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IMRT · IGRT · SBRT

Advances in the Treatment Planning and Delivery of Radiotherapy

Editor
John L. Meyer

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Frequently Used Abbreviations

3DCRT	Three-dimensional conformal radiation therapy
CTV	Clinical target volume
DVH	Dose-volume histogram
EPID	Electronic portal imaging device
GTV	Gross tumor volume
IGRT	Image-guided radiation therapy
IMRT	Intensity-modulated radiation therapy
kV	Kilovoltage
MV	Megavoltage
PTV	Planning target volume
RTOG	Radiation Therapy Oncology Group
SBRT	Stereotactic body radiation therapy
WEB	Online supplement material, www.karger.com/FRATO40_suppl

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Preface

This text offers a guide to the new technologies of radiotherapy and their major applications in the modern radiotherapy clinic. It is intended to be a readable and practical resource, encompassing the several areas of concurrent development that have advanced this field. The volume is divided into three sections. The first offers explanations and discussions of the technologies themselves and technical methods for their implementation. The second section brings these technologies into the radiation clinic with presentations by noted physicians at major centers who have broad experience with these new treatment approaches. In each chapter, the authors offer specific guidelines for current clinical practice. The third section explores the use of these high-precision technologies in the developing field of stereotactic body radiotherapy.

I have planned and developed this volume based on presentations recently given at the San Francisco Radiation Oncology Conference, which is jointly sponsored by the Departments of Radiation Oncology of Stanford University; University of California at San Francisco; Saint Francis Memorial Hospital, San Francisco, and University of California at Davis. Drs. R. Hoppe, W. Wara and S. Vijayakumar joined me in organizing the conference, which carried the same name as this volume. In our planning, we were assisted by the physics directors at these centers, including Drs. A. Boyer, L. Verhey and J. Purdy. I wish to thank all of them. Papers were selected for publication from the conference presentations, and were supplemented by selected additional papers given at a recent meeting on Image-Guided Radiation Therapy held in Las Vegas, USA, and sponsored by the American Society of Radiation Therapists and Oncologists. All presentations have been expanded, updated and integrated for this volume.

Advances in radiologic imaging are the foundation of much of the current work explored in this text. Throughout the volume, examples of this are often presented in more than one format. In addition to the printed illustrations, a website (www.karger.com/FRATO40_suppl) allows the reader to view a number of the important figures in time-elapse video. This is especially useful in understanding the work presented by George Chen and colleagues in their chapter 'Four-Dimensional Imaging and Treatment Planning of Moving Targets' (p 59–71). Other illustrations are also posted on this website for greater clarity and dynamic visualization, and the website is an essential part of these presentations overall.

I wish to thank all of the authors, especially Drs. J. Purdy, B. Kavanagh and R. Timmerman for their excellent contributions and guidance on the volume. I wish to thank Dr. C. Burns for her assistance in the preparation of the manuscripts for publication. Finally I wish to thank Dr. Thomas Karger and Steven Karger, and the many associates of their fine publishing house.

John L. Meyer
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New Technologies in the Radiotherapy Clinic

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Abstract

What are the limitations to the accuracy of our current technologies in radiation oncology? The immobilization of the patient, definition of the target, motion of the target and localization of the target are the major concerns that must be addressed. Current approaches to meet these needs have brought new technical systems with greater precision and new clinical procedures with higher expectations of practice. This text offers discussions on these issues, including advances in intensity-modulated radiotherapy planning, clinical target definition for the major tumor sites, management of organ motion, target localization and image guidance systems, and the expanding applications of high-precision treatment with stereotactic body radiotherapy.

The technologies of radiotherapy planning and delivery have undergone rapid change. While these changes have been welcomed and carefully nurtured for the benefit of the cancer patient, each change has carried with it a spectrum of new concerns about its appropriate application and efficient integration into radiotherapy practice. These technologies, and the clinical treatment programs that bring them into practical use, are the focus of this volume.

