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Clinical Decision-Support Systems in Radiation Therapy

Nilesh L. Jain and Michael G. Kahn

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Clinical Decision-Support Systems in Radiation Therapy

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CLINICAL DECISION-SUPPORT SYSTEMS IN RADIATION THERAPY

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Computers have been used in radiation therapy since the early 1960s to perform dose calculations. In the last decade, researchers have developed computer-based clinical decision-support systems for assisting in different decision-making tasks in radiation therapy. This paper reviews eleven prototype systems developed for target volume delineation, treatment planning, treatment plan evaluation, and treatment machine diagnosis. The advent of three-dimensional (3D) conformal radiation therapy (CRT) provides radiation oncologists with the opportunity to consider innovative beam arrangements which were not possible in two-dimensional class solutions. The difficulty of manually generating the thousands of clinically plausible 3D treatment plans calls for the use of decision-support systems to generate them automatically. The large data sets generated in 3D CRT make manual treatment plan evaluation difficult, and call for the use of decision-support systems for objective radiation treatment plan evaluation. Computer-based optimization of 3D CRT can be then performed by combining the systems for automatic plan generation and objective plan evaluation.

Decision-support systems, Artificial intelligence, Decision theory, Computer-assisted 3D radiation treatment planning, Treatment plan evaluation, Target volume delineation.

INTRODUCTION

Computers have been used in medicine since the late 1950s, about a decade after the appearance of the first electronic computer (44). The first systems were developed primarily for repetitious and labor-intensive tasks, such as processing medical data (7). The need for and success of these early systems along with the phenomenal advances in computer technology has led to the proliferation of computer-based systems in delivering health care. At present, computers are being used mainly to perform medical tasks which can be easily automated. These systems include medical-record systems, hospital information systems, nursing information systems, laboratory systems, pharmacy systems, radiology systems, patient-monitoring systems, and bibliographic-retrieval systems (84).

Radiation therapy, with its need for computation-intensive dose calculations and image processing, was one of the first medical fields to make extensive clinical use of computers (25). Comprehensive treatment planning systems made their appearance in the middle of the 1960s, incorporating the repetitive tasks of calculating dose distributions for various kinds of external beam radiation treatment. Due to the limitations of computer technology, most early treatment planning was two-dimensional. However, with the availability of very fast computers at a reasonable cost

and with the advances in graphics, imaging and display technologies, three-dimensional (3D) treatment planning systems are becoming possible (75). The report of National Cancer Institute's Photon Treatment Planning Collaborative Working Group (85) concluded that 3D radiation treatment planning (RTP) is valuable because it provides a better view of the anatomical relationships and dose distributions (66, 67).

Researchers in medical informatics are interested in using computers to assist physicians and other health care personnel in difficult medical decision making tasks such as diagnosis, therapy selection, and therapy evaluation. *Clinical decision-support systems* are computer programs designed to help health care personnel in making clinical decisions (82). Since one of the first reported systems in 1964 (93), the field has matured considerably and has produced systems for various medical domains. Notable among these are MYCIN for the selection of antibiotic therapy (83), INTERNIST-1 for diagnosis in general internal medicine (51), and ONCOCIN for management of cancer patients (91). The two primary techniques used to construct clinical decision-support systems are *artificial intelligence* and *decision theory*.

Artificial intelligence (AI) is a branch of computer science concerned with the automation of intelligent behavior (45), attempting to make computers do things which people currently do better (73). One of the most visible and commercially-successful products of AI research are *expert systems* (63). An expert system is a computer program that relies on *knowledge* and *reasoning* to perform a task that is usually performed by human experts. Knowledge is stored in a knowledge base using various representation techniques. The most common representation techniques is IF-THEN rules, hence the term rule-based expert systems. Figure 1 contains a typical rule that might be used in radiation therapy treatment selection. Other representation techniques include frames, semantic networks, conceptual graphs, and scripts. *Knowledge acquisition* is the process of eliciting a knowledge base from a domain expert (19). Different reasoning strategies are used to arrive at conclusions based on the problem data and the knowledge base. In rule-based expert systems, the reasoning strategies used are forward chaining where the data are used to arrive at a conclusion, and backward chaining where a conclusion is tentatively assumed and the data are used to justify it. Other applications of AI include planning, vision, learning, and natural language understanding.

```
IF the primary tumor site is lung

THEN use parallel opposed AP/PA beams to deliver 4500 cGy
to the target volume and oblique (off-spinal cord) beams to
deliver an additional 200 cGy to the target volume
```

Fig. 1. A simple IF-THEN rule that can be used in radiation therapy.

Artificial intelligence has been applied to medical problems for the past two decades (10, 50, 89, 90). Most of the applications concentrate on diagnosis, therapy recommendation, and critiquing management plans. Researchers in medical AI have contributed significantly to advancing the state-of-the-art of AI research. They have developed prob-

abilistic reasoning techniques to handle uncertainty (9, 21), and temporal reasoning techniques to handle time (32), all of which are inherent in routine medical decision making.

