OOG OCT 2022 Abstracts

OOG 1: Intraocular Tumors

Choroidal Hemangioma in Pregnancy and Post-Partum: A Case Series

Andron A. A., Gushansky k, Fabian D. I., Vishknevskia-Dai V.

Purpose – To describe 2 cases of symptomatic Choroidal Hemangioma during pregnancy with spontaneous resolution post -partum

Methods – A Case series

Results - A 42-year-old 30-week pregnant woman presented to the ocular oncology service, the Goldschleger eye institute at Sheba Medical Center with new-onset visual deterioration in her right eye. Fundoscopy revealed a pink elevated choroidal lesion in the macular region, with overlying subretinal fluid, also demonstrated on Optical Coherence Tomography (OCT). Ultrasound (US) examination demonstrated a hyperechoic choroidal lesion on B mode with medium- high internal reflectivity on A mode. The working diagnosis was a Choroidal Hemangioma and a decision was made to monitor the patient until after delivery. Post-partum, the patient reported improvement in symptoms and on examination, spontaneous resolution of the subretinal fluid was noticed, demonstrated also on OCT. A 31- year old 29 week primigravida presented to the oncology service with a visual disturbance in her left eye for two weeks. She had a history of a coagulation disorder and was treated with clexane. She had a left sided port – wine stain, prominent episcleral vessels and a diffuse choroidal hemangioma with subretinal fliud in the macular area. She was diagnosed with diffuse choroidal hemangioma with Sturge- Weber syndrome. A watchful waiting approach was taken with this patient as well and post- partum there was complete resolution of subretinal fluid as per Oct.

Conclusions - : Choroidal hemangioma- both circumscribed and diffuse are potentially sight-threatening lesion that may exacerbate during pregnancy. A watchful waiting approach should be considered, as spontaneous resolution of subretinal fluid may occur after delivery.

Surgical options to treat complicated retinal hemangioblastomas

Veckeneer M., Van Overdam K., Bartoszek P.

Purpose: To discuss the results of different vitreoretinal surgical techniques for the treatment of complicated hemangioblastomas.

Methods: Patients with retinal hemangioblastoma that either presented too late for conventional (non-surgical) treatment or that developed complications in spite off/as a result of the treatment were referred to us for vitrectomy.

Results: A total of 33 eyes of 33 patients were included. Treatment consisted of complete vitrectomy and traction release in all eyes. Different additional treatments were used to deal with the angioma's: closing feeder vessel with a suture or with bipolar diathermy forceps followed by intra and post-op laser or complete excision of tumors.

Conclusions: Achieving stable results in these challenging cases may require extensive/multiple surgical interventions. Excision of the tumors usually produces nice initial anatomical results but retinal re-detachments due to aggressive PVR may jeopardize the final outcome. Meticulous surgery with complete release of traction in combination with diathermy and laser but without excision may have favorable functional results.

In silico feasibility study: Retinal blood vessels organoid model to study retinal hemangioblastomas

Bals K., Hajjaj A., Brands T., de Klein A., Kilic E., Brosens E.

Purpose Retinal Hemangioblastomas (RH) are vascularized neoplasms that can present in the setting of Von Hippel-Lindau (VHL) disease. We want to edit control and patient induced pluripotent stem cells (IPSCs) using CRISPRCas9 and differentiate these cells into ocular specific cell types to be used in a blood vessel organoid model system for targeted therapies and prevention strategies. Often, not all relevant genes are expressed after differentiating IPSC into specific cell types. As these type of protocols are very laborious and time consuming, we wanted to evaluate previously published transcriptome datasets before starting our experiments.

Methods We have reanalyzed RNA sequencing derived transcriptomes of human central nervous system micro-vessels, their individual primary cells as well as central nervous system hemangioblastomas. We have compared central nervous system and retinal primary cells to their relevant immature and mature counterparts elsewhere in the body, optimized cell clustering of retinal single cell experiments and derived the transcriptome profiles IPSC derived human retinal primary cells. With deconvolution analysis, expression levels of these cell types were evaluated in choroid, retina, different published IPSC derived blood vessel differentiation protocols and a retinal hemangioblastoma transcriptome.

Results We developed a core marker set that distinguishes these cells from pericytes, endothelial cells, astrocytes and stromal cells of other locations in the body and determined the expression of core-genes needed to be expressed in a RH model system.

Conclusions Although there are differences and optimization of differentiation protocols is needed, it is possible to model RH using retinal blood vessel organoids.

Retinal Vaso Proliferative Tumors

Coman A., Murtagh P., Punic G., Horgan N.

Purpose To describe the clinical characteristics and treatment modalities associated with retinal vasoproliferative tumours (RVPT).

Methods Retrospective chart analysis of 9 patients with a diagnosis of RVPT attending the Ocular Oncology Service between September 2010-April 2022

Results The mean age at diagnosis was 40.4 years (14-55 years), two thirds of which were male. Presenting visual acuity (VA) ranged from 6/6 to Count Fingers. The main indication for presentation was a reduction in visual acuity, with only one patient (11.1%) asymptomatic at presentation. The majority of tumours were isolated to the inferotemporal quadrant (66.7%).

All 9 patients had B scan ultrasonography with a mean tumour thickness of 3.3mm (1.8-5.2mm). With regards to treatment, 1 case underwent argon laser alone, 1 case underwent intravitreal injection of Triamcinolone alone, 1 case required no treatment and 6 patients (66.7%) required multiple treatment modalities with combination of laser, cryotherapy and intravitreal injection of triamcinolone. Associated features found to be contributing to the visual disturbance at presentation included: exudative retinal detachment (44.4%), ERM (33.3%), cystoid macular oedema (22.2%) and vitreous haemorrhage (11.1%). Mean follow-up from diagnosis was 44.8 months.

Conclusions RVPT's are rare diseases entities and we have described a substantial case series of 9 patients. They usually occur in healthy individuals, and although benign, they can have a profound effect on VA as outlined by their associated features. Our findings are similar to previous case series demonstrating the tumour's predilection for the inferotemporal quadrant. Treatment modalities for these lesions vary and the most appropriate treatment choice depends on associated ocular comorbidities.

Mammalian target of Rapamycin Inhibitors for the treatment of Astrocytic Hamartoma in Tuberous Sclerosis Complex (TSC)

Vorobichik Berar O., Tzadok M., Zloto O., Moroz I., Hecht I., Ampaire Musika A.,

Schlomovitz O., Fabian I.D, Vishknevskia-Dai V.

Purpose: The mammalian target of rapamycin (mTOR) inhibitors interfere with the pathological mechanisms of Tuberous sclerosis complex (TSC). The purpose of this study is to assess the effect of mTOR inhibitors on RAH.
Methods: The medical records of all consecutive patients with ocular manifestations of TSC that were treated with mTOR inhibitors at the Sheba Medical Center from January 2014 to December 2018 were retrospectively reviewed Tumor size was assessed by a masked observer, before and after treatment.

Results: Eleven patients with tuberous sclerosis and astrocytic hamartoma were treated with mTOR inhibitors in the study period. Of them, 6 children (11 eyes, 20 tumors), had proper imaging of tumor size before and after treatment. The analysis included these 11 eyes. All six patients had non-ocular manifestations of TSC, including dermatologic (n = 5), neurologic (n = 5), and renal (n = 3) involvement.

Five patients (80%) had tumors near the optic disc, and 4 patients (67%) had foveal tumors. The mean follow-up duration was 2.15 ± 1.4 years (range 10 months to 4.5 years). The average tumor base reduction in the treated group was 17.8% ± 15.9. The average maximal thickness at baseline was 414 ± 174 µm (range 152-686 µm). there was a 14% ± 7.1 reduction after treatment. None of the tumors showed evidence of growth at final follow-up.

Conclusion: The findings of this study suggest that mTOR inhibitors can reduce tumor size, and that it can be considered as an optional treatment in certain conditions.

Choroid metastases from primary lung adenocarcinoma - A case series

O'Brien L., P. Murtagh, N. Horgan

Purpose To describe clinical characteristics and treatment outcomes of patients with choroidal metastases from primary lung adenocarcinoma.

Methods A consecutive series of 3 patients with choroidal metastases from primary lung adenocarcinoma evaluated at an ocular oncology centre July 2018 - April 2022.

Results Mean age at presentation was 42 years (range 33-49). All patients were Caucasian females, non-smokers. In two patients, the underlying cancer diagnosis was not known at the time of presentation. In all three patients, metastasis occurred in the left eye- one patient had two deposits, two patients each had a single juxtapapillary lesion. Average lesion thickness was 2.1mm (1.6-2.5mm). Two patients underwent external beam radiotherapy (EBRT). The third patient was treated with Alectinib, an ALK inhibitor, without EBRT to the choroid. In all three patients the lesions regressed, and visual acuity was 6/6 OU in each patient at last follow-up.

Conclusions Molecular profiling of lung adenocarcinoma in non-smokers facilitates the use of targeted oral treatment such as Alectinib, with less toxicity compared to systemic chemotherapy.

Systemic therapy may allow for EBRT to be avoided if the threat to central vision is not imminent.

We propose a prospective multicentre OOG study to share data from centres on the current management of choroidal metastases from lung adenocarcinoma to evaluate current practice patterns of EBRT versus systemic treatment alone. Although the concept of predilection for the left eye in metastatic choroidal deposits has previously been discounted, it would be interesting to assess laterality in a prospective study of metastatic lung adenocarcinoma.

Intraocular metastases from Cutaneous Melanoma

Lemaitre S., Thaung C., Sagoo M.

