Development a Knowledge-based Medical Diagnosing System for Thyroid Disorders+

Kwun Ik Cho*, Soung Hie Kim* and Jae Bum Noh**

갑상선질환의 진단을 위한 지식기반 의료진단시스템의 개발+

조권익* · 김성희* · 노재범**

Abstract

In this study, we will present a knowledge-based consulting system, called THYCONS, for diagnosing thyroid disorders. It has been developed to make the knowledge and expertise of the human expert more widely available, therefore achieving a high-quality diagnosis.

Frames will be used to represent the medical knowledge of thyroid disorders, and several rules are attached in each slot of a frame. The uncertainty of diagnostic processes is manipulated by the subjective Bayesian method under the assumption that the pieces of evidence are conditionally independent. Searching for the group of diagnostic tests to be carried out and their optimum sequences will be established in order to infer a more correct diagnosis on the basis of maximum information gain with cost and time restrictions. Additionally, differential diagnosis will be carried out based on the information gained.

1. Introduction

The use of computers in the selection of good diagnostic and treatment strategies has received increased attentions in recent years. A major reason for this interest is the desire to improve the ability of the clinician to deal with the difficult problems that can arise in the treatment of a patient. A significant portion of the difficulty stems from the fact that the physician must sort out numerous possibilities and develop a hypothesis about the patient's status. Therefore, making the knowledge and expertise of human experts more widely available through a computer consultation system could be done to achieve high-quality health care.

A number of researchers have studied physiology

+ This work has been done with the assistance of Seoul Nat'l University Medical Center

* Dept. of Industrial Engineering, KAIST

** Sam-Sung Economic Research Institute

and the processes through which it is manipulated, and several systems have been designed. MYCIN and INTERNIST especially are of great interest because they operate inexact reasoning in their diagnostic searches and so are closer to human behavior than the others[3]. And a large number of studies have been done to deal the uncertainty in Expert Systems, which can also be applied to manipulate the inexact reasoning in clinical diagnosis [8].

Our system, called THYCONS(Thyroid Consultation Systems), deals with the relatively small diagnostic problem in internal medicine, i.e. thyroid disorders. This study is organized as follows ; Section 2 explains how the physicians actually carry out the clinical diagnosis. In section 3, the methodology which is used in THYCONS to diagnose is developed and explained ; how to represent medical knowledge, how to proceed the in exact reasoning, and how to choose appropriate tests and put them in sequence. And the architecture and diagnostic processes will be described with the illustrations in section 4 and 5. Finally, the conclusion that we have found in the construction of this system anbd some further research are described in section 6.3

2. Development of THYCONS

This system behaves in the same way that the physician diagnoses a thyroid disorder. The steps of diagnosis are summarized as follows :

1) Checking the patient's initial status by checking the clinical sheet as shown in Table 1. And asking the patient complementary symptoms/signs to get more clinical information, if necessary.

2) Physician roughly determines the suspected pathology by applying the symptoms/signs that the patient complains of.

3) Executing the various tests to make clear the suspicious hypothetical disorders.

4) Making a diagnosis and differential diagnosis by applying the gained evidences and physician's medical knowledge.

5) Recommending treatments and observing the patient's status continuously.