These technical achievements are closely interrelated: one development gives opportunity for another, but often necessitates the creation of a third, and then redefines the use of several others. Understanding this evolving world of new technologies and their applications requires broad perspectives from different vantage points. This volume first takes the viewpoint of computerized treatment planning and delivery with intensity-modulated radiotherapy (IMRT), an elaboration of three-dimensional conformal radiotherapy which has been the subject of prior comprehensive volumes in this series. This new level of treatment precision has brought requirements for image confirmation of the targets during treatment and even automated image guidance of the radiotherapy delivery (image-guided radiation therapy, IGRT). It has also brought an exciting new expansion of radiotherapy into the high-precision realm of accelerated stereotactic body radiotherapy (SBRT) for tumor sites outside the cranium. The practical concerns identified in each of these perspectives will be addressed in the sections of this volume.

Intensity-Modulated Radiation Therapy: Where Are We Now, Where Do We Need to Go?

The intensity modulation of radiation delivery has dramatically changed radiation oncology and greatly expanded the opportunities of the specialty. A little more than a decade ago, IMRT was a new and unconventional idea. Tomotherapy using the Nomos Peacock device was introduced around 1994 and entered use at a few research centers. It was a remarkable innovation, but operationally it carried limiting concerns, including the possible effects that any intratreatment patient motion might have on patient safety or tumor control. By 1996, multileaf collimation had been adapted for IMRT delivery. Its investigation was limited initially to academic centers that were required to develop and maintain appropriate resources in radiation physics not generally available in the community. By the early 2000s, the acquired experience brought confidence that IMRT could be carried out routinely at comprehensive radiotherapy facilities if the necessary quality assurance programs were provided.

To implement IMRT, the patient-specific quality assurance that must be done is additional but important work. Through these efforts, the number and types of patients benefiting from IMRT have expanded. Also, the time required to perform IMRT has decreased significantly, allowing clinics to treat more of their patients with this approach. Clinical results supporting the use of IMRT now exist for head and neck, prostate and other cancers. In many cases, they show that increasing the dose to the tumor can increase rates of local control while decreasing the dose to normal tissues can reduce complications. The clinical results with IMRT are actually occurring as many predicted they would. Yet the development of more precise means of delivering radiotherapy has brought new concerns, especially regarding patient stabilization, organ movement, tumor tracking, and treatment reproducibility.

What has changed? Most importantly, the efficiency of the clinical operations has changed. The efficiency of IMRT planning and delivery is approaching or even exceeding that of complex three-dimensional conformal therapy. Advancements

Table 1. Estimated decrease in planning and treatment times since 2002 for complex head and neck IMRT at UCSF

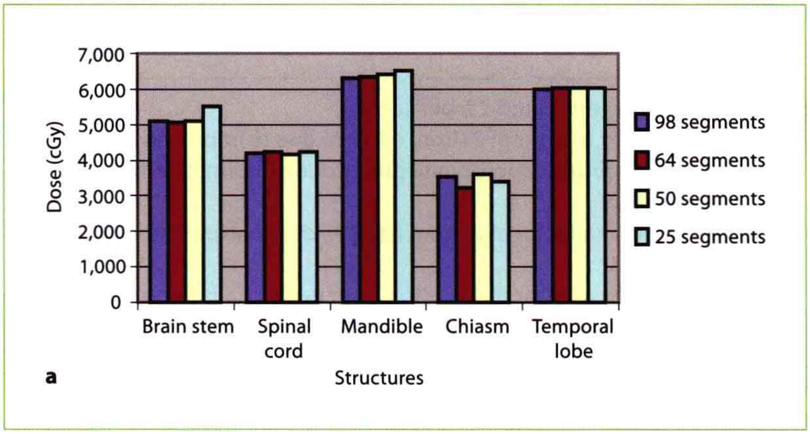
Contouring time	No change (estimated 2 h per case)
Planning time	Decrease by a factor of 2 (from 4 to 2 h) due to improved understanding of appropriate prescription information for optimization
Quality assurance[1]	Decrease by a factor of 2 (from 2 to 1 h) due to experience, better equipment
Treatment time	Decrease by a factor of 4 due to better delivery algorithm, better choice of angles, contour-based inverse planning algorithm (from 120 segments/40 min to 50 segments/10 min as of later in 2005)

