Ophthalmic Radiation Therapy
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Ophthalmic Radiation Therapy
Techniques and Applications

Volume Editors

Arun D. Singh  Cleveland, Ohio
David E. Pelayes  Buenos Aires
Stefan Seregard  Stockholm
Roger Macklis  Cleveland, Ohio

49 figures, 42 in color, and 7 tables, 2013
To my parents who educated me beyond their means, my wife Annapurna, and my children, Nakul and Rahul, who make all my efforts worthwhile. (A.D.S.)

To Veronica, love you forever. We will meet again. (D.E.P.)

To Marie, Louise and Caroline for all your love and support. (S.S.)

For our patients and our students who continue to help us to see with clearer eyes. (R.M.)
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List of Contributors

Mary E. Aronow  
Department of Ophthalmic Oncology  
Cole Eye Institute  
Cleveland Clinic Foundation  
9500 Euclid Avenue  
Cleveland, OH 44195 (USA)  
E-Mail turellm2@gmail.com

Roger Macklis  
Department of Ophthalmic Oncology  
Cole Eye Institute  
Cleveland Clinic Foundation  
9500 Euclid Avenue  
Cleveland, OH 44195 (USA)  
E-Mail macklir@ccf.org

Ehsan H. Balagamwala  
Department of Radiation Oncology  
Taussig Cancer Institute  
Cleveland, OH 44195 (USA)  
E-Mail ehsanhb@gmail.com

Gaurav Marwaha  
Department of Radiation Oncology  
Taussig Cancer Institute  
Cleveland, OH 44195 (USA)  
E-Mail marwahg2@ccf.org

Justis P. Ehlers  
Vitreoretinal Service  
Cleveland Clinic Cole Eye Institute  
9500 Euclid Avenue  
Cleveland, OH 44195 (USA)  
E-Mail ehlersj@ccf.org

Carlos A. Medina Mendez  
Vitreoretinal Service  
Cleveland Clinic Cole Eye Institute  
9500 Euclid Avenue  
Cleveland, OH 44195 (USA)  
E-Mail medina25@hotmail.com

David Y. Kim  
Retina Service  
Department of Ophthalmology  
Massachusetts Eye and Ear Infirmary  
Harvard Medical School  
Boston, MA 02114 (USA)  
E-Mail David_Kim@meei.harvard.edu

Shizuo Mukai  
Retina Service  
Department of Ophthalmology  
Massachusetts Eye and Ear Infirmary  
Harvard Medical School  
Boston, MA 02114 (USA)  
E-Mail Shizuo_Mukai@meei.harvard.edu

Shannon M. MacDonald  
Department of Radiation Oncology  
Massachusetts General Hospital  
Harvard Medical School  
Boston, MA 02114 (USA)  
E-Mail smacdonald@partners.org

David E. Pelayes  
Maimonides University  
Buenos Aires University  
Ciudad Autonoma de Buenos Aires  
Emilio Mitre 477 S A Caballito  
Buenos Aires (Argentina)  
E-Mail davidpelayes@gmail.com
Stefan Seregard
St Eriks Eye Hospital
Karolinska Institutet
Polhemsgatan 50
SE-11 282 Stockholm (Sweden)
E-Mail stefan.seregard@sankterik.se

Roshan V. Sethi
Department of Radiation Oncology
Massachusetts General Hospital
Harvard Medical School
Boston, MA 02114 (USA)
E-Mail rsethi2@partners.org

Arun D. Singh
Department of Ophthalmic Oncology
Cole Eye Institute
Cleveland Clinic Foundation
9500 Euclid Avenue
Cleveland, OH 44195 (USA)
E-Mail singha@ccf.org

Abigail Stockham
Department of Radiation Oncology
Taussig Cancer Institute
Cleveland, OH 44195 (USA)
E-Mail stockha@ccf.org

Allan Wilkinson
Department of Radiation Oncology
Taussig Cancer Institute
Cleveland, OH 44195 (USA)
E-Mail wilkina@ccf.org
Foreword

The physicist W.C. Roentgen discovered X-rays in 1895, which were first named after him mainly in the German-speaking literature. The idea of using X-rays in the treatment of malignant diseases was born in the same year when, upon the initiative of a medical student in Chicago named Emil Grubber, X-rays were used to treat a local relapse of breast cancer. Already in 1897, H. Chalupecki published his experimental results about the effect of the new radiation treatment on rabbit eyes. H.L. Hilgartner wrote the first clinical report on the treatment of a bilateral retinoblastoma with X-rays in 1903. At first, there was a general uncertainty about the exact dosage needed so that medical application only slowly gained general acceptance. The introduction of a unit to calculate the absorbed energy within the irradiated tissue – today measured in ‘Grays’ (1 Gy = 1 Ws/kg) – has been a great step forward.

Furthermore, we had to learn that the biological radiation effect is not only dependent on the absorbed energy, but also on the quality of the rays (ionization density, LET), the dose distribution in time (protraction, fractionation), extension of the radiation field as well as some other factors. For this reason, the term relative biological effectiveness was created. The introduction of brachytherapy with radium contact treatment by Mme S. Laborde in Villejuif in 1925, X-ray brachytherapy by H. Chaoul in 1935, and finally the development of the precise irradiation technique for eyelid cancer by F. Baclesse of the Foundation Curie in Paris in 1939 brought forward the supposition to considerably improve the results after radiation treatment in patients suffering from cancer of the eyelid.

In 1958, A.B. Reese from New York recommended specially shaped irradiation tubes and, with the so-called cross fire technique, was able to considerably improve the outcome after X-ray treatment of children suffering from retinoblastoma. In 1983, J. Schipper was the first to introduce precision megavoltage external beam radiation therapy for retinoblastoma.

