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Using Machine Learning Techniques to improve the behaviour of a medical decision support system for prostate diseases

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Abstract

Prostate gland diseases, including cancer, are estimated to be of the leading causes of male deaths worldwide and their management are based on clinical practice guidelines regarding diagnosis and continuing care. HIROFILOS-II is a prototype hybrid intelligent system for diagnosis and treatment of all prostate diseases based on symptoms and test results from patient health records. It is in contrast to existing efforts that deal with only prostate cancer. The main part of HIROFILOS-II is constructed by extracting rules from patient records via machine learning techniques and then manually transforming them into fuzzy rules. The system comprises crisp as well as fuzzy rules organized in modules. Experimental results show more than satisfactory performance of the system. The machine learning component of the system, which operates off-line, can be periodically used for rule updating, given that enough new patient records have been added to the database.

1. Introduction

In recent years artificial intelligence (AI) techniques using data from patient electronic health records or implementing clinical practice guidelines have been used in many information systems related to the medical field. As computerized health-care support systems are rapidly becoming more knowledge intensive, the need for representation of medical knowledge in a form that enables effective reasoning is growing.

Prostate gland diseases, including cancer, are estimated to be one of the leading cause of male deaths worldwide. Its management is based on guidelines regarding diagnosis, evaluation, treatment and continuing care. Prostate cancer is the most common noncutaneous cancer among males [1]. Diagnosis and treatment of prostate cancer continue to evolve. With the development of prostate-specific antigen (PSA) screening, more men are early identified 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 the age of 60. This number increases to 90% by the age of 85; thus, increasing gland size is considered a normal part of the aging process. Acute prostatitis (AP) is presented 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. AP is usually associated with predisposing risk factors, including bladder outlet obstruction secondary to benign prostatic hyperplasia (BPH) [2].

Different approaches according to medical as well as psychosocial characteristics of patients are usually followed for diagnosis of the above 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 refine a theoretical treatment strategy, a priori established in the guidelines for the corresponding clinical situation, by the specific therapeutic history of the patient [1]. 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

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guideline recommendations. Guideline dependence leads to intelligent decision support systems, based on technologies that provide the "most likely" treatment scenario for the patient [2], [3], [4]. So, the creation of an information system to assist non-expert doctors in making an initial diagnosis is always desirable [5], [6], [7]. Most of the systems that have been proposed and used focus on CP diagnosis , [5], [6], [7], [8].

In order to develop a successful decision-support and knowledge management system, appropriate medical knowledge representation approaches should be employed. A successful information system has to include efficient representations, technologies, and tools that integrate all the important elements that physicians work with: electronic health records, clinical practice guidelines, etc. 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 knowledge via fuzzy sets. During last decade, a number of fuzzy techniques have appeared which, have been extensively applied to medical systems [8], [10], [12]. One of the reasons is that fuzzy logic provides reasoning methods for approximate inference, that is inference with inaccurate (or fuzzy) terms. In this paper, we present an intelligent information system, called HIROFILOS-II, that primarily aims to help in effective diagnosis and treatment of prostate diseases taking into consideration the Lower Urinary Tract Symptoms (LUTS) [1]. It introduces a computer-assisted environment that is able to synthesise patient information with treatment guidelines, perform complex evaluations, and present the results to health professionals quickly.

Its previous version, HIROFILOS-I, was developed based on knowledge elicited from urology experts and bibliographic research ratified with statistical results from clinical practice [9]. Although preliminary experimental results demonstrated acceptable performance for the most common prostate diseases, the system has been improved by using machine learning techniques to extract knowledge, in if-then rule form, from empirical data (i.e. patient records). Thus, it now covers all prostate diseases, as well as CP, which is still poorly understood partly because of its uncertain etiology, but mainly because of lack of clearly distinguishing clinical features.

The structure of the paper is as follows. Section 2 presents the medical knowledge modelling. In Section 3, the system architecture of HERIFOLOS-II is described. In Section 4 implementation issued are presented. Section 5 contains evaluation results. Finally Section 6 concludes.

2. Medical Knowledge Modelling

Appropriate diagnosis of AP, CP, BPH and AC requires urology doctors with long experience in Urology. One of the problems is that there is not a widely acceptable 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 [1].

