

**SCIENTIFIC SESSION 13
UVEAL MELANOMA 3**

Shilpakalavedika Convention Center
Tuesday, January 27, 2004
11:00 AM – 1:00 PM

Chair: Jerry Shields
Co-chair: S Natarajan
Moderator: Gerald Langmann
Session Summary: Gerald Langmann

	Presenter	Title of Presentation	Time
1	Leonidos Zografos	Key Note Lecture : Proton Beam Radiotherapy in Uveal Melanoma	11:00 AM
2	Carlo Mosci	Choroidal Melanoma Treatment with Proton Beam : Ten Years of Experiences of the Genoa Ocular Oncology Group	11:15 AM
3	Jean-Daniel Grange	Local Recurrences after Proton Beam Therapy for Uveal Melanoma	11:25 AM
4	Michael Georgopoulos	LINAC Stereotactic Radiotherapy of Uveal Melanoma	11:35 AM
5	Karin Muller	Effectiveness of Stereotactic Radiation Therapy for Eye Melanoma	11:45 AM
6	Emine Kilic	Reduced Tumor-Related Mortality in Uveal Melanoma by Pre-Enucleation Radiotherapy	11:55 AM
7	Dennis Robertson	Follow-up of Patients with Small Melanomas Treated with Transpupillary Therapy	12:05 PM
8	Myriam Spire	Primary Transpupillary Therapy for Treatment of Small Uveal Melanomas	12:15 PM
9	Andrei Yarovoy	A Comparative Analysis of Ru-106/Rh-106 Brachytherapy and Diode Laser Transpupillary Therapy in Treatment of Small Choroidal Melanoma	12:25 PM
10	Hanneke Joumee-de Korver	Transscleral Therapy for Choroidal Melanoma: From Laboratory to Clinic	12:35 PM
11	Karin Lecuona	The Effect of Different Radiation Dosages on the Recurrence Rate in the Treatment of Medium and Large Choroidal Melanomas with Iodine-125 Plaque	12:45 PM
12	Gerald Langmann	Session Summary	12:55 PM

KEY NOTE LECTURE PROTON BEAM RADIOTHERAPY IN UVEAL MELANOMA

Leonidos Zografos

Hôpital Ophtalmique Jules Gonin, Lausanne, Switzerland

CHOROIDAL MELANOMA TREATMENT WITH PROTON BEAM: TEN YEARS OF EXPERIENCES OF THE GENOA OCULAR ONCOLOGY GROUP

Carlo Mosci, Sandro Squarcia, Pierre Chauvel, Barbara Mascialino, Stefania Donadio, Nicole Iborra

ASL 3 Celesia Hospital, Genova, Italy

PURPOSE: The authors present the statistical results achieved by Genova Ocular Oncology Group during the first ten years in ocular melanoma treatment with proton beam. **METHODS:** The Genoa Ocular Oncology Group is teamwork of ophthalmologists, radiotherapists, and medical and statistician physicists. The application of tantalum clips surrounding the tumor is performed by the Genoa ophthalmological surgical team while proton beam therapy is planned and executed in Central Antine Lacassagne in Nice, France. Patient data are stored in a specialized database and analyzed by a group of medical statisticians of the Genoa University Physics Department. **RESULTS:** Statistical results based on 256 patients show a local tumor control of 96.6%, an eye retention of 94.2% and a survival rate of 86.3% five years after treatment. Hepatic metastasis occurred in 8.4%. **CONCLUSION:** Results of proton beam therapy for melanoma in Italian patients are encouraging.

LOCAL RECURRENCES AFTER PROTON BEAM THERAPY FOR UVEAL MELANOMA

Jean-Daniel Grange, Stephanie, Bruno Jean-Louis, Laurent Kodjikian, Pierre Chauvel, Nicole Iborra

