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General Assembly of the Club Jules Gonin
Vouliagmeni, Greece
10 September 2004

President: Dr. Jack Coleman, **Secretary**: Dr. Nicolas Ducrey
Club members present: 115

1) Approval of the last 2002 committe report
Approval of the preliminary agenda of the 2004 general assembly

2) Movements in committee memberships
a) We express our gratitude to four executive committee members, who are ending their mandate, for their very valuable contribution to the club:

Dr. Jack Coleman, President,
Dr. Nicolas Ducrey, Secretary,
Dr. Rosario Brancato,
Dr. Alain Gaudric.

Dr. Coleman contributed to the Club first as a member for many years, then as Vice-President and finally as President for a total of 14 years in the Executive Committee. Dr. Ducrey had a very long mandate of 22 years as permanent Secretary of the Club. We wish to thank both of them for the tremendous amount of time and energy they have invested for the wellbeing of the Club Jules Gonin

Two committee members were asked to extend their mandates for 4 years

- Dr. Zdenek Gregor
- Dr. Yasuo Tano

Dr. Zdenek Gregor is the new President Elect

Dr. Thomas J. Wolfensberger is elected as the new Secretary of the Club

Three new committee members are elected:

- Dr. Yannick Le Mer, Montreuil, France
- Dr. Francesco Bandello, Udine, Italy
- Dr. Donald D'Amico, Boston, USA

b) The new bylaw for a four year-term of the psesidency is accepted by the floor.

3) Movements in account memberships:

We thank Dr. Michel Gonvers, who is ending his mandate, for his time and expertise.
Dr. Constantin Pournaras, Geneva, Switzerland, is elected as new account member.

4) Movements in memberships

a) Three new **honorary members** are elected:

- Dr. Jean-Jacques De Laey, Ghent, Belgium
- Dr. George Blankenship, Hershey, USA
- Dr. Hal Freemanm, Boston, USA

The updated number of Honorary members is: 21

b) Eleven new **passive memberships** are accepted:

- Dr. Jean-Antoine Bernard, Paris, France
- Dr. Morton S. Cox, Pickney, MI, USA
- Dr. Sergio L. Cunha, Sao Poulo, Brazil
- Dr. Gavin Douglas, Parktown, RSA
- Dr. F. Faulborn, Graz, Austria
- Dr. Froncie Gutman, Chagrin Falls, USA
- Dr. Sylvie Limon, Paris, France
- Dr. Manfred Spitznas, Bonn, Germany
- Dr. Bradley Straatsma, Los Angeles, USA
- Dr. Yuval Yassur, Tel Aviv, Israel

The updated number of passive members is: 71

c) Four **resignations from membership** have been accepted:

- Dr. Hans Gnad, Viena, Austria
- Dr. Horst Laqua, Lübeck, Germany
- Dr. Helge Paulmann, Königswinter, Germany
- Dr. Christiane Trepsat, La Mulatière, France

d) Three **members** of the Club **deceased** this year:

- Dr. Lorimer Fison, honorary member, on February 12th, 2004
- Dr. James Hudson, honorary member, at the beginning of 2004
- Dr. Sam Etzine, member from 1961–1984, at the beginning of 2004

e) Two **memberships** have been **withdrawn**:

- Dr. Robert Sampaolesi, for non-payment of fees
- Dr. Spiros Pollalis for non-payment of fees and non-participation in meetings

f) Thirteen **new active members** are elected:

- Dr. Remzi Avci, Bursa, Turkey
- Dr. Ferdinando Bottoni, Milano, Italy
- Dr. Marta S. Figueroa, Madrid, Spain
- Dr. Glen Jaffe, Durham, USA
- Dr. Arthur Mueller, Munich, Germany
- Dr. Yuichiro Ogura, Nagoya, Japan
- Dr. Ayala Pollack, Rehovot, Israel
- Dr. Kelvin Rivett, East London, RSA
- Dr. Ingrid Scott, Miami, USA
- Dr. Cynthia A. Toth, Durham, USA
- Dr. Panagiotis Theodossiadis, Athens, Greece
- Dr. George A. Williams, Royal Oak, USA
- Dr. Tom H. Williamson, London, UK

The updated number of active members is: 254

5) Financial reports

The financial report of the Club Jules Gonin's accounts and the financial report of the 2002 Meeting in Montreux are presented by Dr. Durcey: no special remarks.

6) Future Meetings

The 2006 Meeting of the Club will take place in Cape Town, South Africa:

The main organiser is: Dr. Louis Kruger, Roosevelt Park, RSA
Dates of the Cape Town Meeting: Sunday October 15th – Friday October 20th
It will be the 3rd joint meeting together with the Retina Society

The 2008 Meeting of the Club will be held in St. Moritz, Switzerland
The organiser is Dr. Thomas J. Wolfensberger, Lausanne, Switzerland

7) Prizes of the Club Jules Gonin

The recipient of the 2004 Hermann Wacker Prize was:
Dr. Gisèle Soubrane, Paris, France
The recipient of the 2004 Gonin Lecture of the Retina Research Foundation was:
Dr. Leonidas Zografos, Lausanne, Switzerland

8) Miscellaneous

a) Graefe's Archives: The journal of the Club Jules Gonin will remain Graefe's Archives printed by Springer. All members will have access to the on-line version and receive the printed version of the journal.

b) New bylaw for membership: The following bylaw concerning the shortening of the time period to become a member of the Club is accepted by the General Assembly:

- In order to become a candidate for membership, the applicant must:
1) send his/her CV with three endorsements from members of the Club to the Secretariat. The documents must be received by May 1st of the year in between congresses (odd number year),

2) have at least 5 recent publications on vitreoretinal subjects in Medline listed journals with senior authorship (1st, 2nd or last author) during the last 10 years,

3) after acceptance of the candidacy by the Executive Committee, give at least one oral presentation at a Club Congress within 4 years. The membership will be voted on the next "in-between" (od number year) Executive Committee Meeting and ratified at the following congress of the Club Jules Gonin by the members at the general Assembly.

A copy of the newly worde requirements for membership will be sent o each member as soon as ready. The bylaw discussed above is subject to a change in the statutes article 3, 1st paragraph, which are to be ratified in 2006 by the General Assembly:

Current version of statutes:
Ophtalmologists and other scientists, of all nationalities, corresponding to the conditions of article 2a), may be eligible for the membership of the Club, after having attended, as guest, at least two meetings over a six year period,
Modifications to be ratified:
Opthalmologists and other scientists, of all nationalities, corresponding to the conditions of article 2a), may be eligible for membership of the club, after having attended, as *candidates*, at least *one* meeting over a *four-year* period.

c) Credit Card Payments: Members can now pay their membership fees either with Visa or Master Cards

Dr. Thomas J. Wolfensberger
Secretatry of the Club Jules Gonin

Meetings of the Club Jules Gonin

1959 Lausanne, Switzerland
1961 Lausanne, Switzerland
1963 Amersfoort, The Netherlands
1965 Villars-sur-Ollon, Switzerland
1966 München, Germany
1968 Cambridge, UK
1970 Lausanne, Switzerland
1972 Miami, USA
1974 La Baule, France
1976 Lausanne, Switzerland
1978 Barcelona, Spain
1980 Crans-Montana, Switzerland
1982 Cordoda, Argentina
1984 Lausanne, Switzerland
1986 Copenhagen, Denmark
1988 Brugges, Belgium
1990 Lausane, Switzerland
1992 Vienna, Austria
1994 Versailles, France
1996 Bern, Switzerland
1998 Edinburgh, Scotland, UK
2000 Taormina, Sicily
2002, Montreux, Switzerland
2004, Athens, Greece

Recipients of the Hermann Wacker Prize

1972 Robert Machemer, Durham
1974 Rudolf Klöti, Zürich
1976 A. Oksala, Finland
1976 Jackson D Coleman, New York
1976 Karl Ossoining, Iowa City
1978 Manfred Spitznas, Bonn
1980 Donald Gass, Miami
1982 Harvey Lincoff, New York
1982 Ernst Custodis, Düsseldolf
1984 John Scott, Cambridge
1986 Relja Zivojnovic, Rotterdam
1988 Norman Byer, Torrance
1990 Charles L. Schepens, Boston
1992 Stanley Chang, New York
1994 Franz Fankhauser, Bern
1996 Pierre Amalric, Albi
1998 Alan C. Bird, London
1998 Raymond Lund, London
2000 Thomas M. Aaberg, Atlanta
2002 Steve Charles, Memphis
2004 Gisèle Soubrane, Creteil

Recipients of the Lecture of the Retina Research Foundation

1996 Evangelos Gragoudas, Boston
1998 Peter Wiedemann, Leipzig
2000 Veit-Peter Gabel, Regensburg
2002 Joan W. Miller, Boston
2004 Leonidas Zografos, Lausanne

Members of the Executive Committee September 2004

President Zdenek Gregor
Secretary Thomas J. Wolfensberger
Members Francesco Bandello
Rafael Cortez
Donald D'Amico
Evangelos Gragoudas
Yannick Le Mer
Einar Stefansson
Yasuo Tano
Peter Wiedemann

Honorary Members of the Club Jules Gonin

Blankenship George, Hershey, USA
Coscas Gabriel, Créteil, France
De Laey Jean-Jacques, Ghent, Belgium
Deutman August F., Nijmegen, The Netherlands
Foulds Wallace, Glasgow, Scotland, UK
Freeman Hal, Boston, USA
Gailloud Claude, Renens, Switzerland
Klöti Rudolf, Zürich, Switzerland
Lincoff Harvey, New York, USA
Machemer Robert, Durham, USA
McPherson Alice, Houston, USA
Nakajima Akira, Bunkyo-ku, Japan
Olivela-Casals, Barcelona, Spain
Ryan Stephen, San Francisco, USA
Schepens Charles, Boston, USA
Scott John, Cambridge, UK
Shimizu Koichi, Itabashiku, Japan
Törnquist Ragnar, Örebro, Sweden
Urrets-Zavalia Alberto, Cordoba, Argentina
Wetzig Paul, Colorado Springs, USA

Presentation of the 2004 Hermann Wacker Prize to Gisèle Soubrane, MD, PhD

Gisèle Soubrane, MD, PhD (Fr) was selected by the executive committee of the Club Jules Gonin as the recipient of the Hermann Wacker Award for 2004. The Hermann Wacker Prize is awarded to a clinician or scientist who has provided exemplary and pioneering work in the understanding and treatment of retinal disease. Dr. Soubrane's selection was based on her pioneering work in the development of flourescein and indocyanine green angiography in the evaluation of the retina. She has also pioneered the use of photodynamic therapy for treating age-related macular degeneration. Her work has played a major role in both retinal imaging technology and in therapeutic stragtegies for treating age-related macular degeneration.

Dr. Soubrane qualified as a medical doctor in 1969 with a thesis on the effect of 5 iodo 2 desoxyuridin on herpes virus at the Medical Faculty of the University of Paris. From 1970-1974 she spent her residency at the Department of Ophthalmology of the University of Paris. This was followed by a fellowship in retinal diseases under Professor Gabriel Coscas from 1974-1976. After working for several years at the Clinique Ophtalmologique Universitaire in Créteil, during which she also spent time at John Hopkins University in Baltimore, USA, as a research associate looking at recurrent neovascularisation after blue-green laser application, she was promoted to Associate Professor with a specialization in Medical Retina, Angiography and Lasers. In 1991 her research work took her to the Institute of Ophthalmology in London to work on vascular casts in minipigs. In 1992 she was awarded a PhD by the Faculté des Sciences Pierre et Marie Curie of the University of Paris for her work on "Ocular angiogenesis in normal and pathologic eyes: Implication of basic fibrolast growth factor". In 1993 followed her promotion to full Professor of Clinical Ophthalmology, and in 1996 she succeeded her mentor, Professor Coscas, as Chair of the Department of Ophthalmology at the University Eye Clinic in Créteil.

Gisèle's career has been punctuated by many highlights. She has received numerous awards internationally, such as the Bietti Medal, the Michaelson Medal, the Médaille d'Or CHIBRET, as well as a Senior Honor Award of the American Academy of Ophthalmology for her clinical and translational research. In 2000 she was also made a Chevalier de la Légion d'Honneur, which is one of the highest awards the French Government can bestow for outstanding service. Gisèle's activities in scientific societies have also been prolific. She has served on the Executive Committee of the Club Jules Gonin from 1992-1998 and has acted as Chairman of the Retina Section for the Association for Research in Vision and Ophthalmology (ARVO). She is the past President of the European Society for Vision and Eye Research and acts as the General Secretary of the European Board of Ophthalmology. She has also worked on the Board of the Société Française d'Ophthalmologie for many years. In addition, Gisèle sits on the editorial board of multiple journals and has been active as a member of many national and international societies in the field of visual science. Her research work continues to be focused on the pathophysiology and diagnosis of age-related macular degeneration, the natural history of choroidal new vessels, new therapeutic approaches for choroidal new vessels as well as experimental models of age-related macular degeneration.

In addition to all these tremendous scientific achievements, all of us know the very special gifts that make Gisèle the individual she is. Her open smile, which makes her instantly accessible, her sense of humour, her tremendous energy, and last but not least her elegant style, all mark her as a truly great person to know. It is therefore my immense pleasure that I present this year's Hermann Wacker Prize to Giséle Soubrane, a very special person, scientist and clinician.

D. Jackson Coleman, MD
Past President Jules Gonin Club

Leonidas Zografos

Radiotherapy in ophthalmology

2004 Jules Gonin Lecture of the Retina Research Foundation

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Radiotherapy has been used in ophthalmology for more than 100 years [10]. Hilgartner (Austin, Texas, USA), in 1903, reported the first successful treatment of a retinoblastoma by x-rays [37]. Three years later, Amman (Winterthur, Switzerland), described the inconclusive results of a trial of external beam radiotherapy for the treatment of a uveal melanoma [4], and Deutschmann (Hamburg, Germany), in 1915, reported the first successful conservative management of this tumor by apposition of mesothorium onto the sclera behind the tumor [20].

Progress in the use of radiotherapy in ophthalmology, despite the inventiveness of the pioneers of this discipline, particularly Axenfeld [7, 8] and Jendralsky [43] in Germany, Marx [57] in Holland, and Schönberg [72], Duncan [23], Janeway [42], and Verhoeff [90] in the United States, was limited during the first 30 years of the 20th century [96]. During this period, when only low-energy x-rays and natural radioisotopes were available, treatment failures were common and complications were often quite serious. However, the rare successes demonstrated in spectacular fashion the efficacy of this treatment in certain well-defined situations.

Application to ocular oncology of the technological advances in the field of radiation physics constituted the main source of progress in ocular radiation oncology, and was accomplished by a series of breakthroughs.

– The use, from 1929 onwards, of radon (^{222}Rn) seeds for interstitial and episcleral radiotherapy of melanomas and retinoblastomas by Foster Moore and Stallard in London [59, 60, 79, 80].
– The 1935 presentation to the New York Academy of Medicine by Martin and Reese of a preliminary report on the treatment of retinoblastomas by fractionated high-dose external beam radiotherapy with a device that allowed the use of small fields and that controlled the direction of the x-ray beam [54–56, 69].
– The successive development by Stallard and Innes, in 1948 and 1950, of radium and ^{60}Co episcleral applicators designed to emit high-energy gamma radiation [40, 81, 82].
– Improvement in external beam irradiation devices with the successive development of orthovoltage apparatuses (150–500 kVp), the betatron in 1941 [45], the ^{60}Co teletherapy in 1951, and the linear accelerator in 1953 [58].
– The development by Lommatzsch, in 1968, of ^{106}Ru/^{106}Rh episcleral applicators that emitted high-energy beta particles [51, 52].
– The design, by Gragoudas and colleagues in 1974, of a device for the treatment of uveal melanomas using an accelerated proton beam [32, 33].
– The report in 1975 by Rotman et al. [70], and the following year that by Sealy et al. [73], of radio-applicators loaded with Iodine 125 (^{125}I) seeds, developed at the Sloan-Kettering Cancer Center [36], that emitted low-energy gamma radiation. Iodine 125 applicators were subsequently chosen by the Collaborative Ocular Melanoma Study (COMS) because of their many theoretical and practical advantages for brachytherapy [24]. They currently constitute the most widely used treatment modality in the United States for the conservative treatment of intraocular tumors.
– The development by Schipper, in 1982, of a system that allows lens-sparing external beam radiotherapy by a linear accelerator of retinoblastomas and metastases located in the posterior segment [71].
– The recent development of conformal teletherapy and radiotherapy delivered by a Gantry connected to a cyclotron; applications to the field of ophthalmology are currently under clinical evaluation.

The concept of conservative management of ocular tumors developed in parallel with the technological advances in radiotherapy, gradually relegated enucleation to second place and limited the indications for which it is considered to be the only solution. This evidence-based progress in treatment was facilitated greatly by concentration of the treatment of ocular tumors in specialized centres. The history of this progress during the second half of the 20th century has been marked by numerous breakthroughs and landmark publications [2, 14, 21, 22, 25, 29, 30, 38, 46, 63, 64, 75, 81, 83–86, 95].

