Series in Medical Physics and Biomedical Engineering

Intelligent and Adaptive Systems in Medicine

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Taylor & Francis
Taylor & Francis Group
New York London

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CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

CRC Press is an imprint of Taylor & Francis Group, an Informa business

Printed in the United States of America on acid-free paper
10 9 8 7 6 5 4 3 2 1

International Standard Book Number-13: 978-0-7503-0994-3 (Hardcover)

Library of Congress Cataloging-in-Publication Data

Intelligent and adaptive systems in medicine / editors, Olivier C.L. Haas and Keith J. Burnham.
p. ; cm. -- (Series in medical physics and biomedical engineering)
Includes bibliographical references and index.
ISBN 978-0-7503-0994-3 (alk. paper)
1. Artificial intelligence--Medical applications--Congresses. 2. Intelligent control systems--Congresses. 3. Biomedical engineering--Computer simulation--Congresses. I. Haas, Olivier. II. Burnham, Keith J. III. Title. IV. Series.
[DNLM: 1. Expert Systems--Congresses. 2. Biomedical Technology--methods--Congresses. 3. Diagnosis, Computer-Assisted--Congresses. 4. Medical Informatics Applications--Congresses. W 26.55.A7 I607 2008]

R859.7.A72I48 2008
610.285--dc22 2007035188

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The Soft Computing Technique of Fuzzy Cognitive Maps for Decision Making in Radiotherapy

Elpiniki Papageorgiou, Chrysostomos Stylios, and Peter Groumpos

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6.1 Introduction

Radiotherapy is the clinical and technological endeavor devoted to cure patients suffering from cancer (and other diseases) using ionizing radiation, alone or combined with other modalities. The aim of radiation therapy is to design and perform a treatment plan for how to deliver a precisely measured dose of radiation to the defined tumor volume with as minimal damage as possible to the surrounding healthy tissue. Successful radiation treatment results in eradication of the tumor, thus high quality of patient's life, and prolongation of survival at a reasonable cost.

The implementation and clinical practice of irradiation is a complex process that involves many professionals who have to take into account a variety of interrelated measurements, tasks, functions, and procedures. Professionals while determining the treatment of a patient have to know how this particular tumor will be destroyed and how the surrounding healthy tissue is likely to be adversely affected by the applied radiation dose. A large number of parameters–factors (medical and technological), which are complementary, similar, and conflicting, are taken into consideration when the radiation treatment procedure is designed. 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].

Experts determine the radiation treatment planning taking into consideration a variety of parameters–factors. The number, nature, and characteristics of factors increase the complexity of the procedure and require the implementation of an advanced technique similar to human reasoning, such as the soft-computing modeling technique of fuzzy cognitive maps (FCMs) [2].

Till today, many approaches and methodologies, algorithms, and mathematical tools have been proposed and used for optimizing radiation therapy treatment plans [3,4]. Dose-calculation algorithms [5,6], dose–volume feasibility search algorithms [7], and biological-objective algorithms have been utilized [8]. Dose distributions have been calculated for the treatment planning systems, satisfying objective criteria and dose–volume constraints [4]. Some algorithms have been proposed for optimizing beam weights and beam directions to improve radiotherapy treatment [9]. 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 [10,11]. Dose–volume histograms analyses the resultant dose distributions, which appears to indicate some merit [12]. Furthermore, methods related to knowledge-based expert systems and neural networks have been proposed for optimizing the treatment variables and developing decision-support systems for radiotherapy planning [13,14]. Much scientific efforts have been made to optimize treatment variables and dose distributions. Toward this direction, there is still a need for a flexible, efficient, and adaptive tool based on an abstract cognitive model, which will be used for clinical practice simulation and decision making [15,16,17].

The complexity and the vagueness of the decision-making process for radiotherapy treatment planning may be handled with soft-computing methods [18]. FCMs is a soft computing technique that incorporates ideas from artificial neural networks (ANNs) and fuzzy logic (FL). Their advantageous modeling features are the flexibility in system design, model, and control; the comprehensive operation; and the abstractive representation of complex systems. We propose the use of FCMs to create a dynamic model for estimating the final dose delivered to the target volume and normal tissues with the ability to evaluate the success of radiotherapy. FCMs have been used to model complex systems that involve discipline and different factors, states, variables, and events. FCMs can integrate and include the partial influence or controversial factors and characteristics in the decision-making problem [18]. The main advantage of implementing FCM in this area is that they can take under consideration causal effect among factors in recalculating the value of concepts that determine the radiation dose, keeping it in a minimum level and at the same time having the best result in destroying tumor with minimum injuries to healthy tissues and organs at risk. This is in accordance with the main goal of any radiation therapy treatment planning [1,19,20].

A decision system based on human knowledge and experience is proposed and developed here, having a two-level hierarchical structure with an FCM in each level, which 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 influences. The upper level FCM models the procedure of the treatment execution and calculates the optimal final dose for 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 [21].

6.2 Soft Computing Techniques for Decision Making

Soft computing differs from conventional (hard) computing. It is tolerant to imprecision, uncertainty, partial truth, and approximation. In effect, the role model for soft computing is the human mind. The principle of soft computing is to exploit the tolerance for imprecision, uncertainty, partial truth, and approximation to achieve tractability and robustness. Soft computing can be seen as a combination and contribution of FL, neural computing (NC), evolutionary computation (EC), machine learning (ML), and probabilistic reasoning (PR), with the latter subsuming belief networks, chaos theory, and parts of learning theory [22–24]. Soft computing can be seen as a partnership where every partner contributes discipline and different methodologies for addressing problems in its domain. In this perspective, the constituent methodologies of soft computing are complementary rather than competitive.

However, it is widely accepted that complex real-world problems require intelligent methods that combine knowledge, techniques, and methodologies from various sources and areas. Intelligent systems are desired to possess humanlike expertise within a specific domain, adapt themselves and learn to do better in changing environments, and explain how they make decisions or take actions. In confronting real-world computing problems, it is frequently advantageous to use several computing techniques synergistically rather than exclusively, resulting in construction of complementary hybrid intelligent systems.

The synergism allows soft computing to incorporate human knowledge effectively, deal with imprecision and uncertainty, and learns to adapt to unknown or changing environment for better performance. For learning and adapting, soft computing requires extensive computation. In this sense, soft computing shares the same characteristics as computational intelligence. Soft computing applications have been used in different areas: diagnostics in medicine, cluster analysis, discriminant analysis, and pattern recognition [25–29].

6.2.1 Description of Fuzzy Cognitive Maps

FCMs have their roots in graph theory. Axelord first used signed digraphs to represent the assertions of information [30]. He adopted the term "cognitive map" for these graphed causal relationships among variables as defined and described by people. The term "fuzzy cognitive map" was coined by Kosko [2]. An FCM model has two significant characteristics.

Causal relationships between nodes are fuzzy numbers. Instead of only using signs to indicate positive or negative causality, a weight is associated with the relationship to express the degree of relationship between two concepts.

The system is dynamic, permitting feedback, where the effect of change in one concept affects other concepts, which in turn can affect the concept initiating the change; the presence of feedback adds a temporal aspect to the operation of the FCM.

Concepts of FCM model reflect attributes, characteristics, qualities, quantities, and senses of the system. Interconnections among concepts of FCM signify the cause and effect relationships among concepts. These weighted interconnections represent the direction and degree with which concepts influence the value of the interconnected concepts. Figure 6.1 illustrates a graphical representation of an FCM model.

The cause and effect interconnection between two ordered nodes C_j and C_i is described with the weight w_{ji}, which takes a value in the range −1 to 1.

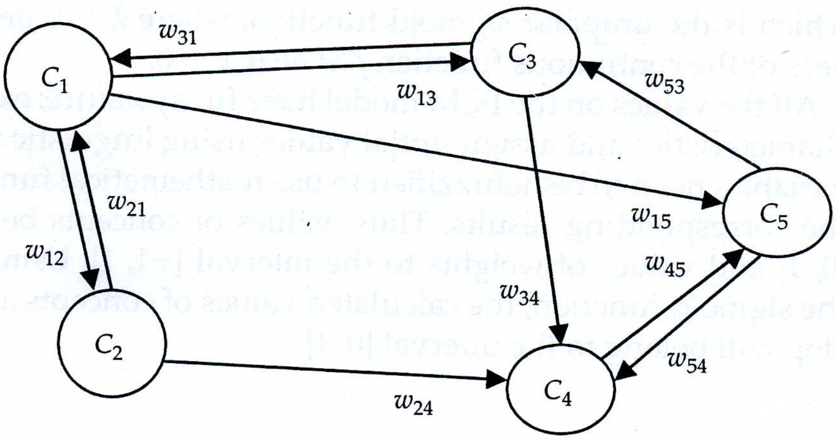

FIGURE 6.1
A simple FCM.

There are three possible types of causal relationships between concepts:

- $w_{ji} > 0$, which indicates positive causality between concepts C_j and C_i. That is, the increase (decrease) in the value of C_j leads to the increase (decrease) in the value of C_i.
- $w_{ji} < 0$, which indicates negative causality between concepts C_j and C_i. That is, the increase (decrease) in the value of C_j leads to the decrease (increase) in the value of C_i.
- $w_{ji} = 0$, which indicates no relationship between C_j and C_i.

Human knowledge and experience on the system are reflected, due to the FCM development procedure on the type and the number of concepts, as well as the initial weights of the FCM. The value A_i of concept C_i expresses the quantity of its corresponding physical value and is derived by the transformation of the fuzzy physical values to numerical ones.

FCM is used to model and simulate the behavior of any system. At each simulation step, the value A_i of a concept is calculated, computing the influence of the interconnected concepts to the specific concept according to the following calculation rule:

$$A_i^{(k+1)} = f\left(A_i^{(k)} + \sum_{\substack{j \neq i \\ j=i}}^{N} A_j^{(k)} \cdot w_{ji} \right) \tag{6.1}$$

where $A_i^{(k+1)}$ is the value of concept C_i at simulation step $k + 1$, $A_j^{(k)}$ is the value of concept C_j at step k, w_{ji} is the weight of the interconnection between concept C_j and concept C_i, and f is a sigmoid threshold function.

The sigmoid function f belongs to the family of squashing functions. Usually the following function is used

$$f(x) = \frac{1}{1 + e^{-\lambda x}} \tag{6.2}$$

which is the unipolar sigmoid function, where $\lambda > 0$ determines the steepness of the continuous function $f(x)$ near $x = 0$.

All the values on the FCM model have fuzzy nature; experts describe FCM characteristics and assign initial values using linguistic notion. These fuzzy variables need to be defuzzified to use mathematical functions and calculate the corresponding results. Thus, values of concepts belong to the interval [0, 1] and values of weights to the interval [−1, 1]. Using Equation 6.1 with the sigmoid function, the calculated values of concepts after each simulation step will belong to the interval [0, 1].

6.2.2 Developing Fuzzy Cognitive Maps

The method that is used to develop and construct the FCM has great importance to sufficiently model a system. The method used depends on the group of experts who operate, monitor, and supervise the system and develop the FCM model. This methodology extracts the knowledge on the system from the experts and exploits their experience on the system's model and behavior [31].

The group of experts determines the number and kind of concepts that comprise the FCM. The expert from his/her experience knows the main factors that describe the behavior of the system; each of these factors is represented by one concept of the FCM. Experts know which elements of the systems influence other elements; for the corresponding concepts, they determine the negative or positive effect of one concept on the others, with a fuzzy degree of causation. In this way, an expert transforms his knowledge in a dynamic weighted graph, the FCM. The methodology of developing an FCM based on fuzzy expressions to describe the interrelationship among concepts is described analytically in Refs. 15 and 31 and is used here. According to the developing methodology, experts are asked to think about and describe the existing relationship between the concepts and so they justify their suggestions. Each expert, in fact, determines the influence of one concept on another as "negative" or "positive" and then evaluates the degree of influence using a linguistic variable, such as "strong influence," "medium influence," and "weak influence."