Purpose Cutaneous melanoma metastatic to the eye is considered to be rare. However, with the increasing incidence of this cancer and improved survival of patients treated with targeted therapies and checkpoint inhibition, it is possible that more cases will be referred to ocular oncology clinics.

Methods Single-centre retrospective study. We included all the patients with a diagnosis of intraocular metastases from cutaneous melanoma.

Results Four patients were seen between 2017 and 2022. Mean duration of follow-up was 12 months (range 4-21). The first patient had unilateral anterior segment and vitreous metastases, the second had bilateral choroidal metastases and unilateral vitreous cells, the third had unilateral amelanotic vitreous metastasis and the fourth had bilateral multifocal choroidal metastases. Interestingly, the two patients with unilateral metastases had a previous history of uveitis in the only affected eye, the two conditions being unrelated. All four patients had synchronous systemic metastases from cutaneous melanoma.

Conclusions The diagnosis of intraocular metastases from cutaneous melanoma is generally clinical but it can be challenging as these metastases sometimes mimic other ocular conditions. The presence of synchronous metastatic sites on screening is very much in favour of the diagnosis. Histological proof combined with genetic analysis is sometimes necessary for diagnosis, especially with amelanotic vitreous debris or in the rare cases where systemic screening is negative. New treatment modalities available for metastatic cutaneous melanoma are expected to help achieve intraocular tumour control and preserve vision.

Metastatic retinal lymphoma secondary to conjunctival MALT lymphoma with transformation into DLCL

Grishina E., Andryukhina O.

Introduction Metastatic retinal lymphoma is exceptionally rare, as systemic lymphomas most often metastasize to the uvea.

Purpose of the work is to report a unique case of metastases into the retina and optic disc from conjunctival lymphoma and discuss the results of treatment of these metastases.

Methods. 41-year-old patient was treated for conjunctival lymphoma 11 years ago. After 11 years blindness of the left eye developed. MRI of the brain, fundus OCT and lumbar puncture were done. Then posterior vitrectomy and FNAB of retinal infiltration were performed

Results. MRI of the brain and lumbar puncture revealed no pathological changes. The diagnosis of metastatic retinal lymphoma was established based on the results of OCT, cytological examination of the punctate of the infiltrated peripapillary retina and PCR examination of the aspirate. It was confirmed by regression of changes in the fundus against the background of antitumor treatment. The patient's follow-up period is 3 years without relapse.

Conclusions. The vital prognosis for patients with metastatic retinal lesion is unfavorable. However, early diagnosis and timely treatment of metastatic lymphoma of the retina and/or optic nerve can restore visual acuity of the affected eye and significantly improve the quality of life of patients.

Spontaneous growth of presumed epi-papillary astrocytic hamartoma

Weinberger Y, Dotan G, Gal-Or O

Purpose: To report a case of a patient with an asymptomatic, epipapillary, presumed astrocytic hamartoma and to describe work-up and management.

Methods: A case report.

Results: A 10-year-old asymptomatic female routinely followed due to unilateral optic nerve head drusen OD. Visual acuity was 20/20 in both eyes, with no clinical signs of optic neuropathy. At 3rd year's follow-up exam, a new epipapillary whitish mass with visible vascularity was observed clinically in her right eye. Work up of the mass included multi-modal imaging. Fundus autofluorescence revealed hyperautofluorescence at the optic nerve head OD. Optical coherence tomography (OCT) cross sectional scans over the optic nerve head revealed peripapillary hyperreflective material and an overlying hyper-reflective mass with no signs of traction OD. OCT angiography revealed flow signal, with no leakage on subsequent fluorescein angiogram. B-scan ultrasonography revealed hyperechogenic lesion at the head of the optic nerve head OD consistent with optic nerve head drusen and an overlying isoechogenic mass protruding to vitreous cavity. Scans of the left eye were unremarkable. Humprey 24-2 Visual field nonspecific, nasal and superior visual field defects OD. Systemic physical revealed no tuberous sclerosis complex stigmata. Head and orbits contrast enhanced magnetic resonance arteriography, venography and imaging was unremarkable.

Conclusion: We present an unusual case of a unilateral epi-papillary mass in a 10-year old asymptomatic patient with optic nerve head drusen. We emphasis the differential diagnosis and the importance of multimodal imaging in intraocular tumors.

OOG 2: Uveal melanoma

Impact of Fitzpatrick Skin Type on Metastatic Risk from Uveal Melanoma in 854 Consecutive Patients at a Single Center

Negretti G., Bayasi F., Goldstein S., Omega M., Taylor O., Ni R., Chiang L., Kim

R., Lien E., Barke M., Shields C.

Purpose To assess the impact of skin color using Fitzpatrick Skin Type (FST) on metastatic risk of uveal melanoma.

Methods Retrospective detailed review of patient charts was performed for FST (type I- white, II-fair, III-average, IV-light brown, V-brown, VI-black), clinical details of the patient and the uveal melanoma, tumor genetic results using The Cancer Genome Atlas (TCGA), and outcome of melanoma-related metastasis and death.

Results The FST classification was type I (n=97 patients), type II (n=665), type III (n=79), type IV (n=11), type V (n=2), type VI (n=0). A comparison of patient FST (type I vs. II vs. III-V) revealed significant differences in mean age at presentation (64.1 vs. 58.5 vs. 49.8 years, $p<0.001$), race white (100% vs. 98% vs. 75%, $p<0.001$), presence of ocular melanocytosis (3% vs. 3% vs. 10%, $p=0.01$), visual acuity <20/200 at presentation (6% vs. 7% vs. 13%, $p=0.03$), mean largest basal diameter (13.2 vs. 12.0 vs. 13.3 mm, $p=0.003$), mean tumor thickness (6.0 vs. 5.6 vs. 6.7 mm, $p=0.03$), genetic results showing TCGA group B tumors (11% vs. 14% vs. 26%, $p=0.01$) or TCGA group D tumors (22% vs. 11% vs. 9%, $p=0.01$), 10-year incidence of melanoma-related metastasis (25% vs. 15% vs. 14%, $p=0.02$) and 10-year incidence of melanoma-related death (9% vs. 3% vs. 4%, $p=0.04$). Cox proportional hazard results showed FST was a significant predictor of melanoma-related metastasis ($p=0.02$, Hazard ratio 2.3).

Conclusions In this large cohort of patients with uveal melanoma, FST was a predictor of melanoma-related metastasis, more common in light compared to dark skin tone.

Secondary Primary Cancers (SPC) in a Polish Cohort of Patients with Uveal Melanoma.

Rospond-Kubiak I., Wroblewska-Zierhoffer M., Kubiak A.

Purpose: to investigate the incidence of second primary carcinomas (SPC) in a Polish cohort of uveal melanoma (UM) patients

Methods: The medical records of the UM patients tretared at the Ocular Oncology Service, Poznań, Poland between 1991-2017, were retrospectively reviewed. The exclusion criteria comprised undocumented follow-up. The survival data were obtained from Greater Poland Cancer Registry.

Results: A total of 653 UM patients was registered in our database: 312 men, 341 women in the median age of 62 years (range 16-98). The treated melanomas were stage T1 in 83 cases, 205 were stage T2, 225 were stage T3 and 97 were stage T4. 125 (19%) patients have developed second primary cancers.

The most common location of SPC was breast, followed by skin and lungs. 71 (57%) patients have developed the second primary neoplasm post the diagnosis of uveal melanoma, 47 (38%) already presented with a history of other cancer. The median follow-up was 35 months (range: 3 to 242 months). The patients who developed the SPC post the diagnosis of UM were significantly younger (p=0,0454) and had a longer survival (p=0,0216, Student's t test) than the patients who presented with the history of cancer. Also, the epitheliod type of melanoma was more common in the first group (p=0,00869, Pearson's chi-squared test)

Conclusions: The recent reports regarding the co-existence of SPC and UM may indicate that UM is probably a part of cancer predisposition syndrome. However, to answer this question the analysis of the bigger database is required.

Non-Invasive testing in UM patients using Circulating Tumor DNA and shallow whole genome sequencing van Poppelen

N.M, de Bruyn D.P., Vaarwater J., Brands T., de Klein A., Brosens E., Kilic E.

Purpose To test the validity of circulating tumor DNA (ctDNA) as a prognostic (genetic) biomarker in the surveillance of enucleated or irradiated uveal melanoma (UM) patients.

Methods CtDNA from 28 patients, 6 with metastatic disease, was isolated from blood-plasma stored in Streck tubes using the Qiagen circulating nucleic acid kit. CtDNA levels were determined using the Stilla Naica dPCR system and used for genome-wide shallow sequencing (0.2X) and Copy number variations (CNV) detection. During radiotherapy (fSRT) material was collected at different time points. Clinical data regarding therapy and disease free survival was collected.

Results CtDNA levels varied between 0-11.2 copies/mL for the patients that underwent radiotherapy. We could not observe a significant change in ctDNA levels ($p > 0.05$) during fSRT, perhaps due to lack of statistical power resulting from the limited number of patients included in this study. CNV analysis revealed alterations in chromosome 1,3 and 8 in one patient with metastatic disease. For the detection of CNV a threshold of 5% ctDNA is needed. Primary UM are often small, tumor ctDNA in the blood is sparse and as a consequence CNV detection is not always possible. Selecting the smaller, tumor derived ctDNA fragments (90 - 150 nucleotides) improved CNV analysis and revealed alterations of chromosomes 1,3 and 8 in another patient with metastatic disease.

Conclusions No change in ctDNA level was detected during radiotherapy. CNV's were detected in only few cases. Protocols and bioinformatic procedures need further optimization before it can be used in UM patient prognostication.

