MEDICAL RADIOLOGY
Diagnostic Imaging and Radiation Oncology

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Hyperthermia has been found to be of great benefit in combination with radiation therapy or chemotherapy in the management of patients with difficult and complicated tumor problems. It has been demonstrated to increase the efficacy of ionising radiation when used locally but also has been of help in combination with systemic chemotherapy where hyperthermia is carried out to the total body.

Problems remain with regard to maximizing the effects of hyperthermia as influenced by blood flow, heat loss, etc.

The present volume defines the current knowledge relative to hyperthermia with radiation therapy and/or chemotherapy, giving a comprehensive overview of its use in cancer management.

Philadelphia/Hamburg, June 1995

L. W. Brady
H.-P. Heilmann
In an attempt to overcome tumor resistance, hypoxia, or unfavorable tumor conditions, oncological research has come to focus on gene therapy, immunotherapy, new cytotoxic agents, and increasingly sophisticated radiotherapy. Radiation research has been directed towards heavy particle therapy and modification of the radiation response by either protecting or sensitizing agents. Improved dose localization using rotational or conformal strategies has also been implemented. Recently, changes in radiation fractionation schedules have shown promise of better results. Hyperthermia in cancer therapy can be viewed similarly as another means to increase the sensitivity of tumors to radio- and chemotherapy.

Hyperthermia (i.e., the application of heat to attain elevated tumor temperatures, usually in the range of 41°–44°C) as an adjuvant to chemo- and radiotherapy is primarily employed to improve local control, while its combination with systemic chemotherapy and sometimes even whole-body radiotherapy obviously aims at the control of systemic metastases as well. It is in local control of the primary lesion that hyperthermia will have the greatest impact, and it is in combination with radiotherapy that hyperthermia appears to have its greatest potential at present. Therefore it should be implemented in patients in whom the percentage of local failure is high, such as those with the common tumors of the brain, breast, lung, oropharynx, upper gastrointestinal tract, and pelvis including the prostate, uterus, cervix, ovary, and bladder. Even if the impact on survival from improved local control were to be as low as 5%, this increase would still represent a very significant number of patients saved from a cancer death.

In cases where no hope for better survival can be expected from improved local control, many patients could still benefit from alleviation of the extremely unpleasant effects of uncontrolled local disease (bleeding, pain, infection, etc.). This is particularly true for breast cancer patients who experience a local failure at the operated breast or chest wall, such failure often being associated with a variety of very distressing symptoms and circumstances. Thus, palliation of uncontrolled local disease is another important indication for hyperthermia.

A general rationale for the use of hyperthermia began to evolve from the laboratory in the early 1960s, but the actual task of inducing and monitoring the heat application clinically proved to be much more technically difficult than was anticipated. Nevertheless, even early clinical trials using crude technical heating equipment sometimes achieved encouraging results when hyperthermia and appropriate radiotherapy where combined.

More recently we have seen some very positive clinical results emerging from well-controlled phase III randomized trials (including malignant brain tumors, melanomas, head and neck and breast tumors) where good quality assurance has been assured. Most of these trials were of multi-institutional design to recruit sufficient numbers of patients within a reasonable period. Studies involving heat in combination with chemotherapy and even triple-modality therapy are now underway for tumors with a high tumor growth fraction or high metastatic potential. Innovative and invasive techniques, such as interstitial and intracavitary hyperthermia, have become available to strengthen our oncological armamentarium. Presently unresolved questions point to the following areas of research:
1. **Biologists** may deepen or even complete our insight into the development of thermotolerance, and specific assays of heat shock proteins may provide us with information about the optimal treatment schedule.

2. **Physiologists and pharmacologists** may induce artificial alterations of the cellular environment by means of specific thermosensitizers, vasodilators, or the infusion of glucose to alter the pH. Using positron emission tomography or magnetic resonance spectroscopy, the induced changes might easily be monitored and used for the prediction of tumor response.

3. **Physicists or engineers** may improve present heating systems: applicators are now being designed to provide broader field sizes, improved control of power deposition, thermal homogeneity and heat delivery to areas of limited access, better shielding of sensitive adjacent normal tissues, better conformity to curved body surfaces, improvement of overall treatment comfort for patients and improved equipment and computer operation for staff.

4. There is a further need for useful noninvasive thermometry techniques, e.g., microwave or ultrasound radiometry, applied potential tomography, or particularly magnetic resonance imaging; however, clinical applications are likely to be some years off.

5. **Clinical oncologists** (surgeons, radiotherapists, and medical oncologists) must cooperate to an even greater extent in multicenter trials and quality control, and design appropriate controlled clinical studies for suitable tumors and body sites.

Despite this “work-in-progress situation,” there is no doubt that the addition of hyperthermia to chemo- and radiotherapy provides a significant and worthwhile improvement in cancer control, and that it holds good promise as a cancer treatment for selected body sites. In the two volumes of *Thermoradiotherapy and Thermochemotherapy* we have aimed to bring together a group of experts of international reknown to present up-to-date knowledge and future perspectives in the fields of hyperthermic biology, physiology, and physics (volume 1) and clinical options for combined hyperthermia and ionizing radiation or chemotherapy (volume 2). The two volumes include 45 contributions (21 chapters in volume 1 and 24 chapters in volume 2) which demonstrate the advanced state of this multidisciplinary field. We have structured the contents of the book into six sections: historical review, biological principles, pathophysiological mechanisms, physical principles and engineering, clinical applications, and multicenter trials and future research.

The logical order of the chapters, the many figures and tables, the concise tabulation of parameters for hyperthermia data evaluation, and the comprehensive subject index provide a clear orientation in the field. The reader will find the important aspects summarized and highlighted at the end of each chapter. The two volumes are designed to allow the specialist as well as the interested newcomer to start with any desired topic or preferred area of research and then easily to proceed to any other topic of interest.

In publishing these two volumes we hope to promote further scientific exchange among the countries of Europe, America, Asia and other areas in order to stimulate the diffusion of knowledge of thermoradio- and thermochemotherapy in all specialized oncological fields. Biological research, technical improvements, and new clinical concepts and therapeutic ideas may pave the way for a broad spectrum of oncological and even nononcological applications. We hope that you will find this book interesting, informative, and stimulating: it certainly was for all three of us as we participated in the writing and editing of it.

Erlangen/London/Stanford

M. Heinrich Seegenschmiedt
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