Technological Basis of Radiation Therapy: Practical Clinical Applications

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Foreword

As I began preparation of the third edition of the *Textbook of Radiotherapy*, it became obvious that the number of pages would have to be increased due to the expanded radiobiology and clinical background. At that time, I decided to add only a minimal amount to the previous edition on clinical physics and special techniques. I soon realized, however, that each "organ" chapter could have included more details on tumor localization, treatment planning, and some of the more recent advances in CT scanning. Not only would such expansion have made the book bulky but it would have diluted the book's specific goals, which were to integrate the treatment of the various diseases into the background of radiobiology and clinical experience. In order for all of this additional material to be presented properly and given the treatment and space it called for, I encouraged Dr. Levitt and Dr. Tapley to write *The Technological Basis of Radiation Therapy: Practical Clinical Applications* as a companion text to the *Textbook of Radiotherapy*. In these times of increasing complexity, a volume such as theirs should prove to be an invaluable source of information to all those involved in the field of practical clinical radiation therapy.

Gilbert H. Fletcher, M.D.

Preface

The concept of this book originated here at the University of Minnesota during the development of the annual postgraduate conferences entitled, "Current Concepts in Radiation Therapy." With the guidance and inspiration of Dr. Gilbert H. Fletcher, Dr. Norah duV. Tapley and I undertook to develop this text which we saw as a complement to Dr. Fletcher's *Textbook of Radiotherapy*. We felt that there was a need for a companion volume to provide more detailed information concerning the actual rationale for and techniques of treatment. With the cooperation of the colleagues who have contributed chapters, we have finally brought this text to publication.

The untimely death of Dr. Norah Tapley was a great loss to society in general, to the radiation therapy community, and to me personally. Dr. Tapley was a great human being, a superb physician, and a compassionate and understanding friend and colleague. Her contributions to this text are immense and it could not have come into being without her.

The chapters herein contain the experiences and advice of individual authors at various institutions whom we felt had a great deal of experience in the practical aspects of the treatment of the cancer patient. The recent growth of and improvement with computerized tomography has had great impact on radiation therapy treatment planning. Although work on this book was initiated a number of years ago, we have tried to update it insofar as possible to include information relative to the utilization of computerized tomography for treatment planning.

I would caution the reader to carefully evaluate the techniques described herein and compare them to their own for evaluation of the validity of the technique in relationship to their own experience and equipment. It is possible that the techniques described are not appropriate for the equipment that the individual institution has. The guidelines are essentially general, and it should be possible for the radiation therapist to modify the techniques to suit the equipment available in the individual department.

Our hope in developing this book was that it would contribute to better treatment for the cancer patient and subsequently improve survival. The accurate localization, adequate treatment, and the ability to duplicate fields used in daily treatment are essential to quality radiation therapy. It is our hope that this volume will provide the radiation therapist with the tools to provide this type of quality radiation therapy to his or her patients.

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Contents

Chapter 1

RATIONALE FOR TREATMENT PLANNING IN RADIATION THERAPY

Carlos A. Perez
James A. Purdy
Don Ragan

Irradiation is an effective antitumor agent that can completely eradicate a malignant process in the irradiated volume in patients treated with curative intent. It can also yield palliative relief to many patients with incurable cancer. The success of radiation therapy depends upon the delivery of an adequate dose to the tumor volume. This chapter reviews the principles of radiotherapeutic strategy and illustrates the significance and methodology of treatment planning.

Although the gross effects of radiation on most normal tissues have been documented, the intricate interrelationship of total dose, fraction size and number, mechanisms of injury repair, and correlation between acute and late effects have not been elucidated. The increasing use of chemotherapeutic agents in the treatment of cancer patients makes this problem more complex because the combination of irradiation with these agents usually results in greater effect on normal tissues. Furthermore, as indicated by Fletcher,[6] the tolerance of the normal tissues is related to the volume irradiated, the nature and function of organs within that volume, and stage of the cancer treated. Recent reports by Herring,[8] Perez et al.,[20] and Shukovsky et al.[22] indicate that there is a close correlation between the dose of radiation given and the probability of tumor control at the primary site or in metastatic lymph nodes. Fletcher has emphasized that such dose-response curves are valid only for homogeneous tumor populations.[6] The doses of radiation depend on the stage and the histologic nature of the tumor. Fletcher has stressed the concept that large masses of tumor require higher doses than small tumors or subclinical microscopic metastases, which are controlled with lower doses.[5] Herring[8] has discussed the theoretic consequences of dose-response curves for tumor control and normal tissue injury. The predicted consequences are based on the precision with which the dose and the volume irradiated are defined. An imprecise treatment system could lead to a high incidence of necrosis with a low probability of tumor control. Reducing radiation doses in an effort to avoid complications will further reduce the probability of achieving tumor control if such action is based on the wrong assumption that complications are only related to radiation dose levels.