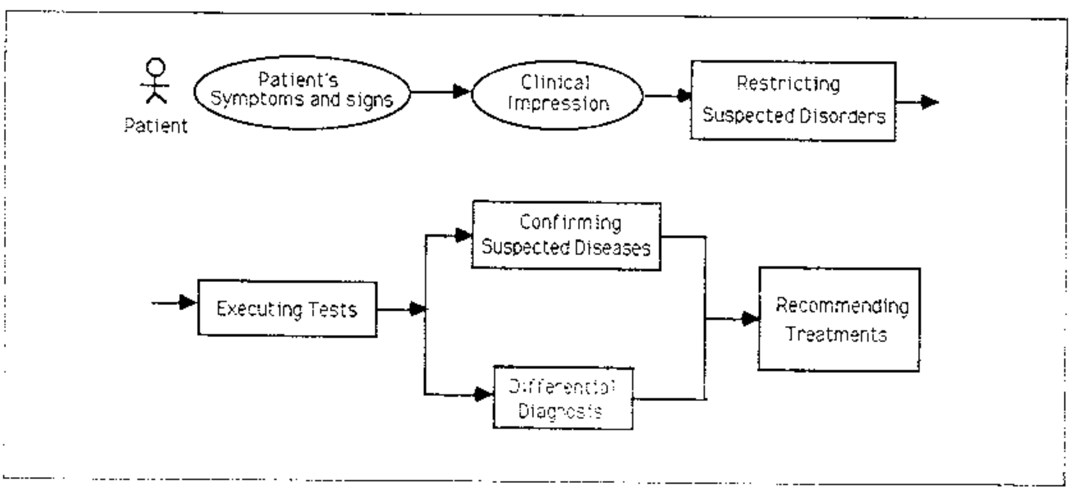


Fig. 1. Diagnostic processes of physicians

Table 1. Chlinical Sheet

Symptoms			Degrees		
Hoarseness			Normal	Mild	Servere
Palpitation		Exist	Not-exist		
Dyspnea	On rest	On Exertion	Normal		
Heat Intolerance	Severe	Mild	Normal		
Cold Intolerance			Normal	Mild	Servere
Sweating	Servere	Mild	Normal	Decreased	
Nervouseness		Exist	Not-exist		
Insomnia		Exist	Not-exist		
Memory Impairment		Exist	Not-exist		
Mens. Amount		Oligomerrhea	Normal	Menorrhgia	
Appetite	Very Good	Good	Normal	Poor	
Defecation	Diarrhea	Hyperd.w/o Diar	Normal	Constipation	
Weight	Servere Lost	Mild Lost	Normal	Mild Gained	Severe Gained
Fatigue	Servere	Mild	Normal		
Goiter Status	Diffuse		Normal	Nodular	
Goiter Size	More larger	Large	Normal	Small	More Smaller
Speech			Normal	Slow	More Slower
Touch of Skin		Moist	Normal	Coarse	Dry
Temperature of Skin		Warm	Normal	Cold	
Pallorness of Skin		Pallor	Normal		
Hand Tremor	Severe	Mild	Normal	Get Better	Get Lost
Hair	Hard	Loss	Normal	Brittle	Become Silky

3. Development of THYCONS

3-1. Knowledge Representation using Frame

THYCONS uses frames for representing knowledge about thyroid disorders which is similar to the PIP(Present Illness Program) [3]. Each frame consists of several slots, which may be filled with various properties, logical and semantic relations, and associated inference rules ; NAME, FINDINGS, IS-SUFFICIENT, MUST-HAVE, MUST-NOT-HAVE, DIFFERENTIAL DIAGNOSIS, and TESTS(Figure 2).

FINDINGS slot contains various important facts associated with the hypothetical disorder which is expressed in NAME slot. Each fact in FINDINGS has its supporting and rejecting likelihood ratio, LS and LN, for the hypothesized disorder where LS and LN show the likelihood ratio for presence and absence of a certain fact respectively. IS-SUFFICIENT covers the case of pathognomonic findings, in which the presence of a single finding is in itself sufficient to confirm the presence of the hypothesized disorder ; logical combinations (NOT, AND, and OR) may also be used to specify more complex criteria. MUST-HAVE and MUST-

NAME *hypothetical disorder*
FINDINGS *findings (LS, LN)*
IS-SUFFICIENT *conditions*
MUST-HAVE *conditions*
MUST-NOT-HAVE *conditions*
DIFFERENTIAL DIAGNOSIS *IF conditions THEN hypothetical disorder*
TESTS *test name (LS, LN)* or
test name LSN(x)

Fig. 2. Typical Structure of a Frame

NOT-HAVE specify necessary conditions, in the absence of which the hypothesis will not be accepted as confirmed. TEST shows the several tests which are used to confirm or disconfirm the hypothetical disorder. And the supporting and rejecting likelihood ratio of a test yielding continuous results are combined into an LSN function. DIFFERENTIAL DIAGNOSIS identifies a set of competing disorders that are to be considered if some appropriate conditions hold. Figure 3 shows an example frame used in THYCONS.