Blood Plasma Metabolomics to Support Uveal Melanoma Diagnosis

Br ossens E., de Bruyn D., Bongaerts M., Bonte R., Vaarwater J., Meester-Smor M.A., Verdijk R., Paridaens D., Naus N.C., de Klein A., Ruijter G.J.G, Kilic E.

Purpose Uveal Melanomas (UM) micro-metastasis can be present prior to diagnosis and relapse after treatment. Earlier detection resulted in an increased incidence of small tumors allowing for novel eye-preserving treatment strategies. These treatments result in reduced availability of tumor tissue needed for prognostic genomic profiling and thus create the need for minimal-invasive methods. We evaluated if metabolite patterns in blood plasma is a viable noninvasive method for UM detection and prognostication.

Methods Peripheral blood plasma was collected at diagnosis, prior to treatment. In this retrospective observational study, discovery (n=53) and replication (n=42) convenience sample sets were included and compared to unaffected control-participants (n=46) as well as across prognostic relevant secondary driver mutation-based subgroups. Metabolite profiles in patients and control-participants were measured using ultra-high performance liquid chromatography mass-spectrometry. After normalization, discriminatory feature patterns were determined using a random forest classifier (RFC) and leave-one-out cross-validation.

Results We detected differential metabolic patterns with a sensitivity of 0.95 and 0.90 and a specificity of 0.98 and 0.98 in positive and negative ion modes, respectively. The accuracy of

the model for classifying the subgroups was insufficient for the discovery (0.600 and 0.614 in the positive and negative ion modes, respectively) and replication cohort (positive ion mode: 0.544 and 0.672 in the positive and negative ion modes, respectively).

Conclusions Minimally-invasive metabolomics does not discriminate between the prognostic relevant mutated UM-subgroups. However, this technique has the potential to allow for minimal invasive screening as it distinguishes metabolite patterns in peripheral blood derived plasma of UM-patients from controls

The prognostic value of chromosome 8q gain in SF3B1-mutated Uveal Melanoma

Nguyen J.Q.N, Vaarwater J., Verdijk R.,de Klein A., Kilic E., Brossens E.

Purpose Gain of chromosome 8q has been associated with poor prognosis in uveal melanoma (UM), with increased numbers of copies of 8q correlated with a shorter survival. *SF3B1*-mutated (*SF3B1*^{MUT}) tumors are characterized by, among others, partial gain of chromosome 8q. A recent subset of *SF3B1*^{MUT} UM with early-onset metastases has been identified, prompting the investigation of the relationship between survival, 8q gain and *SF3B1*^{MUT} UM.

Methods Sixty patients with *SF3B1*^{MUT} tumors were included in this study. Copy number status and gene expression were assessed using SNP array, FISH, karyotyping and RNA-sequencing. Disease-free survival (DFS) was determined and a cut-off of 60 months was used to define early-onset metastasis.

Results Forty-nine patients (82%) had 8q gain (3 copies, 78%; ≥4 copies, 22%). Kaplan-Meier analysis of *SF3B1*^{MUT} UM did not indicate a difference in survival in patients with or without gain of 8q (p=0.8024) nor the total number of additional 8q copies (p=0.6295). The number of 8q copies was also not associated with survival when grouping based on early (p=0.5319) vs late (p=0.2490) metastases. In contrast, presence of 8q gain was correlated with a worse survival in *BAP1*^{MUT} UM (p=0.0134), with a worse survival in increased copy numbers of 8q (p=0.0089).

Conclusions Gain of 8q has no additional predictive value in *SF3B1*^{MUT} tumors, as no correlation was found between 8q gain and early-onset metastasized *SF3B1*^{MUT} tumors. In *BAP1*^{MUT} tumors however, 8q gain is predictive for a worse prognosis. Therefore, 8q gain has additional predictive value for *BAP1*^{MUT} tumors, but not for *SF3B1*^{MUT} tumors.

A retrospective comparative analysis of genetic factors in groups of patients with and without metastases of Uveal Melanoma

Yarovaya V., Yaroyov A., Zaretsky A., Levashov I., Chudakova L.

Purpose: to analyze genetic factors in a retrospective comparative analysis of homogeneous groups of patients with and without metastases.

Methods: This study included 96 patients (96 eyes) with UM after enucleation: 41 NoMTS and 55 MTS. NoMTS were included with follow-up period up to 36 months. NoMTS and MTS groups were statistically homogeneous by all known clinical features (p>0.05). The search for mutations was carried out in GNAQ, GNA11, EIF1AX, SRSF2, and SF3B1. Chromosomes 1, 3, 6 and 8 were analyzed by MLPA. Immunohistochemistry and MLPA were performed for BAP1.

Results: Kaplan-Meier survival analysis showed the GNA11 mutation may indicate an increased risk of metastases at follow-up over 2 years (p = 0.03). EIF1AX gene mutation was

frequently detected in NoMTS and associated with high survival (p <0.0001). BAP1 immunohistochemistry had no association with survival (p=0,98). BAP1 deletion (p=0,012) and deletion of 3p (p=0,004) and 3q (p=0,006) were associated with low survival. Deletion of 8p (p<0,0001) and amplification of 8q (p<0,0001) were associated with low survival as well. SF3B1, 6p, 6q did not reveal significant impact on survival (p>0.05).

On the base of our results comparison of cytogenetic and mutational classifications was performed and revealed the coincidence of classes in 20% (kappa = -0.007).

Conclusions: Retrospective comparative analysis allowed to develop a panel of prognostically significant markers for the development of dissemination of UM.

Multimodal approach in detection of predictors for transformation in Melanocytic Intraocular Tumors

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Purpose. To determine OCT-morphometric and genetic predictors of transformation of melanocytic intraocular tumors.

Methods. 162 (168 eyes) previously untreated patients were examined. All patients underwent standard ophthalmological examinations and special instrumental diagnostic methods (ultrasound examination (US), enhanced depth imaging (EDI) optical coherence tomography (OCT), OCT angiography(OCT-A)). Patients were assigned to the following groups: 1 − with benign choroidal nevus, 2 - with suspicious choroidal nevus, 3 – small choroidal melanoma.

Mutations in GNAQ/GNA11 oncogenes were studied using the analysis of melting curves and polymerase chain reaction - restriction fragment length polymorphism analysis in peripheral blood. The control group was a cohort of individuals without malignancies, comparable in age and sex (n = 62).

Results. Comparative analysis revealed statistically significant predictors of benign choroidal nevus progression into a suspicious choroidal nevus: convex deformation of the retino-choroidal profile, weakening of hyperreflectivity at the choriocapillaries level, expansion of the peritumoral choroidal vessels and their compression in the central zone, local detachment and severe hyperplasia of RPE, slit-like and local detachment of the retinal neuroepithelium, intraretinal microcysts, disorganization of the photoreceptor structure (p<0.05). Malignancy predictors of a suspicious nevus in the small choroidal melanoma were determined: choroidal «excavation», defects in RPE, «shaggy» photoreceptors, accumulation of subretinal hyperreflective deposits (p<0.05).

A quantitative analysis of vascular density at the choriocapillaries level showed an increase in the studied parameter in suspicious choroidal nevus compared with small melanoma and benign nevi (p<0.05), which could be a predictor of tumor growth. A significant increase in the density of perfusion of small choroidal melanoma was revealed when compared with group 2 (p = 0.02).

Mutations in the GNAQ and GNA11 genes in circulating tumor DNA are significantly more common in patients with small melanoma and choroidal nevi. In the control group, oncogenes in circulating tumor DNA were not detected. In patients with small melanoma and suspicious choroidal nevi, mutations in GNAQ/GNA11 in blood are significantly more common than in patients with benign choroidal nevi (1 and 3 groups; p = 0.0004; 1 and 2 groups: p = 0.0008). In groups 2 and 3, there were no significant differences depending on the presence of mutations in GNAQ and GNA11 genes (p>0.05), which may indicate a high risk of transformation of a suspicious nevus into choroidal melanoma.

Conclusion. Complex of predictive markers was revealed using EDI-OCT and OCT-A, including choroidal and tumor associated retinal changes that characterize the progression and malignancy of choroidal nevi. Genetic features in circulating tumor DNA were diagnosed in patients with nevi and small choroidal melanoma. The revealed features can be used to screen patients for choroidal nevi with high risk of malignancy and to carry out an adequate treatment.

OOG 3: Uveal melanoma

FOXD1 is involved in Uveal Melanocyte development and associated w ith high-risk Uveal Melanoma

Van den Bosch Q., Nguyen J.O.N., Brands T., van den Bosch T.P.P, Verdijk R., Paridaens D., Naus N.C., de Klein A., Kilic E., Brosens E.

Purpose Uveal melanoma (UM) arises from melanocytes located in the uveal tract. Secondary driver gene mutations can be used to predict disease progression. *BAP1* mutated UM *(BAP1*-UM) is known to be highly aggressive. In contrast to low-risk UM, transcriptomes of *BAP1*-UM are illustrative of a more stem cell-like profile. We hypothesized that *BAP1*-UM reactivated genes are involved in uveal melanocyte development and increase aggressiveness.

Methods To identify uveal melanocyte developmental genes, we reanalyzed public zebrafish and human scRNA-sequencing datasets. Expression of core melanocyte genes was used to identify melanocytes in embryonic whole zebrafish cells and ocular melanocytes was determined with tissue-specific gene expression (*pmelb).* Identified transcription factors were evaluated in healthy human ocular melanocytes and bulk-RNA sequencing data of UM (n=106). We validated our results in TCGA and ROMS transcriptome datasets of UM. Subsequently, we validated our strongest candidate using immunohistochemistry (IHC, n=60).

