Presentation Title: Cherenkov luminescence imaging for assessment of radioactive plaque position in brachytherapy of uveal melanoma: an in vivo feasibility study

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Abstract: Purpose: To study the feasibility of using Cherenkov luminescence imaging (CLI) to evaluate and document ruthenium plaque position during episcleral brachytherapy for choroidal melanoma. Methods: Ruthenium-106 decays to rhodium-106 by emitting high-energy beta particles. When the electrons propagate through the eyewall, so-called Cherenkov radiation generates visible light, which can be captured by high-sensitive cameras. Five consecutive patients with uveal melanoma located in the posterior pole were studied. All patients underwent brachytherapy with a Ru-106 plaque. The tumors were 6.0-10.2 mm in largest basal diameter and 1.9-3.5 mm in thickness. The plaques had an activity between 7.7-19.1 MBq at the time of examination (24-48 hours after implantation). CLI was performed in complete darkness by a cooled EMCCD-camera (Andor iXon DV887) mounted on a fundus camera (Kowa RC-XV2) modified for long exposures. Results: CLI revealed the actual plaque position by displaying a circular spot of light in the fundus corresponding to the plaque area. The Cherenkov light appeared as a halo surrounding the tumor, which showed some asymmetry if the plaque was slightly displaced. There was a positive correlation between plaque activity and light intensity, and exposure times between 30-60 seconds were necessary to achieve the desired image quality. However, the long exposures made it difficult to maintain stable eye fixation and optimal image sharpness. Conclusion: CLI is a feasible method to assess and document radioactive plaque position in brachytherapy of uveal melanoma. Its main limitation is the long exposure time, which may be solved by improving camera sensitivity and eye fixation.

Presentation Title: The McCannel Brachytherapy Plaque Quick Release Stitch

Authors: Colin McCannel, Tara McCannel
Stein Eye Institute/UCLA, Los Angeles, USA

Abstract: Purpose: To describe a technique to suture brachytherapy plaques in place that allows simplified, efficient removal. Methods: Brachytherapy plaques can be secured to the sclera by means of a quick removal suturing technique. 5-0 VicrylTM suture is passed through the sclera. A loop of the VicrylTM suture is threaded through the islets of the flange of the brachytherapy plaque. A 2-0 Prolene® suture is passed through the VicrylTM loops above the flange, followed by tightening and tying of the VicrylTM suture. For release, the 2-0 Prolene® suture is pulled out and the plaque can then be pulled out by means of a “handle suture” previously attached to the flange. Results: The technique works as expected allowing securing the plaque to the sclera firmly, but allows removal without having to find and cut the sutures that hold the plaque in place. This technique has been used in 187 cases without complications related to the technique of securing the plaque. Among the cases in which the McCannel plaque stitch was used, there have not been any recurrences with a mean follow-up of 18 months. Conclusions: The McCannel plaque stitch can be used to secure and later efficiently remove brachytherapy plaques. Currently there is no detectable disadvantage.
**Presentation Title:** Regression Patterns of Choroidal Melanoma after Plaque Brachytherapy
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**Abstract:** Purpose: To describe the patterns of regression of choroidal melanoma (CM) after treatment with plaque brachytherapy.

**Methods:** Retrospective interventional case series including 170 consecutive patients treated with 103Pd plaque radiation for CM. Outcome measures were changes in tumor thickness, surface characteristics, tumor vascularity, ultrasonography, fluorescein angiography, optical coherence tomography and histopathology.

**Results:** The mean initial tumor thickness of 3.9-mm decreased to 1.7-mm after plaque brachytherapy. On imaging, tumors were pigmented in 51\%(n=86/170), amelanotic in 10\%(n=17/170) and variably pigmented in 39\%(n=67/170). Tumor pigmentation increased in 64\%(n=106/166), decreased in 18\%(n=30/166) and was unchanged in 18\%(n=30/166). Of the 120 that demonstrated intrinsic vascularity, 90\%(n=108/120) showed complete resolution. Subretinal fluid (SRF) was present in 34\%(n=58/170) at presentation, of which, 15\%(n=9/58) had persistent SRF at last follow-up. On ultrasound imaging, 88\%(n=149/170) tumors presented with low-moderate internal reflectivity of which 61\%(n=91/149) showed increased reflectivity on regression. We noted a crescento-decrescendo fluctuation of orange pigment lipofuscin (OP) along with complete resolution of drusenoid retinal pigment epithelial detachments (DRPED). In the entire series of 170 patients, there was 0.5\%(1) failure of local control, 2\%(4) secondary enucleations and 6\%(10) patients developing metastasis.

**Conclusion:** Findings related to choroidal melanoma regression after 103Pd plaque brachytherapy included decreased intrinsic tumor vascularity, decreased tumor related SRF, increased pigmentation, specific changes in OP and DRPED as well as decreased tumor thickness with an increase in internal reflectivity on ultrasound.

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**Presentation Title:** Local tumor control and late complications of fractionated stereotactic radiotherapy in uveal melanoma

**Authors:** Nicole Naus\textsuperscript{1}, Jackelien van Beek\textsuperscript{1}, Caroline van Rij\textsuperscript{1}, Serdar Yavuzyigitoglu\textsuperscript{1}, Dion Paridaens\textsuperscript{2}, Emine Kiliç\textsuperscript{1}

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**Abstract:** Purpose: Fractionated stereotactic radiotherapy (fSRT) for uveal melanoma (UM) treats the tumour, while retaining visual function. The aim of our study is to evaluate tumour control, late complications and survival of patients treated with fSRT. Method: We analyzed 184 small to medium-sized uveal melanoma, treated with fSRT from 1999-2014 in Erasmus University Medical Center Rotterdam and Rotterdam Eye Hospital, the Netherlands. We included tumors with at least 4 years of follow up. Results: The mean tumor thickness decreased from 5.9 mm at baseline to 1.9 mm 4 years after fSRT. Tumor progression was observed in 11 of the melanoma patients after a mean of 46 months. Thirty tumors were secondarily enucleated, due to neovascular glaucoma (n=17), tumor progression (n=11) and other reasons (n=2). The most common side effects were radiation retinopathy in 53, vitreous hemorrhage in 38 and neovascular glaucoma in 36 of the patients. The mean disease free survival was 106 months (range 4-218 months) in the metastatic-free group and the mean survival in the group with metastases was 39 months (range 1-165 months) (p<0.001). Conclusion: The local tumor control rate is 94\% in uveal melanoma patients treated with fSRT with 15 years of follow up.
Presentation Title: Vitreo retinal and ocular surgical procedures for the management of intraocular tumors of ocular tumors: A perspective from an ocular oncologist view
Authors: Ahmet Sarici
Istanbul University-Cerrahpasa, Istanbul, Turkey
Abstract: Purpose: To present the ocular and vitreo retinal surgery options for intraocular tumor management. Methods: Retrospective chart review of patients between 2010 and 2017. Results: There were 27 of who undergone ocular and vitreo retinal surgeries. 16 patients with intraocular melanoma undergone pars plana vitrectomy (3 had primary tumor endoresection, 4 had endoresection for radiation retinopathy, 4 had pars plana vitrectomy and silicone oil to prevent radiation side effects, 1 had subretinal fluid drainage for exudative retinal detachment, 4 had pars plana vitrectomy and endolaser for management of vitreous hemorrhage), 3 patients with hemangioblastoma had plana vitrectomy and endoresection, 5 patients with Coats disease underwent subretinal fluid drainage followed by cryotherapy and endolaser. Conclusion: Vitreo-retinal surgeries contribute and provides better outcomes in the management of patients.

Presentation Title: Features and Incidence of Isolated Choroidal Melanocytosis
Authors: Zelia Correa1,2, Cassandra Brooks3, James Augsburger2
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Abstract: Purpose. To describe the clinical features and course of patients with an isolated patch of choroidal melanosis. Method. Retrospective study of patients with isolated choroidal melanocytosis from a single clinical practice. Cases included presented ≥ 5 mm in basal diameter, homogeneously melanotic, and completely flat by conventional ocular ultrasonography. Results. Thirty-nine patients ranged in age from 2 weeks to 86 years at initial diagnosis. Two patients had bilateral choroidal melanocytosis. Arc length largest basal diameter of the melanotic choroidal lesion ranged 5 to 75 mm (median 34.5 mm). All lesions were flat by ultrasound. The lesion extended beneath the fovea in 17 eyes, to disc margin in 6, and around the disc in 2 eyes. The retina was fully attached in all eyes. Three patients had choroidal melanoma arising from the isolated choroidal melanocytosis. The fellow eye of 1 child had unilateral retinoblastoma, of 1 adult patient had choroidal melanoma, and of 3 adult patients had a choroidal nevus. None of the flat patches of choroidal melanocytosis changed appreciably in size during follow-up ranging from 6.5 months to 35 years (median 24.1 months). Conclusions. Isolated choroidal melanocytosis is a distinct clinical entity in the spectrum of melanocytic lesions of the uveal tract. It must be distinguished from choroidal nevus, choroidal melanoma, acquired bilateral melanotic hyperpigmentation of the posterior choroid, and normal choroidal pigmentation accentuated by patches of choroidal vitiligo. This disorder appears to predispose affected eyes to development of choroidal melanoma arising from the hypermelanotic patch.

Presentation Title: The CURE OM Patient-reported Registry for uveal and conjunctival melanoma.
Authors: Dan Gombos MD FACS1, Richard Carvajal MD2, Bertil Damato MD PhD FRCOphth3, Ivana Kim MD4, Chad Kimbler BSBA MA5, Jacqueline Kraska MS6, Miguel Materin MD7, Linda O’Brien8, Marlana Orloff MD7, Alison Petok MSW LCSW MPH8, Shana Rather MD5, Sara Selig MD MPH6, Carla Tressel6, Renne Zalinsky RN OCN8
1MD Anderson Cancer Center, Houston, USA. 2Columbia University Medical Center, New York, USA. 3Oxford University, Oxford, United Kingdom. 4Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston, USA. 5N/A, N/A, USA. 6Cure OM, Washington DC, USA. 7Duke University Eye Center, Durham, USA. 8Sidney
Kimmel Cancer Center, Thomas Jefferson University Hospital, Philadelphia, USA

Abstract: Purpose. Cure OM (an initiative of the Melanoma Research Foundation) is an organization that is working to improve the lives of patients with ocular melanoma through advocacy, education, counselling and research in the United States and internationally. The aim of this project is to develop a patient-reported registry to enhance opportunities for quality evaluation and research. Methods. The CURE OM Patient-reported Registry will be an online database hosted on a platform in the cloud. Using a structured protocol and study documents approved by a centralized, on-line, independent IRB, the registry will collect, store, maintain and analyze OM data. Patients diagnosed with OM, or their legally-authorized representatives (LARs) will directly input information. Survey questions will be presented using a system of branching logic that presents a series of questions on different OM topics (contact information, demographics, family background, risks, symptoms, diagnosis, treatments, outcomes and quality of life) related specifically to an individual respondent’s answers. Results. The dataset will be based on the registry provider’s standard dataset; applicable oncology standards; and common data elements (CDEs), such as the NIH’s GRDR Registry Model CDEs, the NCI Patient Reported Outcomes-Common Terminology Criteria for Adverse Events (PRO-CTCAE) and Patient-Reported Outcomes Measurement Information System (PROMIS). Patients will be actively engaged longitudinally. Conclusion. The Cure OM patient-reported registry is an important next step in supporting future research and advancing patient outcomes.

Presentation Title: Characterizing uveal melanoma treatment pathways in a large cohort of commercially insured patients
Authors: Prithvi Mruthyunjaya, Daniel Vail
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Abstract: Purpose: We characterize the management of a cohort of commercially insured patients diagnosed with ocular tumors between 2007 and 2015. We estimate the extent to which each treatment pathway is associated with post-treatment retinopathy, enucleation, and other complications. Methods: We use over 7 million records from 27,234 patients with a new diagnosis of an ocular tumor to map all treatments received by every patient, and to identify any diagnoses consistent with post-treatment retinopathy. We use survival models to estimate risks of enucleation and retinopathy based on patients’ treatment pathways. Results: 2,751 patients received treatment for a primary ocular malignancy. The most common initial treatments were plaque brachytherapy (n=1,521), enucleation (n=604), transpupillary thermotherapy (TTT) (n=380), and proton beam radiation (n=246). 32% (n=486) of patients initially treated with plaque brachytherapy developed post-radiation retinopathy within 5 years of treatment. Patients treated with plaque were more likely to develop retinopathy than patients treated with proton beam (HR 2.27, 95% CI 1.54-3.34). 10% of patients treated solely with TTT progressed to enucleation. Conclusions: Characterizing treatment pathways in a large dataset offers insight to the way that health care is experienced at the patient level. We elucidate the most common pathways through care taken by patients with ocular tumors, and associate them with patients’ risk of enucleation and post-treatment retinopathy. We estimate complication risks associated with different treatment strategies, but our primary finding is a more fundamental one: we characterize in detail the real-world treatment pathways taken by a large cohort of patients with eye cancer.

Presentation Title: Improved survival rates in patients with uveal melanoma: Evidence from a nationwide Danish cohort
Authors: Isabel Smidt-Nielsen1, Mette Bagger1, Steffen Heegaard2, Klaus Andersen3, Jens Kiilgaard1
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Abstract: Background: The overall cancer incidence in Denmark is increasing and we aimed to investigate whether this applied to uveal melanoma despite previously described stable incidence rates. Furthermore, we wanted to investigate if an association between centralization of treatment of this infrequent disease and early
detection could be found, thereby improving survival. Methods: We conducted a nationwide retrospective cohort study on Danish patients with uveal melanoma from 1943 through 2017. Incidence rates were estimated as annual percentage change (APC) overall and for AJCC tumor sizes. The age-period-cohort model was applied to estimate the relative risk of calendar period. Relative survival rates were calculated from 1968 through 2017. The cox proportional hazards model was applied to estimate the effect of calendar period on survival. Results: Simultaneously with centralization of treatment regimens, an overall increase in incidence rates were found (APC = 0.25%, 0.07 – 0.42; 95% CI). This was due to an increasing incidence rate of AJCC T1 + T2 tumors (APC = 0.97%, 0.57 – 1.37; 95% CI), whereas no increase in incidence rate of AJCC T3 + T4 tumors was found (APC = -0.01%, -0.26 – 0.25; 95% CI). The relative survival improved for all tumor sizes (HR = 0.98; 0.98 – 0.99; 95% CI). Conclusion: Increasing incidence rates of small melanomas, and improved relative survival rates for all tumor sizes, was found concordantly with centralization of treatment regimens. This supports the hypothesis that early treatment improves survival in patients with uveal melanoma and emphasizes the importance of early detection and prompt workup of suspected lesions.
Presentation Title: Vitreous Cytokines and Chemokines in Choroidal Melanoma Patients
Authors: Hakan Demirci¹, Lu Tang², Cem Ozgonul¹, Yesim Demirci³, Thomas Gardner¹, Jeffrey Sundstrom⁴ ¹Kellogg Eye Center, University of Michigan, Ann Arbor, USA. ²Department of Biosciences, Graduate School Public Health, University of Pittsburgh, Pittsburgh, USA. ³Department of Human Genetics, Graduate School Public Health, University of Pittsburgh, Pittsburgh, USA. ⁴Department of Ophthalmology and Visual Sciences, Penn State University, Hershey, USA
Abstract: Purpose: To evaluate changes in vitreous cytokines and chemokines level in eyes with choroidal melanoma that were treated with plaque radiotherapy. Methods: Vitreous cytokine and chemokine concentrations were measured using a 42-plex cytometric bead immunoassay in 18 choroidal melanoma patients who underwent plaque radiotherapy and in 14 non-choroidal melanoma patients treated for other ocular conditions (epiretinal membrane, symptomatic vitreous floater, or macular hole). Comparisons of Vitreous cytokines and chemokine levels were made both between the choroidal melanoma and non-choroidal melanoma groups and within the choroidal melanoma group (among different prognostic categories as defined by gene expression profiling test: class 1A, 1B, 2). Results: Principal component analysis has revealed a clear separation between the vitreous cytokine/chemokine profiles of choroidal melanoma patients vs. non-choroidal melanoma subjects. A total of twenty-five vitreous cytokines/chemokines showed different concentration (P Conclusion: Analysis of vitreous cytokines and chemokines can provide information about the tumor microenvironment in choroidal melanomas. A subset of vitreous cytokines/chemokines may also differ between class 1 and 2 tumors.

Presentation Title: HIF1 alfa as regulator of inflammation in uveal melanoma
Authors: Martine Jager¹, Niels Brouwer², Gulcin Gezgin², Annemijn Wierenga¹, Robert Verdijk³, Pieter Van der Velden¹, Marina Marinkovic¹, Gre Luyten¹ ¹Dept of Ophthalmology, LUMC, Leiden, Netherlands. ²Dept. of Ophthalmology, LUMC, Leiden, Netherlands. ³Dept of Pathology, LUMC, Leiden, Netherlands. ⁴Dept of Pathology, ErasmusMC, Rotterdam, Netherlands
Abstract: Purpose: An inflammatory infiltrate in uveal melanoma and a high blood vessel density are associated with the presence of monosomy 3 (Maat, IOVS 2008, Bronkhorst, IOVS 2011), but we do not know the pathophysiologic mechanism that links these two. Macrophages are attracted to HIF1alfa; currently, drugs are being developed that interfere with the HIF1alfa-VEGF pathway. We hypothesize that HIF1 alfa expression is increased by tumor size and monosomy 3, and involved in bringing in tumor-infiltrating leukocytes. Methods: Data were available from 52 uveal melanoma from Leiden, all obtained by enucleation. Data were available on clinical and histopathological data, mRNA expression, chromosome and BAP1 status. Results: While HIF1 alfa expression was not related to clinical characteristics such as Largest Basal Diameter, tumor height, or ciliary body involvement, it was significantly related to the expression of T cell markers CD3, CD4, CD8, and macrophage marker CD68 (all P < 0.03). Tumors with extra copies of 8q had a significantly higher HIF1 alfa, but this was due to an association with monosomy 3. Tumors with disomy of chromosome 3 and extra 8q did not have a significantly higher HIF1 alfa (P = 0.08). HIF1 alfa was increased in tumors lacking BAP1 expression. The correlation was stronger with BAP1 status than with chromosome 3 status. Conclusion: The previously observed association between an inflammatory infiltrate and monosomy 3/BAP1 loss may be related to an upregulation of HIF1 alfa. We suggest that chromosome 3 loss/BAP1 loss affects the HIF1 alfa pathway, leading to an inflammatory infiltrate in uveal melanoma.
Presentation Title: Estrogen receptor expression in uveal melanoma
Authors: Lynn Schoenfield, Caroline Craven, Mohamed Abdel-Rahman, Colleen Cebulla
Ohio State University Wexner Medical Center, Columbus, OH, USA
Abstract: Purpose: The purpose of this study is to confirm that estrogen receptors (ER) are present in a subset of uveal melanomas and to determine whether ER expression and gender impact patient outcome (metastasis or dead of disease, DOD). Methods: The study was approved by the OSUWMC IRB. Outcome data of 50 patients with UVM from 2010-17 were analyzed. Tissue was studied by immunohistochemistry (IHC) for ER in 47 cases (brown chromogen) and scored as in breast carcinoma. Statistical analyses were performed. Results: Follow-up was Conclusion: ER expression occurs in over half of cases of uveal melanoma. While significant differences were not demonstrated regarding ER expression in regard to probability of surviving without metastasis or death, the sample size is small and thus the power to detect differences is low. Further study is suggested.

Presentation Title: Long-term visual outcomes for small uveal melanoma staged T1 treated by proton beam radiotherapy
Authors: nathalie cassoux1,2, adelaine toutee1, martina angii3, sylvain Dureau1, remi dendale1, laurence desjardins1
1 Institut Curie, Paris, France. 2 Université Paris V Descartes, Paris, France. 3 IRCCS Istituto Nazionale dei Tumori Foundation, Milan, Italy. 4 Centre de Protonthérapie, Orsay, France
Abstract: AIMS: To investigate the long-term visual outcomes of protonbeam radiotherapy (PBR) for posterior uveal melanoma T1 (T1UM). METHODS: In this retrospective monocentric cohort study, 424 patients with T1UM were treated by PBR between 1991 and 2010 with at least 5-years follow-up. Visual acuity was analyzed for two groups: patients with posterior edge of tumor located at ≥ 3 mm (Group 1) or <3 mm (Group 2) from fovea-optic disc. Primary outcome was visual acuity (VA) and secondary outcomes were local control and radiation therapy related complications. RESULTS: Overall mean follow-up was 122 months. Among the 75 patients of Group 1, mean baseline and final VA were 20/25 and 20/32 respectively and 70.4% patients retained ≥20/40 at 5 years. Among 317 patients of Group 2, mean baseline and final VA were 20/40 and 20/80 respectively. In Group 2, 24.5% patients kept 20/40 and 24.5% kept between 20/200 and 20/40 at follow-up. Final acuity was better for tumors located the furthest away from posterior pole (p=0.03). Risk factors of vision loss were maculopathy (p<0.0001), cataract (p=0.0008) and documented growth (p=0.002). Primary retinal detachment (p=0.02), radiation papillopathy (p<0.0001) and surface of irradiated macula (p<0.0001) increased the risk of radiation maculopathy. No ocular recurrence was observed. CONCLUSION: PBR for T1UM yielded good long-term visual outcomes and local control. Patients of Group 1 retained excellent VA, more than 20/40 in 70.4 % of cases.

