Oncology Issues

ISSN: 1046-3356 (Print) 2573-1777 (Online) Journal homepage: https://www.tandfonline.com/loi/uacc20

Radiation Oncology in the 1990s

Gerald E. Hanks

To cite this article: Gerald E. Hanks (1990) Radiation Oncology in the 1990s, Oncology Issues, 5:2, 11-12, DOI: 10.1080/10463356.1990.11904999

To link to this article: https://doi.org/10.1080/10463356.1990.11904999

RADIATION ONCOLOGY IN THE 1990s

Gerald E. Hanks, M.D.

***Gerald E. Hanks, M.D.,** is Professor and Vice Chairman, Department of Radiation Oncology, University of Pennsylvania, and Chairman, Department of Radiation Oncology, Fox Chase Cancer Center, Philadelphia,*

I believe that we will observe dramatic changes in radiation oncology in the decade of the 90s, and I hope that these predictions or extrapolations from present data will prove to have been too conservative and too limited in scope. Dramatic change does not mean "home runs," but rather a continuous, slow erosion of the cancer problem.

We should begin to see the first benefits from the explosion of knowledge of molecular understandings of resistance to therapy, carcinogenesis, and control of cell proliferation. A molecular-genetic therapeutic approach to selected cancers will begin to replace the gross excisional approach of surgery, the localized but indiscriminant cell killing of radiation therapy, and the systemic toxicity associated with chemotherapy. How this will first be extended into clinical use in the 1990s is open to speculation, but I believe this approach will begin soon in very specialized malignancies.

While we wait for the beginning of the era of genetic engineering in treating cancer, we are still faced with one million cancer patients per year that must be treated and offered the best possible chance for cure. There are at least six areas of improvement that will contribute to the control of more cancers in the 1990s.

Improved Understanding of the Biology of Individual Cancers

It is now possible to assess the cellular radiosensitivity of individual cancers and to allocate resistant tumors to more appropriate therapy. There are several systems of in vitro assay of individual cancer cell populations' radiation sensitivity that were developed during the 1980s. These involve obtaining biopsy material and passing it in short term, in vitro culture to assess its response to radiation. Squamous cell carcinomas of the head and neck have been extensively studied, and correlations with clinical outcome suggest these methods have validity. Certainly, the tumors that are sensitive to radiation will continue to receive standard radiation therapy. Tumors that are relatively resistant to radiation can be directed into modalities with different characteristics of cell killings, such as neutrons, programs combining radiation sensitizers with radiation therapy or, indeed, other modalities.

While we wait for the era of genetic engineering in treating cancer, we are still faced with one million cancer patients per year that must be treated and offered the best possible chance for cure

Improved Interaction of Radiation and Modifiers of Radiation Response

Fluorouracil (5-FU) has now been clearly shown to produce sensitization to radiation in cancer of the anus. There are strong suggestions that it performs a similar function in rectal cancer and cancers of the esophagus. This demonstration that sensitization takes place in human tumors has been 20 plus years in coming, but will help to provide improved outcomes for thousands of patients in the 1990s. The number of tumor sites where this sensitization occurs will also be expanded and other sensitizing agents put into use through appropriate clinical trials.

Hypoxic tumor cell populations have been indicted as responsible for radiation failures since the mid-1950s. More than a decade ago, the first generation of compounds was developed that sensitize the hypoxic cells to radiation damage, providing an improved chance of killing this resistant tumor cell population. Pharmaceutical technology has now produced a second generation of even more effective sensitizers that now appear active in cancers in patients. Worldwide phase III prospective trials in advanced head and neck cancer are under way in the RTOG and other cooperative groups, and apparently are showing an improvement in local control with SR-2508. Combinations of external beam radiation therapy with SR-2508 will be the standard of care for selected tumor sites during the 1990s. In addition to head and neck cancers, there will be a major effort to expand this drug's usefulness to other primary sites where local control and hypoxia are a problem.

There are compounds that protect some normal tissues from radiation damage while not protecting cancer cells. One of these is WR-2721 which, in some experimental systems, protects bone marrow without protecting lymphoma cells in the same animal. Preliminary clinical trials at Fox Chase Cancer Center are under way to investigate the use of WR-2721 with total body irradiation in disseminated lymphomas. Other clinical trials in the United States and China are testing the gastrointestinal protection offered by WR-2721 with radiation therapy of advanced pelvic cancers. These studies may lead to a whole new avenue of approach for reducing radiation morbidity.