Results We characterized ocular melanocyte transcriptomes in zebrafish. Transcription factors *rbfox2, ell2* and *foxd1* were expressed during early development. We were unable to detect *FOXD1* in adult healthy human scRNA-sequencing, suggesting exclusive expression during early embryonic melanocyte development. In UM, *RBFOX2*, *ELL2* and *FOXD1* RNA-expression was associated with poor prognosis where *FOXD1* is nearly exclusively expressed in *BAP1*-UM. IHC of FOXD1 confirmed protein expression which is correlated to poor prognosis as well.

Conclusions Our multi-species approach allowed us to identify novel genes involved in ocular pigmentation and high-risk UM. Our top candidate, *FOXD1,* is correlated to poor prognosis on both RNA and protein level.

Do we need three Uveal Melanoma Cell Types for prognostication?

Yarovoy A., Yarovaya V., Zaretsky A., Levashov I., Shatskih A.

Purpose: The prognosis for uveal melanoma (UM) metastases is individual and depends on a wide range factors. A special place among them is tumor cell type. Spindle-cell (SC) is considered to be “good”, epithelioid-cell (EC) – “poor”. The place of the mixed cell type (MC) remains not entirely clear. The purpose is to determine the prognostic value of UM cell type

Methods: This study included 96 patients (96 eyes) with UM after enucleation: 41 without metastases (NoMTS) with follow-up period up to 36 months, and 55 with metastases (MTS). NoMTS and MTS groups were statistically comparable by age, sex, tumor size and localization, involvement of ciliary body and extrascleral growth ($p>0.05$).

Results: SC type was detected in 44% cases, MC – in 35%, and EC – in 21%. NoMTS were significantly more likely to have the SC type of UM ($p < 0.0001$), MTS - MC and EC UMs were more often detected in MTS ($p < 0.0001$), which is apparently due to the presence of EC in both cell types. Three- and 5-year survival rates of patients with SC UM were significantly higher compared to survival rates of patients with EC or MC UM ($p < 0.001$). Our results were statistically matched with literature data, and will be presented.

Conclusions: Similar survival rates in patients with MC and EC types provide a new insight on prognostication in UM. It is appropriate to assess UM cell type as a prognostic factor using binary approach – "epithelioid cells on" and "epithelioid cells off" in tumor.

Retinal vascular changes following proton beam Radiotherapy in Choroidal Melanoma

Eibenber ger K., Hussain R., Asterios D., Heinmann H.

Purpose To determine morphological and microvascular changes following proton beam radiotherapy (PBR) for the treatment of choroidal melanoma (CM) using optical coherence tomography angiography (OCT-A)

Methods This cross-sectional, clinical trial included patients receiving proton beam radiotherapy for the treatment of CM. For morphologic analysis of the retinal vasculature, OCT-A was performed on the treated study (SE) 6, 12 and 24 months after treatment. The healthy, untreated fellow eyes (FE) served as control. The area and perimeter of the foveal avascular zone (FAZ) were evaluated on OCT-A.

Results 21 patients (6mo: n=6; 12mo: n=12; 24mo: n=3) with a mean age of 61.4±16.3years were included to the study. The base diameter of the CM was 8.44±3.04mm in longitudinal and 8.67±3.07mm in transverse axis, and the mean thickness was 2.52±1.13mm. The initial visual acuity was 0.10±0.17logMar and remained stable at 0.13±0.19logMar, 0.20±0.25logMar and 0.68±0.43logMar 6, 12 and 24 months after treatment (6mo: p=0.05; 12mo: p=0.07; 24mo: p=0.02).

4 patients developed radiation maculopathy 12 months after treatment. The FAZ area was 0.32±0.07mm², 0.36±0.09mm² and 0.34±0.02mm² in the SE at 6, 12 and 24 months compared to 0.31±0.09mm² in the FE (6mo: p=0.03; 12mo and 24mo: p<0.01). The FAZ perimeter was 2148.5±263.7mm, 2287.0±263.7mm and 2189.3±92.0mm in the SE at 6, 12 and 24 months and 2110.1±279.2mm in the FE (all: p<0.001).

Conclusions OCT-A imaging revealed microvascular changes in patients following proton beam radiotherapy, which could be a precursor to the development of radiation retinopathy after PBR.

Proton beam irradiated retino-invasive Uveal Melanomas

Moul in A., Zografos L., Schalenbourg A.

Purpose: Extensive retinal invasion with a propensity to invade the optic nerve without direct choroidal invasion is rarely observed in uveal melanoma. We report the clinico-pathological findings of retinoinvasive uveal melanomas from a single institution.

Methods: Retrospective clinico-pathological files analysis with complementary immunohistochemistry.

Results: 7 cases were identified as retinoinvasive uveal melanomas out of 289 enucleated eyes with uveal melanoma irradiated by proton beam. There were 5 males and 2 females (mean age: 63.5 years). Glaucoma was observed in 66,6% of the cases. Involvement of the

anterior segment or the posterior segment was respectively found in 5 cases and in 6 cases, with a papillary mass in 3 cases. Median time to enucleation was 52 months. 2 patients died of uveal melanomas.

Histopathological analysis revealed a ciliary body and iris involvement in 6/7 cases, with angle and Schlemm's canal invasion in 5 cases. Epiretinal tumor extension was found in all cases, intraretinal and subretinal invasion in 6/7 cases. Involvement of the papilla was found in 5 cases with optic nerve invasion in 3 cases. In all but one case, the tumor cells were epithelioid cells. BAP1 nuclear expression was preserved in all cases. No significant activation of ERK was found within the tumor cells, and limited activation of the PI3K pathway was identified.

Conclusions Retinoinvasive uveal melanoma appears to be an aggressive tumor usually associated with tumor recurrence in the anterior segment that tends to invade the retina and ultimately the optic nerve. These tumors are predominantly composed of epithelioid cells with preserved BAP1 nuclear expression without clear activation of the MAP kinase pathway and limited activation PI3K pathway.

Cerivastatin synergizes with trametinib and enhances its efficacity in the therapy of Uveal Melanoma

Pfeffer U., Amaro A., Tanda E.T., Spagnolo F., Gangemi R., Croce M.

Purpose Metastatic uveal melanoma (MUM) is a highly aggressive and therapy resistant disease. Driver mutations in the Gα-proteins GNAQ and GNA11 activate MAP-kinase and YAP/TAZ pathways of oncogenic signaling. Yet mitogen-activated protein kinase (MAP-kinase) and MEK (mitogen-activated protein kinase kinase) inhibitors do not significantly block MUM progression in patients, likely due to persisting YAP/TAZ signaling. Drugs targeting YAP/TAZ are being developed and drug repurposing could change the management of MUM patients before they become clinically available. Molecular screens revealed that statins can inhibit YAP/TAZ activation by blocking the mevalonate pathway, geranyl-geranylation and subcellular localization of Rho-GTPase. We therefore tested combined treatments of UM cells with MEKi (Trametinib) and statins.

Methods We investigated the sensitivity of six MU cell lines to Trametinib and statins. We established IC_{50} values of the individual drugs and monitored the effects of the combinations in terms of proliferation, cell cycle perturbation and apoptosis. Synergism was detected using isobologram and Chou-Talalay analyses. The most synergistic combination was tested *in vivo* in NSG mice.

Results Synergistic concentrations of trametinib and cerivastatin (T+C) induced a massive arrest of proliferation and cell cycle and an increase of apoptosis 72 hours after the start of treatment, particularly in the monosomic, BAP1 mutated UPMM3 cell line. T+C treatments reduced ERK and AKT phosphorylation and increased the inactive, cytoplasmatic form of YAP. T+C treatment significantly reduced the growth of UM cells with monosomy o chromosome 3 in NSG mice.

Conclusions Statins can potentiate the efficacy of MEK inhibitors in the therapy of UM.

Combined treatment of Juxta & Parapapillary Choroidal Melanoma

Amiryan A. G., Saakyan S.V.

Purpose To estimate the local efficacy of the combined treatment - brachytherapy (BT) with laser coagulation (LC) in patients with of juxta- and parapapillary choroidal melanomas.

Methods 50 patients with choroidal melanoma of juxta- and parapapillary localization were examined and treated, 32 women and 18 men aged from 32 to 76 years old (average - 53.8 ± 9.6 years). The averaged tumor height was 3.8 ± 1.3 mm, basal diameter - 11.2 ± 2.4 mm. The combined eye-preserving treatment included LC close to the optic nerve disc with subsequent BT. The indications for this method were choroidal melanomas of juxta- and parapapillary localization (the distance between the optic nerve disc and the central border of the tumor was no more than 1.5 pd), with the absence of subretinal fluid and retinal detachment in this zone. The follow-up period after the combined treatment ranged from 18 to 102 months (Me = 60 months).

Results Complete tumor resorption was achieved in the majority - 38 (76.0%) of cases, partial - in 11 (22.0%) patients, stabilization of the process - only in one (2.0%) patient, continued growth was not observed in any patient. The initial size of melanoma in patients with complete and partial tumor resorption showed similar averaged values, amounting to 3.8 ± 1.3 mm and 3.6 ± 1.1 mm ($p>0.05$), respectively, basal diameter - 11.1 ± 2.4 mm and 11.4 ± 2.4 mm ($p>0.05$), respectively. According to the duplex scanning, after LC the increasing of distribution of blood flow density in tumor was noted compared with the initial data. Complications included optic neuropathy (88%), hemorrhage (36%) and secondary glaucoma (6%).

Conclusions The combined treatment allows achieving high therapeutic results - 76.0% of complete resorption of juxta- and parapapillary choroidal melanomas and can be used in such patients to increase tumor local treatment efficacy.

Long-term follow-up of Circumscribed Iris Melanomas treated by proton beam therapy

Cassoux N., Matet A., Dendale R., Malaise D., Lumbruso-Le Rouic L.

Purpose: To describe the long-term results in terms of local control (5 years or more), eye preservation and systemic evolution of circumscribed iris melanomas, treated by proton beam irradiation.

Methods: Retrospective review of the charts of patients with circumscribed iris melanoma treated by proton beam therapy between April 1998 and December 2020. Diffuse iris melanomas, ciliary body melanomas with iris involvement or tumours with extrascleral invasion were excluded.

Results: 66 patients have a follow-up of 5 years or more (median follow-up 125 months). 75% patients presented with documented growth lesion. The median clinical diameter was 5.2 mm, the median Ultrasound biomicroscopy thickness 2.1 mm. The iridocorneal angle was invaded by the tumour in 70% of patients and pigmented seeding present for 46%, glaucoma for18%. At the end of follow-up, the survival is 94%, metastatic disease for 3 patients. Local relapse was observed for 4 patients. The main complication was cataract 85% and raised intraocular pressure for 26% patients but no neovascular glaucoma.

Conclusions: Long term follow-up confirms that Proton beam therapy is an excellent treatment for selected cases of localised iris melanomas allowing excellent local tumour control, eye preservation and survival.

Characteristics of Iris Amelanotic Lesions – A Ten-Year Perspective

Shemesh R., Dror S., Vishknevskia-Dai V.

Purpose: Iris amelanotic melanoma and nevi can be challenging to distinguish clinically. This case series provides unique insight into this rare condition and the variable clinical presentations of these lesions.

Methods: A 10-year retrospective analysis of seven patients who were diagnosed with an iris amelanotic lesion (nevi or melanoma) in a tertiary medical center. Demographic, clinical data, surgical reports, pre and postoperative images, complications, and follow-up information were retrieved from a database.

Results: All patients were female. The mean (±SD) age was 46.3 years (±18), with a range of 22-72 years. All patient were caucasian. Occupational exposure to solar ultraviolet radiation was not noted in any of the patients. Six patients (86%) were diagnosed with iris amelanotic nevus and one patient (14%) was diagnosed with melanoma. The mean (±SD) diameter of the lesions was 2.1 mm (±0.2), the mean thickness (±SD) was 0.9 mm (±0.4). Three of the lesions involved the anterior chamber angle (43%). The lesions were located in the inferior iris in 6 patients (86%), 3 patients presented with ectropion uvea (43%) and only one patient presented with a nasal lesion (14%). Hyphema or feathery margins were not noted in any of the patients. A fine meddle aspiration and an incisional biopsy were needed in one suspicious lesion that showed growth and was diagnosed with amelanotic iris melanoma following biopsy and complete tumor removal . Visual acuity and intra-ocular-pressure remained stable with a mean of 0.04 (±0.05) in logMAR and, 13.6(±1.3) mmHg at the first appointment and 0.03 (±0.05) in logMAR, and, 14.1(±1.5) mmHg at the last appointment, (P=0.36), and (P=0.62), respectively. The mean follow-up time (±SD) was 4.2 (±4.8) years.

Conclusions: When presented with an amelanotic iris lesion, clinicians must be vigilant with regular monitoring and have a low threshold for biopsy in lesions of high clinical suspicion.

OOG 4: Retinoblastoma

Favorable clinical outcome of familial retinoblastoma after early postnatal screening, diagnosis, and management

Malaise D., Matet A., Lumbroso-Le Rouic L., Levy C., Gauthier-Villars M., Aerts I., Doz F., Cassoux N.

Purpose To describe clinical of familial retinoblastoma cases having benefited from early screening, diagnosis and management.

Methods Retrospective review of consecutive familial retinoblastoma cases at Institut Curie (France) from January 1995 to January 2018, who underwent first fundus screening according to institutional guidelines: during first week of life if history of bilateral (or unilateral multifocal) retinoblastoma in a parent, first month of life if history of unilateral retinoblastoma in a parent or bilateral (or unilateral multifocal) retinoblastoma in siblings, then repeated according to guidelines.

Results Thirty-seven patients (70 eyes) were included. Average follow-up was 134.8 months [24-269 months]. The mean age at first fundus screening and at retinoblastoma diagnosis was 5.6 days [0-15 days] and 48.1 days [0-219 days], respectively.

Ocular involvement was bilateral at diagnosis in n=19/37 cases (51%), bilateral metachronous in n=14/37 (38%; average time interval between retinoblastoma diagnosis and bilateralization of 16.1 weeks [2-61 weeks]) and unilateral in n=4/37 (11%).

At diagnosis, n=25/37 patients (68%) had at least one affected eye classified most favorably (cT1a).

Conservative treatment was possible for n=69/70 of the affected eyes (98.6%). When assessable, binocular best-corrected decimal visual acuity was greater than 2/10 (0.2) in n=25/26 patients (96%) and greater than 8/10 (0.8) in n=16/26 patients (62%).

No patient presented retinoblastoma metastasis or died. One patient (2.7%) developed pinealoblastoma and another patient (2.7%) osteosarcoma.

Conclusions Following a strict retinoblastoma screening schedule recommendations when a familial history is known is essential to achieve a favorable prognosis in terms of eye preservation and visual acuity.

Familial Retinoblastoma: variations in clinical presentation and management based on material Vs. paternal inheritance

Eiger-Moscovich M., Ruben M., Dockery Ph., Yaghy A., Shields C.

Purpose Several small studies demonstrated the effect of parent-of-origin on retinoblastoma penetrance. We aim to assess differences in clinical presentation of maternally versus paternally inherited familial retinoblastoma.

Methods The clinical records of all children with familial retinoblastoma treated on the Wills Eye Hospital Ocular Oncology Service between December 1975 and May 2020 were reviewed retrospectively.

Results There were 179 patients with familial retinoblastoma. 109 patients (61%) had paternally-inherited retinoblastoma (PI) and 70 (39%) had maternally-inherited retinoblastoma (MI). A comparison (PI versus [vs.] MI) revealed patients with PI were significantly older at presentation (57.2 months vs. 24.4 months, p=0.002). There was no difference in patient sex (53% vs. 57% males, p=0.606) or number of family members affected (3.2 vs. 3.0, p=0.255). PI patients had more advanced International Classification of Retinoblastoma score (ICRB) (Group E 31% vs. 8%, p=0.012); and greater largest tumor in basal diameter (9.0 mm vs. 6.2 mm, p=0.040) and thickness (5.6 mm vs. 4.0 mm, p=0.038), less likely located in the macula (40% vs. 60%, p=0.0041). There was no difference in tumor laterality (69% vs. 64% bilaterality, p=0.530). Those with PI required enucleation more frequently (34% vs. 14%, OR=2.98 [1.35 – 6.60], p=0.007). There was no difference in need for plaque radiotherapy (p=0.86) or chemotherapy (p=0.85). One PI patient developed metastatic retinoblastoma, without retinoblastoma-related deaths.

Conclusions Paternally-inherited retinoblastoma tends to be larger tumors, with more advanced ICRB group, presentation at more advanced age, and more likelihood to require enucleation. This could be due to genetic disease penetrance or imprinting.

Retinoblastoma in the mosaic form of RB1 gene mutation

U shakova T., Yugai O., Kozlova V., Mikhailova S., Polyakov V.

Purpose The causes of retinoblastoma (RB) are mutations of the oncosuppressive gene RB1. The aim of the study was to determine the effect of the mosaic form of the RB1 gene mutation on the clinical course of RB.

Methods The study included 17 patients with RB (21 eyes) at age from 1 week to 39 months, in whom mosaic forms of RB1 gene mutations were detected after using of new generation sequencing, multiplex ligase-dependent amplification.

Results Nonsense mutation was confirmed in 12 out of 17 patients; reading frame shift in 4 out of 17; splicing site mutation – in a single case. Organ-preserving treatment was carried

out in 10 patients (12 eyes), 11 eyes were preserved. Enucleation at the first stage of treatment was performed in 9 patients. Secondary enucleation due to the ineffectiveness of organ-preserving treatment required 1 patient. 6 patients (29%) had a recurrent course of the disease. Among the recurrent forms of the disease, a nonsense mutation was detected in 4 patients, a shift in the reading frame in 2. Relapse-free course of the disease with organ-preserving treatment was observed in 4 patients (5 eyes) and in all children with primary enucleation of the eye. One patient had a metachronous lesion of the eye two months after the detection of monolateral RB. There was not a single case of metastasis and second tumors.

Conclusions The existing experience of observation of patients with RB allows us to conclude about a relatively favorable course of the disease in children with a mosaic form of the RB1 gene mutation.

Lesions simulating retinoblastoma: Pseudoretinoblastomas: the spectrum of pathology and frequency in different age groups.

Volodin D. P., Yaroyov A. A., Yarovaya V. A., Kotelnikova A.V.

Purpose to determine the spectrum of pathology and prevalence of lesions simulating retinoblastoma (Rb) in various age groups.