Decision theory is a branch of operations research which provides an explicit methodology to handle preferences and uncertainty in making optimal decisions depending on the objectives of the decision maker (22, 72). The decision problem is structured as a decision tree starting with the available options (see Figure 2). At each stage, either the decision maker has a choice of other options, or a previous option can lead to few different events. In the latter case, the probability of each event is elicited. The tree is expanded until the final outcomes are reached. If the decision problem has a single objective, the *utility* (desirability) of each final outcome is elicited, the expected utility (based on multiplying utilities and probabilities) of each initial option is computed, and by the principles of normative decision theory, the option with the highest expected utility is chosen. Most non-trivial decision problems require the decision maker to fulfill multiple and often conflicting objectives. In these cases, it is difficult to elicit a single utility value for each outcome. In this setting, each outcome is divided into a number of attributes, each attribute usually corresponding to one of the objectives. Techniques of *multiattribute utility theory* are used for these problems (38, 92). In addition to the utility of each attribute, multiattribute *weights* are elicited to make trade-offs among the conflicting objectives. The overall utility of each outcome is computed by using a suitable combining function for the utilities and weights of the attributes.

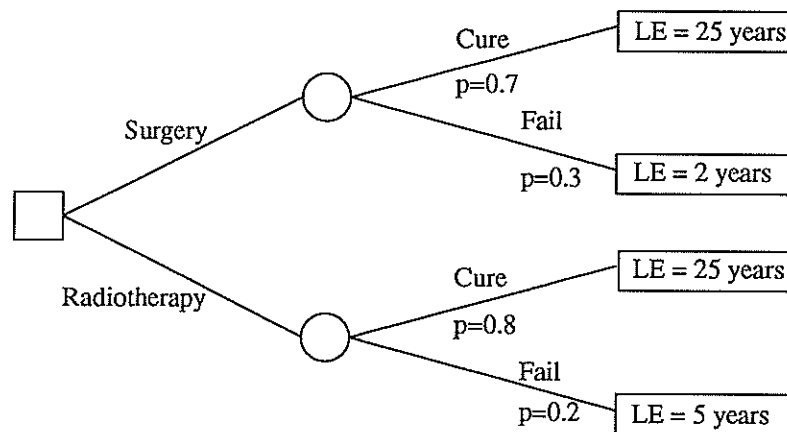


Fig. 2. A simple decision tree for choosing between surgery and radiotherapy. Squares represent choices or decisions, circles represent uncertain events, and rectangles represent final outcomes. (LE = life expectancy)

Clinical decision analysis has been applied to medical decision making problems for the past three decades (37, 65, 86, 94). Representative applications include choosing among treatments, choosing between treatment and no treatment, choosing between treatment and testing, and sequencing of therapy. Researchers developed Markov models to handle large decision trees with time-dependent events (4), uniform outcome measurement scales such as

quality-adjusted life years (69), and cost-effectiveness and cost-benefit analyses to trade-off expected health benefits versus costs (95).

With the advent of 3D conformal radiation therapy (CRT), treatment planning has become more difficult as the class solutions which were used in 2D RTP are no longer optimal (75). Instead of two or three potential plans based on 2D RTP standard solutions, hundreds or thousands of potential plans can be generated in 3D CRT. With the availability of real-time dose calculation, generating each plan is not as time-consuming as it used to be (74). However, current manual treatment planning methods are inadequate to generate all clinically-plausible plans. Hence, researchers have pointed out the need for AI applications to assist in automatically generating treatment plans (33, 36, 43, 97). In addition, the problem of automatic treatment plan optimization has gained renewed interest (52, 56). With the use of unconventional beam arrangements such as non-coplanar beams, the treatment planner can no longer use intuition to infer dose distributions in other planes by looking at the dose distribution in only one plane. Also, 3D CRT produces large data sets which must be used in the evaluation phase of treatment planning. The task of evaluating potential 3D treatment plans has become very difficult (15). Hence, researchers have been pointing out the need for objective plan-evaluation methods which can use this data (76). Since the evaluation of potential plans involves making trade-offs between the doses delivered to the target volumes and to the normal tissues, decision theory can be used for developing such models. The potential use of decision theory in radiation therapy evaluation was first pointed out two decades ago (57, 77). However, nearly ten years passed before the first such model was developed (79).

The past decade has seen an increasing number of decision-support systems in radiation therapy which can be classified into four categories — AI-based systems for target volume generation, AI-based systems for automatically generating treatment plans, decision-theoretic systems for evaluating competing treatment plans, and AI-based systems for diagnosing treatment machine failures. Although decision-support systems have been developed for other aspects of oncology such as diagnosis (3, 11, 13, 46, 64) and selection of treatment modality (47, 48, 49, 53, 54, 68, 87), we review the key features of a selection of systems designed specifically for radiation therapy decision-making.

TARGET VOLUME GENERATION

The consistent addition of margins to the gross tumor to account for possible microextensions of the tumor and patient motion is a difficult problem. We have identified one research group currently developing an AI-based system for the automatic generation of the planning target volume.

