MEDICAL RADIOLOGY
Radiation Oncology

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New Technologies in Radiation Oncology

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With 299 Figures in 416 Separate Illustrations, 246 in Color and 39 Tables

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Foreword

Radiation oncology is one of the most important treatment facilities in the management of malignant tumors. Although this specialty is in the first line a physician's task, a variety of technical equipment and technical know-how is necessary to treat patients in the most effective way possible today.

The book by Schlegel et al., "New Technologies in Radiation Oncology," provides an overview of recent advances in radiation oncology, many of which have originated from physics and engineering sciences. 3D treatment planning, conformal radiotherapy, with consideration of both external radiotherapy and brachytherapy, stereotactic radiotherapy, intensity-modulated radiation therapy, image-guided and adaptive radiotherapy, and radiotherapy with charged particles are described meticulously . Because radiotherapy is a doctor's task, clinically orientated chapters explore the use of therapeutic radiology in different oncologic situations. A chapter on quality assurance concludes this timely publication.

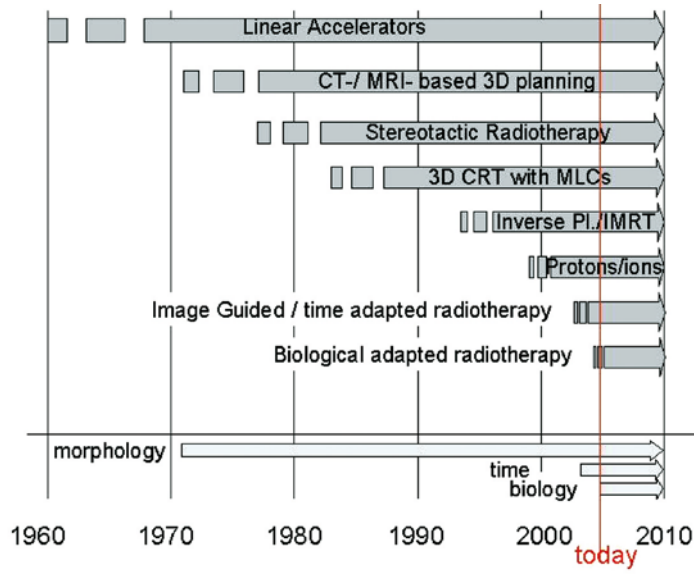
The book will be very helpful for doctors in treating patients as well as for physicists and other individuals interested in oncology.

Philadelphia — Luther W. Brady
Hamburg — Hans-Peter Heilmann
Munich — Michael Molls

Preface

In the 1960s radiation therapy was considered an empirical, clinical discipline with a relatively low probability of success. This situation has changed considerably during the past 40 years.

Radiation therapy is based heavily on fields such as physics, mathematics, computer science and radiation biology as well as electrical and mechanical engineering, making it a truly interdisciplinary field, unparalleled by any other clinical discipline. Now radiation therapy can be applied so safely, precisely and efficiently that the previously feared side effects no longer play a role. At the same time, tumour control, and the probability of cure, has significantly increased for many tumour patients. This change from an empirical and qualitative discipline to a scientifically based, precise clinical science has been accompanied by groundbreaking innovations in physics and technology (Fig. 1).



- The first important step was the replacement of cobalt-60 and betatrons as irradiation sources by electron-linear accelerators (also known as "linacs") between 1960 and 1980. Modern computer-controlled linacs are comparatively compact and reliable, have a high mechanical accuracy and deliver sufficiently high dose rates. Having become the "workhorses" of radiation oncology, they have been introduced in nearly every radiotherapy department in the world, providing the basis of modern precision radiotherapy.
- The next important milestone, which sparked a revolution not only in radiological diagnostics but also in radiotherapy, was the invention of X-ray computed tomography (CT). Computed tomography was introduced to the radiotherapy process at the end of the 1970s, and this resulted in 3D computerized treatment planning, now a standard tool in all radiotherapy departments.