Methods In a retrospective study, we reviewed the charts of 608 patients (871 eyes) that were referred with suspected Rb Ocular Oncology and Radiology department of S. Fyodorov Eye Microsurgery Federal State Institution in the period from 2007 to 2021. The mean age of patients at the time of examination was 21 months (from 1 to 209 months). In 475 patients (78.1%) (715 eyes), after a comprehensive assessment of the eye condition, the diagnosis of Rb was confirmed. 133 patients (156 eyes) (21.9%) had symptoms simulating Rb – pseudoretinoblastomas (p-Rb). All patients with p-Rb were divided into groups of diseases simulating RB, as well as by age groups: from 0 to 1 year, from 1 year to 2 years, from 2 years to 5 years, older than 5 years.

Results Overall, 25 lesions simulating Rb were present in our study. Of the total number of p-Rb, the most common conditions were Coats' disease (n=17, 12.8%), combined hamartoma of retina and RPE (n=12, 9%), retinal detachment (n=11, 8.3%), diffuse vitreous opacities due to intrauterine uveitis (n=11, 8.3%), choroidal hemangioma (n=11, 8.3%), vasoproliferative tumor (VPO) (n=10, 7.5%), retinopathy of prematurity (n=7, 5.3%) and "morning glory" syndrome (n=7, 5.3%). Most of the patients (n=116, 87.2%) had a unilateral lesion.

Conclusions Timely referral of children with suspected RB to specialized ocular oncology centers helps to avoid inappropriate treatment or enucleation in children with p-Rb.

Malignant transformation of retinocytoma

Yarovoy A., Yarovaya V. A.,Kozlova V.M., Ushakova T.L., Kotelnikova A.V.

Introduction: Retinocytoma (RC) is an independent benign tumor capable of malignancy. The absence of a vivid clinical picture and specific complaints significantly complicates the detection of RC. The possibility of its malignant transformation makes RC an urgent problem not only in ophthalmology, but also an important medical and social issue.

Purpose To present clinical case of RC malignant transformation

Methods Among 10 patients with RC (13 eyes), observed between 2009 and 2021, 9 tumors were stable within follow-up from 6 months to 13 years and 1 demonstrated transformation

into retinoblastoma (RB). At the age of 3 the girl was appeared to have left eye deviation and leucocoria. RC was diagnosed: calcinated lesion with thickness of 4,2 mm and basal diameter of 8,1 mm was detected. On 39 months control RB group D with white central tumor mass with massive vitreous and retinal seeding was seen.

Results Two cycles of intra-arterial chemotherapy were performed with low effect that required enucleation. No intravitreal chemotherapy was provided due to 360° ora serrata RB seeding. The pathology exam demonstrated well-differentiated RB of a standard risk.

Conclusions Own experience of observing children and adults with RC has shown that this tumor is stable and rarely undergoes malignant transformation. The possibility of transformation RC into RB at any age makes it a serious challenge. Patients who have been diagnosed with RC need lifelong observation by an ophthalmologist

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Long-term efficacy and safety of intravitreal chemotherapy for vitreous seeding in retinoblastoma

Stathopoulos C.,Beck-Popovic M., Munier F.L.

Purpose: To report 11-year experience of intravitreal chemotherapy (IvitC) for the treatment of active vitreous seeding (VS) in retinoblastoma patients.
Methods: Retrospective review 178 eyes/165 patients treated with IvitC exclusively in Lausanne. Injections were performed according to a previously described safety enhanced technique with intravitreal melphalan and/or topotecan (20-40 µg).
Results: Mean age at initial IvitC was 37 months. Mean number of injections/eye was 5; 93% received intravitreal melphalan only, whereas 7% received both melphalan and topotecan or topotecan only. Overall, 80 % of the injections (n=690/860) were given for 209 occurrences of VS along with other treatments for concomitant retinal/subretinal disease and 20% (n=170/860) to treat 47 occurrences of isolated VS. Complete VS regression was seen after one series of IvitC in 72%(n=128/178), 2 series in 17%(n=30/178), 3 series in 8%(n=14/178), 4 series in 2%(n=4/178) and 5 series in 1%(n=2/178) (mean relapse-free follow-up = 49 months). In the subgroup of eyes with VS at presentation treated within two weeks before and 2 months after their first-line treatment (n=61), the occurrence of isolated vitreous relapses was significantly lower compared to those with VS at presentation (n=39) that did not receive concomitant IvitC along with their first-line treatment (3% versus 51%, P<0.01). There were no secondary enucleations due to uncontrolled VS nor treatment-related deaths or metastasis (mean follow-up since first IvitC: 59 months).
Conclusions: Intravitreal chemotherapy is effective and safe to treat VS. Upfront treatment of VS at presentation seems to be related to a lower rate of isolated intravitreal relapses.

Long term results of organ preserving treatment of retinoblastoma in different years

Saakyan S.V., Tadevosyan S.S.

Purpose. Comparative analysis of the effectiveness of organ-preserving treatment of retinoblastoma (RB) in different periods depending on changes in chemotherapy protocols.

Methods. The study included 555 patients (53.2% male, 46.8% female) who received treatment at the Department of Ophthalmooncology and Radiology of the Helmholtz National Research Center for Eye Diseases in the periods 1994-1998 (n=162), 2004-2008 (n=170), 2014-2017 (n=223). The mean age at the start of treatment was 23.6 ± 1.0 months (median 17 months). The median follow-up period was 132 months. Monocular RB - 383 patients (69%). Binocular RB - 172 patients (31%).

Results. An attempt at organ-preserving treatment was made in 49 of 205 eyes (23.9%) in group 1, in 105 of 230 eyes (45.7%) in group 2, and in 171 of 292 eyes (58.6%) in group 3. Comparative analysis revealed a significant increase in the number of saved eyes in group 3 (152 of 171 eyes; 88.9%) compared with group 1 (35 of 49 eyes; 71.4%; $p<0.01$) and group 2 (75 of 105; 71.4%; $p<0.05$).

In group 1, 33 out of 43 eyes (75.7%) were saved with bilateral RB, 2 out of 6 eyes were saved with monolateral RB. In group 2, 15 out of 30 eyes (50%) were saved with monolateral RB, and 60 out of 75 eyes (80%) with bilateral RB. In group 3, 57 out of 69 eyes (82.6%) were saved with monolateral RB, 95 out of 102 eyes (93.1%) were saved with bilateral RB. The effectiveness of organ-preserving treatment in bilateral RB is higher than in monolateral RB ($p<0.05$).

Conclusion. Improvement in diagnostic methods, cancer alertness of pediatric ophthalmologists, increased detection of the disease at earlier stages, and the introduction of new treatment methods have increased the effectiveness of organ-preserving treatment of RB.

Ru-106 plaque brachytherapy for retinoblastoma at Hadassah- 26 years of experience

Kubossky S., Pe'er J., Eiger-Moscovich M., Frenkel S.

Purpose Retinoblastoma is a radiosensitive tumor. However, treatment veered from EBRT due to increased secondary tumors. Nevertheless, brachytherapy remains an effective therapeutic tool for primary and recurrent retinoblastoma tumors. Here we describe our 26 years of experience with this treatment modality over the past 25 years.

Methods A retrospective review of the medical records of children treated for retinoblastoma at the Hadassah Ocular Oncology Service.

Results From 1994 to 2021, we treated 50 children with Ru-106 plaque brachytherapy. 28 (56%) were boys, and 22 (44%) were girls. The mean age was 2.2 years (range from 3.5 months to 12.5 years, with a Standard Deviation of 2 years). 22 (44%) treatments were given to the right eye, and 28 (56%) treatments were given to the left eye. 13 (26%) of the treatments were primary, and 37 (74%) were secondary treatments. The most used plaque was CCA (31 patients, 62%). The average irradiation dose was 5,561 cGy to the apex and 80,173 cGy to the base. None of the treatments left a retinal scar at these low irradiation doses, as opposed to the retinal scarring after a total dose for uveal melanoma. In 2 of the children, the plaque was moved to cover more than one site in tandem.

Conclusions Ru-106 plaque brachytherapy is effective and safe for both primary and recurrent retinoblastoma.

Results and risk factors of complications of Ru-106 and Sr-90 brachytherapy of retinoblastoma based on 15-year single center experience

Yarovoy A., Yarovaya A.V., Chochaeva A.M., Volodin D.P.

Purpose To present the results and risk factors of complications of Ru-106 and Sr-90 brachytherapy of retinoblastoma.

Methods One hundred thirty-six patients (146 eyes, 206 tumors) were treated with Ru-106 (96 eyes), Sr-90 (34 eyes) plaques or both (16 eyes). Group A was diagnosed in 24 eyes, group B in 55, group C in 28, group D in 39. Mono-focal lesions were observed in 50 eyes (34%), multi-focal in 96 eyes (66%). Mean apical and scleral doses for Ru-irradiation were

89Gy and 330Gy, for Sr-irradiation 136Gy and 680Gy, correspondingly. We used both mono and multi-field irradiation with simultaneous or consequent plaques fixation in multifocal lesions. For small tumors irradiation collimator was used. The follow up was from 3 to 157 months, mean 55 months.

Results Complete tumor regression was achieved in 61.5% (127 tumors), partial in 31.5% (65 tumors), progression was observed in 7% (14 tumors). Complications were observed in 34% (49 eyes) and were associated with Ru-106 plaques in 97% and with Sr-90 only in 3% (4 eyes). Risk factors for complications: tumor thickness >2.5 mm (P=0.0005), basal diameter >7.3 mm (P<0.0001), scleral dose >626Gy (P=0.0002), posterior localization of the tumor (P<0.0001), time from intra-arterial chemotherapy to brachytherapy ≤3 months (P<0.0003). Scleral dose (P=0.0081) and posterior localization (P=0.0028) were the most important risk-factors (Cox regression model).