[1] Measurements in phantom.

in treatment planning algorithms are now providing delivery of simpler treatments with equivalent quality. Image-guided radiotherapy, in one of its several available forms, offers the expectation that the treatment target can be localized as needed at the time of treatment, to decrease margins and make the dose delivery safer. The developing technologies for four-dimensional CT are now being used for planning and dose modification. Complex image-guided radiotherapy, as with daily megavoltage or kilovoltage cone beam CT imaging in the treatment room, can lead to a volumetric analysis of the actual dose delivered to the patient on a daily basis. It will be challenging to use and integrate all of this available information, called dose-guided radiotherapy, yet it offers a new level of understanding and quality assurance for every treatment delivered in a therapy course. Soon it may be an expected standard of care.

IMRT Efficiency and Benefit

IMRT planning and delivery can be examined in each of the work phases to show where efficiencies are improving (table 1). At the University of California, San Francisco (UCSF), the time required for contouring has not changed greatly over the past few years; the algorithms for contouring have improved, but the contouring of tissue volumes still requires about 2 h for an average head and neck case. The planning time itself has decreased by half, from about 4 to 2 h per case, largely because of a better understanding of what specific prescription information leads to the desired dose distributions for a given patient group. This efficiency can be attributed to the greater experience of the planners more than to the development of the planning systems. Quality assurance measurements require about 1 h per patient before the first treatment, again about half the time spent earlier. The actual treatment time, a precious commodity in the operation of any clinic, has diminished by almost a factor of four over the past 3 years. This reflects two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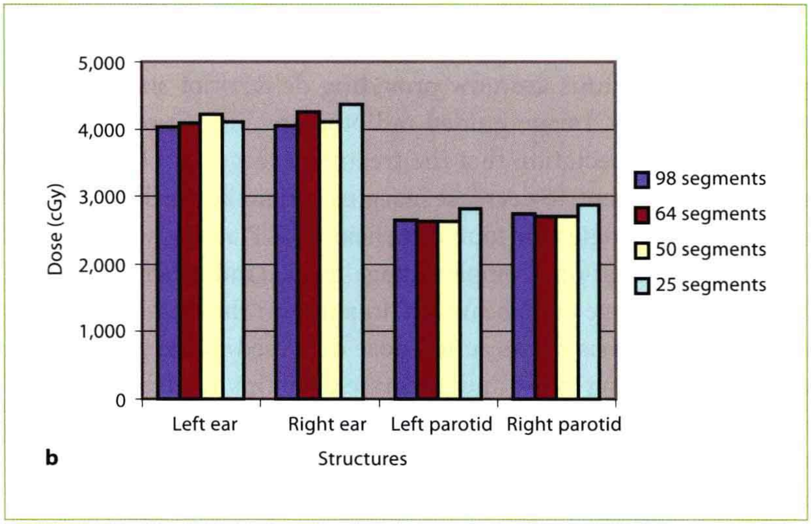
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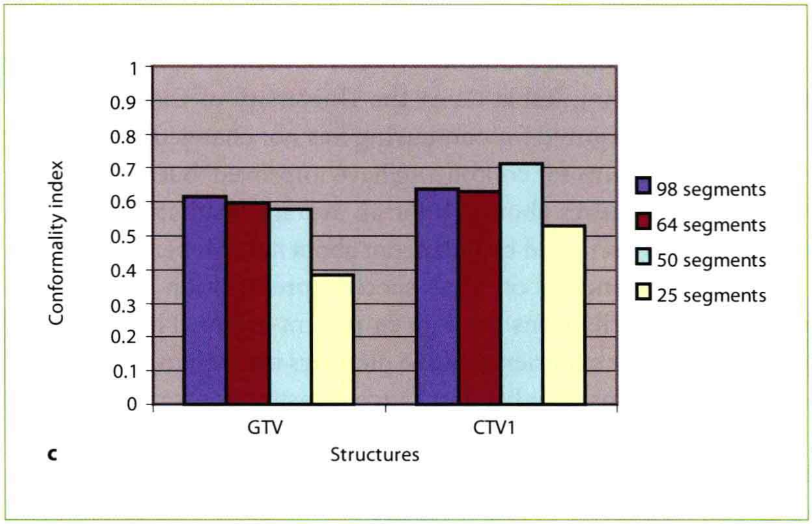
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25 segments
GTV
CTV1
c
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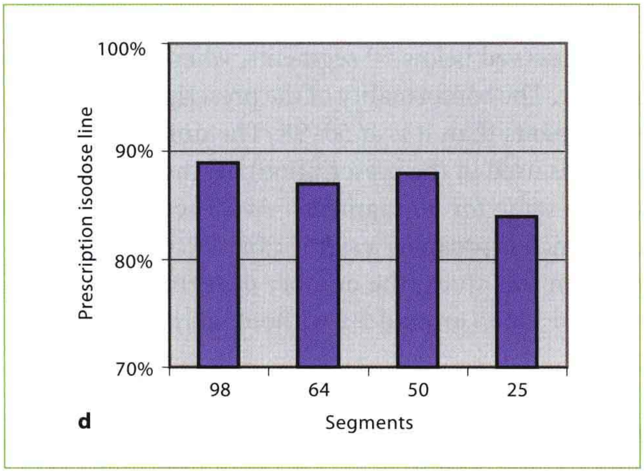

