Goals for the Future of Radiation Oncology

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Although radiation therapy now cures many patients with cancer, approximately one-third still die of recurrence, regardless of the treatment employed. Obviously, significant improvements are necessary for the future.

The general goals of radiation therapy are as follows: to develop a rational basis for radiation oncology, with a good foundation in the biology of cancer and normal tissues; to cure more cancer patients now treated by irradiation with no increase in complications or damage to normal tissues; to extend curative techniques to those patients with cancers not now treated for cure; to improve methods of palliation for patients who can not now, nor in the future, hope for cure.

A further goal is to ensure close interdisciplinary collaboration and cooperation for an early and effective integration of therapy. This is especially important in cancer, since the initial treatment has the highest probability of cure and, if unsuccessful, may compromise later therapy. Of course, combined modality treatment can only be undertaken with a mutual understanding of the expected benefits, risks and limitations of each method.

Collaborative care extends from work-up to follow-up. A team approach is required to define the type and extent of cancer, estimate prognosis, decide on the choice of treatment, its dosage and sequence, recognize and interpret recurrence or complications, and accumulate and examine the results of cures and failures.

In addition, interdisciplinary educational programs in cancer biology, natural history and response to intervention are necessary. The medical community and the public must also be kept fully informed of improvements in radiation therapy.

With these goals in mind, the future is faced with inspiration and optimism. Even modest improvements in biology, physics and clinical care can increase the effectiveness and applicability of radiation oncology, curing or prolonging the lives of more patients.

Several specific goals for the future are discussed below.

Promote Earlier Cancer Detection and Accurate Tumor Definition
The curability of cancer, if detected
early, should be stressed to both the patient and the physician. Effective screening and detection procedures for patients at high-risk of cancer must be sought and popularized. Following recognition of the cancer patient, the extent of clinically evident disease must be established. Accurate predictions of subclinical and occult tumor involvement and extension, based on knowledge of the tumor’s patterns of spread, its location and gross characteristics, are especially important. New techniques, such as computer assisted tomography, may be used to define tumor extent, but will be of even greater value in determining the position and contour of normal structures, thus improving treatment planning. Detection and definition techniques can also help predict the tolerance of regional normal tissues to high doses of radiation, monitor the response of tumor and normal tissues to radiation and permit early recognition of recurrence or complications.

Establish a Data Base on the Natural History of Cancer

A better comprehension of the natural history of cancer is necessary for rational intervention. A data base, founded on clinical observations, biological interpretations and models, is needed to document the pre-recognition period in a patient with cancer and to establish complete records of objective and subjective findings during work-up and management (including pathology, clinical findings and treatment). Information on the patient’s response to treatment and follow-up for prolonged periods of time, including the time-course, location and detailed morphologic descriptions of recurrences, late effects or cures will be helpful.

Produce an Inventory of Radiation Therapy Results

An inventory of radiation’s successes and failures will be developed, and lead to a clinical oncology and radiation biology explanation of results. The numbers and types of cancers treated must be documented, as well as the dose-response relationships for various stages of disease, including those for patients with predicted subclinical involvement. The exact site of initial failure and the time-course of recurrence should be determined, in order to improve local-regional or systemic therapy. Information is required on the frequency and types of early morbidity and late effects on normal tissues, the tolerance of normal tissues involved with tumor cells or other diseases, and the time-course and dose relationship of complications.

Palliative radiation therapy will particularly benefit from a better knowledge of past results. Accumulation of an appropriate data base is difficult, since end points are not well defined and the patient may die of disease extension not included in the treatment volume. However, even short-term observations and evaluations will affect future decisions.

Develop Score Function and Evaluation Processes

A generally acceptable data system for the interdisciplinary and inter-institutional evaluation and examination of results is being devised. Staging systems exist for a number of tumor types, but they require better gradations of disease extent and better measurements of early and late effects and response to treatment of both the tumor and the normal tissues. Such scoring systems will allow for more successful comparisons and a more appropriate evaluation of the risk: benefit ratio of therapeutic intervention.

Identify Characteristics of the Most Effective Current Management

The radiation oncology community is now engaged in a study of the ‘‘Patterns of Cancer Care in Research and Clinical Radiation Therapy,’’ with Dr. Simon
Kramer as the principal investigator. This study aims to determine the present practice and outcome of radiation therapy and to disseminate this information through progress reports, educational and demonstration programs.

Criteria will be established for the most effective current management in the following areas:

- patient work-up and data necessary for definition of gross tumor extent;
- estimation, from past experience, of tumor cell distribution, tumor cell number and tumor cell sensitivity;
- prediction of normal tissue sensitivity and tolerance, as well as possible decreased tolerance because of tumor involvement;
- alternative treatment techniques, doses and goals;
- selection of treatment modalities, time, dose and number of fractions;
- evaluation of dose distribution plans that deliver a minimal dose to normal tissues and high doses to regions with known or suspected high tumor cell numbers;
- localization of treatment portals and prescription of doses and field sizes;
- delivery of repeated fractions of dose, with precision and accuracy;
- re-definition of patient response during the course of treatment;
- supportive care;
- follow-up for observation of cures, failures and late effects.

Following definition and documentation of the most effective present practices, it is hoped that less adequate practices can be up-graded through continuing medical education programs, on the job demonstration of good practice, dissemination of information on requisite staff facilities and personnel, and reimbursement requirements for a viable practice or facility.