Changes Due to Technology

Three Dimensional Treatment Planning. The technology for 3D treatment planning

with virtual image display has provided a means of delivering the radiation dose to some cancers with much more accuracy and with a minimum of radiation to normal surrounding tissues. These technologies are in routine use in a few institutions, including Fox Chase Cancer Center, in cancers of the prostate and the pancreas. This form of more accurate delivery of dose will be the standard of practice for several sites during the 1990s, and patients will benefit through improved cure rates and decreased morbidity.

Neutron Treatment. In the 1980s, we saw a prolonged investigation of neutron and mixed beam (photon/neutron) therapies of common cancers, prompted, in part, because the mechanism of neutron killing is independent of the oxygen effect, and hypoxic tumor cell population should not dominate the response to neutrons. To date, there is a clear advantage for neutron therapy in salivary gland cancers, and a pilot study has shown improved local control in prostate cancer, which is being tested in a phase III prospective trial. Neutrons will continue to be available for the treatment of selected cancers in the 1990s.

Proton beam irradiation has the advantage of greatly increasing the accuracy of delivery of radiation. It may be possible, through this modality, to "escalate" dose in an effort to improve local control of selected cancers, where local recurrence is a problem. Proton therapy is already of proven value in treating selected sites where critical normal structures are at risk. The 1990s will see further clinical investigation of this modality.

Systemic Radiotherapy

This expression refers to the delivery of ionizing radiation in the form of an isotope linked to an antibody. The field is not restricted to radiation therapy, but the ultimate effect is killing through ionizing radiation, and radiation therapists have been prominent in the development of this clinical investigation. Clinical trials are currently ongoing in hepatocellular carcinoma and Hodgkin's disease, as well as other sites, at Johns Hopkins and other centers. The problems of antibody specificity, bone marrow toxicity, antibody-isotope link, isotope selection, and time at the target are immense, but the interest of the National Cancer Institute (NCI) and commercial companies is pushing this field and, it it is likely that in the 1990s, we will see at least one common cancer site where this approach is useful.

Physicians who treat cancer, and the staff at NCI who fund new modality research, are reluctant to accept the time that it takes to develop a biological basis and to prove that a new modality is helpful

The Introduction of New Modalities

It appears that the hypoxic cell sensitizer program has been a success, but one that has taken 20 years to achieve proven efficacy. Physicians who treat cancer, and the staff at NCI who fund new modality research, are reluctant to accept the time that it takes to develop a biological basis and to prove that a new modality is helpful. With some new modalities (first generation hypoxic sensitizers, hyperthermia, photodynamic therapy) there has been too much pressure to transfer the modality to the clinic before sufficient, basic biological data is developed. This runs the risk of terminating clinical investigation and interest in the modality when the initial clinical trials are negative, even though the trials were not properly designed, or the compound tested was not ideal. These developments require patience and deliberate progress.

Photodynamic therapy is one of the new modalities that has undergone many years of generally uncontrolled clinical use. At this time, there is a great interest in controlled clinical trials of this modality (while we still do not know enough about the biology of the substances). Photodynamic therapy should undergo extensive, organized clinical testing, as well as continued laboratory investigations, over the next few years and, one suspects, it will be an area of real clinical benefit in the 1990s.

Changes Due to Standards and Quality Assurance

The field of radiation therapy has a more comprehensive understanding of how it is practiced in the United States than any other specialty (Patterns of Care Study). We have identified what is important, and developed comprehensive standards and quality assurance programs that help to maintain one high level of care for patients in the United States. We have measured the level of care across the entire United States and know that it is generally good, although there are some practice deficits that the specialty is working to eliminate. The identification and correction of deficits through outcome analysis will improve the sum total of radiation therapy in the United States. The knowledge of our national averages for control of common cancers provides us with a database from which we can maintain, and further improve, the quality of radiation therapy care, and attain the ultimate goal of more patients cured and fewer complications across the entire United States, not just in research centers.

Summary

The future of radiation oncology in the 1990s is indeed bright. We will see more appropriate selection of patients for specific therapies, the use of new and emerging modalities, and the assurance of quality through continued monitoring and the improvement of patterns of care. ■