3-2. Handling uncertainty by the Subjective Bayesian method

In THYCONS, the rules expressed in each slot of the hypothetical frame k typically have one of the following forms ;

type 1 : (IF)S_i(then D_k with) (LS_{ik}, LN_{ik})

where S_i denotes a finding or a set of findings combined with logical operators, e.g. symptoms／signs, and tests yielding binary results, and LS_{ik}, LN_{ik} is likelihood ratio of hypothetical disorder D_k when S_i is found and not found respectively.

type 2 : (IF) T_i (then D_k with) $LSN_{ik}(x)$

where T_i is the test yielding continuous results, and $LSN_{ik}(x)$ is the likelihood ratio function of test results. In parts of type 1 and type 2, the underline part will be omitted for simplicity of representation as shown in Figure 3.

The likelihood ratios which are obtained from human experts are defined as follows ;

$$LS_{ik}=P(S_i \mid D_k)/P(S_i \mid \bar{D}_k),$$
$$LN_{ik}=P(\bar{S}_i \mid D_k)/P(\bar{S}_i \mid \bar{D}_k)$$
$$=\{1-P(S_i \mid D_k)\}/\{1-P(S_i \mid \bar{D}_k)\}.$$
$$LSN_{ik}(x)=P(T_i(x) \mid D_k)/P(T_i(x) \mid \bar{D}_k).$$

LS_{ik} is greater than one if S_i is closely related to D_k than to D_k, and is less than one for the reversal case, and LN_{ik} can be interpreted similarly. $LSN_{ik}(x)$ is the confirmation or denial degree of hypothetical disorder D_k where test T_i is done and yields x. A typical $LSN_{ik}(x)$ function has the form as shown in Figure 4. These likelihood ratios are obtained from human expert, and will be stored in Knowledge Base.

In case of presence of a finding i, odd of hypothetical disorder k is updated as ;

$$O(D_k \mid S_i)=LS_{ik} \cdot O(D_k).$$

And for the absence, odd of hypothesis k is modified as follows ;

NAME Graves' Disease

FINDINGS
Pulse rate > 100/min (3,4)
Goiter (3,4)
Nervousness (2,3)
Warm and moist skin (3,3)
Hand tremor (3,3)
Increased sweating (2,3)
Palpitation (4,3)
Heat intolerance (4,3)
Fatigue (1,3)
Weight loss (4,3)
Bruits over thyroid (5,2)
Dyspnea (2,2)
Widened palpebral fissure (2,2)
Infrequence blinking (2,2)
Increased Appetite (3,2)
Insomnia (1,2)
Hyperdefecation without diarrhea (1,1)
Diarrhea (1,1)
Oligomenorrhea (1,1)
Atrial fibrillation (1,0)
Gynecomastia (1,0)
Splenomegaly (1,0)
Sence of irritation in the eye (1,1)
Excessive tearing (1,1)
Exopthalmos (3,1)
Double vision (1,0)
Blurred vision (1,0)
Pretibial myxedema (4,0)

IS-SUFFICIENT

MUST-HAVE

MUST-NOT-HAVE

DIFFERENTIAL DIAGNOSIS
IF (Goiter is absent) and (Skin is cool), THEN (Anxiety state)
IF (Diastolic hypertension is present), THEN (Phenchromocytomn)
IF (TSH > 8uU/ml) and (Alpha subunit TSH > 1uU/ml) and (Pituitary Tumor is present), THEN (TSH Producing Tumor)
IF (TSH > 8uU/ml) and (Alpha subunit TSH < 1uU/ml) and (Pituitary Tumor is absent), THEN (Selective Resistance to TSH)
IF (HCG > 100U/ml), THEN (Trophobiastic Tumor)
IF (Single thyroid nodule is present), THEN (Hyperfunctioning Adenoma)
IF (Multiple thyroid nodule is present), THEN (Toxic Multinodular Goiter)
IF (RAIU < 5%) and (Pain on neck is present), THEN (Subacute Thyroditis)
IF (RAIU < 5%) and (Pain on neck is absent), THEN (Painless Thyroditis)
IF (History of thyroid hormone ingestion is present), THEN (Thyroidtoxicosis Factitia)
IF (Follicular carcinoma is present), THEN (Functioning Follicular Carcinoma)