PTVT

PTVT (Planning Target Volume Tool) is a rule-based expert system to generate the planning target volume developed by Kromhout-Schiro (currently at University of North Carolina, Chapel Hill) et al. at the University of Washington,

Seattle (40). This system is one of a set of 3D CRT tools developed as part of National Cancer Institute's Radiotherapy Treatment Planning Tools Contract (71). PTVT calculates the planning target volume by adding a region of tissue to the gross tumor volume.

Four factors are considered in computing this additional region:

1. areas of tissue adjacent to the visible tumor that may contain microscopic amounts of tumor;
2. errors in positioning the patient for treatment;
3. patient movement during treatment;
4. movement of tumor due to physiologic processes such as breathing.

Data concerning these four factors were gathered from the literature as well as from local radiation oncologists, and were indexed according to the clinical condition of the patient and the clinical characteristics of the tumor. Preliminary evaluation found the generated planning target volumes to be consistent with those manually outlined by the radiation oncologists.

AUTOMATIC TREATMENT PLANNING

The step in RTP investigated by most decision-support investigators is the automatic generation of plausible or optimal radiation treatment plans. We describe the efforts of six research groups which either have developed or are currently developing AI-based systems for automatic treatment planning. Each of these systems focuses on a particular tumor site to make the knowledge acquisition manageable. However, the techniques used in these systems can be applied to other tumor sites by suitable augmentation to the knowledge base.

ROENTGEN

ROENTGEN is a case-based reasoning system for lung cancer currently being developed by Berger et al. at the University of Chicago (5, 6). Case-based reasoning is an AI technique where the solution to the current problem is found by adapting the solution of a previously-solved similar problem (18). All problems and solutions are stored in an indexed case library, the indices are used to retrieve a similar problem, its solution is repaired to account for the differences between the current and the retrieved problem, and the new solution is stored in the case library enabling the system to learn from its problem-solving experience.

ROENTGEN has five modules for the five steps it follows in designing a treatment plan. Given the description of the current patient and the desired prescribed target dose, the *Retriever* module finds a similar prior case from the case library. To facilitate the retrieval, therapy plans have preconditions for their selection based on tumor location and patient geometry. If more than one prior plan satisfies the preconditions, other plan-specific features are used and the prior plan with the best match is retrieved. If this still yields more than one plan, the simplest prior plan based on the

number of beams, and the number of beam energies, is chosen. The *Adapter* module then modifies this retrieved plan to account for the differences between the current patient and the previous patient whose plan was retrieved. The adaptation process also uses the plan-specific features used by the *Retriever* by changing them until they are correct for the current patient. Having obtained a potential current plan, the *Detector* module tries to determine the result of applying the plan by using the resulting dose distribution. It then produces a list of faults indicating areas in the treatment field containing hot spots or cold spots. This list is compared with expected failures which is the fault list of the retrieved prior plan. If an unexpected fault occurs, the *Corrector* module asks a human expert for the relevant knowledge to repair the plan so that this unexpected fault will be eliminated. This plan is passed through the *Detector* again to make sure no new unexpected fault develops. At this point, a new treatment plan has been designed for the current patient, and it is added to the case base by the *Storer* module along with the plan-specific features and other information. Figure 3 contains a simplified system diagram explaining the relationships among the various modules and the working of the system.