More specifically, the causal interrelationships among concepts are declared using the variable *influence*, which is interpreted as a linguistic variable taking values in the universe $U = [-1, 1]$. Its term set $T(influence)$ is suggested to comprise nine variables. Using nine linguistic variables, an expert can describe in detail the influence of one concept on another and can discern between different degrees of influence. The nine variables used here are: $T(influence)$ = {negatively very strong, negatively strong, negatively medium, negatively weak, zero, positively weak, positively medium, positively strong, and positively very strong}. The corresponding membership functions for these terms are shown in Figure 6.2 and they are μ_{nvs}, μ_{ns}, μ_{nm}, μ_{nw}, μ_{z}, μ_{pw}, μ_{pm}, μ_{ps}, and μ_{pvs}.

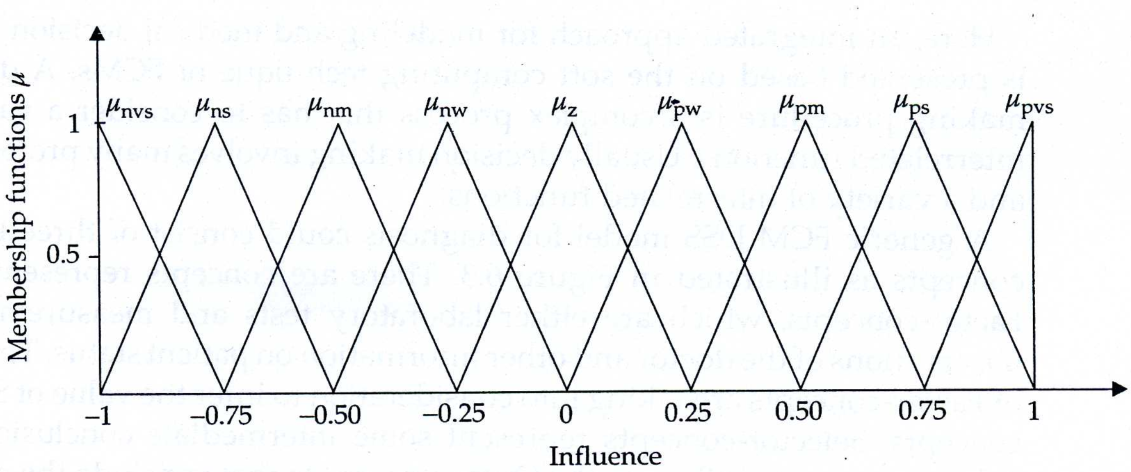

FIGURE 6.2
Membership functions for fuzzy values of FCMs.

Thus, every expert describes each one of the interconnections with a linguistic fuzzy rule; they use IF–THEN rules to justify the cause and effect relationships among concepts, inferring a linguistic weight for each interconnection. Then, the inferred fuzzy weights are integrated using the SUM method, as suggested by experts, and an overall linguistic weight is produced, which with the defuzzification method of center of gravity (CoG) [32] is transformed to a numerical weight w_{ji}, belonging to the interval [−1, 1]. All the weights are gathered into a weight matrix $n \times n$ **W**, where n is the number of concepts.

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**.

Where **B**, **D**, and **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.

6.2.3 Fuzzy Cognitive Map for Decision Support System

Decision support systems (DSS) are widely used in many application areas, from management and operational research sciences to medical applications. DSS are used to suggest solutions and provide advice to people how to conclude to a decision. DSS suggest alternative ways of action based on the advantages, disadvantages, and consequences of each action. DSS are developed utilizing the experience and knowledge of experts in the distinct problem. DSS do not take the decision by themselves but they suggest to human the most appropriate and suitable decision. Especially DSS play a significant role in medical applications, where decisions include humans (patients and doctors), medical equipment, and computers. Medical DSS are used by general practice doctors for specific health problems in order to propose a diagnosis and treatment.

Here, an integrated approach for modeling and medical decision making is presented based on the soft computing technique of FCMs. A decision-making procedure is a complex process that has to consider a variety of interrelated functions. Usually decision making involves many professionals and a variety of interrelated functions.

A generic FCM-DSS model for diagnosis could consist of three kinds of concepts as illustrated in Figure 6.3. There are concepts representing the Factor-concepts, which are either laboratory tests and measurements, or observations of the doctor and other information on patient status. The values of Factor-concepts are taking into consideration to infer the value of Selector-concepts. Selector-concepts represent some intermediate conclusions. The Selector-concepts influence the Output-concepts that conclude the decision. The FCM model can include all the factors and symptoms that can infer a decision along with the existing causal relationships among Factor-concepts, because factors are interdependable and sometimes the existence or lack of a factor requires the existence or lack of another. Moreover, Factor-concepts influence Selector-concepts and the value of each Selector-concept can subsequently influence the degree of the Output-concept of the FCM. This FCM model is an abstract conceptual model of what a doctor does when he makes

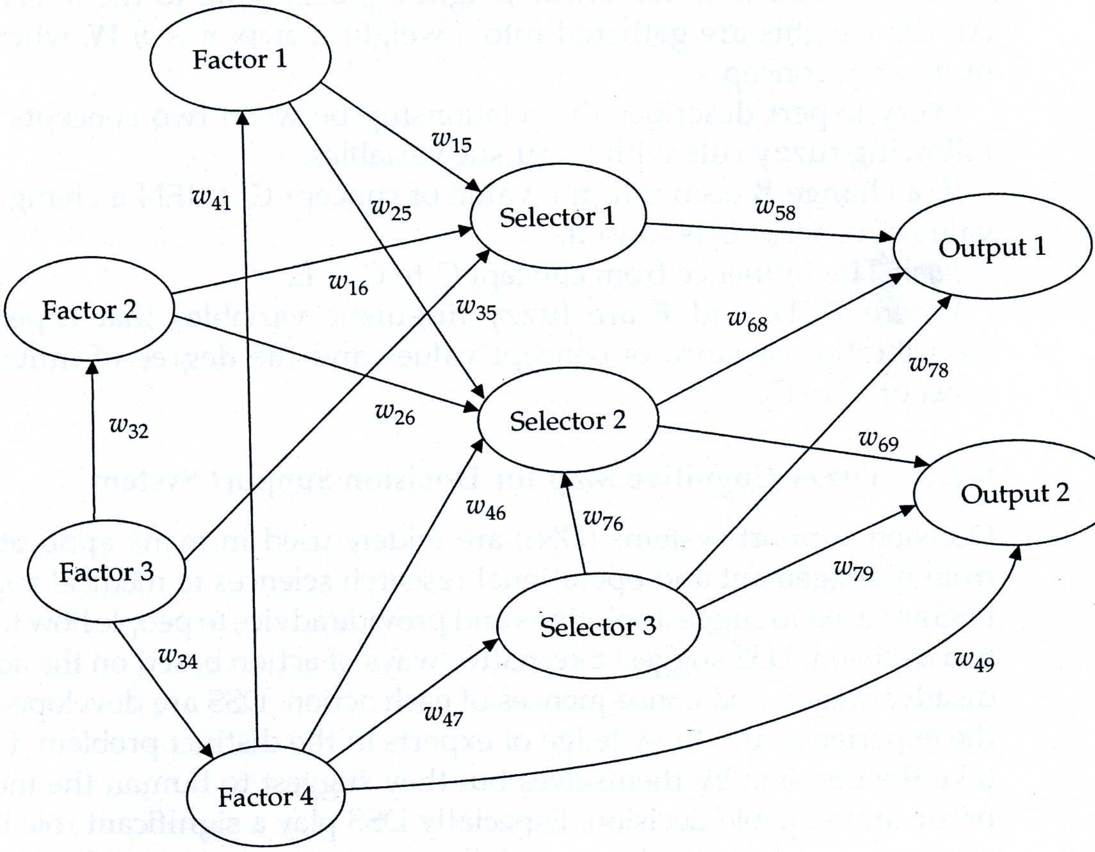

FIGURE 6.3
A generic FCM-DSS model for medical decision making. (From Papageorgiou, E.I., Stylios, C.D., Groumpos, P.P., *IEEE Trans. Biomed. Eng.*, 50(12) 2003. With permission.)

a decision; he reaches some intermediate inferences based on the inputs taking into consideration all the related symptoms, and then according to the intermediate Selector-concepts values, he determines his final decision that in the FCM model are presented as Output-concepts.

6.3 The Nonlinear Hebbian Learning Algorithm

In this section, the nonlinear Hebbian learning (NHL) algorithm that has been proposed to train FCM [33] is described. The NHL algorithm is used to overcome inadequate knowledge of experts and nonacceptable FCM simulation results [33]. The weight adaptation procedure is based on the Hebbian learning rule for nonlinear units [34]. The nonlinear Hebbian-type rule for ANNs learning [35] have been adapted and modified for the FCM case, and the NHL algorithm was proposed [33].

NHL algorithm is based on the premise that all the concepts in FCM model trigger synchronously at each iteration step. During this triggering process, the weight w_{ji} of the causal interconnection of the related concepts is updated and the modified weight $w_{ji}^{(k)}$ is calculated for iteration k.

The value $A_i^{(k+1)}$ of C_i, concept at simulation step $k + 1$, is calculated, computing the influence of interconnected concepts with values A_j to the specific concept C_i due to modified weights $w_{ji}^{(k)}$ at simulation step k, according to Equation 6.1, which takes the form

$$A_i^{(k+1)} = f\left(A_i^{(k)} + \sum_{\substack{j \neq i \\ j=i}}^{N} A_j^{(k)} \cdot w_{ji}^{(k)}\right) \tag{6.3}$$

Furthermore, during the development phase of FCM, experts have defined which concepts of FCM are the decision output concepts (DOCs). These concepts are the outputs of the system that interest us, and we want to estimate their values, which represent the final state of the system. The distinction of FCM concepts as inputs, intermediates, and outputs is determined by the group of experts for each specific problem. Experts select the output concepts and they also define the initial stimulators (Factor-concepts) and the interior concepts (Selector-concepts) of the system.

Taking the advantage of the general nonlinear Hebbian-type learning rule for ANNs, we introduce the mathematical formalism incorporating this learning rule for FCMs, a learning rate parameter and the determination of input and output concepts. This algorithm relates the values of concepts and values of weights in the FCM model.

The proposed learning rule [33] has the general mathematical form for the adjustment of the weights

$$\Delta w_{ji} = \eta_k A_i^{(k-1)} A_j^{(k-1)} - w_{ji}^{(k-1)} (A_i^{(k-1)})^2 \tag{6.4}$$

where the coefficient η_k is a very small positive scalar factor called the "learning parameter" and is determined using an experimental trial and error method to converge the simulation process. $A_j^{(k)}$ is the value of concept C_j, which at next simulation step, k+1, triggers the interconnected concepts.

This simple rule states that if $A_j^{(k)}$ is the value of concept C_i at simulation step k and A_j is the value of the concept C_j that triggers the concept C_i, the corresponding weight from concept C_j toward the concept C_i increases proportional to their product multiplied with the learning rate parameter minus the weight decay at simulation step $k-1$, that is multiplied by the value A_j of triggering concept C_j. All the FCM concepts trigger at the same iteration step and their values are updated synchronously.

