DEVELOPMENT OF THE PRINCIPLES OF FUZZY RULE-BASED SYSTEM FOR HEPATOCELULAR CARCINOMA STAGING

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Abstract

The article proposes the principles for the development of a fuzzy rule-based physician decision support system n to determine the stages of the most common hepatocellular carcinoma (HCC) among malignant tumors of liver. The stages of HCC, i. e., critical situations, are expressed by different combinations of clinical signs of input data and emerging clinical conditions. These combinations shape the multiplicity of possible situations (critical situations) by forming linguistic rules that are in fuzzy relations with one another. The article presents the task of developing a fuzzy rules-based system for HCC staging by classifying the set of possible situations into given classes. In order to solve the problem, fuzzy rules of clinical situations and critical situations deviated from them are developed according to the possible clinical signs of input data. The rules in accordance with the decision-making process are developed in two phases. In the first phase, three input data are developed: nine rules are developed to determine possible clinical conditions based on the number, size, and vascular invasion of tumor. In the second phase, seven rules are developed based on possible combinations of input data on the presence of lymph nodes and metastases in these nine clinical conditions. At this stage, the rules representing the fuzzification of results obtained are also described. The latter provide an interpretation of results and a decision on related stage of HCC. It also proposes a functional scheme of fuzzy rules-based system for HCC staging, and presents the working principle of structural blocks. The fuzzy rule-based system for HCC staging can be used to support physicians to make diagnostic and treatment decisions.

Keywords: stages of hepatocellular carcinoma, physician's decision support, clinical signs, fuzzy rule-based system, knowledge base, decision-making.

1. Introduction

Nowadays, the role of information technology in improving the quality of medical care provided to the population is undeniable, and the global development trend of electronic medicine (e-medicine) proves this. One of the main fields of e-medicine is the development of Information and Communication Technologies (ICT) based tools to support physician decisions [1, 2]. As one of these tools, the creation of intelligent systems based on the knowledge of experienced physician-experts to support diagnostic and treatment decisions is on the agenda. The fact that these systems represent the knowledge and experience of professionals and physician-experts on a particular disease makes them a necessary desktop tool to support physician decisions on diagnosis and treatment.

One of the main tasks of a physician in modern medical practice is to appoint an accurate diagnosis, to prescribe the right treatment in multifactorial uncertainty [3]. Thus, the manifestation of many common diseases with weak and atypical symptoms, incompleteness and inaccuracy of

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information shifts the issues of diagnosis and the appointment of treatment into a fuzzy environment, causing the diagnostic errors [4]. On the other hand, given that medicine is a field of large-scale data production, and that 30 % of the data collected and stored worldwide is medical data [5], it is possible to imagine how difficult the decision-making process is for physicians in this information flood. World Health Organization estimates 20 % of medical errors to be caused by incomplete medical information, incorrect and untimely diagnosis, incorrect prescription of drugs, etc., which affect the quality of medical services. In the US, where 15–18 % of GDP is spent on health care, up to 100,000 people die each year due to medical errors, while in Germany the number of deaths due to medical errors varies from 30,000 to 60,000 [6]. However, physicians' mistakes are not intentional, they are not caused by irresponsibility and unprofessionalism of doctors. Given the abundance of information, physician has to make a decision based on some of this information. The limited ability of the human brain to remember and judge the value of more than 7 indicators [7] leads to shortcomings in medical decisions determined by certain combinations of a large number of indicators. These increase the need to develop intelligent systems that support physician to make error-free treatment and diagnostic decisions by comparatively analyzing large amounts of information in a complex, uncertain information environment.

Today, there is a sufficient methodological basis for creating a new information environment for medical practice, reducing the time spent on medical documentation, developing intelligent systems that support physicians' diagnostic and treatment decisions. However, the use of such systems in clinical condition and as a desktop tool is still unrealized [1, 2].

