An Integrated Two-Level Hierarchical System for Decision Making in Radiation Therapy Based on Fuzzy Cognitive Maps

Elpiniki I. Papageorgiou, Chrysostomos D. Stylios*, *Member, IEEE*, and Peter P. Groumpos, *Member, IEEE*

***Abstract*—The radiation therapy decision-making is a complex process that has to take into consideration a variety of interrelated functions. Many fuzzy factors that must be considered in the calculation of the appropriate dose increase the complexity of the decision-making problem. A novel approach introduces fuzzy cognitive maps (FCMs) as the computational modeling method, which tackles the complexity and allows the analysis and simulation of the clinical radiation procedure. Specifically this approach is used to determine the success of radiation therapy process estimating the final dose delivered to the target volume, based on the soft computing technique of FCMs. Furthermore a two-level integrated hierarchical structure is proposed to supervise and evaluate the radiotherapy process prior to treatment execution. The supervisor determines the treatment variables of cancer therapy and the acceptance level of final radiation dose to the target volume. Two clinical case studies are used to test the proposed methodology and evaluate the simulation results. The usefulness of this two-level hierarchical structure discussed and future research directions are suggested for the clinical use of this methodology.**

***Index Terms*—Decision making, fuzzy cognitive maps, hierarchical intelligent systems, modeling, radiation therapy.**

I. INTRODUCTION

RADIATION oncology is the clinical and scientific endeavor to cure patients with cancer (malignant neoplasis and other diseases) using ionizing radiation and to investigate the biological and physical basis of radiation therapy. The aim of radiation therapy is to deliver a precisely calculated dose of radiation to a defined tumor volume with as minimal damage as possible to the surrounding healthy tissue, resulting in eradication of the tumor, that means high quality of life, and prolongation of survival at a reasonable cost.

The clinical use of irradiation is a complex process that involves many professionals and a variety of interrelated functions and procedures. For determining the treatment of a patient, it is necessary to know how this tumour will be destroyed and how the surrounding healthy tissue is likely to be adversely affected by the applied radiation dose. Different factors some of which are complementary, others similar and others conflicting, are taken into consideration when deciding the radiation treatment procedure. Each factor has a different degree of importance in determining (or influencing) the dose and all factors together determine the success of the therapy [1].

A good number of approaches and methodologies, algorithms, and mathematical tools have been proposed and used for optimizing radiation therapy treatment plans [2], [3]. Dose calculation algorithms [4], [5], dose-volume feasibility search algorithms [6], and biological objective algorithms have been utilized [7] and dose distributions have been calculated for the treatment planning systems, satisfying objective criteria and dose-volume constraints [3]. Algorithms have been proposed for optimizing beam weights and beam directions [8]. Moreover, steepest-descent methods and gradient-descent methods have been used to optimize the objective functions, based on biological or physical indices, and have been employed for optimizing intensity distributions [9], [10]. Dose-volume histograms analyses of the resultant dose distributions appear to indicate some merit to these approaches [11]. Furthermore, knowledge-based expert systems and neural networks have been proposed for the optimization of treatment variables and decision support during radiotherapy planning [12], [13]. Scientists have put much effort into developing the above approaches to optimize treatment variables and dose distributions. This fact makes apparent the need for a fast, flexible, accurate, and adaptive tool, based on an abstract cognitive model, which will be used for the clinical practice simulation and decision-making [14].

The number, kind, and nature of the parameters-factors that have to be taken into consideration in determining the radiation treatment bring up the fuzziness, the complexity and the uncertainty of the whole procedure. These characteristics require the use of soft computing modeling techniques such as FCMs [15] that create a sophisticated approach for decision-making in Radiation Therapy.

FCMs incorporate artificial neural networks and fuzzy logic to create a dynamic model for estimating the final dose received by the target volume and normal tissues and contributes to the success of the whole therapy. FCMs have been successfully used to model complex systems that involve different factors, states, variables, and events. FCMs can integrate and include, in a decision-making process, the partial influence of controversial factors [16]. FCM model makes apparent the cause and effect relationship among the various fuzzy factors that determine the radiation dose, keeping it in a minimum level and at the same time having the best result in destroying tumours with minimum injuries to healthy tissues and organs at risk, and in accordance

Manuscript received May 27, 2002; revised April 3, 2003. *Asterisk indicates corresponding author.*

E. I. Papageorgiou and P. P. Groumpos are with the Laboratory for Automation and Robotics, Department of Electrical and Computer Engineering, University of Patras, Patras 26500, Greece (e-mail: groumpos@ee.upatras.gr).

*C. D. Stylios is with the Computer Science Department, University of Ioannina, P.O. Box 1186, Ioannina, Greece (e-mail: stylios@cs.uoi.gr).

Digital Object Identifier 10.1109/TBME.2003.819845

with the uppermost goal of radiation therapy treatment [1], [17], [18].

The result of this research work is a decision model based on human knowledge and experience, consisting of a two-level hierarchical structure with a FCM in each level that creates an Advanced Decision-Making System. The lower-level FCM models the treatment planning, taking into consideration all the factors and treatment variables and their influence. The upper-level FCM models the procedure of the treatment execution and calculates the final dose during radiation treatment. The upper-level FCM supervises and evaluates the whole radiation therapy process. Thus the proposed two-level integrated structure for supervising the procedure before treatment execution seems a rather realistic approach to the complex decision making process in radiation therapy.

The proposed method can help radiotherapists and physicists to select different treatment variables-factors. With this advanced decision-making system, they can simulate a good number of different treatment planning procedures taking in consideration many different fuzzy factors and so to decide if their selection is acceptable or nonacceptable for the specific treatment case. It is emphasized here that it is not the aim of this study to find the best treatment or the best dose, but to introduce FCM approach in radiation therapy treatment and develop the two-level hierarchical model for the decision-making.

The outline of this paper follows. Section II presents an overview of FCM models, how FCMs are developed and how they model a complex system. Section III discusses the factors, issues, and problems that have to be considered during radiation therapy planning procedure. In Section IV, the FCM model for the radiotherapy planning procedure is designed and developed and this model is implemented for two clinical cases proving the validity of the model. Section V introduces the idea to develop an abstract model to supervise the decision making process for radiation therapy and proposes a two-level hierarchical structure for the radiotherapy decision-making procedure, this structure creates an Advanced Decision-Making System that is implemented for the cases of two treatment procedures and proves the usefulness and importance of the supervision execution procedure. Section VI discusses the proposed methodologies, structures and their contribution and validity and Section VII concludes the paper making suggestions for future research.

II. An Overview of Fuzzy Cognitive Map Models

Fuzzy Cognitive Maps (FCMs) have been successfully used to model complex systems and develop decision support systems. The FCM is a soft computing modeling methodology that follows a method similar to the human reasoning and human decision-making process. It utilizes concepts to illustrate the different aspects of the system's model and behavior and these concepts interact with each other showing the dynamics of the system. FCM structures can be used to represent qualitative and quantitative data. A FCM integrates the accumulated experience and knowledge on the causal relationship between factors/characteristics/components of the system. The advantage of the FCM is due to the way it is constructed, i.e., using human experts that know the system and its behavior under different circumstances [19], [20].

The human knowledge and experience on the system is reflected on the kind and the number of concepts and the weight of the interconnections between concepts of the FCM. Each concept represents one of the key-factors of the modeled system and is characterized by a value A_i. Between concepts there are cause and effect relationships that are illustrated in the FCM graph with the weighted arc w_{ij}. The value of w_{ij} indicates how strongly concept C_i influences concept C_j. The sign of w_{ij} indicates whether the relationship between concepts C_i and C_j is direct or inverse. The direction of causality indicates whether concept C_i causes concept C_j, or vice versa. These parameters have to be considered when assigning a weight w_{ij} to an interconnection. Thus there will be three types of weights between concepts: either expresses positive causality between two concepts $(w_{ij} > 0)$ or negative causality $(w_{ij} < 0)$ or no relationship $(w_{ij} = 0)$.

Every concept in the FCM has a value that expresses the quantity of the corresponding physical quality for which this concept stands for. The value A_i for each concept C_i at time $t + 1$ is influenced by the interconnected concepts and is calculated by the following rule:

$$A_i(t+1) = f\left(A_i(t) + \sum_{\substack{j=1 \\ j\neq i}}^{n} w_{ji} \cdot A_j(t)\right) \tag{1}$$

where $A_i(t)$ is the value of concept C_i at time step t, $A_j(t)$ is the value of concept C_j at time step t, and w_{ji} is the weight of the interconnection from concept C_j toward concept C_i, showing the effect of the change in the value of concept C_j on the value A_i of concept C_i, and f is the threshold function: $f = (1/(1 + e^{-\lambda x})$, where $\lambda > 0$ determines the steepness of the continuous function f and ensures that values of concepts belong to the interval [0, 1].

The methodology for developing FCMs is based on experts who are asked to define concepts and describe relationships among concepts; using IF-THEN rules to justify the cause and effect relationship among concepts and infer a linguistic weight for each interconnection [21]. Every expert describes each one of the interconnection with a fuzzy rule; the inference of the rule is a linguistic variable, which describes the relationship between the two concepts according to everyone expert and gives the grade of causality between two concepts. Then the set of fuzzy weights suggested by experts for each interconnection are integrated using the SUM method and an aggregated fuzzy weight is produced, which with the defuzzification method of center of area (CoA) [22], is transformed to a crisp weight w_{ji}, belonging to the interval $[-1, 1]$.