TESTS
T4 (8ug/dl,-6) (12ug/dl,0) (18ug/dl,6)
T3 (120ug/dl,-6) (100ug/dl,0) (400ug/dl,6)
FT4I (1.5,-4) (3.6,0) (9.7,4)
Free T4 (0.8ug/dl,6) (2ug/dl,0) (4.5ug/dl,6)
RAIU (5%,-6) (30%,0) (45%,3)
TBII (15%,-3) (20%,0) (40%,2)
TSI (50%,-4) (150%,0) (300%,3)
TSH (0uU/ml,1) (4uU/ml,0) (15uU/ml,-6)
TSH Stimulation (2uU/ml,3) (5uU/ml,0) (15uU/ml,-5)

Fig. 3. An Example of the typical Frame

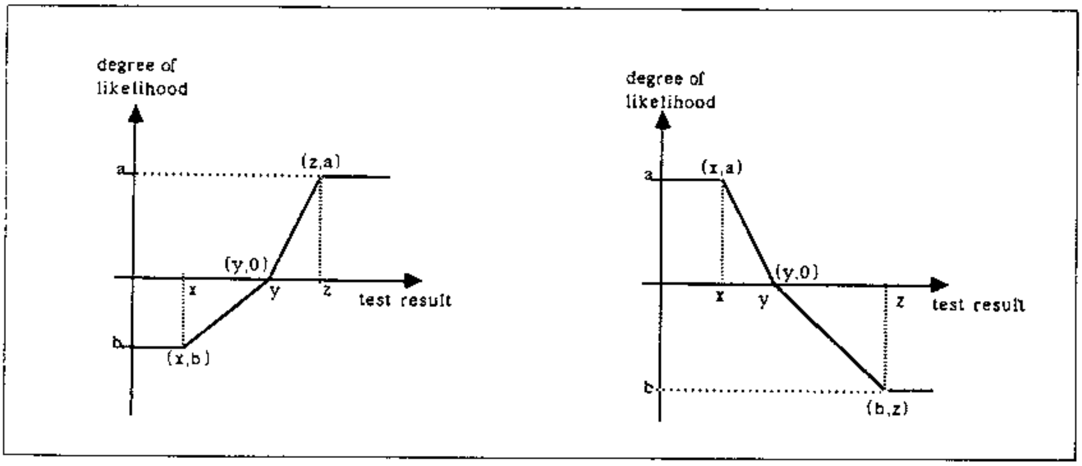


Fig. 4. The form of LSN function

$O(D_k \mid \overline{S_i}) = LN_{ik} \cdot O(D_k)$.

Under assumption that independence is hold between each evidences, posterior odds $O(D_k \mid \{S_i\}_{i \in I} \{S_i\}_{i \in \bar{I}} \{T_j\}_{j \in J})$ after observing symptoms/signs and executing several tests can be modified by the following ;

$$O(D_k \mid \{S_i\}_{i \in I},\ \{S_i\}_{i \in \bar{I}},\ \{T_j\}_{j \in J}) = O(D_k) \cdot \Pi_{i \in I}\ LS_{ik} \cdot \Pi_{i \in \bar{I}}\ LN_{ik} \cdot \Pi_{j \in J}\ LSN_{jk}(x_j) \quad \cdots\cdots\cdots\cdots (1)$$

where I, $\bar{I}$ are the index set of symptoms/signs and binary tests when these are proved to be present and absent respectively, and J is the index set of executed tests yielding continuous results. From equation(1), the probability that the suspected disease would be D_k after observing symptoms/signs and executing several tests will be as follows ;

$$P(D_k \mid \{S_i\}_{i \in I}, \{S_i\}_{i \in \bar{I}}, \{T_j\}_{j \in J}) = O(D_k) / [1 + O(D_k)]$$

3-3. The collecltion of likelihood ratios and odds

Human experts will provide the following numerical medical knowledge ; likelihood ratios and prior odds. But the process of collecting numerical knowledge from experts is a difficult task. As a way to surmount this difficulty, we use the verbal description suggested by Duda et al. [4] which can be transformed into numerical values as shown in Table 2. If Experts express medical knowledge by verbal description, then this knowledge would be transformed automatically into numerical knowledge in THYCONS.