Liver disease is currently one of the leading causes of death in the world [4]. Liver cancer is the second leading cause of death from cancer in the world, accounting for 80 % (90 % in the United States) of HCC [4, 8, 9]. This tumor is most common for people aged 60–70 and often for men (2.5 times more than women), while in high-risk countries, it is observed earlier, in people aged 30–40. HCC is rated the 5–6th most common cancer and the third leading cause of death from cancer. HCC is found in about one million people worldwide every year [4]. Determination of the stages of HCC is the most important issue for its diagnosis and treatment. Solution to this problem depends on the degree of spread of the tumor, the condition of the lymph nodes, the functional state of the liver, the general condition of the body, etc. Of course, each criterion is characterized by certain features. In the context of abundance of information, the stages of HCC are determined according to different combinations of features according to specific schemes. Thus, referring to specific schemes in solving the problem of HCC staging, the prevention of physician errors due to the multiplicity and hierarchy of criteria that form these schemes, the large number of symptoms and their uncertainty and linguistic nature necessitate the development of an appropriate intelligent system and its use as a desktop computer program.

This article provides a conceptual model for HCC staging, referring to the methodology for establishing physician decision support systems (PDSS), and describes the development of a fuzzy rules system that shapes the knowledge base in stages. The article defines the functionalization principles and structural scheme of the fuzzy rule-based system for HCC staging, and presents the working principle of structural components.

2. Materials and methods

Liver is one of the vital organs in the human body, performing many basic functions. There are more than 100 types of liver diseases, for the assessment of which personal and integrated computer models are widely used. At present, the scientific literature refers to the judgments based on artificial neural networks, fuzzy logic, solution tree, genetic algorithms and rules to establish a system for diagnosing liver diseases [10–27].

[10] describes a comprehensive approach based on the analysis of key components and K-proximity methods in the establishment of a liver disease diagnostic system. [11, 12] develop the models based on artificial neural networks for the detection of hepatitis and [13] for the diagnosis of liver disease. [14] uses fuzzy logic to detect hepatitis, and [15] to develop a method for semi-automatic segmentation of liver tumor, and [16] to solve the classification of hepatobiliary diseases [17]. uses solution tree approach to classify liver viruses in chronic hepatitis C and B, and [18] to study

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liver cirrhosis. [19, 20] use the integration of artificial neural networks and fuzzy logic to detect liver disease and [21] to increase the classification accuracy of liver disease. [22, 23] also use this integration to classify liver disease and assess the accuracy of hepatitis prognosis.

[24, 25] use the integration of artificial neural networks and genetic algorithms to detect liver disease and stabilize fibrosis in chronic hepatitis. [26] uses the integration of fuzzy logic and genetic algorithms for the detection of liver disease, and [27] uses the integration of artificial neural networks and genetic algorithms for making decisions on liver transplantation.

For the selection of the prognosis and treatment method of liver cancer, physicians often refer to the degree of tumor spread when determining the stage of the tumor, and for this purpose, they use numerous classifications. However, experience has shown that, unlike other tumors, in addition to the degree of tumor spread in HCC, the functional status of liver and the general condition of the body also play an important role in the prognosis and choice of treatment. Therefore, the classifications developed in recent years take into account the spread of tumor, the parenchyma and general condition of liver [4]. According to the final classification, 5 input data are currently taken into account for HCC staging, namely:

1) number of tumors;
2) size of tumors;
3) vascular invasion;
4) lymph node;
5) presence of distant metastases.

Each input data is identified by clinical signs. For example, the size of tumors often has 4 clinical signs, as less than 2 cm or 2 cm; greater than 2 cm; less than 5 cm; greater than 5 cm. Different standard combinations of possible clinical features of input data, such as the number, size, and vascular invasion of the tumor, define the following 9 clinical conditions:

$$T=<T1a; \ T1b; \ T2a; \ T2b; \ T3; \ T4a; \ T4b; \ T4c; \ T4d>.$$

Here:
$T1a$ – single tumor, 2 cm or less, no vascular invasion;
$T1b$ – single tumor, larger than 2 cm, no vascular invasion;
$T2a$ – single tumor, greater than 2 cm, vascular invasion;
$T2b$ – many tumors, all smaller than 5 cm;
$T3$ – multiple tumors, at least one is larger than 5 cm;
$T4a$ – single or multiple tumors, any size, invasion of large branches of the portal vein;
$T4b$ – single or multiple tumors, any size, invasion of hepatic vein;
$T4c$ – single or multiple tumors, any size, invasion of nearby organs (except gallbladder);
$T4d$ – single or multiple tumors, any size, with perforation of the peritoneum.