Equation 6.4 takes the following form of nonlinear weight adaptation algorithm, if we introduce a weight decay parameter:

$$w_{ji}^{(k)} = \gamma \cdot w_{ji}^{(k-1)} + \eta_k A_i^{(k-1)}(A_j^{(k-1)} - \operatorname{sign}(w_{ji}^{(k-1)}) w_{ji}^{(k-1)} A_i^{(k-1)}) \tag{6.5}$$

where η_k is the learning rate parameter and γ the weight decay parameter.

The value of each concept of FCM is updated through Equation 6.3, where the value of weight $w_{ji}^{(k)}$ is calculated using Equation 6.5.

When the NHL algorithm is applied, only the initial nonzero weights suggested by experts are updated for each iteration step. All the other weights of weight matrix **W** remain equal to zero, which is their initial value.

For the termination of the proposed algorithm, two termination conditions are proposed. One termination condition is the minimization of function F_1. The termination function F_1 that has been proposed for the NHL examines the values of DOCs. It is supposed that for each DOC$_i$, experts have defined a target value T_i. This target value can either be the desired value when DOC$_i$ represents a concept, which has to take a value or the mean value when DOC$_i$ represents a concept whose value has to belong to an interval. Thus, the function F_1 is defined as

$$F_1 = \sqrt{\sum_{i=1}^{l} (\mathrm{DOC}_i - T_i)^2} \tag{6.6}$$

where l is the number of DOCs.

The second termination condition is the minimization of the variation between two subsequent values of DOCs, represented by the following equation:

$$F_2 = \left|\mathrm{DOC}_i^{(k+1)} - \mathrm{DOC}_i^{(k)}\right| < e \tag{6.7}$$

This termination condition helps to terminate the iterative process of the learning algorithm. The term e is a tolerance level keeping the variation of values of DOC(s) as low as possible and it is proposed to be equal to $e = 0.001$, satisfying the termination of the iterative process.

Algorithm 1: "Nonlinear Hebbian learning"
Step 1: Read input concept state A^0 *and initial weight matrix* $\mathbf{W}^0$
Step 2: Repeat for each iteration k
Step 3: Calculate $A_i^{(k)}$ *according to Equation 6.3*
Step 4: Update the weights:
$w_{ji}^{(k)} = \gamma \cdot w_{ji}^{(k-1)} + \eta A_i^{(k-1)}(A_j^{(k-1)} - sgn(w_{ji}) w_{ji}^{(k-1)} A_i^{(k-1)})$
Step 5: Calculate the two termination functions
Step 6: Until the termination conditions are met
Step 7: Return the final weights $\mathbf{W}_{NHL}$

FIGURE 6.4
Pseudo code of NHL algorithm.

Through this training process and when both the termination conditions are met, the final weight matrix $\mathbf{W}_{NHL}$ of FCM is derived.

A generic description of the proposed NHL algorithm for FCMs is given in Figure 6.4.

After a number of experiments and implementation the NHL algorithm in different domains, the upper and lower bounds for the learning rate parameters γ and η have been determined [33]. The bounds of learning rate parameter η are determined as $0 < \eta < 0.1$, and for the weight-decay parameter as $0.9 < \gamma < 1$. Larger η values of 0.1, and smaller γ values of 0.9 do not lead the system in convergence for any initial values.

The flowchart of the proposed NHL procedure implemented in FCMs is given in Figure 6.5. It is mentioned that if the learning procedure repeats for over 1000 iteration steps without converging, it stops and experts are asked to reconstruct the FCM.

Training FCM with the NHL algorithm enhances the FCM model and incorporates the expert's knowledge into a proper FCM model of the process or system. This is the case of supervisor-FCM and when the FCM has to converge in desired equilibrium points after simulation results.

6.4 Radiation Therapy Procedure: Background, Issues, and Factors

Radiotherapy is identified as the external application of beams of photons generated by linear accelerator machines to eliminate tumors and treat cancer patients. There are two objectives for "3-dimensional conformal"

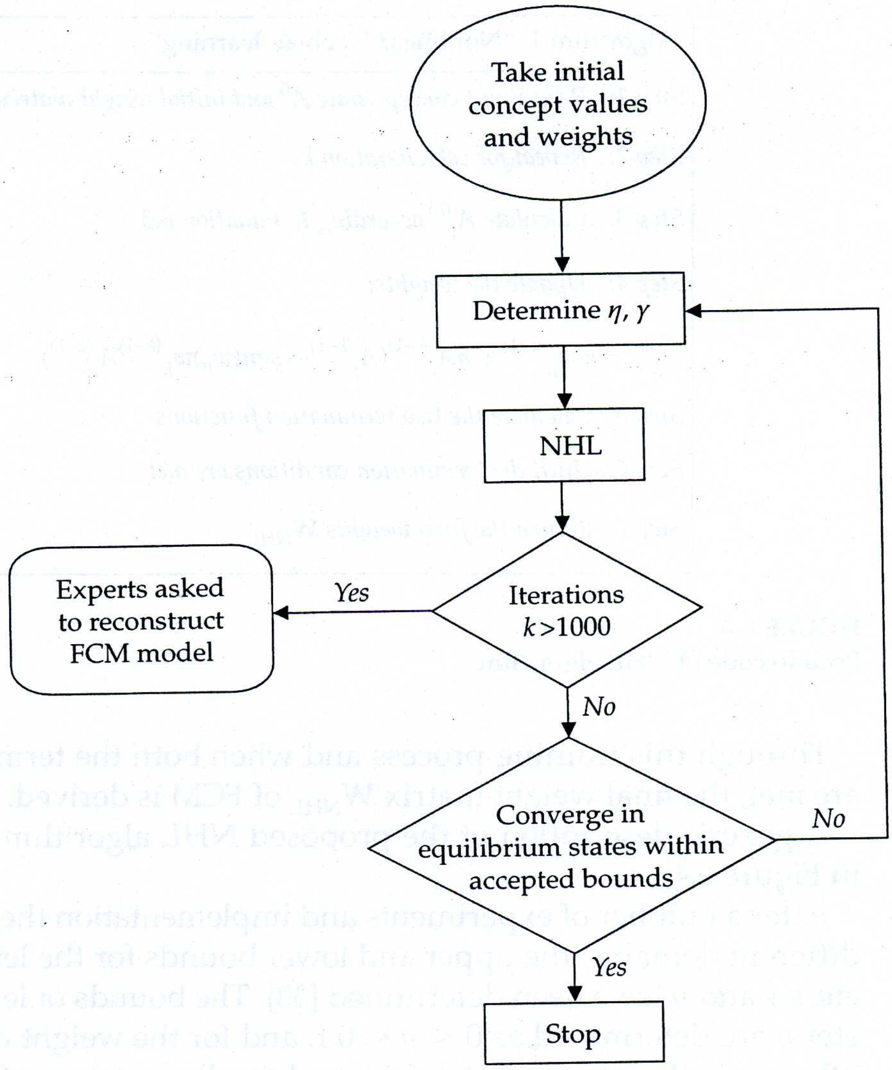

FIGURE 6.5
The flowchart of NHL algorithm.

radiotherapy; the first one is to deliver the highest dose to a volume shaped exactly like the tumor and the second one is to keep the dose level at the minimum for healthy tissues and critical organs. Before the implementation of any beam radiation, a treatment plan is required to be designed. The treatment planning determines how to perform the radiation, which is a complex problem because various complementary of interconnecting conditions and constraints have to be met. The performance criteria for radiation therapy 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 radiation variables and displaying the corresponding dose distribution is repeated till the optimizations of these criteria are met.

The depth of the tumor from the skin surface is probably the most important factor in selecting the appropriate radiation therapy machine, but it is definitely not the only one. For treating complex tumors, a variety of factors are taken into consideration to determine the treatment plan [36–38].

An inexhaustive list of factors may include the following:

1. The depth at which the tumor is located from skin surface.
2. The shape (geometrical or irregular) and the size of the tumor.
3. The location of the tumor in part of the body or head and size of cross section treated.
4. The local invasive capacity of the tumor and its potential spread to the regional lymph nodes.
5. The type of tissue within the tumor, as well as the type of tissue that surrounds the tumor. The presence of inhomogeneities within the irradiated volume such as bone, muscle, lung, fat, and air should be taken into consideration.
6. The dose distribution within the target volume should be reasonably uniform (within ±5%).
7. The tumor position regarding the center of the contour cross section.
8. The existence of radiation-sensitive organs within the irradiated volume, such as eyes, bladder, salivary glands, larynx, spinal cord, anus, and skin. These normal critical structures should not receive doses near or beyond tolerance.
9. Damage to the healthy tissue outside the treatment volume (maximum dose ≤95% of prescribed dose).
10. Patient dimension and contour geometry in treatment region.
11. The number of radiation fields that must be used and the daily dosage on the tumor based on the biological damage of the healthy subcutaneous tissue.
12. Cost—this includes cost of equipment, cost of shielding, and cost of usage of space.
13. The length of time required to administer the treatment—it is difficult to keep a patient immobilized for a long period of time. The length of procedure preparation time (both for patient and staff). The time required for obtaining the optimum treatment plan and the time for calculating the distributed doses within the irradiated volume.
14. Amount of secondary (scattered) radiation that can be tolerated by the patient.
15. Matching of beam overlap volume with target volume.
16. Degree of difficulty in repeatability (flexibility) of setup of the patient and treatment geometry.

However, to achieve a good distribution of the radiation on the tumor as well as to protect the healthy tissues, the following should be taken into consideration:

1. Selection of appropriate size of the radiation field
2. Increase of entry points of the beam (more than one radiation field)
3. Selection of appropriate beam directions
4. Selection of weight of each field (dose contribution from individual fields)
5. Selection of appropriate quality, that is, energy and type of radiation (x-rays, γ-rays, and electrons)
6. Modification of field with cerrobend blocks or multileaf collimators, compensating filters or *bolus*, and wedge filters
7. Use of isocentric stationary beam therapy versus isocentric rotation therapy
8. Patient immobilization
9. Use of conformal (3-D) instead of conventional (2-D) radiotherapy

More information with the necessary theoretical justification and detailed description of the concepts mentioned earlier and related terms are provided in Refs. 36–38.

Treatment planning refers to the description and the selection of implementation procedures and how to reach necessary decisions that have to be made before performing radiation treatment. Both physical and clinical procedures are part of the treatment-planning problem. The treatment-planning process comprises several methods for treatment preparation and simulation toward achieving a reproducible and optimal treatment plan for the patient. Irrespective of the temporal order, these procedures include

- Patient fixation, immobilization, and reference point selection
- Dose prescriptions for target volumes and the tolerance level of organ at risk volumes
- Dose distribution calculation
- Treatment simulation
- Selection and optimization of
  - Radiation modality and treatment technique
  - The number of beam portals
  - The directions of incidence of the beams
  - Beam collimation
  - Beam intensity profiles
  - Fractionation schedule

Thus, the treatment planning is a complex process where a great number of treatment variables have to be considered.

6.5 The Clinical Treatment Simulation Tool for Decision Making in Radiotherapy

Radiotherapists and physicists are asked to construct the FCM model according to their knowledge and experience, thus they are using the factors and treatment variables that were briefly presented in Section 6.4. These factors and characteristics will be the concepts of the FCM decision-making model for radiotherapy treatment planning. They are considering the basic beam data from experimental measurements [39] and the information described at American Association of Physicists in Medicine (AAPM) Task Group (TG) 23 test package [40] to retrieve the main Factors-concepts of the FCM model, selectors, and the relationships among them. The AAPM TG 23 test package is useful for the quantitative analysis of treatment planning systems of photon beam radiation [40,41]. Our test package of basic beam dosimetric data has been developed with experimental measurements [39], which are used here for the determination of initial values of concepts and weights.