2.1 Input-output variables

Based on our expert, we specified a set of parameters that play a role in the diagnosis process and its subprocesses (see Fig. 1). Finally, we resulted in the following parameters, which are distinguished in *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 prostpone 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, medium, 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 Diagnosis Process Model

Based on our expert and the European Association Guidelines, we constructed a model for the prostate diagnosis process, depicted in Fig. 1. According to that model, first the expert defines the existence of Lower Urinary Track Symptoms (LUTS) [1]. If the diagnosis is positive, the performed clinical examination (for pain, fever etc), the results of special urine tests (for pyouria, hematuria, etc), as well as blood tests (for PSA levels) and finally the Direct Ring Examination of prostate (for prostate gland characterization), provide doctors additional information that combined with patients' demographic data (age, etc) helps in concluding about the possible prostate disease and the appropriate therapeutic strategy [1, 9].

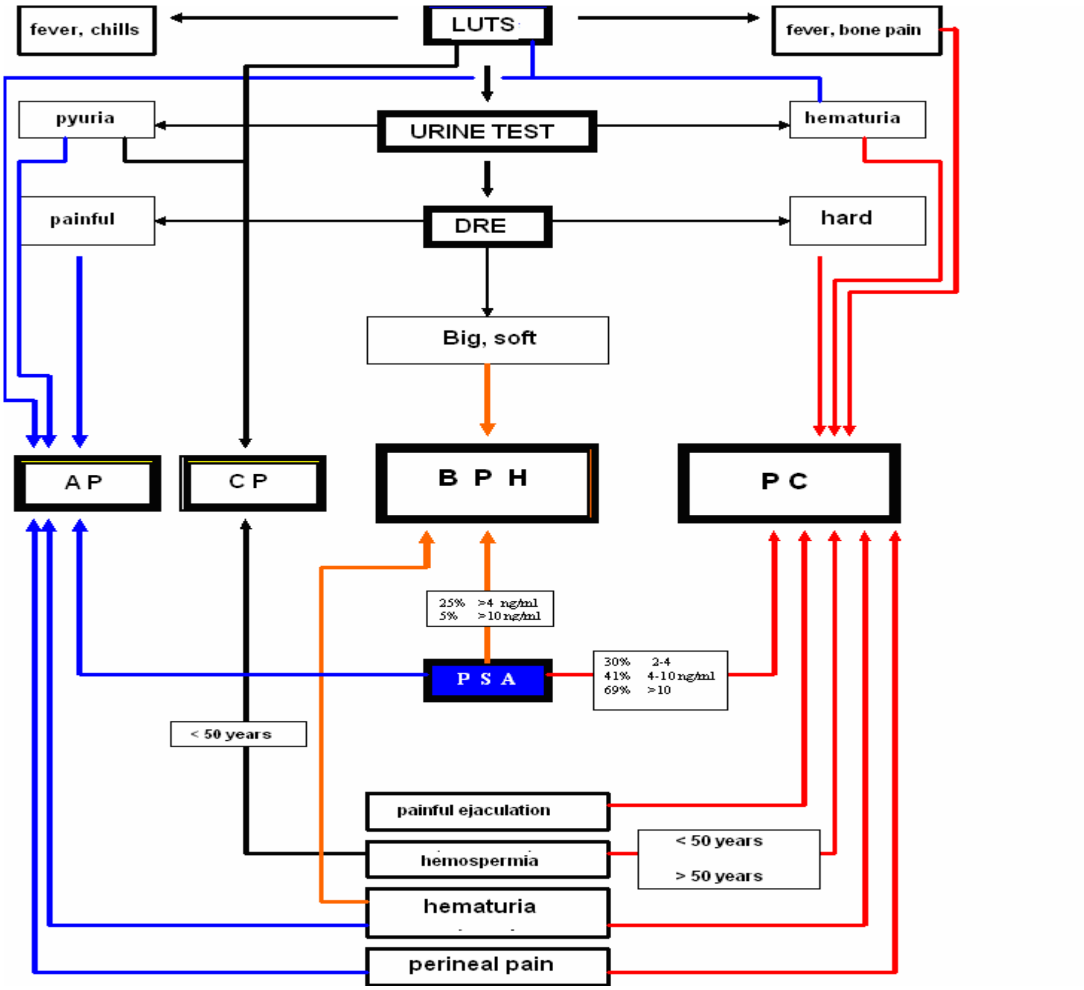

Fig. 1: Prostate Diagnosis Process Model

2.3 Prostate disease diagnosis

To represent the process model, we organized prostate related rules in three groups: *LUTS classification module* (crisp rules), *Prostate Diagnostic module* (fuzzy rules) and *Prostate Treatment module* (fuzzy rules). *LUTS module* classifies the current patient data to a specific patient model according to the calculated LUTS Factor. These values are stored in the patient health record database. A sample of *LUTS rules* can be seen in Table 1.