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In addition to accurate treatment planning, adequate reposition and immobilization techniques are needed to translate the dose optimization formulated in a plan to actual delivery in the patient. Marks et al.[15,16] demonstrated, by systematic use of verification films, a high frequency of localization errors on patients irradiated for head and neck cancer or malignant lymphomas. These errors were corrected with improved immobilization of the patients.

The practice initiated by Baclesse of delivering higher doses of radiation through reducing fields is based on the principle that the center of a tumor contains more cells and a higher hypoxic cell population than the periphery.[6] Extreme care must be taken in defining the volume to be irradiated with this technique because small inaccuracies result in appreciable variations of dose in the critical volume.

Although treatment planning is extremely helpful in determining the best form of therapy, the responsibility for critical judgment and execution rests with the radiation therapist. To treat patients effectively, the therapist must:

1. Have sufficient training to interpret treatment-planning information and to guide the physicist or dosimetrist in achieving the best dose distribution;
2. Be competent to judge the quality of the dose distribution and the technical feasibility and accuracy of a proposed plan;
3. Have the understanding needed to suggest changes and available alternatives;
4. Have sufficient knowledge to select the best possible combination of dose and fractionation for a given site and volume;
5. Understand the capabilities and limitations of the computer in treatment planning.

It is important to emphasize that no computer calculation can correct the therapist's errors of clinical judgment, misunderstanding of physical concepts, or unsatisfactory execution of treatment.

LIMITATIONS OF RADIATION THERAPY

The goal of radiation therapy is to produce the highest possible uncomplicated local and regional control of the tumor. The failure to eradicate a tumor can result not only from suboptimal dosimetry and treatment-planning computations but from a variety of factors:

1. Clinical Factors
   a. Inadequate appraisal of the full extent of the tumor in the surrounding tissues, or inapparent regional lymph node metastases that are not irradiated.
   b. Clinically unrecognized distant metastases at the time of initial treatment are a major cause of failure in some tumors, such as breast or lung primary tumors, and their management requires a systemic therapeutic modality.
2. Physical and Technical Factors
   a. Inaccurate definition of tumor volume to be treated, including a safe margin (particularly in large infiltrating tumors), is a frequent cause of recurrence.
   b. Inadequate treatment planning with inhomogeneous dose distributions in critical target volumes.
   c. Unreliable patient repositioning and immobilization techniques, with faulty reproducibility in daily treatments resulting in inadequate doses or volumes treated.
   d. Lack of adequate in vivo verification-dosimetry techniques, except in cases in which small dosimeters can be introduced into the upper digestive tract, the bladder, and the rectum.
3. Biologic Factors
   a. Initial cell burden because small tumors are more easily eradicated than large tumors.

b. Hypoxic cell subpopulations, which require greater doses of irradiation. This problem is partially resolved by the reoxygenation that occurs between fractionated doses of irradiation.
c. Repair of sublethal or potentially lethal damage between fractions.
d. Limited tolerance of normal tissues to irradiation.
e. Type of supporting tissue involved by the malignant process; a tumor that has not extended into the adjacent soft tissues or the bone is more easily controlled by radiation.
f. Lack of knowledge of human-cell kinetics and biologic equivalents for various dose rate-fractionation regimens.[2,9]

4. Less well-defined factors include the general condition, nutritional status, metabolism, and immune response of the individual patient. This subject has been thoroughly summarized by Bush and Hill.[3]

CONDITIONS FOR OPTIMIZATION OF EXTERNAL-BEAM IRRADIATION

Kitebatake et al.[14] outlined definite requirements for optimal dose distribution with external irradiation in both tumor and normal tissues. The following is a slightly modified list of factors published by these authors:

1. Small entrance and exit dose (except with superficial tumors): Ideally, when the maximum dose is not required at the skin or the subcutaneous tissues, the optimal dose distribution should be at the target volume in the depth of the patient, with lower dose to the skin at the entrance and exit sites.
2. Small side-scattering dose: High-energy-photon beams produce minimal amounts of side-scattered irradiation.
3. Small differential tissue absorption: It is known that with 250 KV x-rays there is significantly greater absorption of irradiation in bone than in soft tissues.[12] This phenomenon disappears with high-energy x-rays due to the decreasing importance of the photo-electric effect and the increasing Compton effect between 1 and 10 MV. At energies of 20 MeV, however, there is an increase of 5% to 10% in the dose in the soft tissues near a bone (high Z) interface.
4. Optimal tumor (target) dose: The aim of good treatment planning is to exploit the maximum therapeutic ratio of a beam arrangement. The target volume should receive a homogeneous dose while delivering as little

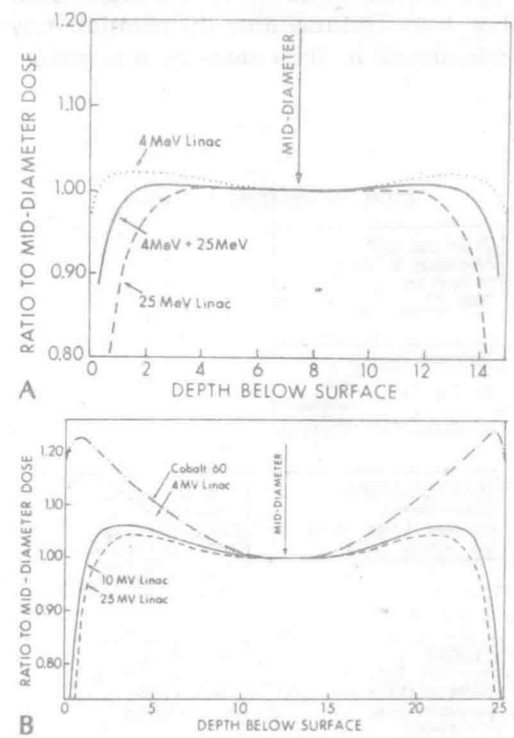

Fig. 1–1. Dose profiles for various energies with parallel opposing beams directed at anatomic areas of different thickness: *(A)* the head and neck, *(B)* the thorax or pelvis. Note the difference in maximum dose necessary to deliver the desired tumor dose (100%) at the midplane.

dose as possible to the surrounding normal tissue.

5. Small integral dose: The ideal situation should be represented by an optimal dose to the target volume with a minimum dose contribution to the rest of the patient.

Either superficial x-rays or low-energy electron beams are used for superficial skin or subcutaneous tumors. Whereas deeply seated tumors require high-energy photons, small cancers of the oral cavity or the genital tract can be treated by brachytherapy. Optimal dose distribution in many tumors requires more than one-beam energy or multiple-beam arrangements. A combination of external beam and intracavitary or interstitial therapy may also be required, depending on the location of the tumor and the beam type and energies used (Fig. 1–1). Optimal dose distribution may be achieved in such cases by a combination of multiple stationary beams or by moving-beam therapy, such as in arc or full-rotational techniques.

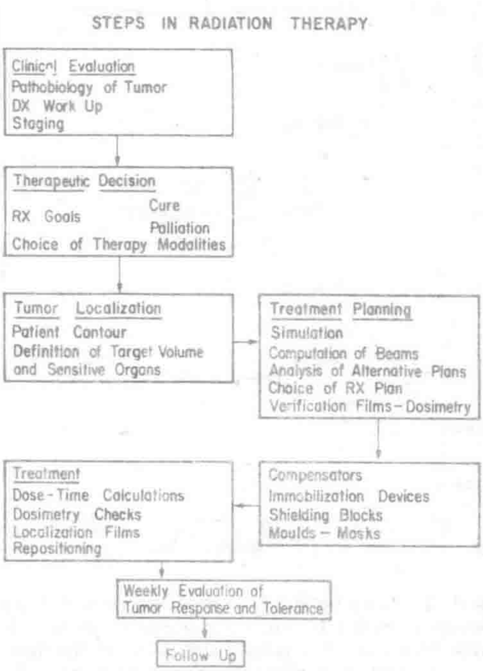

Fig. 1–2. Steps involved in the treatment planning and delivery of radiation therapy.

