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A hybrid fuzzy-ontology based intelligent system to determine level of severity and treatment recommendation for Benign Prostatic Hyperplasia

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ABSTRACT

This paper deals with application of fuzzy intelligent systems in diagnosing severity level and recommending appropriate therapies for patients having Benign Prostatic Hyperplasia. Such an intelligent system can have remarkable impacts on correct diagnosis of the disease and reducing risk of mortality. This system captures various factors from the patients using two modules. The first module determines severity level of the Benign Prostatic Hyperplasia and the second module, which is a decision making unit, obtains output of the first module accompanied by some external knowledge and makes an appropriate treatment decision based on its ontology model and a fuzzy type-1 system. In order to validate efficiency and accuracy of the developed system, a case study is conducted by 44 participants. Then the results are compared with the recommendations of a panel of experts on the experimental data. Then precision and accuracy of the results were investigated based on a statistical analysis.

1. Introduction

Prostate gland is a male organ. This gland may be involved by benign or malignant neoplasms. One of the most prevalent neoplasms among benign category is Benign Prostatic Hyperplasia (BPH). BPH is a considerable health problem to aging men through its associated signs, symptoms, and complications. Although it is not life-threatening, but it can have negative impacts on a patient's quality of life (QOL), as evidenced in community and clinic-based studies [1,2].

BPH is a progressive condition characterized by prostate enlargement accompanied by lower urinary tract symptoms (LUTS) [3,4]. It arises in the per-urethral and transition zones of the prostatic gland and represents an inescapable phenomenon for the aging male population [5]. Although it is uncommon before age 40, approximately 50% of men are involved in BPH-related symptoms at age 50. Incidence of BPH increases by 10% per decade and reaches 80% at approximately 80 year of age [6,7]. An estimated 75% of men with ages more than 50 have symptoms arising from BPH, and 20–30% of men reaching 80 and over 80 years old require surgical intervention for the management of BPH [3,4].

In real world, on one hand, patients having BPH symptoms belong to different social and cultural categories and on the other hand, having access to high level medical experts to determine the level of progression of the disorder may be limited due to weakness of the medical system of the region. This is a great motivation for researchers to develop intelli-

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gent systems such as expert systems to get various signs of the patient and determine level of the disease severity in an intelligent manner.

The first medical expert system which uses symbolic knowledge in a rule-based format, MYCIN, was developed in early 1970s [17]. Adlassnig [32,33] described CADIAG II. Then its successors CADIAG III and CADIAG IV [34], utilized the concepts of fuzzy sets in order to deal with inherent uncertainties in medical knowledge.

Application of intelligent system techniques in the field of prostate disorders is a nice research area. Petrovic et al. [8] have presented a novel case based reasoning (CBR) approach to generate dose plans for prostate cancer patients. In this approach, experience of oncologists in treating previous patients is captured and a dose in two phases is recommended using a modified Dempster–Shafer theory to fuse the dose plans suggested by the most similar cases retrieved from the case base.

Application of fuzzy expert systems in predicting pathological stages of prostate cancer has been investigated in Ref. [9]. In this paper utilizing uncertain variables and approximate reasoning, a fuzzy rule-based system is developed.

Fuzzy sets have been widely used in medical signal processing applications especially in the field of prostatic disorders. In Ref. [10], the concept of ignorance function is defined and used to determine the best threshold in transrectal prostate ultrasound images. Most of efficient classification methods are based on neuro-fuzzy classification (NEFCLASS). In Ref. [11], a new approach based on NEFCLASS to classify prostate cancer is presented. This approach has several features including batch learning, automatic cross validation, and automatic determination of the rule-base size. Since symptoms of BPH and prostate cancer are very similar, medical data related to both categories are obtained to test the system. In a similar study, a neuro-fuzzy system has been developed to predict the presence of prostate cancer [12].

Fuzzy sets and systems have also been used in other medical fields. For example fuzzy clustering has been used in designing efficient in homogeneity compensation models [35], brain MR image segmentation [36], Carotid artery image segmentation [37], analysis of thyroid diseases [38], and heart disease recognition systems [39].

Neural networks are widely used in medical diagnosis during the last two decades. Artificial Neural Networks (ANN) has been utilized in prognosis of prostate cancer in Ref. [13]. In Ref. [13], an ANN is devised that yields a prognostic result indicating whether patients have cancer or not using some of the related medical data. In another research, prostate boundary is detected in ultrasound images using biologically-inspired spiking neural networks. One of the main difficulties in prostate related therapies is insufficient accuracy in decision making based on ultrasound images. In order to solve this problem, Pulse-coupled neural networks (PCNNs) which are capable of extracting edges and segments from images are utilized [14].

Although all these studies have widely used AI techniques in prostatic disorders, but there are still some limitations. First, nearly all these studies focus on prostate cancer while BPH is much more prevalent among men so it is necessary to develop intelligent systems to deal with such an illness. Second, the literature lacks a hybrid intelligent system to be able to reproduce the real decision making processes performed by urologists to be understood by non-technical audiences such as physicians. As a result, since the expert's knowledge in the medical context is mostly linguistic, application of fuzzy logic accompanied by ontologies to represent the semantic structure of the expert's knowledge seems to be necessary. Moreover, there cannot be found a hybrid system to diagnose the BPH level and to recommend appropriate treatment, simultaneously.

In this paper, a hybrid fuzzy intelligent system consisting of two modules is represented. The first module receives several signs from the patient and determines the level of BPH severity on the basis of a rule-base framework. Then, the second module completes the process of therapeutic decision-making based on the output of the first module and several other input parameters. Eventually, ontologies are used to represent the semantic structure of the expert's knowledge and provide a comprehensive formulation of the generated outcomes. This formulation is in the form of a fuzzy rule-based system and decides what the appropriate treatment for the patient is. This system is designed to be applicable in medical environments where the users are less familiar with the technical terms in the literature.

The rest of the paper is organized as follows. In Section 2, a brief introduction to fuzzy logic and ontology modeling is presented. Structure of the developed system and different modules of the system are thoroughly described in Section 3. An experiment which is conducted to evaluate the system and validate its results is given in Section 4. Conclusion remarks and future research issues are represented in Section 5.

2. Background

The proposed system relies on two knowledge representation techniques including ontologies and fuzzy logic. Fuzzy logic was first introduced by Zadeh [21] in order to handle vague concepts. Using fuzzy logic, one can make inference through rule bases using fuzzy variables which are in the form if *if-then* rules [22]. In the following ontology modeling technique is outlined briefly.

2.1. *Ontology modeling*

Ontology is a knowledge representation method with a philosophical concept as "the branch of metaphysics" which has been widely used in science and technology. From computer specialist's perspective, ontology means a vocabulary and a set of terms and relations that define, with the needed accuracy, a set of entities enabling the definition of classes, hierarchies, and other relations among them [25,26].

