HIROFILOS: A Medical Expert System for Prostate Diseases

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Abstract: - Prostate gland diseases, including cancer are estimated to be one of the leading cause of male death worldwide and its management is based on guidelines regarding diagnosis, evaluation, treatment and continuing care. In this study a fuzzy expert system for diagnosing, and learning purpose of the prostate diseases is described. HIROFILOS is a fuzzy expert system for diagnosis and treatment of prostate diseases according to symptoms that are realized in one patient and usually recorded through his clinical examination as well as specific test results. The user-friendly proposed intelligent system is accommodated on a hospital web page for use as a decision support system for resident doctors, as an educational tool for medical students, as well as, an introductory advisory tool for interested patients. It is based on knowledge representation provided from urology experts in combination with rich bibliographic search and study ratified with statistical results from clinical practice. Preliminary experimental results on a real patient hospital database provide an acceptable performance that can be improved using more than one computational intelligence approaches in the future.

Key-Words: - Prostate disease, urology, medical expert system, fuzzy logic.

1 Introduction
Prostate gland diseases, including cancer are estimated to be one of the leading cause of male death worldwide and its management is based on guidelines regarding diagnosis, evaluation, treatment and continuing care. Prostate cancer is the most common noncutaneous cancer among males [1]. The diagnosis and treatment of prostate cancer continue to evolve. With the development of prostate-specific antigen (PSA) screening, more men are identified earlier as having prostate cancer. While prostate cancer can be a slow-growing cancer, thousands of men die of the disease each year. Benign prostatic hyperplasia (BPH) is a noncancerous enlargement of the prostate gland that may restrict the flow of urine from the bladder. BPH involves both the stromal and epithelial elements of the prostate arising in the periurethral and transition zones of the gland; the condition is considered a normal part of the aging process in men and is hormonally dependent on testosterone production. An estimated 50% of men demonstrate histopathologic BPH by age 60 years. This number increases to 90% by age 85 years; thus, increasing gland size is considered a normal part of the aging process. Acute prostatitis (AP) presents as an acute urinary tract infection in men. It is much less common than chronic prostatitis (CP) but is easier to identify because of its more uniform clinical presentation. Chronic prostatitis, is poorly understood partly because of its uncertain etiology and lack of clearly distinguishing clinical features. Acute prostatitis is usually associated with predisposing risk factors, including bladder outlet obstruction secondary to benign prostatic hyperplasia (BPH) [1].

Different approaches according to medical as well as psychosocial characteristics of patients are usually followed for diagnosis of the previous diseases. Like any chronic disease, prostate is complex to manage. Traditionally, an intelligent system that helps clinicians to diagnose and treat diseases is used to identify a patient-specific clinical situation on the basis of key elements of clinical and laboratory examinations and consequently usually refine a theoretical treatment strategy, a priori established in the guideline for the corresponding clinical situation, by the specific therapeutic history of the patient [2]. Depending on the patient's data, it models patient scenarios which drive decision making and are used to synchronize the management of a patient with guideline recommendations. The so-called
guideline-based treatment choice can be considered under the main difference between management of acute and chronic disease that is the time. Guideline dependence introduces a computer-assisted intelligent Decision Support Systems (DSSs), based on technologies that provide to the patient “most likely” treatment scenario [2], [3], [4]. So, the creation of an expert system to assist non-expert doctors in making an initial diagnosis would be very desirable [5], [6], [7]. Most of the systems that have been proposed and used focus on PC diagnosis. Additionally as it is known, real world medical knowledge is often characterized by inaccuracy. Medical terms do not usually have a clear-cut interpretation. Fuzzy logic makes it possible to define inexact medical entities via fuzzy sets. During last decade, a number of fuzzy techniques have appeared which, have been extensively applied to medical systems [8], [9]. One of the reasons is that fuzzy logic provides reasoning methods for approximate inference [8], that is inference with inaccurate (or fuzzy) terms. In this paper, we present a fuzzy expert system for the diagnosis and treatment of prostate diseases (called HIROFILOS from the ancient Greek doctor who first described and named prostate gland). HIROFILOS primarily aims to help in the diagnosis and treatment of prostate diseases effectively under the consideration of LUTS. Also, it can be used by medical students for training purposes on prostate disease management and introduce a computer-assisted environment that is able to synthesise patient specific information with treatment guidelines, perform complex evaluations, and present the results to health professionals quickly.

2 Medical Knowledge Modeling
Appropriate diagnosis of AP, CP, BPH and AC requires urology doctors with long experience in Urology. One of the problems is that there is no a widely accepted approach yet. Therefore, except from the fact that we had a number of interviews with an expert in the field, we also used patient records and bibliographical sources. Our approach to knowledge modeling included three steps. First, we constructed a model of the basic diagnosis and treatment process. We relied on the expert and the literature at this step (Fig. 1). Then, we specified the parameters that played a role in each entity of the process model. At this step, we relied on the expert and the patient records. Finally, we determined the fuzzy models for the values of the resulted linguistic variables. We had, however, to iterate a number of times on this last step to tune the model (Fig. 2).