3-4. The selection of an optimal test flow

One of the decisions a physician frequently confronts is to determine which test should be carried out firstly. In many situations, a single test cannot provide sufficient information to conclude to a certain disorder. Hence two or more tests may be performed in order to prevent jumping the wrong conclusion. Taking account of several tests would make the physician confused, because he/she must consider a number of combinations of tests and interpret the combined test results. In this system, the Entropy concept introduced by Shan-

Table 2. Verbal description for likelihoods and odds

Verbal Description	Level	log (likelihood)
Completely Sufficient	6	6
Extremely Suggestive	5	4
Very Suggestive	4	2
Moderately Suggestive	3	1
Mildly Suggestive	2	0.7
Weakly Suggestive	1	0.3
Indifferent	0	0
Weakly Necessary	-1	-0.3
Mildly Necessary	-2	-0.7
Moderately Necessary	-3	-1
Very Necessary	-4	-2
Extremely Necessary	-5	-4
Absolutely Necessary	-6	-6

Verbal Description	Level	log(odd)
Always Present	4	3
Almost Always Present	3	2
Abundant	2	1
Very Common	1	0.5
Common	0	0
Fairly Common	-1	-0.5
Occasional	-2	-1
Rare	-3	-2
Extremely Rare	-4	-3

non[10] will be applied to find the order of tests with cost and time.

A test can be executable only when its precedent tests have been carried out, and its substituted tests should not be run. Under the situation that m disorders are suspected with their suspicious probability, the amount of information gained by test T_j, $I(D \mid T_j)$, is defined as follows ;

$$I(D \mid T_j) = H(D) - H(D \mid T_j)$$

where $D = (P(D_1), P(D_2), \cdots, P(D_m))$ is the suspected probability for each disorder,

and $H(D) = -\Sigma_{k=1}^{m} P(D_k)\ log O(P_k)$,

$$H(D \mid T_j) = \Sigma_{n=1}^{N} P(T_j = x_n) \cdot$$
$$\{-\Sigma_{k=1}^{m} P(D_k \mid T_j = x_n)\ log P(D_k \mid T_j = x_n)\}.$$

The test yielding continuous results will be discretized its results appropriately to calculate the information gain. A series of tests is chosen among many other tests which prove to be able to carry out based on the maximum information gain with the criteria such as cost, necessary time for the test.

4. The architecture of THYCONS

The architecture of THYCONS is shown in Figure 5. THYCONS can be applied to another areas of which knowledge is organized according to the structure of the system. Primary constituents of THYCONS are as follows ; Domain Knowledge Base, Diseases Interpreter, Test Selector, Data Base, Working Memory, Dialogue Manager.

Domain Knowledge Base Domain Knowledge Base contains the medical knowledge of thyroid disorders in a type of Frames as described in section 3.1. Experts(physicians) can modify and add the knowledge using Knowledge Editor. And the new knowledge can be formed by the knowledge Generator from Data Base where details of patients are recorded.

Data Base Data Base plays a role of recording details of patients and creating new medical knowledge by the knowldedge Generator. The generation of new medical knowledge is done by detecting the common facts which a group of patients suffer having a common disorder.