Possible combinations of the clinical conditions with the clinical signs of input data on the presence of lymph nodes and distant metastases lead to the following 7 critical situations, which indicate the HCC stages:

$$R=<IA, IB, II, IIIA, IIIB, IVA, IVB>.$$

Here: IA, IB, II, $IIIA$, $IIIB$, IVA, IVB are conditional markings of HCC stages determined by clinical signs.

They represent standard combinations of possible clinical signs of input data.

Obviously, the task of HCC staging has a fairly accurate decision-making strategy. The development of an intelligent system for HCC staging, referring to the methodologies presented in [28] for solving problems with an accurate decision-making strategy, involves knowledge modeling related to the subject area.

The uncertainty of input data for HSC staging, the probability of errors in their determination, the inevitability of changes that may occur in the period up to the results require to refer to fuzzy systems for solving the task of HCC staging.

Fuzzy systems are one of the most important areas applying the theory of fuzzy sets [29]. Such systems are often based on a structural model in the form of fuzzy rules. Fuzzy rule-based systems (FRBS), a more advanced version of classical systems referring to IF-THEN rule, use fuzzy logic judgments instead of classical units [30]. Linguistic model of FRBS, based on set of rules IF-THEN, the behavior of the system can be described in natural expressions. As a result, the activity to be performed or belonging to any class is determined.

FRBS is composed of linguistic rules and includes fuzzy judgments, in which the antecedent and the consequent are in fuzzy implication and composition with each other [31]. When a set of conditions IF-THEN in fuzzy rules is fulfilled in the FRBS knowledge base, the output mechanism module and a set of consequents representing the fuzzification interface are activated, the fuzzy rule is defuzzified and delivered to the user as a result.

3. Problem statement and solution

The goal of the current work is to develop FRBS to prevent physician errors in HCC staging, to support physician decisions, and to make better decisions taking into account the uncertainties in decision-making process. This system has to implement HCC staging referring to 5 input data, i. e., select one of the 7 critical situations and make a decision according to the current situation.

The development of the FRBS for HCC staging requires the solution of the following stages:
1. Formation of a fuzzy rules system for determining the clinical situation.
2. Formation of a fuzzy rules system for determining critical situations (HSC staging).
3. Development of the functioning principles of FRBS for HCC staging.
The problem is solved in the following steps.

3. 1. Formation of a fuzzy rules system for determining the possible clinical situations

The first input data for HCC staging includes the number of tumors ($t1$). According to the number of tumors, two clinical signs are distinguished: single tumor and multiple tumors (**Table 1**).

Table 1
Clinical signs and linguistic variables of input data on the number of tumors

Input data	Level	Clinical signs	Conditional expression	Linguistic variables
Number of tumors ($t1$)	$=1$	single tumor	$t1a$	Positive (P)
	>1	multiple tumors	$t1b$	High positive (YP)

The size of the tumors ($t2$) is taken into account as the second input data. **Table 2** presents the clinical signs of tumors according to their size.

Table 2
Clinical signs and linguistic variables of input data on the size of tumors

Input data	Level	Clinical signs	Conditional expression	Linguistic variables
Size of tumors ($t2$)	≤ 2 cm	2 cm or less	$t2a$	Little (K)
	>2 cm	greater than 2 cm	$t2b$	Medium (O)
	<5 cm	Less than 5 cm	$t2c$	Large (B)
	>5 cm	greater than 5 cm	$t2d$	Very large (ÇB)

The third input data for HCC staging includes vascular invasion ($t3$). **Table 3** presents possible clinical signs and linguistic variables for vascular invasion.

The standard combination of the number and size of tumor and the possible clinical signs of vascular invasion is identified as the following 9 clinical conditions based on expert evaluation (**Table 4**).