Fig. 1. Effect of the number of segments. Control of dose to normal tissues, conformality and uniformity indexes decrease below 50 segments. **a** Average maximum dose to 1 cc of serial structures. **b** Average mean dose for parallel structures. **c** Average conformality index. **d** Average uniformity index.

changes. First, the new algorithms for inverse planning that use optimization based on anatomic contours or apertures, instead of pixels, have reduced treatment time by half. Second, the number of treatment segments has been reduced by about 50% with no appreciable loss of quality. At UCSF, the most complex IMRT cases now use about 50 segments delivered over an average of 7 angles, which require about 10 min to deliver after the patient is set up. Previously, treatments required 25–35 min, and as long as 40 min for complex cases that were using 120–150 segments. This improvement is a breakthrough in efficiency, and anticipates a time in the near future when the most complex cases need only 15 min in the treatment room.

What level of IMRT complexity should be used? The balance between clinical efficiency and therapeutic benefit of IMRT segmentation has been approached in work at UCSF [1]. Their previous experience with pixel-based optimization algorithms showed that for simple head and neck cases, IMRT plans typically required 90 segments with 6–7 beam angles, but for complex head and neck cases as many as 130–160 segments with 9 beam angles were needed. The question is, can plans with equivalent quality be obtained with fewer segments? New planning algorithms have potentially made this possible. Using an aperture-based optimization algorithm implemented in the Pinnacle planning system, the maximum number of segments permitted in the optimized plan can be specified. Figure 1 shows the effect of 98, 64, 50 or 25 segments on several normal tissues, shown as serial or parallel organs.

As seen particularly for brain stem volumes, it is evident that there is a deterioration of the quality of the plan observed below 50 segments, whereas the results for 50 or more segments are similar. The conformality of the prescription dose line is significantly different at 25 segments than it is at 50–98. The uniformity index (the prescription isodose line that is used in the prescription) begins at about 89% for 98 segments, and is about the same for 50 segments. At 25 segments, it has diminished to around 84–85%, which is probably a significant decrease clinically. For the complex treatment plans in this study, the number of segments could be reduced by about half, from around 100 to around 50, without sacrificing quality.