Radiotherapy experts, following the generic FCM-decision support model presented in Section 6.2.3, identified and divided the concepts, which consist of the FCM model for radiotherapy treatment planning, into three categories: Factor-concepts, Selector-concepts, and Output-concepts. Factors and selectors concepts could be seen as inputs, they represent treatment variables with given, measured, or calculated values, and the corresponding causal weights are identified from experimental data, and data from AAPM TG 23 test package [39–42]. The values of the Selector-concepts are influenced by the value of the Factor-concepts with the corresponding causal weights. The values of the Output-concepts are influenced and determined by the values of the Factor-concepts and the Selector-concepts with the corresponding causal weights. The decision-making procedure is based on the determination of the values of the Output-concepts that lead to the final decision.

The values of concepts in the FCM model can generally take crisp, numeric, and linguistic values. It is considered that the values of concepts in the FCM-DSS model take five positive linguistic variables depending on the characteristics of each particular concept, such as very high, high, medium, weak, and near zero. When concepts represent events or discrete variables, there is a threshold (0.5) that determines if an event is activated or not. All the values of concepts in the FCM belong to the interval [0, 1]. The degree of the influence between concepts 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, and negative very low} [15,21].

Experts developed the FCM that models the radiotherapy treatment planning procedure, according to the test packages and experimental data. So, the clinical treatment simulation tool based on fuzzy cognitive map (CTST-FCM) model consists of 26 concepts that are described in Table 6.1.

Concepts F-C1 to F-C13 are the Factor-concepts, concepts S-C1 to S-C10 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 the mean clinical target volume (CTV), which has to be more than 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 has to be as small as possible, less than 5% of the volume receiving the prescribed dose. The value of concept OUT-C3 represents the volume of organ at risk (OAR) receiving a dose, which should be less than the 10% of volume receiving the prescribed dose. The objective of the FCM model is to keep the values of the OUT-Cs, in the following range:

$$\text{OUT-C1} \geq 0.90 \tag{6.8}$$

$$\text{OUT-C2} < 0.05 \tag{6.9}$$

$$\text{OUT-C3} < 0.10 \tag{6.10}$$

The values of Output-concepts are acceptable when they satisfy the performance criteria in Equations 6.8 through 6.10.

Using the development methodology for FCMs as described in Section 6.2.2, every expert describes each interconnection using a fuzzy rule. Fuzzy rules are evaluated in parallel using fuzzy reasoning and the inferred fuzzy weights are combined so that an aggregated linguistic weight is produced, which is then defuzzified 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 and Factor-concepts, are determined. Five examples are now described to illustrate the determination of the weights for some interconnections.

Example 6.1

One expert describes the influence from the 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 S-C3, THEN a small change is caused in the value of 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,

TABLE 6.1

Concepts of the CTST-FCM: Description and Type of Values

Concepts	Description	Number and Type of Values Scaled
F-C1	Accuracy of depth of tumor	Five fuzzy
F-C2	Size of tumor	Seven fuzzy (very small, small, positive small, medium, negative large, large, and very large)
F-C3	Shape of tumor	Three fuzzy (small, medium, and large)
F-C4	Location of tumor size at cross section	Three fuzzy
F-C5	Regional metastasis of tumor (sites of body)	Five fuzzy
F-C6	Type of irradiated tissues—presence of inhomogeneities	Five fuzzy
F-C7	Dose uniformity (including 90% isodose) within target volume	One fixed
F-C8	Skin sparing—amount of patient skin dose	Three fuzzy (low, medium, and high)
F-C9	Amount of patient thickness irradiated	Five fuzzy
F-C10	Accuracy of patient's contour (taken from CT-scans and portal films)	Five fuzzy
F-C11	Amount of scattered radiation received by patient	Five fuzzy
F-C12	Time required for treatment procedure or preparation	Five fuzzy
F-C13	Amount of perfect match of beam to target volume	Three fuzzy
S-C1	Quality of radiation—four types of machines (orthovoltage, supervoltage, megavoltage and teletherapy)	Four discrete
S-C2	Type of radiation (photons, electrons, protons, and heavy particles)	Four discrete
S-C3	Size of radiation field	Five fuzzy
S-C4	Single or multiple field arrangements	Two discrete
S-C5	Beam direction(s) (angles of beam orientation)	Continuous
S-C6	Weight of each field (percentage of each field)	Continuous
S-C7	Stationery versus rotation—isocentric beam therapy	Continuous
S-C8	Field modification (no field modification, blocks, wedges, filters, and multileaf-collimator shaping blocks)	Five discrete
S-C9	Patient immobilization	Three discrete
S-C10	Use of 2-D or 3-D conformal technique	Two discrete
Out-C1	Dose given to treatment volume (must be within accepted limits)	Five fuzzy
Out-C2	Amount of irradiated volume of healthy tissues	Five fuzzy
Out-C3	Amount of irradiated volume of sensitive organs (OAR)	Five fuzzy

Source: Papageorgiou, E.I., Stylios, C.D., Groumpos, P.P., *IEEE Trans. Biomed. Eng.*, 50, 12, 2003. With permission.

increasing the amount of dose. So, the influence of S-C3 to OUT-C1 is positively small.

The inferred linguistic weight for this interconnection will be aggregated with other linguistic weights proposed by the other experts and an overall linguistic weight will be produced, which will be defuzzified.

Example 6.2

The influence from the F-C2 toward the S-C3 representing the size of radiation field is inferred:

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

This means that the size of the tumor, determined by the radiotherapist, influences the size of radiation field. If the size of target volume is increased by a small amount, the size of radiation field is increased by a larger amount. The influence of F-C2 to S-C3 is inferred as positively strong.

Example 6.3

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

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

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

Example 6.4

The influence from S-C4 toward the F-C13 representing the amount of perfect match of beam to target volume-tumor is inferred as

IF a large change occurs in the value of S-C4, THEN a very large change is caused in the value of F-C13.

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

Example 6.5

The influence from Output-concept OUT-C1 toward the Output-concept OUT-C2 is inferred as

IF a small change occurs in the value of OUT-C1, THEN a large change is caused in the value of OUT-C2.

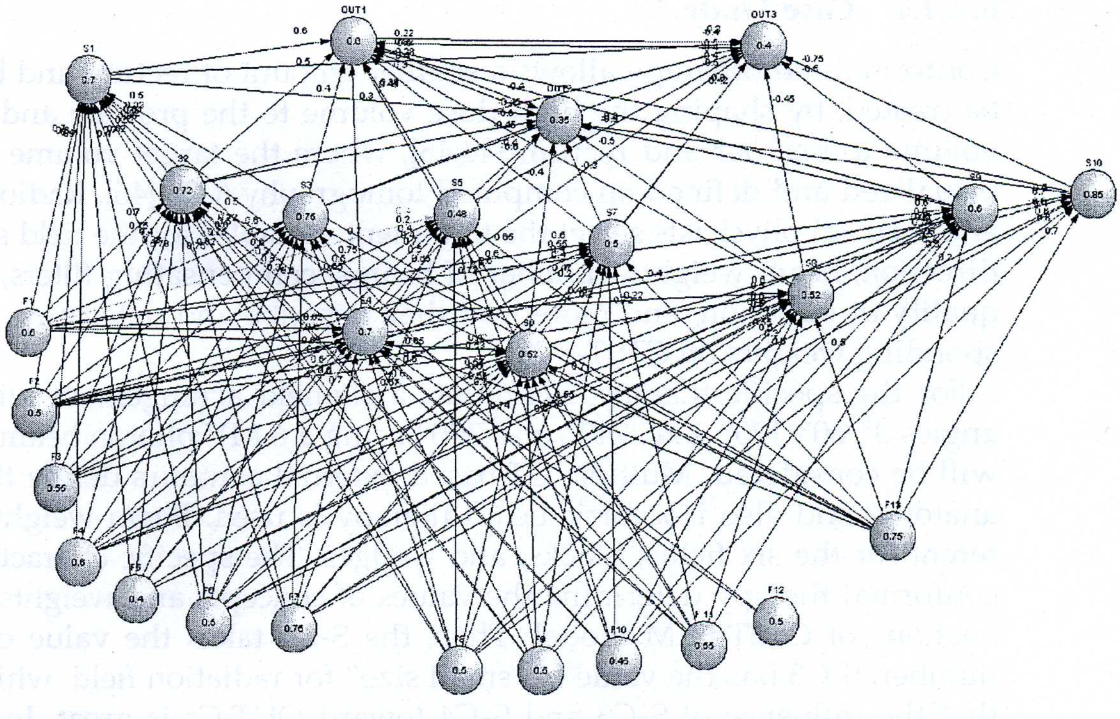

FIGURE 6.6
The CTST-FCM model with 26 concepts and 156 interrelationships. (From Papageorgiou, E.I., Stylios, C.D., Groumpos, P.P., *IEEE Trans. Biomed. Eng.*, 50(12), 2003. With permission.)

> 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 among Factor-concepts, Selector-concepts, and Output-concepts.

The CTST-FCM model for the decision making in radiotherapy is developed and illustrated in Figure 6.6. It consists of 26 concepts and 156 interconnections. Initial values of concepts are taken from the data set of the AAPM TG 23 [40, 43] and from experimental data [39], and are identified according to each specific treatment technique, then these values are normalized and transformed in the interval [0, 1].

6.5.1 Testing of the Clinical Treatment Simulation Tool for Two Radiotherapy Planning Case Studies

The treatment of localized prostate cancer is commonly treated with the use of radical radiotherapy. In this section, two different treatment cases for prostate cancer therapy have been examined using the CTST-FCM 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.

6.5.1.1 Case Study 1

Conformal radiotherapy allows a smaller amount of rectum and bladder to be treated, by shaping the high dose volume to the prostate and low-dose volume to bladder and rectum [44,45], where the target volume is readily visualized and defined on computed tomography (CT) [46]. Radiotherapists and medical physicists select the treatment variables for the field size, beam direction, beam weights, number of beams, compensating filters, type and quality of radiation, and moreover, they describe and determine the corresponding weights on CTST-FCM.

For the specific therapy technique, a six-field arrangement with gantry angles 0°, 60°, 120°, 180°, 240°, and 300° using a 6 MV photon beam radiation will be considered. Multiple CT-based external contours define the patient anatomy and also isocentric beam therapy is used. Beam weights are different for the six fields, blocks, and wedges. The specific characteristics of conformal therapy determine the values of concepts and weights interconnections of CTST-FCM model. Thus, the S-C4 takes the value of six-field number; S-C3 has the value of "small size" for radiation field, which 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 on OUT-Cs because different beam directions and weights of radiation beams are used. S-C8 takes the value for the selected blocks and wedges, influencing the OUT-Cs. The S-C7 takes the discrete value of isocentric beam therapy. The S-C9 takes a value for accurate patient positioning and the S-C10 takes the discrete value of 3-D radiotherapy.

Thus, for the specific technique considering the earlier discussion, 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 is given in Table 6.2. Tables 6.3 and 6.4 contain the weights of interconnections

TABLE 6.2
Weights Representing Relationships among Selector-Concepts and Output-Concepts for First Case Study

Selectors	OUT-C1	OUT-C2	OUT-C3
S-C1	0.6	−0.45	−0.4
S-C2	0.50	−0.6	−0.5
S-C3	0.4	−0.45	−0.4
S-C4	0.3	−0.6	−0.5
S-C5	0.38	−0.40	−0.4
S-C6	0.45	−0.4	−0.4
S-C7	0.30	−0.30	−0.30
S-C8	0.4	−0.5	−0.45
S-C9	0.4	−0.5	−0.45
S-C10	0.6	−0.5	−0.5

Source: Papageorgiou, E.I., Stylios, C.D., Groumpos, P.P., *IEEE Trans. Biomed. Eng.*, 50, 12, 2003. With permission.