Ontology tries to describe and represent a knowledge domain. Therefore, ontology of a domain is a form of computer-acceptable representation of knowledge about a part of an abstract or real world. Generally, an ontology model Ω can be represented in the form of a set C of concepts and a finite family of ontological models M_k, $k = 1, 2, \ldots K$ defined as relationships described on selected subsets of C. The relationships may be of various kinds such as named roles or binary

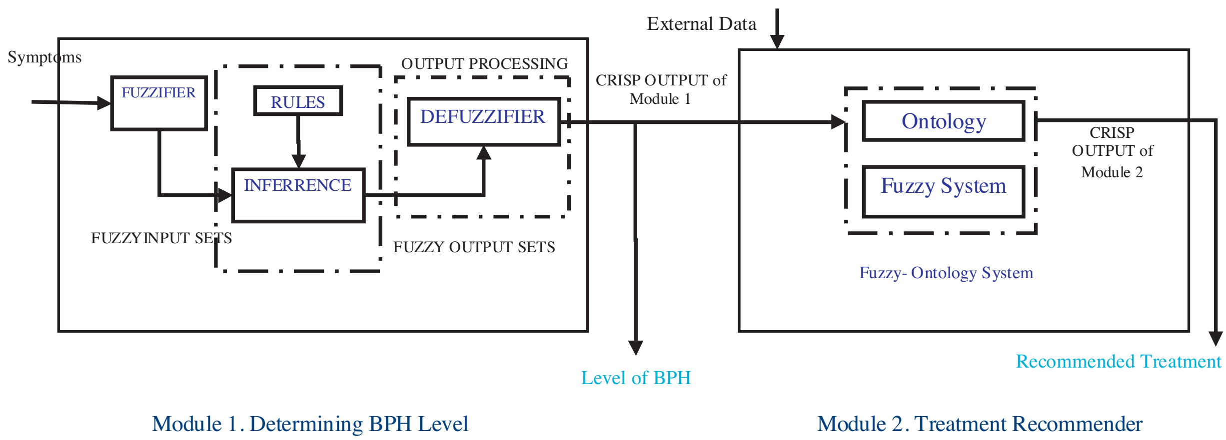

Fig. 1 – The structure of the proposed system.

relations. However, taxonomies T_i, $i = 1, 2, \ldots I$ of the concepts are mandatory elements of ontology [23].

Web Ontology Language (OWL) is the current standard language to formalize ontologies. OWL is a semantic web tool based on description logics to represent knowledge and support a wide range of reasoning facilities [27]. Description logics (DLs) ([28]) are a family of concept-based knowledge representation formalisms mobilized with well-defined model-theoretic semantics [29].

Although powerful reasoning tools that exist for DLs make ontologies so ideal to encode knowledge in a plethora of applications but they have some constraints in handling vague concepts. Hence, in this paper we develop a hybrid fuzzy-ontology system to benefit from both modeling capabilities of ontologies and vagueness handling capabilities of fuzzy logic.

Application of ontologies in the area of medical sciences is growing day by day but in the field of prostatic dysfunctions relevant studies are rare. For instance in Ref. [30], Prostate Cancer Ontology (PCO) is created for the development of the Prostate Cancer Information System (PCIS). The developed information system is then applied to demonstrate how the ontology is utilized to solve the semantic heterogeneity problems. Lack of existence of an effective and reliable intelligent system in this area can be felt, so in the next sections we develop a novel fuzzy-ontology intelligent system to control the severity level and to recommend appropriate treatments for BPH.

3. Method

BPH is a global problem and most elderly men may be involved in this problem. Identificationof the system (developing knowledge base and inference algorithm) is performed based on direct approaches [15,16].

Generally, there are two different approaches when developing an expert system: *direct* approach and *indirect* approach. When using the *direct* approach, the relations between input and output variables of the system are discovered by collecting data from physicians and informative patients. *Indirect* approach deals with discovering knowledge from various sources of data using several techniques such as clustering and other data mining methods. In this research we adopt *direct* approach to develop the system.

The proposed system consists of two main modules. The first module is devoted to determine the level of BPH and the second module which is a decision-making unit, recommends appropriate therapy for patients having BPH. The structure of the system is presented in Fig. 1.

The methodology being adopted in this section is based upon designing knowledge acquisition stages for both modules and then proposing a knowledge representation method accompanied by a fuzzy reasoning technique which aims to support clinician's everyday practice.

The first module of the developed system tries to get symptoms of patients and to determine the level of BPH. There are two general views for identifying input variables when developing intelligent systems in medical researches: physician's perception and patient's perception [17]. In this paper, focus of the knowledge acquisition process has been on patient's view to expedite mechanism of evaluation.

Second module of the developed system is responsible for decision-making. This module is in charge of: (a) encoding high-level medical knowledge acquired from physicians and specialized medical written documents such as books, medical papers, and guidelines; (b) making inference based upon some features discussed in the next sub-sections. These features are selected to be implemented in the second module according to physician's opinions and some of the main resources in the literature including [18] and [31]. According to these features, the system tries to recommend the most reliable treatment for the patient. These treatments are grouped in three categories including watchful waiting, medical therapies, and surgical therapies.

In the following, knowledge acquisition and knowledge representation stages for both modules are thoroughly discussed.

3.1. *Knowledge acquisition*

The objective of knowledge acquisition is to compile a body of knowledge on the problem of interest that can be encoded

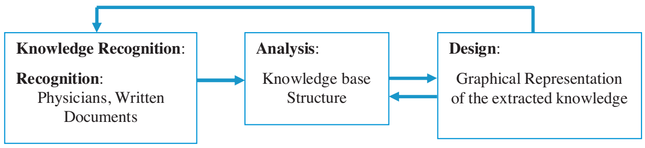

Fig. 2 – Knowledge acquisition cycle.

in the expert system [17]. Sources of this knowledge can be domain experts, books, guidelines, and etc.

In medicine context, application of knowledge acquisition techniques aims to make the implicit body of medical knowledge, known as tacit knowledge, more explicit at motivating physicians to provide an explanation to their actions [23].

The process of knowledge acquisition in this paper is divided to two parts. The next two sub-sections describe knowledge acquisition for the first and the second modules, respectively.

3.1.1. *Knowledge acquisition for module 1*

Process of knowledge acquisition in module 1 consists of three main stages as depicted in Fig. 2. During the first stage, problem recognition, the main aspects of BPH is studied and the main sources of knowledge are detected. In this phase, two main sources are detected: Physicians, and written sources [18]. According to physician's experience and written documents, a checklist is designed to capture symptoms of the patients. During this phase, input variables and the inherent uncertainties are investigated. During the second stage, analysis, these data are thoroughly interpreted and structure of the knowledge base of the first module is recognized. In the final phase, design, a schematic view and input/output variables is obtained and represented by general inference network (GIN) (Fig. 3).

In the following, the variables represented in Fig. 3 are introduced.

Also a fuzzy set respecting each linguistic variable is represented.

- *Incomplete emptying*: number of having sensation of not emptying the patient's bladder after finishing urinating. It can be categorized into 6 linguistic classes: Not at all ([0, 0, 1]), About less than 1 time in 5 ([0, 1, 2]), Less than half the time ([1, 2, 3]), About half the time ([2, 3, 4]), More than half the time ([3, 4, 5]), Almost always ([4, 5, 5]).
- *Frequency*: this variable represents the number of urinating less than two hours after finishing urinating and is classified in 6 groups: Never ([0, 0, 1]), About less than 1 time in 5 ([0, 1, 2]), Less than half the time ([1, 2, 3]), About half the time ([2, 3, 4]), More than half the time ([3, 4, 5]), Almost always ([4, 5, 5]).