Current modalities of radiotherapy for uveal melanomas

Cobalt 60 plaques, which were the “gold standard” of brachytherapy for uveal melanomas for a long time [98], have now been abandoned, primarily because of concerns regarding radioprotection. The treatments used most widely at the present time are ^{106}Ru/^{106}Rh applicators, ^{125}I applicators and proton beam radiotherapy. Other methods and treatment modalities used by some groups include palladium (^{103}Pd) applicators [27] loaded with a radioisotope that emits gamma radiation with a lower energy than that emitted by ^{125}I; gamma knife, which delivers circumscribed irradiation, although with wide diffusion around the target [47, 94]; and linear accelerator, combined with Schipper's device [12] or a conformal stereotactic technique [11, 93].

Ruthenium/Rhodium 106 (^{106}Ru/^{106}Rh) applicators

Ruthenium/Rhodium 106 applicators emit high-energy beta particles that are able to penetrate tissues to a depth of 6 to 7 mm, but with rapid, progressive and considerable attenuation of the irradiation away from the radioactive plaque. Consequently, when the tumor is prominent, the base receives an irradiation dose several times higher than the therapeutic dose of 90–100 Gy delivered to the apex and, if for a mechanical reason the plaque becomes detached from the sclera, the apex may receive an insufficient dose of irradiation. We have estimated that, in such a situation, the dose to the apex is reduced by about one-half if the plaque is displaced a mere 1 mm from the scleral wall.

The isodose configuration of the irradiation emitted by these applicators makes them particularly suitable for the treatment of dome-shaped melanomas that do not exceed 5 mm in thickness. The low diffusion of irradiation around the target volume, which reduces adverse effects on the healthy tissues that surround the tumor, and the high irradiation dose that is delivered to the tumor base, which induces radiation necrosis and rapid reduction of tumor volume, thereby reducing the harmful effects produced by the residual tumor mass, confer certain theoretical advantages to this type of applicator. However, these theoretical advantages are counterbalanced by a risk of tumor recurrence, estimated to be between 10% and 40% at 5 to 15 years after treatment [53, 87, 92].

Iodine 125 (^{125}I) applicators

Iodine 125 applicators are monodirectional brachytherapy devices that emit low-energy gamma radiation. In the ^{125}I applicators designed for the COMS study, radioactive seeds are placed in the bottom of a gold shell with walls of 3 mm thickness, which are available in several standardized shapes and diameters [26]. This configuration of radioactive sources, set at a distance from the wall of the eyeball, helps to ensure a more homogeneous irradiation dose delivered to the target while minimizing side scatter, thereby ensuring better radioprotection of adjacent healthy tissues. Dosimetry is performed with various simplified calculation models, considering ^{125}I seeds to be a point irradiation source, with no correction for anisotropy [5, 6, 44].

This type of applicator, used for the treatment of medium-sized melanomas, ensures 5- and 10-year local tumor control rates of 85% to 95% [28, 34, 41, 68]. The main advantage of ^{125}I applicators is their commercial availability, which allows all retinal surgeons working in the field of ocular oncology to treat with a good chance of success most small and medium-sized uveal melanomas. The low energy of the gamma radiation emitted by these applicators is a second advantage, as it allows effective shielding that protects orbital tissues and also has low ambient diffusion of radiation, thereby contributing to the radioprotection of both patients and healthcare personnel.

However, the relatively short half-life (about two months) of ^{125}I is one of the major disadvantage of this type of radioactive applicator, as it requires frequent replacement of the seeds, which contributes to increased cost of treatment. Furthermore, there can be difficulty in exactly positioning the^{125}I plaques in some cases, especially when the tumor surrounds or covers the optic disc, which is another disadvantage of this type of brachytherapy, because they can result in incomplete irradiation, possibly leading to recurrence.

Proton beam irradiation

Treatment of uveal melanomas by proton beam radiotherapy was performed first by Gragoudas et al. in 1975 [32, 33]. Two years later, Char et al. developed a similar radiotherapy technique using an accelerated helium ion beam [17]; at the same time, Brovkina et al., in Moscow, began to use a lower energy particle accelerator for the treatment of melanomas of the iridociliary complex and anterior choroid, without surgical localization of the tumor [13]. We introduced proton beam irradiation into Western Europe in 1984, in the context of a joint project between Jules Gonin Eye Hospital and the Paul Scherrer Institut (PSI).