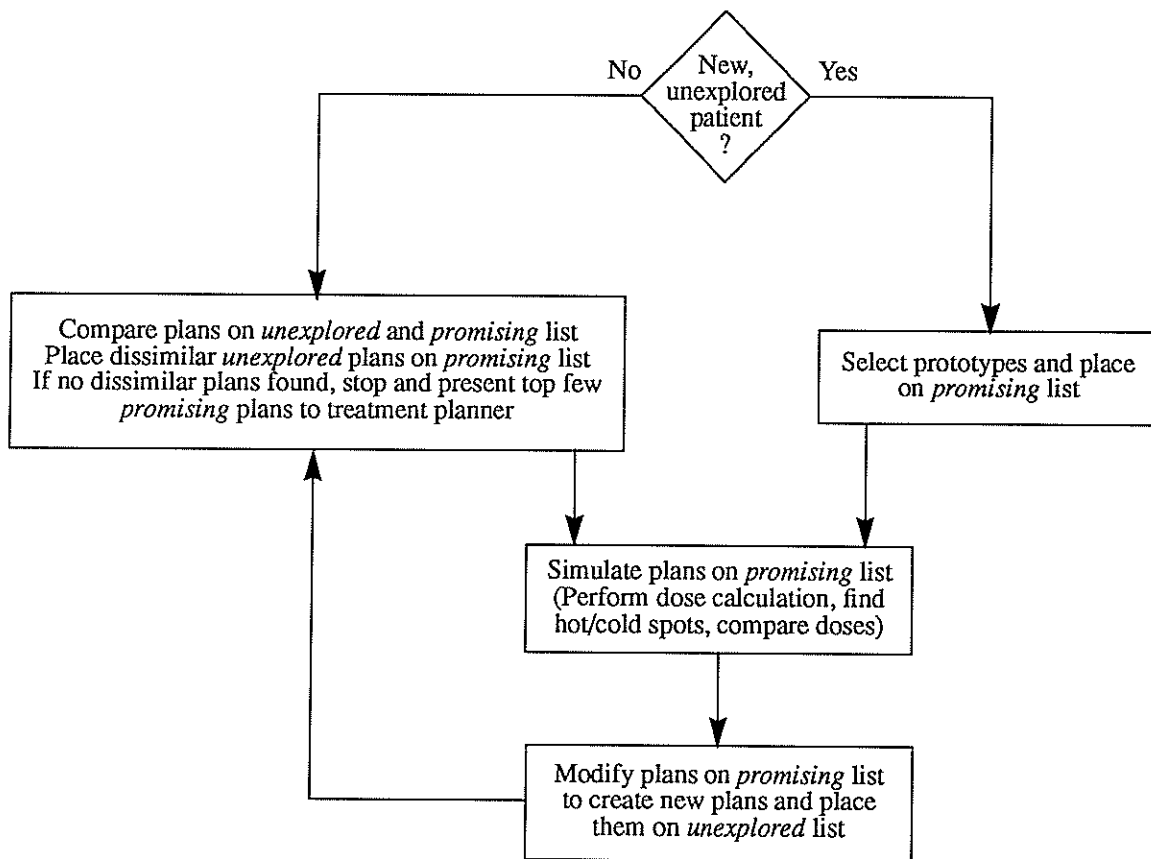


Fig. 3. Simplified system diagram for ROENTGEN. (Modified from: Berger, J. ROENTGEN: Case-based reasoning and radiation therapy planning. In: Frisse, M. E., ed. Proceedings of the Sixteenth Annual Symposium on Computer Applications in Medical Care. New York, NY: McGraw-Hill; 1992:210-214.)

It is important to note that ROENTGEN only designs a plausible treatment plan, and leaves it up to the human designer to decide whether this plan is optimal or not. Individual modules can be used for different tasks. The *Retriever* and *Adapter* can suggest plans to a novice designer. The *Detector* can be used as a critic for manually generated plans.

RADEK

RADEK is a rule-based expert system for head and neck tumors developed by Paluszynski (currently at University of Wroclaw, Poland) et al. at the University of Washington, Seattle (58). Initially, a simple rule-based system determines the treatment modality and the prescription dose for the primary tumor and nodal metastases (35). In RADEK, treatment planning begins by selecting with one or more prototypic plans from a library of standard starting plans traditionally used by the local treatment planners, and placing them on a list of *promising* plans (34, 60). This selection is based on the tumor site, shape and size of the patient, and prescription dose.

RADEK must evaluate *promising* plans to determine if they are clinically acceptable, if they can lead to acceptable plans, or if they should be discarded. The system performs this evaluation by plan simulation which involves calculating the dose distribution, determining the volume of hot and/or cold spots, and comparing the peak doses and integral doses in the various tissues (59). Based on the results of this evaluation, some *promising* plans are modified to create new treatment plans which are marked as *unexplored*. Because this step can generate a large number of *unexplored* plans and the evaluation can become time-consuming, *unexplored* plans are compared to previously evaluated *promising* plans to prune plans that are very similar (59). Only dissimilar plans are placed on the *promising* list to be evaluated. The planning process stops when no new plans are placed on the *promising* list after the similarity-based pruning. This resulting plan is presented to the treatment planner. Figure 4 contains a simplified system diagram.

CARTES

CARTES (Computer Aided RadioTherapy Expert System) is a decision-support system for inoperable non-small cell lung cancer developed by Hyödynmaa, Kolari et al. at the Technical Research Center, Finland (39). It is a part of the Nordic program CART (Computer Aided RadioTherapy) to develop an integrated information system for radiotherapy (42). Three stages in cancer therapy were identified where AI techniques could be applied — treatment decision making, design of new treatment protocols, and analysis of treatment results. CARTES is a prototype of the first and third stages, and no prototype was built for the second stage.

The prototype for the first stage (treatment decision making) uses relevant data and information about the social and medical history of the patient, clinical signs and symptoms, results of various tests and examinations, and the intention of the therapy (23, 39). The information is obtained automatically from an integrated clinical database, or directly from the user. CARTES acts as a critiquing system by checking if the diagnosis made by the physician agrees