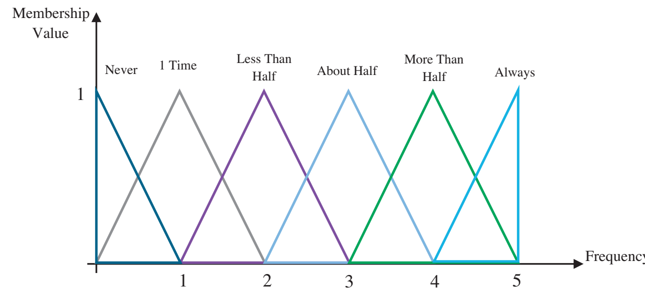

Fig. 4 – Membership function of Frequency.

- *Intermittency*: number of times a patient founds himself stops urinating and starting again several times during urinating. Its linguistic variables are: Not at all ([0, 0, 0]), About less than 1 time in 5 ([0, 1, 2]), Less than half the time ([1, 2, 3]), About half the time ([2, 3, 4]), More than half the time ([3, 4, 5]), Almost always ([5, 5, 5]).
- *Urgency*: number of times patient feels that he cannot postpone urinating with variables: Not at all ([0, 0, 0.5, 1]), About less than 1 time in 5 ([0, 0.5, 1.5, 2]), Less than half the time ([1, 1.5, 2.5, 3]), About half the time ([2, 2.5, 3.5, 4]), More than half the time ([3, 3.5, 4.5, 5]), Almost always ([4, 4.5, 5, 5]).
- *Weak stream*: number of times during the past month that the patient had weak urinary stream. Its classification is the same as *Urgency*.
- *Straining*: number of the times a patient had to have pushed or strain to begin urination. Its variables are: Never ([0, 0, 1]), About less than 1 time in 5 ([0, 1, 2]), Less than half the time ([1, 2, 3]), About half the time ([2, 3, 4]), More than half the time ([3, 4, 5]), Almost always ([4, 5, 5]).
- *Nocturia*: number of the times a patient got up to urinate from the time he went to bed at night until getting up in the morning. This factor is classified in six groups: None ([0, 0, 1]), About 1 time ([0,1,2]), About 2 times ([1,2 3]), About 3 times ([2, 3, 4]), About 4 times ([3, 4, 5]), About 5 times or more ([4, 5, 5]).

Graphical representations of membership functions of the extracted factors *Frequency* and *Urgency* are represented as an example in Figs. 4 and 5, respectively. Finally, the fuzzy out-

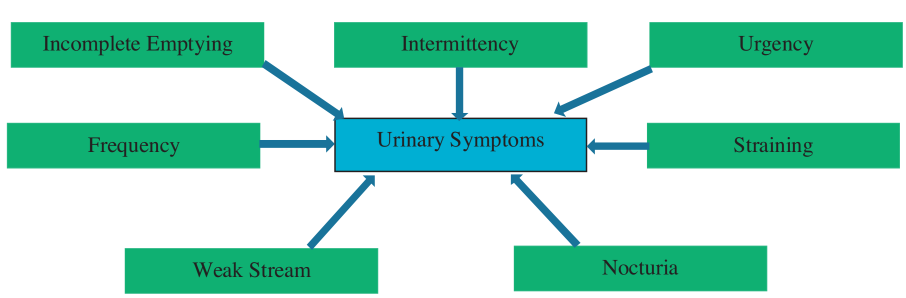

Fig. 3 – General inference network (GIN) of variables extracted from knowledge acquisition phase.

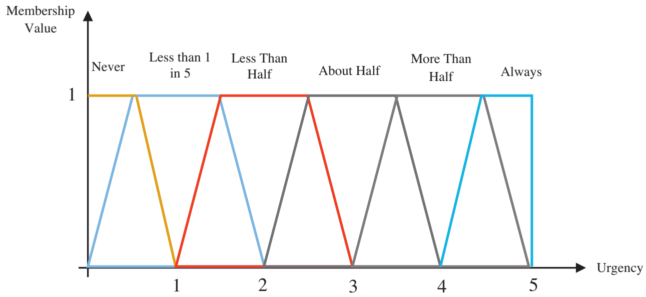

Fig. 5 – Membership function of Urgency.

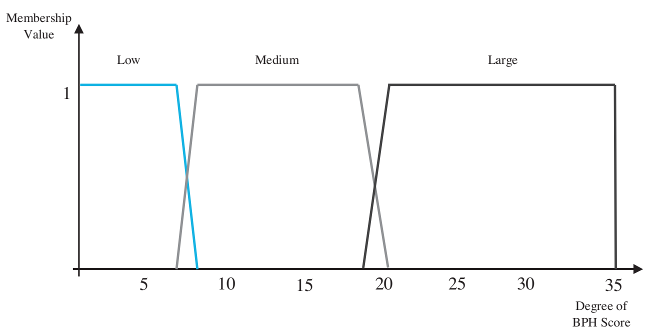

Fig. 6 – Membership function of BPH score.

Table 1 – Values and fuzzy intervals for BPH symptom score.

Symptom score	Fuzzy Interval
Low	[0, 0, 7, 8]
Moderate	[7, 8, 19, 20]
High	[19, 20, 35, 35]

put variables of the module1 are represented in Fig. 6 and its details are provided in Table 1.

It should be emphasized that the membership functions being adopted in this system are designed through long negotiations with the experts. Then, the experts tuned the corresponding fuzzy intervals and their respective membership functions through reaching a consensus.

3.1.2. *Knowledge acquisition for module 2*

The main goal of knowledge acquisition procedure applied in module 2 is to obtain descriptive and procedural knowledge

Table 2 – Influential features on the recommended treatment.

Feature	Linguistic label
Prostatic size	Low, Medium, Large
BPH Bothering Symptoms	None, Medium, High
Cardiac risk[a]	Low, High
Urinary retention	None, High
Quality of life (QOL)[b]	Terrible, Pleased, Mostly Satisfied, Mixed about equally satisfied and unsatisfied, Mostly dissatisfied, Unhappy, Terrible

[a] Based on Ref. [31].
[b] Based on International Prostate Symposium Score (IPSS).

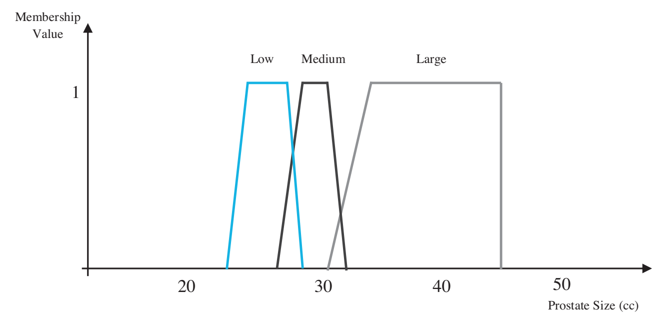

Fig. 7 – Membership function of prostate size.

of the domain in order to make an appropriate decision for recommending reliable treatment. Therefore, to gain this goal, a group of physicians in Arya Hospital (Mashhad, Iran) were requested to present their suggestions about influential variables on BPH and their corresponding values through a brainstorming process. Then they reached a consensus on these variables which are represented in Table 2. These features including their variables are iteratively tuned with collaboration of the physicians.