The technique developed in Boston, and still used today with only minimal modifications [67, 74, 97], comprises an energy modulator connected to a device that allows three-dimensional localization of the position of the tantalum clips fixed around the tumor base for the definition of the target volume. Treatment planning is performed on a computerized ocular model [31].

Treatment of uveal melanomas by accelerated proton beam is a widely used treatment option in Europe, being performed in Switzerland, France (Centre d'Orsay–Foundation Curie, Paris; Centre Lacassagne, Nice), the United Kingdom (Clatebridge), Italy (Catania), and Germany (Berlin).

In Lausanne and at the PSI, between 1984 and 2004, we have treated more than 4,000 cases of melanoma. On the basis of the experience acquired, we have gradually improved the local tumor control (98.8% at 10 years) and eye retention probability (95.6% at 10 years). We have also demonstrated, by means of subgroup analyses, the efficacy of this treatment in specific situations, such as those involving melanomas with extrascleral extension, melanomas associated with massive ocular melanocytosis, and diffuse melanomas of the iridociliary complex. In this last situation, due to the risk of severe dry eye syndrome secondary to complete irradiation of the anterior segment, we now harvest limbus stem cells prior to radiotherapy, which are then transplanted immediately after completion of radiotherapy.

Having achieved excellent local tumor control by circumscribed radiotherapy, especially with accelerated proton beam, the future objectives of conservative management of melanoma are primarily improvement of the functional result (elimination of the residual tumor, decreased irradiation to adjacent healthy tissues) and control of any microscopic metastases present at the time of treatment. Based on the effectiveness of intrahepatic fotemustine chemotherapy for liver metastases [50], we have initiated a prospective study of adjuvant intrahepatic fotemustine chemotherapy. Preliminary results of this study for the treatment of high-risk cases (tumor diameter ≥22 mm or tumor diameter ≥15 mm with extrascleral extension) are favourable, although the final results are still under evaluation.

Current modalities of irradiation of retinoblastomas

Whole-eye radiotherapy and circumscribed radiotherapy are part of the global therapeutic approach to retinoblastoma [9]. The choice of treatment modality, however, must be individualized for each case, and should take into account the extent of the tumor, the state of the fellow eye and the risk of complications, particularly the risk for development of a radiation-induced second orbital tumor [1].

In the majority of complex cases, chemoreduction is now typically the first step in treatment [30, 49, 63, 75], and is designed to make the tumor accessible to therapies that are less aggressive than irradiation such as photocoagulation, cryotherapy, or thermochemotherapy, thereby limiting as much as possible the use of radiotherapy.

External beam radiotherapy

External beam radiotherapy is delivered by either whole-eye irradiation techniques or lens-sparing techniques. Regardless of delivery method, well- documented results indicate a success rate of about 80% [39, 89].

One of the most widely used protocols consists of a total dose of 45 Gy delivered at 2 Gy fractions per session, 5 times per week [15]. In selected cases, highly fractionated doses can be used to reduce the risks of radiation retinopathy [18]. In contrast, dose escalation may be necessary, such as in the case of massive invasion of the vitreous, although malignancies do not always respond favourably to radiotherapy.

The current indications for external beam radiotherapy for retinoblastoma are limited, and its use should be avoided in children under the age of 1 year. However, this type of treatment is justified in well-defined situations [9]:

- Primary or adjuvant therapy of advanced tumors.
- Tumors that are in contact with the optic disc after reduction, and those that are inaccessible to brachytherapy or other focal treatment modalities.
- Presence of vitreous seeding that cannot be treated by cryotherapy, brachytherapy or chemotherapy alone.
- Subretinal or vitreous seeding that is refractory to treatment or that is recurrent after focal therapy or chemotherapy, with or without retinal detachment in patients with only one eye.
- Orbital exteriorization of the tumor or optic nerve invasion after enucleation.

Two lines of research have been developed in an attempt to limit irradiation outside of the target volume. The first approach consists of proton beam irradiation of the entire eye or vitreous cavity. Preliminary results have demonstrated the effectiveness of this method in terms of local tumor control [61, 62], but it did not eliminate the high dose of irradiation delivered at the radiation port.

