Fuzzy System For Breast Disease Diagnosing Based On Image Analysis

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Abstract. In the article, the authors investigated the process of breast disease diagnosis based on the cytological and histological image analysis. One of the main disadvantages in diagnosing is a physician's subjective decision-making, therefore, it is urgent to develop a system that would confirm a preliminary diagnosis. The researchers have examined modern systems of diagnosing in various fields of medicine and proved the effective use of fuzzy logic apparatus to create such a system. The developed system includes two main fuzzy subsystems for breast pre-cancer diagnosing based on the cytological and histological image analysis, which work similarly to the practical work of a doctor-diagnostician. These subsystems are modeled in the Matlab environment. Computer simulation of their work confirmed the efficiency of the developed system and the possibility of its further software or hardware application in medical practice.

Keywords: biomedical image, breast precancerous condition, cytological image, histological image, fuzzy system, telemedicine, Matlab.

1 Introduction

Telemedicine has an increasing tendency for the development today, as it is widely perceived as a resource capable of revolutionizing access to health care services. The important areas of effective use of telemedicine include teleconsultation, telediagnostics, telemedicine, teletraining, teleprogramming, telemonitoring, and telesupport. Telemedicine has the undeniable advantages; however, there are many urgent issues and ethical problems that need to be solved. Telemedicine is becoming a part of human lives and its importance in the health care system is increasing [1, 2].

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One of the main tasks of telemedicine is to quickly diagnose patient's urgent conditions; therefore, it is necessary to develop new methods and tools to assist the physicians in timely diagnosing.

Breast cancer is one of the biggest problems of modern women [3]. The diagnosis is made on the basis of histological and cytological image analysis processed by the doctor. However, there is a risk of medical error or other subjective causes of misdiagnosis or late diagnosis. Therefore, the development of an automated system for analyzing such images, which is a part of telemedicine complexes, is an urgent task.

2 Literature review

The use of communication technologies improves the methods of fast and accurate diagnosing, as well as methods of providing medical care [4]. Fast communication between doctors and patients are provided by means of the advancement of telemedicine technologies. For example, in a research study [5], the authors developed a new method to diagnose traumatized spleen in the presence of laceration, contusion, active bleeding or hematoma via abdominal trauma using tablet based telemedicine. Clinicians used e-mails to inform about the diagnosed pathological findings of 10 patients. The fast diagnostic system proposed by the authors decreases the mortality and morbidity of emergency patients.

Many scientists use artificial intelligence methods to develop new systems of diagnosis including the fuzzy logic apparatus.

In research [6], the authors proposed a fuzzy based decision-making system for breast cancer diagnosis. Breast cancer is a serious disease; therefore, primary breast cancer detection is important. The authors of the research study developed the artificial intellectual method such as fuzzy logic for correct and accurate decision-making. Based on fuzzy rules, expert knowledge is used to treat the patient's symptoms and make accurate decisions according to the constructed rules [6]

The authors of [7] summarized the significant differences in the Maddani-type and Sugeno-type fuzzy systems for the diagnosis of diabetes. The developers have used MATLAB fuzzy logic toolbox. Fuzzy rule-driven systems are suitable for the medical area where interpretability is a major concern. The medical domain is extremely important to the data and uses electronic medical records to build the knowledge base; therefore, the fuzzy sets are important. Multiple variables are often necessary to determine the correct and personalized diagnosis, and it is often difficult to make accurate and timely decisions.

In research [8], a new semantically interpreted knowledge base structure for the diagnosis of diabetes was developed and implemented. This system employs multiple aspects of fuzzy inference, ontology reasoning, and a fuzzy analytical hierarchy process to provide a more intuitive and accurate design. The proposed system offers many unique and critical enhancements to the implementation of an accurate, dynamic, semantically interpretable knowledge base. The developed system considers the ontology semantic similarity of diabetes symptoms in the process of fuzzy rules' evaluation. It has been tested using a real data set, and the results show how the proposed system helps physicians to accurately diagnose diabetes.

Improving the fuzzy system, such as in [9, 10], allows building effective diagnostic models that can be successfully used in modern telemedicine.

The analysis of modern publications in the field of telemedicine confirms that the use of fuzzy logic allows developing fast high-performance systems for diagnosing pathological conditions of patients.

3 Problem statement

The literature review shows that diagnosis of breast precancerous conditions is an urgent task. Therefore, the purpose of this study is to develop a subsystem of the telemedicine complex for the breast pre-cancer diagnosis based on the cytological and histological image analysis using the fuzzy logic apparatus.