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Table 3

Clinical signs and linguistic variables for vascular invasion

Input data	Clinical signs	Conditional expression	Linguistic variables
	no vascular invasion	$t3a$	Negative (N)
	vascular invasion presents	$t3b$	Positive (P)
	invasion of large branches of the portal vein	$t3c$	High positive (YP)
Vascular invasion ($t3$)	invasion of the hepatic vein	$t3d$	Very high positive (ÇYP)
	invasion of nearby organs (except the gallbladder)	$t3e$	Extremely positive (HÇP)
	perforation of the peritoneum	$t3f$	Absolutely positive (AP)

Table 4

Determination of standard clinical condition according to clinical signs

No.	Clinical condition	Number of tumors	Size of tumors	Vascular invasion
1	$T1a$	Single tumor	2 cm or less	No vascular invasion
2	$T1b$	Single tumor	greater than 2 cm	No vascular invasion
3	$T2a$	Single tumor	greater than 2 cm	Vascular invasion presents
4	$T2b$	Multiple tumors	all less than 5 cm	Any possible situation
5	$T3$	Multiple tumors	At least one is greater than 5 cm	Any possible situation
6	$T4a$	Single or multiple tumors	Any size	Invasion of large branches of the portal vein
7	$T4b$	Single or multiple tumors	Any size	Invasion of the hepatic vein
8	$T4c$	Single or multiple tumors	Any size	Invasion of nearby organs (except the gallbladder)
9	$T4d$	Single or multiple tumors	Any size	Peritoneum perforation

Based on **Table 4**, the following fuzzy rules of clinical situations described by linguistic variables are formed in the knowledge base of FRBS:

Rule 1. If ($t1$ *is P*) *and* ($t2$ *is K*) *and* ($t3$ *is N*) *then* (T *is T1a*).

Rule 2. If ($t1$ *is P*) *and* ($t2$ *is O*) *and* ($t3$ *is N*) *then* (T *is T1b*).

Rule 3. If ($t1$ *is P*) *and* ($t2$ *is O*) *and* ($t3$ *is P*) *then* (T *is T2a*).

Rule 4. If ($t1$ *is YP*) *and* ($\forall t$: $t2$ *is B*) *then* (T *is T2b*).

Rule 5. If ($t1$ *is YP*) *and* ($\exists t$: $t2$ *is ÇB*) *then* (T *is T3*).

Rule 6. If (($t1$ *is P*) *or* ($t1$ *is YP*)) *and* (($t2$ *is K*) *or* ($t2$ *is O*) *or* ($t2$ *is B*) *or* ($t2$ *is ÇB*)) *and* ($t3$ *is YP*) *then* (T *is T4a*).

Rule 7. If (($t1$ *is P*) *or* ($t1$ *is YP*)) *and* (($t2$ *is K*) *or* ($t2$ *is O*) *or* ($t2$ *is B*) *or* ($t2$ *is ÇB*)) *and* ($t3$ *is ÇYP*) *then* (T *is T4b*).

Rule 8. If (($t1$ *is P*) *or* ($t1$ *is YP*)) *and* (($t2$ *is K*) *or* ($t2$ *is O*) *or* ($t2$ *is B*) *or* ($t2$ *is ÇB*)) *and* ($t3$ *is HÇP*) *then* (T *is T4c*).

Rule 9. If (($t1$ *is P*) *or* ($t1$ *is YP*)) *and* (($t2$ *is K*) *or* ($t2$ *is O*) *or* ($t2$ *is B*) *or* ($t2$ *is ÇB*)) *and* ($t3$ *is AP*) *then* (T *is T4d*).