Presentation Title: Outcomes after proton irradiation for patients who are eligible for investigational AU-011 treatment
Authors: Evangelos Gragoudas1,2, Anne Lane1,2, Ivana Kim1,2
1 Massachusetts Eye and Ear, Boston, USA. 2 Harvard Medical School, Boston, USA
Abstract: Purpose: Vision loss is common in patients treated with radiotherapy for choroidal melanomas. With protons, maximum radiation dose is delivered to the tumor with a sharp dose reduction outside the tumor. However, radiation complications can develop when tumors are located near the optic nerve or macula. Treatment with light-activated AU-011, an investigational product which specifically targets tumors cells, may avoid these complications. We evaluated outcomes in patients who fit eligibility criteria for AU-011 treatment and were treated with proton irradiation. Methods: Two hundred and seventy-four eligible patients were identified for analysis. Rates of visual acuity, radiation-induced complications, eye loss, and tumor recurrence were calculated using the Kaplan-Meier method. Results: Median tumor height was 2.1 mm (1.2-2.9), median largest basal diameter was 9.0 mm (4.0-10.0), and 75.1% of tumors were within 2 disc diameters of the optic disc and/or fovea. Median follow-up was 5.7 years (1.3 months-30.2 years). Visual acuity of 20/40 or better was observed in 86.1%, 68.2% and 53.4% of patients at 1, 3 and 5 years after proton irradiation, respectively. Maculopathy developed in 39.5%, papillopathy in 20.9%, and NVG in 3.1% but the majority of patients (66.5%) retained visual acuity of 20/200 at 5 years after proton irradiation. Eye loss (2%) and tumor recurrence (1%) were rare. Conclusion: Despite the advantageous dose distribution of protons, vision loss can still occur particularly in patients with tumors located near critical structures. Treatment with AU-011 may prove to be beneficial for improving visual outcome in these patients.
Unsupervised clustering of SNP array CNV profiles predicts survival in Uveal Melanoma patients

Authors: Emine Kilic1, Wojtek Drabarek2, Serdar Yavuzyigitoglu1, Askar Obulkasim3, Job Van Riet4, Kyra Smil2, Natasha Van Poppelen1, Jolanda Vaarwater1, Tom Brands2, Bert Eussen5, Robert Verdijk6, Nicole Naus1, Hanneke Mensink7, Dion Paridaens2, Eric Boersma8, Harmen Van Werken4, Annelies De Klein5, Martine Jager4, Tara McCannel and Amit Arora

Abstract: Purpose:Uveal Melanoma (UM) is characterized by multiple chromosomal rearrangements and recurrent mutated genes. The aim of this study is to investigate if copy number variations (CNV) alone and in combination with other genetic and clinico-histopathological variables can be used to stratify for disease-free survival (DFS) in uveal melanoma (UM) patients.Methods:We analyzed SNP array data of primary tumors and other clinical variables of 214 UM patients from the Rotterdam Ocular Melanoma Study (ROMS) cohort. Weighted hierarchical clustering of SNP array data was used to identify molecular subclasses with distinct CNV patterns. The subclasses associate with mutational status of either BAP1, SF3B1 or EIF1AX. Cox proportional hazard models were then utilized to study the predictive performance of clinico-histopathological-, SNP array cluster-and mutation data, and their combination for study endpoint risk.Results:Five clusters with distinct CNV patterns and concomitant mutations in BAP1, SF3B1 or EIF1AX were identified. The sample's cluster allocation contributed significantly to mutational status of samples in predicting the incidence of metastasis during a median of 45.6 (interquartile range [IQR]: 24.7 - 81.8) month follow-up (P << 0.001) and vice versa. Furthermore, incorporating all data sources in one model yielded a 0.81 (95% confidence interval [CI]: 0.74 - 0.88) c-score during 100 months follow up which indicates good performance for UM-related DFS prediction.

miR-145/miR-205 interacting with miR-200c synergistically attenuates the metastatic characteristics of uveal melanoma cells

Authors: Yang Li, Bin Wei

Abstract: Purpose: MicroRNAs (miRNAs) contribute to tumorigenesis by acting as either oncogenes or tumor suppressor genes. In this study, we investigated the mechanism of miR-145/miR-205 and miR-200c in uveal melanoma cell metastasis and malignant transformation.Method: Quantitative real-time polymerase chain reaction was used to screen the expression levels of miR-205, miR-200c, -miR205/miR-200c, miR145, miR145/miR-200c in uveal melanoma cell lines. Lenti-virus expression system was used to construct OCM-1A and C918 cell lines with miR-205, miR-200c, -miR205/miR-200c, miR145, miR145/miR-200c. Cell proliferation, cell cycle, cell apoptosis and migration of these overexpression cell lines were examined by MTT assay, flow cytometry and traswell respectively.Results: MIR-205, miR-200c, -miR205/miR-200c, miR145, miR145/miR-200c inhibited the proliferation and migration of uveal melanoma cell lines. Among them, miR145/miR-200c inhibited the migration of tumor cells most significantly.Conclusion: MI145/miR-200c can significantly inhibit tumor cell migration.
Presentation Title: Function of BAP1 in vertebrate development sheds light on its role in the metastasis of uveal melanoma

Authors: J. William Harbour¹,²,³, Jeffim Kuznetsov¹, Dawn Owens¹, Tristan Aguero⁴, Mary King⁴

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Abstract: Purpose: The tumor suppressor BRCA1-associated protein 1 (BAP1) is frequently mutated in uveal melanoma, leading to metastasis and poor patient outcome. This study sought to identify the function of BAP1 in normal development in order to provide potential insights into its role in cancer. Method: The effect of depleting BAP1 in Xenopus laevis embryos was analyzed using morphologic analysis, immunohistochemistry, RNA-seq, and ChIP-seq. Results: Alterations caused by BAP1 loss affected multiple embryonic lineages and paralleled those associated with BAP1 loss in human uveal melanoma. This model was used to conduct a novel high throughput drug screening strategy to identify compounds that reverse the effects of BAP1 loss. Conclusion: These findings reveal a complex role for BAP1 in the epigenetic control of cell identity during normal development, and they provide insights into its role in uveal melanoma that may lead to new therapeutic strategies.

Presentation Title: Correlation of BRCA1-Associated Protein-1 Immunoreactivity and Gene expression profiling as an indicator of risk of metastasis in patient with primary uveal melanoma

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Abstract: Purpose: To determine the correlation of BRCA1- associated protein-1 (BAP1) immunoreactivity and gene expression profile (GEP) classification in a series of patients with primary uveal melanoma, and to describe their clinicopathologic features. Methods: A retrospective chart reviewed of the clinical history, histopathologic findings and gene expression profile classification. Formalin-fixed paraffin-embedded tissues were stained for BAP1. Collected data (patient demographics, clinical findings, BAP1 Immunoreactivity testing result, and gene expression profile classification) were then analyzed statistically. Results: Thirty (30) patients with primary uveal melanoma who had undergone enucleation met the inclusion criteria. Sixteen (53%) of them were male and 14 (47%) were female. The mean age was 62 ± 15.68 years old with a range of 24-92. Only nuclear BAP1 staining was highly correlated with the GEP classification. Among the 30 cases, all (7/7) GEP Class 1A have high nuclear BAP1 expression. In Class 1b, 4/8 (50%) have high nuclear BAP1 expression and 4/8 (50%) have low nuclear expression. In Class 2, 15/15 (100%) have low nuclear BAP1 expression. Conclusions: Nuclear BAP1 immunohistochemical staining of enucleated uveal melanoma patients highly correlates with GEP classification with a Cohen’s k for agreement of 0.73 and a Fisher’s exact test of p<0.001 in GEP class 2 versus 1 tumors, indicating substantial agreement between the two prognostic tests.

Presentation Title: Genetic Background In Pediatric Uveal Melanoma

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Abstract: Purpose: Uveal melanoma (UM) is the most common primary adult intraocular malignancy; familial and pediatric uveal melanoma (PUM) remains rare. BAP1 has been identified as a predisposition gene for UM. Purpose of this study is to elucidate the role of BAP1 germline mutations in pediatric uveal melanoma (PUM). Method: Collaborative multicenter Ocular Oncology Group (OOG) study. Patients with PUM were included if blood or formalin fixed paraffin embedded tissue was available. Samples were sent in from different European countries. The Ion Torrent next-generation sequencing platform was used for germline analysis of the BAP1 gene in normal tissue or blood. When tumor tissue was available immunohistochemistry (IHC) of BAP1 was performed. When
there was lack of BAP1 expression a mutations in the BAP1gene was assumed. Clinical data was collected from each center in an online database. ResultsIn total, 68 patients from 12 different centers were included. From 45 patients results of IHC of tumor tissue or germline testing for BAP1is available. BAP1 staining was performed on 27 UM sections. There was BAP1 expression in 17 UM and lack of expression was observed in 10 sections. Blood samples were tested from 18 patients, which did not show a germline BAP1mutation. In one patient a previously described p.Leu570fs*40 mutation was found in normal tissue. ConclusionAn absent BAP1 expression using IHC was observed in tumor tissue of PUM patients indicating the presence of a BAP1mutation. However, no preference for BAP1germline mutations in PUM could be identified so far.
Presentation Title: Small Incision Guarded Hydroaspiration of Iris Melanoma
Authors: Arun Singh  
_Cole Eye Institute, Cleveland, USA_

Abstract: Purpose: To describe the technique and results of a minimally invasive surgical technique for resection of small iris melanoma. Methods: Case report. Results: A 43 year old female who noted recent change in long standing (20 years) iris pigmented lesion of the right eye. Uncorrected visual acuity was 20/20 OU and normal intraocular pressure OU. On anterior segment examination of the right eye, a 2 mm x 2 mm x 1 mm melanocytic iris stromal mass with fascicular surface and corectopia was noted at 6:30 o’clock. Gonioscopy excluded angle involvement. By ultrasound biomicroscopy, the stromal mass had maximal iris thickening of 1.0 mm. The lesion was excised using small incision approach (3.0 mm) with straight and curved cutting scissors (23-gauge), approximately 1mm beyond the visible margin. The wedge like excised tumor (with surrounding normal iris tissue) was aspirated into DSEK inserter that had been preloaded with viscoelastic. Pupilloplasty was then performed using a single 10-0 prolene suture through an additional 2.4 mm corneal incision. Both corneal wounds were closed with a single 10- nylon suture. Postoperatively, there were no complications and the refraction remained unchanged (plano, 20/20). Histopathology revealed the lesion to spindle cell melanoma with clear margins. Conclusions: Small incision guarded hydroaspiration is a minimally invasive surgical technique for resection of select small iris lesions. Use of multiple small corneal incisions avoids morbidity associated with a single large corneoscleral incision and use of guarded aspiration eliminates the risk of wound contamination by the malignant tumor.

Presentation Title: Class 2 gene expression profile of a hemorrhagic pigment epithelial detachment misdiagnosed as melanoma
Authors: Claudine Bellerive1,2, Elaine Binkley1, Arun Singh1  
1_Cole Eye Institute, Cleveland Clinic, Cleveland, USA. 2Centre Hospitalier Universitaire de Quebec, Quebec, Canada_

Abstract: Purpose: To describe a case of a hemorrhagic pigment epithelial detachment that was initially misdiagnosed as a choroidal melanoma and had a class 2 gene expression profile (GEP) on prognostication fine needle aspiration biopsy (FNAB). Methods: Retrospective case report. Results: A 79-year-old man with a history of atrial fibrillation treated with warfarin presented for guidance regarding systemic surveillance after undergoing prognostic FNAB at the time of episcleral plaque brachytherapy for a presumed cilio-choroidal melanoma. The results of GEP testing were consistent with a class 2 molecular profile. At three month and eight month follow up, the clinical, echographic, and optical coherence tomography (OCT) findings were consistent with a hemorrhagic pigment epithelial detachment (PED) rather than melanoma. By eight months, the lesion had completely resolved. Conclusion: This is the first reported case of a GEP class 2 profile obtained from prognostic FNAB of a non-malignant lesion. Given that GEP is not a diagnostic test, it and can lead to erroneous prognostic information in the setting of non-melanoma choroidal lesions.

Presentation Title: Percutaneous oncolytic rose bengal disodium for metastatic uveal melanoma patients with hepatic metastasis
Authors: Sapna Patel1, Gener Balmes1, Portia Velasquez1, Masood Iqbal1, Jessie Richard1, Michelle Rohlf1, Jocelyn Joseph1, Chrystia Zobniw1, Jaime Anderson1, Van Trinh1, Ravi Murthy1, Eric Wachter2
Abstract: Purpose: Rose bengal disodium (PV-10) is a small molecule oncolytic immunotherapy in clinical development for treatment of solid tumors. When administered by intralesional injection, PV-10 can produce an immunogenic cell death that may induce a T-cell mediated immune response against treatment-refractory and immunologically-cold tumors. Given this mechanism of action, we investigated treatment of metastatic uveal melanoma with percutaneous hepatic PV-10.

Methods: PV-10-LC-01 (NCT00986661) is an open-label Phase 1 study evaluating the safety, tolerability, and preliminary efficacy of intralesional PV-10 in patients with solid tumors metastatic to the liver. A single percutaneous injection of PV-10 is administered to a designated hepatic tumor 1.0-4.9 cm in diameter. Response assessments are performed at Day 28, then every 3 months. Patients with multiple injectable tumors may receive further PV-10 after Day 28.

Results: PV-10-LC-01 includes a single-center cohort of 10 uveal melanoma patients with hepatic metastases. Eligible patients may receive standard of care checkpoint blockade immunotherapy during treatment with PV-10.

Conclusion: To date, the study has screened 9 patients with metastatic uveal melanoma. Five patients have been consented, enrolled, and treated; two have received a second treatment with intralesional hepatic PV-10. One patient has received PV-10 with standard of care immunotherapy. Updated enrollment as well as preliminary safety and efficacy data of the uveal melanoma cohort will be presented at the meeting.

Presentation Title: Lights, KAMRA… trouble

Authors: Magdalena Edington, Julie Connolly, David Lockington, Paul Cauchi, Vikas Chadha
Tennent Institute of Ophthalmology, Glasgow, United Kingdom

Abstract: Purpose: The trend for refractive procedures addressing presbyopia is rising, with a variety of corneal onlays and inlays available. One such device is the KAMRA small aperture inlay, which functions on the principle of pinhole optics. It has previously been reported that the device does not impair clinical examination or imaging. We present a case where a KAMRA inlay potentially masked an intraocular tumour.

Method: Retrospective report of case

Results: A 62-year-old female attended her optician with reduced vision and visual field defect in her left eye. She had had bilateral LASIK and left KAMRA corneal inlay done in 2015. The optician reported a limited fundal view and referred the patient. On examination visual acuity was reduced to 6/60 in the left eye. The shadow from corneal inlay limited the posterior segment examination even on dilated fundoscopy, but there appeared to be a raised lesion temporally. Ocular ultrasound confirmed a large intraocular tumour consistent with malignant melanoma, measuring 21 mm across and 13.3 mm high with associated retinal detachment. Due to the tumour size, the decision was made to enucleate the eye. Conclusion: We raise concerns regarding the use of ocular devices that limit the ocular examination, and wish to emphasize the importance of appropriate consenting of patients. In this case, the elective insertion of a refractive technology potentially masked an intraocular tumour due to creating pinhole conditions for both patient and clinician. Enucleation may have been avoided if the lesion had been identified at an earlier stage.

Presentation Title: Bilateral Simultaneous Primary Choroidal Melanomas: Treated with Palladium-103 Plaque Radiation

Authors: Abhilasha Maheshwari1,2, Paul Finger2
1Centre for sight, Hyderabad, India. 2New York eye cancer center, New York, USA

Abstract: Purpose: To provide a clinical description of a case of bilateral choroidal melanoma in a patient treated with palladium-103 (103Pd) plaque brachytherapy. Methods: An 81-year old man presented with choroidal melanoma in both eyes. In consideration of tumor sizes and locations; treatment involved insertion of 103Pd radioactive plaque in the right eye followed by the left, at an interval of 2 months. Results: At 1-year follow up, bilateral local control has been associated with apical tumor height regression and visual acuity has been preserved (20/20 in the right eye and 20/25 in the left). Exudative subretinal fluid has resolved. There has been no metastasis.
Conclusion: Bilateral choroidal melanomas are rare, reported to be either simultaneous or sequential as well as treatable. In this case, we were able to achieve tumor regression and preserve visual acuity in both eyes for after plaque brachytherapy.

Presentation Title: Optic Nerve Invasion of Choroidal Melanoma
Authors: Hans Grossniklaus, Eszter Szalai, Jill Wells
Emory University, Atlanta, USA
Abstract: Purpose: To describe a case of optic nerve invasion of uveal melanoma. Methods: The clinical features and pathologic findings in a patient who developed optic nerve invasion of a choroidal melanoma were reviewed. Results: A 58-year-old man was followed for one year after plaque brachytherapy for a choroidal melanoma. The melanoma was found to invade the optic nerve and his eye was enucleated. Pathologic findings showed direct invasion of the optic nerve from melanoma in the peripapillary choroid. Conclusions: Mechanisms of optic nerve invasion of choroidal melanoma include via the vitreous, extension through the retina, invasion from the peripapillary choroid, and combined mechanisms. Patients should be followed for this as this is an indication for enucleation.

Presentation Title: Choroidal Melanoma Metastatic to the Ipsilateral Choroid
Authors: Paul T Finger1,2,3, Anna C Pavlick3,4, Puneet Jain1, Moanes Morkos5
1 The New York Eye and Ear Infirmary of Mt. Sinai, New York, USA. 2 The New York University School of Medicine, New York, USA. 3 New York University Cancer Center, New York, USA. 4 New York University School of Medicine, New York, USA. 5 The New York Eye and Ear Infirmary, New York, USA
Abstract: Purpose: To report a case choroidal melanoma metastatic to the Ipsilateral choroid which responded to checkpoint chemotherapy. Methods: Local control of a primary choroidal melanoma was achieved with palladium-103 plaque radiation therapy. Radiation maculopathy occurred 2.5 year later and was successfully suppressed with periodic intravitreal anti-VEGF injections for 5 additional years. Then, in 2017 she developed a new, discrete choroidal melanoma in the same left eye. Restaging with magnetic resonance imaging of the orbits and abdomen/pelvis as well as computed tomography of the chest revealed multi-organ systemic metastasis in the eye, the liver and lymph nodes. Treatment involved systemic combination immunotherapy with ipilimumab (3 mg/kg) and nivolumab (1 mg/kg) IV every 3 weeks for 4 cycles followed by nivolumab (3 mg/kg) IV every 4 weeks as maintenance. Ophthalmic ultrasound and systemic imaging restaging was performed every 12 weeks. Results: Intraocular, liver and nodal metastases all regressed on systemic immunotherapy. After 14 months, ophthalmic ultrasound revealed that the intraocular metastasis was reduced from 6.6 to 1.5 mm in thickness. Serial computed tomography revealed progressive shrinkage and disappearance of hepatic/nodal metastasis. Continued intravitreal anti-VEGF therapy suppressed her radiation maculopathy resulting in a visual acuity of 20/25, now 8 1/2 years after plaque therapy. Conclusion: This study presents a unique case of metastatic choroidal melanoma that presented in the liver, nodes and the same eye as the primary tumor. Systemic immunotherapy controlled the systemic metastases and aided intraocular diagnosis by controlling the metastatic uveal melanoma.

Presentation Title: What will be with an eye after Ru-106 irradiation with a scleral dose over 5000 Gy?
Authors: Andrey Yarovoy, Anna Shatskikh, Vera Yarovaya, Egor Korobov, Roman Loginov
S.Fyodorov Eye Microsurgery Federal State Institution, Moscow, Russian Federation
Abstract: Purpose: to present a case of inadvertent irradiation of the eye with a huge overdose. Method: A 27-year old Asian female with cilio-choroidal melanoma was treated with Ru-106 brachytherapy. Tumor thickness was 7.9 mm, maximum basal diameter 18.2 mm. The eye had scleral and choroidal melanosis. Prescribed scleral dose was 1896 Gy. At that period the patient had some psychological problems and on the day before plaque removal she left the clinic and went home. She came back few days later. At the time of plaque removal the scleral dose was 5618 Gy. Results: Patient was under the follow up within 3 years with tumor regression to the thickness of 6.0
mm when the scleral melt was diagnosed. The eye was enucleated. Results of histological and genetic examinations will be presented. Five years after enucleation orbital reconstruction with polyethylene prosthesis implantation was fulfilled. Follow up after diagnosis is 9 years. Patient is free of metastases. Conclusion: This exceptional case shows that despite the huge overdose the eye changes were similar to those after irradiation with much less doses. This can be explained by well-known fact of tissue radio protection by intensive pigmentation.
**Presentation Title:** Variability of Bad Prognosis in Uveal Melanoma  
**Authors:** Arun Singh, Yusra Shao, Jose Echegaray, Nakul Singh  
*Cole Eye Institute, Cleveland, USA*  
**Abstract:** Purpose: To explore variability in survival of patients with uveal melanoma classified to have bad prognosis. Methods: We searched PUBMED, MEDLINE and EMBASE for studies reporting survival data for uveal melanoma undergoing prognostic testing with chromosome 3 status by FISH, CGH, MSA, MLPA, SNP, GEP class and exon sequencing. Results: Of the initial search of 49 studies, only 12 studies met inclusion criteria. Three studies reported survival data for FISH, 1 for CGH, 1 for MSA, 3 for MLPA, 3 for SNP, 3 for GEP, and 2 for combination of tests. No studies reported survival data for exon sequencing. Reported outcome measures included percent free of metastatic death (6), metastases free survival (MFS) (2), reported overall survival (OS) (2), and probability of metastasis (2). MFS (5 year) for monosomy 3 by FISH was 40-60%, by MLPA was 30-40%, by SNP was 72% and for GEP Class 2 was not reported. Overall survival (5 year) for monosomy 3 (and disomy 8) tumors by MLPA and GEP Class 2 were not comparable (81% and 55% respectively). Conclusion: Variability exists in reported survival for bad prognosis uveal melanoma. Composition of study population (tumor size, exclusion of iris melanoma, duration of follow up), method of obtaining tumor sample, type of prognostic test, method of determining metastases, and use of variable outcome measures can explain some of the observed differences in survival. Standardization of study methods and outcome measures will allow comparison of survival data derived from different prognostic tests.

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**Presentation Title:** Multiplex Ligation Probe Amplification (MLPA) Assay in Metastatic Prognosis for Uveal Melanoma: A Multi-Center Collaborative International Report  
**Authors:** Tara McCannel¹, Vidal Soberon², Armin Afshar³, Bertil Damato³, Robert Johnson⁴, Katherine Paton⁵, Carol Shields⁶, Arun Singh⁷, Ezekiel Weis⁸  
¹University of California, Los Angeles, Los Angeles, USA. ²University of Los Angeles, Los Angeles, USA. ³University of California, San Francisco, San Francisco, USA. ⁴West Coast Retina, San Francisco, USA. ⁵University of British Columbia, Vancouver, Canada. ⁶Wills Eye Institute, Philadelphia, USA. ⁷Cleveland Clinic, Cleveland, USA. ⁸University of Alberta, Edmonton, Canada  
**Abstract:** Purpose: To correlate the DNA-based multiplex-ligation probe amplification (MLPA) platform result with metastatic outcome in an international multi-centered collaboration. Methods: Patients from seven ocular oncology centers in the United States and Canada, diagnosed with choroidal and/or ciliary body uveal melanoma who underwent fine needle aspiration biopsy for molecular prognostication were included. MLPA was performed on biopsy specimens where foci on chromosomes 1, 3, 6 and 8 were tested. In some cases, sequencing for GNAQ, GNA11, EIF1AX, or SF3B1 was performed. Pearson’s chi square test, Fisher’s exact test and Wilcoxon rank sum test were used to correlate chromosomal aberrations and mutations, and tumor dimensions with metastatic outcome. Kaplan-Meier plots were performed for survival correlations. Results: A total of 312 patients were included, with average follow-up of 18 months. Average tumor greatest diameter was 11.6 mm, average tumor thickness was 5.0 mm. Twenty-seven (8.6%) patients developed metastasis. All cases that developed metastasis had monosomy 3 identified by MLPA. The strongest correlations with metastasis were the presence of 8q gain (p=0.00003966); tumor diameter (p=0.000083); presence of monosomy 3 (p=0.0002879); and tumor thickness (p=0.0001379). Two metastatic cases revealed no chromosomal aberration or other mutation. Conclusions: The MLPA prognostic assay provides a highly accurate and transparent method of not only providing prognostic
information, but also the sequencing for tumor-specific mutations providing an internal control as to whether or not uveal melanoma tissue was sampled.