2.1 Input-output variables
Based on our expert, we specified a set of parameters that play a role for each of the entities in the process model that represent patient data (Fig. 1). Finally, we resulted in the following parameters for each entity in the process model. According to the model, we distinguish between input, intermediate and final parameters at each sub process.

Input parameters: (a) bladder not empty sensation, (b) less than 2 hours urination, (c) urination stopping, (d) difficulty to postpone urination, (e) night urination (1 to 5), (f) quality of life, (g) fever, (i) hematuria, (j) hemospermia, (k) painful ejaculation, (l) fever, (m) chills, (n) perineal pain, (o) bone pain, (p) pyuria, (q) age.

Intermediate output parameters: (a) LUTS (yes, no), (b) DRE (normal, big, painful, stony).

Intermediate input parameters: (a) LUTS (yes, no), (b) PSA (normal, middle, high).

Final output parameters: (a) Prostate disease (AP, CP, BPH, PC) (b) Biopsy

Final treatment parameters: Final treatment according to current Prostate disease (a) simple follow up (b) medication (antibiotics, etc) and (c) surgery (open, urethral, laser, microwaves)

2.2 LUTS diagnosis
The knowledge base of the expert system includes production rules, which are symbolic (if-then) rules with Boolean or crisp variables (e.g. age, smoke, cholesterol, etc). The variables of the conditions (or antecedents) of a rule are inputs and the variable of its conclusion (or consequent) an output of the system. To represent the process model, we organized production rules in three groups: LUTS classification rules, prostate diagnostic rules and treatment rules inspired form model presented in Fig. 1. The current patient data are stored in the Patient Database, as facts. Each time that the reasoning process requires a parameter value, it gets it from the database or the user. In a pure interactive mode, it could be given only by the user.
Table 1. Lower Urinary Tract Symptoms classification rules (partial)

<table>
<thead>
<tr>
<th>Stop urination</th>
<th>Weak urination</th>
<th>Night Urination</th>
<th>...</th>
<th>LUTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1</td>
<td>Less than 1</td>
<td>1</td>
<td>...</td>
<td>No</td>
</tr>
<tr>
<td>Less than half</td>
<td>Less than half</td>
<td>1</td>
<td>...</td>
<td>No</td>
</tr>
<tr>
<td>About half</td>
<td>Less than half</td>
<td>1 to 3</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>More than half</td>
<td>Less than half</td>
<td>1 to 3</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Always</td>
<td>About half</td>
<td>1 to 3</td>
<td>...</td>
<td>Yes</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
<td>1 to 3</td>
<td>...</td>
<td>Yes</td>
</tr>
</tbody>
</table>

2.3 Prostate disease diagnosis
To represent the process model, we organized production rules in two groups: LUTS classification Rules and Prostate Diagnostic Rules. LUTS rules classify the current patient data to a specific patient model according to the calculated LUTS Factor. These values are stored in the patient database. A sample of LUTS rules can be seen in Table 1.

Table 2. Prostate diseases diagnostic rules (partial)

<table>
<thead>
<tr>
<th>INTERMEDIATE INPUT</th>
<th>DIAGNOSTIC RULES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PSA</td>
</tr>
<tr>
<td>Yes</td>
<td>Hard</td>
</tr>
<tr>
<td>Yes</td>
<td>Hard</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

For each patient dataset that is stored in the Patient Database, Prostate diagnosis Rules decide to ask for the parameter PSA values in order to give to the user the final diagnosis. Each time that the reasoning process requires a value, it gets it from the database or from user interaction. A sample of Prostate diagnosis rules can be seen in Table 1. Finally there are a small number of Treatment rules, which according to the resulted disease provide the appropriate treatment strategy.

3 HIROFILOS architecture
The developed fuzzy expert system has the structure...
of Fig. 2, which is similar to the typical structure of such systems [8], [9]. The knowledge base of the expert system includes fuzzy rules, which are symbolic (if-then) rules with linguistic variables (e.g. age). Linguistic variables take linguistic values (e.g., middleaged, old). Each linguistic value is represented by a fuzzy set: a range of crisp (i.e. non-linguistic) values with different degrees of membership to the set. The degrees are specified via a membership function. The variables of the conditions (or antecedents) of a rule are inputs and the variable of its conclusion (or consequent) an output of the system.