Membership functions for the features represented in Table 2 are represented in Figs. 7–11. Also the membership function of the system output is represented in Fig. 12.

Prostate size is an influential factor on the patient's quality of life. Prostate size has a range between 23 and 43 cc. According to the expert's knowledge, prostate size is considered to have three fuzzy intervals: [23; 24; 27; 28] for Low size, [27; 28; 30; 31] for Medium size, and [30; 32; 45; 45] for Large size (Fig. 7).

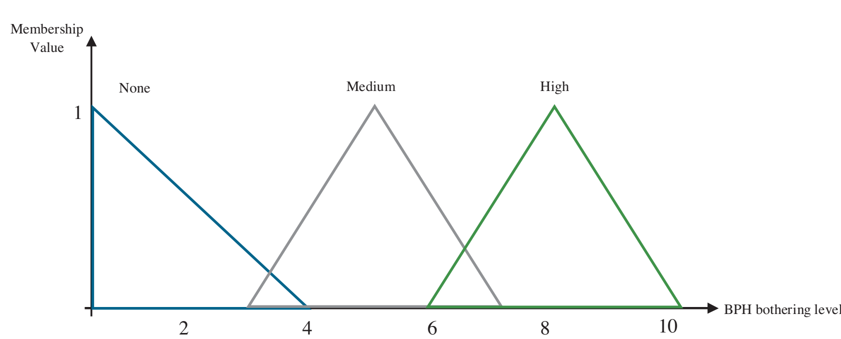

Fig. 8 – Membership function of BPH bothering level.

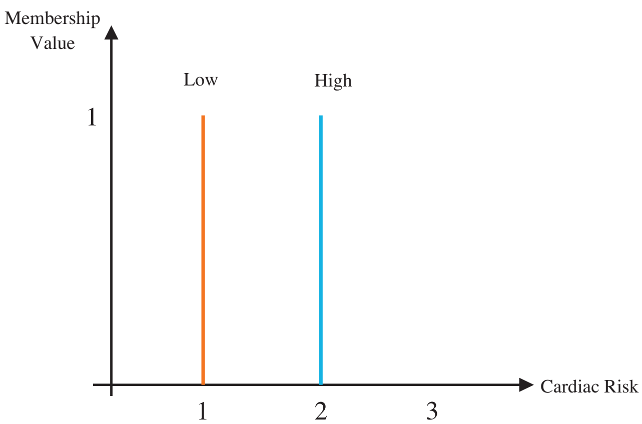

Fig. 9 – Membership function of cardiac risk.

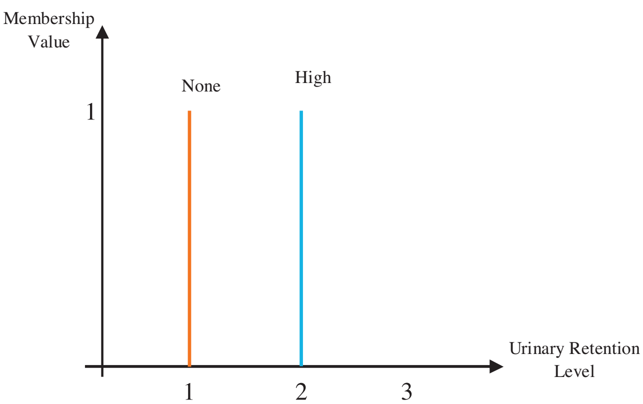

Fig. 10 – Membership function of urinary retention.

In the literature, cardiac risk is demonstrated to have negative impact on the appropriate treatment of the BPH. Hence, membership function of this parameter has been considered to have two crisp values: Low and High which are the result of negotiating with the experts (Fig. 9). Similarly, urinary retention is also considered to have two crisp values where if the patient has urinary retention the membership value is none and in case of having retention, High membership value is devoted to the patient (Fig. 10). Since both membership functions in Figs. 9 and 10 are highly critical, the experts decided to consider these two parameters as crisp values.

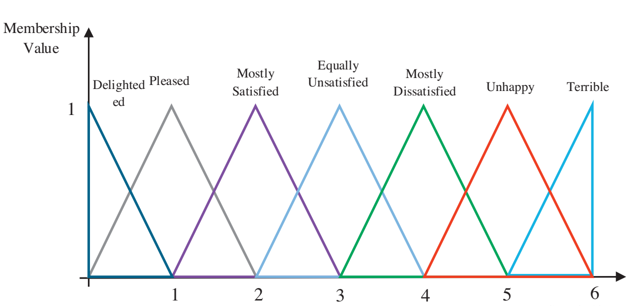

Fig. 11 – Membership function of quality of life.

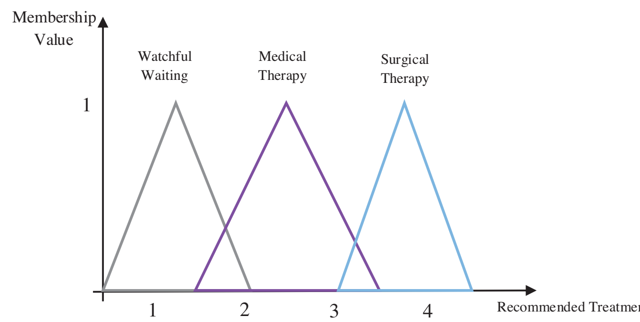

Fig. 12 – Membership function of module 2 output.

As noted in Table 2, quality of life is divided into seven different sets. On the basis of this groups and the knowledge of the experts, quality of life for patients having BPH has been considered as six fuzzy intervals represented in Fig. 11.

The output of the second module includes three kinds of treatments. These treatments include watchful waiting, medical therapy, and surgical therapy which are determined via reaching a consensus among the experts. The membership functions of these therapies are represented in Fig. 12.

3.2. *Knowledge representation*

3.2.1. *Knowledge representation for module 1*

According to the fuzzy intervals and membership values obtained from the knowledge acquisition phase, the knowledge derived from the experts and other sources of knowledge are represented in the knowledge base of the module 1 of the system in the form of *if-then* rules. These rules are of the form of evaluation rules.

Evaluation rules capture input variables of symptoms for each patient and result in BPH score for the patient. Although there are several numbers of rules but in Fig. 13, some of these rules are represented.

It should be mentioned that in the first module, we have used Mamdani inference method to reach the final result since Mamdani inference technique has been proved to be precise when dealing with fuzzy rule-bases which have fuzzy variables in both antecedent and consequent parts. In the following, a brief representation on Mamdani inference mechanism is presented.