**Presentation Title:** Five-year clinical outcomes of a prospective, multi-center cohort tested with the 15-gene expression profile test for uveal melanoma and impact of test results on metastatic surveillance intensity

**Authors:** Thomas Aaberg¹,², Kyle Covington³, Tony Tsai⁴, Yevgeniy Shildkrot⁵, Kristen Plasseraud³, Kristen Oelschlager⁶, Federico Monzon³

¹Retina Specialists of Michigan, Grand Rapids, USA. ²Michigan State University, Grand Rapids, USA. ³Castle Biosciences, Inc., Friendswood, USA. ⁴Retina Consultants, Sacramento, USA. ⁵University of Virginia, Charlottesville, USA. ⁶Castle Biosciences, Inc., Phoenix, USA

**Abstract:** Purpose: This multicentered prospective registry (NCT102376920) study evaluated 5-year metastasis-free survival (MFS) and management recommendations for patients clinically tested with the uveal melanoma 15-gene expression profile (GEP) test. Methods: Patients with GEP results were consented and enrolled (n=89). Physician recommendations for patient management were collected. Clinical outcomes were collected bi-annually. Annual surveillance imaging and/or liver function testing (LFT) was considered low intensity; quarterly to biannual imaging and/or LFT was considered high intensity. Results: 49 (55%) patients had low-risk Class 1 (38 Class 1A; 11 Class 1B) and 40 (45%) had high-risk Class 2 tumors. Class 2 median largest basal diameter was greater than Class 1 (p=0.008). Median follow-up for event-free cases was 4.7 years (1.1-8.0 years). Three Class 1 (6%) and 22 (55%) Class 2 patients experienced metastasis (p<0.0001). Median times to metastasis were 3.2 and 2.5 years for Class 1 and 2 patients. Five-year MFS rates for Class 1 and 2 patients were 92% (84-100%) and 42% (27-64%) (p<0.0001). In multivariate analysis, GEP Class 2 was the only independent predictor of metastasis (HR: 12.02; p<0.0001). All Class 2 patients had high intensity surveillance compared to 20% of Class 1 patients (p<0.0001). No Class 1 patients received systemic adjuvant therapy. Four Class 2 patients received systemic adjuvant therapy, and two of these patients were metastasis-free at last follow-up. Conclusions: These results confirm the clinical utility of the UM GEP test and are consistent with previous studies. GEP results guide risk-appropriate surveillance plans, now reflected in national guidelines.

**Presentation Title:** Cytogenetic and Molecular Prognostic Classifications of Uveal Melanoma: Do They Match?

**Authors:** Vera Yarovaya¹, Andrey Yarovoy¹, Andrey Zaretsky²,³, Lidia Chudakova², Boris Malyugin¹, Egor Korobov¹

¹S. Fyodorov Eye Microsurgery Federal State Institution, Moscow, Russian Federation. ²LLC «Eurogen», Moscow, Russian Federation. ³Pirogov Russian National Research Medical University, Moscow, Russian Federation

**Abstract:** Purpose: To compare cytogenetic (CC) and mutational prognostic classifications (MC) of uveal melanoma (UM). Methods: UM tissue samples from 139 eyes treated either with eye-sparing methods (n=88) or enucleation (n=51) were analyzed prospectively. Eye-sparing treatment included Ru-106 brachytherapy (n=72), gamma-knife radiosurgery (n=2), transscleral resection (n=2), and en-doresection (n=12). Pathology review, FISH for monosomy 3 and 8q gain, PCR for GNAQ, GNA11, EIF1AX and SF3B1 mutations and immunohistochemistry (IHC) for BAP1 expression were performed. Patients were divided into prognostic classes using FISH data (CC) and mutation+IHC data (MC). Results: In 28% of cases no genetic class used in MC was found (no BAP1 inactivation, EIF1AX mutation or SF3B1 mutation was found). Unusual combination of EIF1AX mutation with monosomy 3 or BAP1 inactivation was seen in 4%. EIF1AX mutation never described before was detected. Matching analysis was performed in 61 patients and showed discrepancy between CC and MC in 80% of cases. In those cases, metastatic risk was estimated according to the “worst”. Conclusion: UM molecular testing using several sets of biomarkers is widely used nowadays for estimation of metastatic risk. However, no prospective comparison of CC and MC UM markers has been ever performed. Prognostic significance of the discrepancy between two UM classifications is currently unknown. Further research is needed.
**Presentation Title:** Whole exome sequencing to identify candidate genes associated with hereditary predisposition to uveal melanoma

**Authors:** Mohamed Abdel-Rahman\textsuperscript{1,2}, Klarke Sample\textsuperscript{1}, Ben Kelly\textsuperscript{3}, David Gordon\textsuperscript{2}, Peter Johansson\textsuperscript{4}, Robert Pilarski\textsuperscript{2}, Getachew Boru\textsuperscript{1}, Timothy Grosel\textsuperscript{1}, James Massengill\textsuperscript{1}, Daniel Kinnamon\textsuperscript{2}, Frederick Davidorf\textsuperscript{1}, Nicholas Hayward\textsuperscript{4}, Peter White\textsuperscript{3}, Colleen Cebulla\textsuperscript{1}

\textsuperscript{1}Havener Eye Institute, Department of Ophthalmology and Visual Science, The Ohio State University Wexner Medical Center, Columbus, USA. \textsuperscript{2}The Ohio State University Wexner Medical Center Division of Human Genetics, Department of Internal Medicine and Comprehensive Cancer Center, Columbus, USA. \textsuperscript{3}The Institute for Genomic Medicine, Nationwide Children’s Hospital, Columbus, USA. \textsuperscript{4}QIMR Berghofer Medical Research Institute, Brisbane, Australia

**Abstract:**

**Purpose:** The goal of this study was to identify novel genes associated with hereditary predisposition to uveal melanoma (UM).

**Methods:** Exome sequencing was carried out for 29 unrelated high-risk UM patients, with no detectable mutations or deletions in BAP1, and 10 of their relatives. The probands included 25 with familial UM, one with bilateral UM, one with congenital UM and 2 patients with strong family history of cancers observed in the BAP1-Tumor Predisposition. Results: We focused our initial analysis on genes with established association with hereditary predisposition to cancer, which are routinely tested in diagnostic laboratories. We identified coding pathogenic or potentially pathogenic variants in 5 cancer predisposition genes (CHEK2, MLH1, PALB2, SMARCE1, RECQL4 and COL7A1) in 6 patients. Biallelic inactivation of PALB2 and MLH1 were observed in the tumors from the respective patients. Variants in cancer associated genes, mostly missense variants of uncertain significance, were identified in 24/29 patients. In 17 of those, more than one gene was impacted. Several of these variants were in genes in the DNA damage repair pathway. In one family, we confirmed functional alterations in three potential candidate tumor suppressor genes. Conclusions: The study provides evidence of a germline mutation in PALB2 and MLH1 with hereditary predisposition to UM. It also identifies several other potential candidate genes. The results suggest locus heterogeneity in predisposition to UM and potential multi-genic etiology in a subset of patients. Validation in a larger UM cohort is warranted.
Date: Saturday 23.3.19  
Time: 3:20pm - 3:55pm  
Session: Free Paper Session: Imaging Modalities for Melanoma and Radiation Changes  
Session Chair: Arun Singh  
Moderators: Thomas Aaberg and Svetlana Saakyan

Presentation Title: Optical coherent tomography – angiography in benign and suspicious choroidal nevus and small choroidal melanoma

Authors: Svetlana Saakyan, Elena Myakoshina 
Helmholtz Moscow Research Institute of Eye Diseases, Moscow, Russian Federation

Abstract: Purpose. To examine features imaged by optical coherence tomography angiography (OCTA) in eyes with benign and suspicious choroidal nevus and small choroidal melanoma. Methods. In this retrospective, noninvasive, observational study 128 patients diagnosed with benign (45 eyes) and suspicious (42 eyes) choroidal nevus and small choroidal melanoma (41 eyes) who underwent dilated fundus examination, ocular ultrasonography (thickness <0.5 mm, basal diameter <8.0 mm) and OCTA images were compared. OCTA RTVue XR Avanti (Optovue, USA) at the level of the choroid was used. Results. In benign choroidal nevus of all patient, OCTA demonstrated homogeneous (isoreflective) choriocapillaries with brightness similar to surrounding vascular plexus. In suspicious choroidal nevus presence of hyperreflective homogeneous dilated choriocapillaries with brighter glow compared with the surrounding choriocapillaries - 92.9%. Avascular zone in the central region of the tumor with surrounding dilated hyperreflective choriocapillaries - 7.1%. In small choroidal melanoma under RPE - neovascular component with limiting avascular zone - 46.3%. Looped articulated with uneven clearance heterogeneous tumor vessels with numerous bends and weaves, located under retinal vessels. The combination of hyperreflective vascular component and looped convoluted. On the periphery of tumor hyperreflective choriocapillaries. Conclusion. OCT-A allows you to identify vascular changes in melanocytic tumors of the choroid in 100% of cases. OCT-A makes it possible to distinguish tumor vessels and choriocapillaries in case of nevi and small choroidal melanoma. OCTA provides an opportunity to establish the correct diagnosis in order to provide timely tactics for managing patients with benign and malignant choroidal tumors.

Presentation Title: Swept-source optical coherence tomography angiography in choroidal melanoma: an Analysis of 22 Consecutive Cases.

Authors: Marco Pellegrini, Federico Corvi, Alessandro Invernizzi, Vittoria Ravera, Matteo Cereda, Giovanni Staurenghi 
Eye Clinic, Department of Biomedical and Clinical Sciences “Luigi Sacco”, Luigi Sacco Hospital, University of Milan, Milan, Italy

Abstract: Purpose: To describe the imaging features of choroidal melanoma using swept-source optical coherence tomography angiography (SS-OCT-A) and to evaluate its ability to display tumor intrinsic vasculature. Methods: Consecutive patients diagnosed with choroidal melanoma underwent a complete ophthalmic evaluation including best-corrected visual acuity, color fundus photography, ultrasonography, fluorescein angiography and indocyanine green angiography and SS-OCT-A (PLEX Elite 9000; Carl Zeiss Meditec, Dublin, Ca). Results: Twenty-two eyes of 22 consecutive patients were included in the study; 11 cases (50%) were treatment naive. Three lesions (14%) were located at the macula, 14 (63%) between the macula and equator, and 5 (23%) between the equator and the ora serrata. The mean tumor base and thickness were 10.3 mm (range 5-15 mm) and 4.3 mm (range 1.5-8.9 mm). Seventeen lesions (77%) were dome shaped, whereas 5 (23%) had a mushroom configuration. Thirteen lesions (59%) were pigmented, 5 (23%) partially pigmented, and 4 (18%) amelanotic. An exudative retinal detachment was documented in 13 eyes (59%). Fluorescein angiography and indocyanine green angiography were performed in 20 patients and disclosed intrinsic microvasculature of the tumor, respectively, in 4 (20%) and 20 (100%) cases. SS-OCT-A was performed in 22 eyes and detected tumor microvasculature in 14 eyes (64%) using the automated choroid segmentation, 16 eyes (73%) using the automated whole eye.
segmentation, and in 22 eyes (100%) with fine manual adjustments of segmentation lines.

CONCLUSION: In our series SS-OCT-A disclosed tumor intrinsic microvasculature in all cases despite their size, location, pigmentation and history of previous treatments.

**Presentation Title:** Longitudinal Detection of Radiation-Induced Peripapillary and Macular Retinal Capillary Ischemia Using Optical Coherence Tomography Angiography

**Authors:** Alison Skalet¹,², Liang Liu¹, Audra Miller¹, Christina Binder², Richard Crilly², Arthur Hung², Charles Thomas, Jr.², David Wilson¹, David Huang¹, Yali Jia¹

¹Casey Eye Institute, Oregon Health & Science University, Portland, USA. ²Radiation Medicine, Oregon Health & Science University, Portland, USA

**Abstract:** Purpose: To study changes in retinal capillary circulation in eyes with uveal melanoma treated with I-125 plaque brachytherapy using optical coherence tomography angiography (OCTA). Methods: Longitudinal study of 21 participants. Eyes were imaged with AngioVue (Optovue, Inc.) prior to I-125 plaque brachytherapy and 12- and 24-months post-radiation. Optic disc (4.5 x 4.5 mm) and macular (3 x 3 mm) OCTA scans were acquired. The peripapillary nerve fiber layer capillary density (pNFL_CD), macular superficial vascular complex density (mSVC_VD) and foveal avascular zone (FAZ) area were calculated. Results: Compared with eyes prior to treatment (48.4 ±4.1%), the pNFL_CD was reduced in treated eyes at 12 months (46.7 ± 5.0%; P=0.04, Wilcoxon signed-rank test) and 24 months (44.5 ±6.1%; P< 0.0001). Similarly, the mSVC_VD (48.4 ± 3.6%) was reduced in treated eyes at 12 months (43.4 ± 5.9%; P=0.01) and 24 months (38.9 ± 7.8%; P=0.0002). The FAZ area increased in treated eyes at 12 months (0.350 ± 0.22; P=0.009) and 24 months (0.699 ± 0.97; P=0.002) as compared with baseline (0.262 ± 0.10). When only eyes with clinically-evident radiation changes were evaluated (8 eyes at 24 months, 38.1%), the changes in pNFL_CD, mSVC_VD, and FAZ area were more pronounced. Notably, even eyes without RR or RON at 24 months had reduced pNFLC_VD and mSVC_CD. Conclusion: OCTA demonstrates early emergence of peripapillary and macular capillary vasculature changes after I-125 plaque brachytherapy. OCTA provides a quantitative measurement of retinal capillary changes associated with ischemia that may prove useful in predicting development of radiation-induced retinal toxicity.

**Presentation Title:** Wide-field swept-source optical coherence tomography angiography of the retina after plaque radiotherapy of choroidal melanoma

**Authors:** Li-Anne Lim¹, David Camp, David Ancona-Lezama¹, Mehdi Mazloumi, Carol Shields

¹Wills Eye Hospital, Philadelphia, USA

**Abstract:** Purpose: To evaluate retinal microvasculature abnormalities after plaque radiotherapy of choroidal melanoma using wide-field swept-source optical coherence tomography angiography (SS-OCT-A). Methods: Retrospective analysis of 105 choroidal melanomas treated with I-125 plaque radiotherapy imaged with wide-field 15x9mm SS-OCT-A. Results: At mean follow-up of 49 months after plaque radiotherapy, SS-OCT-A observations included enlargement (24/105, 23%) and discontinuity (39/105, 37%) of the foveal avascular zone (FAZ), retinal ischemia in the superficial (91/105, 87%) and deep plexus (92/105, 88%), loss of choriocapillaris (89/105, 85%) and large choroidal vessels (40/105, 38%). In eyes with clinically evident radiation retinopathy (CERR), FAZ mean area was enlarged (irradiated vs contralateral eye) (1.7 vs 0.23 mm², p=0.03) and vascular density reduced in the superficial and deep plexus and choriocapillaris in the total wide-field (p<0.001) and peripapillary region (p<0.001). In eyes without CERR, mean FAZ area was preserved (1.2 vs 0.23 mm², p=0.16), only the superficial plexus (p<0.008) and choriocapillaris (p<0.001) of the total wide-field and choriocapillaris of the peripapillary region (p<0.001) were reduced. Comparison of eyes with and without CERR showed significant difference between superficial and deep vascular density of the total wide-field (p<0.006 and p<0.02) and peripapillary region (p<0.001 and p<0.01). Mean logMAR visual acuity was reduced in irradiated eyes (p=0.004), significantly differing between eyes with and without CERR (1 vs 0.6, p=0.002). Conclusion: Wide-field SS-OCT-A demonstrates retinal microvascular alterations in multiple vascular layers of the eye after plaque radiotherapy for choroidal melanoma, even in eyes without clinically evident radiation retinopathy.
Presentation Title: Ocular Brachytherapy: The Evidence Supporting Systematic Dose De-escalation in Choroidal Melanoma.

Authors: Richard Jennelle1, Jesse Berry1, Jonathan Kim1, Bao Le2, Melvin Astrahan3

1University of Southern California, Los Angeles, CA, USA. 2University of Hawaii, Honolulu, HI, USA. 3Eye Physics, Los Angeles, CA, USA

Abstract: Purpose: To identify evidence in support of systematic dose de-escalation in choroidal melanoma.Method: Though systematic review of the literature, we identified both prospective and retrospective studies supporting the effectiveness of de-escalated doses in the management of patients with brachytherapy, proton beam radiotherapy and radiosurgery. We used standard dose modeling methodology to allow comparison of dose between different forms of radiotherapy.Results: Substantial prospective and retrospective data exists to support systematic dose de-escalation in the management of choroidal melanoma using proton beam radiotherapy and radiosurgery. Retrospective data exists supporting dose de-escalation in brachytherapy but this data is not systematic in nature. Dose modeling suggests that accurately calculated brachytherapy doses on the order of 70 Gy may be sufficient in the management of choroidal melanoma so long as dose inhomogeneity and geometric considerations are properly controlled for.Conclusion: The ocular oncology community should consider efforts to standardize dose calculation regarding inhomogeneity and geometric effects and build upon this standardized framework to support a properly designed multi-institution trial that safely investigates dose de-escalation.

Presentation Title: Histopathology and molecular profiling of uveal melanoma in eyes enucleated due to radiotherapy complications

Authors: Hatem Krema, Normand Laperriere, Mostafa Hanout, Zaid Kamel, Danny Ghazarian, Suzanne Kamel-Reid

University of Toronto, Toronto, Canada

Abstract: Purpose: To report the histopathologic and molecular profiling features of uveal melanoma in eyes that underwent secondary enucleation for radiation induced complications not for tumour recurrence.Methods:Review of patient records was conducted for patients that underwent secondary enucleation to treat intractable radiation complications, despite the clinical evidence of tumour control post radiotherapy. Histopathology and Molecular profiling using Next Generation Sequencing (NGS) – melanoma panel were reviewed.Results: Eleven patients met the inclusion criteria. Viable tumour as evidenced by mitotic activity was detectable in 9/11 specimens. The mean interval between irradiation and enucleation was 32 months (range: 12 -80 months). Predominant cell types were: Epithelioid 4/11 samples, mixed 4/11 and spindle 3/11. Scleral invasion was detected in 3/11, optic nerve invasion in 2/11 and Vortex vein invasion in one sample. NGS showed actionable variants for genes GNAQ, GNA11, SF3B1, and BAP1Conclusions:Residual viable melanoma cells could still be detected in the majority of enucleated eyes with clinically manifested controlled melanoma at an average of 3 years post radiotherapy.

Presentation Title: Prospective Randomized Trial of Ranibizumab for Radiation Retinopathy (RRR): Two year Anatomic Outcomes

Authors: Amy Schefler1,2, Rajiv Anand3, Dwain Fuller3, Timothy Fuller3, Maria Bretana1,2, Ryan Kim4

1Blanton Eye Institute, Houston Methodist Hospital, Houston, USA. 2Retina Consultants of Houston, Houston, USA. 3Texas Retina Associates, Dallas, USA. 4University of Texas Health Sciences Center at Houston, Houston, USA
Abstract: PURPOSE: To evaluate the anatomic retinal changes in patients undergoing intravitreal ranibizumab with or without targeted panretinal photocoagulation for radiation retinopathy-related macular edema (RR-CME). METHODS: This was a Phase II, prospective, multicenter, randomized trial. In the second year of the trial, all patients were assigned to a treat-and-extend regimen following pre-specified SD-OCT re-injection criteria. This presentation will focus specifically on the anatomic outcomes in the first and second year of the trial. RESULTS: At study entry, the mean central retinal thickness (CMT) was 385 μm. At one year, the mean change in CMT was -97 μm, -105 μm, and -87 μm in the monthly, monthly plus laser, and PRN cohorts, respectively. There was a statistically significant difference between mean CMT in the monthly cohort and the PRN cohort (p=0.002) at one year, as well as a statistically significant difference in the mean CMT between the monthly plus laser cohort and the PRN cohort (p=0.002). There was a statistically significant decrease in retinal hemorrhages, exudates, and ischemia in all three cohorts compared to baseline at one year (p CONCLUSIONS: Patients in all three cohorts in the RRR trial had a mean improvement in central macular thickness as measured by SD-OCT at one year. Two year results reflecting less frequent treatment, more reflective of real world care, will demonstrate the durability of the improvement observed in year one.

Presentation Title: Anti-VEGF treatment ameliorates radiation retinopathy - a randomized clinical trial Authors: Antonia Joussen1, Ira Seibel2, Martin Hellmich3
1Charité University Medicine Berlin, Berlin, Germany. 2Charité, Berlin, Germany. 3CTCC Center for Clinical Trials, Cologne, Germany
Abstract: Purpose: to demonstrate the superior efficacy of Ranibizumab 0.5 mg to focal and peripheral laser treatment regarding change from baseline in BCVA over 6 months in patients with radiation-retinopathy in uveal melanoma. Methods: Phase II, two-arm, randomized, parallel-group clinical trial. Ranibizumab was administered as three initial monthly intravitreal injections. Subsequent injections were given if visual acuity dropped by >5 letters and evidence of macula or optic disc edema. Laser treatment of the macula served as comparator treatment. Inclusion criteria comprised: patients with radiation retinopathy (cotton wool spots, hemorrhages, vascular ischemia), visual impairment due to focal or diffuse ME in the irradiated eye that is eligible for laser treatment, age ≥18 years, and BCVA less than 20/32. Results: The Full Analysis Set (FAS) included 31 patients who were randomly assigned to ranibizumab (n=15) or laser treatment (n=16). The Per-Protocol Set (PPS) included 19 patients (n=7 ranibizumab group, n=12 laser group). Efficacy: Regarding the primary outcome measure ‘average change in BCVA from baseline over 26 weeks’, treatment with ranibizumab was superior compared to laser treatment, with a mean advantage of 0.14 logMAR (i.e. 7 ETDRS chart letters). Subgroup analyses by dose to macula/disc and gender did not indicate any interaction with treatment. The positive effect of ranibizumab vanished following week 26, i.e. after treatment was stopped. Conclusions: This small randomized clinical trial showed a statistically significant improvement of visual acuity under treatment with ranibizumab compared to laser treatment.