Conclusions Brachytherapy using ^{106}Ru and ^{90}Sr plaques is an effective treatment of retinoblastoma. Sr-90 irradiation is safer than Ru-106 one.

Thermotherapy in children with Retinoblastoma: Approaches and long-term results

Volodin D.P, Yaroyov A.A, Yarovaya V.A.

Purpose To evaluate the efficacy of transpupillary thermotherapy of retinoblastoma.

Methods In a retrospective study, we reviewed the charts of 206 children with retinoblastoma (1251 tumors in 266 eyes) treated with transpupillary thermotherapy at the S. Fyodorov Eye Microsurgery Federal State Institution in Moscow between October 2011 and December 2021. The median patient age at the time of treatment was 17 months. The mean tumor thickness was 1.1 mm (from 0.3 to 4.5), the mean basal diameter was 2.2 mm (from 0.3 to 13.4). Transpupillary thermotherapy was performed using a diode laser with the following parameters: wave length-810 nm, spot diameter-1200 microns, power from 180 to 900 mW (mean - 430 mW), exposure-from 3 to 15 s in the application mode, and continuous in the scanning mode.

Results Overall tumor control was achieved in 92% (1157 tumors). Tumor recurrence was observed in 8% (94 tumors). 249 eyes (94%) were preserved. 17 eyes (6%) were enucleated due to the tumor progression, total vitreous hemorrhage, total retinal detachment, or subatrophy of the eyeball. Complications were present in 8 eyes and included local vitreous hemorrhage, pretumoral hemorrhage, local vitreous opacities and iris atrophy.

Conclusions Transpupillary thermotherapy is a highly-effective treatment for retinoblastoma with excellent local tumor control and few complications.

Primary silicone orbital prosthesis implantation in patients with Retinoblastoma

Kotelnikova A., Yaroyov A.V., Ushakova T.L., Yarovaya A.V.

Purpose To present our experience of primary silicone orbital prosthesis implantation in patients with retinoblastoma (RB).

Methods Formation of locomotor stump with primary silicone orbital prosthesis implantation was carried out in 24 children (24 eyes) with RB. Implantation was performed in the absence of extrabulbar tumor growth and invasion of the optic nerve (ON) that was intraoperatively approved under a microscopic examination.

Results A satisfactory cosmetic effect was achieved in all cases. No tumor recurrences were seen during the mean follow-up period of 20.5 months (range from 3 to 79 months).

Complications found in 4 patients with silicone endoprosthesis were successfully managed. The external beam therapy was performed in 3 cases and it did not cause further complications

Conclusions Primary orbital endoprosthesis implantation in children with RB is a safe and necessary method of cosmetic rehabilitation taking into account the absence of tumor recurrence in the orbit within a follow-up period up to 79 months and rare complications in the postopertive period. A wide size range allows the use of this type of implant in children under 1 year old. Replacement of the endoprosthesis with compensation of the orbit volume and cosmetic purpose is possible with complete remission of the tumor in children who are regularly monitored.

Extraocular retinoblastoma: intracranial retinoblastoma involving the visual tract

Ushakova T., Polyakov V., Rodina A.

Purpose To date, the survival rates of patients with RB reach almost 100% with timely and adequate diagnosis. High-dose chemotherapy (HDCT) with auto-transplantation of hematopoietic stem cells (auto-THSC), it allows to increase relapse-free survival in patients without metastatic lesions of the CNS, but the prognosis of survival is extremely unfavorable.

We report a case of bilateral RB: OD- with extraocular and intracranial spread of the tumor along the optic nerve with a lesion of the chiasm and a transition to the initial parts of the visual tracts. OS - with intraocular tumor growth in a 3-year-old child.

Methods After chemotherapy, including intrathecal, a simultaneous two-stage operation was performed in the volume of bone-plastic pterionic craniotomy with prechiasmal resection of the right optic nerve (ON) and enucleation of the right eye. In the postoperative period, chemotherapy was performed, followed by HDCT with auto-THSC. Radiation therapy (RT) has become the final stage of treatment. Brachytherapy for OS tumor and RT for craniospinal region, right orbit, optic nerve stump with chiasm and pituitary pedicle were successively performed.

Results After 14 months from the beginning of treatment and 5 months after its completion, a leptomeningeal relapse of the disease was detected.

Conclusions Among the causes of mortality in patients with extraocular RB, the main one is metastasis in the central nervous system. In addition to studying the features of the course of the tumor process and an effective approach to antitumor treatment, the basis of a favorable prognosis for the disease is early diagnosis .

OOG 5: Ocular Adnexal Tumors and Systemic Therapy

miR-196b-5p and mir-107 Expression differentiates Ocular Sebaceous Carcinoma from Squamous Cell Carcinoma of the Conjunctiva

de Keizer R.O.B., Vriends A.L.M, Hötte J.H., Paridaens D., Wiemer E.A.C, Verdijk R.

Purpose An Ocular Sebaceous Carcinoma (OSC) is a rare malignant tumor for which initial clin-ical and pathological diagnosis is often incorrect. OSCs can mimic Squamous Cell Carcinomas of the Conjunctiva (SCCC). The aim of this study was to find microRNA biomarkers to distinguish OSCs and SCCCs from normal tissue and from each other.

Methods Clinical OSC and SCCC case files and the corresponding histopathological slides were collected and reviewed. Micro dissected forma-lin-fixed paraffin-embedded tumor and control tissues were subjected to semi-high throughput microRNA profiling. MicroRNA

expression distinguishes OSCs and SCCCs from corresponding control tissues. Selected differentially expressed miRNAs were validated using single RT-PCR assays.

Results No prognostic miRNAs could be identified that reliably predict SCCC metastasis or OSC recurrence. A comparison between OSCs (n = 14) and SCCCs (n = 18) revealed 38 differentially expressed microRNAs ($p < 0.05$). Differentially expressed miRNAs were selected for validation in the discovery cohort and an independent validation cohort (OSCs, n = 11; SCCCs, n = 12). At least two miRNAs, miR-196b-5p ($p \leq 0.05$) and miR-107 ($p \leq 0.001$), displayed a statistically significant differential expression between OSCs and SCCCs with miR-196b-5p upregulated in SCCCs and miR-107 upregulated in OSCs. In the validation cohort, microRNA miR-493-3p also showed sig-nificant upregulation in SCCCs when compared to OSCs ($p \leq 0.05$). ROC analyses indicated that the combined miR-196b-5p and miR-107 expression levels predicted OSCs with 90.0% sensitivity and 83.3% specificity.

Conclusions The combined testing of miR-196b-5p and miR-107, can be of additional use in routine diagnostics to discriminate OSCs from SCCCs.

Viral and genomic drivers of carcinomas arising in the conjunctiva and lachrymal dr ainage system

Heegard S., Viera F., Toft P.B., von Buchwald C., Funding M., Ramberg L.

Purpose Five percent of all solid cancers are caused by human papillomavirus (HPV). In the ocular adnexa, the conjunctiva and lacrimal drainage system (LDS) epithelia are potential locations for HPV-driven carcinogenesis. In the light of available prophylactic vaccines and the major research interest in therapies for HPV-associated cancers, further investigations of HPV in ocular adnexal carcinoma are timely. We aimed to investigate HPV transcription and the correlating genomic profile of conjunctival and LDS squamous cell carcinomas (SCC) and their precursors.

Methods Consecutive patients of LDS papilloma and carcinoma (*n* = 31) and SCC *in-situ* and SCC of the conjunctiva (*n* = 33) were included. HPV analysis was performed using HPV DNA PCR, E6/E7 mRNA *in-situ* hybridization, and p16-immunohistochemistry. The TSO500 panel (Illumina) covering 523 cancer-related genes was applied for paired-end DNA sequencing.

Results HPV transcripts were detected in SCC of the LDS (67%) and the conjunctiva (21%), most frequently HPV16. HPV16-positive SCC harbored a distinct molecular profile compared to HPV-negative. The HPV16-positive carcinomas were driven by PI3K-AKT signaling (*PIK3CA*, *FGFR3*, *AKT1* and *PIKR1* mutations (13 out of 15, 87%)) and the oncogenic effects of HPV16 (all cases). The tumors were further characterized by p16 expression and wild-type *TP53* (all cases). In contrast, somatic loss-of-function in *TP53*, *CDKN2A* and *RB1* were frequent in HPV-negative SCC.

Conclusions Transcription of HPV oncogenes supports a causal role of HPV in subsets of LDS and conjunctival SCC. Further, the distinct genomic profiles based on HPV status point to differential carcinogenic mechanisms with possible implications for future treatment strategies.

The use of electroporation in the treatment of Conjunctival Melanoma

Kapelushnik N., Abdelkader A., Blum S., Sharabi S., Fabian D.I.

Purpose Conjunctival melanoma is a rare but deadly malignancy of the ocular surface. Its mainstay of treatment is surgical resection and adjuvant focal therapy. However, local disease recurrences are relatively common, some of which cases may be fatal.

Electroporation is a technique in which tissues are exposed to external electrical fields. Irreversible electroporation permeabilize the cell membrane in a manner leading to cell death. Preliminary ex-vivo studies have shown promising results in treating conjunctival melanoma. The purpose of this study was to investigate the optimal treatment setup of electroporation for conjunctival melanoma in a rabbit model.

Methods The study was conducted using six New-Zealand white Rabbits. Human melanoma cells were injected to the rabbit's conjunctiva. Seven days post inoculation, small pigmented conjunctival tumors were detected, and treated with irreversible electroporation in 3 different voltages:500V, 600V and 800V. Three days post-treatment, the residual tumor mass was extracted and treatment adverse effect on surrounding tissue was assessed. After additional 2 week the eyes were enucleated. Tumors and eyes were sent for pathological analysis.