Based on these fuzzy rules, the determination of the current clinical signs in accordance with the clinical status of input data is implemented in the following sequence:

1. The current values of the 3 input data input enter the system, which generate a fuzzy vector of clinical signs as the input values of the current situation:

T=(number of tumors <single; multiple>, size of tumors <2 cm or less; greater than 2 cm; less than 5 cm; greater than 5 cm>, vascular invasion < no vascular invasion; vascular invasion presents; invasion of large branches of the portal vein; invasion of the hepatic vein; invasion of nearby organs (except the gallbladder); perforation of the peritoneum)

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or

$$T = (t1 < t1a;\ t1b >,\ t2 < t2a;\ t2b;\ t2c;\ t2d >,\ t3 < t3a;\ t3b;\ t3c;\ t3d;\ t3e;\ t3f >).$$

2. The fuzzification procedure is performed, the signs are expressed by linguistic variables in the clinical signs vector, the fuzzy vector of linguistic variables is obtained:

$$T = (t1 < P;\ YP >,\ t2 < K;\ O;\ B;\ ÇB >,\ t3 < N;\ P;\ YP;\ ÇYP;\ HÇP,\ AP >).$$

3. Through fuzzy extraction program IF-THEN, each possible fuzzy vector of linguistic variables is opposed to one output vector from the knowledge base, i. e., clinical situation.

4. According to the standard combinations of clinical signs of 3 input data viewed, one of the 9 clinical conditions is selected, i.e., defuzzification is performed, the clinical condition is determined, the result is obtained.

Fig. 1 schematically describes the mechanism for determining the clinical conditions $T1a$, $T1b$, $T4d$ according to the clinical signs of input data.
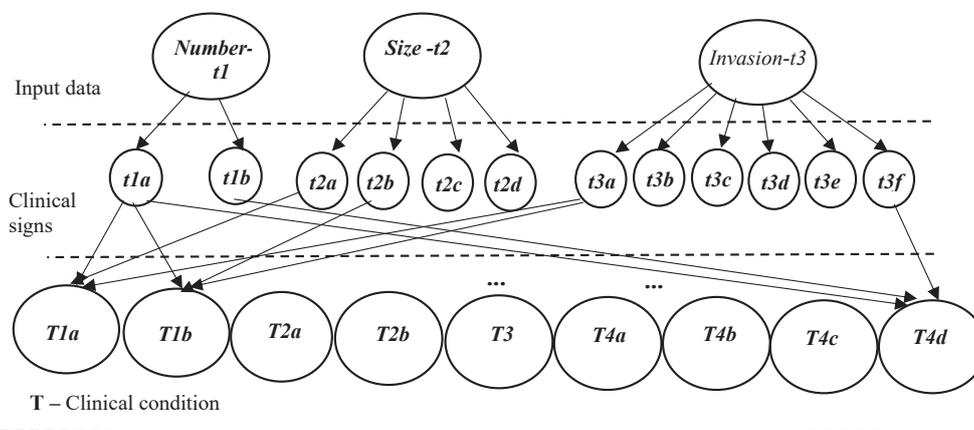
Fig. 1. Schematic description of the tumor of clinical condition according to the clinical signs for the number and size of tumors and the vascular invasion

Fig. 1 visually shows that:
– the clinical condition $T1a$ is determined by a combination of clinical signs, such as a single tumor, a tumor of 2 cm or less, and no vascular invasion;
– the clinical condition $T1b$ is determined by a combination of clinical signs, such as a single tumor, a tumor greater than 2 cm, and the absence of vascular invasion;
– the clinical condition $T4d$ is determined by a combination of clinical signs, such as peritoneal perforation as a result of vascular invasion, regardless of single or multiple tumors.
This description also visually illustrates the formation of Rule 1, Rule 2 and Rule 9.

3. 2. Formation of a fuzzy rules system of critical situations
The lymph node (N) is considered as the fourth input data for HCC staging, i. e., critical situations, and **Table 5** presents the possible clinical signs it may acquire.

Table 5
Clinical signs and linguistic variables for lymph nodes

Input data	Clinical signs	Conditional expression	Linguistic variables
Lymph node (N)	lymph node is not identified	Nx	Negative (Neq)
	no metastasis in lymph node	$N0$	Positive (P)
	metastasis in lymph node presents	$N1$	High positive (YP)

Distant metastasis (*M*) is considered as the fifth input data for HCC staging, and it is determined by 2 clinical signs (**Table 6**).