The use of radon seeds by R.F. Moore, H.B. Stallard and J.G. Milner in 1931 provided a new method for the treatment of intraocular melanomas using brachytherapy and thus avoiding enucleation. In 1960, H.B. Stallard presented his first patients suffering from choroidal melanoma who had been treated successfully by shell-shaped $^{60}$Co applicators sutured onto the scleral surface at the base of the intraocular tumor.
The ball-shaped $^{60}$Co applicators developed by B. Rosengreen and B. Tengroth did not gain acceptance. Unfortunately, these gamma ray sources caused severe radiation-induced side effects in the course of time. For this reason, a number of alternative radionuclides were introduced to improve therapeutic outcome: $^{106}$Ru/$^{106}$Rh plaques by P.K. Lommatzsch, R. Vollmar and G. Vormum, $^{125}$I plaques by M. Rothman and S. Packer, $^{192}$Ir plaques by D. Grange, $^{90}$Sr/$^{90}$Y plaques by L. Missotten, $^{103}$Pa plaques by P. Finger, and finally the binuclid applicator ($^{106}$Ru/$^{106}$Rh in combination with $^{125}$I) by N. Bornfeld. Herewith, the functional results could be remarkably improved, especially in cases with small and medium-sized tumors. H.L. Friedell, C.J. Thomas and J.S. Krohmer constructed some concave mirror-like $^{90}$Sr/90Y applicators. With them, M. Lederman from the Royal Marsden Hospital in London considerably improved his postradiation results in eyes with conjunctival melanomas, as reported 1966.

C. Haye, H. Jammet and M.A. Dollfus published their two volumes of 'L'oïl et les radiations ionisantes' in 1965 and lay the theoretical and practical foundations for radiation therapy of malignant eye tumors.

The introduction of particulate radiation into medicine was an important step forward. Taking advantage of the 'Bragg peak', we were enabled to optimize the dose distribution even within larger intraocular tumors, and at the same to protect structures of the eye from not being involved in the malignant tumor. E.S. Gragoudas introduced proton beam therapy in 1978 and D.H. Char the use of accelerated helium ions in 1986 for the treatment of intraocular melanomas. In addition, the development of stereotactic radiation techniques either with the linear accelerator (LINAC) or with the gamma knife ($^{60}$Co) gave us the opportunity to optimize the tumor dose in a similar fashion as the much more expensive proton beams.

Radiotherapy of choroidal melanomas can destroy the local tumor; however, it does not prevent the patients from death due to metastasis in about 50% (Collaborative Ocular Melanoma Study Group, 2004). Monosomy in chromosome 3 and gain of chromosome 8 in melanoma cells are significant features when seeking an increased probability for the development of metastases, as we have recently seen in the results of numerous publications, especially those by B. Horstemke, E. Passarge and N. Bornfeld. Consequently, human genetic examinations of tissue from choroidal melanomas become increasingly important to detect micro metastases, thus enabling to commence an effective adjuvant treatment in patients with a high risk of developing metastases.

The management of patients with an ophthalmic tumor can be particularly challenging. That is why intensive cooperation between experienced ophthalmologists, radiologists and radiation physicists is a necessary and fundamental condition to successfully utilize all types of ionizing radiation in order to treat tumors of the eye and its adnexa. Because of the slow regression of most tumors after irradiation as well as the chance of tumor recurrence and radiation-induced side effects, it seems mandatory to perform well-organized follow-up examinations of each irradiated patient.

The last comprehensive book on this topic, 'Radiotherapy of Intraocular and Orbital Tumors', was published by E. Alberti and R.H. Sagerman in 1993. Since then, 20...
years have passed and many new therapeutic procedures and a lot of clinical trials have appeared in the literature.

Therefore, we welcome Arun D. Singh as an international experienced colleague who is well noted in the field of ophthalmic oncology for taking the initiative to compose and present our current knowledge of radiation therapy in ophthalmology in this volume of *Developments in Ophthalmology*.

He has made use of his good reputation to bring together eminent experts from around the world to produce an up-to-date and comprehensive overview of radiation therapy in ophthalmology.

This book will be most valuable not only to trainees but also to mature ophthalmologists, oncologists, radiologists and other specialists participating in the care of patients, especially those with ophthalmic tumors.

Only a well-founded knowledge of all the pros and cons of ionizing radiation for medical purposes can meet the requirements to apply radiotherapy properly.

In any case, the principle in medicine ‘nihil nocere’ should be especially noted.

*Peter K. Lommatzsch, MD, Leipzig*
Preface

Ophthalmic tumors are rare and diverse, hence their diagnosis and treatment usually requires special expertise and equipment, and in many instances is controversial. Increasingly, the care of such patients is provided by a multidisciplinary team, comprising ocular oncologists, general oncologists, radiation therapists, radiation oncologists and other specialists. The field of radiation oncology is advancing rapidly, because of accelerating progress in tumor biology, pharmacology, and instrumentation. For all these reasons, we felt that there was scope for a monograph dedicated to radiation therapy of ocular tumors, offering a comprehensive source of authoritative information on the subject of ocular and adnexal radiation therapy.

This monograph, a conjoint effort of ocular oncologists and radiation oncologists, comprises of 10 chapters covering basic and advanced radiation therapy techniques followed by specific indications by location (uveal, retinal, orbital tumors, eyelid and conjunctival tumors) and complications of radiation therapy. We have also included a chapter on investigational use of radiation therapy for age-related macular degeneration.

It is our sincere hope that readers will find as much pleasure reading this textbook as we had writing and editing it.

Arun D. Singh, MD, Cleveland, Ohio, USA
David E. Pelayes, MD, PhD, Buenos Aires, Argentina
Stefan Seregard, MD, Stockholm, Sweden
Roger Macklis, MD, Cleveland, Ohio, USA