TABLE 6.3

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
F-C1	0.7	0.7	0.6	0.62	0.4	0.42	0.6	0.6	0.2	0
F-C2	0.65	0.6	0.7	0.6	0.2	0.53	0.55	0.5	0.6	0.5
F-C3	0.4	0.4	0.6	0.63	0.45	0	0.4	0	0	0.7
F-C4	0.7	0.38	0.3	0.6	0.4	0.52	0.4	0.6	0.7	0
F-C5	0.4	0.78	0.8	0.6	0.7	0.6	0	0.45	0	0
F-C6	0.7	0.75	0.32	0.6	0.5	0.55	0.47	0.5	0	0.6
F-C7	0.62	0.62	0.6	0.7	0.65	0.6	0.2	0.74	0.5	0.4
F-C8	0.52	0.75	0.65	0.67	0.72	0.74	0.45	0.55	0	0.6
F-C9	0.35	0.6	0.5	0.6	0.6	0.6	0.2	0.5	0.5	0
F-C10	0.22	0.5	0	0	0.6	0.58	0.72	0.3	0.7	0.6
F-C11	0.61	0.72	0.75	0.6	0.6	0.55	0.22	0.6	0	0
F-C12	0.33	0	0	0.52	0	0	0	0	0.5	0
F-C13	0.50	0.50	0.7	0.65	0.65	0.7	0.4	0.2	0.6	0.7

Source: Papageorgiou, E.I., Stylios, C.D., Groumpos, P.P., *IEEE Trans. Biomed. Eng.*, 50, 12, 2003. With permission.

TABLE 6.4

Weights of the Interconnections among Output-Concepts

Outputs	OUT-C1	OUT-C2	OUT-C3
OUT-C1	0	0.6	0.6
OUT-C2	−0.7	0	0
OUT-C3	−0.6	0	0

Source: Papageorgiou, E.I., Stylios, C.D., Groumpos, P.P., *IEEE Trans. Biomed. Eng.*, 50, 12, 2003. With permission.

between Factor-concepts and Selector-concepts, and Output-concepts to Output-concepts respectively.

The following matrix is formed with the initial values for this particular treatment technique:

$$A_1^{\text{lower level}} = \begin{matrix}[0.75\ 0.5\ 0.5\ 0.6\ 0\ 0.5\ 0.8\ 0.5\ 0.55\ 0.7\ 0.4 \\ 0.5\ 1\ 0.75\ 0\ 0.4\ 1\ 0.7\ 0.2\ 0.6\ 0.5\ 1\ 1\ 0\ 0\ 0]\end{matrix}$$

where A_i is the value of concept C_i.

When the initial values of concepts have been assigned, the CTST-FCM starts to interact and simulate the radiation procedure. Equation 6.3 calculates the new values of concepts after each simulation step and Figure 6.7 illustrates the values of concepts for eight simulation steps. From Figure 6.7, it is concluded that after the fifth simulation step, the FCM reaches an equilibrium region, where the resulting values of OUT-Cs are OUT-C1 = 0.99, OUT-C2 = 0.025, and OUT-C3 = 0.04.

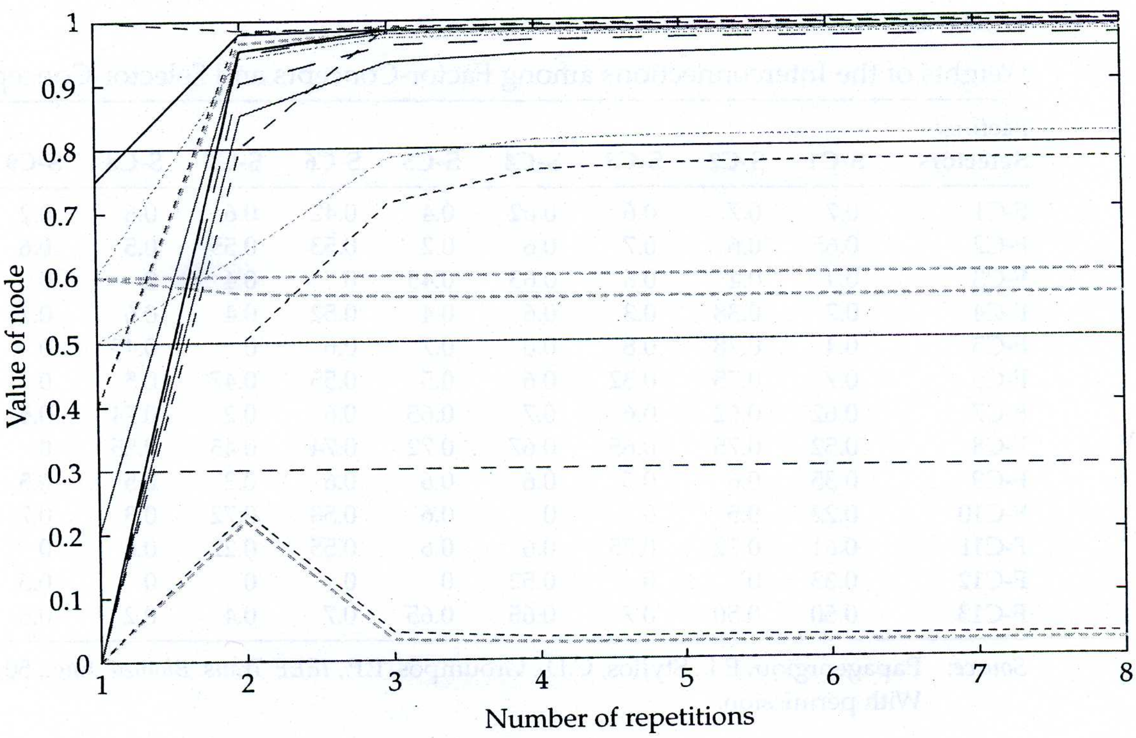

FIGURE 6.7
Variation of values of 26 concepts for the CTST-FCM for the first case for eight simulation steps.

The values of the CTST-FCM concepts at equilibrium region are $A_{leq}^{lower\ level}$ = [0.75 0.5 0.5 0.5564 0 0.5 0.8 0.5 0.55 0.7 0.4 0.779 0.819 0.991 0.99 0.987 0.993 0.99 0.995 0.987 0.99 0.978 0.99 0.025 0.040].

Based on the referred performance criteria in Section 6.5, the calculated values of output concepts are accepted. The calculated value of OUT-C1 is 0.99, which means that the CTV receives the 99% of the amount of the prescribed dose, so it is accepted. The value of OUT-C2 that represents the amount of the surrounding healthy tissues' volume received a dose is found equal to 0.025, so that 2.5% of the volume of healthy tissues receives the prescribed dose of 81 Gy. The value of OUT-C3 that represents the amount of the critical organ's volume (bladder and rectum) is equal to 0.034, which means that the 3.4% of the volume receives the prescribed dose of 81 Gy. The values of OUT-Cs satisfy the performance criteria in Equations 6.8 through 6.10. It is clear that the CTST-FCM model with the initial values of treatment variables and their interconnections which radiotherapists and medical physicists proposed for the specific technique of prostate cancer converged to a set of values that satisfy the performance criteria. Thus, the CTST-FCM suggests that the treatment planning can be executed and there will be acceptable results for the treatment.

6.5.1.2 *Case Study 2*

For the second case study, the conventional four-field box technique is implemented for the prostate cancer treatment. This radiotherapy technique consists of a four-field box arrangement with gantry angles 0°, 90°, 180°, and 270°.

A single external contour defines the patient anatomy and the isocentric beam therapy is used. Beam weights have the same value for four fields and moreover, no blocks, wedges, collimator settings, and compensating filters are used.

For this case, the CTST-FCM has to be reconstructed, which means that radiotherapists have to reassign weights and interconnections because a different treatment technique is used [45–48]. Data from AAPM TG 23 and experiments determine the treatment variables and their interrelationships, and they modify 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 directions and weights of radiation beams are used. S-C8 has 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 conformal treatment case mentioned earlier. The S-C9 takes a low value for no accurate patient positioning and the S-C10 takes the discrete value of 2-D radiotherapy.

The weights between S-Cs and OUT-Cs for this case are given in Table 6.5. If we compare Table 6.5 with Table 6.2, which contains the weights for the first case, we will see that some weighted 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 example starts with the following initial values of concepts:

$$\mathbf{A}_2^{\text{lower level}} = \begin{matrix}[0.5\ 0.5\ 0.5\ 0.6\ 0\ 0.5\ 0.6\ 0\ 0.5\ 0.3\ 0.6\ 0.5\\ 0.5\ 0.75\ 0\ 0.2\ 1\ 0.4\ 0.4\ 0.6\ 0\ 0\ 0\ 0\ 0\ 0]\end{matrix}$$

The values of concepts are calculated using Equation 6.3 and the variation of values of 26 concepts after eight simulation steps are illustrated in Figure 6.8.

TABLE 6.5

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	−0.6	−0.48
S-C3	0.27	−0.2	−0.20
S-C4	0.24	−0.4	−0.4
S-C5	0.22	−0.25	−0.2
S-C6	0.25	−0.20	−0.20
S-C7	0.30	−0.30	−0.30
S-C8	0	0	0
S-C9	0.28	−0.30	−0.2
S-C10	0.20	−0.25	−0.20

Source: Papageorgiou, E.I., Stylios, C.D., Groumpos, P.P., *IEEE Trans. Biomed. Eng.*, 50, 12, 2003. With permission.

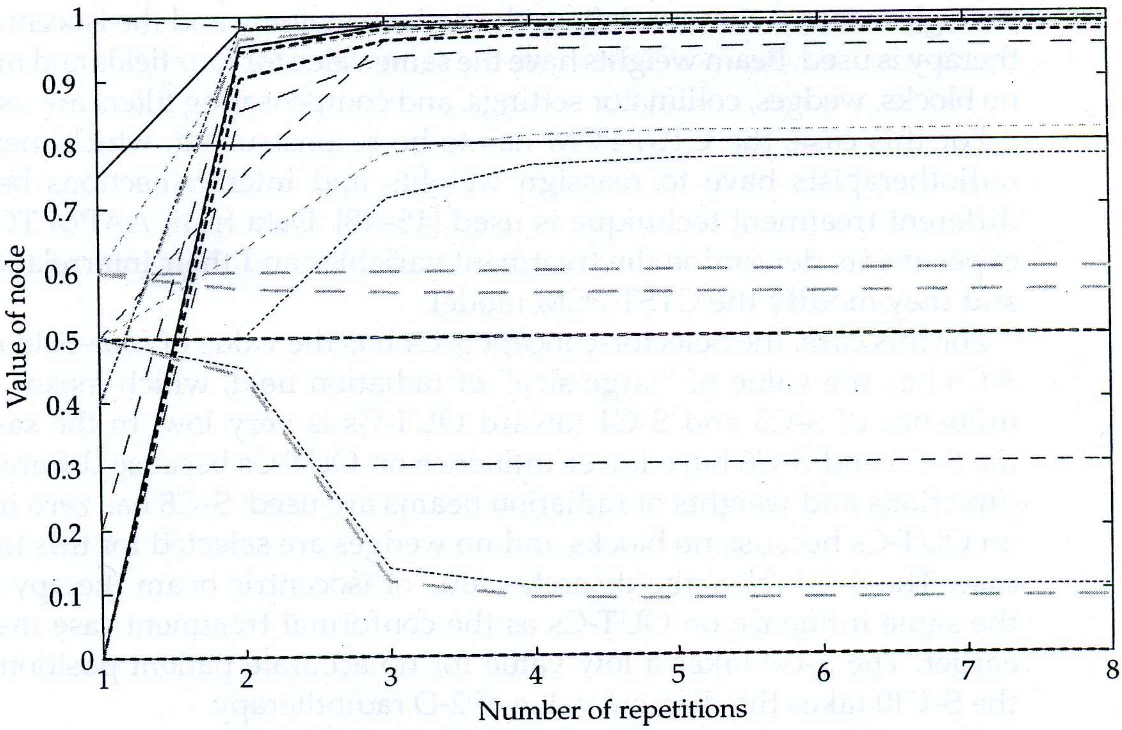

FIGURE 6.8
Variation of values of 26 concepts of CTST-FCM for the second example, with the classical treatment planning case for eight simulation steps.