Reasoning in such a system includes three stages: fuzzification, inference, defuzzification. In fuzzification, the crisp input values (from the fact database) are converted to membership degrees, by applying the corresponding membership functions, that become the truth degrees of the corresponding conditions of the fuzzy rules. In the inference stage, first, the degrees of the conditions of the fuzzy rules are combined to produce the degrees of truth of the conclusions. The MIN method is used here. According to that, the degree of truth of a conclusion is the minimum of the degrees of the conditions of the corresponding rule (AND fuzzy operation) and its membership function is clipped off at a height corresponding to that minimum. Afterwards, all the degrees assigned to same conclusions (i.e. rule outputs) are combined into a single degree using the MAX method. According to that, the combined output degree of truth is the maximum of the degrees (OR fuzzy operation) and its membership function is clipped off at a height corresponding to that maximum. Finally, the clipped off membership functions of all outputs are aggregated to form the combined fuzzy output. In defuzzification, the fuzzy output is converted to a crisp value. Here, the well-known centroid method is used. According to that method, the crisp output value is the x-coordinate value of the center of gravity of the aggregate membership function [1].

To represent the process model, we organized fuzzy rules in three groups: classification rules, diagnostic rules and treatment rules. The current patient data are stored in the Database, as facts. Each time that the reasoning process requires a value, it gets it from the database. In an interactive mode, it could be given by the user. Fig.3 presents how the rule groups and the facts/user are used/participates during the reasoning process to simulate the diagnosis process.

4 Implementation Issues

The user interface has been developed with Macromedia Flash 8.0, and the fuzzy expert system has been developed in FuzzyCLIPS 6.1b Expert System Shell. Finally, about 84 rules have been constructed. Patient data in the Database are organized by using FuzzyCLIPS templates. For example, the following rules are presented.

Next rule asks the user to input parameters about LUTS:
(defrule Questions_LUTS "ask-question" (initial-fact) => (printout t "Question About LUTS ") (bind ?empty (ask-question "Do you feel your bladder is not quite empty after you have been to pass urine (yes/no)?" yes no) ) (assert (empty ?empty))

Next group of rules gives the intermediate diagnosis of LUTS:
(defrule_5 (declare(salience 40)) (or(pass_urine yes) (flow yes) (trickles yes) (thinner yes) (empty yes) (get_up yes) (daytime yes) (straight yes) (mean yes)) => (assert (A yes)))

...
(defrule print_a
  (A yes)
  (end yes)
  =>
  (printout t "*** you have severe symptoms and should consult your own doctor ** You may need an examination, and possibly a blood test. Your doctor may consider referring you for an operation to remove the prostate gland, or may consider putting you on a course of tablets **" crlf))

Next rule inserts as final diagnosis Prostate Cancer,

Rule 46: If patient **LUTS** is yes and **haematuria** is yes and **painful ejaculation** is yes or **fever** is yes then disease is **Prostate Cancer.**

has been implemented in FuzzyCLIPS as follows:

(defrule _46
  (declare(salience 20)
  (and(luts haematuria)
  (luts haemo_spermia)
  (luts painful_ejaculation)
  (luts fever))
  =>
  (assert(PCA (value yes))))

To implement reasoning flow, different priorities have been used for different rule groups (named `salience(?)`).

5 Experimental Results
We used HIROFILOS for a number of 105 patient records from the Hospital Database with different types of prostate diseases. The corresponding treatment results were compared to the results of our expert doctor. To evaluate HIROFILOS, we used three metrics, commonly used for this purpose: accuracy, sensitivity and specificity (abbreviated as Acc, Sen and Spec respectively), defined as follows:

\[ Acc = \frac{a + d}{a + b + c + d}, \]
\[ Sen = \frac{a}{a + b}, \]
\[ Spec = \frac{d}{c + d} \]

where, \( a \) is the number of positive cases correctly classified, \( b \) is the number of positive cases that are misclassified, \( d \) is the number of negative cases correctly classified and \( c \) is the number of negative cases that are misclassified. By ‘positive’ we mean that a case belongs to the group of the corresponding initial treatment and by negative that it doesn’t. The evaluation results are presented in Table 3 and show an acceptable performance.

<table>
<thead>
<tr>
<th></th>
<th>EXPERT</th>
<th>HIROFILOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACCURACY</td>
<td>0.95</td>
<td>0.76</td>
</tr>
<tr>
<td>SENSITIVITY</td>
<td>0.98</td>
<td>0.79</td>
</tr>
<tr>
<td>SPECIFICITY</td>
<td>0.99</td>
<td>0.75</td>
</tr>
</tbody>
</table>
6 Conclusions

In this paper, we present the design, implementation and evaluation of HIROFILOS, a fuzzy expert system that deals with diagnosis and treatment of prostate diseases except prostate cancer that is the usual diagnosis of most similar approaches in the same medical field [2], [3], [6]. The diagnosis process was modeled based on expert’s knowledge and existing literature. Linguistic variables were specified based again on expert’s knowledge and the statistical analysis of the records of 105 patients from a hospital database. Linguistic values were determined by the help of expert, the statistical analysis and bibliographical sources. Experimental results showed that HIROFILOS did quite better than non-expert urologists, but worse than the expert. A possible reason for that may be the determination of the values (fuzzy sets) of the linguistic variables and their membership functions. Better choices may give better results. One the other hand, use of alternative or more advanced representation methods, like hybrid ones [6], [10], [11] may give better results.

References: