Animal Models in Ocular Oncology

Guest Editors
Martine J. Jager, Leiden
Sarah E. Coupland, Liverpool
A comprehensive source of authoritative information on ocular and adnexal radiation therapy

Ophthalmic Radiation Therapy

Techniques and Applications

Editors:
Arun D. Singh
David E. Pelayes
Stefan Seregard
Roger Macklis

This publication, a joint effort by ocular oncologists and radiation oncologists, comprises ten 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. A chapter on investigational use of radiation therapy for age-related macular degeneration is also included. The contributions are illustrated by photographs, imaging studies, and detailed treatment plans to clearly convey the fundamental concepts. Additional tables, flow diagrams, graphs or charts support the understanding of the subject.

To ocular oncologists, radiation physicists, radiation therapists, and radiation oncologists this volume is a comprehensive source of authoritative information on the subject of ocular and adnexal radiation therapy.

Contents

Foreword: Lommatzsch, P.K.

• Teletherapy: Advanced Techniques: Stockholm, A.; Balagamwala, E.H.; Singh, A.D.; Macklis, R.
• Brachytherapy: Marwaha, G.; Macklis, R.; Singh, A.D.; Wilkinson, A.
• Radiation Therapy: Uveal Tumors: Seregard, S.; Pelayes, D.E.; Singh, A.D.
• Radiation Therapy: Retinal Tumors: Sethi, R.V.; MacDonald, S.M.; Kim, D.Y.; Mukai, S.
• Radiation Therapy: Age-Related Macular Degeneration: Medina Mendez, C.A.; Ehlers, J.P.
• Radiation Therapy: Conjunctival and Eyelid Tumors: Aronow, M.; Macklis, R.; Singh, A.D.
• Radiation Therapy: Orbital Tumors: Marwaha, G.; Macklis, R.; Singh, A.D.
• Radiation Therapy: Anterior Segment Complications: Medina Mendez, C.A.; Singh, A.D.

Subject Index

Dear Librarian
I have reviewed this publication and would like to recommend it for our library.
Recommended by:

Department:

Date:

Signature:

Orders may be placed with any bookshop, subscription agency, directly with the publisher or through a Karger distributor.

The easiest way to order: www.karger.com/deoph

KARGER
Contents

See the journal website for contents
Ocular Oncology and Pathology

Editors-in-Chief
A.D. Singh, Cleveland, Ohio
H.E. Grossniklaus, Atlanta, Ga.

Editorial Board Members
P. Chévez-Barrios, Houston, Tex.
B. Damato, San Francisco, Calif.
S. Heegaard, Copenhagen
S. Seregard, Stockholm
G.K. Vemuganti, Hyderabad
M.W. Wilson, Memphis, Tenn.
Guidelines for Authors

Submission
Manuscripts in English are considered for publication and should be submitted online.

Online Manuscript Submission
Should you experience any problems with your submission, please contact the Editorial Office at:

doop@karger.com
S. Karger AG
Editorial Office ‘Ocular Oncology and Pathology’
P.O. Box
CH–4009 Basel (Switzerland)
Fax +41 61 306 1434

Conditions
All manuscripts are subject to editorial review. Manuscripts are received with the explicit understand-
ing that they are not under simultaneous consideration by any other publication.
A cover letter with the name, address, and telephone and telefax numbers of the corresponding author must accompany each manuscript. This letter must include a statement that affirms that all authors concur with the submission.
Submission of an article for publication implies transfer of the copyright from the author to the publisher upon acceptance. Accepted papers become the permanent property of Ocular Oncology and Pathology and may not be reproduced by any means, in whole or in part, without the written consent of the publisher.
It is the author’s responsibility to obtain permission to reproduce illustrations, tables, etc. from other publi-
cations.

Conflicts of Interest
Authors are required to disclose any sponsorship or funding arrangements relating to their research and all authors should disclose any possible conflicts of inter-
est. Conflict of interest statements will be published at the end of the article.

Ethics
Published research must comply with the guidelines for human studies and animal welfare regulations. Authors should state that subjects have given their informed consent and that the study protocol has been approved by the institute’s committee on human research. Fur-
ther, they should also state that animal experiments conform to institutional standards.

Plagiarism Policy
Whether intentional or not, plagiarism is a serious vio-
lation. We define plagiarism as a case in which a paper reproduces another work with at least 25% similarity and without citation.
If evidence of plagiarism is found before/after accept-
ance or after publication of the paper, the author will be offered a chance for rebuttal. If the arguments are not found to be satisfactory, the manuscript will be re-
tracted and the author sanctioned from publishing pa-
ers for a period to be determined by the responsible Editor(s).

Types of Papers
Editorials
Review Articles
Clinical Research
Basic Science Research
Case Series and Brief Reports

Arrangement
Title page: The first page of each paper should indi-
cate the title, the authors’ names, the institute where the work was conducted, and a short title for use as running head.
Full address: The exact postal address of the corre-
responding author complete with postal code must be given at the bottom of the title page. Please also sup-
ply phone and fax numbers, as well as e-mail address.
Key words: Please supply 3–10 key words in English that reflect the content of the paper.
Abstract: Each paper needs an abstract in English of not more than 200 words.
The abstract is of utmost importance. It should contain the following information: purpose of the study, pro-
cedures, results, conclusions and message of the paper.
Footnotes: Avoid footnotes.
Tables and illustrations: Tables and illustrations (both numbered in Arabic numerals) should be sent in sepa-
rate files. Tables require a heading and figures a leg-
end, also in a separate file. Due to technical reasons, figures with a screen background should not be submit-
ted. When possible, group several illustrations in one block for reproduction (max. size 180 x 223 mm). Black and white half-tone and color illustrations must have a final resolution of 300 dpi after scaling, line drawings one of 800–1,200 dpi.

Color Illustrations
Online edition: Color illustrations are reproduced free of charge. In the print version, the illustrations are re-
produced in black and white. Please avoid referring to the colors in the text and figure legends.
Print edition: Up to 6 color illustrations per page can be integrated within the text at CHF 800.00 per page.

References
In the text identify references by Arabic numerals [in square brackets]. Material submitted for publication but not yet accepted should be noted as [unpublished data] and not be included in the reference list. The list of references should include only those publications which are cited in the text. Do not alphabetize; numer-
number references in the order in which they are first men-
tioned in the text. The surnames of the authors followed by initials should be given. There should be no punc-
tuation other than a comma to separate the authors. Preferably, please cite all authors. Cite all authors, ‘et al’ is not sufficient. Abbreviate journal names accord-
ing to the Index Medicus system. Also see International-
al Committee of Medical Journal Editors: Uniform re-
requirements for manuscripts submitted to biomedical journals (www.icmje.org).

Examples
(a) Papers published in periodicals: Chatel J-M, Ber-
nard H, Orson FM: Isolation and characterization of two complete Ara h 2 isoforms cDNA. Int Arch Allergy
(b) Papers published only with DOI numbers: Theoh-
rides TC, Boucher W, Spear K: Serum interleukin-6 reflects disease severity and osteoporosis in mas-
tocytosis patients. Int Arch Allergy Immunol DOI:
10.1159/000063858.
(c) Monographs: Matthews DE, Farewell VT: Using and Understanding Medical Statistics, 3rd, revised. Basel,
Karger, 1996.
(d) Edited books: Tarou LR, Bloomsmith MA, Hoff MP,
Erwin JM, Maple TL: The behavior of aged great apes;
in Erwin JM, Hoff PR (eds): Aging in Nonhuman Pri-
mates. Interdiscip Top Gerontol. Basel, Karger, 2002,
vol 31, pp 209–231.

Reference Management Software: Use of EndNote is rec-
commended for easy management and formatting of cita-
tions and reference lists.

Digital Object Identifier (DOI)
S. Karger Publishers supports DOIs as unique identi-
fiers for articles. A DOI number will be printed on the tu-
ble page of each article. DOIs can be useful in the fu-
ture for identifying and citing articles published online
without volume or issue information. More informa-
tion can be found at www.doi.org

Supplementary Material
Supplementary material is restricted to additional data
that are not necessary for the scientific integrity and con-
cclusions of the paper. Please note that all supple-
mentary files will undergo editorial review and should
be submitted together with the original manuscript.
The Editors reserve the right to limit the scope and
length of the supplementary material. Supplementary
material must meet production quality standards for
Web publication without the need for any modifica-
tion or editing. In general, supplementary files should
not exceed 10 Mb in size. All figures and tables should
have titles and legends and all files should be supplied
separately and named clearly. Acceptable files and for-
mats are: Word or PDF files, Excel spreadsheets (only
if the data cannot be converted properly to a PDF file),
and video files (.mov, .avi, .mpeg).

Author’s Choice™
Karger’s Author’s Choice™ service broadens the reach
of your article and gives all users worldwide free and
full access for reading, downloading and printing at
www.Karger.com. The option is available for a one-
time fee of CHF 3,000.00, which is a permissible cost
in grant allocation. More information can be found at
www.karger.com/authors_choice.

NIH-Funded Research
The U.S. National Institutes of Health (NIH) mandates
under the NIH Public Access Policy that final, peer-
reviewed manuscripts appear in its digital database
within 12 months of the official publication date. As
a service to authors, Karger submits your manuscript
on your behalf to PubMed Central (PMIC) immediately
upon publication. It usually receives a PMCID within
approximately a month and will appear in PMC after
12 months. For those selecting our premium Author’s Choice™ service, the usual embargo will be overrid-
ed, accelerating the accessibility of your work. More
details on NIH’s Public Access Policy are available here.

Self-Archiving
Karger permits authors to archive their pre-prints (i.e.
pre-refereeing) or post-prints (i.e. final draft post-ref-
ereeing) on their personal or institution's servers, pro-
vided the following conditions are met: Articles may
not be used for commercial purposes, must be linked to
the publisher's version, and must acknowledge the
publisher's copyright. Authors selecting Karger’s Au-
thor’s Choice™ feature, however, are also permitted
to archive the final, published version of their article,
which includes copyediting and design improvements
as well as citation links.
Page Charges
There are no page charges for papers of 5 or fewer printed pages (including tables, illustrations and references). Each additional complete or partial page is charged to the author at CHF 325.00. The allotted size of a paper is equal to approx. 8 manuscript pages (including tables, illustrations and references).

Proofs
Unless indicated otherwise, proofs are sent to the corresponding author and should be returned with the least possible delay. Alterations other than the correction of printer's errors are charged to the author.

Reprints
Order forms and a price list are sent with the proofs. Orders submitted after the issue is printed are subject to considerably higher prices.

ESASO Course Series

This new book series makes the essentials of the courses of the European School for Advanced Studies in Ophthalmology (ESASO) available to interested ophthalmologists, optometrists, technicians and residents all over the world. The presentations of the courses are published regularly featuring a wide range of ophthalmological topics from vitreoretinal pathology to retinal surgery, retinal diseases, cornea and refractive surgery or cataract.

ESASO Course Series

Read it online: www.karger.com/ESASO

Series Editors
F. Bandello, Milan
B. Corcóstegui, Barcelona

Vol. 5: Orbital Surgery
Editors: Medel R. (Barcelona); Vásquez L.M. (Barcelona)
VIII + 116 p., 87 fig., 82 in color, 3 tab., 2014
CHF 98.00 / EUR 82.00 / USD 115.00
(soft cover)
CHF 118.00 / EUR 98.00 / USD 138.00
(online)
ISBN 978-3-318-02605-4
e-ISBN 978-3-318-02606-1

Vol. 4: Optical Coherence Tomography
Editors: Coscas, G. (Citéd'Paris); Loewenstein, A. (Tel Aviv); Bandello, F. (Milan)
XII + 134 p., 137 fig., 97 in color, 9 tab., 2014
CHF 98.00 / EUR 82.00 / USD 115.00
(soft cover)
CHF 118.00 / EUR 98.00 / USD 138.00
(online)
ISBN 978-3-318-02563-7
e-ISBN 978-3-318-02564-4

Vol. 3: Cataract
Editor: Güell, J.L. (Barcelona)
VIII + 140 p., 178 fig., 168 in color, 5 tab., 2013
CHF 98.00 / EUR 82.00 / USD 115.00
(soft cover)
CHF 118.00 / EUR 98.00 / USD 138.00
(online)
ISBN 978-3-318-02410-4
e-ISBN 978-3-318-02411-1

Vol. 2: Surgical Retina
ESASO modules 2009 and 2010: Selected contributions
Editors: Bandello, F. (Milan); Battaglia Parodi, M. (Milan)
X + 178 p., 89 fig., 56 in color, 23 tab., 2012
CHF 98.00 / EUR 82.00 / USD 115.00
(soft cover)
CHF 118.00 / EUR 98.00 / USD 138.00
(online)

Online version for institutional purchase
Prices subject to change. EUR price for Germany, USD price for USA and Latin America only

ESASO Course Series

Founded 2012
Field of Interest: Ophthalmology
ISSN 1664–882X
e-ISSN 1664–8838

Included in
www.karger.com/ophthalmology-package

© 2015 S. Karger AG, Basel
E-Mail karger@karger.com
www.karger.com

The Guidelines for Authors are available at:
www.karger.com/int
### ESASO Programme 2015

<table>
<thead>
<tr>
<th>Event</th>
<th>Dates</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oculoplastic Surgery</td>
<td>19-23.01.15</td>
<td>La Valletta</td>
</tr>
<tr>
<td>Medical Retina</td>
<td>02-06.02.15</td>
<td>Lugano</td>
</tr>
<tr>
<td>Medical &amp; Surgical Retina</td>
<td>27-30.03.15</td>
<td>Singapore</td>
</tr>
<tr>
<td>Cataract &amp; Intraocular Refractive Surgery</td>
<td>26-30.04.15</td>
<td>Sharjah</td>
</tr>
<tr>
<td>Cataract &amp; Intraocular Refractive Surgery</td>
<td>04-08.05.15</td>
<td>Barcelona</td>
</tr>
<tr>
<td>Surgical Retina</td>
<td>01-05.06.15</td>
<td>Lugano</td>
</tr>
<tr>
<td>Medical Retina</td>
<td>08-12.06.15</td>
<td>Lugano</td>
</tr>
<tr>
<td>Cataract &amp; Intraocular Refractive Surgery</td>
<td>22-26.06.15</td>
<td>St. Petersburg</td>
</tr>
<tr>
<td>Medical &amp; Surgical Retina</td>
<td>23-26.07.15</td>
<td>Singapore</td>
</tr>
<tr>
<td>Medical Retina</td>
<td>07-11.09.15</td>
<td>Lugano</td>
</tr>
<tr>
<td>Medical &amp; Surgical Retina</td>
<td>28.09-02.10.15</td>
<td>Ankara</td>
</tr>
</tbody>
</table>

**15th ESASO Retina Academy 2015**

22 – 24 October 2015  
Barcelona, Spain

![Save the date!](www.esaso.org)
Current Concepts in Uveal Melanoma

Editors
Martine J. Jager
Laurence Desjardins
Tero Kivelä
Bertil E. Damato

Contents

Diagnosis of Uveal Melanoma: Kivelä, T.
Treatment Selection for Uveal Melanoma: Damato, B.E.

Ruthenium-106 Brachytherapy: Pe'ee, J.


Stereotactic Photon Beam Irradiation of Uveal Melanoma: Zehetmayer, M.

Local Resection of Uveal Melanoma: Damato, B.E.

Biopsies in Uveal Melanoma: Midena, E.; Parrozzani, R.

Analysis of Intraocular Biopsies: Coupland, S.E.

Antiangiogenic Therapy in Uveal Melanoma: el Filali, M.; van der Velden, P.A.; Luyten, G.P.M.; Jager, M.J.

Immunotherapy of Uveal Melanoma: Bosch, J.J.

Genetic Determinants of Uveal Melanoma: Couturier, J.; Saule, S.

Therapeutic Options in Metastatic Uveal Melanoma: Mariani, P.; Servois, V.; Piperno-Neumann, S.

Uveal melanoma is an aggressive form of cancer that can involve the iris, the ciliary body, and/or the choroid, which is the main location of this tumor. Patients often wish to be informed about treatment choices and the results of different approaches. Important current clinical questions are whether a biopsy should be taken of choroidal melanomas, what should be done with this biopsy, and whether high-risk patients should be screened regularly.

This volume describes the clinical characteristics of uveal melanoma along with the different current techniques available for treatment, such as radioactive plaque treatment, proton beam therapy, and local tumor resection. Furthermore, techniques for taking biopsies and characterizing biopsy material are demonstrated. Future therapies such as anti-VEGF treatment and options for the treatment of metastases are also discussed.

Residents with an interest in ocular oncology, ophthalmologists or physicians dealing with uveal melanoma, as well as patients wishing to know more about this malignancy will find a topical update on uveal melanoma in this publication.
Knowing One’s Medical Fate in Advance
Challenges for Diagnosis and Treatment, Philosophy, Ethics and Religion

Editors
Georg Pfleiderer
Manuel Battegay
Klaus Lindpaintner

Contents
Introduction: Pfleiderer, G.; Battegay, M.; Lindpaintner, K.

Medical Perspectives
• Evolving Therapy and Prognosis in HIV – How Knowing One’s Medical Fate in Advance Can Change Dramatically: Battegay, M.
• Related to Human Cognition: Is Personalization Feasible and Desirable?: Papassotriopoulos, A.

Ethical and Juridical Perspectives
• Ethical Decision-Making on Genetic Diagnosis Facing the Challenges of Knowing One’s Medical Fate in Advance: Bahrer, G.
• Predictive Medicine – Changes in Our View of Ourselves and Others: Birnbacher, D.
• Current Challenges for the Law: Disclosure Dilemmas in Predictive Medicine: Dörre, B.S.

Religious Perspectives
• Fate and Judaism – Philosophical and Clinical Aspects: Gesundheit, B.
• Modern Medicine and My Future Life: A Christian-Theological Perspective: Pfleiderer, G.
• Karma, Contingency, and the ‘Point of No Return’: Predictive Medicine and Buddhist Perspectives: Schlieter, J.

Author Index
Subject Index

Modern medicine is now in a position to make advanced prognoses that chart the entire course of illness and recovery. Paradoxically, this is coupled with a new dimension of uncertainty for the patient, i.e. coming to terms with discovering they have an increased risk of a particular disease and deciding what appropriate steps to take. In this publication, renowned experts in their fields discuss these issues. The certainty and uncertainty of one’s fate are discussed from both methodological and epidemiological perspectives, using examples of diseases for which treatment and prognosis have dramatically changed. Despite profound insights into the human genome, personalized genetically tailored medicine still lies in the future. Religious, spiritual and philosophical dimensions are discussed, as are the ways in which they may help people cope with these new insights into their future, e.g. the promise of an afterlife.

This publication aims to bridge the different fields dealing with this area by addressing the challenges faced and encouraging dialogue. It will be of interest to all readers who deal with ethical problems of prognosis, particularly in medicine, as well as to theologians and sociologists.

Please send: ___ copy/ies
Postage and handling free with prepayment

Payment:
Please charge to my credit card
☐ American Express ☐ Diners
☐ MasterCard ☐ Visa

Card No: _____________________________
Exp. date: __/___

(Note: 3 digits in the signature field on the back of Visa and MasterCard)
☐ Check enclosed ☐ Please bill me

Orders may be placed with any bookshop, subscription agency, directly with the publisher or through a Karger distributor.

Fax: +41 61 306 12 34
S. Karger AG, P.O. Box, CH–4009 Basel (Switzerland)
E-Mail orders@karger.ch, www.karger.com

Name/Address:

Date: _____________________________

Signature: _____________________________
Ophthalmic Research features original papers, reviews and short communications reporting on translational and clinical studies. Authors from throughout the world cover topics on glaucoma, cataract and refractive surgery, retina, uveitis, and other fields in connection with physical, physiologic, pharmacological, biochemical and molecular biological aspects of ophthalmology. This journal provides a record of international clinical research for both researchers and clinicians in ophthalmology.

The journal further offers, at a reasonable price, the possibility of publishing dedicated supplements and abstracts of conferences and symposia. Please consult the managing editor for this.

Ophthalmic Research
Journal for Translational and Clinical Research

Editor
José Cunha-Vaz, Coimbra

Associate Editors
Age-Related Macular Degeneration
José-Alain Sahel, Paris

Diabetic Retinopathy and Retinal Vascular Diseases
Reinier O. Schlingemann, Amsterdam

Genetics
Bart Leroy, Ghent

Glucoma
Ingeborg Stalmans, Leuven

Immunology and Infectious Diseases
Dorairajan Balasubramanian, Hyderabad

Imaging
Tunde Peto, London

Oncology and Pathology
Eduardo Midenes, Padua

Surgery
Yuichiro Ogura, Nagoya

Neuro-Ophthalmology and Visual Function
Birgit Lorenz, Giessen

Anterior Segment
Marie-José Tassin, Arpont

EVICR.net
Cecilia Martinho, Coimbra

Epidemiology
Cécile Delcourt, Bordeaux

Educational – ESASO
Bruno Falcomatà, Lugano

Maurizio Battaglia Parodi, Milan

New Editor
José Cunha-Vaz, Coimbra

Selected contributions
• Expression of CREB in Primary Pterygium and Correlation with Cyclin D1, ki-67, MMP7, p53, Survivin and Vimentin: Nubile, M.; Curcio, C.; Lanzini, M.; Callejo, R.; Iezzi, M.; Mastropasqua, A.; Di Nicola, M.; Mastropasqua, L. (Chieti/Pescara)
• Progenitor Cells for Ocular Surface Regenerative Therapy: Casale-Marano, R.P.; Nieto-Nicolau, N.; Martinez-Conesa, E.M. (Barcelona)
• The Effect of Chronic Smoking on the Pupil and Photostress Recovery Time: Sobac, C.; Erdem, Ü.; Gundogdu, F.; Musayev, S. (Bilkent)
• Ocular Surface Temperature Gradient Is Increased in Eyes with Bacterial Corneal Ulcers: Klamann, M.K.J.; Maier, A.-K.B.; Gonnermann, J.; Klein, J.P.; Bertelmann, E.; Pleyer, U. (Berlin)
• High Vitreous Concentration of IL-6 and IL-8, but Not of Adhesion Molecules in Relation to Plasma Concentrations in Proliferative Diabetic Retinopathy: Koskela, U.E.; Kuusisto, S.M.; Nissinen, A.E.; Savolainen, M.J.; Liinamaa, M.J. (Oulu)

More information at www.karger.com/ore
Karger Publishers – 125 Years of Experience in Medical and Scientific Publishing

Karger Publishers – independent, family-run and Swiss-based.

It is our goal to promote the global scientific community with innovative and outstanding publications in every field of medical science. This means dedication to maintaining the highest standards of quality, as well as personalized service for authors, editors and readers.

www.karger.com

Please order a free copy of the Karger Festschrift ‘Connecting the World of Biomedical Science’ by sending your address to 125years@karger.com.
The last decade has observed significant progress in both basic and translational research, and in treatment options in the field of ocular oncology. Despite this, we are still seeking the ‘holy grail’ of effective therapeutics in disseminated ocular malignancies. We remain reliant on pre-clinical in vitro and in vivo models for testing drug efficacy.

Today, a range of animal models are available for studying ocular tumors, including uveal melanoma, conjunctival melanoma, retinoblastoma and vitreoretinal lymphoma. These models can also be used to determine how the host responds to tumors immunologically or to find out how certain genes or cytokines contribute to tumor growth.

Experts in the field of ocular oncology have contributed to this publication with a range of comprehensive reviews on the use of animal modeling for ocular tumors, including chick embryos, drosophila, zebrafish, mice, rats, rabbits and others. This volume will represent a useful background resource for researchers in the field.