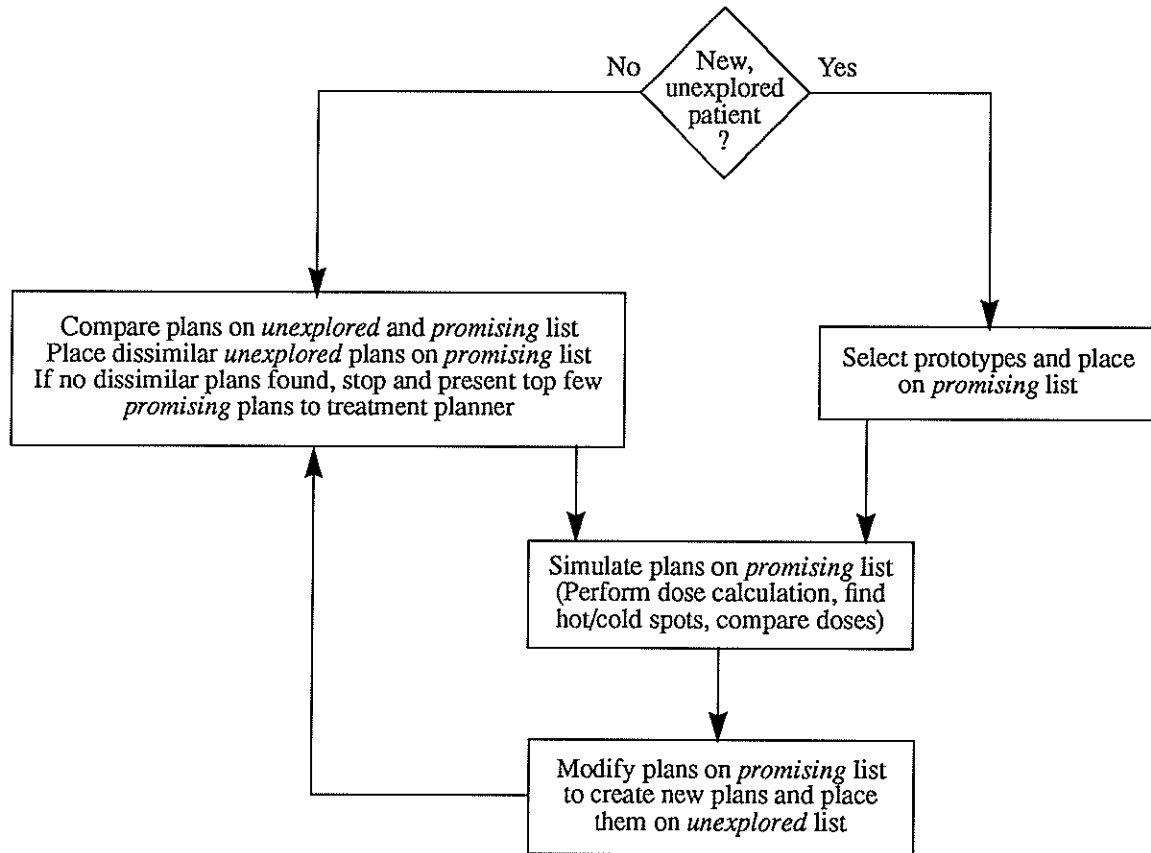


Fig. 4. Simplified system diagram for RADEK. (Modified from: Paluszynski, W. Designing Radiation Therapy for Cancer: An Approach to Knowledge-Based Optimization. Ph.D. Dissertation, Department of Computer Science. Seattle, WA: University of Washington; 1990.)

with the patient's clinical data, and whether the chosen therapy intent is appropriate in this case. It also determines if the patient has any symptoms which would indicate immediate treatment. The intended users of this first stage prototype are young physicians without much experience in cancer therapy.

The prototype for the third stage (analysis of treatment results) uses the treatment results and follow-up data gathered from a set of treated patients (24). This data comes from the clinical register which acts as a data bank for all therapeutic information. The goal is to provide the oncologist with an intelligent user interface to a statistical analysis software package to assist in preparation and specification of data, problem formulation, and interpretation of the outcome. This statistical analysis helps in quality assurance of the therapy and can provide feedback to the prototype for the first stage performing treatment decision making.

RADONCOL

RADONCOL is a rule-based system for head and neck tumors developed by Ionescu-Farca et al. at Rätisches Kantons- und Regionalspital, Switzerland (27, 28). It uses clinical information such as the case description, tumor site, extent of disease, staging, Karnofsky performance of the patient and other factors to recommend the appropriate treatment. The system is built using a commercial expert system shell and has about 300 rules. It uses backward chaining — it reasons from the goal of finding the appropriate therapy to the available clinical data. Certainty factors are used to handle multiple solutions. RADONCOL provides explanation about its reasoning, and the knowledge base can be modified and augmented.

Given the clinical data, RADONCOL determines the primary treatment modality, and the chronological order when more than one modality is indicated. If radiation therapy is one of the selected modalities, the system prescribes the dose and fractionation, and recommends a basic or standard beam arrangement based on a library of prototypical plans.