It is necessary to do the following:

- analyze modern cytological and histological images of precancerous breast conditions and identify the main features of such pathologies;
- formulate the diagnostic rules of precancerous breast conditions based on images of the specified type with the help of an expert;
- determine the apparatus of fuzzy conclusion and build an appropriate knowledge base for the development of the diagnostic system;
- develop modeling of the general scheme and its main parts of the diagnosis of breast precancerous conditions on the basis of cytological and histological image analysis;
- carry out the experimental research and analyze the application of the developed fuzzy system in modern telemedicine complexes.

4 Cytological and histological image analysis of breast precancerous conditions

Cytological examination of epithelial cells and their structures allows identifying the degree of epithelial proliferation. The appearance of compressed apocrine epithelium, papillary growths in the cytogram and a secretory function of cells allows to cytologically differentiate the cystic mastopathy and intra-ductal papilloma from fibroadenoma and adenoma. Systematization of cytological images of breast disease (mastopathy) and fibroadenoma shows the possibility of applying a cytological method in diagnosing [11, 12].

Qualitative characteristics of non-proliferative breast disease diagnosing are the following:

1) flattened apocrine epithelium;
2) papillary structures formation;
3) presence of secretory activity in cells;
4) centrally-located rounded hyperchromic nuclei;

5) small number of hyperchromic monomorphic cells;
6) cells are located in layers;
7) there are many phagocytes and histiocytes in the background;
8) presence of secret in the cellular space.

The graphical representation of these characteristics is shown in Figure 1.

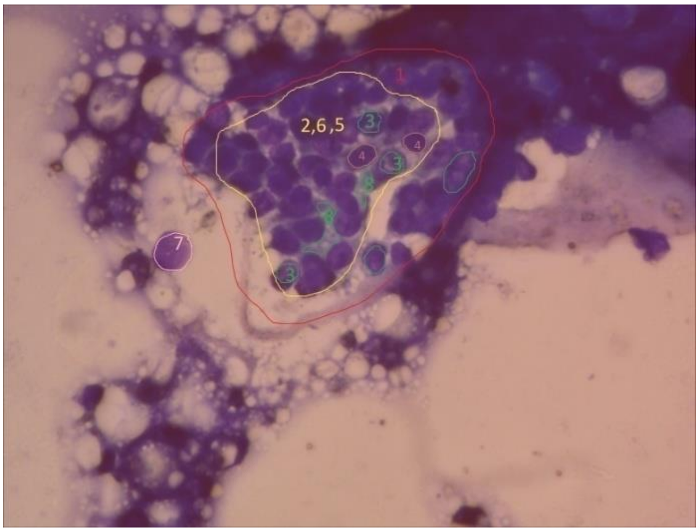

Fig. 1. Expert characteristics of non-proliferative breast disease diagnosis.

The rule for non-proliferative breast disease diagnosis is the following:

IF there is flattened apocrine epithelium; AND papillary structures; AND presence of secretory activity in cells; AND centrally located rounded hyperchromic nuclei; AND a small number of hyperchromic monomorphic cells; AND cells are located in layers; AND there are many phagocytes and histiocytes, AND presence of secret in cells; THEN it is a non-proliferative breast disease (mastopathy).

The qualitative characteristics of proliferative breast disease are the following:

1) formation of cellular complexes (acinus).

2) formation of papillary complexes with dense cells placement in multilayer layers.

3) large cell sizes.

4) large sizes of nuclei with intensely expressed chromatin.

The graphical representation of these characteristics is shown in Figure 2.

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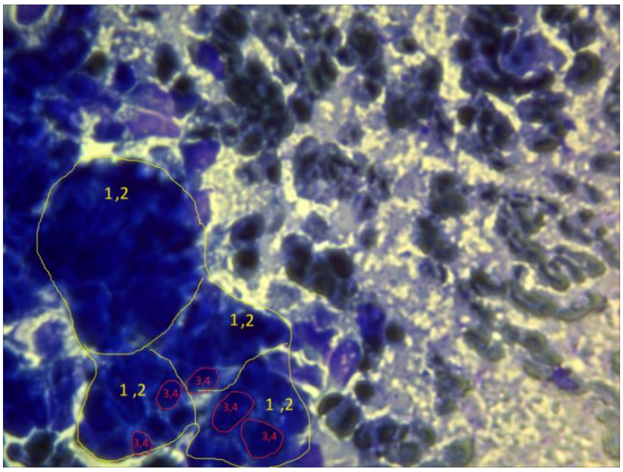

Fig. 2. Expert characteristics for proliferative breast disease diagnosis.

The main characteristics of fibroadenoma are the following:

1) papillary structures formation;
2) flattened apocrine epithelium;
3) cells are increased in size;
4) intensely expressed nuclei;
5) narrow rim of intensely colored cytoplasm;
6) rounded hyperchromatic nuclei;
7) fibroblasts.