STEPS INVOLVED IN TREATMENT PLANNING (FIGURE 1–2)

The procedures involved in effective administration of radiation therapy comprise a complex, closely integrated operation that should include the following:

1. Thorough knowledge of the natural history and pathologic characteristics of the tumor.
2. Adequate evaluation of the patient and staging procedures to determine the full extent of the tumor.
3. Definition of treatment strategy, to select the best modality or combinations to be applied. This may depend on the stage, type of tumor to be treated, and the routes of spread.
4. Treatment simulation, with accurate definition of the tumor volume to be treated and the portals to be used.
5. Treatment planning, to determine the distribution of irradiation within the volume of interest.
6. Accurate and reproducible repositioning and immobilization techniques for daily treatment delivery.
7. Applicable dosimetry, portal localization, and verification procedures, to insure quality control throughout the therapy.
8. Periodic evaluation of the patient during and after therapy, to assess the effects of treatment on the tumor and the tolerance of the patient.

The treatment strategy must include, in addition to clinical, physical, and radiobiological concepts that may provide rational basis for the therapy, thoughtful consideration of the treatment's psychological repercussions, side-effects, and sequelae, all of which may affect the quality of life of the patient. Supportive care during treatment is important.

Even though general policies of treatment may be established and atlases compiled, it is mandatory to remember that the treatment plan must be individualized to suit each patient's needs.

PROBLEMS WITH PRESENT TREATMENT-PLANNING TECHNIQUES

Several problem areas still exist in regard to treatment-planning computation. The most pertinent include: 1) surface and buildup doses; 2) the effect of tissue inhomogeneities;[17] 3) irregular field effects due to secondary blocking; 4) beam modifiers such as wedges and compensators;[1] 5) combination of interstitial and intracavitary isodoses with external-beam dose distributions; 6) tridimensional dose computations and display; and 7) dose optimization.

The effect of the patient's shape and of consequent oblique-beam incidence must be taken into account in treatment planning, as must the patient's internal anatomy and the differences among intervening tissues. Methods developed to handle the problem of oblique incidence include the effective source-to-skin-distance (SSD) method, the effective attenuation coefficient method, and the isodose curve shift method. All these methods are approximations and result in an inaccurate description of the surface dose and the dose in the build-up region. The surface dose and the dose in the build-up region are largely determined by collimator design and diaphragm–surface distance and are therefore machine-specific. In the case of high-energy x-rays (25 MV) generated by a linear accelerator, the maximum dose depth changes from 4.0 cm for a 4 cm × 4 cm field size to 2.5 cm for a 25 cm × 25 cm field (Figure 1–3). Although this phenomenon is not well understood, we suspect that it is caused by electrons from the flattening filter and collimator jaws.

Correction for inhomogeneities in the medium is primarily done by the "isodose shift method." The isodose value is shifted to a distance proportional to the path length through the inconsistent medium (i.e., a downward shift if the inhomogeneity has a density of less than one or an upward shift if the inhomogeneity has greater than unit density). A method has been described using an absorption equivalent density and an inverse square law correction (effective density).[18] Interface effects, although important for high-energy photons (over 20 MV), are neglected in most cases.

The effect of a wedge or shielding block

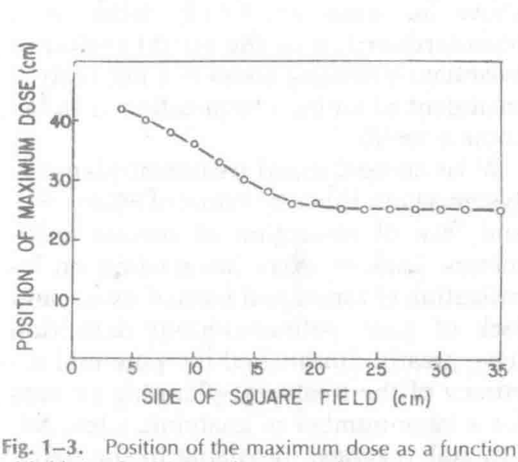

Fig. 1–3. Position of the maximum dose as a function of field size for 25 MeV linear-accelerator x-ray beam. Note the displacement toward the surface as the field size increases.