Make Present Radiation Oncology Programs Widely Available

Since many medical facilities do not have a radiation therapist to participate in cancer patient care or even to discuss alternatives of care, consideration of this mode of treatment is often not considered. In fact, several medical schools do not teach the principles, practices and benefits of radiation therapy and, thus, many physicians have no comprehension of its place in the cure or palliation of patients with cancer.

It is proposed that:

- outreach and consultation programs are developed;
- present results and benefits, as well as opportunities for the future, are publicized;
- an adequate number of new therapists, physicists and radiation therapy technologists are trained;
- administrators, civic agencies and health care insurers are provided with the requisites for facilities, personnel, status and reimbursement for good practice.

Reduce Radiation Morbidity and Complications

Current practice and investigations have been aimed toward local cancer control rather than reduction of injury to normal structures. Thus, a two-phase program is underway: the first strives to understand and document clinical injury produced by radiation, and the second, to seek out biologic modifications of the injured tissues, thus promoting better healing and less late fibrosis and injury. A clinical data base is necessary to separate the acute morbidity associated with good radiation therapy practices from the expected and unavoidable small incidence of complications. Both of these situations must be differentiated from unnecessary injuries and complications that result from bad radiation therapy. Also needed are animal models of the syndromes of radiation injury in many tissues and a system to score the injuries with regard to their severity and the amount of deficit produced. A registry
of anecdotal reports of injuries is of some value, but the frequency of the given injury related to the dose administered and the results of radiation therapy must be determined. Finally, the mechanisms of injury and their role in the development of late radiation effects must be studied. This includes:

- normal stem cell damage;
- small vessel damage;
- interstitial tissue or ground substance injury;
- injury to connective tissue precursor cells.

Observations of clinically evident late effects are being collected, and methods of measuring subclinical injuries are being sought. It must be recognized, however, that tumor infiltration and compromise of normal tissues or previous treatment modifies the tolerance of normal tissue by any therapeutic intervention. Successful radiation therapy will produce a small incidence of adverse late effects. However, the scale must be weighted to account for the fact that failure to control a tumor locally may be the most significant complication of inadequate therapy.

**Improve the Planning and Delivery of Radiation Therapy**

If the criteria of a "best treatment plan" can be agreed on with an unambiguous statement of the dose distribution required for tumor cure and normal tissue tolerance, computer calculation systems can then be utilized to assist in developing an optimal treatment plan. A treatment system must accomplish the delivery of multiple daily fractions of radiation to the target volume with high precision and accuracy, since small variations from the appropriate dose may result in either failure or complication.

**Utilize and Investigate New Biology and Physics Mechanisms**

The application of new biological and physics techniques, for example, radiation sensitizers, hyperthermia, high LET radiation and interstitial insertion of moderate-lifed radioactive isotope sources, will contribute to increased local and regional control of cancer with an improved probability of normal healing. However, these new techniques require controlled clinical trials with observation of patients for prolonged periods. Analysis of the time-course of failures and estimation of the number of surviving or remaining tumor cells suggest that modern improvements in the therapeutic ratio result in increased cure rates for many patients.

New biological mechanisms are continually being investigated. Efforts are now underway to uncover the biological processes that contribute to a positive therapeutic ratio. Models of the relationship between time, dose and volume for tumor cure and low frequency of injury have been developed. These models do not fit well with those developed from radiation biology observations and principles. An opportunity, therefore exists to discover and prove new clinical and biological models of selected depopulation of tumor cells with regrowth of normal tissue, a phenomenon observed in cured patients.

**Extend the Benefits of Improved Radiation Therapy to Cancers Not Now Treated by Radiation**

In some of the more aggressive neoplasms, such as cancers of the kidney, colon, rectum, pancreas, stomach, melanoma, bone and soft tissue sarcomas, results have improved only slightly over the past decade. These patients are often not considered to be candidates for radiation therapy, either because the tumors are thought to be radioresistant or, alternatively, responsive but so intimately associated with sensitive normal tissues that treatment, even if successful to cure, might cause excessive damage and destruction of vital normal structures. Twenty years ago, Hodgkin's disease
was regarded as incurable, due to both radiation resistance and wide dissemination. Inoperable breast cancer was considered non-responsive to radiation, although long-term local control of metastases was commonly observed. Today, radiation has been used successfully to cure Hodgkin's disease, even at moderately advanced stages, and inoperable breast cancer has been controlled in local regional sites. The success of radiation therapy in these common and lethal diseases has been rewarding not only in the number of patients cured, but also in the vindication of clinical and biological predictions on the effectiveness of aggressive therapy.

Radiation therapy for cure of these common tumors demands the development of tumor localization and dose limitation techniques that permit the delivery of an adequate dosage. Success depends on the ability to predict the extent of disease and to monitor tumor response. With the advent of successful chemotherapy programs, optimal multimodality therapy will produce the highest cure and the fewest complications.

**Extend Radiation Therapy to Patients with Disseminated Disease**

Control of occult metastases requires better control of the primary tumor and its clinical extension. An example is the successful management of Wilms' tumor, rhabdomyosarcoma and osteosarcoma through aggressive surgical or radiation therapy for local and regional control of the primary and clinically apparent metastases, and systemic therapy for occult distant metastases. Systemic therapy contributes to depopulation of the local disease, as well as distant metastases, and may improve local and regional control of a large bulky primary or metastatic tumor by radiation therapy or surgery.

A model or prediction system is needed to estimate the local adverse effects of combination therapy, based on an understanding, although limited, of the local and systemic effects of each modality alone. Adequate supportive care for the cancer patient undergoing combination therapy must also be developed in the future.