The graphical representation of these characteristics is shown in Figure 3.

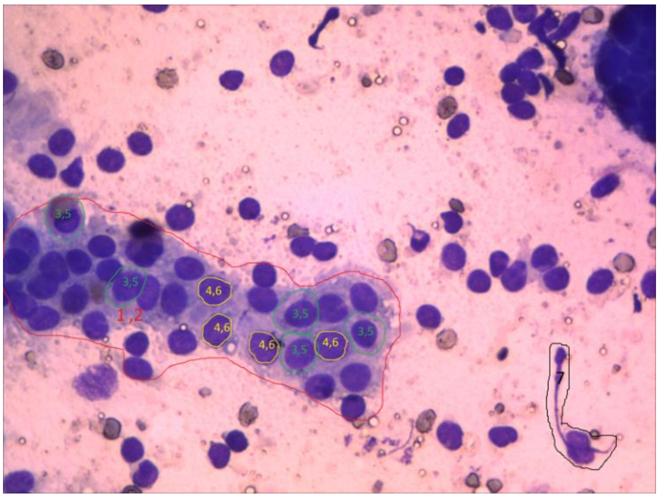

Fig. 3. Expert characteristics of fibroadenoma diagnosis.

The rule for fibroadenoma diagnosis is the following:

IF there are papillary structures; AND flattened apocrine epithelium; AND cells are increased in size; AND there are intensely expressed nuclei; AND there is a narrow rim of intensely colored cytoplasm; AND there are rounded hyperchromatic nuclei; AND fibroblasts, THEN it is a fibroadenoma.

Histological images are images of preparations of thin sections of biological tissue, as shown in Figure 4. The authors used a test sample of cytological and histological images [13, 14]. The input variables are the geometric features of the image data [15, 16].

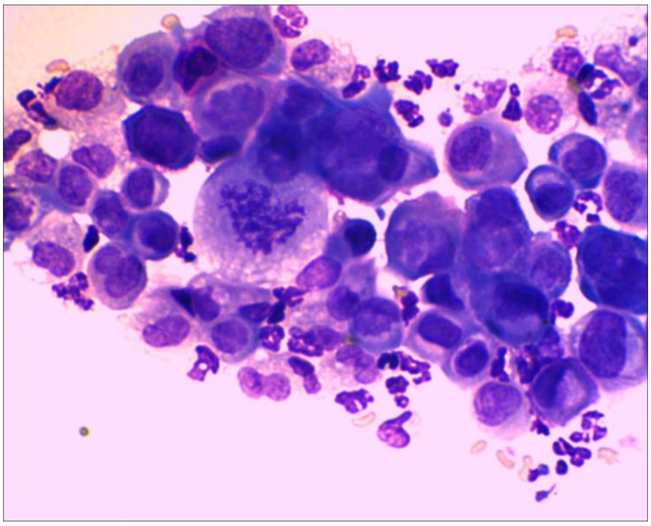

Fig. 4. Histological image

The primary variable is formed on the basis of expert's conclusions about the input variables about the diagnosis and consists of five fuzzy sets, namely: proliferative breast disease (mastopathy), nonproliferative breast disease (mastopathy), and fibroadenoma.

The membership functions of the developed fuzzy system are based on the expert's knowledge about the features of pathological conditions. For example, the features of fibroadenoma diagnosis are the following:

1) proliferation of alveoli;
2) proliferation of intra-lobe ducts;
3) the presence of loose basophilic connective tissue;
4) tenderness of coarse oxyphilic connective tissue;
5) ducts lined with epithelium and myoepithelium of different functional state;
6) microepithelium (elongated dark cells or light with globular inclusions);
7) formation of false glandular structures;
8) connective tissue hyalinosis and epithelial atrophy.

The following features confirm the non-proliferative mastopathy diagnosis:

1) shallow cysts of alveoli;
2) cysts form nests;
3) cystic dilated ducts;
4) hyalinosis of connective tissue;
5) proliferation of connective tissue;
6) metaplasia of dark epithelium into white (light);
7) a lot of connective tissue around glands and ducts;
8) pseudo papillary structures;
9) atrophy of glandular areas and formation of cysts.

Features that confirm the diagnosis of proliferative mastopathy are the following:

1) proliferation of myoepithelium and endothelium of small ducts;
2) extension between the ducts;
3) proliferation of small ducts and alveoli;
4) slight partial stroma;
5) absence of basement membrane;
6) proliferating myoepithelial cells move into the intra-chaotic connective tissue and become similar to smooth muscle.