Table 6

Clinical signs and linguistic variables for lymph nodes

Input data	Clinical signs	Conditional expression	Linguistic variables
Distant metastasis (*M*)	No distant metastasis	*M*0	Negative (*Neg*)
	Distant metastasis presents	*M*1	Positive (*P*)

According to the stages of HCC, 7 critical situations (*R*) are possible (**Fig. 2**):

$$R = <R1; R2; R3; R4; R5; R6; R7>.$$

Rule 10. *If* (*R is R*1) *then* (*HCC is in stage IA*).
Rule 11. *If* (*R is R*2) *then* (*HCC is in stage IB*).
Rule 12. *If* (*R is R*3) *then* (*HCC is in stage II*).
Rule 13*. If* (*R is R*4) *then* (*HCC is in stage IIIA*).
Rule 14. *If* (*R is R*5) *then* (*HCC is in stage IIIB*).
Rule 15. *If* (*R is R*6) *then* (*HCC is in stage IVA*).
Rule 16. *If* (*R is R*7) *then* (*HCC is in stage IVB*).

Thus, the rules generated in FRBS knowledge base for determining the critical situation are described as follows:

Rule 17*. If* (*T is T*1*a*) *and* (*N is P*) *and* (*M is N*) *then* (*R is R*1).
Rule 18*. If* (*T is T*1*b*) *and* (*N is P*) *and* (*M is N*) *then* (*R is R*2).
Rule 19*. If* ((*T is T*2*a*) *or* (*T is T*2*b*)) *and* ((*N is P*) *and* (*M is N*) *then* (*R is R*3).
Rule 20*. If* (*T is T*3) *and* (*N is P*) *and* (*M is N*) *then* (*R is R*4).
Rule 21*. If* ((*T is T*4*a*) *or* (*T is T*4*b*) *or* (*T is T*4*c*) *or* (*T is T*4*d*)) *and* (*N is P*) *and* (*M is N*) *then* (*R is R*5).
Rule 22*. If* ((*T is T*1*a*) *or* (*T is T*1*b*) *or* (*T is T*2*a*) *or* (*T is T*2*b*) *or* (*T is T*3) *or* (*T is T*4*a*) *or* (*T is T*4*b*) *or* (*T is T*4*c*) *or* (*T is T*4*d*)) *and* (*N is YP*) *and* (*M is N*) *then* (*R is R*6).
Rule 23*. If* ((*T is T*1*a*) *or* (*T is T*1*b*) *or* (*T is T*2*a*) *or* (*T is T*2*b*) *or* (*T is T*3) *or* (*T is T*4*a*) *or* (*T is T*4*b*) *or* (*T is T*4*c*) *or* (*T is T*4*d*)) *and* ((*N is Neq*) *or* (*N is P*) *or* (*N is YP*)) *and* (*M is P*) *then* (*R is R*7).

The scheme of determination of HCC stages *IB* and *IIIB* is presented (**Fig. 2**).
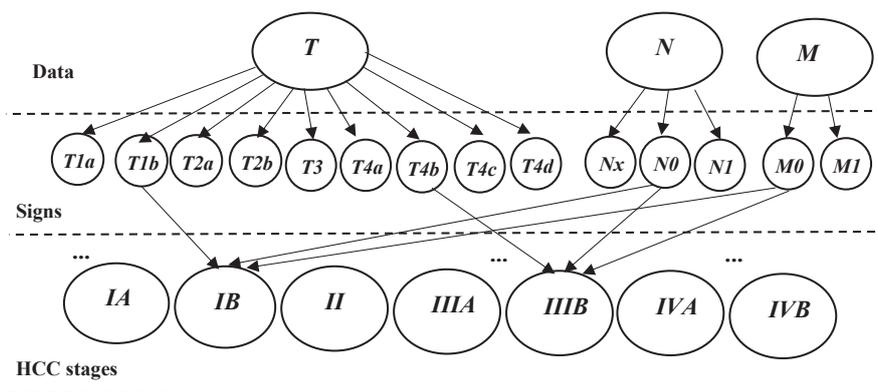
Fig. 2. Hierarchical structure of HCC staging, scheme of determination of *IB* and *IIIB* stages

Fig. 2 shows that in cases of absence of lymph node metastasis and the absence of distant metastasis, the critical situation corresponding to the clinical condition *T*1*b* corresponds to stage *IB* of HCC. This section covers the implementation of Rule 11 and Rule 18.