Heterogeneity Correction
The manner of dose calculation is an essential aspect of accuracy in the planning process. The use of dose heterogeneity corrections for planning throughout the body is now considered standard in most radiation therapy clinics, and is especially important in thoracic sites. There are several different methods used to perform dose heterogeneity corrections, and some can approach (within a few percentage points) the results of exhaustive Monte-Carlo-based calculations. Convolution superposition has become a standard algorithm over the past few years. While the results obtained by these methods can vary, these differences are far smaller than the effects of not using heterogeneity corrections.

Image Guidance in Radiation Therapy

Tumor and normal tissues move with time, and this movement may be clinically significant from second to second, day to day, week to week, or longer. The movement may be periodic and predictable (like respiratory motion), irregular (like peristalsis), or even permanent (like tumor shrinkage). From a radiotherapy point of view, these variations may be considered *intratreatment* or *intertreatment.* In actuality, every tumor site will show both of these effects to varying degrees; some will be dosimetrically significant while others will not. For instance, a lung tumor may move with respiration; show three-dimensional rotational changes from day to day; be affected gradually by changing atelectasis, edema and fluid, and gradually shrink during a therapy course. Even repeated CT scanning will have difficulty in capturing all of these changes in each snapshot of imaging.

Each tumor site (and to some extent, every tumor) will have its own characteristics of movement. For thoracic tumors, periodic respiratory motion often predominates the pattern of change, while for head and neck tumors it is gradual tumor shrinkage over time. Prostate tumors may change position primarily day by day, though additional momentary and irregular changes can occur as a result of peristalsis in a minority of patients. However, no tumor appears to be immune from some combination of *all* of these momentary and more gradual changes, some of which may be complex and unpredictable. For all of these differences, how can the delivery of uniform radiotherapy dose to the targeted tissues be guaranteed? To embark on this journey, work in radiotherapy has begun to tame periodic motion through restriction of motion (e.g. breath hold, with or without assistance), prediction of motion (e.g. gating, four-dimensional CT reconstructions), or tracking of motion through robotics or other dynamic approaches, and will be discussed in this volume.

Intertreatment Changes

At present, radiation oncologists have the greatest opportunity to immediately improve therapy delivery through the identification and correction of change occurring between therapy fractions. Intertreatment motion can be studied by imaging the patient using megavoltage or kilovoltage cone beam systems referenced to the planning system or by other approaches. The imaging can be obtained on a regular, predefined basis or at specific points during a course of therapy.

Evaluation of intertreatment change is important in several areas, especially the head and neck region. Figure 2 projects the IMRT dose distributions for a head and neck cancer patient treated at UCSF; 70 Gy is planned to the gross tumor volume (GTV) and 59.4 Gy to the clinical target volume. In figure 2a, the treatment plan based on the initial CT is shown. After 21 treatment fractions were given, the tumor had markedly regressed and the patient had lost 5% of his body weight. A second CT was obtained, and figure 2b shows that the original plan now projects differently on the tissue structures, since some of the volumes have changed. For instance, the dose to the spinal cord is much higher than intended. Figure 2c shows the reoptimized plan based on the second CT.

Similar work was performed in a series of patients at UCSF; CT studies were repeated in head and neck cancer patients if their contour had noticeably changed, which is fairly common in this patient group [2]. The two CT studies were typically 4–5 weeks apart. For each case, a recalculation of the doses was performed, with endpoints being the dose to 95% of the target volumes, the maximum doses to the spinal cord and brain stem, the mean doses to parallel structures (mainly the parotid glands), and the total doses. Analysis of the normal and tumor tissue volumes indicates that the doses to the right and left parotid glands were reduced by 15.6 and 21.5%, respectively, and the clinical target volume dose decreased by 7.5%. Figure 3a illustrates the dose to 95% of the GTV that would have been delivered with or without replanning. Substantially lower doses would have been delivered to the GTV than intended by the initial plan in most cases. Figure 3b shows the spinal cord doses predicted by three plans for each case: an initial plan and a second reoptimized plan, and a third showing the first intensity patterns applied