Using a histological sample of histological images and their qualitative features, it is necessary to build membership functions.

5 Structure of a fuzzy system for breast pre-cancer diagnosing

This study offers a fuzzy system for histological and cytological image processing of breast tissues for the rapid diagnosis of precancerous conditions.

In general, the system has three main blocks: a computer system for storing and processing the knowledge base, the features of pathological conditions and the rules of their processing, a fuzzy system of diagnosis, and a block of processing and storage of diagnosis, which is connected to the knowledge base of the computer. An expert (physician- diagnostician) takes part in the process of creating a knowledge base and analyzing the results of the fuzzy system (Figure 5) and makes the final diagnosis. The computer system works in two modes: "accumulation of knowledge" (an expert is directly involved in the process) and processing of the knowledge base (with the help of a fuzzy system).

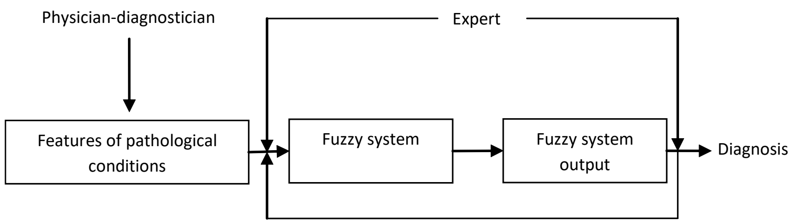

Fig. 5 General scheme of diagnosing based on fuzzy logic

Since the expert makes a preliminary diagnosis on the basis of cytological image analysis and then confirms the diagnosis on the basis of histological image analysis, it is proposed to build this fuzzy system on the basis of two independent modules - fuzzy systems of cytological and histological images, which together with a set of rules are located in the knowledge base of the computer system (Figure 6).

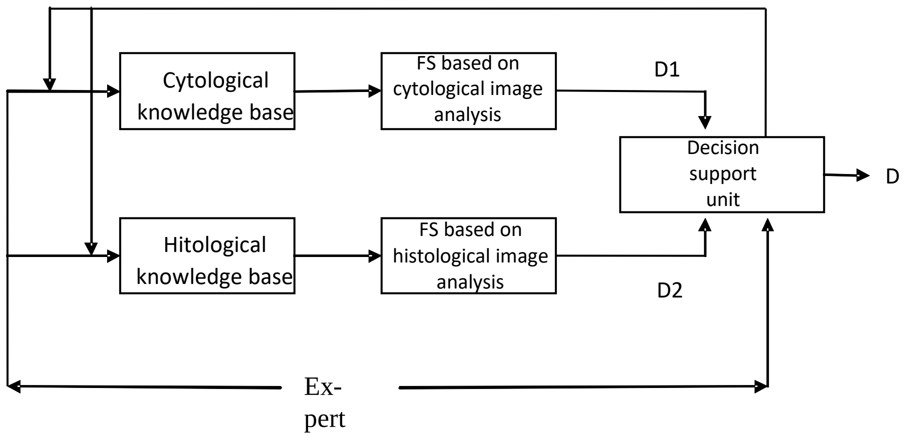

Fig. 6. Diagnosing process by the developed system

The decision support unit receives input D1, which corresponds to the diagnosis of the breast pathological state based on the cytological image analysis, as well as D2, which corresponds to the diagnosis made on the basis of histological image analysis. Since D2 is the confirmation of the final diagnosis, in the case when D1≠D2, the decision-making unit submits the diagnosis D2. In other cases, when D1= D2 or if D2 is not specified, D1 is output.

Fuzzy sets are indicated by a certain base scale B and a membership function - μ(x), x is B, which takes a value in the interval [0… 1]. Thus, the fuzzy set B is the set of pairs of type (x, μ (x)), where x is B. The following expression is common:

$$B = \sum_{i=1}^{n} \frac{x_i}{\mu(x_i)}, \qquad (1)$$

where (x_i) – is the i-th value of the base scale.

The membership function determines the subjective degree of the expert's belief that a given value of the base scale corresponds to the value of a fuzzy set.

The choice of productive rules is based on the definition of such fuzzy rules so that the control module generates certain output signals when receiving input signals. Therefore, it is necessary to divide the space of the input and output signals into sets and define the corresponding membership functions for them. It is important to write fuzzy rules based on experimental sampling, create a table to record a productive rule base and a rule table (presence or absence of features), identify the degree of truth, generate the appropriate rules, and form a base of fuzzy rules.

Fuzzy modeling in the Matlab environment is based on the application of the Fuzzy Logic Toolbox extension package, which presents a large number of functions of fuzzy logic and fuzzy inference.