The second line of research consists of the application of conformal radiotherapy; this is currently being studied in Lausanne. This irradiation technique, which is guided by three-dimensional software, employs multiple beams, each specifically collimated. The advantage of this technique is that it reduces considerably the irradiation dose delivered around the target volume. Conformal radiotherapy has already been used successfully for the treatment of various other types of tumors [16, 48, 88, 91], and preliminary results of its application to the treatment of retinoblastoma are also encouraging.

Circumscribed radiotherapy

Circumscribed radiotherapy is performed by use of either radioactive plaques (brachytherapy) or accelerated proton beam, after definition of the target volume by means of tantalum clips.

The use of ^{60}Co plaques, in which the internal surface comprises a radius of curvature adapted to the child's eye, was abandoned for reasons of radioprotection, even though no case of secondary orbital tumor related to the use of ^{60}Co plaques has been reported in the literature. In routine clinical practice, ^{106}Ru/^{106}Rh plaques and ^{125}I plaques are used for this type of treatment. The choice between these two types of plaque must take into account the tumor diameter, thickness and site.

Brachytherapy is indicated for tumors with a diameter between 4 and 15 mm and a thickness not exceeding 9 mm [35], that cannot be treated by photocoagulation, cryotherapy or thermochemotherapy. Brachytherapy is indicated also for treatment of residual tumors or recurrences after external beam radiotherapy or other focal therapies [19, 77, 78].

The recommended irradiation dose is about 40 Gy to the apex of the tumor, in which cases local tumor control is obtained in 80–90% of patients [3, 76, 77]. The most commonly encountered complications are proliferative retinopathy, radiation maculopathy, radiation neuropathy and cataract.

Because the 40 Gy isodoses of radioactive plaques are adapted primarily for the treatment of dome-shaped tumors, and in view of the frequently spherical shape of retinoblastomas, a plaque with a diameter that is quite a bit larger than that of the tumor base must be used to include all of the tumor. This disadvantage, together with the technical problems of precise positioning and fixation of radioactive plaques in young children with a posterior tumor, has led us to the possibility of treating some retinoblastomas by proton beam therapy after surgical localization of the tumor with tantalum clips.

Proton beam therapy has the advantage of delivering a homogeneous irradiation dose to a predefined target, regardless of its shape or site inside the eyeball, which theoretically minimizes the risk of radiation-induced complications and increases the rate of local control. However, with the currently available devices, which have been adapted to the treatment of ocular tumors in adults, in whom the head is maintained immobile in the sitting position, we have been able to successfully treat only children over the age of 3 years who have a recurrent retinoblastoma.

The efficacy of this circumscribed radiotherapy, similar to that observed for melanoma, has led us to investigate a new device whereby radiation is delivered via a Gantry [65, 66], which directs the beam by a spot scanning technique to children who are under general anaesthesia. This device, which is still under construction, will likely be operational in 2006 for experimental studies at the Institut Paul Scherrer.

Conclusions

Considerable progress has been made in the field of radiotherapy in ophthalmology, which now allows both local tumor control and eye retention in the majority of patients with a malignant intraocular tumor. However, further progress is necessary to improve the functional results by reducing the harmful effects of the tumor itself and of the radiation. Combined therapies and highly circumscribed irradiation techniques, currently under clinical evaluation, are a giant step in this direction, and should improve still more the outcome of treatment of intraocular tumors.

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Leonidas Zografos, MD : Curriculum vitae

Date of birth: 1947

Training, academic and hospital appointments

1972
- Degree in medicine of the University of Athenes - Greece

1973-1980
- Resident and Cheif resident in ophthalmology, University of Lausanne

1980-1984
- Research fellow and part-time consultant in ocular oncology, University Eye Clinic, Lausanne

1987
- Doctor in medecine, University of Lausanne

1989-1996
- Privat Docent, University of Lausanne

1993
- Swiss federal degree of medecine

1996-present
- Professor of Ophthalmology and Chairman of the University Eye Clinic, Lausanne
- Medical director of the Jules Gonin Eye hospital
- Scientific director of the IRO

Honors and Awards

1987
- Vogt price

1987
- Medal of the Italian society of ophthalmology

1988
- Cesar Roux price of the University of Lausanne

1991
- 4th Aquilana Gold medal of ophthalmology

1999
- Gold medal of the Tunisian ophthalmological society

2002
- Annual report of the French society of ophthalmology

2003
- Doctor Honoris Causa in medical science, University of Alger

2004
- Doctor Honoris Causa, Faculty of medicine, University of Athenes

2005
- Gold medal of the Ophthalmological society of Marocco