Every expert describes the relationship between two concepts using the following fuzzy rule with linguistic variables:

IF a change **B** occurs in the value of concept C_j
THEN a change **D** in the value of concept $C_i$is caused.
Infer: The influence from concept C_j to C_i is **E.**

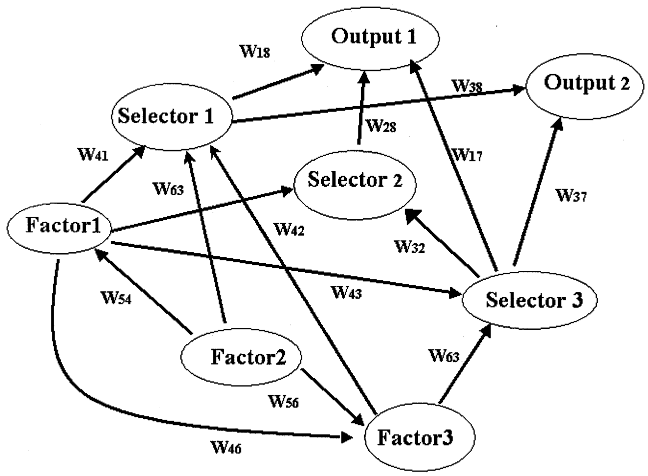

Fig. 1. The general decision support FCM model consisted of selectors, factors, and outputs.

Where $\mathbf{B}, \mathbf{D}$, and $\mathbf{E}$ are fuzzy linguistic variables that experts use to describe the variance of concept values and the degree of influence from concept C_j to C_i.

The FCM development method have been improved and supplied with the Activation Hebbian Learning (AHL) algorithm to train FCM and adjust the values of weights. AHL algorithm considers that the value of weight w_{ji} is dependent on time t; so (1) is updated to a new calculation rule that takes under consideration the asynchronous updating of weights between concepts, as AHL proposes. The proposed learning algorithm overcomes inadequate knowledge of experts and/or nonacceptable FCM simulation results [23]. This AHL algorithm is described in Appendix A.

A generic FCM-model for decision-making in radiotherapy could be consisted of three kinds of concepts as it is illustrated in Fig. 1. There are concepts representing the **Factor**-concepts that are taking into consideration in determining the value of the Selector-concepts. **Selector-**concepts are the concepts that influence the **Output-**concepts that represent the final decision. The FCM model can include all the factors and selectors, along with the existing causal relationships among Factor-concepts because factors are interdependable. Moreover, Factor-concepts influence Selector-concepts and the value of each Selector-concept can subsequently influence the degree of the Output-desired concept of the decision support system. This FCM model is a very abstract model of what a doctor does when he takes a differential decision on the radiation therapy procedure; he determines the selectors and their values, taking into consideration all the related factors, and then according to the Selector-concepts values he determines his final decision that in the model is presented as Output-concepts.

III. Radiation Therapy Process and Treatment Planning: Issues and Factors

The most common method of treating cancer patients with radiation is externally applied beams of photons generated by linear accelerator machines. The objective goal of "three-dimensional (3-D) conformal" radiotherapy is to deliver the highest dose to a volume shaped exactly with the tumour shape and to keep the dose level at the minimum value for healthy tissues and critical organs. The treatment planning is a complex problem because of intercontracting constraints. The performance criteria are: maximization of dose and dose uniformity within the target region and dose minimization to surrounding critical organs and normal tissues. The process of adjusting treatment variables and displaying the corresponding dose distribution is repeated till the optimizations of these criteria are met.

According to ICRU Report 42, the set of procedures applied in Radiotherapy treatment planning [24], are anatomic patient data, definition of the target volume, prescription of the target absorbed dose, selection and computation of provisional beam arrangements, best dose distribution according to the radiation field arrangement, fractionation scheme and simulation of the components of the plan before the first fraction is applied to the patient, and the first setup. At every step of the treatment planning procedure doctors may decide to go back to the previous one if undesirable or unacceptable simulation results are encountered.

The treatment planning is a complex process where a great number of treatment variables have to be taken under consideration. The treatment variables could vary according to each plan and each patient; they are the number of beams, beam weights, beam orientation, wedge angles, collimator settings, and block arrangements. The process of adjusting treatment variables and displaying the corresponding dose distribution is repeated till the objective criteria of maximum dose, dose uniformity within the target region and dose minimization to surrounding healthy tissues and critical organs are considered optimized.

In order to achieve a good distribution of the radiation on the tumour, as well as to protect the healthy tissues the following factors should be taken into consideration [25], [26] (more details of the related terms are provided in [27]).

1) Selection of appropriate size for radiation field.
2) Increase entry points of the beam (multiple radiation field).
3) Selection of the appropriate beam directions.
4) Selection of the weight of each field (dose contribution of each individual field).
5) Selection the appropriate quality, i.e., energy and type of radiation (x-rays, γ-rays, electrons, protons).
6) Modification of field with wedge filters.
7) Processing the outline of the patient with addition of compensating filter or bolus in place of the missing tissue.
8) Modification of field with cerrobend blocks or multileaf collimators.
9) Use of isocentric stationary beam therapy versus isocentric rotation therapy.
10) Patient immobilization.
11) Use of conformal (3-D) instead of conventional two-dimensional (2-D) radiotherapy.

IV. A Clinical Treatment Simulation Tool (CTST-FCM) for Decision-Making in Radiotherapy

In the previous section a brief analysis and description of most factors and treatment variables, that have to be taken into consideration in determining the radiotherapy treatment procedure was done. These factors and characteristics will be the concepts consisting the FCM model for the decision-making procedure of the radiotherapy treatment.

Radiotherapists and physicists experts are asked to construct the FCM model taking under consideration the basic beam data from experimental measurements [28] and the information described at AAPM Task Group 23 test package [29] in order to retrieve the main factors, selectors and the relationships among them. The AAPM Task Group 23 test package is useful for the quantitative analysis of treatment planning systems of photon beam radiation [30]. Our test package of basic beam dosimetric data has been developed with experimental measurements, [28], which is used here for the determination of initial values of concepts and weights.

The concepts of the FCM model for radiotherapy treatment are divided into three categories: Factor-concepts, Selector-concepts, and Output-concepts. Input (factors and selectors) concepts, represent treatment variables with given or measured or desired values, and the corresponding causal weights are calculated from experimental data [28], and data from AAPM Task Group 23 test package [31], [32]. The values of the Selector-concepts are influenced by the Factor-concepts with the corresponding causal weights and the values of the Output-concepts are influenced and determined by the Factor-concepts and the Selector-concepts with the corresponding causal weights. The final decision-making is based on the determination of the values of the Output-concepts that figure out the final decision.

Values of concepts are described using five positive linguistic variables depending on the characteristics of each particular concept, such as very high, high, medium, weak, and zero. The degree of the influence is represented by a linguistic variable of the fuzzy set {positive very high, positive high, positive medium, positive weak, zero, negative weak, negative medium, negative low, negative very low} [33]. When concepts represent events and/or discrete variables, there is a threshold (0.5) that determines if the event is activated.

Experts develop the FCM model of the radiotherapy treatment procedure, that it is consisted of the 33 concepts that are described in Table I. Concepts F-C1 to F-C18 are the Factor-concepts, concepts S-C1 to S-C12 are the Selector-concepts and the concepts OUT-C1 to OUT-C3 are the Output concepts. The value of the Output-concept OUT-C1 represents the amount of dose applied to mean Clinical Target Volume (CTV), which have to be larger than the 90% of the amount of prescribed dose to the tumor. The value of concept OUT-C2 represents the amount of the surrounding healthy tissues' volume received a dose, which have to be as less as possible, less than the 5% of volume received the prescribed dose. The value of concept OUT-C3 represents the amount of Organs At Risk (OAR) volume received a dose, which have to be less than the 10% of volume received the prescribed dose. The values of Output-concepts can be acceptable or not acceptable, satisfying or not the performance criteria (according to the doctors and the corresponding protocols).

Using the development methodology for FCMs [21], the fuzzy rules for each interconnection are evaluated in parallel using fuzzy reasoning and the inferred fuzzy weights are combined and deffuzified and the result is a crisp value representing the weight of each interconnection. In this way, the weights of interconnections among Factor-concepts and Selector-concepts, Selector-concepts and Output-concepts, and Output-concepts to Output-concepts, are determined. As an example, the determination of some weights are described:

Experts describe the influence from S-C3 toward OUT-C1 representing the amount of dose to target volume using the following fuzzy rule:

IF a small change occurs in the value of $\mathrm{S{-}C3}$,
THEN a small change is caused in the value of $\mathrm{OUT{-}C1}$.

This means that if a small change occurs in the size of radiation field, then a small change in the value of dose to the target volume is caused, increasing the amount of dose. So, the influence of S-C3 to OUT-C1 is positively small.

The influence from the F-C2 toward the S-C3 representing the size of radiation field, is described as

IF a small change occurs in the value of $\mathrm{F{-}C2}$,
THEN a large change is caused in the value of $\mathrm{S{-}C3}$.

This means that the size of the tumor, determined by doctor, influences the size of radiation field. Increasing at a small amount the size of target volume, the size of radiation field increases at a larger amount, so influence of F-C2 to S-C3 is inferred as positively strong.

The influence from F-C1 toward the OUT-C2 representing the healthy tissues' volume received a prescribed dose, is described as

IF a large change occurs in the value of $\mathrm{F{-}C1}$,
THEN a very large change is caused in the value of $\mathrm{OUT{-}C2}$.

This means that the increase in depth of tumor increases very much the amount of healthy tissues' volume received the prescribed dose. Thus the influence is positively very strong.

The influence from S-C4 toward the F-C15 representing the amount of perfect match of beam to target volume-tumor, is inferred as

IF a large change occurs in the value of $\mathrm{S{-}C4}$,
THEN a very large change is caused in the value of $\mathrm{F{-}C15}$.

This means that if more field arrangements are used, the match of beam to the target volume increases at a very large amount. Thus the influence is positively very strong.

The influence from OUT-C1 toward OUT-C2, is inferred as

IF a small change occurs in the value of $\mathrm{OUT{-}C1}$,
THEN a large change is caused in $\mathrm{OUT{-}C2}$.