In fuzzy modeling, the Mamdani format is usually used, in which the antecedence and the consequence of the rules are defined by fuzzy sets, such as "low", "medium", "high", etc. In the fuzzy conclusion of the Mamdani type, the knowledge base consists of the rules "IF/THEN".

Fuzzy models based on Mamdani's fuzzy inference device are accessible; their structure is meaningfully interpreted in terms that are understandable to both developers with high mathematical qualifications and customers, such as doctors, economists, or managers. The availability of fuzzy Mamdani models is one of the major advantages. Because of fuzzy logic, they are successfully competing with other methods, especially for those applications where meaningful interpretation is more important than accuracy of modeling.

In a fuzzy system of cytological image processing for diagnosis of breast pathological conditions, the input variables are features (signs) of pathological conditions that are present in the image [17]. The following features are used:

c1 – flattened apocrine epithelium;

c2 – formation of papillary structures;

c3 – presence of secretory activity in cells;

c4 – centrally located rounded hyperchromic nuclei;

c5 – a small number of hyperchromic monomorphic cells;

c6 – cells are located in layers;

c7 – there are many phagocytes and histiocytes in the background;

c8 – presence of secret in the cell space;

c9 – formation of cell complexes;

c10 – formation of papillary complexes with dense structures of cells in multi-layers;

c11 – large cell sizes;

c12 – large nuclei with intense chromatin;

c13 – intensively expressed nuclei;

c14 –a narrow rim of intensely stained cytoplasm;

c15 –rounded hyperchromic nuclei;

c16 – fibroblasts.

Each of the features is set with only two fuzzy states of "presence" or "absence" in the image.

For the diagnosis of non-proliferative breast disease, proliferative breast disease and fibroadenoma, there are no mutually exclusive features in cytological images. However, there are some features that may be present or others that must be present.

In particular, to confirm the diagnosis of non-proliferative breast disease in the cytological image, the diagnostic physician should always see the features c1, c3, c4 and c5. In addition, usually there will be features c2, c5, c6 or c1, c3, or c1, c3, c8. Based on this, we can conclude that to confirm the diagnosis of non-proliferative breast disease, it is necessary to develop a base of 16 rules.

Proliferative breast disease and fibroadenoma can be confirmed only if there are features of c9, c10, c11 and c12 (in case of breast disease) in the image, and c1, c2, c11, c13, c14, c15, c16 (in case of fibroadenoma).

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In general, a fuzzy system is developed based on 18 rules of the "IF_THEN" type:

1. If (c1 is present) and (c3 is present) and (c4 is present) and (c5 is present) then (diagnosis-cytology is unprolif-mastopaty)
2. If (c1 is present) and (c2 is present) and (c3 is present) and (c4 is present) and (c5 is present) then (diagnosis-cytology is unprolif-mastopaty)
3. If (c1 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c6 is present) then (diagnosis-cytology is unprolif-mastopaty)
4. If (c1 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c7 is present) then (diagnosis-cytology is unprolif-mastopaty)
5. If (c1 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c8 is present) then (diagnosis-cytology is unprolif-mastopaty)
6. If (c1 is present) and (c2 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c6 is present) then (diagnosis-cytology is unprolif-mastopaty)
7. If (c1 is present) and (c2 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c7 is present) then (diagnosis-cytology is unprolif-mastopaty)
8. If (c1 is present) and (c2 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c8 is present) then (diagnosis-cytology is unprolif-mastopaty)
9. If (c1 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c6 is present) and (c7 is present) then (diagnosis-cytology is unprolif-mastopaty)
10. If (c1 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c6 is present) and (c8 is present) then (diagnosis-cytology is unprolif-mastopaty)
11. If (c1 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c7 is present) and (c8 is present) then (diagnosis-cytology is unprolif-mastopaty)
12. If (c1 is present) and (c2 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c6 is present) and (c7 is present) then (diagnosis-cytology is unprolif-mastopaty)
13. If (c1 is present) and (c2 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c6 is present) and (c8 is present) then (diagnosis-cytology is unprolif-mastopaty)
14. If (c1 is present) and (c2 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c7 is present) and (c8 is present) then (diagnosis-cytology is unprolif-mastopaty)
15. If (c1 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c6 is present) and (c7 is present) and (c8 is present) then (diagnosis-cytology is unprolif-mastopaty)

16. If (c1 is present) and (c2 is present) and (c3 is present) and (c4 is present) and (c5 is present) and (c6 is present) and (c7 is present) and (c8 is present) then (diagnosis-cytology is unprolif-mastopaty)

17. If (c9 is present) and (c10 is present) and (c11 is present) and (c12 is present) then (diagnosis-cytology is prolif-mastopaty)

18. If (c1 is present) and (c2 is present) and (c11 is present) and (c13 is present) and (c14 is present) and (c15 is present) and (c16 is present) then (diagnosis-cytology is fibroadenoma)

The fuzzy cytological image analysis system is modeled in Matlab using FuzzyLogicToolbox.