Presentation Title: Study of Ophthalmic Radiation Therapy Toxicity (SORTT): a prospective international survey. Authors: Wolfgang Sauerwein1, Paul Finger2, Yuliya Gavrylyuk3, Brenda Gallie4,5
1University Duisburg-Essen, Essen, Germany. 2The New York Eye Cancer Center, New York, USA. 3Princess Margaret Cancer Center, Toronto, Canada. 4University of Toronto, Toronto, Canada. 5Princess Margaret Cancer Centre, Toronto, Canada
Abstract: For the SORTT study group Purpose: Radiation plays a vital role in the treatment of ophthalmic malignancies. Though many different radiation modalities can be used to destroy ocular tumors, each varies in the incidence and location of side effects as well as in functional outcomes. However, there are not only strikingly few comparative studies or staging systems available to collect the incidence and impact of ophthalmic radiation. Methods: After plenary meetings during the First and Second Cancer Working Days in Paris and Sydney, a prospective international survey was started. Both ophthalmic and radiation-related data elements were fashioned to collect both treatment and outcomes. Working with Health Informatics Research IT team, all patient
privacy and ethics regulations were incorporated into an internet-based registry to prospectively track outcomes for patients after ophthalmic radiotherapy. These include plaque brachytherapy, proton-beam, photon-beam and stereotactic radiosurgery. After an initial year-long enrollment period, patients will be followed for at least 3 additional years. ResultsTwenty-one centers from all continents have agreed to join this prospective registry. They are currently obtaining local IRB and ethics approvals. We plan to launch patient accrual on January 1, 2019.ConclusionsThis database will support the creation of several ophthalmic radiation side effects grading systems, and accumulate evidence about risks associated with currently used ophthalmic radiation modalities. Such data may lead to preferred radiation practice patterns and staging systems in treatment of ocular tumors. We hope this study will lead to improved local control and less toxicity among ocular tumor patients.
Presentation Title: Intraocular seeding of choroidal melanoma after biopsy with a 25-gauge vitrector
Authors: Jill Wells, Chris Bergstrom, Hans Grossniklaus
1Emory University, Atlanta, USA. 2Retina Consultants of Carolina, Greenville, USA
Abstract: Purpose: To present a case of a second intraocular melanoma occurring at the port site after transretinal fine needle aspiration of a choroidal melanoma. Methods: Interventional case report. Results: A 55-year-old Caucasian woman with a history of breast cancer was found to have a partially pigmented choroidal mass in her macula. A diagnostic biopsy using a 25-gauge trochar vitrectomy set up was performed at the same time as plaque placement and pathology confirmed melanoma. The melanoma regressed in size but nearly three years later a new intraocular mass developed at one of the trochar sites. A transcleral biopsy of the second mass was performed at the time of plaque placement and pathology was consistent with melanoma. One year later, both melanomas are well treated although her vision is poor secondary to radiation retinopathy. Conclusion: Transretinal biopsy of choroidal melanoma provides important diagnostic and prognostic information but in rare cases may be responsible for tumor seeding.

Presentation Title: Aflibercept for Radiation Maculopathy (ARM Study): A Prospective, Randomized Clinical Study
Authors: Timothy Murray, Aaron Gold
1Baptist Cancer Center, Miami, USA. 2Miami Ocular Oncology and Reia, Miami, USA
Abstract: Purpose: To evaluate a randomized, prospective clinical study approach comparing aflibercept delivered by either a q6 week treatment interval or a treat-and-adjust interval for radiation maculopathy. Methods: 40 consecutive patients were enrolled in an IRB approved clinical trial and randomized to aflibercept treatment via one of two regimens: Fixed, every six-week treatment OR Variable, treat-and-adjust centered around 6 weeks. All patients had visually compromising radiation maculopathy confirmed by a decline in best-corrected visual acuity AND sdOCT. Aflibercept was delivered via intravitreal injection (2.0 mg/0.05 ml). Treat-and-adjust interval was determined by sdOCT analysis. The primary outcome measures were visual acuity and sdOCT CPT at 1 year follow up. Results: Thirty-nine of 40 patients completed the trial (97.5%) with one-year follow-up. Patient #9 relocated out of the USA after 8 months of treatment (Entry VA 20/100, Last VA 20/25). Baseline study entry best-corrected VA was 20/63 and improved to 20/62 at study conclusion at 60 weeks (1 year). At the study conclusion, 42.5 % (17/40) eyes were better than 20/50, and only 5% (2/40) eyes ended with a VA below 20/200. SD OCT declined from 423 microns to 294 microns at study conclusion. In the q6 treatment arm, patients received 9 injections while in the treat-and-adjust study arm patients received 8.4 injections (p-value, .088). Conclusion: Aflibercept is successful in limiting vision loss associated with radiation maculopathy. Remarkably almost half of all treated patients maintained 20/50 better vision throughout one year of treatment.

Presentation Title: The spontaneously regressed presumed Small Pigmented Choroid Lesion shift into a T0 Choroid Melanoma. A four stages story.
Authors: Vincenzina Mazzeo Simonini, Laura Lodi
1Studio Oculistico, Ferrara, Italy. 2UOC Oculistica Ospedale Maggiore, Bologna, Italy
Abstract: To describe the 17 years follow-up of the spontaneously regressed "Small Pigmented Choroid Lesion" (SPL) presented at the ICOO conference in 2013 till it became a small Melanoma. A dome shaped SPL was found in the RE of a 31 y-o lady during her first pregnancy in 2000. The lesion was less than 2 mm thick and highly
reflective on ultrasonography. No fluid was present and it was circumscribed by tiny bright yellow spots. After 10 years and just after her second pregnancy, the lesion shrunk to less than a mm. In 2016 no thickness change but a thin satellite serous RD was found on OCT and a little contour change on the posterior border was present. In September 2017 the tumor was found to be little less than 3 mm thick, have a larger base (T0), different profile and one low reflective area. General work-up and conservative treatment followed. Few cases of spontaneously regressed Choroid Melanoma (CM) are reported in the literature a less re-growth with time. The longest follow-up of a spontaneously regressed and recurred CM is 16 years and 9 months. Two SPL regressions in two female patients 23- and 71 y-o, with 4- and 6 years follow-up respectively. The present case has longer follow-up and the presence of two pregnancies in the clinical history. Is spontaneous regression the malignancy key diagnostic criterium in SPL?

Presentation Title: Uveal melanoma in young children
Authors: Wolfgang Sauerwein¹, Joël Herault², Norbert Bornfeld¹, Clare Stannard³
¹University Duisburg-Essen, Essen, Germany. ²Centre Antoine Lacassagne, Nice, France. ³Groote Schuur Hospital, Cape Town, South Africa

Abstract: Purpose: Uveal melanoma is rare in children and therefore may not be recognised until the tumour is large thus making management more challenging. Method: We report on 3 children, under 10 years old, with large uveal melanomas. The tumour was invading the orbit in the first child. Enucleation was followed by an iodine-125 implant into the orbit. The 2nd child had a 9mm thick tumour with a large exudative retinal detachment and the 3rd child had a tumour involving the ciliary body and iris. These two were treated with proton therapy. Results: The first child has been followed up for 12 years and remains clear of disease. The growth and development of the face is normal and symmetrical, the prosthesis does not cause problems. The follow up of the other two children is less than a year, but thus far they have retained good vision, although one has secondary glaucoma. Conclusion: We observed 3 large melanomas in children due to delayed diagnosis. These required dedicated radiation techniques. It was challenging to adapt the conventional adult proton therapy technique to the smaller size of young patients.

Presentation Title: Delayed transcleral recurrence of choroidal melanoma treated by I-125 plaque
Authors: Zelia Correa
Wilmer Eye Institute, Johns Hopkins Medicine, Baltimore, USA

Abstract: Purpose: To report a case of broad base choroidal melanoma presenting 2 marginal recurrences treated by laser and delayed transcleral recurrence into the orbit 27 years after plaque brachytherapy. Method: retrospective single case report. Results: Patient was initially treated by I-125 plaque for a choroidal melanoma in 1991 and 5 sessions of laser thermotherapy at another institution. Her other eye is amblyopic. She presented 2 marginal recurrences also treated by laser (last treatment 7 years ago). She went on to develop radiation retinopathy and chronic macular edema responsive to intravitreal steroid. She presented for an evaluation to assess the possibility of treatment of her radiation-induced macular edema. Diagnostic ultrasound revealed a hypo-reflective retrobulbar nodule measuring 3.7 by 2.5 mm nasal to the optic disc. Conclusions: Delayed development of orbital recurrence of choroidal melanoma following aggressive laser treatment is possible due to the scleral weakening secondary to repeat injury of the sclera and radiation therapy.

Presentation Title: Unexpected Survival Of Delayed Metastatic Choroidal Melanoma With Local Recurrence After Brachytherapy
Authors: Christian Campos¹, Marcio Nehemy¹, Zelia Correa²
¹Federal University of Minas Gerais, Belo Horizonte, Brazil. ²Johns Hopkins University, Baltimore, USA

Abstract: PURPOSE: To describe the case of long-term survival of a patient with metastatic choroidal melanoma and local recurrence 18 years after brachytherapy. METHODS: Interventional single case report. RESULTS: A 20-year-old woman with choroidal melanoma (CM) of the left eye treatment with
an episcleral I-125 plaque. Five-years after treatment she was thought to be “cured” of her cancer. Fundus examination revealed the presence of local recurrence of her choroidal melanoma 14 years later but she declined enucleation. Subsequently, she was diagnosed with a new metastatic liver nodule 18 years after initial treatment. She was submitted to local resection of her liver metastasis and chemotherapy but 2 years later she developed new metastatic disease in the liver, lungs and brain. Surprisingly, she had an excellent response to immunotherapy and has now survived for over 5 years with metastatic choroidal melanoma, CONCLUSION: We report a case of a long-term survival with metastatic choroidal melanoma metastasis with untreated local recurrence and its potential impact on survival and progression of metastatic disease.

Presentation Title: Delayed diagnosis of diffuse choroidal melanoma
Authors: Rafaela Faraj¹, Zelia Correa²
¹Santa Casa, Belo Horizonte, Brazil. ²Wilmer Eye Institute, Baltimore, USA
Abstract: PURPOSE: to report a case of delayed diagnostic of Diffuse Choroidal Melanoma, which developed extensive liver metastasis and mesenteric lymph node involvement.METHODS: Single case report. An 80 year-old woman referred for a suspicious of Choroidal Melanoma and ocular pain in her left eye. Her family members report she had a suspicious lesion in the back of the eye since 2016. At that time, she was evaluated by color fundus photos, ultrasound of the left eye, brain, chest and abdominal CT. All scans were normal. Because no diagnosis was defined at that time, the family decided to forego periodic follow up after 4 months. Fifteen days ago she started to have intense ocular pain in her OS. At ocular examination, her visual acuity was 20/400 OD and LP OS. Biomicroscopy OD showed normal anterior segment and cataract; OS revealed mild corneal edema, shallow anterior chamber, iris neovascularization, and sentinel vessels superiorly. There was no funds view OS.RESULTS: B-scan ultrasound OS showed an extensive choroidal tumor involving all posterior pole and superior periphery, measuring 3.0 mm in maximal thickness. Basal diameter could not be measured because it was too extensive. The patient was referred for new CT scans of the chest and abdomen. The CT showed multifocal liver metastasis and suspicious mesenteric lymph node.CONCLUSION: Differential diagnosis of relatively thin, diffuse choroidal tumors can be challenging. Clinicians should be aware of clinical features and the important of early diagnosis since these tumors carry a higher risk of metastatic spread.
Presentation Title: UMMethylSig: A novel prognostic marker for Uveal Melanoma based on multi-locus DNA methylation signature of the primary tumor.

Authors: Arupa Ganguly¹, Julie Crafferty¹, Emilie Lalonde¹, Carol Shields²
¹University of Pennsylvania, Philadelphia, USA. ²Will's Eye Hospital, Philadelphia, USA

Abstract: Purpose: Uveal melanoma (UM) is a rare, but deadly, cancer in which 50% of patients progress to metastasis within 10 years of diagnosis, which is almost always fatal. Current genetic tests offer prognostic assessment using chromosomal aberrations, genetic mutations, RNA expression and/or clinicopathological variables of the primary tumor. Recently, targetable epigenetic modifications have catalyzed efforts to develop epigenetic therapeutics. Work by The Cancer Genome Atlas (TCGA) project has shown that there are four uveal melanoma subtypes based on DNA methylation; but to date, DNA methylation has not been investigated as a prognostic tool for UM. Methods: To identify a multi-locus prognostic signature, the TCGA cohort (n=80) was used for feature selection and model training using standard cross-validation and machine learning approaches. The model was tested using genome-wide methylation profiling of 41 primary UM tumors with at least 2 years follow-up. Results: A multi-locus DNA methylation signature consisting of 63 probes achieved an area under the curve of ~84% in the independent validation set. The classification was prognostic for metastasis (hazard ratio: 7.72; 95% confidence interval 2.76-21.6; p = 9.75e-5). When combined with an established clinicogenomic model based on chromosomal status and clinicopathological variables, the methylation signature demonstrated the potential to improve current clinical models. Conclusion: This study provides a promising biomarker for identifying primary UM at risk of aggressive metastasis.

Presentation Title: Comprehensive Analysis Of Germline Bap1 Variants In Finnish Uveal Melanoma Patients

Authors: Tero Kivelä¹, Pauliina Repo², Reetta-Stiina Järvinen², Johannes Jäntti², Martin Täll¹, Virpi Raivio¹, Anna-Elina Lehesjoki², Joni Turunen¹.²
¹Department of Ophthalmology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland. ²Folkhälsan Institute of Genetics, Biomedicum Helsinki, Helsinki, Finland

Abstract: Purpose. Germline pathogenic variants in BRCA1-associated protein 1 (BAP1) gene cause BAP1 tumor predisposition syndrome (TPDS). The main tumor types are uveal melanoma (UM), mesothelioma, renal cell carcinoma, cutaneous melanoma, and meningioma. Two percent of unselected UM patients harbor a germline BAP1 pathogenic variant. We report comprehensive screening of exonic, intronic and regulatory regions of BAP1 in 438 Finnish UM patients.

Methods. Targeted Sanger sequencing and next generation sequencing were used to detect variants and MLPA to screen for copy number variations (CNV). Variants were interpreted in view of clinical data, public databases, in silico predictions, and functional assays that target core functions of BAP1 protein: nuclear localization and deubiquitinase activity.

Results. We identified 6 patients with a loss-of-function variant: 4 with exon 14 single-base insertion, and 2 with intron 2 splice site variant. Five additional patients had non-synonymous heterozygous variants in one of three exons: 5, 9 and 13. Functional studies showed that exon 5 and 9 variants were likely pathogenic. Finally, one non-coding variant, 25 bp deletion in intron 1, disrupted a splicing branch point. No CNVs were detected. Frequency of BAP1 pathogenic variants was 2.1% (9/438; 95% CI 0.9-3.9); 5/9 had relatives with UM and 7/9 with any TPDS cancers.

Conclusion. Coding region and essential splice site variants are the most common BAP1 pathogenic variants, but regulatory regions can also harbor such variants. Extending mutation analysis to the non-coding areas and utilizing functional assays in interpretation of pathogenicity is recommended to enhance sensitivity and specificity.
**Presentation Title:** Intraocular Biopsy in the Diagnosis of Indeterminate Lesions of the Choroid and Ciliary Body Technique and Pathohistological vs Molecular Genetic Workup

**Authors:** Norbert Bornfeld¹, Stefan Kreis¹, Claudia Le Guin¹, Michael Zeschnigk², Klaus Metz³, Nikolaos Bechrakis¹

¹University Eye Clinic, Essen, Germany. ²Institute of Human Genetics University Essen, Essen, Germany. ³Institute of Pathology University Essen, Essen, Germany

**Abstract:**
Purpose: To evaluate pathohistological and molecular genetic workup in intraocular biopsies of patients with indeterminate intraocular lesions

Method: Consecutive series of 123 intraocular biopsies over 12 months of indeterminate intraocular lesions (113 transretinal biopsies using either forceps or a 25G vitreous cutter, 10 transscleral biopsies). Molecular genetic work-up was available in 108/123 biopsies. 19/123 patients had a history of extraocular tumours.

Results: Diagnosis of a uveal melanoma could be confirmed in 95/123 patients and a diagnosis of uveal metastasis in 6/123 patients. Pathohistological diagnosis of an “indeterminate potentially malignant melanocytic lesion” was established in 24 patients (melanocytic tumour with metaplasia and low proliferation rate (4/24), probe to small (5/24), suspected melanocytoma (2/24), no differentiation between nevus and melanoma (5/24)). From 24 patients with inconclusive pathohistological diagnosis monosomy 3 was detectable in 6 probes. GNAQ mutations in codon 209 were detectable in 2/24 patients, but 3/6 patients with a histological diagnosis of a hemangioma had a GNAQ mutation as well. 1 patient with the histological diagnosis of choroidal metastasis had monosomy 3 in the biopsy probe.

Conclusion: A high percentage of intraocular biopsies are informative. Molecular genetic processing can establish a diagnosis in unclear cases, whereby the role of a GNAQ mutation remains to be clarified.

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**Presentation Title:** Brazilian Model for Addressing Gaps in Access to Ocular Oncology

**Authors:** Rubens Belfort, Aline Sutili, Patricia Ferraz, Marcio Costa, Melina Morales

Ocular Oncology Service - Department of Ophthalmology and Visual Sciences, Federal University of São Paulo, São Paulo, Brazil

**Abstract:**
Purpose: To present challenges in offering ocular oncology care in Brazil and to recommend new strategies to improve care by promoting early diagnosis and efficient care despite the issue of financial constraints, including the use of telemedicine and internet-based teaching.

Methods: We reported several strategies, including establishing of a new ocular cancer center in the Amazon, using the “Oncophone” which is a Whatsapp channel for second opinion in ocular oncology free to all ophthalmologists in Brazil, utilizing our YouTube-based ocular oncology videos for patients and ophthalmologists (www.cancerocular.com.br), and formulating low-cost strategies for tumor treatment. We also took advantage of the social media to invite more patients with diseases that present high risk of ocular cancer for consultation and examination.

Results: The Amazon ocular oncology center received an average of 120 patients per year, while the “Oncophone” received an average of 10 new cases per week. Meanwhile, our YouTube channel gained more than 69,000 views. Through our social media approach, we were also able to receive 31 new xeroderma pigmentosum patients on a single day. Results of our melanoma primary endoresection and laser for conjunctival tumors have already been published.

Conclusion: Despite the lack of financial resources, we were able to start a number of initiatives to promote early diagnosis and treatment for ocular oncology patients, including the use of internet-based platforms that are free and readily available, allowing for the expansion of this project to other developing countries.
Presentation Title: 2018 International TSC Consensus Guidelines: Ocular Oncology Update
Authors: Mary Aronow
Chair, Ophthalmology Section, 2018 International TSC Consensus Group, Silver Spring, USA. Retina Service, Massachusetts Eye and Ear, Harvard Medical School, Boston, USA

Abstract: Purpose: To provide a practical update on the 2018 International Tuberous Sclerosis Complex (TSC) Consensus Guidelines.Methods: An ophthalmology chair perspective is provided based upon the 2018 World TSC Conference and Consensus Group Meeting. Results: TSC occurs in approximately 1 in 6,000 individuals due to mutations in the TSC1 and TSC2 genes. Ophthalmic features (astrocytic hamartoma and retinal achromic patch) are present in nearly 40% of affected individuals and play an important role in diagnosis as major and minor clinical diagnostic criteria. A current update on the diagnostic criteria, surveillance approach, and management recommendations will be presented. Additionally, this update will serve as a call to action to the ocular oncology community regarding specific ophthalmic concerns from the TSC Consensus Group (a multi-disciplinary panel of experts including pediatric neurologists, nephrologists, cardiologists, pulmonologists, neurosurgeons, dermatologists, and others). There will be a focus on the role of mTOR inhibitors in treating aggressive astrocytic hamartoma and screening recommendations as it relates to ocular toxicity of vigabatrin, a commonly used first-line antiepileptic. Conclusion: Ophthalmologists, and in particular ocular oncologists, play a central role in the diagnosis and management of individuals with TSC. There is a pressing need for more active engagement between eye care professionals and the TSC community.

Presentation Title: Ophthalmic Immune-Related Adverse Events of Immunotherapy—A Single-Site Case Series
Authors: Renelle Lim, Jenna Kim, Miguel Materin, Mario Sznol, Harriet Kluger, Sarah Weiss, Jessica Chow, Kathleen Stoessel, Ninani Kombo, Lucian Del Priore
Yale University, New Haven, USA

Abstract: Purpose: To evaluate ophthalmic immune-related adverse events in the setting of immune checkpoint inhibitors. We report the largest case series of ophthalmic side effects from nivolumab with or without ipilimumab.Methods: Observational, retrospective, noncomparative case series in a single institution of the 1,474 patients treated with Nivolumab monotherapy or in combination with ipilimumab, 12 patients developed ophthalmic adverse events during treatment.Results: Over the course of 7 years (2011-2018), 12 patients had ophthalmic immune-related adverse events (IRAE) including spontaneous corneal perforation, uveitis, Vogt-Koyanagi-Harada-like serous retinal detachments, melanoma-associated retinopathy, myasthenia gravis, and optic disc edema. Depending on the severity of ophthalmic IRAE, a range of recommendations were made ranging from observation to hospital admission for high-dose intravenous steroids, immunoglobulins, and pyridostigmine. Six (50%) of these patients had progression of their metastatic disease[LR1].Conclusion: Ophthalmic IRAE can range from dry eyes to corneal perforation and permanent vision loss despite cessation of immunotherapy and institution of systemic immunosuppressive therapy. Ophthalmic events may have little correlation with systemic response to immunotherapy.[LR1]Need more info… after stopping immunotherapy?
**Presentation Title:** Photodynamic therapy (PDT) for retinal hemangioblastoma: tumor control, visual outcome, and exudative response in 17 consecutive patients  
**Authors:** Maura Di Nicola$^{1,2}$, Basil Williams$^{2,1}$, Jing Hua$^1$, Vladislav Bekerman$^1$, Arman Mashayekhi$^1$, Jerry Shields$^1$, Carol Shields$^1$  
$^1$Ocular Oncology Service - Wills Eye Hospital, Philadelphia, PA, USA. $^2$Department of Ophthalmology - University of Cincinnati College of Medicine, Cincinnati, OH, USA  
**Abstract:** Purpose: To evaluate clinical features and treatment outcomes of patients with retinal hemangioblastoma (RH) treated with photodynamic therapy (PDT). Methods: Retrospective case series of 18 RHs in 17 patients treated with PDT at the Ocular Oncology Service of Wills Eye Hospital, Philadelphia between November 2002 and February 2017. Demographic, clinical and treatment features were collected. Data were analyzed with regard to the primary outcome measures, which included tumor control, final visual acuity (VA) and exudative response (subretinal fluid [SRF] and cystoid macular edema [CME]) after PDT. Results: Seven of 17 patients had von-Hippel Lindau disease. Mean age was 35 years (range 7-67) and mean follow up was 46 months (range 2-144). Visual acuity was ≥20/40 (n=9), 20/50-20/150 (n=4), and ≤20/200 (n=5). Location was post-equatorial (n=10) (juxtapapillary or macular). Mean tumor thickness and diameter were 2.4 mm and 3.4 mm, respectively. Subretinal fluid was present in 16 cases with subfoveal involvement in 14 cases and CME was found in 11 eyes. Photodynamic therapy was used as primary treatment (n=7) or secondary treatment (n=11). Tumor control was achieved in 15/18 (83%), visual acuity was stable or improved in 11/17 (65%), SRF showed partial or complete regression in 12/16 (75%) and CME resolved in 6/11 (55%). Conclusion: Photodynamic therapy can be an effective treatment for RH, providing tumor control, resolution of SRF and CME, with visual stabilization in most cases.