CAVCAV

CAVCAV is a rule-based expert system for cavum cancers developed by Aletti et al. at the Alexis Vautrin Center, France and Haton et al. at the University of Nancy, France (1, 2, 20). The system performs treatment planning in three phases. The first phase consists of the basic treatment up to 40 Grays. Using information about the tumor and abnormal ganglions, the system specifies a beam arrangement, nature and energy of the beams, and protective devices needed for sensitive organs such as the eye. In the second or boost phase ranging from 40 to 50 Grays, the precise location and shape of the target volume is used to arrive at an optimal treatment plan. The criteria used to determine optimality include maximization of tumor coverage, and minimization of surface inside the 90% isodose. The third phase consists of scheduling the extra irradiation based on the tumor irradiation in the first two phases and the patient's availability for treatment.

National Institute for Cancer Research, Italy

Paoli et al. at the National Institute of Cancer Research, Italy have developed an expert system for head and neck cancers (62, 78). The expert system consists of two parts:

1. a neural network to arrive at a general treatment plan;
2. a rule-based system to define the complete treatment plan.

The neural network uses anatomical, morphological and functional data obtained from CT images to determine the standard treatment plan which has the highest probability of success. The rule-based expert system then starts with this plan, uses clinical and dosimetric data from a relational database, and a heuristic knowledge base encoding the treatment planning expertise of local experts to arrive at a complete treatment plan.

This group is currently working on a rule-based expert system for total body irradiation in leukemia (61).

TREATMENT PLAN EVALUATION

In addition to generating treatment plans, another significant and interesting problem is the evaluation of competing radiation treatment plans. Currently, most treatment plan evaluation is performed manually by radiation oncologists using subjective techniques. We describe two research projects which have used multiattribute utility theory for the objective evaluation of competing radiation treatment plans.

Schultheiss' Model

Schultheiss (currently at Fox Chase Cancer Center, Philadelphia) at Eastern Virginia Medical School, Norfolk, used multiattribute utility theory for the evaluation and optimization of radiation treatment plans (79, 80, 81). The component attributes of his multiattribute model were the possible clinical complications of treatment such as non-eradication of the tumor and radiation-induced damage to the healthy normal tissues appearing in the treatment field. For each attribute, he computed its *utility* by combining the *probability* that the associated complication occurs with a *weight* representing the morbidity of the complication. The utilities of all the attributes were multiplied together to arrive at the overall utility for the plan known as its *figure of merit (FOM)* using:

$$FOM = \prod_i^{\text{complications}} (1 - \text{probability}_i \times \text{weight}_i) \quad (1)$$

The *FOM* was used as an objective function for an automatic optimization algorithm that attempted to obtain a statistically optimal treatment plan. Complication probabilities were obtained from dose-response models developed by Schultheiss. Weights were the subjective judgment of the physician about the morbidity of the complication. However, while evaluating his decision-theoretic model, Schultheiss set $\text{weight}_i = 1$ so that the *FOM* effectively computed the probability that no complication occurs.

Jain's Model

Jain et al. at Washington University, St. Louis extended Schultheiss' model to include the treatment preferences of the radiation oncologist as well as the clinical condition of the patient (30, 31). Like PTVT, this system is also one of the tools being developed as part of National Cancer Institute's Radiotherapy Treatment Planning Tools Contract (71). The model extension was done by making the *weight* a function of two quantities: *prototypical weight* and *modifier*. The prototypical weight represents the morbidity of the complication for an average patient for the treating radiation oncologist. The modifier encodes the clinical condition of the patient which would change the prototypical weight. The probability of complication was computed from radiobiological probability computation models such as the Tumor Control Probability (TCP) (16) and the Normal Tissue Complication Probability (NTCP) (41).

Unlike Schultheiss, Jain elicited weights from radiation oncologists for three tumor sites — prostate, lung, and head and neck. Two different methodologies were used — Level of Concern (30) and Level of Enthusiasm (31) — both of which were variants of the direct rating method of multiattribute weight elicitation. In response to physicians' concerns, additional attributes were added to the model to handle different fractions of the volume of a tissue exceeding threshold dose. A clinical study is underway to validate this model in the context of three-dimensional radiation treatment of non-small cell lung cancer (17).

Preliminary evaluation of the model indicated some shortcomings due to the unreliability of the TCP and NTCP models as well as the low values for the complication probabilities. Research is underway to investigate a new model which eliminates the shortcomings in the current model (29).

TREATMENT MACHINE DIAGNOSIS

In addition to the clinical systems described in the previous three sections, researchers have also focused on the non-clinical aspects of radiation therapy such as delivery of the radiation. This step can be hindered by the failure of the treatment machine. Two research groups have developed expert systems for the diagnosis and troubleshooting of different treatment machines.

TROUBLESHOOTER

TROUBLESHOOTER is a rule-based expert system developed by Curran et al. at the Tufts–New England Medical Center to handle hardware failures and operator errors that may occur with Varian Clinac 4/100 and 6/100 linear accelerators during clinical operation (12, 88). The system is built using a commercial expert system shell and has about 400 rules. The system first elicits the symptoms from the user through a series of menus. Backward chaining is used to evaluate the possible malfunctions using a pre-specified list of potential subsystem failures. Forward chaining is then used to arrive at the precise diagnosis and to make repair suggestions.