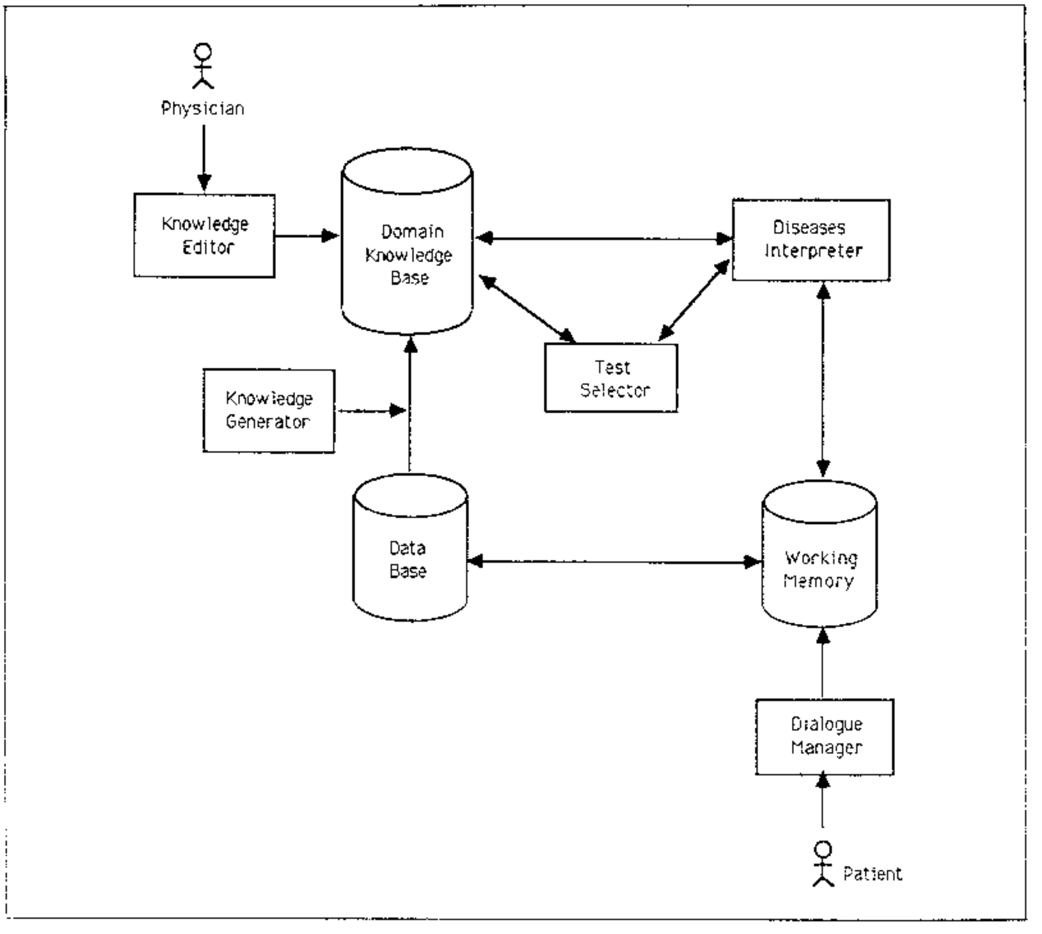


Fig. 5. The Architecture of THYCONS

Working Memory The state of a patient is stored in Working Memory while diagnosing and trying to cure the disease.

Test Selector Tests should be executed to identify a disorder from which patient is suspected to suffer from. Test Selector suggests appropriate tests and their sequence for diagnosing more precisely.

Diseases Interprter Based on several results, i.e. symptoms, signs and results of tests which the patient reveals, Diseases Interpreter will identify a disorder and carry out differential diagnosis.

5. Diagnostic processes of THYCONS

THYCONS will carry out a diagnosis for a patient who suffers from a disorder related to the thyroid gland as shown in Figure 6.

Step 1 A user(patient) complains of maor pains,. according to the clinical sheet presented from the Dialogue Manager, and details of pains are stored in the Working Memory. The items in the clinical sheet are closely related to the syndromes of the thyroid disorder as seen. After interac-