**Presentation Title:** Single photodynamic therapy protocol for exudative circumscribed choroidal hemangioma. Clinical series in 37 patients  
**Authors:** Patrick De Potter, Paulina Bartoszek, Xavier Proumen, Ann-Pascale Guagnini  
**Abstract:** Purpose: To evaluate the effectiveness of our protocol using a single session of PDT for exudative circumscribed choroidal hemangiomas (CCH) Methods: Prospective non comparative case series including 37 patients with symptomatic exudative CCH. Our protocol included a single session of PDT performed 2 minutes after IV bolus injection of verteporfin (6mg/m2) at 689nm with a light dose of 100J/cm2 for 166 seconds. The Wilcoxon signed ranks test and Spearman’s rank correlation coefficient were applied as statistical analyses with a predictive analytics software (SPPSS 21.0, Chicago, IL) Results: The mean tumor thickness before PDT was 4.4 mm and the mean largest TBD was 7.8 mm. After a mean follow-up of 100 months (range, 6-150), all CCH (100%) showed regressed tumor thickness, resolution of subretinal fluid and no recurrent leakage. Visual improvement was documented in 26 eyes (70%), P Conclusion: This protocol with a single session of PDT offered a safe and effective option in treating symptomatic exudative CCH in terms of visual recovery, tumor thickness regression, and resolution of subretinal fluid with exudative recurrence.

**Presentation Title:** Simple treatment for circumscribed choroidal hemangiomas.  
**Authors:** Juan Valenzuela, Arturo Irarrázaval  
**Abstract:** Purpose: To evaluate the effectiveness of our protocol using a single session of PDT for exudative circumscribed choroidal hemangiomas (CCH) Methods: Prospective non comparative case series including 37 patients with symptomatic exudative CCH. Our protocol included a single session of PDT performed 2 minutes after IV bolus injection of verteporfin (6mg/m2) at 689nm with a light dose of 100J/cm2 for 166 seconds. The Wilcoxon signed ranks test and Spearman’s rank correlation coefficient were applied as statistical analyses with a predictive analytics software (SPPSS 21.0, Chicago, IL) Results: The mean tumor thickness before PDT was 4.4 mm and the mean largest TBD was 7.8 mm. After a mean follow-up of 100 months (range, 6-150), all CCH (100%) showed regressed tumor thickness, resolution of subretinal fluid and no recurrent leakage. Visual improvement was documented in 26 eyes (70%), P Conclusion: This protocol with a single session of PDT offered a safe and effective option in treating symptomatic exudative CCH in terms of visual recovery, tumor thickness regression, and resolution of subretinal fluid with exudative recurrence.
**Abstract:** Purpose: The aim of this study was to evaluate the safety and efficacy of transpupillary thermotherapy (TTT) as a simple, cheap and safe treatment for circumscribed choroidal haemangioma (CCH). The goal of transpupillary thermotherapy is to achieve the resolution of exudative detachment of the fovea and the improvement of vision when possible. Procedures: This is a retrospective cohort study of 20 patients undergoing TTT for CCH in a single centre between 2000 and 2018, and a review of previously published studies. Results: Twenty patients with CCH received TTT, with an average follow up of 48 months, ranging from 0 to 71 months. Three never showed up to the follow up and were excluded from the results. In all eyes but one the foveal detachment subsided. In 10 eyes with pretreatment visual acuity (VA) > 0.05 (20/400), it increased in 6 eyes (60%), remained unchanged in 1 eye (10%) and worsened in 3 (30%). On the other hand, in 7 patients with pretreatment visual acuity < 0.05 the visual acuity increased in 2 eyes (29%), remained unchanged in 4 eyes (57%) and and worsened in 1 (14%). Conclusions: TTT is a safe and effective treatment for CCH which results in both structural and functional improvements. In all parafoveal cases we had the same efficacy as PDT. Initial low visual acuity and delay of treatment were the worst prognostic factors in achieving improvement of VA.

**Presentation Title:** Outcomes of Ruthenium106 (Ru106) Plaque Brachytherapy in Circumscribed and Diffuse Choroidal Hemangioma.

**Authors:** Mrittika Sen, Sumeet Lahane, Sonal Chaugule, Surbhi Joshi, Raksha Rao, Vishal Sharma, Vijay Reddy, Santosh Honavar

**Centre for Sight Superspecialty Eye Hospital, Hyderabad, India**

**Abstract:** PURPOSE: To evaluate the efficacy and safety of Ru106 plaque brachytherapy in the treatment of diffuse and circumscribed choroidal hemangioma. METHODS: Retrospective interventional case series including 80 eyes of 80 patients, 67 with circumscribed choroidal hemangioma (CCH) and 13 with diffuse choroidal hemangioma (DCH) with Sturge-Weber syndrome who underwent Ru-106 plaque brachytherapy. Mean dose of 3830±620cGy was delivered over a mean period of 46±21 hours. Tumor regression, subretinal fluid (SRF) resolution and improvement in vision were the primary outcome measures. RESULTS: Mean tumor diameter was 10.6±3.4mm and mean tumor height was 4.4±1.4mm. Mean follow up was 14±16 months (range 6-108). Tumor regression and resolution of SRF was noted in 77 (96%) eyes. Vision improved (>2 Snellen lines) in 52 (65%) and was stable in 26 (33%) eyes. Radiation retinopathy was noted in one eye. CONCLUSION: Ruthenium-106 plaque radiotherapy is an effective and safe method of treatment for circumscribed and diffuse choroidal hemangiomas.

**Presentation Title:** Regional hemodynamic changes in patients with intraocular tumors

**Authors:** Anush Amiryan, Svetlana Saakyan

**Moscow Helmholtz research institute of eye disease, Moscow, Russian Federation**

**Abstract:** Purpose. To determine the regional hemodynamic changes in patients with various intraocular tumors. Methods. 178 patients with intraocular tumors were examined, 60 of them with choroidal hemangioma (mean age 48.1 ± 12.2), 31 patients (40 eyes) with metastatic choroidal tumor (mean age 48.2 ± 7.7) and 87 patients with choroidal melanoma (mean age 56.3 ± 10.3). Assessment of hemodynamic in the main eye vessels (CRA, CRV, OA) in examined intraocular tumors was performed on the ultrasound system Voluson730-Pro (GE Healthcare, Austria). The control was the symmetrical blood flow indicators on the healthy side. Results. In patients with choroidal haemangioma no hemodynamic disturbances were observed. In malignant lesions - metastatic tumors and melanomas, a decrease of blood flow features (Vps, Ved, TAMX) in the CRA was revealed in comparison with the contralateral healthy side (p 0.05). In addition, hemodynamic disturbances in CRA correlated with tumor size, which consisted in a significant decrease in blood flow velocities with increasing tumor thickness (p Conclusion. The revealed hemodynamic disorders in the main eye vessels in various intraocular tumors can be considered as an additional differential diagnostic criterion in the complex diagnosis of these tumors and explains some pathogenetic aspects in the course of choroid tumors.
Presentation Title: Metastasis to the retina and vitreous from systemic cancer  
Authors: Jill Wells¹, Hans Grossniklaus¹, Christopher Stelton², Hakan Demirci³, Carolyn Craven⁴, Chris Bergstrom⁵  
¹Emory University, Atlanta, USA. ²SK Retina, Sarasota, USA. ³University of Michigan, Ann Arbor, USA. ⁴Ohio State University, Columbus, USA. ⁵Retina Consultants of Carolina, Greenville, USA  
Abstract: Purpose: To describe the clinical features and outcomes of patients with retinal and/or vitreous metastasis from systemic cancer. Method: Retrospective case series. Results: Fourteen patients with retinal and/or vitreous metastases were included (largest case series). The average age was 60 and the presenting visual acuity ranged from 20/20 to counting fingers. Two patients had bilateral disease. Referring initial misdiagnoses included acute retinal necrosis, pigmentary dispersion, vascular occlusion, and toxoplasmosis. Twelve patients had a known primary systemic cancer. There was pathologic confirmation in 10/14 patients. Nine patients received external beam radiation and one patient underwent a series of intravitreal melphalan. Three patients are still alive (all with metastatic cutaneous melanoma to the retina and/or vitreous), six died an average of ten months after ocular metastasis, and the fate of the remaining five remains unknown. Conclusion: Retinal and/or vitreous metastasis from systemic cancer is rare and may be misdiagnosed as infectious retinitis. Life prognosis is typically poor but in recent years patients are living longer with immunotherapy and as a result ocular oncologists may start to see more cases.

Presentation Title: Uveal metastasis: Clinical features and survival outcome of 2214 tumors in 1111 patients based on primary tumor origin  
Authors: Carol Shields¹2, R. Joel Welch², Kunal Malik², Luis Acaba-Berrocal², Evan Selzer², Jennifer Newman², Eileen Mayro², Jerry Shields²¹  
¹Thomas Jefferson University, Philadelphia, USA. ²Wills Eye Hospital, Philadelphia, USA  
Abstract: Purpose: To evaluate uveal metastasis based on primary tumor site. Methods: Retrospective analysis. Results: There were 1111 consecutive patients with uveal metastasis. Patients were mean 60 years old, Caucasian race (88%), and female gender (64%). The primary tumor originated in the breast (37%), lung (26%), kidney (4%), gastrointestinal (GI) tract (4%), cutaneous melanoma (2%), lung carcinoid (2%), prostate (2%), thyroid (1%), pancreas (1%), others (19%). Based on the 5 most common primary sites (breast, lung, kidney, GI tract, cutaneous melanoma), mean patient survival was poor (22.2, 11.5, 8.6, 12.4, 11.4 months) and Kaplan Meier analysis revealed 5-year survival (24%, 13%, 0%, 14%, 21%). Poorest survival was found with pancreatic metastasis (mean 4.2 months) and most favorable survival with lung carcinoid (92% @5 years). Conclusion: Uveal metastasis typically originate from cancer in the breast, lung, kidney, GI tract, cutaneous melanoma, or others. Overall prognosis at 5 years was 23%.

Presentation Title: Choroidal amelanotic tumors: Clinical differentiation of benign from malignant lesions in 5586 cases  
Authors: R Joel Welch, Jennifer Newman, Stephanie Honig, Eileen Mayro, Mark McGarrey, Alexander Graf, Evan Selzer, Luis Acaba-Berrocal, Sean Considine, Kunal Malik, Jerry Shields, Carol Shields  
Wills Eye Hospital, Philadelphia, USA
Abstract: Purpose: To investigate demographics and clinical features of patients with amelanotic choroidal tumors. Design: Retrospective analysis. Methods: Comparison of demographic and clinical features of various amelanotic choroidal tumors based on stratification by patient age, sex, and tumor diameter. Included were all patients with amelanotic choroidal tumors evaluated on the Ocular Oncology Service, Wills Eye Hospital, Philadelphia, PA, USA over a 45-year time period. Results: A total of 5586 amelanotic choroidal tumors in 4638 eyes of 4441 patients were included with mean age at presentation of 58 years (median 60, range 0.1-100 years). Most patients were white (95%), female (56%), and with unilateral lesion (96%). By comparison, amelanotic melanoma presented at a younger mean age (57 years) compared to metastasis (60 years). Conclusion: Understanding the demographic and clinical features of amelanotic choroidal melanoma and other amelanotic lesions could lead to earlier and more accurate diagnosis.

Presentation Title: Protein expression of the intraocular epithelium: An analysis of the potential utility of cytokeratin OSCAR and SOX10 in the diagnosis of epithelial tumors

Authors: Charles Biscotti, Thomas Plesec, Arun Singh
Cleveland Clinic, Cleveland, USA

Abstract: Purpose: Diagnosis of intraocular epithelial lesions challenges cytologists, especially distinguishing pigmented epithelial adenomas from melanocytic neoplasms. Ocular epithelium variably expresses some melanocytic and epithelial differentiation markers further complicating diagnosis. We analyzed four enucleation specimens for epithelial and melanocytic differentiation to assess the diagnostic potential of cytokeratin (CK) OSCAR and SOX10. Method: The specimens included three normal eyes, removed in en bloc cancer resections, and one blind eye removed for pain and scleral abscess. Formalin fixed paraffin embedded sections were immunostained for epithelial differentiation (CK OSCAR, CK CAM 5.2, and EMA) and melanocytic differentiation (SOX10 and HMB45). One of the authors (CVB) scored each stain as negative, focally positive, or diffusely positive in the intraocular epithelium (RPE, ciliary epithelium (CE), and iris epithelium (anterior and posterior). Results: Ocular epithelia expressed CK OSCAR as follows: RPE (100%), Non-pigmented CE (100%), pigmented CE (100%), anterior iris (75%), and posterior iris (0%). CAM 5.2 expression occurred slightly less often: RPE (100%), non-pigmented CE (75%), pigmented CE (75%), anterior iris (50%), posterior iris (0%). EMA was limited to focal anterior iris expression in a single case. RPE expressed SOX 10, albeit weakly and focally, in all cases. CE and iris epithelium did not express SOX10. HMB45 had variable expression including RPE (100%), non-pigmented CE (25%), pigmented CE (75%), anterior iris (50%), and posterior iris (0%). Conclusion: Our results suggest that CK OSCAR has potential as an intraocular epithelial tumor marker. It outperformed other epithelial markers studied. Further, RPE SOX10 expression is a potential diagnostic pitfall.
Presentation Title: Preliminary data of circulating tumor cells and circulating tumor DNA in uveal melanoma

Authors: Carol Hall, Josh Upshaw, Vanessa Sarli, Salyna Meas, Anthony Lucci, Sapna Patel
The University of Texas MD Anderson Cancer Center, Houston, USA

Abstract: Purpose: Treatment of primary uveal melanoma (UM) is often very effective, with local recurrence rate of less than 5%. However, distant recurrence after treatment of the primary tumor is as high as 50%, suggesting the presence of micrometastases by the time of primary tumor treatment. A few pilot reports have studied circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) in metastatic UM. The aim of this study is to serially monitor CTC presence and characterize ctDNA in non-metastatic and metastatic uveal patients.

Methods: CTCs and ctDNA were assessed in 49 UM patients using the CellSearchTM system and ThermoFisher Oncomine TMPan Cancer ctDNA Panel.

Results: CTCs were identified in 20/49 (41%) of patients at first blood collection; 3/5 (60%) Class 1, 5/17 (29%), Class 2, 3/8 (38%) unknown, and 9/19 (47%) of metastatic patients. CTCs were identified (in draw 1, 2, or 3) in 5/7 (71%) of Class 2 patients and in 13/17 (76%) metastatic patient blood draws before, during or at the time of progression by imaging. Tumor and ctDNA GNAQ/GNA11 mutations were concordant in 5/7 (71%) patients. Serial ctDNA analysis demonstrated increasing GNAQ/GNA11 mutation allele frequency that was associated with progression.

Conclusion: CTCs can be identified in UM before, during, and at the time of disease progression. ctDNA and tumor GNAQ/GNA11 mutations were concordant, and the ctDNA mutation burden increased with disease progression. These data warrant larger studies to determine if serial CTC/ctDNA assessments could be beneficial in UM management.

Presentation Title: Clinical Application of Circulating Tumour Cells and Circulating Tumour DNA in Uveal Melanoma

Authors: Timothy Isaacs1,2, Aaron Beasley3, Elin Gray3, Muhummad Khattak4, James Freeman3, Richard Allcock5, Fred Chen6, Michelle Pereira3, Kyle Yau5, Jaqueline Bentel7, Tersia Vermeulen7, Leslie Caprese3, Michael Millward8, Melanie Ziman3
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Abstract: Purpose: To investigate circulating tumour cells (CTCs) and circulating tumour DNA (ctDNA) in peripheral blood specimens for prognostic analysis in uveal melanoma (UM). Methods: Serum samples from patients undergoing treatment for UM were analysed for the presence of CTCs and ctDNA. CTC were immunocaptured to magnetic beads, and immunostained for MART1/gp100/S100β. ctDNA was quantified using droplet digital PCR assay for mutations in the GNAQ, GNA11, PLCβ4 and CYSLTR2 genes. Low coverage whole genome sequencing (WGS) was used to determine somatic chromosomal copy number alterations (SCNA) in primary UM tumour, ctDNA and whole genome amplified CTCs.

Results: In a cohort of 30 primary UM patients, CTCs were detected in 58% of patients (1-37 CTCs per 8 mL of blood), while only 26% of cases had detectable ctDNA (1.6-29 copies/mL). Neither the presence of CTC or ctDNA were associated with tumour size or other prognostic markers. However, we demonstrate that SCNA analysis of CTCs showed great concordance with the enucleated primary tumour. These results support a model in which CTCs can be used to derive tumour specific SCNA relevant for prognosis. In addition, monitoring of ctDNA after treatment of the primary tumour allowed
detection of metastatic disease earlier than 18F-labeled fluorodeoxyglucose PET in two patients who developed metastatic disease during the course of the study. Conclusion: The presence of CTCs in peripheral blood specimens can be used to determine prognostic SCNA. Peripheral blood ctDNA can be used to monitor patients for early evidence of metastatic disease.

**Presentation Title:** Eighteen month results of a phase 1b/2 open-label clinical trial of AU-011 for the treatment of small to medium choroidal melanoma

**Authors:** Ivana Kim1, Abdhish Bhavsar2, Antonio Capone, Jr.3, Hakan Demirci4, Brian Marr5, Tara McCannel6, Cadmus Rich7, Amy Scheffler8, Carol Shields9

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**Abstract:** PurposeTo present interim results of a trial evaluating the safety and preliminary efficacy of a potential vision-sparing targeted therapy for patients with choroidal melanoma. Methods Patients with choroidal melanoma with an apical height between 1.5 - 3.4 mm and largest basal diameter of ≤ 16 mm received intravitreal administration of a viral-like particle bioconjugate (AU-011) at doses of 20 µg, 40 µg, or 80µg followed by light-activation with a 689 nm laser at a fluence of 50 J/cm2. Regimens consisting of single as well as 2 and 3 repeat injections followed by 1 or 2 laser applications were evaluated. Results 36 patients have been treated with up to 80 µg x 3 doses and followed for 4 to 24 months. Local tumor control has been observed in the majority of subjects. Five subjects have received additional radiotherapy; 1 with protocol-defined disease progression and 4 at investigator discretion. Mild/moderate adverse events (AEs), including intraocular inflammation and increased IOP, were clinically manageable. There were no related serious or severe AEs. Tumor thickness, tumor diameter and BCVA results by visit will be presented. Conclusions This study has shown preliminary safety and efficacy of AU-011. Long-term vision change is rare. Further randomized controlled studies will be initiated to confirm the safety and efficacy of AU-011 and its potential as an alternative to radiotherapy.

**Presentation Title:** Adjuvant therapy for high risk uveal melanoma: Assessing five-year survival outcomes

**Authors:** Elaine Binkley1,2, Pierre Triozzi3, Lisa Rybicky1, Paul Elson4, Susan Achberger1, Wayne Aldrich1, Arun Singh1

1Cleveland Clinic, Cleveland, USA. 2University of Iowa, Iowa City, USA. 3Wake Forest Baptist Health, Winston-Salem, USA. 4Cleveland, Clinic, USA

**Abstract:** Purpose: Survival after diagnosis of metastasis from uveal melanoma is poor. Identifying individuals at high-risk for metastasis and developing adjuvant therapy to prevent clinically-apparent metastasis could improve survival. We conducted an adjuvant trial of sequential, low-dose dacarbazine (DTIC) and interferon-alpha-2b (IFN-α-2b) in patients with cytogenetic high-risk uveal melanoma. Methods: Patients with iris, ciliary body, or choroidal melanoma and high-risk tumor cytogenetics (monosomy 3) were offered adjuvant treatment with low-dose DTIC and IFN-α-2b following primary therapy. Eligible but not-enrolled patients were observed. DTIC was administered at 850 mg/m2intravenously on days 1 and 28. IFN-α-2b was administered at 3 million units (MU) subcutaneously three times weekly for 24 weeks beginning at week 9. Hepatic imaging was performed before adjuvant therapy and at least every 6 months. Survival data were collected for five years after enrollment. Results: Prospective data from 150 patients were available. Thirty-three patients (22%) were treated, 29 (19%) were observed, and 88 (59%) were ineligible. Estimated 5-year metastasis-free-survival (MFS) was 64% (95% confidence interval [CI] 44-78) for treated and 33% (15-52) for observed patients (p=0.05). Estimated 5-year overall-survival (OS) was 66% (45-80) for treated and 37% (19-55) for observed patients (p=0.02). When adjusted for variations in significant prognostic factors between treatment and observation groups, survival differences were no longer significant (p=0.56 MFS and p=0.92 OS). Conclusion: Differences in baseline tumor characteristics between treated and observed patients...
can influence interpretation of results. Both clinical and molecular data must be considered when assessing outcomes in adjuvant trials for uveal melanoma.

Presentation Title: Utilizing T-cell activation signals 1, 2 and 3 for tumor-infiltrating lymphocytes (TIL) expansion: the advantage over the sole use of interleukin-2 in uveal melanoma
Authors: Marie-Andrée Forget, Cara Haymaker, René Tavera, Young Uk Kim, Orenthial Fulbright, Rodabe Amaria, Patrick Hwu, Dan Gombos, Sapna Patel, Chantale Bernatchez
The University of Texas MD Anderson Cancer Center, Houston, USA
Abstract: Purpose: In this study, we address two major challenges encountered in TIL therapy for uveal melanoma 1) the feasibility of growing a suitable TIL product and 2) the time needed for proper propagation.
Methods: We hypothesized that TCR activation in the first phase of expansion combined with an agonistic stimulation of CD137/4-1BB and IL-2 would enable the growth of TIL from a higher percentage of uveal patient (primary and metastatic), favoring as well a preferential expansion of CD8+ TIL.
Results: As predicted, this 3-signal approach platform for optimal T-cell propagation allowed for successful expansion of TIL from primary and metastatic uveal melanoma tumors in 100% (n=12). This expansion was rapid (less than 3 weeks) and more consistently composed of CD8+CD3+ TIL. Providing the three signals attributed to optimal T-cell activation led to expansion of TIL capable of recognizing their tumor counterpart.
Conclusions: This new methodology for the initial phase of TIL expansion brings a new opportunity for translation of TIL therapy in challenging malignancies such as uveal melanoma.