- The CT-based treatment planning was later supplemented with medical resonance imaging (MRI). By combining CT and MRI, and using registered images for radiotherapy planning, it is now possible to assess tumour morphology more precisely, and thus achieve improved definition of planning target volumes (PTV), improving both percutaneous radiotherapy and brachytherapy.
- The computer revolution, characterized by the development of small, powerful and inexpensive desktop computers, had tremendous impact on radiation therapy. With new tools from 3D computer graphics, implemented in parallel with 3D treatment planning, it was possible to establish "virtual radiotherapy planning", a method to plan and simulate 3D irradiation techniques. New 3D dose calculation algorithms (e.g. "pencil-beam algorithms") made it possible to precalculate the 3D dose distributions with sufficient accuracy and with acceptable computing times.
- With the aforementioned advent of 3D imaging, 3D virtual therapy simulation and 3D dose calculation, the preconditions for introducing an individualized, effective local radiation treatment of tumours were fulfilled. What was still missing was the possibility to transfer the computer plans to the patient with high accuracy. This gap was filled by the introduction of stereotaxy into radiotherapy in the early 1980s. Prior to this development, stereotaxy was used in neurosurgery as a tool to precalculate target points in the brain and to precisely guide probes to these target points within the tumour in order to take biopsies or implant radioactive seeds. The transfer of this technique to radiotherapy resulted in significantly enhanced accuracy in patient positioning and adjustment of radiation beams. Stereotactic treatment techniques were first developed for single-dose irradiations (called "radiosurgery"), then for fractionated treatments in the brain and the head and neck region ("stereotactic radiotherapy"). Later, it became possible to transfer stereotactic positioning to extracranial tumour locations ("extracranial stereotactic radiotherapy") as well. This opened up the possibility for high-precision treatments of tumours in nearly all organs and locations.
- The next important step which revolutionized radiotherapy came again from the field of engineering. The development of computerized multi-leaf collimators (MLCs) in the middle of the 1980s ensured the clinical breakthrough of 3D conformal radiotherapy. With the advent of MLCs, the time-consuming fabrication of irregularly shaped beams with cerrobend blocks could be abandoned. Conformal treatments became less expensive and considerably faster, and were applied with increasing frequency. The combination of 3D treatment planning and 3D conformal beam delivery resulted in safe and efficient treatment techniques, which allowed therapists to escalate tumour doses while at the same time lowering the dose in organs at risk and normal tissues.
- By the mid 1990s, 3D conformal radiotherapy was supplemented by a new treatment technique, which is currently becoming a standard tool in modern clinics: intensity-modulated radiotherapy (IMRT) using MLC-beam delivery or tomotherapy, in combination with inverse treatment planning. In IMRT the combination of hardware and software techniques solves the problem of irradiating complex target volumes with concave parts in the close vicinity of critical structures, a problem with which radio-oncologists have had to struggle from the very beginning of radiotherapy. In many modern clinics around the world, IMRT is successfully applied, e.g. in the head and neck and in prostate cancer. It has the potential to improve results in many other cancer treatments as well.
- The IMRT with photon beams can achieve a level of conformity of the dose distribution within the target volume which can, from a physical point of view, not be improved further; however, the absolute dose which can be delivered to the target volume is still limited by the unavoidable irradiation exposure of the surrounding normal tissue. A further improvement of this situation is possible by using particle radiation. Compared with photon beams, the interaction of particle beams (like protons or heavier charged particles) with tissue is completely different. For a single beam, the dose delivered to

the patient has a maximum shortly before the end of the range of the particles. This is much more favourable compared with photons, where the dose maximum is located just 2–3 cm below the surface of the patient's body. By selecting an appropriate energy for the particle beams and by scanning particle pencil beams over the whole target volume, highly conformal dose distributions can be reached, with a very steep dose fall-off to surrounding tissue, and a much lower "dose bath" to the whole irradiated normal tissue volume. Furthermore, from the use of heavier charged particles, such as carbon-12 or oxygen-16, an increase in RBE can be observed shortly before the end of the range of the particles. It is expected that this radiobiological advantage over photons and protons will result in a further improvement in local control, especially for radioresistant tumours. However, particle therapy, both with protons and heavier charged particles, is still in the early stages of clinical application and evaluation on a broad scale. Ongoing and future clinical trials must demonstrate the benefit of these promising, but costly, particle-beam treatments.