The figure also depicts a combination of components shaping a critical situation in accordance with stage *IIIB* of HCC. Thus, this critical situation is determined by the clinical condition of *T4b* in the absence of lymph node metastases and in the absence of distant metastases. This section visualizes the implementation of Rule 14 and Rule 21, and so on.

3. 3. Functional scheme of FRBS for HCC staging

According to the structure of the traditional PDSS, the FRBS includes three main components for HCC staging: KB, logical reasoning mechanism, and the interaction interface [3, 32]. Based on 16 fuzzy rules that make up the KB, the result is generated in logical reasoning mechanism and transmitted to the user (physician) through the interface. This outcome is the answer to the user's request entered to FRBS that is the decision of the system.

Fig. 3 presents the functional structure of proposed FRBS for HCC staging.
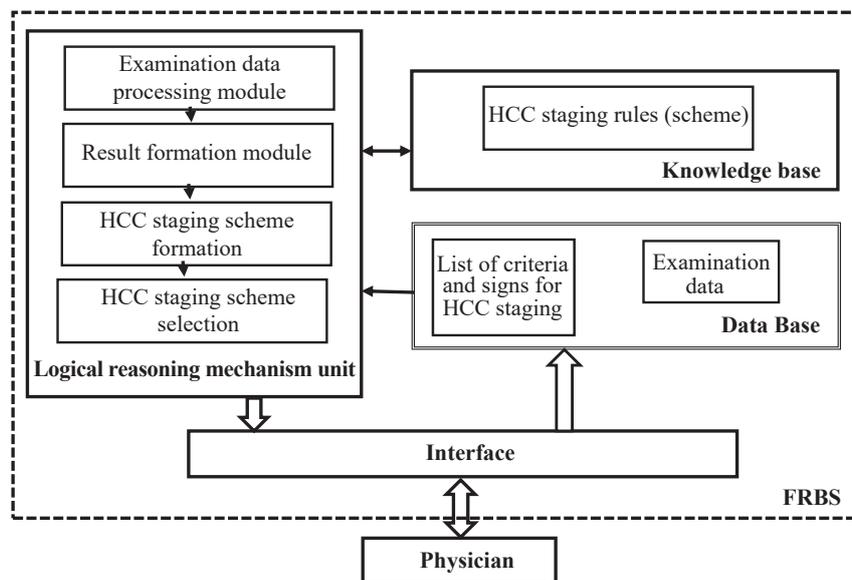
Fig. 3. The FRBS structure for HCC staging

The **database** stores input data for HCC staging and a complete list of their clinical signs, the current results of the patient's examination (examination data) in a single format.

The **KB** includes the subject area, specifically, *fuzzy rules in accordance with the production model of the description of knowledge for* HCC staging.

The **logical reasoning mechanism** generates a new fact based on the current input data (clinical signs of input data) received from the working memory. It is compared with the antecedent part of the fuzzy rules in KB (schemes for HCC staging), and the factual rule is activated and the result is transmitted to the user as logical reasoning mechanism result. These processes are implemented in the interaction of the relevant modules of logical reasoning mechanism with KB.

The interface block provides communication between the user (physician) and the FRBS, enables entering the patient's examination data (current symptoms) into the system, and delivers the results obtained in logical reasoning mechanism to the user.

4. Results

FRBS was performed on Delphi programming platform for HCC staging, and the software was implemented in the following stages: Database Development; KB Development; logical reasoning mechanism development. The system database includes the tables representing the following information necessary for HCC staging:

1) number of tumors;
2) size of tumors;

3) presence of vascular invasion;

4) presence of lymph nodes;

5) metastasis of tumors in the body.