Croix-Rousse Hospital, University Eye Clinic, Lyon, France

PURPOSE: To analyze rate and localizations of recurrences after proton therapy for uveal melanoma, also correlations between recurrences and initial tumor volume, tumor localizations and metastasis. **METHODS:** After placement of Tantalum rings, proton therapy was delivered at the Biomedical Cyclotron at a 60 GY Cobalt equivalent dose, in 365 eyes between June 1991 and 2003. Patients were followed every 4 months the 1st year, every 6 months the 2nd year, then each year. Ocular echographic measurements were performed each time and hepatic ultrasonography each semester. Fluorescein angiography was done if recurrence occurred. **RESULTS:** With a mean follow-up of 36 months, 19 recurrences (5.2%) were observed 11 were marginal, 5 uncontrolled tumors, 1 ring melanoma and 2 extrascleral extension. Mean initial tumor thickness was 6.6 mm and mean initial largest tumor diameter (LTD) 16.23 mm. 68% of recurrent tumors (13) were choroidal, 32% (6) on ciliary body. Mean time of recurrence was 28.4 months (3-84). 9 recurrences were treated with enucleation, 7 with protons, 4 developed metastasis. **CONCLUSION:** A low rate of recurrences is observed. Marginal recurrences were predominant. Comparing with larger series, similar observations could be done between the risk of recurrence and tumor height, LTD, and localization. Identical proportions of second treatments were also observed. A higher risk of hepatic dissemination was also correlated with recurrence.

LINAC STEREOTACTIC RADIOTHERAPY OF UVEAL MELANOMA

Michael Georgopoulos, Martin Zehetmayer, Karl Kircher, Karin Dieckmann, Richard Pötter

Department of Ophthalmology, Medical University of Vienna, Vienna, Austria

PURPOSE: We investigated long term local tumor control and clinical outcome after fractionated stereotactic radiotherapy with linear accelerator (LINAC) of uveal melanoma. **METHODS:** Between June 1997 and June 2003 135 patients with uveal melanoma have been treated with a 6MV stereotactic LINAC. Tumors included in this prospective study were either located unfavorably with respect to macula and optical disc (<3 mm distance) or presented with a thickness >7 mm. 133 patients presented with choroidal melanomas. Mean tumor thickness and volume were 5.2mm and 304mm³, respectively. The head was immobilized with a noninvasive head mask system. The eye was stabilized with an optical fixation system. 3D delineation and planning were performed with CT/MRI image fusion. Patients have been treated with 60-70Gy marginal dose (80% isodose) divided into 5 fractions. **RESULTS:** Local tumor control was achieved in 97%. The mean relative tumor prominence reductions were 13%, 23%, 32%, 36%, 38% and 43% at 0.5, 1, 2, 3, 4 and 5 years, respectively. Side effects included neovascular glaucoma (20 eyes), retinopathy (49 eyes), and cataract (51 eyes). Eleven eyes had to be enucleated. Five patients developed metastases. **CONCLUSION:** Fractionated LINAC with total doses of 60-70Gy results in good local tumor control and represents a highly effective method to treat uveal melanomas.

EFFECTIVENESS OF STEREOTACTIC RADIATION THERAPY FOR EYE MELANOMA

Karin Muller, Peter Levendag, Connie de Pan, Gre Luyten

Erasmus University, Rotterdam, The Netherlands

PURPOSE: To study the effectiveness and acute side effects of Stereotactic Radiation Therapy (SRT) for eye melanoma. **METHODS:** A blinking light (in front of the unaffected eye) and a camera (to monitor the position of the diseased eye) are attached to a non-invasive relocatable stereotactic frame. Primary endpoints are local control at 3, 12 and 24 months and acute toxicity (3 months). **RESULTS:** 38 Patients were included (median FU 18 months). All patients received 5 fractions of 10 Gy within 5 days (isodose 80%). After three months (38 patients) the local control was 100%, after 12 months (21 patients), one patient received a TTT because the tumor size did not decrease, after 24 months (8 patients) no recurrences were seen. The acute side effects were: conjunctival symptoms (7), loss of lashes or hair (6), visual symptoms (6), fatigue (5), dry eye (1), cataract (1), and pain (1). One patient underwent an enucleation 2 months after therapy. **CONCLUSION:** SRT is an effective and safe treatment modality for eye melanoma with an excellent local control and mild acute side effects. The FU should be prolonged to study both local controls at long-term and late toxicity.

REDUCED TUMOR-RELATED MORTALITY IN UVEAL MELANOMA BY PRE-ENUCLEATION RADIOTHERAPY

Emine Kilic, Theo Stijnen, Neeltje Mooy, Wilhelmina Eijkenboom, Paulus de Jong, Gre Luyten

Erasmus MC Department of Ophthalmology, Rotterdam, The Netherlands

PURPOSE: Pre-enucleation radiotherapy (PER) of uveal melanoma patients has been initiated in order to reduce enucleation-induced metastasis. Earlier studies with a follow-up period of 5 to 7 years did not demonstrate a significant effect on survival. Therefore, we studied the effect of PER on tumor-related mortality after a mean follow-up of 9.25 years. **METHODS:** In a prospective study, 167 uveal melanoma patients were treated between 1971 and 1992 by irradiation with 8 Gy given in two fractions two days before enucleation.

