of Fuzzy Inference System For White Blood Cell Cancer Detection Using DSP [19]	Just mentioned High accuracy
Automated Blood Cancer Detection [10]	high accuracy in comparison other traditional methods
The proposed system	95

6. Conclusions

This paper proposed a fuzzy expert system to diagnose acute lymphocytic leukemia in children. The FES were evaluated on real patients data set. This system can assist experts' decision making for diagnosis of the ALL cancer in children and also is applicable for early diagnosis of even suspected people. This approach is promising to assist early diagnosis of this type of cancer in the children and consequently providing suitable follow-up and treatment to save more children lives. Our future work is to extend the FES for diagnosis of other types of the leukemia.

References

- Shortliffe EH, Cimino JJ. Biomedical informatics: computer applications in health care and biomedicine. New York: Springer; 2006.
- Durkin J., Expert Systems: Design and Development, Prentice Hall, New York, 1994.
- Edward A, Feigenbaum BG, Buchanan D, and Meta D, Roots of Knowledge Systems and Expert System Applications, Artificial Intelligent 59 (1933), no. 1-2, 233-240.
- Shortliffe EH, Computer-based Medical Consultations: MYCIN, Elsevier Science Publishers, New York (1976).
- Roger Jang, Neuro-Fuzzy and Soft Computing ,Chapter 1&3& 4 , Introduction to Fuzzy Systems &Fuzzy Rules and Fuzzy reasoning &Fuzzy Inference System FIS , 1997.
- Armin Ghasem Azar 1 Zohreh Mohammad Alizadeh 2 Department of Computer Science 1,2 , International Journal Of Computer & Information Technologies (IJOCIT) ISSN= 2345-3877 ,2013 Designing an Expert System to Diagnose and Propose about Therapy of Leukemia.
- H. Islami NosratAbadi, S. Mohsen Taheri, A Fuzzy Expert System for Diagnosis of Blood Cancer, in the proceeding of 6th International Conference of ICT Management.
- Acute lymphocytic leukemia(ALL), Children's Cancer Research Fund, available at : <http://www.childrenscancer.org>
- America cancer society, www.cancer.org (-800-227-2345), 2015.
- Nur Alom Talukdar 1 Daizy Deb 2 Sudipta Roy³ , "International Journal Of Advanced Research in Computer Science and Software Engineering " ISSN:2277 128X ,Automated Blood Cancer Detection Using Image Processing Based on Fuzzy System.
- Adewunmi M.Tosin 1 Adekunle Y.A 2 , " International Journal of Advanced Research in Computer Science and Software Engineering " ,ISSN:2277 128X,Clinical Decision Support System for Diagnosis of Pneumonia in children, 2013.
- J.C. ,Imianvan A.A , " GLOBAL JOURNAL OF COMPUTER SCIENCE AND TECHNOLOGY " ,ISSN:0975-4350, Interactive Neuro-Fuzzy Expert System for Diagnosis of Leukemia ,2011.
- Roger Jang, Neuro-Fuzzy and Soft Computing ,Chapter 1&3& 4 , Introduction to Fuzzy Systems &Fuzzy Rules and Fuzzy reasoning &Fuzzy Inference System FIS , 1997.
- R. Hosseini, S. D. Qanadli, S. Barman, M. Mazinani, T.Ellis, and J. Dehmeshki, An Automatic Approach for Learning and Tuning Gaussian Interval Type-2 Fuzzy Membership Functions Applied to Lung CAD Classification System, *IEEE Transactions on Fuzzy Systems*, vol. 20, No. 2, April, pp. 224-234 (2012).
- R. Khezri, R. Hosseini and M. Mazinani, A Fuzzy Rule-Based Expert System for The Prognosis of The Risk of Development of The Breast Cancer, International Journal of Engineering Transactions A: Basics, vol. 27, No. 10, pp. 1557-1564, (October 2014).
- Maliheh Noorzadeh, Rahil Hosseini, Acute Leukaemia Diagnosis using A Fuzzy Expert System, In Proc. of the 14th Fuzzy Systems Association Conference , Tabriz, Iran, August 2014.
- Rahil Hosseini, Mahdi Mazinani, In Proc. of 9th Symposium of Advances in Science and Technology, Classification of Uncertainty Sources in Intelligent Image Processing and Analysis Systems, November 2014, Mashhad, Iran.
- Jaun M. Corchado 1 Jaun F. Depaz 2 Sara Rodriguez 3 Javier Bajo, Artificial Intelligence in Medicine 46 ,179-200 , Model of experts for decision support in the diagnosis of leukemia patients,2009.
- Devesh D.Nawgaje 1Dr.Rajendra D.Kanphade 2, "International Journal of Engineering Science and Technology (IJEST)",Implementation of Fuzzy Inference System for White Blood Cell Cancer Detection Using DSP TMS320C6711.
- Azim Mehrvar, Mahak Hospital Manager, Interview , JameJam NewsPaer, May 2012