TABLE I
THE CONCEPTS OF THE CTST-FCM: DESCRIPTION AND TYPE OF VALUES

Concepts	Description	Type & Number of scaled values
F-C 1	Accuracy of depth of tumor	Five fuzzy
F-C 2	Size of tumor	Seven fuzzy
F-C 3	Shape of tumor	Three fuzzy (small, medium, large)
F-C 4	Location of tumor-size at cross section	Three fuzzy
F-C 5	Regional metastasis of tumor (sites of body)	Five fuzzy
F-C 6	Type of irradiated tissues-presence of inhomogeneities	Five fuzzy
F-C 7	Dose uniformity within target volume	One fixed
F-C 8	90% isodose surrounding treatment volume	One fixed
F-C 9	Skin sparing (amount of skin dose)	Three fuzzy
F-C 10	Amount of patient thickness irradiated	Five fuzzy
F-C 11	Accuracy of patient's contour (taken from CT-scans, portal films)	Five fuzzy
F-C 12	Amount of scattered radiation received by patient	Five fuzzy
F-C 13	Time required for treatment procedure or preparation	Five fuzzy
F-C 14	Cost of equipment, shielding, space	Five fuzzy
F-C 15	Perfect match of beam to target volume	Three fuzzy
F-C 16	Edge effect-amount of lateral electron scattering	Three fuzzy (low, medium, high)
F-C 17	Tumor position regarding center of contour cross section	Three fuzzy
F-C 18	Irradiation of one side of skin surface (entry points of the beam)	Three fuzzy
S-C 1	Quality of radiation; 4 machines (orthovoltage, supervoltage, megavoltage, teletherapy)	Four discrete
S-C 2	Type of radiation (photons, electrons, protons, heavy particles)	Four discrete
S-C 3	Size of radiation field	Five fuzzy
S-C 4	Single or multiple field	Two discrete
S-C 5	Beam direction(s) (orientation angles)	Continuous
S-C 6	Weight of each field (percentage of each field)	Continuous
S-C 7	Stationery vs. rotation-isocentric beam therapy	Continuous
S-C 8	Blocks (no blocks, physical blocks and multileaf-collimator shaping)	Three discrete
S-C 9	Wedge filters (no wedge, physical and dynamical wedge)	Three discrete
S-C 10	Use of compensating filter or bolus	Two discrete
S-C 11	Patient immobilization	Three discrete
S-C 12	Use of 2D or 3D conformal technique	Two discrete
Out-C 1	Dose given to treatment volume (must be within accepted limits)	Five fuzzy
Out-C 2	Amount of irradiated volume of healthy tissues	Five fuzzy
Out-C 3	Amount of irradiated volume of sensitive organs	Five fuzzy

This means that if the dose given to the tumor increases, a larger amount of healthy tissues' volume receives the prescribed dose given to the tumor. The influence of OUT-C1 to OUT-C2 is inferred as positively strong.

Analogous is the methodology of determining all the existent influences between Factor-concepts, Selector-concepts and Output-concepts.

The Clinical Treatment Simulation Tool based on FCM model (CTST-FCM) for the decision-making in radiotherapy is illustrated on Fig. 2 and it is consisted of 33 concepts and 195 interconnections with numerical weights. Initial values of concepts are taken from data set AAPM TG 23 [29] and from experimental data [28], and they are normalized and transformed in the interval [0, 1].

A. Implementation of a Clinical Treatment Simulation Tool (CTST-FCM) for Two Radiotherapy Planning Case Studies

Radical radiotherapy is commonly used to treat localized prostate cancer. In this section, we will examine two different treatment cases for prostate cancer therapy using the CTST-FCM model in order to test the validity of the model. In the first case the 3-D conformal technique consisting of six-field arrangement is suggested and in the second one the conventional four-field box technique. Radiotherapy physicians and medical physicists choose and specify the initial values of concepts and weights of the proposed CTST-FCM model, for each case.

1) Case Study 1: Conformal radiotherapy allows a smaller amount of rectum and bladder to be treated, by shaping the

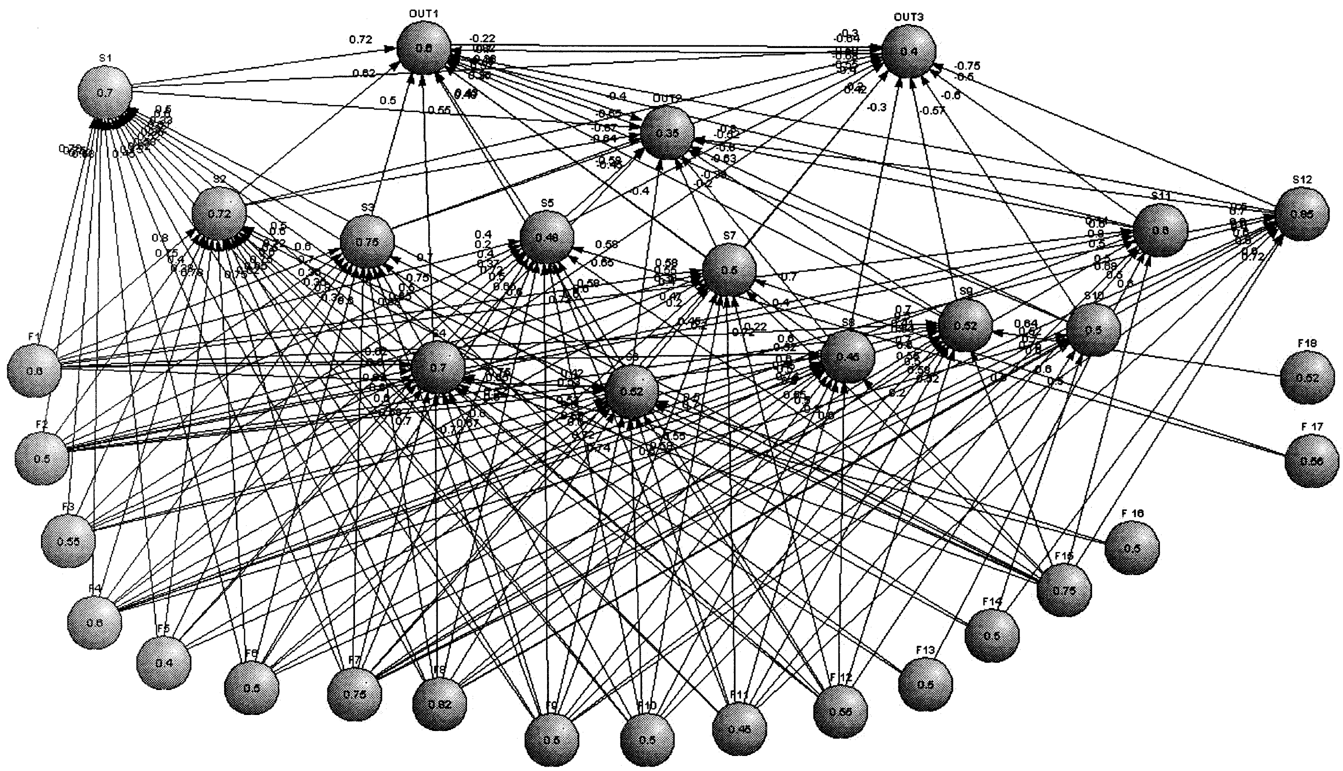

Fig. 2. The CTST-FCM model with 33 concepts and 195 interconnections.

high-dose volume to the prostate and low-dose volume to bladder and rectum, [34], [35], where the target volume is readily visualized and defined on computed tomography (CT) [36]. Radiotherapists and medical physicists select the treatment variables, such as field size, beam direction, beam weights, number of beams, compensating filters, type and quality of radiation and they determine the corresponding weights on CTST-FCM.

For this therapy technique there will be considered a six-field arrangement with gantry angles 0°, 60°, 120°, 180°, 240°, and 300°, using a 6-MV photon beam radiation. Multiple CT-based external contours define the patient anatomy and isocentric beam therapy is used. Beam weights are different for the six fields, and blocks, wedges are used. The specific characteristics of conformal therapy determine the values of concepts and weights interconnections of CTST-FCM model. So, the S-C4 takes the value of six-field number; S-C3 has the value of “small-size” for radiation field that means that the influence of S-C3 and S-C4 toward OUT-Cs is great. In the same way the S-C5 and S-C6 have great influence at OUT-Cs because different beam directions and weights of radiation beams are used. Concepts S-C8 and S-C9 take values for the selected blocks and wedges, influencing the OUT-Cs. The S-C7 takes the discrete value of isocentric beam therapy. The S-C11 takes a value for accurate patient positioning and the S-C12 takes the discrete value of 3-D radiotherapy.

So, considering the above, the initial values of concepts and weights of interconnections between S-Cs and OUT-Cs are suggested. The value of weights between S-Cs and OUT-Cs are given in Table III. Tables II and IV gather the weights of interconnections between Factor-concepts and Selector-concepts, and Output-concepts to Output-concepts, respectively.

The following initial vector is formed for this particular treatment technique:

$$\begin{aligned}\mathbf{A}_1^{\mathrm{lower-level}} \\ &= [0.66\ 0.57\ 0.54\ 0.67\ 0.51\ 0.58\ 0.75 \\ &\quad 0.75\ 0.6\ 0.56\ 0.51\ 0.67\ 0.59\ 0.68 \\ &\quad 0.85\ 0.55\ 0.56\ 0.62\ 0.72\ 0.65\ 0.4\ 0.65 \\ &\quad 0.7\ 0.45\ 0.6\ 0.6\ 0.5\ 0.4\ 0.65\ 0.75\ 0.45\ 0.53\ 0.45],\end{aligned}$$

where A_i is the value of concept C_i.

When the initial values of concepts have assigned, CTST-FCM starts to interact and simulates the radiation procedure. Equation (1) calculates the new values of concepts after each simulation step and Fig. 3 illustrates the values of concepts for eight simulation steps, where is concluded that after the 5th simulation step FCM reaches an equilibrium region, outlined with the following values of OUT-Cs: for OUT-C1 is 0.98, for OUT-C2 is 0.01 and for OUT-C3 is 0.04.