3.2.1.1. *Mamdani inference mechanism*. Mamdani inference mechanism [40] is a method to compute the final output of a fuzzy rule-based system. Such a mechanism begins with fuzzification of inputs of the system. Then, it combines fuzzy inputs according to fuzzy ruled and computes the firing strength of each rule. After then, using firing strength of each rule, consequences of the rules are obtained and then consequence values are computed. Such values are finally defuzzified in order to find the output of the rule-based system. Fig. 14 represents a sample fuzzy rule-based with two inputs and output.

1. **IF** [Incomplete Emptying is Never] **AND** [Frequency is About 1 Time] **AND** [Intermittency is Less than 1 time in half] **AND** [Urgency is about half] **AND** [Weak Streamis not at all] **AND** [Straining is not at all] **AND** [Nocturia is not at all] **THEN** [BPH score is low]

2. **IF** [Incomplete Emptying is less than half] **AND** [Frequency is about half] **AND** [Intermittency is more than half] **AND** [Urgency is always] **AND** [Weak Streamis less than half] **AND** [Straining is less than 1 in 5] **AND** [Nocturia is not at all] **THEN** [BPH score is moderate]

3. **IF** [Incomplete Emptying is always] **AND** [Frequency is more than half] **AND** [Intermittency is about half] **AND** [Urgency is about half] **AND** [Weak Streamis about half] **AND** [Straining is more than half] **AND** [Nocturia is always] **THEN** [BPH score is high]

4. **IF** [Incomplete Emptying is about half] **AND** [Frequency is less than half] **AND** [Intermittency is Less than 1 time in half] **AND** [Urgency is not at all] **AND** [Weak Streamis less than1 in half] **AND** [Straining is less than half] **AND** [Nocturia is about half] **THEN** [BPH score is moderate]

Fig. 13 – A schematic view of some rules embedded in the knowledge base.

3.2.2. *Knowledge representation for module 2*

The process of knowledge representation for the second module is based upon ontology and fuzzy modeling. Descriptive knowledge acquired in knowledge acquisition stage in association with the output of module1 is characterized by the developed ontology. Knowledge representation structure and the ontology model devised in this paper are represented in Figs. 15 and 16, respectively.

As it can be observed in Fig. 15, the knowledge representation process in this paper is divided into two separate stages. In the following, these steps are thoroughly described as follows:

- Ontology modeling

Ontology model devised in this paper is a five layer model. These layers are

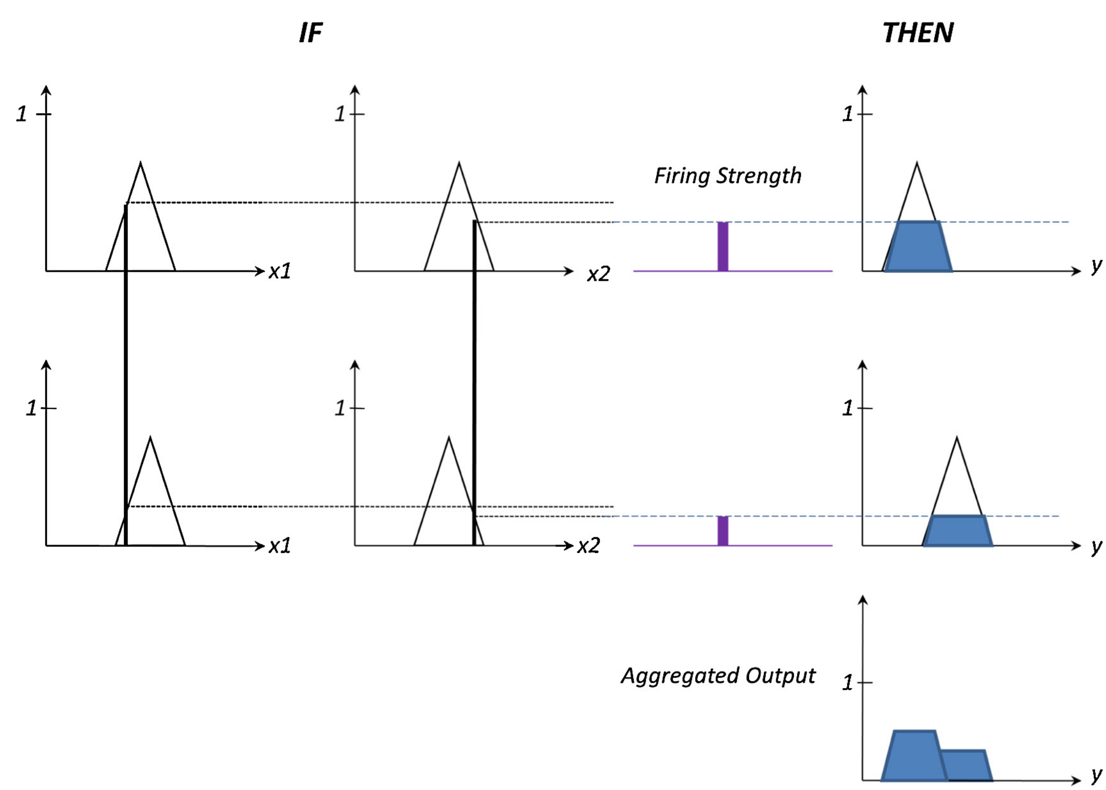

Fig. 14 – A schematic view of Mamdani inference mechanism.

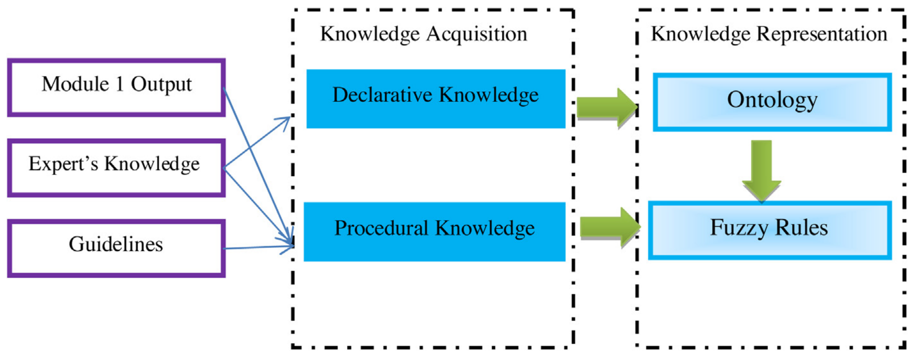

Fig. 15 – Schematic view of the knowledge representation process in module2.

I. *Domain layer*: This is the top layer of the model and model tries to obtain an appropriate treatment for this layer.

II. *Therapy layer*: Although there may be some other pertinent therapies in addition to the three therapies presented in therapy layer, but since these three therapies are the most prevalent all around the world, our system prototype only considers these three issues.

III. *BPH severity level*: This level is in fact the output of module1 in the system. It is the result of the expert system developed for module1 that gets several symptoms of the patient and then determines the BPH severity.