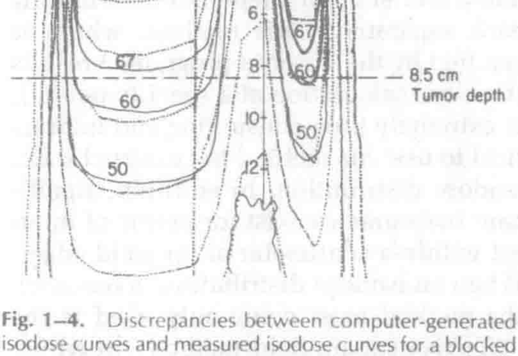

Fig. 1–4. Discrepancies between computer-generated isodose curves and measured isodose curves for a blocked field that includes a full-thickness spinal shield. Dashed lines represent computer-generated curves. The solid lines represent ionization measurements.

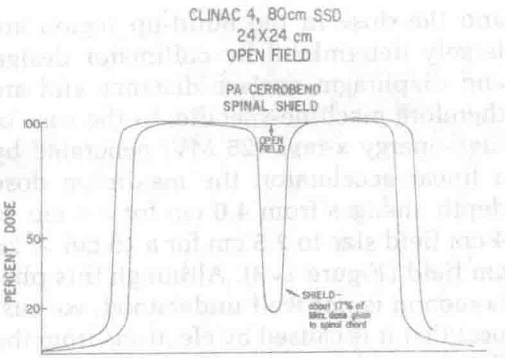

Fig. 1–5. The dose profile in a field treated by 4 MeV x-rays in which a 5 half-value layer (HVL) block is interposed in the middle (e.g., in the thorax PA portal to shield the spinal cord). Note that a 17% dose is delivered under the block at 10 cm depth. This is mostly contributed by scattered irradiation, although a small percentage is due to transmission through the shielding block. Neglecting to consider this 17% dosage contribution may result in significant inaccuracies in treatment planning.

on dose distribution is due to changes produced in the beam profile. In order for a beam-generation program to be related as closely as possible to the physical situation, the actual location, dimensions, and physical characteristics of the wedge or beam block must be entered into the program. Depending on the thickness and the attenuation coefficient of the wedge, attenuation factors can be calculated along various phantom lines applied to the primary dose and the scatter dose.

At present, irregular-field calculations are accomplished by dividing the dose at a given point into a primary component and a scatter component and determining each separately. This method, which is typified by the Toronto programs,[4] results in a dose calculation at a specific point. It is extremely time-consuming and impractical to use this method to construct a full isodose distribution. In addition, significant inaccuracies exist for points of interest within a centimeter of the field edges. When an isodose distribution is required, the method most commonly used is the "effective-square-field method" in which the irregular field is approximated by an effective rectangular field, isodose curves are obtained using a rectangular field. Serious errors may result especially in the penumbra region or when special shielding blocks (e.g., full- or half-value-thickness spinal-cord shield) are used (Figs. 1–4 and 1–5).

Although the methods mentioned above are much faster than hand calculations, they still require considerable time in computation and final display. This problem is compounded by the need for interaction among the physicist, the physician, and the computer technologist. Plans are usually done by a treatment-planning technologist using a prescription given to him by the physician. The plans are given to the physician for review. Corrections are made, if needed, and the process is repeated. To circumvent these problems, small computers have been developed to allow the physician to participate directly in the treatment-planning process. In practice, though, most institutions still employ treatment-planning technologists to compute the treatment plans. An additional problem is that there is no wide agreement as to how to specify treatment-planning doses. The doses to the center of the tumor volume are normally used; other specifications include maximum, minimum, or modal dose. There are numerous arguments for and against the use of all of the above but none are totally satisfactory. Standardization in the specification of treatment-planning doses is a necessity if treatment planning optimization is to become a reality.

Most computerized treatment-planning systems have inherent errors of 5% to 15%, and lack of resolution of several millimeters. Lack of exact information on localization of tumor and normal tissue, and lack of clear patient-contour definition have greatly diminished the potential accuracy of the treatment-planning process for a large number of anatomic sites. Additional vagaries, inevitable in the delivery of successive treatments of radiation therapy, have resulted in the need for