Based on the referred performance criteria in Section IV, the calculated values of output concepts are accepted. The calculated value of OUT-C1 is 0.98, which means that the CTV receives the 98% of the amount of the prescribed dose, which is accepted. The value of OUT-C2 that represents the amount of the surrounding healthy tissues’ volume received a dose is found equal to 0.01, so the 1% of the volume of healthy tissues receives the prescribed dose of 81 Gy. The value of OUT-C3 that

TABLE II
THE WEIGHTS OF THE INTERCONNECTIONS AMONG FACTOR-CONCEPTS AND SELECTOR-CONCEPTS

Factors/ Selectors	S-C1	S-C2	S-C3	S-C4	S-C5	S-C6	S-C7	S-C8	S-C9	S-C10	S-C11	S-C12
F-C1	0.78	0.8	0.6	0.62	0.4	0.42	0.58	0.6	0.7	0	0.2	0
F-C2	0.75	0.75	0.7	0.6	0.2	0.53	0.55	0.52	0.5	0	0.6	0.5
F-C3	0.42	0.4	0.6	0.63	0.4	0	0.38	0	0.41	0	0	0.7
F-C4	0.68	0.38	0.36	0.6	0.37	0.52	0.4	0.6	0.54	0.52	0.8	0
F-C5	0.45	0.78	0.8	0.6	0.72	0.6	0	0.45	0	0	0	0
F-C6	0.75	0.75	0.32	0.58	0.5	0.55	0.47	0.5	0	0	0	0.6
F-C7	0.62	0.62	0.6	0.7	0.65	0.6	0.2	0.74	0.7	0.7	0.5	0.4
F-C8	0.58	0.65	0.68	0.72	0.6	0.72	0	0.6	0.6	0.75	0	0.4
F-C9	0.52	0.75	0.65	0.67	0.72	0.74	0.45	0.55	0.55	0.6	0	0.6
F-C10	0.35	0.6	0.5	0.6	0.6	0.6	0.2	0.5	0.5	0	0.5	0
F-C11	0.22	0.5	0	0	0.6	0.58	0.72	0.3	0.58	0	0.68	0.6
F-C12	0.61	0.72	0.75	0.6	0.58	0.55	0.22	0.6	0.52	0.6	0	0
F-C13	0.33	0	0	0.52	0	0	0	0	0	0	0.5	0
F-C14	0.60	0.60	0	0	0	0	0	0	0	0.5	0	0.6
F-C15	0.50	0.50	0.7	0.65	0.65	0.7	0.4	0.2	0.5	0	0.6	0.72
F-C16	0	0	0	0.75	0	0.5	0	0	0	0	0	0
F-C17	0	0	0	0	0.58	0	0.7	0	0	0	0	0
F-C18	0	0	0	0	0	0	0	0	0.64	0	0	0

TABLE III
THE WEIGHTS REPRESENTING RELATIONSHIPS AMONG SELECTOR-CONCEPTS AND OUTPUT-CONCEPTS FOR FIRST CASE STUDY

Selectors	OUT-C1	OUT-C2	OUT-C3
S-C1	0.52	-0.45	-0.44
S-C2	0.50	-0.57	-0.48
S-C3	0.45	-0.45	-0.4
S-C4	0.33	-0.58	-0.55
S-C5	0.38	-0.40	-0.38
S-C6	0.45	-0.42	-0.4
S-C7	0.30	-0.30	-0.30
S-C8	0,42	-0.48	-0.45
S-C9	0.45	-0.42	-0.40
S-C10	0.25	-0.23	-0.24
S-C11	0.43	-0.48	-0.45
S-C12	0.62	-0.52	-0.48

TABLE IV
THE WEIGHTS OF THE INTERCONNECTIONS AMONG OUTPUT-CONCEPTS

OUTPUTS	OUT-C1	OUT-C2	OUT-C3
OUT-C1	0	0.61	0.65
OUT-C2	-0.68	0	0
OUT-C3	-0.63	0	0

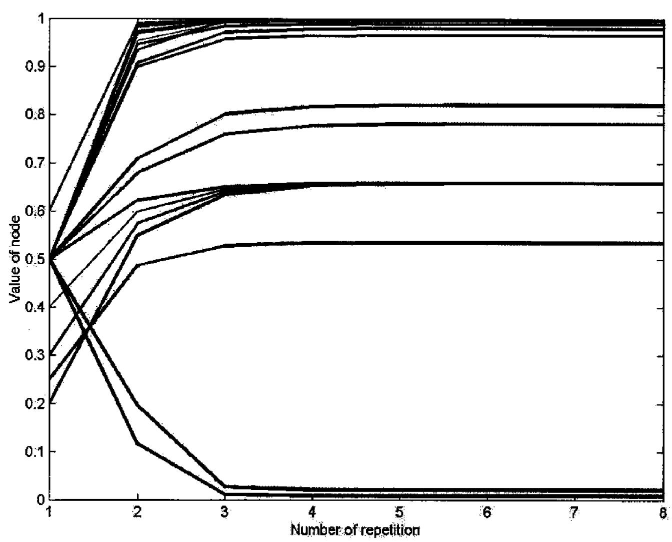

Fig. 3. Variation of values of 33 concepts for the CTST-FCM for the CTST-FCM for the first case for eight simulation steps.

represents the amount of the critical organ's volume (bladder and rectum) is equal to 0.04, which means that the 4% of the volume receives the prescribed dose of 81 Gy, which is accepted because a volume less than the 10% of volume of organs at risk is accepted to receive a prescribed dose 81 Gy.

After this discussion it is obvious that the CTST-FCM model, with the initial values of treatment variables and their interconnections that radiotherapists and medical physicists proposed for the specific technique of prostate cancer, reach a set of values that satisfy the performance criteria. So, according to the CTST-FCM model for this technique, the treatment could be executed with acceptable results.

2) Case Study 2: In the second case study, the conventional four-field box technique is implemented for the prostate cancer treatment. This technique is consisted of a four-field box arrangement with gantry angles 0°, 90°, 180°, and 270°. A single external contour defines the patient anatomy and isocentric beam therapy is used. Beam weights have the same value for four fields and no blocks, wedges, collimator settings, and compensating filters are used. For this case, the CTST-FCM has to be reconstructed that means that radiotherapists [34] have to reassign weights and interconnections because a different treatment technique is used. Data from AAPM TG 23 and experiments [28], [29] determine the treatment variables and their interrelationships and so modifying the CTST-FCM model. For this case, the Selector-concept S-C4 has the value of four-field number; S-C3 has the value of "large-size" of radiation field, which means that the influence of S-C3 and S-C4 toward OUT-Cs is very low. In the same way the S-C5 and S-C6 have lower influence on OUT-Cs because different beam

TABLE V
THE SELECTOR-CONCEPTS-OUTPUT-CONCEPTS WEIGHTS FOR THE SECOND RADIOTHERAPY CASE STUDY

Selectors	OUT-C1	OUT-C2	OUT-C3
S-C1	0.52	-0.45	-0.44
S-C2	0.50	-0.57	-0.48
S-C3	0.27	-0.23	-0.19
S-C4	0.24	-0.42	-0.38
S-C5	0.22	0.25	0.23
S-C6	0.25	0.22	0.20
S-C7	0.30	0.30	0.30
S-C8	0	0	0
S-C9	0	0	0
S-C10	0.25	-0.23	0.24
S-C11	0.28	-0.30	-0.27
S-C12	0.20	-0.25	-0.20

directions and weights of radiation beams are used. S-C8 and S-C9 have zero influence on OUT-Cs because no blocks and no wedges are selected for this treatment case. The S-C7 takes the discrete value of isocentric beam therapy and has the same influence on OUT-Cs as the above conformal treatment case. The S-C11 takes a low value for no accurate patient positioning and the S-C12 takes the discrete value of 2-D radiotherapy.

The weights between S-Cs and OUT-Cs for this case are given in Table V. If we compare Table V with Table III that gathers the weights for the first case, we will see that some interconnections have different values.

Using this new CTST-FCM model, with the new modified weight matrix, the simulation of the radiotherapy procedure for this case starts with the following initial values of concepts:

$$\begin{aligned}\mathbf{A}_2^{\text{lower-level}} = [&0.53\ 0.48\ 0.43\ 0.57\ 0.39\ 0.58\ 0.75\ 0.75\\ &0.52\ 0.48\ 0.41\ 0.5\ 0.45\ 0.61\ 0.72\ 0.59\\ &0.54\ 0.48\ 0.72\ 0.65\ 0.7\ 0.45\ 0.4\ 0.6\ 0.62\\ &0.3\ 0.2\ 0.4\ 0.42\ 0.3\ 0.42\ 0.35\ 0.54].\end{aligned}$$

The values of 33 concepts are calculated using (1) and the variation of their values after eight simulation steps are illustrated in Fig. 4. This shows that the FCM interacts and reaches an equilibrium region, where the final values of OUT-Cs are as follows: for OUT-C1, 0.97; for OUT-C2, 0.06; and for OUT-C3, 0.15. The calculated value of concept OUT-C1 is within the desired limits but the values of concept OUT-C2 and concept OUT-C3 are not accepted. The value of OUT-C2 is equal to 0.06, which means that the 6% of the volume of healthy tissues receives a prescribed dose of 81 Gy. The calculated value of OUT-C3 describes that the 15% of volume of organs at risk receives an amount of the prescribed dose. These values for OUT-C2 and OUT-C3 are not accepted according to related protocols [35].

If these suggested values for Output-concepts were adopted, the patient would receive a larger amount of dose than the desired one on the normal tissues and sensitive organs. So, it is important to examine all the factors and selectors and their cause and effect toward the Output-concepts and suggest new treatment variable values changing the planning procedure.