The input variables of this fuzzy system are the features c1-c16 described above. The output of the proposed system (diagnosis-cytology) is the diagnosis of non-proliferative breast disease (unprolif-mastopaty), proliferative breast disease (prolif-mastopaty) and fibroadenoma (fibroadenoma). A general outline of the fuzzy cytological diagnosis system is given in Figure 7.

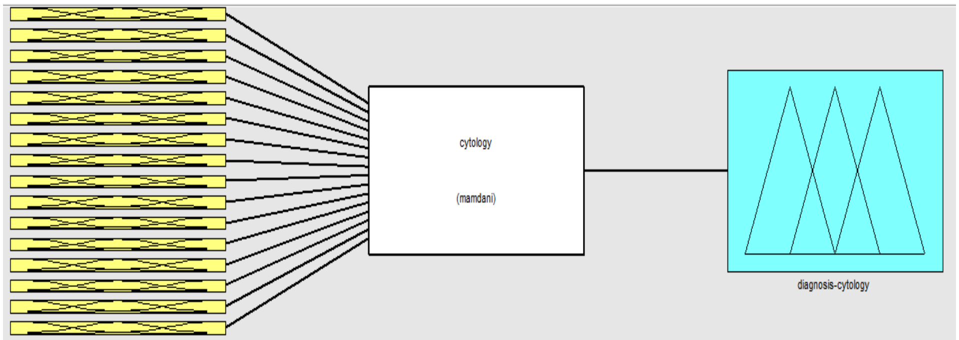

Fig. 7. General view of the developed fuzzy system

The membership functions of the input variables, that is, signs C1-C16, are given a bell-shaped form that reflects two sets of values of each of them, namely, "present" or "absent" feature in the image (Figure 8) [8].

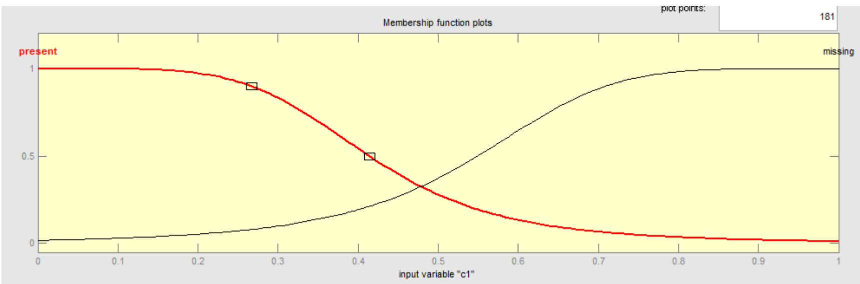

Fig. 8. Membership functions of input variables on the example of C1

A triangular shape was used to set the membership functions (Figure 9).

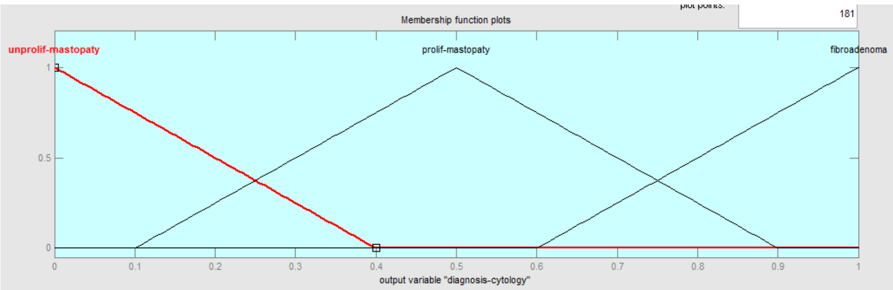

Fig. 9. Membership functions of a variable diagnosis-cytology

In a fuzzy diagnosis system, based on histological image analysis, qualitative features of breast precancerous conditions are input, and correct diagnosis is output (Figure 10).