A group of 108 uveal melanoma patients, treated between 1971 and 1992 by enucleation only (EO) in the same hospital, served as a historical control group. Patients were followed until December 2002 or until death. **RESULTS:** Tumor-related death was observed in 32.3% of the PER treated group and in 40.7% of the EO group. A significant difference in survival was observed after a period of 48 months in favor of the PER group. After 15 years of follow-up the estimated survival rates for melanoma-related death in the PER group and EO group were 63.7% and 51.0%, respectively. For death due to all causes these percentages were 47.5% and 25.2%, respectively. In both groups, women had a better prognostic outcome than men. **CONCLUSION:** This study is suggestive that PER improves long-term survival in uveal melanoma patients.

FOLLOW-UP OF PATIENTS WITH SMALL MELANOMAS TREATED WITH TRANSPUPILLARY THERMOTHERAPY

Dennis Robertson, Peter Winn, Helmut Buettner, Steven Bennett

Mayo Clinic, Rochester, MN, USA

PURPOSE: To provide a critical intermediate follow-up analysis of small choroidal melanomas treated with transpupillary thermotherapy (TTT). **METHODS:** Since 1996, 40 eyes with suspected small choroidal melanomas have been treated with TTT, using a diode laser (810 nm). Follow-up ranged from one to seven years. The mean follow-up of the first 20 patients was 57 months. Mean follow-up of the recent 20 patients was 28 months. **RESULTS:** Ages of the patients ranged from 26 to 82 years (mean 58). Tumor thickness ranged from 1.0 to 3.2 mm (mean 2.0). Twenty-three tumors were reduced to a flat scar within six months. Five tumors (13%) developed edge recurrences and were satisfactorily managed with additional TTT and/or cryotherapy. Edge recurrences were seen as long as 71 months after TTT. Four tumors (10%), showed progressive growth not controlled with additional TTT; two were enucleated, one was treated with brachytherapy, and one was treated with proton radiation. **CONCLUSION:** Most tumors treated with TTT were reduced to a flat scar and did not recur following single treatment. Overall, nine tumors had recurrences. Recurrences were observed as long as 71 months after TTT.

PRIMARY TRANSPUPILLARY THERMOTHERAPY FOR TREATMENT OF SMALL UVEAL MELANOMAS

Myriam Spire, Laurent Kodjikian, Mojgan Sishe-Born Devouassoux, Jean-Daniel Grange

Hôpital de la Croix Rousse, Lyon, France

PURPOSE: In ophthalmology, heat has been recently evaluated: beyond 60°C for photocoagulation, between 42°C and 45°C in association with radiotherapy, and between 45°C and 60°C for isolated transpupillary thermotherapy (TTT). We performed TTT with diode laser at 810 nm for the treatment of small posterior pole uveal melanomas. **METHODS:** We treated 18 patients presenting posterior pole uveal melanoma between 2.5 and 4 mm thickness. Mean tumor thickness was 3.25 mm; mean diameter 7.11 mm, the localization inside posterior pole being variable. Patients received between 1 and 3 sessions, for an exposure time of one minute, an intensity adapted to the coloration of the fundus impact and a diameter beam depending of the laser type (2 or 3 mm). **RESULTS:** Among 18 patients, we report 8 tumor regressions (5 in and out posterior pole, 3 macular localization's), 10 tumor recurrences (5 juxta-papillary, 3 macular, and 2 in and out tumors). Treatment of recurrences required 3 enucleating, 6 proton beam-therapy, one tumor being controlled with a second session. **CONCLUSION:** Despite encouraging initial but still experimental results, the possible occurrence of severe complications, especially recurrences, should awake our

reflection about modalities and indications of primary TTT even for small uveal melanomas.

A COMPARATIVE ANALYSIS OF RU-106/RH-106 BRACHYTHERAPY AND DIODE LASER TRANSPUPILLARY THERMOTHERAPY IN TREATMENT OF SMALL CHOROIDAL MELANOMAS

Andrei Yarovoy, Leonid Linnik, Dzhavid Magaramov, Tatiana Syomikova, Evgenia Bulgakova