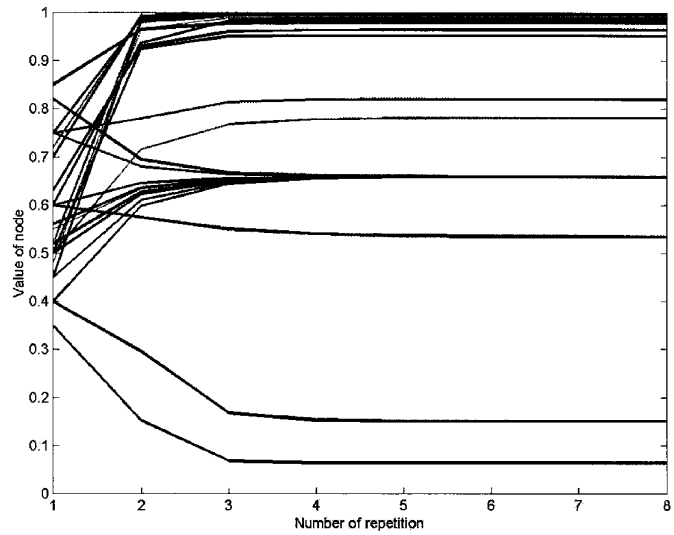

Fig. 4. Variation of values of 33 concepts of CTST-FCM for the second example, with the classical treatment planning case for eight simulation steps.

3) Discussion of Case Studies: During the treatment planning procedure some treatment parameters have great influence to the treatment execution and to the determination of the final dose that is actually received by the target volume and the patient. On the CTST-FCM model standard treatment techniques are suggested which can be implemented in clinical practice, and the outcome advise the radiotherapists if this treatment planning technique is acceptable or not for the specific case.

For complex treatment planning problems where the surrounding normal tissues and organs at risk, place severe constrains on the prescription dose as in the case of prostate cancer, CTST-FCM model provides an efficient tool for decision making, treatment variables determination and acceptance of a treatment technique.

However, in practice, the patient receives a different amount of dose than that determined from the treatment planning, due to the presence of some other factors, more general, as machine factors and human factors, that are involved in the treatment execution [37]. Also, some of the existent factors referred on the CTST-FCM model, such as tumor localization and patient positioning change their values easily and it is necessary to take them into consideration during the final decision-making process, with a more generic mode for all the patient cases. Thus, there is a need to determine a concept, named "Final Dose" (FD), affected by the previous referred parameters and the OUT-Cs, describing the final decision-making. The concept of "Final Dose" is an extremely important concept describing the success of radiation treatment and so the prolongation of patient's life. The purpose of our approach is not the accuracy of calculated amount of FD received by the patient, but to describe the success of radiation therapy process in general, examining the value of FD.

V. THE HIERARCHICAL STRUCTURE

The CTST-FCM model for the radiotherapy treatment planning process could be enhanced if an upper-level is considered for supervising the radiation therapy process, creating an

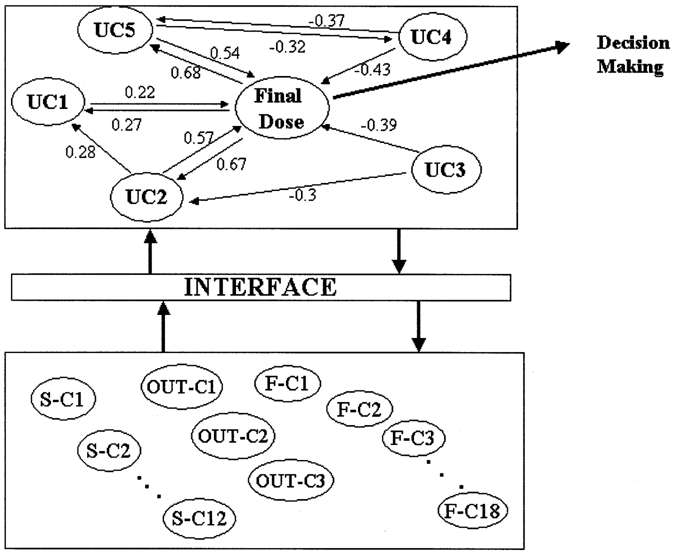

Fig. 5. The integrated two-level hierarchical structure for decision-making in radiation therapy.

integrated hierarchical structure model, which is illustrated on Fig. 5. In the lower-level of the structure, there is the CTST-FCM model of 33 concepts that models the treatment planning and calculates the dose to the target volume, normal tissues and organs at risk. In the upper-level, a Supervisor-FCM model, consisting of six concepts, is used for the parameters analysis and the final acceptance or not of the treatment therapy for the specific treatment technique. The Supervisor-FCM handles important information from concepts of the CTST-FCM model for the description and determination of the specific treatment outcome and evaluates the whole process. Some of the treatment parameters represented by the Selector-concepts such as tumor localization based on CT-scans or portal films, patient positioning and immobilization; and the concepts of treatment dose to target volume, normal tissues and critical organs, are crucial factors for the treatment execution and they influence the Supervisor-FCM. The three parameters referred as Output-concepts on the CTST-FCM contribute a lot to the "Final Dose" and to the successful of treatment process.

The proposed Supervisor-FCM model is developed utilizing the expert's knowledge, which actually supervise and take decisions for the radiation therapy process using the notion and values of tumor localization, patient positioning and the calculated dose from the treatment planning system in order to determine the Final Dose [38]. Also, experts suggest that human factors and machine factors take part in the determination of the "Final Dose" [37].

According to experts the Supervisor-FCM is consisted of the following concepts:

UC_1) *Tumor Localization*. It is dependent on patient contour, sensitive critical organs, and tumor volume. It embodies the value and influence of these three Factor-concepts of CTST-FCM model.

UC_2) *Dose prescribed from Treatment Planning*. This concept describes the prescribed dose and is depending on OUT-C1, OUT-C2, and OUT-C3 concepts of CTST-FCM model.

UC_3) *Machine factors*. This concept describes the equipment characteristics, maintenance etc.

UC_4) *Human factors*. A concept describing the experience and training level of medical staff

UC_5) *Patient positioning and immobilization*. This concept describes the cooperation of the patient with the doctors and following instructions.

UC_6) *Final Dose given to the target volume*. A measurement of the radiation dose received by the target tumor.

Using the same methodology that was presented in Section II, the Supervisor-FCM is developed. Experts used the data from AAPM test packages and experimental data from Radiation Therapy Oncology Group [35] to describe the relationships among concepts. The connections among the concepts of Supervisor-FCM are described in Table VI, then the linguistic variables of weights are defuzzified and transformed in numerical values and the following weight matrix for the Supervisor-FCM is produced:

$$W^{\text{upper-level}} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0.43 \\ 0.28 & 0 & 0 & 0 & 0 & 0.57 \\ 0 & -0.3 & 0 & 0 & 0 & -0.39 \\ 0 & 0 & 0 & 0 & -0.32 & -0.43 \\ 0 & 0 & 0 & -0.37 & 0 & 0.68 \\ 0.22 & 0.67 & 0 & 0 & 0.54 & 0 \end{bmatrix}.$$

The objective of the Supervisor-FCM is to keep the amount of concept "Final Dose," which is delivered to the patient, between some limits, an upper limit $\mathrm{FD}_{\max}$ and a low limit $\mathrm{FD}_{\min}$. Another objective is to keep the "Dose from Treatment Planning" between a maximum value $\mathrm{D}_{\max}$ and a minimum value $\mathrm{D}_{\min}$. These objectives are defined by the related ICRU protocols that describe the accepted dose levels for each organ and region of human body [39]. The Supervisor-FCM evaluates the success or failure of the treatment estimating the value of the "Final Dose" concept. So, the objective for the Supervisor-FCM is to keep the values of corresponding concepts for "Final Dose" and "Dose from Treatment Planning" in the range of values:

- $\mathrm{FD}_{\min} \le \mathrm{FD} \le \mathrm{FD}_{\max}$;
- $\mathrm{D}_{\min} \le \mathrm{D} \le \mathrm{D}_{\max}$.

The Supervisor-FCM model is, a generic decision support model that can be implemented in all clinical treatment cases. However, the CTST-FCM model is used for standard treatment techniques in clinical practice, and using the Supervisor-FCM, a fast and accurate suggestion can be derived, which will help the radiotherapist-doctor to decide if the technique could be implemented or not. When the result is undesirable or unacceptable, we return on the lower-level through an interface, where a procedure takes place suggesting new treatment variables and interconnections among them, changing the values of concepts and weights. This procedure can be either the selection of another treatment technique or modification of the used one. Then, through the interface, we return on the upper-level where the "Final Dose" is calculated and this iterative process is following till the result is acceptable.