The tables describing the clinical signs of these 5 input data are composed of the following areas:

1. Key area.

2. Disease code.

3. Code of clinical signs.

4. Clinical signs.

5. Clinical condition.

The following algorithm is used during the implementation of FRBS for HCC staging.

At the interpretation stage of the system development, the methods for specific problem statement to be solved, for initial data acquisition and obtaining the result were identified.

At the conceptualization stage, the structure of the knowledge related to the subject area, terminology, basic concepts and their attributes, the structure of input and output data, decision-making strategy, etc. were identified.

The expert knowledge obtained was transformed at the formalization stage, and fuzzy rules were formed. At the implementation phase, a prototype of FRBS, which includes a knowledge base, a logical reasoning mechanism, and other units, was developed on Delphi programming platform.

During the trial phase of the system, the ease and adequacy of the input/output interface, the effectiveness of the control strategy, the quality of the trial samples and their adequacy to reality were tested.

During trials conducted with the involvement of relevant experts, importance of FRBS for making correct diagnostic decisions is emphasized. The system is evaluated as a necessary instrumental tool to prevent physician errors.

5. Discussion of experimental results

The task of developing a software product for HCC staging was raised by relevant experts. The goal was to prevent physician errors that may occur when results were obtained based on their standard combinations of a large number of clinical signs. For this purpose, FRBS was developed referring to fuzzy rules for automatic HCC staging. The subject area for the system development was studied, the input data necessary for HCC staging were identified, the decision-making process and the mechanism of formation of physician's decisions were analyzed in detail. Fuzzy rules were referred to as an adequate solution mechanism for decision-making process. Physician-expert knowledge related to HCC staging was transformed into FRBS for the first time. A system of fuzzy rules was formed, and the theoretical and methodological basis of FRBS was developed to support physician's decision. In addition, the article described the FRBS implementation scheme, the operation principle of structural units, and developed an appropriate software product for the system implementation. In this regard, the article presented both the scientific and theoretical and practical basis for the establishment of FRBS.

Obviously, the systems based on expert knowledge often cover the modeling of a narrow subject area and are aimed at solving the problems faced by physicians in practice. The system developed in this regard can be used to support decisions on HCC staging only. Respectively, the input data, their number, clinical signs, etc. were developed for this disease. And these limited the use of FRBS in the diagnosis of other diseases. However, the approach proposed in the article can be used as a methodological basis for the diagnosis of other diseases. The most important and difficult moments in the implementation of this approach were related to the acquisition of expert knowledge in the field, the transformation of natural knowledge into artificial knowledge and its modeling. Of course, this required an individual approach to each disease, and the development of knowledge engineering.

The approach proposed in the article was the first step in the development of an intelligent system for liver disease and its transplantation, using established FRBS as a module of that system. The authors are currently conducting research to develop a system for decision support

in the treatment of liver disease and its transplantation. However, on the one hand, difficulties in collecting, systematizing and transforming expert knowledge, and on the other hand, in the current COVID-19 pandemic, the lack of time and limited contact create certain difficulties in conducting this research.

6. Conclusions

FRBS was designed to provide accurate information to physicians for selection of diagnostic and treatment methods of HCC for its staging.

The use of the system as a desktop tool by specialists in the relevant field enables physicians to eliminate errors in HCC staging, and to reduce the time spent on this process. The system development principles can be used for staging of other oncological diseases.

HCC staging system, like all other PDSSs, increases access to scientific facts, clinical recommendations, knowledge and expert knowledge related to the disease. The accumulation of expert knowledge on typical and atypical situations in these systems ensures its (knowledge) permanence, and prevents the loss of knowledge arisen in connection with the physician's physical, psychological, moral, etc. condition.

The use of such systems allows for successful applications in the development of telemedicine, benefitting from the knowledge of physician-experts in environments dangerous for human life.

These advantages require the development of similar systems for the diagnosis (treatment) of other diseases, the strengthening and deepening of research in this context for the advancement of e-medicine in Azerbaijan. In this regard, the main goal of the authors' perspective research is the creation of PDSS for the treatment and transplantation of liver diseases, and the developed intelligent system for HCC staging is one of its key subsystems.

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