Presentation Title: Tumor infiltrating lymphocyte (TIL) harvest and ex vivo expansion from primary and metastatic uveal melanoma tumors: the MD Anderson experience
Authors: Meredith Pelster, Marie Forget, Chantale Bernatchez, Cara Haymaker, Patrick Hwu, Rodabe Amaria, Dan Gombos, Sapna Patel
MD Anderson Cancer Center, Houston, USA
Abstract: PURPOSE: To describe the success rates of tumor infiltrating lymphocyte (TIL) harvesting and subsequent ex vivo expansion of cells from primary and metastatic uveal melanoma tumors.
METHODS: Patients age 18 and older with documented uveal melanoma were consented to an IRB-approved protocol for TIL harvest.
RESULTS: Between 2006 and 2018, 63 uveal melanoma patients were consented and underwent TIL harvest. Median age was 54 years (range: 28 – 86), 56% of the subjects were male, 78% Caucasian, 9% Hispanic, and 13% unknown ethnicity. Overall successful ex vivo expansion of TIL occurred in 40% of subjects. Primary tumor was harvested for TIL in 17 of 63 of cases (27%), and metastatic tumor was harvested in 46 of 63 cases (73%). Ex vivo expansion was successful in 17.6% of primary TIL harvests and 48% of metastatic TIL harvests. Median days in culture for successful ex vivo expansion was 35 days in both cohorts. With respect to the metastatic cohort, 14 of 46 (30%) harvests were from liver metastases. Successful T cell expansion was observed in 43% of liver TIL harvests with a median of 34.5 days in culture. Overall, the median number of TIL expanded from culture and frozen for clinical use was 86.2 million (range: 34 - 460).
CONCLUSION: Uveal melanoma TIL harvest and successful ex vivo expansion of cells is more successful from metastatic tumors, including liver metastases, than from primary tumors. Techniques for expanding cells ex vivo are being refined to increase yield.
Presentation Title: Treatment of vitreo-retinal lymphoma - 20 years of experience
Authors: Jacob Pe'er¹, Zohar Habot-Wilner²,³, Shahar Frenkel¹
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Abstract: Purpose: To describe our 20 years of experience in treating vitreoretinal involvement of primary central nervous system lymphoma, by intravitreal injections of methotrexate (MTX). Methods: Intravitreal MTX (400 mg/0.05 ml) was administered twice weekly for 4 weeks, once weekly for 8 weeks, and then once monthly for 9 months, for a total of 25 injections. Data were collected from the patients' records and included, inter alia, response to intravitreal MTX measured by time to disappearance of vitreal cells and retinal infiltrates, changes in visual acuity, and clinical recurrence rate. Results: 130 eyes of 81 patients (49 women, 60.5%) were diagnosed at the mean age (±SD) of 62.0 ±16.9 years. 32 patients had monocular involvement and 49 had binocular. 35 (43.2%) patients also had CNSL and 5 (6.2%) had previous systemic lymphoma. Clinical remission was reached after 5.2 (±4.0) (1–16) injections of MTX (mean (±SD) (range)), with 90% of the eyes needing 11 injections or less to be cleared of malignant cells. Two patients had an intraocular recurrence which responded to the same treatment. Among the side effects, the most common was corneal epitheliopathy, which usually appeared after the third injection and began to subside when the intervals between injections increased. 13 patients (16.0%) developed NVG.Conclusions: Vitreoretinal involvement of lymphoma can be controlled effectively and without serious adverse reactions by intravitreal MTX injections. This is an effective treatment protocol with bearable side effects. We recommend this as a standard of care in the management of vitreo-retinal lymphoma.

Presentation Title: Intravitreal melphalan for vitreoretinal lymphoma
Authors: Arman Mashayekhi¹, Carol Shields¹, Emil Say², Jerry Shields¹
¹Oncology Service, Wills Eye Hospital, Philadelphia, USA. ²Medical University of South Carolina, Charleston, USA
Abstract: Purpose: To determine the efficacy of intravitreal melphalan for treatment of vitreoretinal (VR) lymphoma. Methods: Intravitreal melphalan (10 μg/0.05 mL) was injected on a monthly basis. Results: 12 eyes of 6 patients with VR lymphoma were studied. Three patients were male and 3 were female. Patient age ranged from 59 to 91 years. One patient had history of cutaneous large B-cell lymphoma and 3 patients developed central nervous system lymphoma during follow-up. All eyes had vitreous involvement and 10 eyes of 5 patients had sub-retinal pigment epithelial (sub-RPE) infiltrates. Cytopathologic examination was performed on samples obtained by needle biopsy of sub-RPE infiltrates (3 patients) or by pars plana vitrectomy (3 patients). The number of melphalan injections per eye ranged from 2 to 14. Duration of follow-up ranged from 3 to 31 months. At last follow-up tumor control was achieved in 9 of 12 eyes. One patient with bilateral involvement had regression in one eye and recurrent vitreous lymphoma in the other eye. Two eyes of one patient showed resolution of vitreous lymphoma but persistent sub-RPE infiltrates subsequently treated successfully with intravitreal methotrexate. Visual acuity remained stable in 7 eyes, increased in 3 eyes, and decreased in 2 eyes. Conclusion: Intravitreal melphalan (10 μg/0.05 mL given monthly) was effective in causing tumor regression in 9 of 12 eyes with VR lymphoma. Further studies are needed to determine the optimal dosage and interval between injections.
Presentation Title: Expanding clinical spectrum of ocular melanocytomas

Authors: Jerry Shields1,2, Carol Shields1,2

1Wills Eye Hospital, Philadelphia, USA. 2Thomas Jefferson University, Philadelphia, USA

Abstract: Purpose: To highlight new observations on ocular melanocytomas based on further clinical and/or histopathologic observations. Methods: Chart review to specifically identify new clinical findings. Results: We identified melanocytomas involving the optic disc, choroid, ciliary body, and iris. Those in the choroid were dark brown to black in color and none were amelanotic. They resembled a typical nevus or low grade melanoma. Optic disc melanocytomas showed growth in about 20% of cases. There were few that demonstrated growth into low grade melanoma, but none developed metastasis. The vision in optic disc and choroidal melanocytomas varied from 20/20 to no light perception; the latter being due to severe necrosis in the tumor. Secondary central retinal vein obstruction and central retinal artery obstruction developed in 2 separate cases. Iris melanocytomas were found to have unique features of a uniform dark brown to black color with granular multinodular surface. Some iris have shown enlargement but were believed to be benign despite slow growth, confirmed on histopathology. In the early part of this study, iris tumors showing growth were treated with iridectomy or iridocyclectomy, but it was eventually found that they were benign pathologically despite the enlargement. In addition, iris melanocytoma can be giant in size with extensive pigment dispersion and secondary glaucoma. Conclusion: Our knowledge of ocular melanocytoma has evolved in recent years. This tumor can occur not only in the optic nerve but throughout the uvea. The vast majority of melanocytomas are benign and transformation into low grade melanoma is extremely rare.

Presentation Title: Adenomas and adenocarcinomas of the retinal pigment epithelium: clinical and imaging characteristics, treatment options and histopathologic findings in 51 consecutive patients

Authors: Basil Williams1,2, Maura Di Nicola2,1, Luis Acaba2, José Antonio Lucio-Alvarez2, Jerry Shields2, Carol Shields2

1Department of Ophthalmology - University of Cincinnati College of Medicine, Cincinnati, OH, USA. 2Ocular Oncology Service - Wills Eye Hospital, Philadelphia, PA, USA

Abstract: Purpose: To describe the clinical and imaging characteristics, treatment options and pathologic features of 51 consecutive cases of adenoma and adenocarcinoma of the retinal pigment epithelium (RPE). Methods: Retrospective case series of 51 patients diagnosed with adenoma or adenocarcinoma of the RPE at the Ocular Oncology Service of Wills Eye Hospital, Philadelphia between October 1980 and February 2018. Referring diagnosis, demographic and clinical features, and treatment modality were documented. Multimodal imaging, cytologic and histopathological features were assessed. Results: Mean age was 51 years (range 18-83) and most common referring diagnosis was choroidal melanoma (n=19, 37%). Visual acuity (VA) was ≥20/40 (n=30, 59%), 20/50-20/150 (n=7, 14%) and ≤20/200 (n=14, 27%). Mean tumor thickness and diameter were 3.5 mm and 6.1 mm, respectively. Most lesions appeared black (n=28, 55%) and abruptly elevated (n=42, 82%). Feeder vessels (n=31, 61%), lipid exudation (n=28, 55%), congenital hypertrophy of the RPE (n=11, 22%) and exudative retinal detachment (n=11, 22%) were observed. Primary treatments included observation (n=29, 57%), partial lamellar sclerouvectomy (n=9, 18%), enucleation (n=5, 10%), radiotherapy (n=3, 6%), intravitreal anti-vascular endothelial growth factor or corticosteroids (n=3, 6%) and laser photocoagulation (n=2, 4%). Mean follow-up was 82 months (n=35, range 0.3-354). Final VA was stable or improved in 17/32 (53%). Tumor growth was observed in 12/35 (34%) and eye retention rate was 32/39 (82%). Conclusion: RPE adenoma or adenocarcinoma can be identified by clinical and imaging characteristics. Observation is preferred in asymptomatic patients, treatment for progressive lesions should be individualized.
Presentation Title: Pigmented Peripapillary Lesion
Authors: Tara McCannel, Vidal Soberon
University of California, Los Angeles, Los Angeles, USA
Abstract: Purpose: To report the case of a papillary and peripapillary pigmented lesion in the right eye of a 68 year old man with no visual complaints. Method: Clinical examination findings, and imaging studies (ultrasonography, fluorescein angiography and optical coherence tomography (OCT)) were reviewed. Results: Visual acuity was 20/20 in both eyes, with normal intraocular pressure. Funduscopy of the right eye revealed a variably pigmented inferior papillary and choroidal lesion with drusen and no sub retinal fluid. Ultrasonography revealed a lesion height of 2.57 mm and high reflectivity on A scan. Fluorescein angiography revealed mixed early blockage and late staining of the lesion, with no active leakage. OCT revealed a hyperreflective granular appearance in the retina surrounding the optic nerve, and a choroidal component inferior to the nerve with cystic-appearing spaces in the middle layers of the retina. Conclusion: The findings suggest that this case represents a combined melanocytoma and choroidal nevus. Observation was recommended.

Presentation Title: An unusual case of serpiginous maculopathy
Authors: Marco Pellegrini, Chiara Preziosa, Giovanni Staurenghi
Eye Clinic, Department of Biomedical and Clinical Science “Luigi Sacco”, Luigi Sacco Hospital, University of Milan, Milan, Italy
Abstract: Purpose: To document a case of unilateral retinal pigment epithelium dysgenesis (URPED) complicated by a choroidal neovascularization (CNV) Methods: Case reportResults: A 51-year-old woman referred to our ocular oncology service for a possible choroidal osteoma in her left eye. Patient was in therapy with systemic prednisone, topic dexamethasone and ketorolac since three months for a previous diagnosis of serpiginous choroiditis. Best corrected visual acuity (BCVA) at baseline was 20/200. A complete ophthalmological evaluation including color fundus photography, fundus autofluorescence, fluorescein angiography, indocyanine green angiography, optical coherence tomography and OCTA was performed with a final diagnosis of URPED complicated by CNV. After two intravitreal injections of bevacizumab, the BCVA improved to 20/50 and OCTA showed a progressive contraction of the CNV. URPED margins remained stable at consecutive follow up.Conclusions: URPED is a rare clinical entity with unique appearance and often mimicking other inflammatory or neoplastic conditions. OCTA may be used for a detailed imaging and follow up of URPED-associated CNVs and anti-vascular endothelial growth factor (VEGF) agents represent an effective therapy for the treatment of CNV in patients with this disease.

Presentation Title: Another amelomatic iris nodule
Authors: Hakan Demirci, Ersin Muz, Victor Elner
Kellogg Eye Center, University of Michigan, Ann Arbor, USA
Abstract: Purpose: To report a rare case of thyroid glandular epithelial choristoma of the irisMethod: A case reportResult: A healthy 76-year-old man, who has a right iris mass present since birth, presented with its enlargement. Visual acuity was 20/60 OD and 20/20 OS. Slit-lamp biomicroscopy of the right eye showed a solitary yellow-white mass with multiple cysts and intrinsic vessels located in the midzone of the iris leaflet at 6 o’clock. It measured 4x3x1.7 mm. Otherwise, his ocular examination was unremarkable. Ultrasound
Biomicroscopy showed a solid lesion containing small cysts, and highly reflective spots that cast shadow behind. There was no anterior chamber angle or ciliary body involvement. The patient underwent iridectomy. Histopathology showed glandular tissue with follicles containing colloid, fibrosis, and calcification, consistent with thyroid glandular epithelial choristoma. Immunohistochemistry was positive for nuclear thyroid transcription factor-1 (TTF-1), cytoplasmic cytokeratin, and cytoplasmic and follicular thyroglobulin. Staining was negative for calcitonin and chromogranin A. His systemic work-up for metastatic thyroid cancer was unremarkable. After 1-year follow-up, no local recurrence or systemic problems were observed. Conclusion: Thyroid glandular epithelial choristoma is a rare presentation of amelanotic iris lesions.

Presentation Title: Pediatric Intraocular Tumor or Not?  
Authors: Carol Shields  
Wills Eye Hospital, Philadelphia, USA. Thomas Jefferson University, Philadelphia, USA  
Abstract: A 3 year old boy developed preseptal cellulitis, photophobia, and pain that was treated with Amoxicillin. He was subsequently found to have an intraocular tumor, presumed to be retinoblastoma or amelanotic melanoma. Referral to our department and careful examination lead to tips that established the correct diagnosis and management that will be revealed at the meeting.

Presentation Title: Conservative Management of Necrotic Ciliary Body Melanocytoma  
Authors: Elaine Binkley¹,², Charles Biscotti¹, Annapurna Singh¹, Jonathan Sears¹, Arun Singh¹  
¹Cleveland Clinic, Cleveland, USA. ²University of Iowa, Iowa City, USA  
Abstract: Purpose: To describe a case of a necrotic ciliary body melanocytoma associated with ocular inflammation that was managed conservatively. Methods: Case report. Results: A 69-year-old man presented with an acute decline in vision (counting fingers) accompanied by eye pain due to extensive anterior chamber inflammation and elevated intraocular pressure. There was no view to the posterior pole. Ultrasonography revealed a low-reflective ciliary body mass. The patient was initially managed conservatively with topical steroids with improvement in the inflammation and he underwent laser peripheral iridotomy for secondary angle closure. Diagnostic trans-scleral fine-needle aspiration biopsy favored a diagnosis of melanocytoma. The lesion was followed closely by serial observation with spontaneous decrease in size from 9.0 millimeters in height at presentation to 5.5 millimeters after two years. Following cataract surgery and vitrectomy (for residual vitreous debris) the final visual acuity was 20/40. Vitreous biopsy revealed pigment laden macrophages similar to his initial biopsy and absence of melanoma. Conclusion: Necrotic melanocytoma and necrotic ciliary body melanoma can have similar clinical and ultrasonographic features. This case highlights the utility of diagnostic fine-needle aspiration biopsy in distinguishing between these entities. A careful, tailored management and follow up strategy should be employed for ciliary body lesions suspected to be benign.

Presentation Title: Genomic Profile of Solitary Choroidal Hemangioma  
Authors: Jasmine Francis¹, Tatyana Milman², Hans Grossniklaus³, Daniel Albert⁴, Robert Folberg⁵, Gregory Levitin⁶, Sarah Coupland⁷, Federica Catalanotti⁸, Cyriac Kandoth¹, Klaus Busam¹, David Abramson¹  
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Abstract: Purpose: Solitary choroidal hemangiomas are benign vascular hamatomas, which, unlike their diffuse counterpart, are not associated with systemic findings. Both solitary and diffuse choroidal hemangiomas have the potential of threatening vision. Methods: Case presentation of solitary choroidal hemangioma evaluated with Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT), a hybridization capture-based next-generation sequencing assay for targeted deep sequencing of all exons and selected introns of 468 key cancer genes in formalin-fixed, paraffin-embedded tumors. Results: MSK-IMPACT...
reveals a unique genetic profile to this solitary choroidal hemangioma: specifically in an actionable mutation. Conclusion: This case of a solitary choroidal hemangioma reveals an actionable genomic event. This has implications for potential visual rehabilitation/maintenance with appropriate targeted therapy.

Presentation Title: Tumor or not?
Authors: Jerry Shields
Wills Eye Hospital, Philadelphia, USA. Thomas Jefferson University, Philadelphia, USA
Abstract: A 68 year old white female was referred with blurred vision and a choroidal mass on OCT with subretinal fluid. Following multimodal imaging a unique diagnosis was found. Review of the literature revealed only several similar published cases of this unique entity. The diagnosis will be revealed at the meeting.

Presentation Title: Mystery Case
Authors: Pukhraj Rishi
Sankara Nethralya, Chennai, India
Abstract: Purpose: To report the outcomes of I-125 plaque radiation for ciliary body medulloepithelioma in 13-year-old Asian girl Methods: A 13 year-old-girl presented with complaints of pain and decreased vision in the left eye of 15 days duration. Examination revealed BCVA of 6/12(P) in affected left eye. Right eye was essentially normal. Examination revealed anterior chamber reaction, rubeosis iridis, ectropion uveae, synechial closure of iridocorneal angle, neovascularization at optic disc, inferior vitreous hemorrhage, old laser photocoagulation marks, cystoid macular edema, and intraocular pressure (IOP) of 42 mmHg. Her systemic history was unremarkable. There was no history of bleeding diathesis or trauma. Gonioscopy revealed a whitish-gray ciliary body tumor extending from 4 to 10 o’clock meridian and measured 5.9 x 6.7 x 5.9 mm in size. Retrolental neoplastic membrane was adherent to tumor apex. IOP was controlled with oral and topical antiglaucoma medications. Clinical diagnosis of ciliary body medulloepithelioma was confirmed with FNAB which revealed multiple clumps of large sized cohesive cells with high nucleocytoplasmic ratio, arranged in an eosinophilic matrix. Some cells showed formation of duct like structures. The family chose plaque radiation with I-125 over enucleation, at treatment dose of 40Gy. Results: Two years later, the patient underwent cataract surgery. At 4 years follow-up, there was no recurrence or metastasis. Visual acuity recorded at last follow-up was 6/60 and IOP was controlled. Conclusion: This case demonstrates the effectiveness of I-125 plaque radiation therapy for CB Medulloepithelioma till 4 years of follow-up.
Presentation Title: Leukocoria in a baby girl.
Authors: Alexandre Moulin, Christina Stathopoulos, Pascal Escher, Francis Munier
1Jules-Gonin Eye Hospital, Lausanne University, Lausanne, Switzerland. 2Universitätsklinik für Augenheilkunde, Inselspital, Bern, Switzerland
Abstract: PURPOSE: To document to the best of our knowledge the youngest retinal giant cell astrocytoma reported to date. METHOD: Case report
RESULTS: A 2 weeks old girl was referred due to a right leukocoria. Slit lamp examination revealed dilated iris vessels in right eye. There was a complete retinal detachment with tortuous vessels touching the lens. On B-Scan the retina appeared thickened and cystic without calcifications. Fundus of the left eye revealed three small nodular greyish masses, arising within the inner retinal layers as shown by OCT. Brain MRI revealed multiple infra- and supratentorial tubers, several subependymal nodules as well as a posterior supratentorial radial hyperintensity in T2 sequence. Germline mutation TSC2 mutation from blood PBMC was found. Enucleation of the right eye was performed. Macroscopy revealed a complete retinal detachment with solid areas alternating with cystic, creamy or gelatinous areas. Microscopy demonstrated a very extensive partially necrotic retinal giant cell astrocytoma without choroid invasion. Activation of S6 was found in gemistocytic astrocytes. CONCLUSIONS: Retinal giant cell astrocytoma should be part of the differential diagnosis of leukocoria in the context of retinal hamartomas and tuberous sclerosis. We also document for the first time an activation of S6 in retinal giant cell astrocytoma. Targeted therapy with mTOR inhibition has been used in the management of smaller retinal astrocytomases.

Presentation Title: Claudin-4 immunostaining allows for the diagnosis of choroidal metastasis in a challenging case
Authors: Martina Angi, Jessica Sergenti, Biagio Paolini, Barbara Valeri
Istituto Nazionale Tumori, Milan, Italy
Abstract: Purpose: To describe the clinical and pathological features of a rare case of choroidal metastasis from gastric adenocarcinoma presenting as hemorrhagic retinal detachment
Method: Report of a case and literature review
Results: A 62-year-old male with stage IV gastric adenocarcinoma treated with paclitaxel and ramucirumab with achievement of stable disease, presented to his local hospital with visual loss in his left eye and was diagnosed with hemorrhagic retinal detachment. During surgery, an amelanotic choroidal mass was noticed and the patient was referred to the Ocular Oncology Centre. Because of the silicon oil filling, ultrasound and MRI were not meaningful, so a transretinal choroidal biopsy was performed. Despite a heavily hemorrhagic background, the use of Claudin-4 immunostaining allowed for the identification of scattered neoplastic epithelial cells, hence the diagnosis of choroidal metastasis. Intensity-modulated radiation therapy was planned, but the eye become blind and painful and the patient underwent enucleation. Conclusion: Choroidal metastasis can occur in patients with apparent good control of systemic disease and masquerade as hemorrhagic retinal detachment. Diagnostic biopsy can be challenging and requires a skilled Pathologist and the choice of suitable immunostaining.

Presentation Title: Mystery Case
Authors: Mary Aronow
Retina Service, Massachusetts Eye and Ear, Harvard Medical School, Boston, USA
Abstract: Purpose: To present a challenging diagnostic case of an unlikely intraocular metastasis. Methods: Case presentation. Results: A 59-year old Caucasian male presented with blurry vision in the left eye. His vision was 20/20 in the right eye and 20/30 in the affected left eye. Intraocular pressures were 18 and 20 mm Hg in the right and left eye, respectively. The right eye was unremarkable. In the left eye, an intraocular mass was visible in the angle at 5:00 with posterior extension to the ciliary body and peripheral choroid. Slit lamp photographs, ultrasound biomicroscopy, B/A scan ultrasonography, and color fundus photography will be shown. The findings were clinically consistent with intraocular metastasis. The patient had known head and neck squamous cell carcinoma of the left pyriform sinus responsive to pembrolizumab, but developed progressive disease in the lungs despite continued therapy. A second primary lung malignancy was suspected. Tissue from the intraocular tumor was sampled via a transcorneal fine-needle aspiration biopsy. Cytology revealed intraocular squamous cell carcinoma consistent with his known head and neck primary. The eye was successfully treated with proton beam irradiation. Conclusion: Intraocular metastasis from head and neck squamous cell carcinoma is a rare entity but should be recognized by the ocular oncologist.

Presentation Title: A young man, a rare tumor and a happy ending
Authors: Priscilla Ballalai, Patricia Picciarelli
University of Sao Paulo Medical School (USP), Sao Paulo, Brazil
Abstract: The authors report a case of a 33 years old white male, presenting with an extensive and rare ciliary body tumor, managed by “en block” resection and phacoemulsification with IOL implantation.