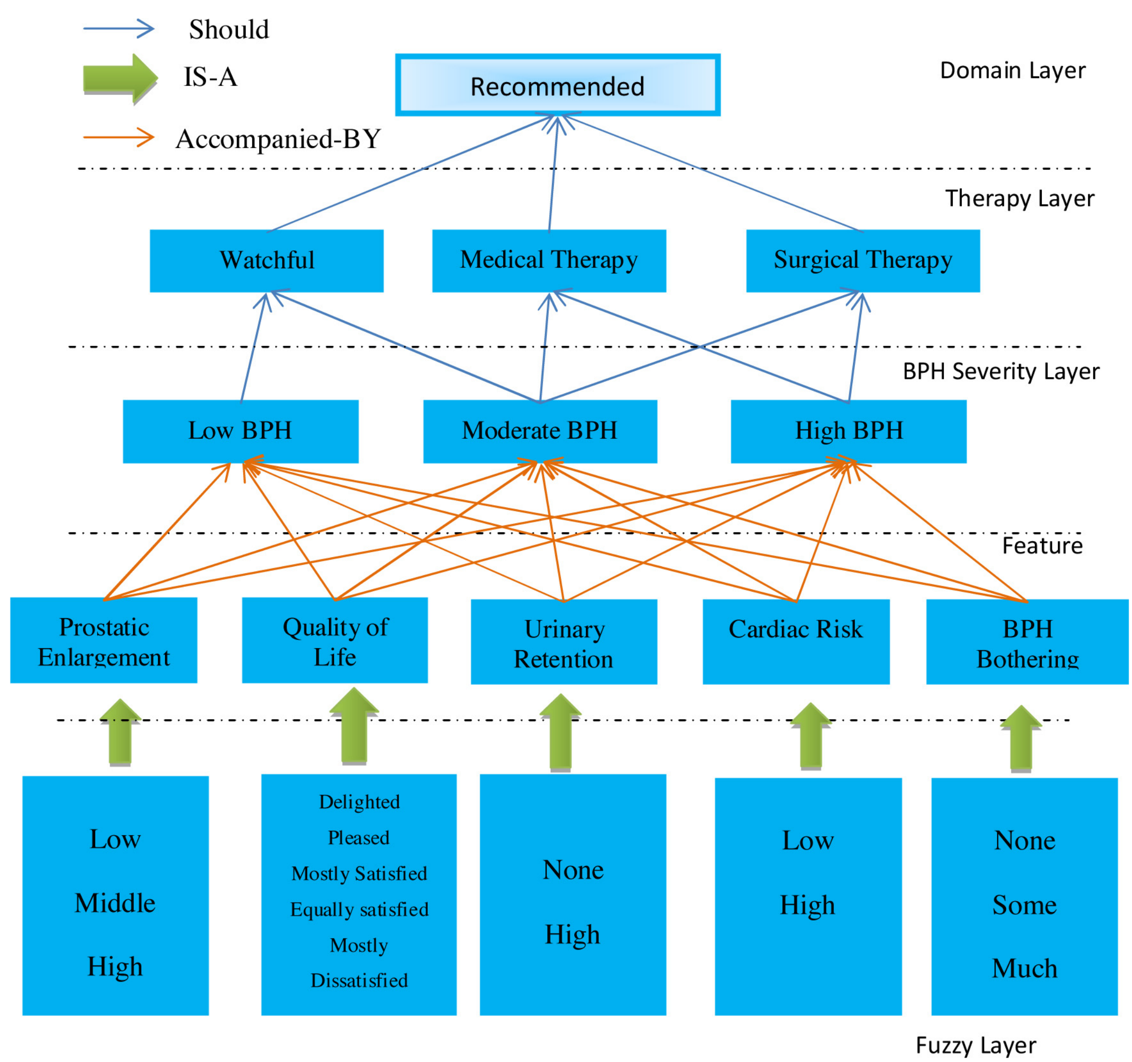

Fig. 16 – Schematic view of the developed ontology.

1. **IF** [ProstaticEnlargementIsLow] **AND** [QualityOfLifeIs (Delighted **OR** Pleased **OR** Mostly Satisfied)] **AND** [UrinaryRetentionIsNone] **AND** [CardiacRiskIsLow] **AND** [BPHBotheringSymptomsIs(None **OR** Some)] **AND** [BPHSeverityIs (Low **OR** Moderate)] **THEN** [WatchfulWaitingShouldBeRecommended]

2. **IF** [ProstaticEnlargementIsMiddle] **AND** [QualityOfLifeIs (Delighted **OR** Pleased **OR** Mostly Satisfied)] **AND** [UrinaryRetentionIsNone] **AND** [CardiacRiskIsLow] **AND**BPHBotheringSymptomsIs [(None **OR** Some)] **AND** [BPHSeverityIs(Low **OR** Moderate)] **THEN**WatchfulWaitingShouldBeRecommended

3. **IF** [ProstaticEnlargementIs(Middle **OR** High)] **AND** [QualityOfLifeIs(Delighted **OR** Pleased **OR** Mostly Satisfied)] **AND** [UrinaryRetentionIsNone] **AND** [CardiacRiskIsLow] **AND** [BPHBotheringSymptomsIs (Some **OR** Much)] **AND** [BPHSeverityIs (Moderate **OR** High)] **THEN**MedicalTherapyShouldBeRecommended

4. **IF** [ProstaticEnlargementIs Middle] **AND** [QualityOfLifeIs (Delighted **OR** Pleased **OR** Mostly Satisfied)] **AND** [UrinaryRetentionIs High] **AND** [CardiacRiskIs High] **AND** [BPHBotheringSymptomsIs (None **OR** Some)] **AND** [BPHSeverityIs (Low **OR** Moderate)] **THEN**MedicalTherapyShouldBeRecommended

5. **IF** [ProstaticEnlargementIs (Middle **OR** High)] **AND** [QualityOfLifeIs (Delighted **OR** Pleased **OR** Mostly Satisfied **OR**EquallyUnsatisfied)] **AND** [UrinaryRetentionIs High] **AND** [CardiacRiskIs Low] **AND** [BPHBotheringSymptomsIs (None **OR** Some)] **AND** [BPHSeverityIs Moderate] **THEN**MedicalTherapyShouldBeRecommended

6. **IF** [ProstaticEnlargementIs Middle] **AND** [QualityOfLifeIs (Mostly Dissatisfied **OR** Unhappy **OR** Terrible)] **AND** [UrinaryRetentionIs High] **AND** [CardiacRiskIs High] **AND** [BPHBotheringSymptomsIs (Some **OR** Much)] **AND** [BPHSeverityIs High] **THEN**SurgicalTherapyShouldBeRecommended

7. **IF** [ProstaticEnlargementIs Middle] **AND** [QualityOfLifeIs (Unhappy **OR** Terrible)] **AND** [UrinaryRetentionIs High] **AND** [CardiacRiskIs High] **AND** [BPHBotheringSymptomsIs Much] **AND** [BPHSeverityIs High] **THEN**SurgicalTherapyShouldBeRecommended

8. **IF** [ProstaticEnlargementIs Low] **AND** [QualityOfLifeIs (Delighted **OR** Pleased **OR** Mostly Satisfied)] **AND** [UrinaryRetentionIs None] **AND** [CardiacRiskIs Low] **AND** [BPHBotheringSymptomsIs (None **OR** Some)] **AND** [BPHSeverityIs (Moderate **OR** High)] **THEN**MedicalTherapyShouldBeRecommended

9. **IF** [ProstaticEnlargementIsHigh] **THEN**SurgicalTherapyShouldBeRecommended

10. **IF[**CardiacRiskIsHigh] **THEN**SurgicalTherapyShouldBeRecommended

11. **IF** [ProstaticEnlargementIs High] **AND [**BPHSeverityIs High] **THEN**SurgicalTherapyShouldBeRecommended

12. **IF** [ProstaticEnlargementIs Low] **AND [**BPHSeverityIs (Low **OR** Moderate)] **THEN**WatchfulWaitingShouldBeRecommended

Fig. 17 – Schematic view of the knowledge base of module 2.