Results No recurrence was observed in any of the treated eyes within the 2 weeks following tumor excision. No apparent damage to surrounding structures was observed. Tumors treated with 500V showed dense mass of viable tumor cells. Tumors treated with 600V showed rarified tissue with small number of viable cells. Tumors treated with 800V showed significant infiltration of lymphocytes with minimal number of viable appearing tumor cells.

Conclusions In this present *in-vivo* study, histopathological analysis following Irreversible electroporation and tumor excision showed that 800V resulted with minimum of residual malignant tumor cells. No damage to ocular structures or side effects were found post treatment except mild edema surrounding the treatment site. These encouraging results suggest that electroporation is a viable and effective neoadjuvant treatment in the management of conjunctival melanoma.

Lacrimal system and sinonasal recurrence of conjunctival melanoma: A case series

Green F., Lemaitre S., Thaung C., Sagoo M.

Purpose Recurrence of conjunctival melanoma in the ipsilateral lacrimal system or sinonasal region is rare. Two main mechanisms of recurrence are hypothesised: direct extension into the nasolacrimal system or seeding of free melanoma cells present in tears into the nasolacrimal system or sinonasal region. One known risk factor is the melanoma location (medial conjunctiva, plica semilunaris and caruncle).

Methods Single-centre retrospective study. All patients treated for conjunctival melanoma at one institution since 2010 with subsequent recurrence in the lacrimal system, nasal cavity or paranasal sinuses were included.

Results 3 patients developed recurrence in the lacrimal system, with one extending into the nasal cavity and sinuses. Primary tumour location was medial in two cases and temporal in one. Prior to lacrimal system recurrence, all three patients had had at least one local relapse of conjunctival melanoma. Interestingly, neither of the three patients had undergone adjuvant radiotherapy after their first excision of conjunctival melanoma. All three had underlying primary acquired melanosis but only one received Mitomycin C treatment.
Conclusions We suggest that multiple recurrences on the ocular surface (likely favoured by lack of adjuvant radiotherapy and/or mitomycin C after excision of the primary tumour) may be a risk factor for lacrimal system or sinonasal recurrence of conjunctival melanoma.

There is currently no consensus in the management of lacrimal system melanoma recurrence. If the treatment intent is curative, these cases raise questions about the role of secondary exenteration. All patients reporting ongoing nasolacrimal symptoms after treatment of conjunctival melanoma should undergo prompt imaging.

Systemic management of Conjunctival Sqamous Cell Carcinoma with orbital e xtension: case repot and review of literature

Sergenti J., Lanza F.B., Guzzo M., Angi M.

Purpose To analyze the role of immune checkpoint inhibitors (ICIs) in the management of advanced conjunctival squamous cell carcinoma (cSCC) with orbital invasion.
Methods Case report and review of the literature.
Results A 46-year-old male was referred to us because of a painful large pink mass in his left eye. A conjunctival lesion was excised two years before but no histological examination was performed. At presentation, the lesion involved the nasal bulbar, inferior and superior tarsal conjunctiva with inferior and posterior extension into the orbit. BCVA was 20/25. Globe compression with choroidal folds was noticeable. MRI confirmed the presence of a solid conjunctival mass of 33x18mm extending into the orbit with involvement of medial rectus and inferior oblique and no bone erosion. Systemic work-up was unremarkable. Incisional biopsy confirmed the diagnosis of cSCC. Since the patient declined surgery, pembrolizumab was started. At 3 months, the mass regressed to 27x13mm with resolution of bulbar compression. At 7 months, the lesion was stable but the patient reported pain. Therefore, cetuximab was added. After 3 months of combined therapy, the lesion showed further growth and orbital exenteration was carried out with patient's consent.
Conclusions ICIs are gaining popularity as globe-sparing therapy for advanced cSCC, although in some cases they might only delay surgery. A review of the current literature will be presented and discussion on possible collaborative protocols will be encouraged.

Periorbital Solitary Plasmacytoma Vs. Multiple Myeloma: presentation and outcomes

Zloto O., Vahdani K., Stack R., Verity D.H., Rose G.E.

Aims: To describe patients with periocular solitary extramedullary plasmacytoma (SEMP) and multiple myeloma (MM), together with an estimate of the risk of progression from SEMP to MM.

Patients and methods: A retrospective case-note review for patients seen between 1978 and 2020, examining demographics, presentation, imaging, pathology, management, and outcome.

Results: Twenty patients (10 male; 50%) presented at a mean age of 60.9 years, with an average symptom duration of 4.5 months. Ten (50%) patients had known systemic myeloma at ophthalmic presentation (the MM group) and, on average, they presented one decade earlier than those with occult MM discovered after orbital biopsy (p = 0.06); the majority (9/15; 60%) of patients with MM were female, whereas there was a male bias (4/5; 80%) with SEMP (p = 0.30). Most tumors (15/20; 75%) were within the anterior part of the orbit, especially superolaterally (16 patients; 80%), and the soft-tissue mass often appeared to "explode" from the frontal bone or greater wing of the sphenoid (16/20; 80%). Full treatment details were known for 19 patients: 6 (32%) had solely orbital radiotherapy, 4 (21%) chemotherapy, 6 (32%) combined chemoradiation, and 3 (16%) had combined chemoradiation with stem-cell transplant (Table 3). After an average follow up of 58 months, 1/5 (20%) patients with SEMP and 11/15 (73%) with MM had tumor-related death. The overall survival probability for all 20 patients with periocular plasmacytoma was 34% at 5 and 10 years, with MM patients having a worse outlook (27% 5-year, and 18% 10-year survival) compared with SEMP (53% survival at 5 and 10 years) (p = 0.18). None of the 5 patients with SEMP progressed to systemic MM over an average follow up of 9.1 years.

Conclusions: Although 50% patients with periocular plasmacytoma appear to have a SEMP at ophthalmic presentation, a half of these patients were found to have occult MM within 6

months of biopsy. Of those without systemic disease around the time of biopsy, none developed MM over an average follow up of more than 9 years.

Checkpoint inhibitor immune therapy-ophthalmic sides effects.

Gr aeff E., Meyer P.

Ocular Melanoma of Unknown Origin: Atypical Uveal or Late Isolated Metastasis of Cutaneous Melanoma.

Arazi M., Fabian D. I.

Purpose To present the case of a patient with a history of primary cutaneous melanoma who developed isolated ocular metastasis 11 years after initial presentation and treatment.
Case presentation A 75-year-old male was referred for a clinical picture of pan-uveitis in the right eye. Eleven years prior, the patient was treated for non-metastatic cutaneous melanoma of the right flank with no follow-up recurrences. Full workup including complete uveitis panel, PET CT, brain MRI, lumbar puncture, and vitreous tap for uveitis workup as well as lymphoma, demonstrated no abnormal findings. On decompensation of the right eye, an additional vitreous biopsy was done, found positive for melanoma markers, however unable to differentiate between metastatic cutaneous or atypical uveal melanoma. Following enucleation, and awaiting pathology analysis, the patient developed recurrent orbital disease. Initial genetic results demonstrated activating BRAF V600E mutations, confirming metastatic cutaneous melanoma in origin. The patient began immunotherapy treatment and was referred for exenteration after a positive response to therapy.
Discussion Ocular metastasis from primary cutaneous melanoma is rare, accounting for less than 5% of all metastases to the eye and orbit, with most patients having at least one other non-ocular distant metastasis at ocular presentation. Furthermore, differentiation between atypical uveal and metastatic cutaneous melanoma can be difficult clinically, with the latter typically bilateral, multifocal as well as aggressive. A proper oncological history as well as genetic testing can aid in final diagnosis.

Eyelid specimen comparison, ophthalmology vs plastics departments

Levinkron O., Briscoe D.

Background: Eyelid lesions are excised and biopsied by Ophthalmologists and by Plastic surgeons. We retrospectively compared eyelid specimen that were excised by both the disciplines for the same population.
Methods: We reviewed the clinical and epidemiologic features of benign and malignant eyelid lesions from 2015- 2020 in Emek medical center, Afula, Israel. 1428 eyelid specimens were included. 5 specimens were dropped because of pathologic diagnosis was not set.
Results: Among 1423 specimens, histopathology confirmed 1210 (85.0%) were benign lesions and 213 (15.0%) were malignant/pre-malignant tumors.
The mean age at diagnosis was higher in patients with malignant eyelid tumors than those with benign eyelid tumors (76 and 59 years, resp.).
The most common benign lesions from all eyelid lesions were Fibroma (20.1%), seborrheic keratosis (11.0%) and Melanocytic Nevus (10.3%).
The most common malignant/pre-malignant tumors of all eyelid lesions were basal cell carcinoma (BCC) (9.2%), followed by solar keratosis (2.5%) and Bowen's disease (1.9%). Therefore, the risk of BCC is approximately 1 of 10.
37 of 683 (5.4%) of the lesions removed by ophthalmology were malignant/pre-malignant.
142 of 740 (19.2%) of the lesions removed by plastic were malignant/pre-malignant.
Of the lesions caused by UV exposure, 270 (70.0%) were removed by Plastic and 116 (30.0%) were removed by Ophthalmology.

Conclusions: Ophthalmology department eyelid specimens tend to be more benign, infectious/inflammatory with younger individuals.
Plastic department eyelid specimens tend to be more malignant, UV-exposure related with older individuals.