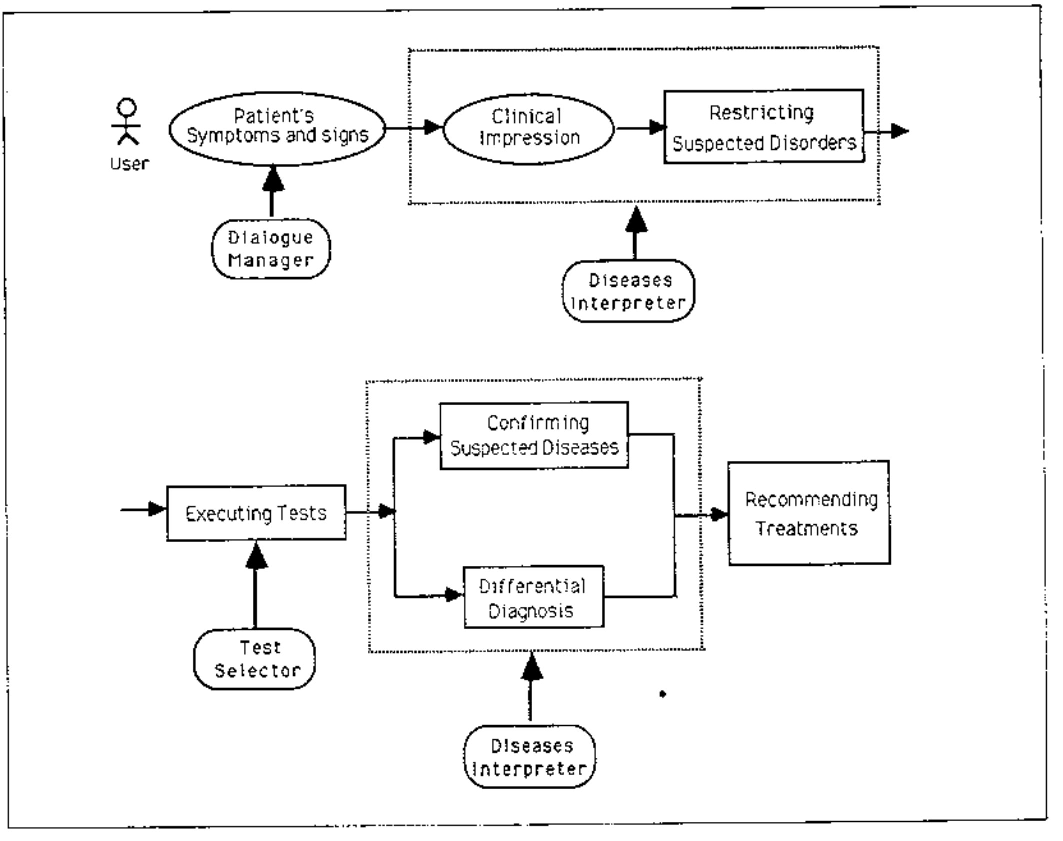


Fig. 6. Diagnostic Processes of THYCONS

ting with user, the various symptoms/signs which the patient reveals are summarized as(a) in Figure 7.

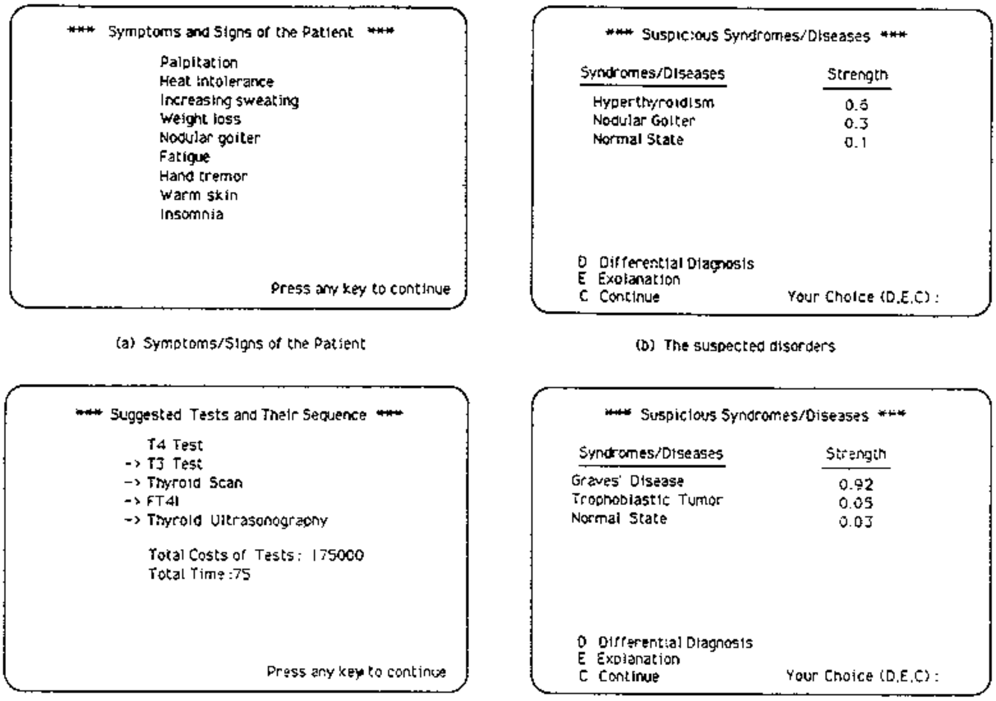
Step 2 Based on symptoms/signs that the patient conmplains, the THYCONS draws a deduction of possible syndromes/diseases. The suspected degrees of each disorder are computed by Disease Interpreter using knowledge in Knowledge Base and displayed as(b) in Figure 7.