Philips SL-25 Linac Diagnostics

Myers (currently at University of Pennsylvania, Philadelphia) et al. at University of California, Los Angeles developed a rule-based expert system for general machine diagnosis and troubleshooting of the Philips SL-25 Linac (55). Knowledge is organized in a hybrid of object-oriented and rule-based framework. The objects include components arranged in a semantic network, as well as symptoms and tests. The system assists the user in navigating through the semantic net to find the minimum replaceable component. The knowledge base is updated after each session so that the system becomes more efficient as it is used.

FUTURE DIRECTIONS

A patient diagnosed with cancer is treated using one or more of surgery, radiotherapy and chemotherapy. If radiation therapy is one of the selected treatment modalities, the following steps are undertaken to deliver it:

1. The patient undergoes imaging using computerized tomography (CT) or magnetic resonance imaging (MRI) to determine his/her internal anatomy. Typically 20-30 slices/scans are taken to cover the region of interest.
2. The radiation oncologist delineates the target volumes on all images and prescribes a radiation dose.
3. Normal tissues occurring near the target volume are also contoured as the dose delivered to them needs to be minimized to prevent radiation-induced damage.
4. Various treatment plans are designed for the patient.
5. The competing plans are evaluated to select an optimal plan.
6. The patient is filmed in the proposed treatment position to simulate the treatment and verify that the treatment achieves its goal.
7. The treatment is delivered.

The systems described in this paper represent promising prototypes for steps 2, 4, 5, and 7. However, most of these steps will have to be revisited in the 3D CRT era which is going to pose new unforeseen challenges requiring computer-based decision-support. In this section, we outline some of the opportunities or the grand challenges for future decision-support systems in radiation therapy.

Target Volume Delineation

The International Commission on Radiation Units and Measurements (ICRU) soon will be publishing its report defining the three target volumes which should be specified by the radiation oncologists for treatment planning (26). The Gross Tumor Volume (GTV) will refer to the gross palpable or visible/demonstrable extent and location of the tumor. The Clinical Target Volume (CTV) will extend the GTV to include the microscopic extensions that need to be treated. The Planning Target Volume (PTV) will add margins to the CTV to account for organ and patient movement, and inaccuracies in beam and patient set up. Additionally, ICRU will require investigators to report three dose values for the target dose – maximum dose, minimum dose, and dose at the ICRU reference point which is a point in the PTV where the dose can be accurately measured and is not in a region having a steep dose gradient. Such standardization is necessary for meaningful comparison of tumor control data from clinical trials performed at different institutions. Radiation oncologists will need assistance to consistently follow these guidelines in defining GTV, CTV and PTV, and reporting target volume doses (70).

Initial difficulty for the radiation oncologists in following these recommendations will occur as most institutions currently follow their own standard. Knowledge-based decision-support systems like PTVT will be invaluable for consistent use of the ICRU recommendations. Although PTVT is a prescriptive tool, it could be modified into a

critiquing-based tool which ensures that the volumes being used by the radiation oncologist are consistent with the ICRU terminology.

Normal Tissue Contouring

Outlining normal tissues on all CT or MR images is a labor-intensive and time-consuming task (14). Research is underway in structural biology to build a knowledge base about the anatomical structure of the human body (8). The knowledge base will have two kinds of information — spatial and symbolic. The spatial information will be in the form of CT slices of a male and female cadaver to encode the physical structure of the human body. This will be annotated by symbolic information containing the names of the tissues, their hierarchy and other anatomical facts. Such a knowledge base can be used to enhance automatic contouring algorithms which attempt to perform the time-consuming task of contouring normal tissues on each image. Since the anatomical knowledge base will be composed of CT slices, the location of the image within the body will give information on the tissues expected on that slice along with their approximate shape. This will enable edge-detection algorithms to make intelligent choices when the image contrast is not that high on a particular portion of the slice. The knowledge base will also facilitate consistent inclusion or exclusion of tissue in the low contrast regions to develop a consistent 3D reconstruction of the tissue.

Treatment Plan Generation

Perhaps the most challenging task in the radiation therapy process is treatment plan generation, bringing to bear all the skills and experience of the treatment planners. The advent of 3D CRT makes heavy demands on treatment planners as the class solutions used in traditional 2D RTP are not optimal. Also, treatment planners no longer are restricted to a single plane, but can plan and deliver treatments having non-coplanar beams. The relaxing of these restrictions makes the solution space of plausible 3D treatment plans much larger than that for 2D RTP. Conservative estimates of simple four beam plans suggest that the number of possible treatment plans may run into the millions of millions, though not all of them will be clinically plausible. Even with real-time 3D dose calculation, the time required to examine each of them automatically to find the optimal solution will be impractical. Clearly, there is need for knowledge-based techniques to generate plausible treatment plans automatically.