The proposed integrating two-level hierarchical structure is used to model the complex radiotherapy process. The decision maker evaluates the value of the "Final Dose" given to the target

TABLE VI
CONNECTIONS AMONG THE CONCEPTS OF SUPERVISOR-FCM

Linkage	Direction of Influence	Description
L_1	UC1 to UC6	Medium influence from Tumor Localization towards Final Dose
L_2	UC2 to UC1	Small influence from Dose of treatment planning towards tumor localization
L_3	UC2 to UC6	High influence from dose of treatment planning towards Final Dose
L_4	UC3 to UC2	Negative small influence from machine parameters towards the Dose of treatment planning
L_5	UC3 to UC6	Negative medium influence from machine parameters towards Final Dose
L_6	UC4 to UC6	Negative medium influence from human factors towards the Final Dose
L_7	UC4 to UC5	Negative small influence from human factors towards the patient positioning
L_8	UC5 to UC4	Negative medium influence from patient positioning towards human factors
L_9	UC5 to UC6	High influence from patient positioning towards the Final Dose
L_{10}	UC6 to UC5	Medium influence from Final Dose towards patient positioning
L_{11}	UC6 to UC1	Small influence from Final Dose towards the Tumor Localization
L_{12}	UC6 to UC2	High influence from Final Dose towards the Dose of treatment planning

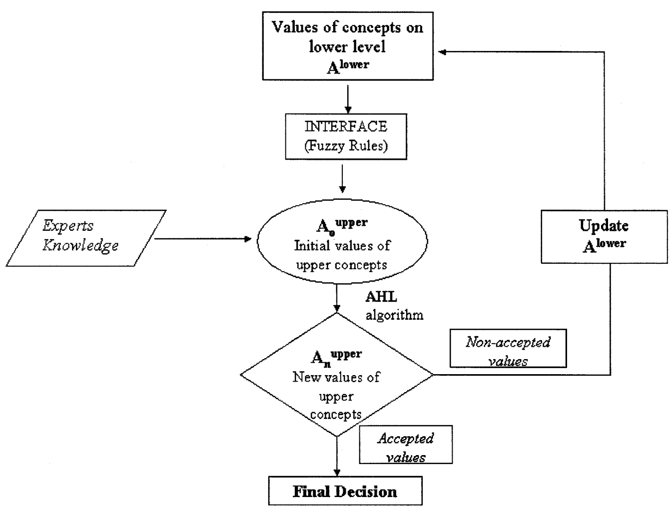

Fig. 6. The flowchart of the algorithm for supervision execution and interaction between the two levels of decision support.

volume, and in the case of unacceptable value of "Final Dose," some concepts on the CTST-FCM model are influenced through the interface, so they take new values that cause the CTST-FCM model to interact. When the lower-level CTST-FCM reaches an equilibrium region information pass to the supervisor-FCM, which decides if the new calculated value of "Final Dose" is accepted or not. The flowchart of this procedure is depicted on Fig. 6.

The interface transmits information from the CTST-FCM on the lower-level to the Supervisor-FCM on the upper-level and vice versa. This interface is consisted of two parts, one part transmit information from lower to upper and the other part from upper to lower. Generally, the information from two or more concepts on the CTST-FCM model are aggregated and through the interface influence one concept in the Supervisor-FCM, and an analogous interface exists for the inverse transmission of information. For example, information from the machine parameters concepts at CTST-FCM model (Selector-concepts S-C7, S-C9, S-C10) pass through the interface and influence the concept of UC3 "machine factors" at Supervisor-FCM. Also, information from the Output-concepts (OUT-C1, OUT-C2, OUT-C3) influences the UC2 "Dose from Treatment Planning."

The interface is a set of fuzzy rules. The influences between values of concepts from one level to the other are representing using the IF-THEN rules that are embedded into the interface. The fuzzy rules have as input the values of concepts from the CTST-FCM model at lower-level and infer the value of concepts on the Supervisor-FCM.

We have tested and proposed the following fuzzy rules that describe the part of the interface from lower-level toward the upper-level.

- **IF** value of OUT-C1 is very high **AND** values of (OUT-C2 **AND** OUT-C3) are very low, **THEN** value of UC2 is very high.
- **IF** value of OUT-C1 is the highest **AND** values of (OUT-C2 **AND** OUT-C3) are the lowest, **THEN** value of UC2 is highest.
- **IF** value of OUT-C1 is high **AND** values of (OUT-C2 OR OUT-C3) are low, **THEN** value of UC2 is high.
- **IF** value of OUT-C1 is very high **AND** values of (OUT-C2 OR OUT-C3) are low, **THEN** value of UC2 is high.
- **IF** value of S-C3 is very low **AND** values of (S-C7 **AND** S-C9 **AND** S-C10) are very high, **THEN** value of UC3 is high.
- **IF** value of S-C3 is very low **AND** values of (S-C7 **AND** S-C9 and S-C10) are the highest, **THEN** value of UC3 is very high.

- **IF** value of S-C3 is very low **AND** values of (S-C7 OR S-C9 OR S-C10) are very high, **THEN** value of UC3 is high.
- **IF** value of S-C3 is medium **AND** values of (S-C7 OR S-C9 OR S-C10) are medium, **THEN** value of UC3 is medium.
- **IF** value of S-C11 is very high, **THEN** value of concept UC5 is very high.
- **IF** value of S-C11 is highest, **THEN** value of concept UC5 is highest.

In the same way, with a corresponding set of fuzzy rules the interface from the upper-level toward the lower-level is developed describing analogous influences from the concepts of Supervisor-FCM toward the Selector-concepts of the CTST-FCM.

A. Simulation to Estimate the Successful or Not of the Radiation Therapy Treatment Case—First Example

The initial values of concepts on Supervisor-FCM are determined by the values of concepts of lower-level CTST-FCM model, through the above-described interface, and the user determines the external inputs of the values of concepts referred as UC5 "human factors" and UC1 "Tumor localization."

The CTST-FCM that was presented at Section IV for the first test case is the lower-level FCM. As was presented this FCM after the simulation had reached an equilibrium region and the values of Factor-concepts, Selector-concepts, and Output-concepts could be used for the desired treatment planning and calculation of dose on the target volume, normal tissues, and sensitive organs. These values are inputs to the fuzzy rules consisting the interface and so they determine the initial values of concepts on Supervisor-FCM that are given in the following matrix:

$$\mathbf{A}_1^0 = [0.76\ 0.84\ 0.66\ 0.57\ 0.73\ 0.81]$$

For these values of concepts, the Supervisor-FCM with the initial weights $\mathbf{W}^{\text{upper}-\text{level}}$ is able to examine if they are within the accepted limits for the radiotherapy execution. The Supervisor-FCM is updating by the implementation of AHL rule that is described in Appendix A and the (A.3) is used to modify the weights of Supervisor-FCM, and (1) is used to calculate the values of concepts after each simulation step. After 43 simulation steps, the Supervisor-FCM reaches an equilibrium region, where the resultant values of concepts are

$$\mathbf{A}_1^{\text{upper}-\text{level}} = [0.91\ 0.84\ 0.94\ 0.50\ 0.85\ 0.90]$$

and the new weight matrix derived after training using the AHL algorithm is

$$\mathbf{W}_{\text{firstcase}}^{\text{supervisor}} = \begin{bmatrix} 0 & 0.12 & 0.47 & 0.10 & 0.12 & 0.45 \\ 0.75 & 0 & 0.45 & 0.09 & 0.11 & 0.55 \\ 0.13 & -0.24 & 0 & 0.09 & 0.12 & -0.17 \\ 0.08 & 0.07 & 0.33 & 0 & -0.38 & -0.25 \\ 0.12 & 0.11 & 0.44 & -0.98 & 0 & 0.62 \\ 0.62 & 0.95 & 0.50 & 0.09 & 0.89 & 0 \end{bmatrix}$$

The AHL algorithm assumes that there is a time relationship in the changes of concepts values. When the value of one-concept changes, in the next time unit the value of another one concept changes based on the influence of the first one, and this is referred to as a simulation time step.

Protocols and experimental data prescript the final dose to patient for every treatment case. This information is used to check out our model. For this first example the calculated value of UC6 "Final Dose" is 0.90, which is an acceptable value according to the ICRU protocol [38]. Thus, radiotherapists can follow the suggested values and the treatment will be executed with successful results.

B. Second Case

In this subsection, it will be considered the second test case of prostate cancer, presented at Section IV, where the CTST-FCM on the lower-level reach the equilibrium region and through the interface the following initial concept values for the Supervisor-FCM is produced:

$$\mathbf{A}_2^0 = [0.40\ 0.67\ 0.20\ 0.25\ 0.32\ 0.35].$$

The AHL algorithm is applied to the Supervisor-FCM, so (A.3) is used to calculate the values of weights and (1) calculates the values of concepts after each simulation step. The simulation starts and after 49 simulation steps the Supervisor-FCM reaches an equilibrium region where the values of concepts are

$$\mathbf{A}_2^{\text{upper}-\text{level}} = [0.90\ 0.81\ 0.93\ 0.47\ 0.83\ 0.86].$$

and the produced weight matrix of Supervisor-FCM is

$$\mathbf{W}_{\text{secondcase}}^{\text{supervisor}} = \begin{bmatrix} 0 & 0.10 & 0.52 & 0.07 & 0.08 & 0.43 \\ 0.77 & 0 & 0.53 & 0.06 & 0.07 & 0.54 \\ 0.10 & -0.29 & 0 & 0.06 & 0.08 & -0.23 \\ 0.06 & 0.05 & 0.30 & 0 & -0.43 & -0.30 \\ 0.09 & 0.07 & 0.40 & -0.99 & 0 & 0.61 \\ 0.61 & 0.94 & 0.42 & 0.05 & 0.89 & 0 \end{bmatrix}$$

The value of UC6 "Final Dose" is 0.86 that is out of range of the desired-accepted value for execution dose [38]. Thus, the value of concept "Final Dose" is not accepted and the radiotherapy would not have the expected results. The supervision execution procedure as is depicted on Fig. 6, suggests updating the values of concepts on the lower-level FCM and changing the values of Factor-concepts. In order to update the values of concepts at lower-level, we follow the upper-lower interface and we influence the values of the most important Factor-concepts and Selector-concepts according to the fuzzy rules. So, new values are assigned to size of radiation field (S-C3), beam direction (S-C5), weight of each field (S-C6), patient immobilization (S-C9), perfect match of beam to the target volume (F-C15). These values along with the rest of the values of $\mathbf{A}_2^{\text{lower}-\text{level}}$ for the second case study are resulting in producing the following values for the concept of lower-level

$$\mathbf{A}_{21}^{\text{lower}-\text{level}} = [0.53\ 0.48\ 0.43\ 0.57\ 0.39\ 0.58\ 0.75\ 0.75\ 0.52\ 0.48\ 0.41\ 0.5\ 0.45\ 0.61\ 0.83\ 0.59\ 0.54\ 0.48\ 0.72\ 0.65\ 0.7\ 0.45\ 0.63\ 0.72\ 0.6\ 0.3\ 0.55\ 0.4\ 0.4\ 0.3\ 0.42\ 0.35\ 0.54].$$

The CTST-FCM with the values $\mathbf{A}_{21}^{\text{lower}-\text{level}}$ interacts and new values for the 33 concepts are calculated according to the (1) and the new calculated values for Output-concepts are:

OUT-C1 is 0.98, OUT-C2 is 0.03, and OUT-C3 is 0.07. These calculated values of Output-concepts are within the accepted limits for the CTST-FCM model. So, these new updated values of concepts from CTST-FCM model influence again through the interface the upper level concepts of Supervisor-FCM, determining the new concept values

$$\mathbf{A}_{21}^{\text{upper}-\text{level}} = [0.87\ 0.81\ 0.93\ 0.47\ 0.85\ 0.86].$$

Then, implementing the AHL algorithm for the Supervisor-FCM, the following values of concepts on upper-level are calculated:

$$\mathbf{A}^{\text{upper}-\text{level}} = [0.92\ 0.84\ 0.94\ 0.48\ 0.85\ 0.91].$$

The value of concept UC6, 0.91, is accepted for the treatment execution. If the calculated "Final Dose" was not accepted, then the above procedure could continue until the calculated value of concept "Final Dose" would be accepted. In this way, the supervisor-FCM models and supervises the treatment for prostate cancer therapy with external beam radiation and more generally the whole procedure.