Step 3 To make clear the suspicious diseases, THYCONS may make inquiries about additional pains by Dialogue Manager. And the suspected degrees of each hypothetical disorder are also updated based on these pains.

Step 4 To find a series of tests which are used to make a correct diagnosis, the patient will be asked about cost and time that he/she is willing to allow for executing tests. Then a group of tests which are proved executable and their precedence relation are suggested by Test Selector as(c) in Figure 7.

Step 5 After carrying out a test(tests), THYCONS makes a diagnosis and differential diagnosis using test results by Disease Interpreter as(b) in Figure 7.

Step 6 The details of a patient are stored in Data Base to reuse some time later when the patient revisits to cure the disease, and infer new medical knowledge.



(a) Symptoms/Signs of the Patient (b) The suspected disorders

(c) Executable Tests and their Sequence (d) Final Diagnosis

Fig. 7. Example Session of Diagnostic Processes

6. Conclusion

In this study, we have developed a consulting system for diagnosing thyroid disorders. This system includes about 20 hypothetical frames and additional frames will be added. The system can give good results in a rather narrow domain of thyroid disorders.

There are additional works as follows : the subjective Bayesian method which is used to infer the suspicious syndromes/diseases can operate well only when the pieces of evidences are conditionally indepenedent, which differs frem most real situations. Therefore, the methodology that can deal with the dependence successfully should be developed and implemented to the better system. Using the Fuzzy Reasoning may be regarded as a solution. Knowledge generation from the Data Base of patients is hard to implement since the physician is not willing to accept the generated knoledge. So the complementary knowledge generation method must be developed to give well-defined knowledge. The mentioned subects will remain for further research.

Acknowledgement

In the development of THYCONS, staffs of Seoul Nat'l University Medical Center gave us many assistance and advices. We thanks for their efforts and especially to Chang Soon Ko, Bo Yun Cho, and Myung Sik Lee.

References

[1] H. Anna, Knowledge Acquisition for Exper System, McGraw-Hill, 1986.

[2] N Baba, "Least cost testing sequence problem with unknown rejecting probabilities," Information Science 12, pp. 157-162, 1977.

[3] W.J. Clancey, E.H. Shortliffe, Readings in Medical Artificial Intelligence, Addison-Wesley, 1984.

[4] R.O. Duda, P.E. Hart, and N.J. Nilsson, "Subjective Bayesian Methods for Rulebased Inference Systems," SRI Technical Note 124, 1976.

[5] A.O. Esogbue, R.C. Elder, "Fuzzy sets and the modelling of physician decision processes, Part I : The initial interview-information gathering session," Fuzzy Sets and Systems 2, pp. 279-291, 1979.

[6] . Fichefet, J.P. Lecleria, "Microcomputer-Assisted Identification of Bacteria and Multicriteria Decision Models," Computers and Operation Research, vol 11. No. 4, pp. 361-372, 1984.

[7] C.F. Hess, K. Brodda, "On the optimum selection of diagnostic tests in computer aided differential diagnosis," Computers and Biomedical Research 17, pp. 389-398, 1984.

[8] L.N Kanal, .F. Lemmer, Uncertainty in Artificial Intellignece, North-Holland, 1986.

[9] R.I Levine, E.D. Drang, and B. Edelson, A Comprehensive Guide to AI and Expert Systems using Turbo Pascal, McGraw-Hill, 1988.

[10] A.M. Mathi, P.N. Rathie, Basic Concepts in Information Theory and Statistics-Axiomatic Foundations and Applications, John-Wiley & Sons, 1975.

[11] J.A. Reggia, S. Tuhrim, Computer-Assisted Medical Decision Making, vol 1 & vol 2, Springer-Verlag, 1985.

[12] H.U. Shaolin, Y.Y. Haimes, and R.S. Galen, "Optimal selection of a battery of tests ; A multiobjective optimization methodology," Medical Decision Making 8, pp. 19-32, 1988.

[13] D.A. Waterman, A Guide to Expert Systems, Addison-Wesley, 1986.

[14] T.F. Weyant, Optimization of Generalized Sequential Decision Schemes for Medical Diagnosis, University of California, 1982.