It shows that the CTST-FCM interacts and reaches an equilibrium region. The values of concepts at equilibrium region are $\mathbf{A}_{2eq}^{\text{lower level}} =$ [0.5 0.5 0.5 0.566 00.5 0.6 0 0.5 0.3 0.6 0.777 0.818 0.986 0.983 0.981 0.99 0.983 0.991 0.976 0.985 0.97 0.943 0.983 0.087 0.011].

At this equilibrium region, the final values of OUT-Cs are OUT-C1 = 0.983, OUT-C2 = 0.087, and OUT-C3 = 0.11. 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 0.087, which means that the 8.7% of the volume of healthy tissues receives a prescribed dose of 81 Gy. The calculated value of OUT-C3 describes that the 11% 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 [45].

If these suggested values for Output-concepts were adopted, the patient's normal tissues and sensitive organs would receive a larger amount of dose than that desired, which is not accepted. Thus, 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 in order to reschedule the planning procedure. This prompts the need for a higher level to lead the rescheduling and supervise the whole treatment planning.

6.5.2 Discussion of the Results on the Two Case Studies

CTST-FCM model integrates different treatment planning procedures where treatment parameters can have different degrees of influence to the treatment execution. CTST-FCM model estimates the final dose, which is actually received by the target volume and the patient. CTST-FCM was modified for some standard treatment techniques that are implemented in clinical practice, and then the CTST-FCM run and advised radiotherapists about the acceptance of the treatment planning technique.

The CTST-FCM model is an efficient and useful tool especially for this case of complex radiotherapy 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. In practice, the patient receives a different amount of dose than that determined during the treatment planning due to the presence of some other factors, more general, as machine factors, human factors, and quality processes [37,49] that influence the treatment execution. In addition to this, there are some factors on the CTST-FCM model, such as tumor localization and patient positioning, which 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, a better solution would be the designing of higher level with a new key-concept named "final dose" (FD). Concept FD would be affected by the parameters referred earlier and the OUT-Cs. The concept of "FD" is an extremely important concept describing the success of radiation treatment and so the prolongation of the patient's life. The purpose of the proposed approach is not to accurately calculate the amount of FD received by the patient, but to describe the success of the radiation therapy process in general and determining the value of FD. This highlights the need to construct a supervisor level.

6.6 Abstract Supervisor-FCM Model for Radiation Therapy Process

The supervisor level is higher than CTST-FCM model and is used for the parameters analyses and the final acceptance of the treatment planning technique. The two-level structure creates an advanced integrated system, which handles abstract information. The supervisor is modeled as an FCM that models, monitors, and evaluates the whole process of radiation therapy.

The supervisor-FCM is developed exploiting and utilizing experts' knowledge (doctors), who actually supervise the process. Radiotherapists usually use the notion and values of tumor localization, patient positioning, and the calculated dose by the treatment planning system to determine the FD [49,50]. They also mentioned that human factors and machine factors play an important role in the determination of the FD and they usually take these values into consideration. Experts, using this method of thinking and concluding, suggested the concepts of the supervisor-FCM.

The suggested supervisor-FCM consists of seven concepts to supervise the decision-making process during the radiation therapy process and it is

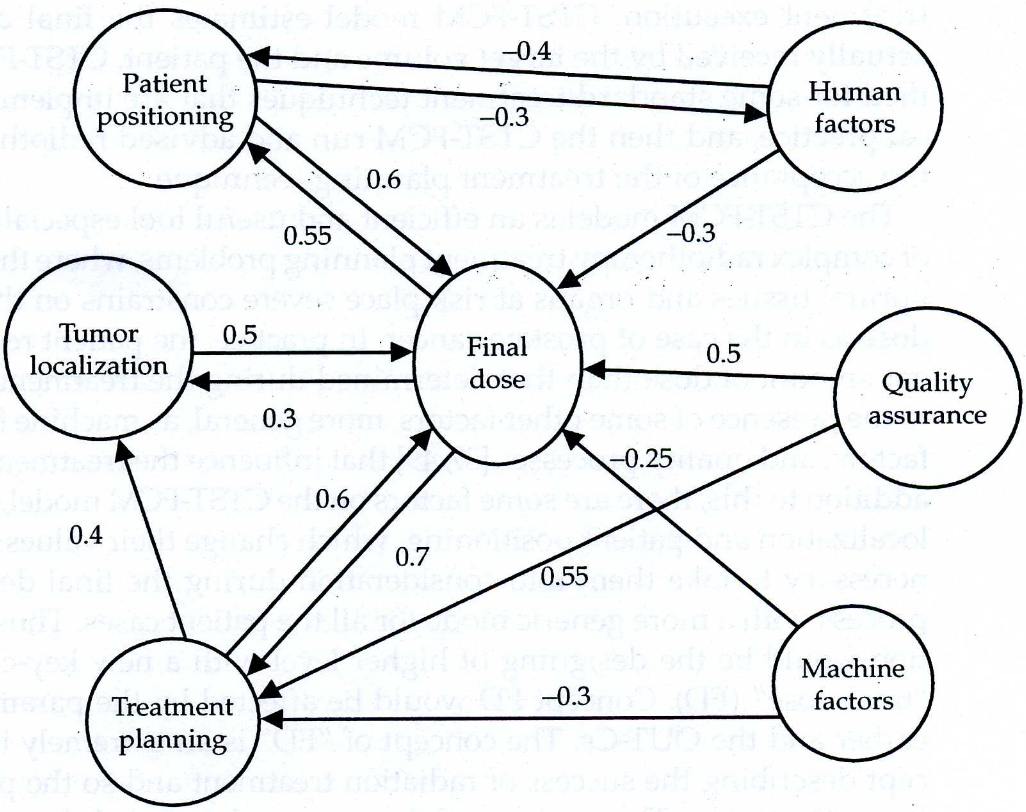

FIGURE 6.9
The Supervisor-FCM model of the radiotherapy process.

depicted in Figure 6.9. This model updates the first introduced supervisor-FCM and now one more concept has been added [21]. This new concept represents the quality assurance (QA) of the whole radiotherapy process. QA refers to the whole range of procedures and technical systems for assuring that the quality parameters of the process are in accordance with the national and international standards (preset) such as the International Standards Organization (ISO standards). Treatment planning systems, imaging devices, simulators, treatment units, checks of beam quality and inhomogeneity, and clinical dose measurements determine the QA process.

The concepts suggested by experts to include in the supervisor-FCM are as follows:

UC_1 *(tumor localization)*. It is dependent on the following three factors concepts of the lower level FCM: patient contour, sensitive critical organs, and tumor volume. It embodies the value and influences these three Factor-concepts.

UC_2 *(dose prescribed from treatment planning [TPD])*. This concept represents the prescribed dose and is dependent on the following concepts of the CTST-FCM model: the delivered dose to target volume, normal tissues, and critical organs that are calculated at the treatment planning model of the lower level FCM.

UC_3 (*machine factors*). This concept represents the equipment characteristics, reliability, efficiency, and maintenance.

UC_4 (*human factors*). A general concept that evaluates the experience and knowledge of medical staff, involved in the treatment.

UC_5 (*patient positioning and immobilization*). This concept describes the cooperation of the patient with the doctors and if the patient accurately follows their instructions.

UC_6 (*QA*). This represents and evaluates the qualifications of staff, the efficiency of therapeutic procedures, and the performance of technical systems for complying with the preset standards.

UC_7 (*final dose given to the target volume [FD]*). An estimation of the radiation dose received by the target tumor.

The methodology presented in Section 6.2 is used here to construct the supervisor-FCM. The experts are asked to describe the relationships among concepts and they use IF–THEN rules to justify the cause and effect relationship among concepts and infer a linguistic weight for each interconnection. The degree of the influence is a linguistic variable, member of the fuzzy set *T*{*influence*} as illustrated in Figure 6.2.

Experts suggested the following connections among the earlier-described concepts of supervisor-FCM:

Linkage 1. Connects UC_1 with UC_7: it relates the tumor localization with the delivered FD. Higher the value of tumor localization, greater the delivered final dose is.

Linkage 2. Relates concept UC_2 with UC_1: when the dose derived from treatment planning is high, the value of tumor localization increases by a small amount.

Linkage 3. Connects UC_2 with UC_7: when the prescribed dose from treatment planning is high, the FD given to the patient will also be high.

Linkage 4. Relates UC_3 with UC_2: when the performance of machine parameters increases, the dose from treatment planning decreases.

Linkage 5. Connects UC_3 with UC_7: any decrease to machine parameters influences negatively, the FD given to target volume.

Linkage 6. Relates UC_4 with UC_7: the human factors cause decrease in the FD.

Linkage 7. Connects UC_4 with UC_5: the presence of human factors causes decrease on the patient positioning.

Linkage 8. Relates UC_5 with UC_4: any decrease on the patient positioning negatively influences the human factors.

Linkage 9. Connects UC_5 with UC_7: when the patient positioning increases, the FD also increases.

Linkage 10. Relates UC_6 with UC_2: any increase on the QA (control) checks, positively influences the treatment planning.

Linkage 11. Connects UC_6 with UC_7: any increase on the QA (control) checks positively influences the FD.

Linkage 12. Relates UC_7 with UC_5: when the FD reaches an upper value, the patient positioning is influenced positively.

Linkage 13. Connects UC_7 with UC_1: any change in FD causes change in tumor localization.

Linkage 14. Connects UC_7 with UC_2: when the FD increases to an acceptable value, the dose from treatment planning increases to a desired one.

After the determination of the relationships and the kind of linkages among concepts, each one of the experts suggests one linguistic weight for each linkage. The linguistic weights for each linkage are aggregated to an overall linguistic weight, which is defuzzified and transformed into crisp weight, corresponding to each linkage. Thus, the following weight matrix for the supervisor-FCM is produced, with the following numerical linkage weights:

$$W^{\text{second level}} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0.5 \\ 0.4 & 0 & 0 & 0 & 0 & 0 & 0.6 \\ 0 & -0.3 & 0 & 0 & 0 & 0 & -0.22 \\ 0 & 0 & 0 & 0 & -0.3 & 0 & -0.3 \\ 0 & 0 & 0 & -0.4 & 0 & 0 & 0.6 \\ 0 & 0.55 & 0 & 0 & 0 & 0 & 0.5 \\ 0.3 & 0.7 & 0 & 0 & 0.55 & 0 & 0 \end{bmatrix}$$

Experts describe the goals of supervisor-FCM and set the objectives. One objective of the supervisor-FCM is to keep the amount of FD, which is delivered to the patient, between some limits, an upper FD_{max} and a lower limit FD_{min}. Another objective is to keep the TPD between maximum value TPD_{max} and minimum value TPD_{min}. These objectives are defined at the related AAPM and International Commission on Radiological Protection (ICRP) protocols [1,11,12], where the accepted dose levels for each organ and region of human body are determined. So, the overall objective for the upper level, the supervisor-FCM, is to keep the values of corresponding concepts, FD given to the target volume and TPD in the range of values:

$$0.90 \leq FD \leq 0.95 \tag{6.11}$$

$$0.80 \leq TPD \leq 0.95 \tag{6.12}$$

The supervisor-FCM evaluates the success or failure of the treatment by checking the value of the FD concept, whether the suggested treatment process is within the accepted limits or not for the specified case of treatment [50].