For each patient record that is stored in the Patient Database, *Prostate diagnosis module* decides 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 disease diagnosis rules* can be seen in Table 2. Finally there are a small number of *Prostate treatment* rules, which according to the resulted disease provide the appropriate treatment strategy.

Table 1. Lower Urinary Tract Symptoms classification rules (partial)

Stop urination	Weak urination	Night Urination	…	LUTS
Less than 1	Less than 1	1		No
Less than half	Less than half	1	…	No
About half	Less than half	1 to 3		Yes
More than half	Less than half	1 to 3		yes
Always	About ahalf	1 to 3	…	Yes
…	…	1 to 3		yes

Table 2. Prostate diseases diagnostic rules (partial)

INTERMEDIATE INPUT			DIAGNOSTIC RULES			
LUTS	DRE	PSA	AP	CP	BPH	PCA
Yes	Hard	High	No	No	No	Yes
Yes	Hard	High	Yes	No	No	Yes
Yes	Painful	Middle	Yes	Yes	Yes	No
Yes	Painful	Middle	Yes	Yes	No	No

	…	…				
No	No	Normal	No	No	No	No

3. HIROFILOS-II Architecture and Design

The developed intelligent system for all prostate diseases has the structure of Fig. 2. The core of the system is a fuzzy expert system [8], [11] augmented by an off-line machine learning component. The *knowledge base* of the expert system includes *crisp or fuzzy rules*, distributed in groups. Fuzzy rules are symbolic (if-then) rules with linguistic variables (e.g. age), which 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* [10, 11]. The variables of the conditions (or antecedents) of a rule represent 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. 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 [11].

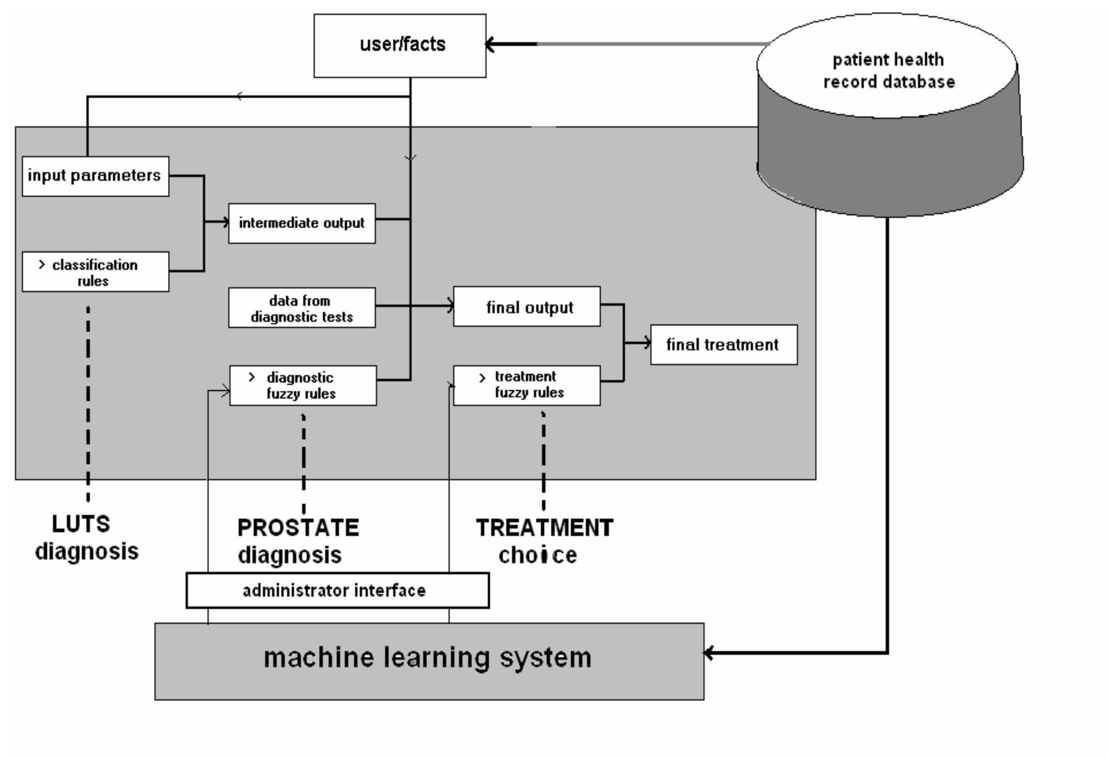

Fig. 2. The general structure of and reasoning flow in HIROFILOS-II

To represent the process model, we organized rules in three groups: *classification rules*, *diagnostic rules* and *treatment rules*. From those, the first contains crisp rules, whereas the other two fuzzy rules. The current patient data are stored in the System Database, as *facts*. Each time the reasoning process requires a value, it gets it from the database. In an interactive mode, it could be given by the user. Fig.2 presents how the rule groups and the facts/user are used/participates during the reasoning process to simulate the diagnosis process.