Presentation Title: Vitreoretinal Leukemia in a Child
Authors: Vicktoria Vishnevskia-Dai
Ocular Oncology Service, The Goldschleger eye institute, Sheba Medical Center, Tel-Hashomer, Israel. Sackler School of medicine Tel Aviv University, Israel, Rumut Gun, Israel
Abstract: A 3 years old child was admitted to our hospital with recurrent falls and known acute lymphocytic leukemia (ALL) on remission. On her ocular examination massive optic nerve infiltration with serous retinal detachment OD and severe vitreous opacifications on the LE were observed. Biopsy proven vitreoretinal leukemia was diagnosed. The child was treated locally with reported intravitreal Methotrexate injections in addition to systemic and and intrathecal chemotherapy. Full remission was achieved. On 7 years follow up the patient is alive and well.

Presentation Title: Metastasis of Urothelial Carcinoma to the Choroid of the Human Eye: A Case Report of Diagnosis and Treatment with Systemic Erdafitinib.
Authors: Peter Hovland1, Amanda Mason1, Gregory Kotnis2, Chase DiMarco3
1Colorado Retina Associates, Denver, USA. 2Unipath, LLC, Denver, USA. 3St. James School of Medicine, Park Ridge, USA
Abstract: Purpose: To describe a case of metastasis of urothelial carcinoma to the choroid of the eye. A review of the literature suggests that this is an unusual manifestation of this disease. Methods: A 50 year-old female with a one month history of metastatic urothelial carcinoma developed photopsias in the right eye. Examination revealed a subretinal tumor (3.5 mm depth x 11 mm diameter) in the macula. A 27-gauge fine needle aspirate biopsy was performed using a standard 25g pars plana vitrectomy approach. Pathology technique included monolayer and cell block evaluation with immunohistochemistry. Chemotherapy with gemcitabine and cisplatin was stopped after 2 cycles due to rapid systemic disease progression. Palliative radiotherapy included treatment of the eye with a 3,000 cGy fractionated dose. The patient was enrolled in a clinical trial of Erdafitinib, (Janssen Research and Development, LLC) a fibroblast growth factor receptor inhibitor. Results: The biopsy specimen was positive for Cytokeratin 7 and GATA 3, and nonreactive for S100, and was compared to reported findings of the original biopsy of the primary tumor. These results were consistent with a diagnosis of metastatic urothelial carcinoma.
Clinically, the tumor in the eye and other metastases regressed rapidly after the systemic therapy with Erdafitinib. The eye tumor thickness decreased to 341 microns with visual acuity improvement from 20/400 to 20/20.

Conclusion: This is the first report of biopsy-confirmed urothelial carcinoma metastasis to the choroid of the human eye. This condition appears to respond favorably to treatment with external radiation and Erdafitinib.

Presentation Title: Ciliary Body Tumor Treated Topically
Authors: Yahya Alzahrani
King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia
Abstract: Purpose: To report a rare case of ciliary body mass treated topically.
Method: Case report.
Result: A case of a 65-year-old female presented with gradual visual loss, pain, and redness in her right eye for 6 months. Best corrected visual acuity of the right eye was hand motion, and of the left eye was 20/25. The right eye showed circumcorneal congestion. A brownish multilobulated lesion detected supero-temporal with iridocorneal touch temporally, mass was seen from 7 to 12 o’clock position with sever cellular and fibrinous reaction. There was no view to the fundus in right eye. UBM of the right eye showed a ciliary body from 7 to 12 o’clock measured (11.30 mm length with 5.58 mm elevation). B scan shows mild vitreous opacity with flat retina. All the investigations were within normal limits. The diagnosis of inflammatory tumor was made. She was treated with topical steroid tapered weekly over next 8 weeks then she continued on once daily. Her symptoms gradually improved and the ciliary body mass also decreased in size both clinically and in the UBM images. There was no recurrence in the next 10 months after which patient underwent a cataract extraction surgery. There was no recurrence a year later with final best corrected visual acuity of 20/40 and UBM measurement showed significant improvement compared to size at presentation with very minimal thickening of ciliary body (1.11 mm elevation).
Conclusion: Inflammatory etiology of the ciliary body tumor should be considered as differential.

Presentation Title: Ocular circulation in optic disc melanocytoma
Authors: Iku Kikuchi1,2, Satoru Kase2, Kan Ishijima2, Yuki Hashimoto2, Kiriko Hirooka2, Susumu Ishida2
1Department of Surgery, Obihiro social work association Obihiro Hospital, Obihiro, Japan. 2Department of Ophthalmology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Hokkaido, Japan
Abstract: Purpose: To examine relationship between ocular circulation and visual field in optic disc melanocytoma (ODM). Methods: Five eyes in 5 patients were enrolled in this study. All patients were diagnosed with ODM in Department of Ophthalmology, Hokkaido university hospital from March 2009 to November 2017. Ophthalmological findings, optical coherence tomography angiography (OCTA), and laser speckle flowgraphy (LSFG) findings were retrospectively analyzed. Results: The 5 ODM cases consisted of 2 females and 3 males. Age of the patients ranged from 47 to 82 years (mean: 54 years). Follow-up periods were from 4 to 105 months. Visual acuity deteriorated in 1 out of 5 eyes. Fluorescein angiography displayed hypo-fluorescence throughout the examination in all the 4 eyes examined. OCTA detected radial blood vessel networks in the tumor in 2 out of 5 eyes. Nasal visual field defects were found in the other 2 eyes, which were correlated with locations of the tumor, and absent of the blood vessel networks. One ODM eye without marked visual field defects and pigmentation showed lower mean blur rates determined by LSFG in optic disc vessel and tissue circulations than those of the contralateral eye. During follow-up, tumor enlargements were not seen in all cases. Conclusion: LSFG demonstrated reduced blood flow in the optic disc of ODM without visual field defects. This study further showed relationship between deficit of blood vessel networks in ODM and apparent visual field defects, suggesting that circulation disorders in the optic disc might result in the visual field defect.

Presentation Title: Fractionated Stereotactic Radiosurgery in Patients with Very Large (AJCC T4) Choroidal Melanoma
Authors: Anthony Daniels, Alexander de Castro-Abeger, Guozhen Luo, Gregory Twork, Diandra Ayala-Peacock
Abstract: Purpose: To describe a series of patients with very large (AJCC T4) uveal melanoma (UM) treated with fractionated stereotactic radiosurgery (fSRS). Methods: A series of patients with T4 UM is described. All were treated with fSRS instead of enucleation. Surgically-implanted fiducial markers were not used. Tumor control rates, globe retention, major vascular complications, and patient survival are described. Results: During a 9-month period, 10 patients presented with T4 UM. 1 was excluded because of prior brachytherapy, 1 could be treated with plaque, and 2 chose primary enucleation. Thus, 6 patients underwent fSRS. Median basal diameter was 21 mm and median height was 9.2 mm. At 1-year, tumor control was achieved in 6/6 (100%) eyes (primary endpoint). At 1-year, no eyes required secondary enucleation (100% globe retention) and no eyes (0%) developed vascular complications (secondary endpoints). By 2-years, 1 eye required secondary enucleation for persistent tumor cells in the vitreous, despite clear regression of the treated choroidal tumor mass. Thus, 2-year tumor control rate and globe retention were both 83% (5/6). However, by 2-years, 4/5 of the remaining eyes developed NVG, manageable with drops and/or bevacizumab and/or panretinal photocoagulation. The last eye developed NVG at 26 months. 3/4 eyes that presented with acuity ≥20/100 retained acuity ≥20/100 at final follow-up. No metastases or deaths occurred. 3-year follow-up data will also be presented. Conclusions: The majority of eyes with T4 UM treated with fSRS were salvaged, with surprising retention of vision, although most developed (easily treatable) NVG.
Abstract:
We recently described the first small animal (rabbit) model of intra-arterial chemotherapy with xenografted human retinoblastoma tumors as a platform to assess toxicity and efficacy of novel compounds in vivo. We subsequently described an extensive toxicity assessment platform for this model. Our purpose here is to describe our use of this combined model (rabbit IAC, tumor xenograft, toxicity assessment platform) to assess the efficacy and toxicity of various traditional chemotherapies and molecularly-targeted antineoplastic agents.

Methods: For IAC, each rabbit’s dominant ophthalmic artery was endovascularly cannulated, and each drug was injected at various doses. For intravitreal experiments, 1-3 weekly injections of each drug were performed. For both, retinal structure and function were assessed by electroretinography, photography, fluorescein angiography, OCT, and OCT-Angiography, both before and after treatment. Human WERI-Rb1 xenografts were treated with either intravenous, intra-arterial, or intravitreal chemotherapy. Assessment of efficacy against vitreous seeds was by both direct quantification of seed burden (vitreous harvesting and cell counting) and by assessment of apoptosis induction.

Results: Toxicity was dose-dependent and drug-specific. The clinically-observed toxicities of intra-arterial melphalan and carboplatin could be recapitulated. Various doses of intravitreal topotecan were studied, and in vivo efficacy was equivalent to intravitreal melphalan with much lower toxicity. A new class of inhibitor targeting gene expression in retinoblastoma was studied. It was equally effective to melphalan, without the associated retinal toxicity.

Conclusions: For the first time, intra-arterial chemotherapies, alone or in combination with intravitreal chemotherapies, can be studied for both efficacy and toxicity in a preclinical model, identifying potential alternative agents.

Abstract:
Penetration of topotecan in retinoblastoma tumorspheres

Authors: Ursula Winter1, Federico Fuentes2, Santiago Zugbi1, Rosario Aschero1, Mariana Sgroi1, Claudia Sampor1, Angel Carcaboso3, David Abramson4, Guillermo Chantada1, Paula Schiaiquiche1

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Purpose: RETINOBLASTOMA VITREOUS SEEDS ARE STILL THE MAJOR CAUSE OF THERAPEUTIC FAILURE IN EYES WITH INTRAOCULAR TUMORS. A PRECLINICAL MODEL WOULD BE HELPFUL IN THE UNDERSTANDING OF SEED BEHAVIOR, DRUG PENETRATION, AND RESPONSE TO CHEMOTHERAPY. OUR AIM WAS TO DEVELOP AN IN VITRO MODEL OF VITREOUS SEEDS OR TUMORSHERVES TO ASSESS CHEMOTHERAPY PENETRATION BY MEANS OF LIVE-CELL IMAGING.
METHODS: Cell cultures from two patients with retinoblastoma who underwent upfront enucleation were established and thoroughly characterized for retinal lineage-markers. The correlation between the in vitro tumorspheres and the in vivo vitreous seeds was established. Subsequently, confocal microscopy was used to quantify real-time fluorescence of topotecan as a measure of its penetration into different sizes of tumorspheres. Tumorsphere viability was determined after chemotherapy penetration.

RESULTS: The tumorsphere model was able to recapitulate the morphology, phenotype, and genotype of patient vitreous seeds. The larger the size of the tumorsphere, the longer the time required for the drug to fully penetrate into the core (p<0.05). Topotecan penetration correlated with its cytotoxic activity.

DISCUSSION: The tumorsphere model recapitulated several characteristics of vitreous seeds observed in patients with retinoblastoma and was successfully used to assess live-cell imaging of chemotherapy penetration for drug distribution studies.

Presentation Title: The Retinoblastoma Tumor Microenvironment Contributes to Drug Resistance
Authors: Matthew Wilson1,2, Zachary Goldsmith1, M Brouner1, Rachel Brennan2,1, Benjaamin King2,1, Vanessa Morales-Tirado1
1Hamilton Eye Institute, Memphis, TN, USA. 2St Jude Children's Research Hospital, Memphis, TN, USA
Abstract: Purpose: Vitreous seeding remains the greatest challenge in treating retinoblastoma (Rb) in part due to their unique location and resistance to current therapies. Previously, we demonstrated the presence of members of the ATP-binding cassette (ABC) transporter family in Rb. These proteins are involved in drug efflux of both carboplatin and melphalan and may warrant therapeutic value to reduce vitreous seed drug resistance. Methods: Using RNA isolated from nine naive Rb patients with vitreous seeding, we quantified levels of primary ABC transporters (ABCB1, ABCC1, ABCC2, and ABCG2) and CD44 and compared to 5 healthy human vitreous controls by qPCR. We measured ABC transporter function through use of a cell-permeable fluorescent dye by flow cytometry. We also examined the percentage of Y79 Rb cells expressing CD44 by flow cytometry. Furthering our previous studies on PDGF-PDGFRb signaling, we investigated the role of this pathway in Rb drug resistance. Results: We measured high mRNA expression of all ABC transporters as well as CD44 in Rb patients relative to healthy vitreous. We also demonstrated an abundance of CD44+ Y79 Rb cells, which was reduced after disruption of PDGF-PDGFRb signaling. Conclusion: In this study we demonstrate expression of key players implicated in drug resistance in the vitreous of Rb patients. Furthermore, as previous work from our group has shown the importance of PDGF-PDGFRb signaling in Rb cell survival, we demonstrated how disruption of this signaling cascade may aid in reducing drug resistance of Rb cells.

Presentation Title: Topotecan in patients with advanced intraocular retinoblastoma: Moving beyond PK-guidance
Authors: Rachel Brennan1,2, Michala Burges1, Olivia Campagne1, Clinton Stewart1, Matthew Wilson1,2
1St. Jude Children's Research Hospital, Memphis, USA. 2University of Tennessee Health Science Center, Memphis, USA
Abstract: Purpose: Topotecan is effective in the treatment of advanced intraocular retinoblastoma. To enable the generalization of this strategy, results from a pharmacokinetic (PK)-guided dosing approach used in an institutional protocol were analyzed. Methods: Patients with advanced intraocular retinoblastoma were enrolled on SJRET6 (NCT01783535). Topotecan dosing was PK-guided to achieve the protocol defined systemic exposure (i.e., 140 +/- 20 ng-hr/mL). Using prior clinical data, the initial topotecan dosage in SJRET6 was stratified based upon age. PK studies were completed in all patients for courses 1 and 2; those not within target range were re-studied during courses 5, 8, and 11. Results: Twenty-one patients from SJRET6 with 89 PK studies were analyzed; 38% (8 of 21) of patients on SJRET6 were within target range after the first dose in course 1. Six of 21 patients (29%) required PK adjustment of dosage in courses 5, 8, or 11. Twelve patients were above the target range (range 162-200ng-hr/mL, median 172ng-hr/mL); 42% (5 of 12 patients) were < 6 months of age and 58% (7 of 12 patients) were < 9 months old at the time of topotecan administration. Topotecan adjustments were expected for others based on
clinical factors (increased creatinine, difficulty tolerating therapy, underlying genetic condition). The median dosage decrease was 20% (range 6-39%), with no further dosage adjustment required in those < 12 months of age. Conclusions: Age-adjusted dosing for topotecan is feasible, but patients younger than 12 months of age should receive initial PK-guided dosing to avoid potential toxicity.
Presentation Title: An early-maturing cone photoreceptor origin of retinoblastoma tumors
Authors: Hardeep Singh¹, Sunhye Lee¹, Sijia Wang¹, Kevin Stachek¹, Martin Triska¹, Matthew Thornton², Cheryl Craft², Brendan Grubbs², David Cobrinik²,¹
¹Children's Hospital Los Angeles, Los Angeles, USA. ²Keck School of Medicine, University of Southern California, Los Angeles, USA
Abstract: Purpose: The retinoblastoma cell-of-origin has been debated for more than a century. Identification of this cell type is needed in order to define its therapeutic vulnerabilities. Prior studies suggested a cone precursor cell-of-origin based on the cone-like phenotype of retinoblastoma cells and the cone precursors' proliferative responses to RB loss; however, the appearance of the earliest retinoblastomas in the inner retina suggested an inner retina (non-cone) origin. Here, we examined retinal cell responses to RB loss in intact retina cultures in order to observe how retinoblastomas form.
Methods: Cultured retinae were transduced with RB-directed or control shRNAs and with fluorescent markers of transduction and L/M cone maturation. Retinae were live-imaged with 2-photon videomicroscopy, immunostained for cell-type and proliferation markers, and dissociated for single cell transcriptome profiling via scRNA-seq.
Results: RB depletion caused cone precursor cell cycle entry, proliferation, withdrawal to a retinoma-like state, and emergence of retinoblastoma-like masses. Many RB-depleted cone precursors migrated from the outer nuclear layer to the outer plexiform layer. Only maturing (cone arrestin+) cone precursors entered the cell cycle, yet the most mature cone precursors with highest L/M-opsin were refractory. scRNA-seq segregated immature, early-maturing, and late-maturing cone precursor populations and revealed that only RB-depleted early-maturing cone precursors proliferated.
Conclusions: RB-depleted early-maturing cone precursors have properties of the retinoblastoma cell-of-origin, including their migration towards the inner retina, proliferation, and genesis of retinoma- and retinoblastoma-like masses. Further characterization of this population may enable novel retinoblastoma treatment and prevention approaches.

Presentation Title: Non invasive diagnosis of retinoblastoma using cell free DNA
Authors: Manoj Parulekar¹, Amy Gerrish², Stephanie Allen³, Edward Stone⁴, Samuel Clokie⁴, John Ainsworth³, Carol Hitchcott⁴, Maureen McCalla⁴, Helen Jenkinson⁴, Isabel Colmenero⁴, Trevor Cole⁴
¹Birmingham Women's and Children's Hospital, Birmingham, United Kingdom. ²Birmingham Women's and Children's Hospital, Birmingham, United Kingdom. ³Birmingham Women's and Children's Hospital, Birmingham, United Kingdom.
Abstract: Purpose: To develop and validate a minimally invasive test for detecting retinoblastoma mutation in unilateral retinoblastoma. Distinguishing between somatic and germline retinoblastoma is crucial. An important strategy to confirm the somatic nature of the tumour includes identifying mutations in tumour tissue, and excluding the from blood DNA. Modern eye saving treatment (systemic, intra-arterial and intra-vitreal) has resulted in fewer enucleations, and tumour tissue is not always available. Intravitreal techniques involve aspiration of aqueous humour, providing a novel sample source for analysis. Method: Cell free (cf)DNA in aqueous humour (AH) fluid of eyes affected with retinoblastoma was analysed using next generation sequencing.
Results: The results obtained with fluid from enucleated eyes were concordant with tumour tissue in all 10 cases. In addition, AH analysis from 2 patients undergoing IVC successfully identified somatic variants in both cases.
Conclusion: AH fluid is a promising source of tumour-derived DNA in retinoblastoma for analysis. Testing for DNA in AH samples can help confirm somatic cases in a minimally invasive fashion, reducing the need for screening family members.
Presentation Title: Prognostic information for mosaic and high penetrant carriers of RB1 mutations
Authors: M. Reddy1,2, Mussa Butt1, Anne-Marie Hinds2, Catrina Duncan1,3, Tanzina Chowdhury3,1, Elizabeth Price1, Mandeep Sagoo1,2, Zerrin Onadim1
1Royal London Hospital, Barts Health NHS Trust, London, United Kingdom. 2Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom. 3Great Ormond St Hospital NHS Foundation Trust, London, United Kingdom

Abstract: PURPOSEThe role of mosaicism in Retinoblastoma (Rb) is increasingly being recognised as molecular genetic tests become more sensitive. Providing information regarding laterality and tumor number for mosaic and heterozygous RB1 mutation carriers would be helpful for clinicians and parents. METHODS A retrospective analysis of mosaic and heterozygous RB1 mutation carriers (low penetrant [LP] and high penetrant [HP]) from 1992 to 2017 was conducted. Tumor number per eye was assessed in patients classified with A, B and C tumors using the International Intraocular Retinoblastoma Classification system. Patients with D or E group eyes were assessed based upon age at diagnosis. RESULTS Data were analysed for 107 patients: 64 were full germline familial patients (53 HP and 11 LP) and 43 mosaic patients. 25% of high penetrant patients were unilateral at presentation and 9 of 13 (69%) developed tumors in their previously unaffected eye. 72% of mosaic patients were unilateral and only 1 of 31 (3%) developed tumors in their unaffected eye. Age at diagnosis was higher in mosaic patients (median 16 months range 2-117) than HP patients (median 7 range 2-33) (p<0.001). Tumor number per eye was lower in mosaic patients (median 1.5 tumors range 1-6) than highly penetrant patients (median 3 range 1-8) (p=0.009). There were only 3 gaugeable eyes regarding tumor number with LP. CONCLUSION This is the first study to provide prognostic information in the form of tumor number. Children with mosaicism have fewer tumors in eyes presenting with Rb compared to HP carriers.

Presentation Title: Genomic Analysis of Aqueous Humor cell-free DNA in Retinoblastoma Predicts Eye Salvage: The Surrogate Tumor Biopsy for Retinoblastoma
Authors: Jesse L Berry1, Liya Xu2, Irsan Kooi2, A. Linn Murphree1, Rishvanth K Prabakar4, Mark Reid1, Kevin Stachelek1, Bao Han A Le1, Lisa Welter2, Bibiana J Reiser1, Patricia Chevez-Barrios5, Rima Jubran1, Thomas Lee1, Jonathan W Kim1, Peter Kuhn3, David Cobrinik1, James Hicks2
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Abstract: Purpose: To identify tumor-derived cell-free DNA (cfDNA) in the aqueous humor (AH) of retinoblastoma eyes and correlate somatic chromosomal copy number alterations (SCNAs) in the AH with clinical outcomes, specifically eye salvage.

Methods: AH was extracted via paracentesis during intravitreal injection of chemotherapy or enucleation. CfDNA was isolated; shallow whole genome sequencing performed to assess tumor DNA fractions and highly recurrent SCNAs including gain of 1q, 2p, 6p, loss of 13q, 16q and focal MYCN amplification. Clinical features, treatment regimen and eye salvage were recorded. Clinical analysis was retrospective.

Results: Sixty-three samples of AH from 29 eyes of 26 patients were evaluated; 13 eyes were enucleated and 16 were salvaged. The presence of detectable SCNAs was 92% in enucleated eyes versus 38% in salvaged eyes (p=0.006). 6p gain was the most common SCNA found in 77% of enucleated versus 25% of salvaged eyes (p=0.0092). 6p gain was associated with a ten-fold increased odds of enucleation (OR=10.95%;CI:1.8-55.6). The mean amplitude of 6p gain was 1.47 in enucleated versus 1.07 in salvaged eyes (p=0.001). The probability of ocular survival was higher in eyes without detectable SCNAs in the AH (p=0.0028).

Conclusions: This is the first study to show that clinical outcomes correlate with highly-recurrent SCNAs in the AH from retinoblastoma eyes. These preliminary results suggest that AH can reliably serve as a surrogate to tumor
biopsy. This novel approach may provide additional objective information beyond clinical classification to determine the likelihood of globe salvage for patients with advanced retinoblastoma.