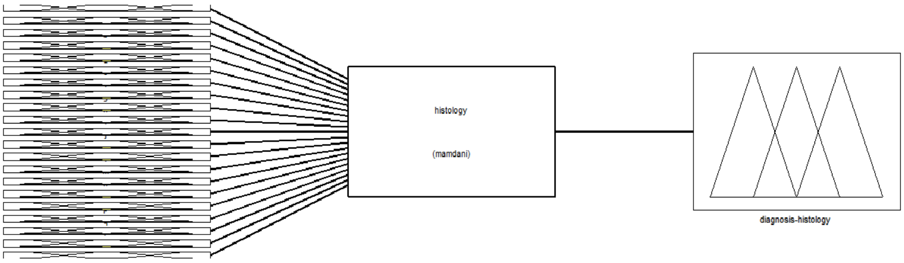

Fig.10. Fuzzy system developed in the Fuzzy Logic Toolbox Editor

The input data are the features of pathological conditions described above; they are given in the form of a bell-shaped membership function. It is worth noting that all input variables can only be present or absent in histological image, therefore, they are represented by the fuzzy sets presented in Figure 11.

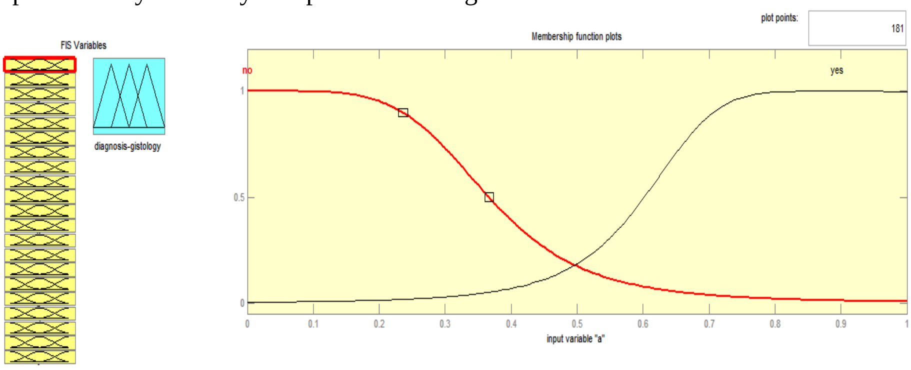

Fig. 11. Membership functions of the input variables of the fuzzy diagnosis system

The output data are actually diagnoses derived from the productive rules, so they will look like a triangular membership function, as shown in Figure 12.

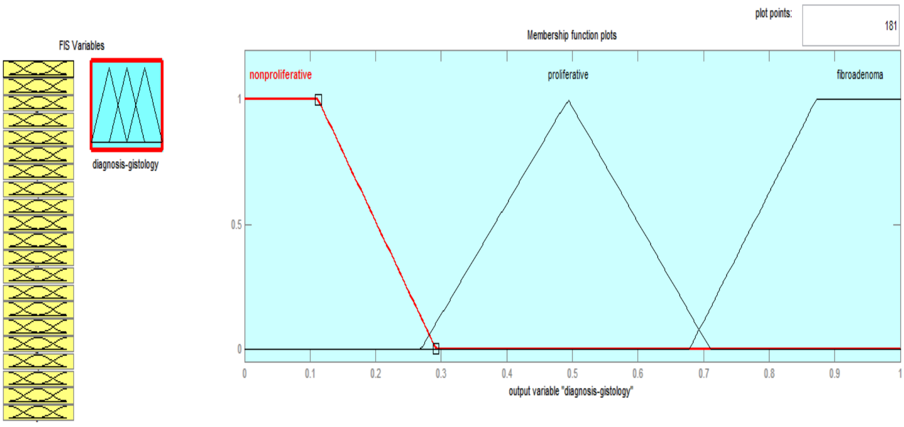

Fig. 12. Membership functions of output data

Productive rules are an integral part of the knowledge base. Each productive rule reflects a separate piece of knowledge from an expert. Productive rules can be modified as a single unit, regardless of other rules.

In the medical expert system, such rules are used to establish links between symptoms or qualitative features and diagnosis.

In the developed fuzzy system, there are 519 productive rules of the "IF/THEN" type [18].

6 Evaluation of operation correctness of the developed fuzzy system

To evaluate the efficiency of the developed fuzzy systems and the possibility of their software or hardware realization, it is necessary to analyze the rule base and the correctness of the fuzzy conclusion, depending on the input values of features of pathological conditions.

The correctness of work of the fuzzy system of cytological image analysis follows from the analysis of the fuzzy conclusion obtained during the operation of the defined rule base (Figure 13).