VI. Overall Discussion of Results

The proposed two-level decision model for radiation treatment procedure takes under consideration an extremely large number of factors that are evaluated with the use of FCMs. This dynamic decision-making model for the radiotherapy treatment process uses the experts' knowledge and follows a reasoning similar to the one doctors adopt while deciding on a treatment plan.

The proposed CTST-FCM model is evaluated for different treatment cases but it arises the need for an abstract model that will supervise it. An integrated two-level hierarchical structure is proposed, that uses two-level FCMs to evaluate the radiotherapy planning procedure. The Supervisor-FCM stands as a second level control for prediction, decision analysis, and determination of the "Final Dose." Supervisor-FCM model is improved and becoming more generic with the implementation of the AHL algorithm that adjusts the weights and ensures the success of the treatment therapy procedure.

In this stage the research work was focused on the study of knowledge representation and on the development of a two level hierarchical model based on FCMs. The following have been achieved:

- Development of a radiotherapy-planning model, the CTST-FCM model on the lower-level.
- Validation of the Clinical Treatment Simulation Tool (CTST-FCM) for two cases.
- Development of an abstract generic model to supervise the process that was enhanced with learning methods to have better convergence results.
- Description of an interface to transform information between the levels of hierarchy.
- Proposing an algorithm to describe the flow and exchange of information within the integrated hierarchical system.

Using the FCM-methodology at lower-level we are able to model the process of treatment planning, adjusting the treatment variables and calculating the corresponding dose to the target volumes, organs at risk and normal tissues. Using the same methodology at upper-level we are able to supervise the whole procedure of radiation therapy, adjusting the interconnections between the generic treatment variables of upper-level and calculating the "Final Dose."

We believe that this modeling method based on FCMs helps the radiotherapist to simulate the treatment procedure, decide if the treatment execution will or not be successful, keeping the prescribed dose between the accepted limits. This decision-making system was developed to improve planning efficiency and consistency for treatment cases, selecting the related factors and treatment variables, and describing and determining the causal relationships among them.

Unlike most optimization methods are used to solve complex treatment planning problems; the proposed FCM approach is not intended to generate novel plan designs in terms of beam ballistics (directions, apertures, weights, and wedges) or intensity modulation, but rather to create a simulation tool to help physicians and medical physicists to select the treatment variables, to save time determining the treatment technique and make decisions before the treatment execution. Calculating dose distributions, making optimization on treatment technique and scheduling treatment therapy is beyond the scope of our research at this point, these optimization methods are used in mathematical models such as the gradient descent or MOGA or Pareto cost functions. The primary purpose for using the FCM approach is to develop a clinical treatment simulation tool for decision-making in radiotherapy, which will facilitate the iterative process used by medical physicists and radiotherapists off-line. In the future more concepts [40] and optimization cost functions could be considered in developing further the Supervisor-FCM.

VII. Conclusions and Future Directions

The most common approaches used today for optimization of treatment variables and the methods for optimizing complex beam arrangements or intensity-modulated beam shaping have appeared to have limited clinical applicability, due in part to practical constrains on the number of beams, orientation of beams collimator settings, wedge angles, based on the construction and function of treatment machines and in part to the computational time required to obtain an optimized plan. A major problem is the complexity of the decision-making process for Radiotherapy and the fact that many fuzzy factors must be taken under consideration that make it too complicated to be modeled precisely. Here a two-level hierarchical structure based on the soft computing modeling technique of FCMs was proposed, that is implemented in the decision making process for Radiotherapy.

The proposed structure is easily implemented in clinical practice and provides a fast, accurate, reliable, and flexible tool for decision-making in radiotherapy procedure. The test cases that were investigated proved the feasibility and validity of the model giving very promising results. At present, the system is not used clinically, but it has been tested with clinical data, with similar and/or either better result than the usual treatment practice reported on the medical literature.

Future direction of this research effort could include:

- further improvement of the Supervisor-FCM model;
- investigation of the optimization methods of soft computing techniques in order to eliminate the present limitation of the proposed method as mentioned earlier;
- running simulations with new clinical data;
- validation of the proposed CTST-FCM tool under real-time medical radiotherapy treatment;
- sensitivity analysis.

APPENDIX

The AHL algorithm introduces the asynchronous updating for the weights of FCM and the calculation of the desired values of concepts. The asynchronous mode suggests that for each time step, during the simulation run there is only one activation concept at the FCM. The new value of the activation concept acts as a trigger, which causes updating of the weights of the connections between the activation concept and the others. It should be noticed here that experts initially choose the activation concept for every time step, according to the infrastructure of the fuzzy cognitive map. So, experts who determine the most important factors-concepts that affect the desired value of concept define the sequence of activation steps between concepts.

The AHL adjust the weights between interconnections using the following discrete type of asynchronous mode:

$$w_{ij}(t+1) = a \cdot w_{ij}(t) + \eta(t) \cdot A_i^{\text{act}}(t) \cdot A_j(t). \qquad \text{(A.1)}$$

Here, it is supposed that concept C_i with value A_i is the activation concept. $A_i^{\text{act}}(t)$ is the value of the activation concept C_i on the iteration t and $A_j(t)$ is the value of interconnected concept at the same iteration. The coefficients a and $\eta(t)$ take positive values, $0 < a < 1$ and $0 < \eta(t) < 1$, and it is also supposed that $a > \eta(t)$.

According to the established procedure of constructing FCM [21], initially experts draw the FCM and suggest the weights w_{ij}. It is desirable to keep in mind their suggestions. Thus the coefficient a is suggested to take values near to one but it never becomes equal to it. Coefficient $\eta(t)$ is the learning rate coefficient that affects concepts at any iteration t and determines the modification of the values of weights. After some iterations, it is desirable to eliminate the influence of A_i^{act} on $w_{ij}(t+1)$, so it is proposed that the coefficient $\eta(t)$ decreases exponentially and finally, after a number of iterations, takes very small value. The learning rate coefficient is expressed as

$$\eta(t) = k \cdot \exp(-\lambda \cdot t) \qquad \text{(A.2)}$$

where k is a constant coefficient with value 0.02 that has been proven to be the best choice after many simulation experiments [23]. The parameter λ is chosen so that the value of $\eta(t)$ to decrease slowly with no sharply attenuation for the first 20 steps. The suggested value of λ is between 0.1–0.2 and here the used one is 0.1 [23].

Thus, the AHL rule of (A.1) with substitute of (A.2) is transformed in the following equation that calculates the new value of weight w_{ij} at iteration $t+1$:

$$w_{ij}(t+1) = a \cdot w_{ij}(t) + 0.02 \cdot \exp(-0.1 \cdot t) \cdot A_i^{\text{act}}(t) \cdot A_j(t). \qquad \text{(A.3)}$$

ACKNOWLEDGMENT

The authors would like to thank A. Lotsari-Groumpos, University of Patras, for her helpful suggestions in English grammar and language.