IV. *Feature level*: This level consists of several features which are obtained by module 2 in order to match them with the output of module1.
V. *Fuzzy layer*: This layer belongs to its upper layer and contains fuzzy values related to the diagnosing features. The membership functions related to these features were represented in Section 3.1.2.

Construction process of the developed ontology is bottom-up. In such a manner, feature level is firstly constructed by receiving the necessary information with their respective fuzzy membership values from the user. Then the system receives the output values of module1 and decides what therapy to offer. However, final decision making is performed in the next sub-section of fuzzy modeling which will be described.

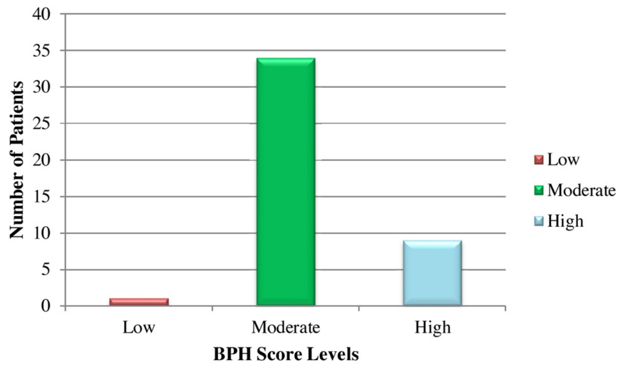

Fig. 18 – Distribution of patients with BPH symptoms in the test.

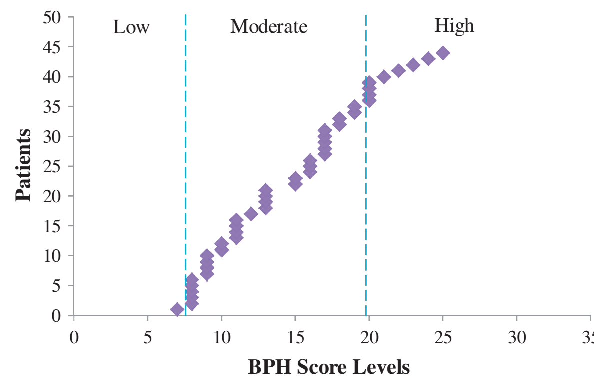

Fig. 19 – Results of the system based on patients symptoms.

- Fuzzy modeling

Procedural knowledge obtained from external sources and knowledge structure obtained from the ontology are compacted in this stage and transformed to *if-then* rules to be used in module 2. According to the obtained knowledge, the knowledge base of this module is formed in this stage. Here the entire rules in the knowledge base of the system are presented below (Fig. 17):

It should be mentioned that module 2 may need additional information from other sources in order to result in more appropriate treatments. Such additional information can be closeness of the patient residence location to medical services or the quality of medical services available in the area and etc. (Fig. 1).

4. System evaluation

The developed system is coded by MATLAB 7.12.0 programming language. In order to validate accurate and precise performance of the developed system, an experiment has been conducted in Arya hospital, Mashhad, Iran. This experiment has been approved by the Mashhad Azad University of Medical Sciences. In this experiment, 44 patients with ages between 44 and 80 years old had participated. Validation process of the developed system is performed in two stages: evaluation of module1 and evaluation of the module 2.

4.1. *Evaluation of module 1*

I. BPH scores for this group of patients were obtained from physicians and they were grouped into three categories: Low, Moderate, and High. These results are represented in Fig. 18.

II. Input variables for each patient were entered to the developed system and the output results were analyzed. BPH score levels obtained from the developed system are represented in Fig. 19. According to discussions before, results are classified into three different categories including Low (0–7), Moderate (8–19), and High (20–35).

As it can be observed in Fig. 19, the system determines the BPH severity level for each patient correctly. In Fig. 19, the vertical axis represents the number of patients which are 44 patients and the horizontal axis represents the calculated BPH score for each patient. In order to enhance the readability of the results in Fig. 19, we have divided the horizontal axis into three zones according to the fuzzy intervals defined in Section 3: Low, Moderate, and High. It is clear that only 1 patient exists in Low zone, 34 patients in Moderate zone, and 9 patients exist in High zone. This result is totally in accordance with the given information in Fig. 18.

III. In order to evaluate the results obtained from the system, a statistical comparison between the physician's opinions and system outputs must be made. In this paper we have used Cohen Kappa statistic which is used to measure the agreement between two raters who each classify N items to C mutually exclusive categories [19,20]. The equation for this statistic is as below: 19

$$k = \frac{Pr(a) - Pr(e)}{1 - Pr(e)} \tag{3}$$

where$Pr(a)$ and $Pr(e)$ are the relative observed agreement among raters and hypothetical probability of chance agreement, respectively. Table 3, represents the evaluation results of physicians and the system.According to Eq. (3), we have:

$$Pr(a) = \frac{1+34+9}{44} = 1,\ Pr(e)_{\text{Physician::Low}} = \frac{1}{44} = 0.02273,\ \text{and}\ Pr(e)_{\text{System::Low}} = \frac{1}{44} = 0.02273$$

Therefore,

$$Pr(e)_{\text{Low}} = Pr(e)_{\text{Physician::Low}} \times Pr(e)_{\text{System::Low}} = 0.02273 \times 0.02273 = 0.00052$$

In the same manner, other parameters are as follows:

$$Pr(e)_{\text{Moderate}} = 0.5976,\ Pr(e)_{\text{High}} = 0.042$$

Table 3 – Evaluation comparison of physician and the system.

	Physician: Low	Physician: Moderate	Physician: High
System: Low	1	0	0
System: Moderate	0	34	0
System: High	0	0	9

Table 4 – Evaluation comparison of physician and the system output.

	Physicians: watchful waiting	Physicians: medical therapy	Physicians: surgical therapy
System: watchful waiting	8	2	0
System: medical therapy	0	16	1
System: surgical therapy	0	0	17

At last, the final Pr(*e*) is:

$$Pr(e) = Pr(e)_{\text{Low}} + Pr(e)_{\text{Moderate}} + Pr(e)_{\text{High}} = 0.64012$$

Therefore, the kappa coefficient will be:

$$k = \frac{1 - 0.64012}{1 - 0.64012} = 1$$

Since $k = 1$, it is proved that the system results have complete correspondence with the opinions of the experts and therefore validity of the system results is demonstrated.

4.2. *Evaluation of module 2*

Recommending appropriate treatment for the patients is highly critical. Therefore the developed system must be reliable enough to recommend the needed treatment precisely. In this section the module 2 of the developed system is tested using the medical data of 44 patients having BPH.