SN Fyodorov State Institution Eye Microsurgery, Moscow, Russia

PURPOSE: To perform a comparative analysis of efficacy of diode laser transpupillary thermotherapy (TTT) and brachytherapy (BT) in patients with small choroidal melanomas. **METHODS:** 55 patients were treated, 29 by diode laser TTT (average follow-up: 12.3 months), 26 by brachytherapy (average follow-up: 39.7 months). Before the treatment, the average tumor height was 2.14 and 2.71 mm, average diameter was 8.0 and 9.0 mm, and the average initial visual acuity was 0.52 and 0.58 respectively. **RESULTS:** The height of residual tumor (as percent of initial thickness) was 40% after TTT and 67.7% after BT. There was no metastasis in the TT group. In the BT group 2 patients were dead due to metastatic disease. Visual acuity in the TTT group decreased on an average by 4%, from 0.52 to 0.5, and in the BT group by 49.6%, from 0.58 to 0.29. Complications of TTT were thrombosis of branch retinal vein (n=1), subretinal vascularization (n=1), retinal traction (n=3), retinal hemorrhage (n=7), local vitritis (n=2) and retinoschisis (n=1). Complications of TTT were hemophthalmia (n=4), vitreous condensation (n=10), secondary glaucoma (n=1), retinal detachment (n=7), and optic neuropathy (n=7). **CONCLUSION:** TTT of small choroidal melanomas allows local tumor control as good as BT. TTT has better functional preservation. For a further complex evaluation of TTT results in small choroidal melanomas, a longer follow-up is necessary.

TRANSSCLERAL THERMOTHERAPY FOR CHOROIDAL MELANOMA: FROM LABORATORY TO CLINIC

H.G. Journée-de Korver, A.I. Rem, E.R. Barthen, J.E.E. Keunen

Leiden University Medical center, Leiden, The Netherlands

PURPOSE: Development of parameters for transscleral thermotherapy (TSTT) in the treatment of patients with choroidal melanoma. The aim of TSTT is to destroy the base of the tumor as well as the intrasclerally located tumor cells if present. **METHODS:** Experiments on the heat tolerance of the sclera was tested in specimens of donor sclera and in healthy rabbits. Depth of tumor necrosis by a single application of TSTT was tested in hamsters, subcutaneously implanted with Greene melanomas, which were covered with a specimen of human donor sclera. TSTT was performed in patients with large choroidal melanoma prior to their planned enucleation with permission of the Commission Medical Ethics of the Leiden University Medical Center end after informed consent was obtained from the patient. TSTT was performed with a newly developed applicator, diameter 5 mm, which combined infrared laser-induced heating with additional conductive episcleral heating at 60°C. **RESULTS:** Conductive episcleral heating up to 60°C was well tolerated by the sclera. TSTT with laser-parameters, power range 750-1250 mW, beam diameter 2-3 mm and a one-minute exposure time per application combined with additional episcleral heating of 60°C was well tolerated by the sclera. It resulted in tumor necrosis with occlusion of blood vessels with a depth of about 4 mm in hamster Greene melanoma; pre-enucleation TSTT in patients with choroidal melanoma resulted in a depth of about 3 mm. **CONCLUSION:** Experimental research on TSTT provided parameters that enabled us to perform pre-enucleation TSTT in patients with large choroidal melanoma.

THE EFFECT OF DIFFERENT RADIATION DOSAGES ON THE RECURRENCE RATE IN THE TREATMENT OF MEDIUM AND LARGE CHOROIDAL MELANOMAS WITH IODINE-125 PLAQUE

Karin Lecuona, Clare Stannard, Ross Sealy, Egbert Herring, Ruth Knowles, Seddick Isaacs

Groote Schuur Hospital and University of Cape Town, Cape Town, South Africa

PURPOSE: From 1983 to 1994 an apparent apical dose of 42 Gray was given. It was assumed to be 60 gray as calculations were based on a Relative Biological Effect (RBE) of 1.5 relative to Iridium 192. Subsequent information revealed an RBE of 1 and the dose was modified accordingly from 1 May 1994. **METHODS:** Retrospective review of data to assess the effect of the change in dosage to tumor control. **RESULTS:** 217 patients were treated for choroidal melanoma with I-125 plaque over 19 years. 88 patients were treated with a median apical dose of 46.19 Gray. 28 eyes were enucleated and 26 developed recurrences. 129 patients were treated with a median apical dose of 60.15 Gray. 13 eyes were enucleated and 11 patients developed recurrences. The eight-year recurrence rate under the two treatment groups was compared using the logrank test. No statistically significant difference between the groups ($p < 0.02$) was observed. **CONCLUSION:** No statistical difference could be demonstrated in the recurrence rate of choroidal melanomas irradiated with a dosage of 42 Gray compared with 60 Gray.

SESSION SUMMARY

Gerald Langmann

University Eye Clinic, Graz, Austria