At the beginning of the new millennium, the field of adaptive radiotherapy evolved from radio-oncology:

- After 3D CT and MRI enabled a much better understanding of tumour morphology, and thus spatial delineation of target volumes, the time has arrived where the temporal alterations of the target volume can also be assessed and taken into account. Image-guided and time-adapted radiotherapy (IGRT and ART) are characterized by the integration of 2D and 3D imaging modalities into the radiotherapy work flow. The vision is to detect deformations and motion between fractions (inter-fractional IGRT) and during irradiation (intra-fractional IGRT), and to correct for these changes either by gating or tracking of the irradiation beam. Several companies in medical engineering are currently addressing this technical challenge, with the goal of implementing IGRT and ART in radiotherapy as a fast, safe and efficient treatment technique.
- Another innovation which is currently on the horizon is biological adaptive radiotherapy. The old hypothesis that the tumour consists of homogeneous tissue, and therefore a homogeneous dose distribution is sufficient, can no longer be sustained. We now know that a tumour may consist of different subvolumes with varying radiobiological properties. We are trying to characterize these properties more appropriately by functional and molecular imaging using new tracers in PET and SPECT imaging and by functional MRI (fMRI) and MR spectroscopy, for example. We now have to develop concepts to include and integrate this information into radiotherapy planning and beam delivery, firstly by complementing the morphological gross tumour volume (GTV) by a biological target volume (BTV) consisting of subvolumes of varying radioresistance, and secondly by delivering appropriate inhomogeneous dose distributions with the new tools of photon- and particle-IMRT techniques ("dose painting"). Furthermore, biological imaging can give additional information concerning tumour extension and tumour response to radiotherapy or radiochemotherapy.

Currently, we have reached a point where, besides the 3D tumour morphology, time variations and biological variability within the tumour can also be taken into account. The repertoire of radiation oncology has thus been expanded tremendously. Tools and methods applied to radiotherapy are increasing in number and complexity. The speed of these developments is sometimes breathtaking, as radiation oncologists are faced more and more with the problem of following and understanding these modern innovations in their profession, and putting the new developments into practice. This book gives an introduction into the aforementioned areas. The authors of the various chapters are specialists from the involved disciplines, either working in research and development or in integrating and using the new methods in clinical application. The authors endeavoured to explain the very often complicated and complex subject matter in an understandable manner. Naturally, such a

collection of contributions from a heterogeneous board of authors cannot completely cover the whole field of innovations. Some overlap, and variations in the depth of descriptions and explanations were unavoidable. We hope that the book will be particularly helpful for physicians and medical physicists who are working in radiation oncology or just entering the field, and who are trying to achieve an overview and a better understanding of the new technologies in radiation oncology.

The motivation to compile this book can be traced back to the editors of the book series Medical Radiology/Radiation Oncology, by Michael Molls, Munich, Luther Brady, Philadelphia, and Hans-Peter Heilmann, Hamburg. We thank them for continuous encouragement and for not losing the belief that the work will eventually be finished. We extend thanks to Alan Bellinger, Ursula Davis, Karin Teichmann and Kurt Teichmann, who did such an excellent job in preparing the book. Most of all, thanks to all the authors, who wrote their chapters according to our suggestions, and a very special thanks to those who did this work within the short period of time before the deadline.

Heidelberg — Wolfgang Schlegel
Boston — Thomas Bortfeld
Munich — Anca-Ligia Grosu

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