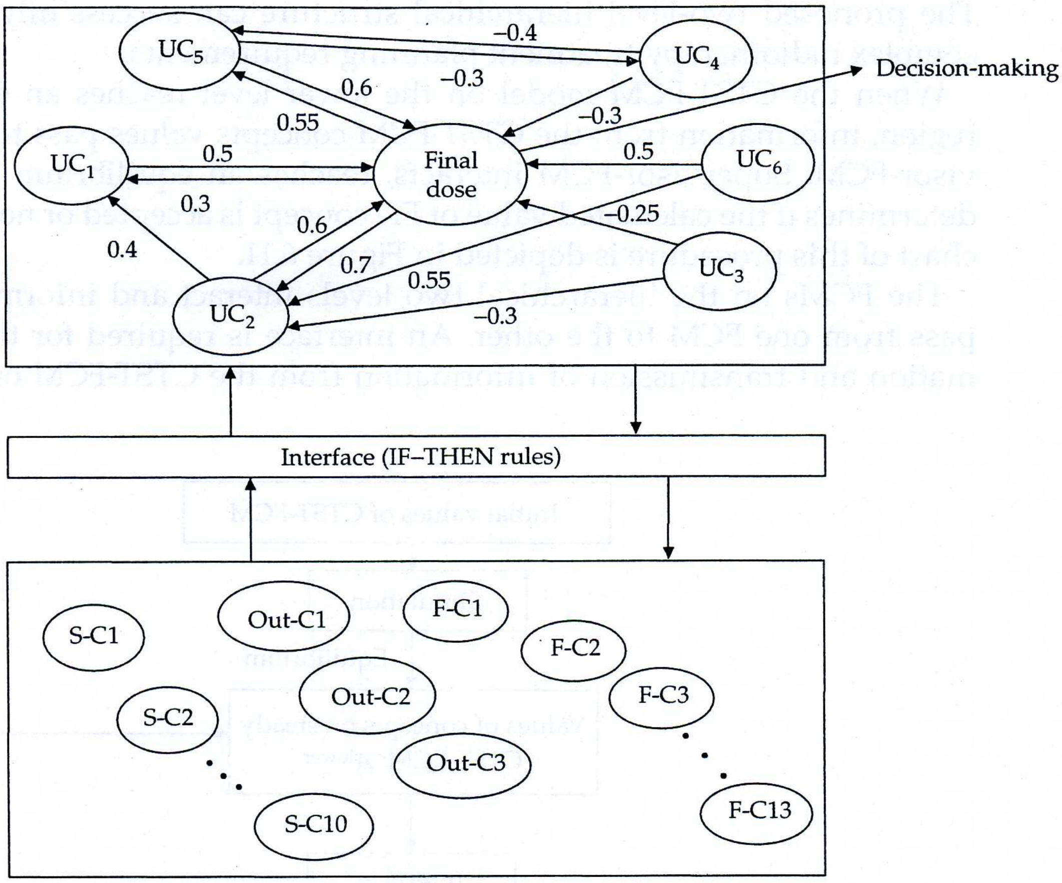

FIGURE 6.10
The integrated two-level hierarchical structure for decision making in radiation therapy.

A two-level hierarchical structure is proposed, which is illustrated in Figure 6.10. The CTST-FCM model for the radiotherapy treatment planning process, which was discussed in Section 6.5, is the lower level, where the 26 concepts of CTST-FCM model the treatment planning and the dose distribution to the target volume and normal tissues. Supervisor-FCM is the upper level, which is used for the determination of acceptance of the treatment therapy.

6.7 An Integrated Hierarchical Structure of Radiotherapy Decision Support System

The integrated hierarchical structure, consisting of the supervisor-FCM and the CTST-FCM, is the advanced DSS, which advises the radiotherapist–doctor on the decisions about the success of treatment therapy and the optimum treatment outcome. The supervisor-FCM aims to plan strategically and to detect and analyze unacceptable treatment before the execution of the treatment procedure. The main supervisory task is the coordination of the whole system, determining the amount of FD given to the target volume.

The proposed two-level hierarchical structure can successfully model the complex radiotherapy treatment planning requirements.

When the CTST-FCM model on the lower level reaches an equilibrium region, information from the CTST-FCM concepts values pass to the supervisor-FCM. Supervisor-FCM interacts, reaches an equilibrium region that determines if the calculated value of FD concept is accepted or not. The flowchart of this procedure is depicted in Figure 6.11.

The FCMs on the hierarchical two levels interact and information must pass from one FCM to the other. An interface is required for the transformation and transmission of information from the CTST-FCM on the lower

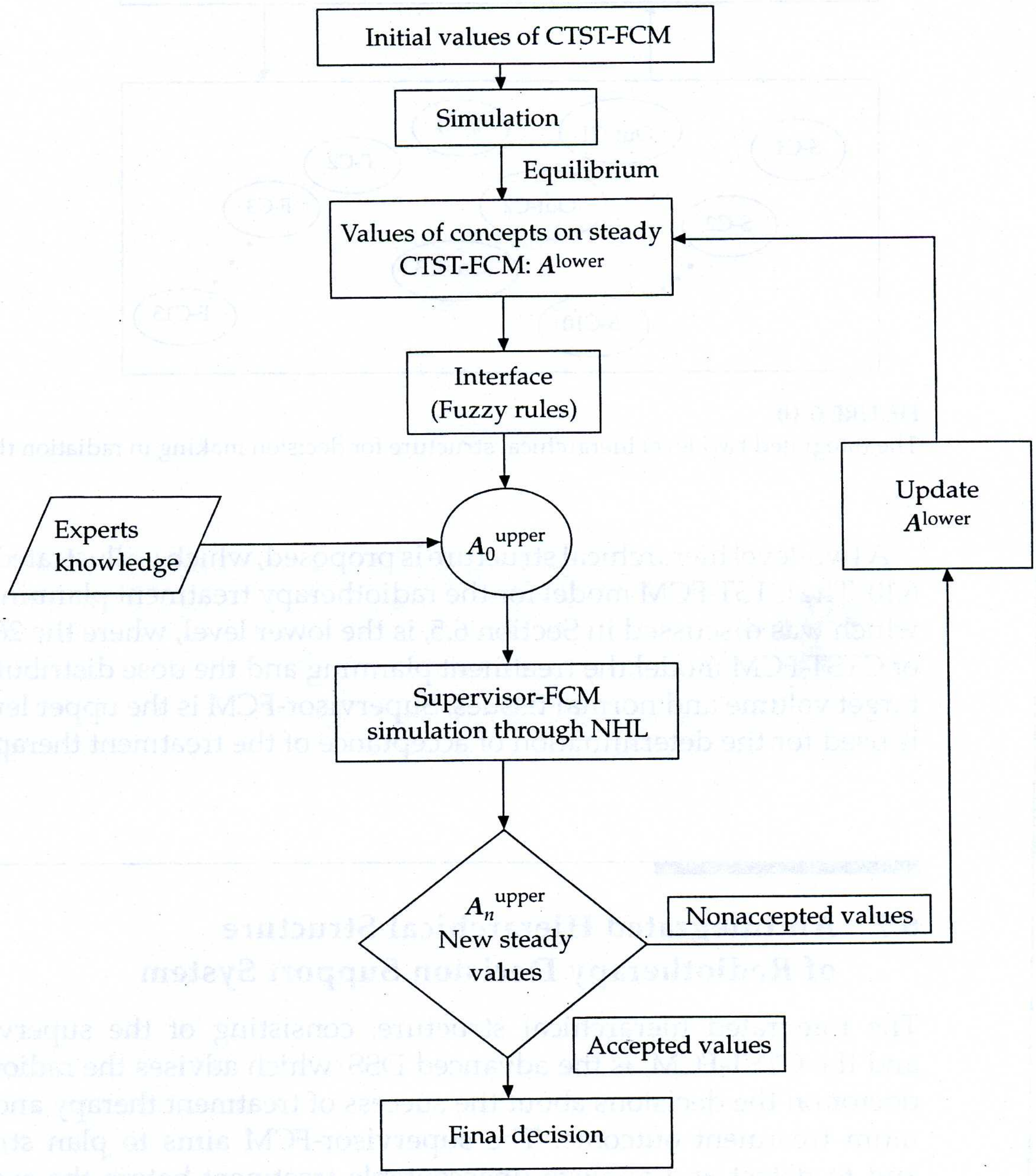

FIGURE 6.11
Schematic representation of the algorithm for supervision execution.

level to the supervisor-FCM on the upper level and vice versa. This interface consists of two parts; one part transmits information from lower level to upper level and the other part from upper level to lower level. Generally, the information from two or more concepts on the lower level CTST-FCM pass through the interface is aggregated and influence one concept in the upper level, and an analogous interface exists for the inverse transformation and transmission of information.

The interface is designed as a set of fuzzy rules. The transformation and transmission of information between concepts of two-level structures are representing using the IF–THEN rules that are embedded into the interface. The fuzzy rules take the values of concept as input from the lower level and infer the value of concepts on the supervisor-FCM. For example, information from the concepts of machine parameters at the lower level (Selector-concepts S-C7 and S-C8) pass through the interface and influence the concept of UC_3 "machine factors" at the upper level. Also, information from the Output-concepts (OUT-C1, OUT-C2, and OUT-C3) influences the UC_2 "dose from the treatment planning system." The following fuzzy rules 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 UC_2 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 UC_2 is the highest.
- IF value of OUT-C1 is high AND values of OUT-C2 OR OUT-C3 are low THEN value of UC_2 is high.
- IF value of OUT-C1 is very high AND values of OUT-C2 OR OUT-C3 are low THEN value of UC_2 is high.
- IF value of S-C3 is very low AND values of S-C7 AND S-C8 are very high THEN value of UC_3 is high.
- IF value of S-C3 is very low AND values of S-C7 AND S-C8 are the highest THEN value of UC_3 is very high.
- IF value of S-C3 is very low AND values of S-C7 OR S-C8 are very high THEN value of UC_3 is high.
- IF value of S-C3 is medium AND values of S-C7 OR S-C8 are medium THEN value of UC_3 is medium.
- IF value of S-C9 is very high THEN value of concept UC_5 is very high.
- IF value of S-C9 is the highest THEN value of concept UC_5 is the 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.

6.7.1 Estimation of the Success or Failure of the Treatment Therapy

The initial values of concepts on supervisor-FCM are determined by the values of concepts of lower level CTST-FCM model, through the interface described earlier, and also there are some external inputs for the values of concepts referred to as UC_5 "human factors" and UC_1 "tumor localization."

6.7.1.1 *Case Study 1*

Here, the case of Section 6.5 will be discussed under the aspects of the hierarchical two-level structure. The CTST-FCM that was used for the first test case of prostate cancer is the lower level FCM. As presented, this CTST-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:

$$A_1^0 = [0.75 \ \ 0.8 \ \ 0.3 \ \ 0.6 \ \ 0.7 \ \ 0.5 \ \ 0.65]$$

For these values of concepts, the supervisor-FCM is able to examine if they are within the accepted limits for the radiotherapy execution. The supervisor-FCM simulates through Equation 6.1 using the initial matrix A_1^0 and the initial weight matrix $\mathbf{W}^{\text{upper level}}$, to find an equilibrium region.