The machine learning system includes some of the well known data mining tools (such as those included in WEKA) as off-line developers, to extract rules from the patient records. It has been initially used for constructing the expert system, but it will be mainly used to periodically evolve the fuzzy expert systems, based on new patient cases stored in the database. Health record data was used for induction, and the exported/constructed rules have been transformed into the fuzzy knowledge base by the administrator of the system and finally integrated with the expert knowledge (Fig. 2).

4. Implementation Issues

The user interface of the system has been developed with C#.NET v2003, in order to be used as a web-based application on a hospital web server, and the fuzzy expert system has been developed in FuzzyCLIPS 6.1b Expert System Shell. We used WEKA (more specifically, algorithm *J48)* for tree-form rule extraction to produce an initial number of rules. Then rules were modified based on expert advice. Finally, about 84 rules have been constructed. To implement reasoning flow, we implemented each rule group as a *module* in CLIPS. Patient health records from the Database are recognized by using FuzzyCLIPS *templates*. Following are some example rules:

Next rule asks the user to input parameters about LUTS:

```
(defrule   Questions_LUTS     "ask-
question"
(initial-fact)
=>
(printout  t "Question About LUTS "
t)
…
(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 rule 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 (LUTS yes)))
(defrule print_LUTS
(LUTS  yes)
(end yes)
=>
(printout   t  "***  you have severe
LUT  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 is a fuzzy rule that concerns prostate cancer final diagnosis:

```
 (defrule R_4
 (declare (CF 0.1))
 (and(fever  no)(GRN  enlarged)(PSA
high))
 =>
  (assert (PCA (value yes))
)
```

5. Experimental results

HIROFILOS-I was tested on a number of 200 patient records from a Hospital Database with different types of prostate diseases. Data that was the input to the system, was taken from electronic health records that were recorded in the hospital by the doctors. The type of data that is usually stored in these records, are numeric as well linguistic. To evaluate HIROFILOS-II, the same test set has been used and three statistical metrics were calculated for this purpose: accuracy, sensitivity and specificity. The gold standard that used was the 90% for all metrics as sensitivity and specificity, for all the classes in this problem. The final corresponding diagnosis results were compared to the results of a specialized urology doctor for prostate cancer (PC). The evaluation results are presented in Table 3 and show an elevated performance for the final system on the present database.

Table 3. Evaluation results for initial diagnosis of prostate cancer patients using HIROFILOS-I & II

Metrics	SPECIALIZED DOCTOR	HIROFILOS-I	HIROFILOS-II
ACCURACY	0.95	0.76	0.93
SENSITIVITY	0.98	0.79	0.97
SPECIFICITY	0.99	0.75	0.99

6. Conclusions

In this paper, we present the design, implementation and evaluation of HIROFILOS-II, an intelligent system that deals with diagnosis and treatment of almost all prostate diseases. This is in contrast to existing efforts that mainly deal with prostate cancer only [3], [4], [5], [9]. The system comprises three modules, one dealing with LUTS, the other dealing with prostate diseases diagnosis process and the third concerning treatment proposals.

The predecessor of HIROFILOS-II, called HIROFILOS-I, was constructed based on expert knowledge only and using crisp rules. HIROFILOS-II has been constructed by extracting rules from a set of patient records via a machine learning algorithm (WEKA-J48) and transforming them into fuzzy rules taking account their medical usefulness. Additionally results from the machine learning algorithm showed that not all of the parameters identified by the expert are necessary for making decisions. Also, HIROFILOS-II has had a much better performance than HIROFILOS-I. On the other hand, the machine learning component will be periodically used to update existing rules based on new patient data gathered in the database.

At present, HIROFILOS-II is accommodated on a hospital server for use as: a decision-support system for resident doctors, as well as an e-learning platform for medical students. Furthermore, it can be used as an introductory advisory agent for interested patients having access through secure wireless network. In addition, more experiments are on the way as future steps in order to improve the system and to cover rare patient cases. Also, the extend of this system can be used as a model with other electronic health records in other hospitals of the country as well as other diseases.

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