According to discussions represented in Section 3, there are 6 variables as inputs of the module 2 and its output is the recommended treatment including: watchful waiting, medical therapy, and surgical therapy. Using the available data for this set of patients, the resulting output of the system is represented in Fig. 20. As it is observed, the system gives the following results: watchful waiting for 10 patients, medical therapy for 17 patients, and surgical therapy for 17 patients. It should be mentioned that in Fig. 20, recommended therapies 1, 2, and 3 are interpreted as watchful waiting, medical therapy, and surgical therapy, respectively.

In order to validate precision and accuracy of the developed system, several urologists as experts were requested to present their treatment recommendation on the set of patients. After reaching a consensus their recommendations were aggregated. The aggregation process was as follows: One of the authors of this paper has played the role of the head of a panel. Then, we conducted a brainstorming session where the experts and the head of the panel had participated. According to the brainstorming rules, firstly, opinions of each expert were collected. Their opinions in most cases were similar and only for a few number of patients there were conflicts among the experts.

To aggregate the opinions of experts, experts with similar opinions tried to convince the other expert through discussions in order to find a final and comprehensive result.

The method used in this paper is based on brainstorming procedure. Since all the experts participated in this experiment were highly qualified, their opinions were not that different especially because BPH is not that sophisticated. Of course in some other disorders such as cancer it would be harder for the panel to reach a consensus soon. In some cases where condition of the patient is critical then changes in decision making process may be different but in our cases it does not matter.

The results of their offered treatments, which are formed based on reaching a consensus, are presented in Fig. 21.

Table 5 – Statistical analysis of treatments offered by the system and experts.

System	Physician
$Pr(e)_{WatchfulWaiting} = 0.227$	$Pr(e)_{WatchfulWaiting} = 0.182$
$Pr(e)_{MedicalTreatment} = 0.3864$	$Pr(e)_{MedicalTreatment} = 0.41$
$Pr(e)_{SurgicalTreatment} = 0.3864$	$Pr(e)_{SurgicalTreatment} = 0.41$

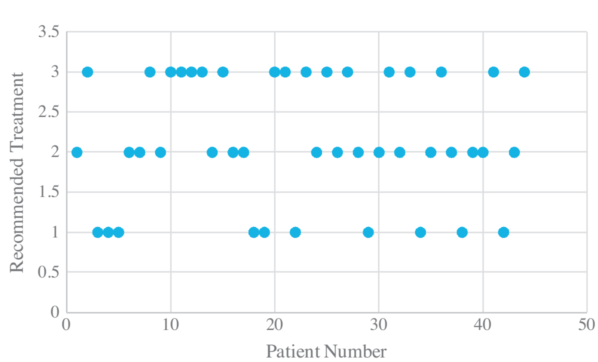

Fig. 20 – Output of module 1 for 44 patients.

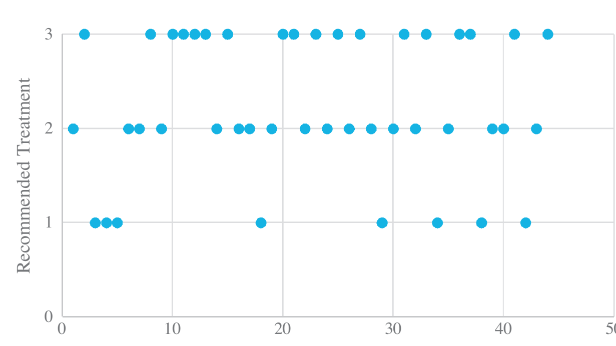

Fig. 21 – Recommended treatments by the experts for 44 patients.

Table 6 – Cohen's statistical analysis.

$Pr(e)_{Therapies}$	$Pr(e)$	$Pr(a)$	k
$Pr(e)_{Watchful\ Waiting} = 0.041314$ $Pr(e)_{Medical\ Treatment} = 0.15843$ $Pr(e)_{Surgical\ Treatment} = 0.15843$	$Pr(e) = 0.358174$	$Pr(a) = 0.932$	$k = 0.895$

In the same way as the last subsection, in order to compare the correctness of the outputs given by the system a statistical analysis using Cohen's statistic has been performed. The total comparison based on Figs. 20 and 21 is represented in Table 4 and the information of the statistical analysis is presented in Tables 5 and 6.

According to the results of Table 6, it is shown that for the available data set, the developed system gives correct answer for nearly 90% of the patients. In other words, the resulting therapies recommended by the system conforms the expert's treatment for nearly 90% percent which is high.

Medical treatments mostly depend on the physician's perception and most of the times two physicians may recommend two different therapies for the same patient. Therefore developing a comprehensive system to cover all these differences is a daunting task. In this paper the developed system gives very reliable results by using fuzzy techniques and can be extended to more detail systems which are even able to offer the dosage of drug to be used and various surgical therapies.

5. Conclusions

Benign Prostatic Hyperplasia (BPH) is a prevalent disorder among old men around the world. Although lots of researches have been performed during recent years in diagnosing and treatment areas but many important factors involved in this disease have been overlooked. Diagnoses and therapies recommended by physicians are based on experience and knowledge of the physician, simultaneously. This means that different physicians may recommend different therapies for a specific case. This is true in most cases since physician's judgments are inherently vague. This is a nice area to use logics to handle the vagueness such as fuzzy logic.

In this paper a hybrid fuzzy-ontology intelligent system is presented to determine BPH level and recommending appropriate therapy. The proposed approach in this article has a unique feature. It is one of the very first methods to combine BPH diagnosis using fuzzy-ontology based expert systems. Unfortunately, most of the existing studies on prostate problems which use soft computing methods concentrate on prostate cancers, which are different from BPH, so we could not compare them with our approach. For example in Refs. [9,11–13] the authors consider prostate cancer which is prevalent among men. On the other hand, other studies which are basically medical-based, not soft computing-based, propose completely different approaches which have no direct connection to the field of computational intelligence. Therefore, it was not possible to make direct comparison with the existing approaches.

The developed system consists of two main modules. module 1 is responsible to capture several factors and infer BPH symptom score for the patient. Module 2 is responsible to suggest appropriate therapy for the patients according to the results of the module 1.

Also in this research, an experiment was conducted in Arya hospital, Mashhad, Iran, to evaluate and validate performance of the developed system. In this test, 44 patients aging between 44 and 80 years old were participating. Experimental results demonstrate that the developed system is completely in correspondence with the physician's opinions when determining the severity level of BPH and has nearly 90% of correspondence with the physician's treatments; this demonstrates power of the developed intelligent system.

Application of intelligent systems in the field of medical diagnosis especially in BPH is a novel field of research. Expanding the developed system to use fuzzy Type-2 inference mechanisms in order to minimize inherent vagueness in medical data and as a result, minimizing risks of suggesting wrong therapies can be pursued as future study. Also use of soft computing methods such as various clustering techniques to develop data-driven intelligent systems can be a nice research field.

6. Conflict of interests

The authors declare that they have no financial or personal conflict of interest that could inappropriately influence the writing or publication of this manuscript.

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