The systems described in the section **Automatic Treatment Planning** use *ad hoc* rules to move or add beams to generate treatment plans, giving rise to the possibility of generating clinically implausible plans. The anatomical knowledge base described in the previous subsection could be used to perform the kind of anatomical reasoning performed by treatment planners while manually designing treatment plans. Such a system would reason about the shape and position of the various tissues in the treatment field, and attempt to design beams which spare the critical normal tissues as much as possible, and at the same time deliver the prescribed dose to the planning target volume. The system can also be given information about the relative importance of the various tissues in the treatment field to make tradeoffs among the tissues while positioning a beam. Anatomical reasoning is similar to the spatial reasoning problem being investigated by researchers in robotic planning.

Systems performing anatomical reasoning will endeavor to generate a treatment plan from scratch, and thus will need to contain a vast amount of treatment planning knowledge. An alternative to this approach uses case-based reasoning, as exemplified by ROENTGEN. By sharing treatment plans across institutions, it would be possible to build large case libraries containing many of the possible variation in the types and locations of tumors. The decision-support challenge will then be to devise a suitable metric to categorize patients, tumors and treatment plans to facilitate the accurate retrieval of one or more similar treatment plans.

Treatment Plan Evaluation

The treatment plan evaluation systems described here, as well as the mathematical optimization algorithms investigated by other researchers, are increasingly relying on TCP and NTCP values to characterize outcomes. While these concepts represent the ultimate bottom line for outcomes, state-of-the-art TCP and NTCP models are still not reliable and have not gained clinical acceptance. This lack of reliability is evident from the caveats mentioned by most authors while defending the use of current TCP and NTCP models (15, 31, 56). One way of getting more realistic outcomes data may be to construct a national (or international) outcome database of patients which contains image data along with dose distributions of the administered treatment plan. Patient follow-up and outcomes will allow researchers to use actual outcomes data for treatment plan evaluation and optimization. This data also can assist in validating current and future TCP and NTCP models.

With 3D CRT, it is possible to deliver higher doses to the target volume while keeping normal tissues below acceptable thresholds. This new capability is allowing radiation oncologists to increase the target dose to test the hypothesis that increased target dose improves local control (96). Such dose escalation studies are a major focus of current clinical radiation oncology research. An NCI-sponsored multi-institutional clinical trial to study the impact of dose escalation in carcinoma of the prostate is scheduled to begin this year. One project goal is to create a national outcomes resource database for 3D CRT prostate treatment planning data.

Evaluating treatment plans at escalated dose levels is difficult for two reasons — TCP models which are unreliable at normal prescription dose levels are equally or perhaps more unreliable at higher levels, and not enough clinical data is available to make subjective estimates of the tumor control rate. Hence the evaluation of plans has to rely on other criteria to characterize the outcomes. Treatment objectives can be stated in terms of prescribed target dose and the desire to minimize dose to the normal tissues. Decision theory provides the framework to elicit utility functions to indicate how closely these objectives are met. This information could be used to compute the overall utility of the plan or its figure of merit and could be used for treatment plan evaluation.

Treatment Optimization

We earlier highlighted the difficulty of manually generating all the clinically plausible 3D treatment plans and the need for decision-support systems to perform this task. A similar argument could be made for the manual optimiza-

tion of 3D plans as the treatment planner would have to consider all plausible plans to select the most optimal plan. Objective plan-evaluation models could be used for the automatic optimization of treatment plans by detecting the clinically plausible 3D plan with the highest figure of merit. Since 3D dose calculations can be performed in real-time, the computational cost of performing such optimization will not be very high (74).

Decision-support systems can also be developed to assist in the manual or semi-automated optimization of treatment plans. Using an anatomical knowledge base, a critiquing system could examine a proposed treatment plan and suggest possible improvements to it. By combining this critiquing system with objective plan-evaluation models, it could suggest the change which would result in the greatest improvement in the figure of merit of the plan. This design would be the best kind of decision-support system for treatment planners who want to remain in the optimization loop as it would work using the starting points suggested by the treatment planner.

Treatment Delivery

One of the neglected issues in treatment plan evaluation and optimization has been the complexity of delivering the treatment plan. The use of multiple energies, or other complex maneuvers, leads to an increased chance of error in delivering the treatment. While there has been a steady increase in the number of computer-controlled treatment machines, the need to incorporate the treatment plan complexity into the evaluation and optimization of radiation treatment plans is still required. Artificial intelligence techniques such as case-based reasoning possibly could be used for computing the complexity of a treatment plan. Research also needs to be done on decision-support systems for diagnosis and repair of treatment machines.

CONCLUSION

This paper examines eleven prototype decision-support systems developed to assist in various steps in the radiation therapy of a cancer patient. With the imminent 3D CRT era, a complete transformation will occur in the way in which radiation therapy personnel perform their tasks. The increased number of possibilities and amount of information will require radiation therapy to use decision-support technology to best exploit the advantages of 3D conformal therapy. We have described some of the specific advances that we foresee or that are necessary for better decision-support. Completely untapped is the potential pedagogical use for the tools that could be developed to instruct residents in the art of designing, evaluating and optimizing 3D radiation treatment plans.

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