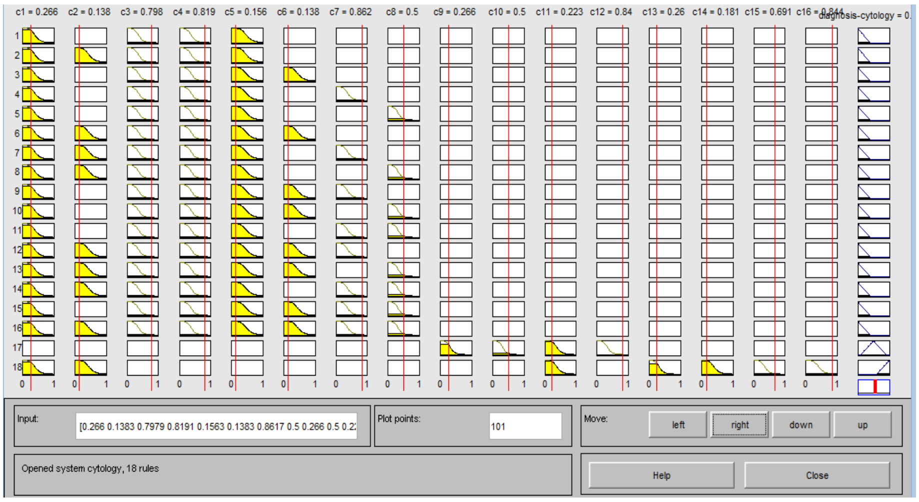

Fig. 13. The result of operation of a fuzzy system for the diagnosis of breast pathological conditions based on cytological image analysis

The fuzzy system is evaluated by analyzing the productive rules base (Figure 14).

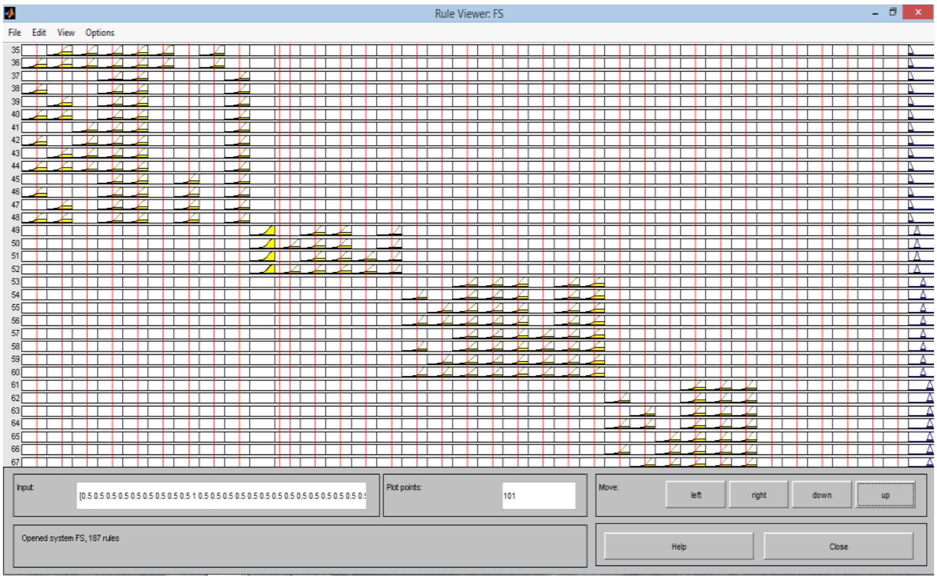

Fig. 14. An example of the productive rules base of the developed fuzzy system based on histological image analysis

The features of pathological conditions on histological images were provided by experts and used in the study. Analysis of the work of a fuzzy system confirms its efficiency and correctness of work. Therefore, it can be argued that hardware or software realization of the proposed fuzzy system for breast disease diagnosing can be used in telemedicine to make an accurate diagnosis excluding the subjective nature of a doctor's diagnosis.

Conclusions

1. In this research study, the analysis of the current state and tendencies in telemedicine and its application for solving medical problems are carried out.

2. The main problems of breast pre-cancer diagnosing are identified and it is suggested to use the fuzzy logic apparatus to solve them.

3. Modern diagnostic systems based on fuzzy logic are analyzed.

4. The cytological and histological image analysis is carried out, the basic features are identified, and the productive rules for the breast pre-cancer diagnosis are formulated.

5. A fuzzy knowledge base for cytological and histological image processing is presented. Based on the developed rules of fuzzy conclusion, a system for diagnosing the breast pathological conditions was constructed.

6. This fuzzy system solves the main problem of diagnosis of the breast pathological conditions, namely the subjectivity in doctor’s diagnosis during the cytological image analysis. In addition, the system can be used in questionable diagnoses as a confirmation of experts’ opinion.

Areas for further research

The first direction is the expansion of the database of histological and cytological images with new types of breast dysplastic and cancerous conditions, the search for new informational features for diagnosis. This direction requires the involvement of expert cytologists and histologists.

The second direction is the hardware application of the developed fuzzy system for breast disease diagnosis. This will allow using this diagnostic tool to pre-diagnose or confirm the preliminary diagnosis of a physician independently from telemedicine networks.

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