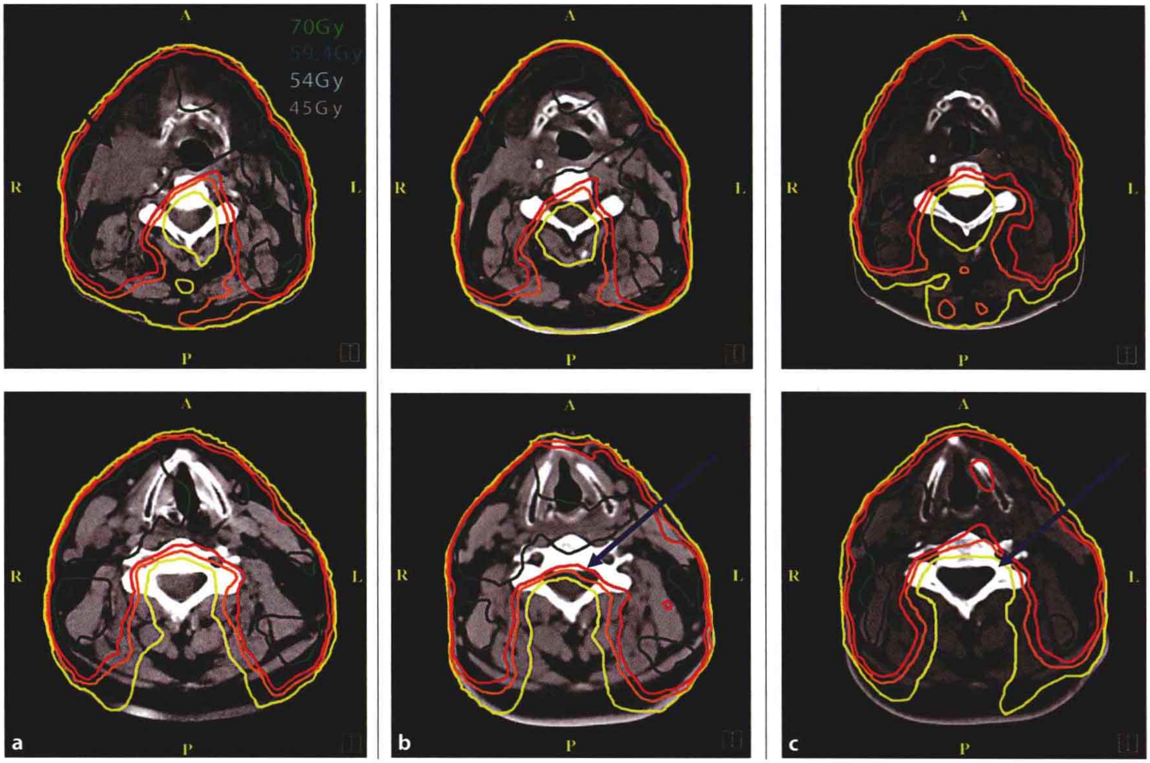

Fig. 2. IMRT treatment isodoses for a T4N2c base of tongue cancer in a 54-year-old male. Top row: level of hyoid bone; bottom row: lower neck. **a** CT 1: initial plan, before therapy. **b** CT 2: same plan shown on repeat CT scan after 21 fractions; tumor has regressed (black arrow) and patient has lost 5% of his body weight. Note that spinal cord dose has become unacceptable (blue arrow). **c** CT 2: reoptimized plan.

to the second CT scan. If replanning and reoptimization were not performed, significantly higher doses might have been given to the spinal cord than were intended. It is important to follow the patient and perform replanning when needed, and detection of significant soft tissue changes may be one of the most useful applications of image guidance with cone beam technology.

Intratreatment Motion and Tumor Tracking

The issues involved in imaging, tracking and managing motion during the treatment itself are challenging, though they may ultimately provide the best answers to treatment verification. Platforms now exist for three-dimensional radiographic tracking of passive implanted fiducial seeds and the radiofrequency tracking of implanted interactive seeds. Flat-panel technologies used in cone beam CT offer the potential for fluoroscopic monitoring of anatomy or fiducials at kilovoltage or