After 10 iteration steps, an equilibrium region is reached and Figure 6.12 gives the subsequent values of calculated concepts. Values of concepts UC_2

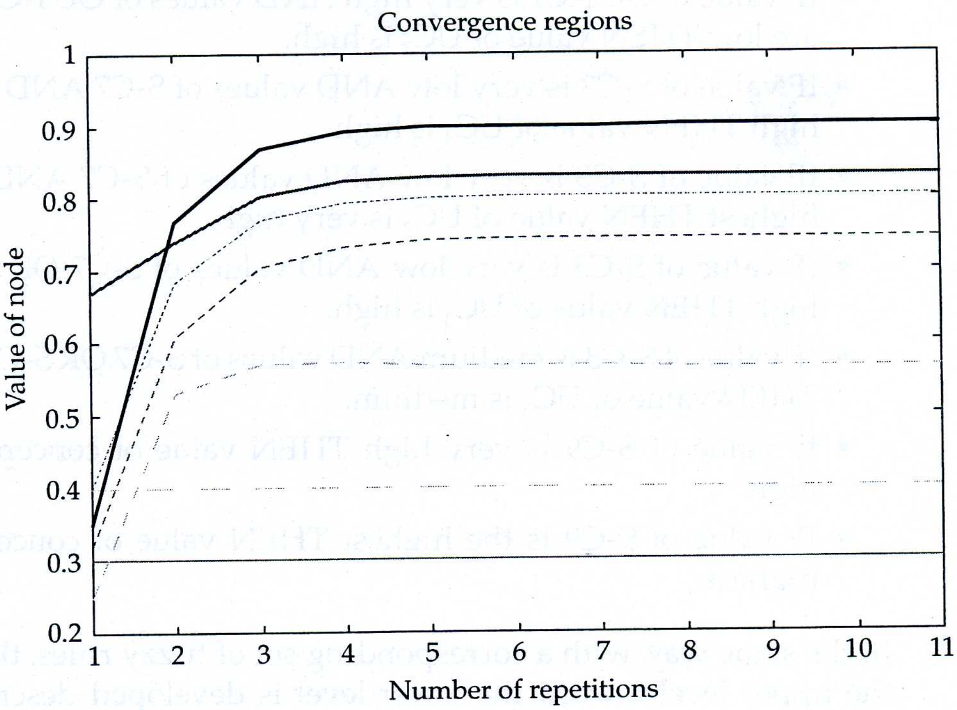

FIGURE 6.12
Equilibrium state for Supervisor-FCM model.

and UC_7, in the equilibrium region, are equal to the values 0.8033 and 0.89 where the value of FD is out of the suggested desired regions in Equations 6.11 and 6.12. Then according to the algorithm of supervision of Figure 6.11, we continue implementing the NHL algorithm.

The supervisor-FCM updates by the implementation of NHL algorithm, which is described in Section 6.3. After trial and error experiments for the specific supervisor-FCM model, the values of learning parameters η and γ have been determined as 0.04 and 0.98, respectively. The desired target values for each of the two DOCs are the mean values of the corresponding Equations 6.11 and 6.12: $T_1 = 0.875$ for the concept TPD and $T_2 = 0.925$ for the FD.

Equation 6.5 is used to modify the weights of supervisor-FCM, and Equation 6.3 is used to calculate the values of concepts after each simulation step. After 11 simulation steps, the supervisor-FCM reaches an equilibrium region, satisfying the criteria of algorithm in Equations 6.6 and 6.7:

$$\mathbf{A}_1^{\text{upper level}} = [0.8325\ \ 0.8462\ \ 0.3000\ \ 0.6055\ \ 0.7693\ \ 0.5000\ \ 0.9236]$$

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

$$\mathbf{W}_{\text{NHL}}^{\text{supervisor}} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0.54 \\ 0.465 & 0 & 0 & 0 & 0 & 0 & 0.61 \\ 0 & -0.1 & 0 & 0 & 0 & 0 & -0.043 \\ 0 & 0 & 0 & 0 & -0.105 & 0 & -0.078 \\ 0 & 0 & 0 & -0.23 & 0 & 0 & 0.611 \\ 0 & 0.52 & 0 & 0 & 0 & 0 & 0.386 \\ 0.409 & 0.681 & 0 & 0 & 0.54 & 0 & 0 \end{bmatrix}$$

The updated weights keep their initial suggested signs and directions, and their values within the initial ranges derived from the fuzzy linguistic variables, as suggested by expert doctors. Protocols and experimental data prescribe the final dose to patient for every treatment case.

In the first example, the calculated values for output concepts are TPD = 0.8462 and FD = 0.9236, respectively, which are within the acceptable values according to Equations 6.11 and 6.12 [50]. Radiotherapists can follow the suggested values and the treatment will be executed with successful results.

6.7.1.2 *Case Study 2*

To update the values of concepts at lower level, we follow the upper-lower interface and we change the values of the most important Factor-concepts and Selector-concepts. Also, at the same time, for the new employed technique or clinical case, we redefine some of the weights between SCs and OUT-Cs based on experts' suggestions. So, new values are assigned to the size of the radiation field (S-C3), beam direction (S-C5), weight of each field (S-C6), patient immobilization (S-C9), and increase the amount of perfect match of beam to the target volume (F-C15). These values along with the rest of the values of matrix $\mathbf{A}_2^{\text{lower level}}$ for the second case study result in producing the following matrix for the lower level:

$$\mathbf{A}_{21}^{\text{lower level}} = \begin{matrix}[0.5\ 0.5\ 0.5\ 0.6\ 1\ 0.5\ 1\ 0\ 0.5\ 0.3\ 0.6\ 0.5\ 0.5 \\ 0.75\ 0\ 0.8\ 1\ 0.8\ 0.4\ 0.6\ 0.5\ 0.5\ 0\ 0.8\ 0.2\ 0.4]\end{matrix}$$

The CTST-FCM with the new $\mathbf{A}_{21}^{\text{lower level}}$ interacts and new values for the 26 concepts are calculated according to Equation 6.3 and the newly 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 newly updated values of concepts from CTST-FCM model influence the upper concepts of supervisor-FCM through the interface again, determining the next new initial concept values:

$$\mathbf{A}_{21}^{\text{upper level}} = [0.87\ \ 0.81\ \ 0.2\ \ 0.4\ \ 0.65\ \ 0.5\ \ 0.86]$$

Then implementing the NHL algorithm for the supervisor-FCM, the following values of concepts on upper level are calculated: $\mathbf{A}^{\text{upper level}} = [0.857\ \ 0.832\ \ 0.2\ \ 0.621\ \ 0.85\ \ 0.5\ \ 0.91]$.

Thus, the value of UC_7 is FD $= 0.91$ and the value of UC_2 is TPD $= 0.832$, which are accepted for the treatment execution.

If the calculated values of TPD and FD were not accepted, then the procedure mentioned earlier for the final decision could continue until the calculated values of concepts FD and TPD would be accepted. In this way, the supervisor-FCM supervises the treatment for prostate cancer therapy with external beam radiation and more generally the whole procedure.

6.7.2 Evaluation of the Proposed Model

In this research, the FCM modeling methodology is introduced and utilized at lower level 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. The same modeling methodology is used at upper level to model abstractly and supervise the whole procedure of radiation therapy. For the supervisor-FCM, a novel training algorithm, the NHL is utilized to adjust the interconnections between the generic treatment variables of upper level and calculate the FD.

Weight adaptation and fine-tuning of supervisor-FCM causal links have great importance in updating the model to achieve acceptable results for radiotherapy techniques. This is the reason why we implement the NHL in the supervisor-FCM. Also, we should emphasize that using the NHL algorithm, we combine the human experts' structural knowledge with the data for each specific case. This is exactly the same with the reaction of a human expert who adapts his approach to the input data.

The doctor in charge usually evaluates the value of the FD given to the target volume, and the supervisor-FCM does exactly the same. In the case of unacceptable values for TPD and FD, some concepts on the lower level CTST-FCM have to be influenced; they take new values that causes the lower level CTST-FCM to interact. Then, the new calculated values of lower level, through the interface, determine again the values of upper level supervisor-FCM concepts. Implementing the NHL algorithm, the supervisor-FCM interacts and after some simulation steps, converges to an equilibrium region, which can be accepted or not, according to the related protocols.

Thus, radiotherapists can follow the suggested values and the treatment will be executed with successful results. The proposed approach is efficient and very useful for the FCM-controlled clinical radiotherapy process. The utilization of NHL algorithm recalculates all weights that participate in the simulation process, which enhances the supervisor-FCM model that was initially determined by expert doctors. Its importance to the radiotherapists is underlined by the fact that they will be able to introduce clinical cases based on a range of accepted values for the Output-concepts of the model.

Some requirements and limitations of the proposed approach are

- Experts should have great knowledge and know the proper operation of the whole system to provide useful information on desired values of Output-concepts.
- The proposed training algorithm does not derive new interconnections and there is no influence on the architecture of the FCM model.

6.8 Discussion and Conclusions

The soft computing approach of FCMs is used to determine the success of the radiation therapy process estimating the FD delivered to the target volume. The scope of this research is to advise radiotherapists to find the best treatment or the best dose. Furthermore, a two-level integrated hierarchical structure is proposed to supervise and evaluate the radiotherapy process before treatment execution. The supervisor-FCM determines the treatment variables of cancer therapy and the acceptance level of final radiation dose to the target volume. Two clinical case studies have been used to test the proposed methodology with successful results and demonstrate the efficiency of the CTST-FCM tool.

The proposed CTST-FCM model is evaluated for different treatment cases but it raises the need for an abstract model that will supervise it. An integrated two-level hierarchical structure is proposed, consisting of two-level FCMs to evaluate the radiotherapy planning procedure. The supervisor-FCM represents a second higher level control for prediction, decision analysis, and determination of the FD. The supervisor-FCM model is updated with the implementation of the NHL algorithm that adjusts the weights and ensures the success of the treatment therapy procedure.

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

This research work was focused on the study of knowledge representation and on the introduction of a two-level hierarchical model based on FCMs. For the radiotherapy planning model, the CTST-FCM model on the lower level was proposed and an abstract generic model to supervise the whole process was suggested, which was enhanced with learning methods to have better convergence results. Furthermore, an interface to transform and transmit information between the levels of hierarchy was described and an algorithm to ensure the flow and exchange of information within the integrated hierarchical system was proposed.

The proposed modeling method based on FCMs could improve the radiotherapist's ability to simulate the treatment procedure and decide whether the treatment execution will or will not be successful by taking into consideration the prescribed dose between the accepted limits. In addition to this, the radiotherapist can simulate the procedure before the treatment process starts. This proposed approach for decision making in radiotherapy was introduced to improve planning efficiency and consistency for treatment cases, selecting the related factors and treatment variables, describing and determining the causal relationships among them.

The proposed hierarchical structure can be easily implemented in clinical practice and thus provides the physicians and medical physicists with a fast, accurate, reliable, and flexible tool for decision making in radiotherapy procedures. The test cases, presented in this work, demonstrate the efficiency of the proposed integrated approach and give very promising results to develop intelligent and adaptive decision support systems for medical applications.

Acknowledgment

The work of Elpiniki I. Papageorgiou was supported by a postdoctoral research grant from Greek State Scholarship Foundation (I.K.Y.).

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