REFERENCES

[1] F. Khan, *The Physics of Radiation Therapy*, 2nd ed. Baltimore, MD: Williams & Wilkins, 1994.
[2] A. Brahme, "Optimization of radiation therapy and the development of multileaf collimation," *Int. J. Radiat. Oncol., Biol. Phys.*, vol. 25, no. 2, pp. 373–375, 1993.
[3] ——, "Optimization of radiation therapy," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 28, pp. 785–787, 1994.
[4] J. P. Gibbons, D. N. Mihailidis, and H. A. Alkhatib, "A novel method for treatment plan optimization," *Proc. 22nd Annu. Int. Conf. IEEE EMBS*, vol. 4, pp. 3093–3095, July 2000.
[5] G. S. Mageras and R. Mohan, "Application of fast simulated annealing to optimization of conformal radiation treatments," *Med. Phys.*, vol. 20, pp. 447–639, 1993.
[6] G. Starkschall, A. Pollack, and C. W. Stevens, "Treatment planning using dose-volume feasibility search algorithm," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 49, pp. 1419–1427, 2001.
[7] A. Brahme, "Treatment optimization using physical and biological objective functions," in *Radiation Therapy Physics*, A. Smith, Ed. Berlin, Germany: Springer-Verlag, 1995, pp. 209–246.
[8] C. G. Rowbottom *et al.*, "Simultaneous optimization of beam orientations and beam weights in conformal radiotherapy," *Med. Phys.*, vol. 28, p. 1696, 2001.
[9] S. Soderstrom, "Radiobiologically Based Optimization of External Beam Radiotherapy Techniques Using a Small Number of Fields," masters thesis, Stockholm Univ., Stockholm, Sweden, 1995.
[10] G. Kutcher and C. Burman, "Calculation of complication probability factors for nonuniform normal tissue irradiation: The effective volume method," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 16, pp. 1623–1630, 1989.
[11] L. J. Beard, M. van den Brink, A. M. Bruce, T. Shouman, L. Gras, A. te Velde, and J. V. Lebesque, "Estimation of the incidence of late bladder and rectum complications after high-dose (70–78 Gy) conformal radiotherapy for prostate cancer, using dose-volume histograms," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 41, pp. 83–99, 1998.
[12] T. Willoughby, G. Starkschall, N. Janjan, and I. Rosen, "Evaluation and scoring of radiotherapy treatment plans using an artificial neural network," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 34, no. 4, pp. 923–930, 1996.
[13] D. Wells and J. Niederer, "A medical expert system approach using artificial neural networks for standardized treatment planning," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 41, no. 1, pp. 173–182, 1998.
[14] C. D. Stylios and P. P. Groumpos, "Fuzzy cognitive maps in modeling supervisory control systems," *J. Intell. Fuzzy Syst.*, vol. 8, pp. 83–98, 2000.
[15] B. Kosko, *Neural Networks and Fuzzy Systems*. Englewood Cliffs, NJ: Prentice-Hall, 1992.
[16] ——, "Fuzzy cognitive maps," *Int. J. Man-Machine Studies*, vol. 24, pp. 65–75, 1986.
[17] "Prescribing, Recording and Reporting Photon Beam Therapy," International Commission on Radiation Units and Measurements (ICRU), Washington, DC, Rep. 50, 1993.
[18] "Determination of Absorbed Dose in a Patient Irradiated by Beams of X or Gamma Rays in Radiotherapy Procedures," International Commission on Radiation Units and Measurements (ICRU), Washington, DC, Rep. 24, 1976.
[19] M. Schneider, E. Shnaider, A. Kandel, and G. Chew, "Automatic construction of FCMs," *Fuzzy Sets Syst.*, vol. 93, pp. 161–172, 1998.

[20] B. Kosko, *Fuzzy Engineering*, New Jersey: Prentice-Hall, 1997.
[21] C. D. Stylios, P. P. Groumpos, and V. C. Georgopoulos, "An fuzzy cognitive maps approach to process control systems," *J. Adv. Computational Intell.*, vol. 3, no. 5, pp. 409–417, 1999.
[22] C. T. Lin and C. S. G Lee, *Neural Fuzzy Systems: A Neuro-Fuzzy Synergism to Intelligent Systems*. Upper Saddle River, N.J.: Prentice-Hall, 1996.
[23] E. Papageorgiou, C. D. Stylios, and P. P. Groumpos, "Activation hebbian learning rule for fuzzy cognitive maps," in *Proc. 15th IFAC World Congress Int. Federation of Automatic Control*, Barcelona, Spain, July 21–26, 2002. Available: CD-ROM.
[24] "Use of Computers in External Beam Radiotherapy Procedures with High Energy Photons and Electrons," International Commission on Radiation Units and Measurements (ICRU), Bathesda, M.D., Rep. 42, 1987.
[25] R. Mohan, G. S. Mageras, B. Baldwin, L. J. Brewster, G. J. Kutcher, S. Leibel, C. M. Burman, C. C. Ling, and Z. Fuks, "Clinically relevant optimization of 3D-conformal treatments," *Med. Phys.*, vol. 4, no. 19, pp. 933–943, July/Aug. 1992.
[26] I. Turesson and A. Brahme, *Clinical Rationale for High Precision Radiotherapy*, Malmo, Sweden: ESTRO (Eur. Soc. Therapeutic Radiat. Oncol.), 1992.
[27] E. Papageorgiou, C. D. Stylios, and P. P. Groumpos, "Decision making in external beam radiation therapy based on FCMs," in *Proc. 1st IEEE Int. Symp. Intelligent Systems 2002*, Bulgaria, 2002. Available: CD-ROM.
[28] E. Papageorgiou, "A model for dose calculation in treatment planning using pencil beam kernels," master thesis, Univ. Med. Sch. Patras, Patras, Greece, June 2000.
[29] "Radiation treatment planning dosimetry verification," Amer. Assoc. Physicists in Medicine, Amer. Inst. Physics (AAPM), Woodbury, N.Y., Task Group 23 Rep. 55., 1995.
[30] J. Venselaar and H. Welleweerd, "Application of a test package in an intercomparison of the photon dose calculation performance of treatment planning systems used in a clinical setting," *Radiotherapy Oncol.*, vol. 60, pp. 203–213, 2001.
[31] R. Alam, G. S. Ibbott, R. Pourang, and R. Nath, "Application of AAPM radiation therapy committee task group 23 test package for comparison of two treatment planning systems for photon external beam radiotherapy," *Med. Phys.*, vol. 24, pp. 2043–2054, 1997.
[32] F. Dechlich, K. Fumasoni, P. Mangili, G. M. Cattaneo, and M. Iori, "Dosimetric evaluation of a commercial 3-D treatment planning system using Report 55 by AAPM Task Group 23," *Radiotherapy Oncol.*, vol. 52, pp. 69–77, 1999.
[33] J. S. Jang, C. T. Sun, and E. Mizutani, *Neuro-Fuzzy and Soft Computing*. Upper Saddle River, N.J.: Prentice-Hall, 1997.
[34] A. Pollack *et al.*, "Conventional vs. conformal radiotherapy for prostate cancer: Preliminary results of dosimetry and acute toxicity," *Int. J. Radiat. Oncology Biol. Phys.*, vol. 34, no. 4, pp. 555–564, 1996.
[35] *A Phase I/II Dose Escalation Study Using Three-Dimensional Conformal Radiation Therapy for Adenocarcinoma of the Prostate*, 1996.
[36] J. Armstrong, "Three-dimensional conformal radiation therapy: Evidence-based treatment of prostate cancer," *Radiotherapy Oncol.*, vol. 64, pp. 235–237, 2002.
[37] G. Leunes, J. Verstaete, W. Van de Bogaert, J. Van Dam, A. Dutreix, and E. Van der Schueren, "Human errors in data transfer during the preparation and delivery of radiation treatment affecting the final result: 'Garbage in, garbage out"," *Radiotherapy Oncol.*, vol. 23, pp. 217–222, 1992.
[38] "Dose specification for reporting external beam therapy with photons and celectrons," International Commission on Radiation Units and Measurements (ICRU), Washington, DC, Rep. 29, 1978.
[39] M. J. Zelefsky *et al.*, "The effect of treatment positioning on normal tissue dose in patients with prostate cancer treated with three-dimensional conformal radiotherapy," *Int. J. Radiat. Oncol. Biol. Phys.*, vol. 37, pp. 13–19, 1997.
[40] J. Meyer, A. J. Mills, L.C.O. Haas, J. K. Burnham, and E. Parvin, "Accommodation of couch constraints for coplanar intensity modulated radiation therapy," *Radiotherapy Oncol.*, vol. 61, pp. 23–32, 2001.

Elpiniki I. Papageorgiou was born in Larisa, Greece, in 1975. She graduated from the Physics department at University of Patras in 1997 and received the M.Sc. degree in medical physics from University of Patras, in 2000. She is currently working towards the Ph.D. degree in the Department of Electrical and Computer Engineering at the University of Patras, Greece.

Her research interests are intelligent control, fuzzy logic, learning algorithms, and neural networks.

Ms. Papageorgiou is the recipient of a scholarship form the Greek Scholarships Foundation (I.K.Y).

Chrysostomos D. Stylios (S'96–A'01–M'03) received the diploma in electrical engineering from the Aristotle University of Thessaloniki, Thessaloniki, Greece, in 1992 and the Ph.D. degree from Department of Electrical and Computer Engineering, University of Patras, Patras, Greece in 1999.

He is currently adjunct faculty member at the Computer Science Department, University of Ioannina, Ioannina, Greece (since 2000). He has published over 40 journals and conference papers, book chapters, and technical reports. His research interests include soft computing and artificial intelligence techniques, modeling of complex systems, supervisory control, intelligent systems, decision support systems for medical application.

Dr. Stylios is a member of the EUSFLAT and the National Technical Chamber of Greece.

Peter P. Groumpos (S'73–M'78) received the Ph.D. degree in electrical engineering from the State University of New York, Buffalo, in 1978.

He is professor in the Department of Electrical and Computer Engineering at the University of Patras, Patras, Greece. He is also the head of the department and director of the Laboratory for Automation and Robotics. He was on the faculty at Cleveland State University, Cleveland, OH, 1979 to 1989. He was the director of the Communication Research Laboratory from 1981 to 1986 and a member of the Technical Committee of the Advanced Manufacturing Center from 1985 to 1987 at Cleveland State University, Cleveland, OH. He participated on a Technology Transfer Program with the Ministry of Higher Education of Egypt from 1981 to 1984.

For the academic year 1987–1988 he was a *Fulbright visiting scholar* at the University of Patras. He was the Greek National Representative to the High-Level Group for EUREKA and to EC Program ESPRIT 1991–1994. He is consultant to a number of companies in the USA and Greece. He was an Associate Editor for Book Reviews for the *IEEE Control Systems Magazine* from 1980 to 1985. He has published over 90 journals and conference papers, book chapters, and technical reports. His main research interests are modeling of complex systems, intelligent manufacturing systems, process control, robotics, simulation methods, hierarchical and large-scale systems control and adaptive control.

Prof. Groumpos is the Greek NMO representative to IFAC and he is the vice-chairman of the IFAC TC "Large Scale Systems." He is an associate Editor for the international journals *Computers and Electrical Engineering*, *Computers in Industry* and *Studies in Informatics and Control*. He is a member of the Honorary Societies Eta Kappa Nu and Tau Beta Pi. He was the Coordinator of the ESPRIT Network of Excellence in Intelligent Controls and Integrated Manufacturing Systems (ICIMS-NOE).