Presentation Title: Therapeutic Targeting of the RB1 Pathway in Retinoblastoma with the Oncolytic Adenovirus VCN-01

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Abstract: Purpose. Retinoblastoma is initiated upon the homozygous disruption of the RB1 gene in developing retinal cells. VCN-01 is an oncolytic adenovirus designed to replicate selectively in tumor cells with high free levels of E2F-1 transcription factor due to a dysfunctional retinoblastoma pathway. Our purpose was to evaluate the activity of VCN-01 against retinoblastoma.Methods. We studied the expression of E2F-1 in enucleated eyes. We performed in vivo and in vivo assays to study the activity of VCN-01 against human retinoblastoma. We evaluated the distribution and toxicity of VCN-01 upon intravitreous injection in juvenile rabbits. We designed and initiated a Phase 1 clinical trial in children with refractory retinoblastoma (NCT03284268).Results. 94% (31 out of 33) of human tumors expressed E2F-1 in tumor cells. In vitro, VCN-01 killed multiple patient-derived retinoblastomas. In mice, administration of VCN-01 in intravitreous xenografts induced tumor necrosis, improved ocular survival compared to chemotherapy and prevented metastasis. VCN-01 did not replicate in rabbit retinas, induced minor local side effects and was shed at low and transient levels in blood. Two patients were treated with two intravitreous injections of VCN-01 separated by 14 days. The patients did not present systemic complications, local inflammation was found, and antitumor activity was observed. Conclusions. VCN-01 shows preclinical efficacy in retinoblastoma and has been successfully translated to a first-in-children Phase I trial.

Presentation Title: The Histone Methyltransferase NSD2/WHSC1 is Selectively Expressed in Retinoblastoma and Positively Regulates its Growth

Authors: Zhenhua Zou, Rajesh Rao

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Abstract: PURPOSE: Retinoblastoma (RB) is the most common primary intraocular cancer in children, and the third most common cancer overall in infants. No molecular-targeted therapy for this potentially deadly tumor exists. We recently showed that EZH2, a histone methyltransferase (HMT), is highly expressed in RB and its trimethyl catalytic activity on histone H3 lysine 27 (H3K27me3) is required for RB cell survival (Laboratory Investigation95, 1278–1290 (2015)). Since EZH2 promotes expression of NSD2/WHSC1, an HMT for H3K36me, we reasoned that NSD2 might regulate human RB tumorigenesis.METHODS: The expression levels of NSD2 in 43 primary enucleated human retinoblastoma specimens, and two RB (Y79 and Weri-Rb1) cell lines were compared by RT-PCR, immunohistochemistry and Western blotting. shRNA was used to knockdown NSD2, and changes in histone modifications were verified with specific antibodies. The consequences of NSD2 knockdown were detected in ATP-based cell proliferation assay, PI/Annexin V-based apoptosis assay and PI/5'EDU-based cell cycle assay. RESULTS: NSD2 was detected in tumor cells of all 43 analyzed human RB specimens, but not normal retina. To assess the role of NSD2 in RB cell viability and growth, we used shNSD2 in RB cell lines and found that NSD2 accelerates S-phase progression in RB cell cycle and inhibits apoptosis. Using shRNA, we found that NSD2 regulates H3K36me2, H4K20me2 and H3K27me3 with different patterns in RB cell lines. CONCLUSION: NSD2 is a histopathologic biomarker for human RB and shows promise as a novel epigenetic target for RB.
Presentation Title: Spontaneous regression of malignant teratoid medulloepithelioma with massive maxillary and skull base recurrence
Authors: Dan Gombos MD FACS1,2,3,4, Daniel Chelius MD FACS2,3, Mehmet Okcu MD PhD2,3, Patricia Chevez-Barrios MD1,2
1MD Anderson Cancer Center, Houston, USA. 2Texas Children’s Hospital, Houston, USA. 3Baylor College of Medicine, Houston, USA. 4The Methodist Institute, Houston, USA
Abstract: Purpose: To describe a case of recurrent malignant teratoid medulloepithelioma following evisceration and subsequent regression. Methods: Single case report. Results: An 18 month old arab male from the gulf presented with leukocoria. Subsequent hyphema, glaucoma and retinal detachment was treated by vitrectomy. Uncontrolled glaucoma led to evisceration and placement of an implant at age 5. Modified enucleation followed three years later with presentation at our center. Pathology confirmed malignant teratoid medulloepithelioma with infiltration of the surrounding tissue & vasculature. MRI was suggestive of residual disease. The child underwent exenteration of the residual orbital contents including biopsy of adjacent bone. Final pathology was negative for malignancy. The orbital defect was reconstructed with a free flap and no additional adjuvant therapy was administered. Five months later massive recurrence was detected in the maxillary sinus and skull base. Conclusions: Malignant teratoid medulloepithelioma may recur despite complete regression on pathology. The risk is highest in patients who undergo open globe procedures.

Presentation Title: Orbital Angiomyxoid Tumor in an Infant
Authors: Mrittika Sen, Sumeet Lahane, Kaustubh Mulay, Vijay Reddy, Santosh Honavar
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Abstract: Purpose: To report a rare case of an orbital Plexiform Angiomyxoid Tumor in an infant. Method: A retrospective case report. Results: A four-month-old boy presented with progressive abaxial proptosis from the right eye for 2 months. Examination revealed a firm, irregular mass in the superolateral quadrant of the orbit. CT scan showed a cystic mass in the superotemporal orbit with areas of calcification and erosion of the roof. Initial incisional biopsy showed features of intraosseous myxoma. An excisional biopsy was performed with removal of all the involved bone. Final histopathology showed with stellate and spindle shaped cells with myxoid stroma, rich in thin walled vascular channels, suggestive of low grade angiomyxoid tumour. The cells were positive for smooth muscle actin and vimentin and negative for CD34, S100, EMA, myogenin and desmin. The child was treated with stereotactic external beam radiotherapy (4200 cGy in 14 fractions). The child is free of local tumor recurrence and systemic metastasis at 1 year follow-up. Conclusion: Angiomyxoid tumour of the orbit is extremely rare and is reported in the third to fourth decade. This is an unusual presentation in an infant. Complete excision with adjuvant radiotherapy seems to be a reasonable treatment option.

Presentation Title: Minimally Disseminated Disease And Outcome In Overt Orbital Retinoblastoma
Authors: Rosario Aschero1, Ana Torbidoni1, Claudia Sampor1, Viviana Laurent1, Santiago Zugbi1, Ursula Winter1, Fabiana Lubiniecki1, Daniel Alonso2, Paula Schaiquevich1,3, Guillermo Chantada1,3
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Abstract: Purpose: To report the occurrence of minimally disseminated disease (MDD) and outcome in a series of overt orbital retinoblastoma. Methods: This is a retrospective study of patients with overt orbital retinoblastoma.
diagnosed from 2007 to 2017. In all cases, bone marrow (BM) and cerebrospinal fluid (CSF) were collected to evaluate MDD. MDD was evaluated using Cone-rod homeobox (CRX) and/or beta-1,4-N-acetyl-galactosaminyltransferase 1 (GD2 synthase).

Results: During the study period of 363 newly diagnosed cases, 11 patients were diagnosed with overt orbital retinoblastoma. One case was excluded since MDD evaluations were not done, so 10 patients were analyzed in this report. Five cases (50%) showed overt orbital retinoblastoma at diagnosis and 5 upon relapse. MDD was detected in four cases (one in the bone marrow, two in the CSF and in one case in both sites). All patients received conventional chemotherapy following previously published protocols. Four patients received orbital radiotherapy. Seven patients showed tumor relapse or progression (6 cases included CSF and 1 case had systemic relapse), all of them died after this event. Three patients remain in continuous complete remission. There was no apparent correlation between MDD and final outcome.

Conclusions: Overt orbital retinoblastoma was uncommon in our setting, representing a heterogeneous group with general poor outcome. MDD was detected in 40% of the cases highlighting the need for intensive treatment with both systemic and CNS coverage. This study was partially supported by the Fund for Ophthalmic Knowledge (NY) and the Fundacion Natalia Flexer (Argentina).

Presentation Title: Optical coherence tomography in Retinoblastoma: Diagnosis of massive choroidal invasion
Authors: Sameh Soliman, Leslie Mackeen, Cynthia Hawkins, Brenda Gallie
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Abstract: Purpose: To describe the optical coherence tomography (OCT) features of choroidal invasion in a unilateral eye with refractory retinoblastoma with clear view of the optic nerve and fovea. Tumor extension into choroid occurred after 4 cycles of intra-arterial chemotherapy, 4 cycles of systemic chemotherapy and multiple laser sessions over 1 year of active treatment.

Methods: A rapid tumor regrowth was observed within a white-scarred area 5 weeks after previous examination and laser treatment. The recurrence did not involve the optic nerve head or vitreous seeds. It was 1.5 mm elevation on B-scan. OCT was performed to assess tumor features.

Results: OCT showed tumor within the retina in a dome shaped configuration suggestive of active tumor growth. The hyper-reflective retinal pigment epithelium (RPE) was elevated and irregular. A ball-growth under the RPE measured to be around 5x6 mm in diameter and 0.7 mm in elevation, highly suggestive of massive choroidal invasion. Using both horizontal and vertical OCT scans, a volumetric map of the suspected choroidal invasion was constructed. In retrospect, the previous OCT showed a smaller active tumor with interruption of the underlying RPE line without a distinct sub-retinal growth. Enucleation was performed with parental consent. Histopathology confirmed massive (>3 mm) choroidal invasion, pathological stage pT3a (TNMH 8th ed.). The child received 4 cycles adjuvant systemic chemotherapy.

Conclusion: OCT was critical in recognition of choroidal extension of retinoblastoma after treatment.
Presentation Title: Global Retinoblastoma Presentation 2017

Authors: Ido Didi Fabian1, Andrew Stacey2, Covadonga Bascaran1, Marcia Zondervan1, Allen Foster1, Richard Bowman1

1London School of Hygiene and Tropical Medicine, London, United Kingdom. 2Department of Ophthalmology, University of Washington, Seattle, Washington, USA

Abstract: Purpose: To collect baseline clinical information on the mode of presentation of patients with retinoblastoma (Rb) across the world in 2017. Methods: In 2017/8, Rb centers from across the world were recruited to join a 1-year retrospective study. Inclusion criteria were treatment-naive Rb patients that presented to participating centers from January-December 2017. Parameters included presentation age, sex, laterality, country of origin, Rb family history, first symptom and sign, clinical examination findings, and primary treatment offered. Results: During the study period, 227 centers from 123 countries submitted data on 3,504 patients who resided in 147 countries (Latin America and the Caribbean’s (8%), North America (4%), Europe (15%), Asia (51%), Africa (23%) and Oceania (<1%)). Data integrity remained robust with >95% of the parameters submitted for 90% of the children. The most common presenting sign was leukocoria (n=2,099 (62%)), mean presentation age was 26.8 ±23.7 months, 1,095 (32%) of children had bilateral disease, 158 (5%) family history of Rb, 726 (22%) extraocular disease, 236 (7%) metastatic spread and 46 (1%) died at or soon after presentation. Over 5% (n=195) of patients travelled across country borders for treatment, and treatment refusal was recorded in 7% (n=225). Conclusion: This study, which represent nearly half of the estimated annual global incidence of Rb during a calendar year, is the first to characterize Rb presentation on a global scale. The network herein created, in which approximately 75% of the world’s countries are represented, may be used for further large-scale multinational collaborations.

Presentation Title: Statistical Analysis of the Global Retinoblastoma Presentation 2017 Cross-Section: All Children are Created Equal, but Equality Ends There

Authors: Andrew Stacey1, Covadonga Bascaran2, Marcia Zondervan2, Allen Foster2, Richard Bowman2, Ido Didi Fabian2

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Abstract: Purpose: Retinoblastoma (Rb) outcomes have improved in recent years in high-income countries, however this improvement has not been seen in most low and middle-income countries (LMICs). The aim of this study is to investigate the mode of Rb presentation globally over a single year according to national income level. Methods: A 1-year cross-sectional analysis of the presentation of treatment-naive Rb patients that presented to participating centers during 2017. Data were submitted by centers from January-June 2018. Associations between clinical parameters at presentation and national income levels were explored. Results: The cohort included 3,105 children, 437 (14%) from low-income, 2,143 (69%) from middle-income and 525 (17%) from high-income countries. A statistically significant correlation was found when a country’s income level was compared to a number of factors (low, lower-middle, upper-middle and high-income countries, respectively; p<0.001): presentation age (unilateral Rb: 37, 33, 29 and 26 months; bilateral Rb: 23, 21, 15 and 11 months); proportion of familial Rb (2%, 4%, 5% and 9%), extraocular disease (49%, 27%, 10% and 2%), metastatic spread (17%, 8%, 7% and <1%), and death at presentation (28 cases, all from LMICs). Conclusions: Children from LMICs (>80% of the cohort) present at a later age, with more advanced disease, and are at higher risk of death from metastatic disease. There
was significantly less familial disease in LMICs possibly due to late presentation resulting in death. Given that Rb is a curable disease, these data are alarming, necessitating immediate intervention at local and global levels.

Presentation Title: The impact of monocular vision on motor function and quality of life in survivors of retinoblastoma
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Abstract: Purpose: Monocular vision has been found to have a negative effect on children’s motion processing and motor functions. Yet, the knowledge of the motor function of survivors of retinoblastoma (RB) with monocular vision (due to enucleation, for example) is limited. This study examined the motor function and its relationship to visual-related and health-related quality of life (HRQOL) in survivors of RB with monocular vision. Methods: Parents of 27 survivors of RB, who underwent an enucleation of one eye resulting in monocular vision, and of 21 typically developing children between the ages of 6–12, were administered questionnaires relating to their children’s motor function (DCDQ), as well as vision-related function (CVFQ) and HRQOL (PedsQL). Results: Of the 27 survivors of RB, 7 (25.6%) were found to have difficulties in motor functions, compared to 1 (4.8%) child in the control group. The difficulties were mainly in daily function requiring control during movement, including jumping, running, and ball playing. Additionally, significant correlations were found between motor functions and children’s QOL. Finally, survivors of RB with monocular vision were found to have lower QOL, specifically Physical- and School-related QOL. Conclusion: Survivors of RB who have monocular vision are at a higher risk of decreased motor function leading to lower QOL. These results point to a need for ongoing assessment of survivors of RB to allow timely detection of motor deficits and to institute appropriate therapeutic interventions.

Presentation Title: Globe salvage in retinoblastoma patients treated with intra-arterial chemotherapy, six years' experience in Medellin, Colombia
Authors: Maria Gonzalez Alviar1, Martha Gaviria Bravo1, Andrea Correa Acosta1, Mariana Lopez Posada1, Sergio Vargas1, Carlos Diaz1, Oscar Villada Ochoa1,2
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Abstract: PURPOSE To summarize our outcomes of intra-arterial chemotherapy (IAC) in retinoblastoma in a developing country METHODSThis is a retrospective, single institution review of all retinoblastoma eyes treated with IAC at San Vicente Hospital, between August 2011 and June 2017. The Kaplan-Meier method was used to estimate globe salvage. RESULTS This retrospective review included 77 retinoblastoma eyes of 66 patients treated with IAC. There were 386 chemotherapy injections (median, five per eye). The majority of our patients were classified D and E groups (61.13%). Bilateral disease was seen in 62% and the treatment was secondary in 59.7%. The median follow-up was 27 months (range 15-55 months). 24 patients had one eye enucleated and the eye was salvaged in 20 of the patients. Overall ocular survival was 80.52%, 58.33% for ICRB group E, 71.42% for ICRB group D, and 100% for ICRB groups A, B and C. There were no treatment-related deaths or ophthalmic artery occlusion CONCLUSION In developing countries where late diagnosis and difficult health system access are the main causes of enucleation, IAC has become a good and safe option to preserve eyes with advanced retinoblastoma or recurrent and persistent disease.

Presentation Title: Management of unilateral intraocular retinoblastoma in sub-Saharan Africa: Mali experience
Authors: TRAORE FOUSSEYNI1, SYLLA FATOU2, TRAORE CHEIK B3, TOGO BOUBACAR1, DESJARDINS LAURENCE4, BEY PIERRE5
Abstract: Purpose: Retinoblastoma (RB) is the most common malignant intraocular tumor in children and the unilateral form represents 70% of cases. Enucleation at early stage of disease may improve the survival rate in developing countries. Patients and method: It was a prospective study from 01/11/2011 to 31/12/2015, aimed to evaluate treatment result of intraocular RB, rehabilitation of orbits after enucleation and survival rates (OS and EFS) in all patients. Were included Intraocular unilateral RB without signs of clinical and radiological extraocular extension. At admission all patients received ophthalmological and oncological assessment. The Tumors were classified according to the IIROC classification. Patients were treated according to the guidelines of the French-African pediatric oncology (GFAOP-RB1). Results: Fifty patients were included. The median age was 30 months. The sex ratio was 0.6. The majority of patients were Malians (84%). The first symptoms were leucocoria (88%) and strabismus (12%). According to the IIROC classification, group E patients represented 64%, group D (28%) and group B (8%). The enucleation rate was 84%. Twelve percent of patients received primary enucleation. Thirty-five patients (70%) received neoadjuvant chemotherapy. We recorded 38% hematological toxicity and 4% toxic death. The remission rate was 78%, with median follow up of 2.3 years. Conclusion: Intraocular RB remains a diagnostic challenge for the physicians in sub-Saharan Africa. The enucleation decision must not be delayed because the conservative treatment is inaccessible. Keywords: Intraocular retinoblastoma, enucleation, Mali.

Presentation Title: Outcome of 100 intraocular topotecan injections for retinoblastoma in 31 eyes– A 5 years Prospective Study in Asians.

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Abstract: Purpose: To evaluate the efficacy and outcome of intravitreal and intracameral topotecan in eyes with retinoblastoma (RB). Method: This multicenter, prospective, non-randomized, interventional study was conducted in a tertiary referral center for RB in India and China in patients who received intraocular topotecan from September 2013 to 2018 with more than 6 months follow up. Primary outcome assessed was disease regression and complications. Results: Of the 40 eyes that received intraocular topotecan injection, 31 were included in the study and, 8 patients were one eyed. Primary management was intra-arterial and intravenous chemotherapy in 52% (n=16) and 48% (n=15) patients respectively. Of the total 100 injections administered, 97 injections were intravitreal for recurrent vitreous seeds (n=13), persistent vitreous seeds (n=12), recurrent subretinal seeds (n=4), recurrent endophytic tumor (n=1) and both vitreous and subretinal seeds (n=1). One eye received 3 intracameral topotecan injections for anterior chamber seeds (ACS). Vitreous seeds were classified as spherules (n=12), dusting (n=1), clouds (n=1) and mixed (n=12). At a mean follow up of 14 ± 10 (median= 11; range= 6 to 51) months, there was complete regression in all eyes (100%). The mean injections for complete regression was 3±2 (median=2.5; range= 1 to 12). Most common complication was focal subconjunctival hemorrhage (25%) followed by conjunctival scarring (13%) and epithelial inclusion cyst (3%). Conclusion: Intra-ocular topotecan injection is an alternative to melphalan and, is safe and effective for VS and/or SRS and ACS in RB. Our study showed promising results with 100 % regression of the disease.
Presentation Title: Neonatal Retinoblastoma: clinical data and therapeutic outcome.
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Abstract: Purpose: To identify patients with retinoblastoma diagnosed at the age of 1 month and describe their clinical features and treatment outcome. Methods: A retrospective study of 715 cases of retinoblastoma diagnosed and treated at the Retinoblastoma Referral Center University of Siena between 1980 and 2018 has been performed. Results: Thirty-six patients diagnosed within the first month of life have been identified. The majority of them had a bilateral form (28/36); among the unilateral ones some of them developed metachronous tumors in the fellow eye. Family history was positive in 47% of them. The follow-up range was 1 to 37 years. Management included early enucleation, systemic chemotherapy, bridge chemotherapy followed by intraarterial chemotherapy and focal treatments. None of them developed metastatic disease or second tumors. Conclusions: Family history prompted early diagnosis in most cases. However, early diagnosis does not always mean early stage of the disease and better prognosis.

Presentation Title: Association of RB1 mutation type and the age at detection of the first retinoblastoma tumor in children at risk for familial retinoblastoma.
Authors: Annette Moll¹, Milo van Hoofen Wijsard¹, Armida Fabius¹, Erika Maka², Vicktoria Vishnevskia-Dai³, Rejin Kebudi⁴, Samuray Tuncer⁴, Theodore Hadjistilianou⁵, Elisa Gelli⁵, Carol Shields⁶, Kareem Sioufi⁶, Theodore Hadjistilianou⁵, Elisa Gelli⁵, Carol Shields⁶, Kareem Sioufi⁶, Francis Munier⁷, Livia Lumbroso⁸, Claude Houdayer⁸, Kalle Nummi⁹, Tero Kivela⁹
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Abstract: Purpose: If RB1 mutation type influences the time of Rb tumor presentation, personalized screening based on germline mutation could reduce unnecessary exposure to anesthesia. The aim of this study is to explore the genotype-phenotype relation between the germline RB1 mutations and the age at detection of the first Rb tumor. Methods: All patients at risk for familial Rb who were screened from birth and with a known RB1 gene mutation from nine study centers were included in this study. Patients were categorized by mutational type based on its effect on the RB1 protein: nonsense, frameshift, splice site, missense, gross deletions/insertions and chromosomal rearrangements and we compared age at first Rb tumor between the groups. Results: One hundred-forty-six (146) patients from 113 families were included in this study. The median age at diagnosis of the first tumor for all familial Rb patients was 25 days (interquartile range (IQR) 8-88). Per mutational type the age at time of first tumor has a median of 16 days (IQR 6.7-37.5) for nonsense, 40 days (IQR 16.0-197.0) for splice site-, 40 days (IQR 13.3-76.0) for frameshift- and 104 days (IQR 24.0-219.5) for missense mutations, 17.5 days (IQR 7.3-101.3) for gross deletions/insertions and 24 days (IQR 11.5-218.0) for chromosomal rearrangements. ANOVA on the log transformed data showed a significant difference between mutational types (p=0.01). Conclusion: Preliminary analysis shows a difference in a patients’ age at Rb diagnosis between RB1 mutational groups.
Presentation Title: Quantity and quality of optic nerve invasion matters in Retinoblastoma

Authors: Patricia Chevez-Barrios\textsuperscript{1,2}, Claudia Prospero Ponce\textsuperscript{1}, Murali Chintagumpala\textsuperscript{3,2}, Stephen Chen\textsuperscript{4,2}, Frank Lin\textsuperscript{3,2}, Cynthia Herzong\textsuperscript{5,2}, Jonathan Kim\textsuperscript{6,7}, Dan Gombos\textsuperscript{5,2}

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Abstract: Purpose: To investigate the features that may impose higher risk for CNS recurrence in this population.

Methods: Retrospective study of consecutive enucleated eyes from 2015-2018 to investigate the type of tumor invasion and outcome in these patients.

Results: We found 108 cases during this period and of these 62 had no optic nerve invasion, 32 had prelaminar or laminar optic nerve invasion and 14 had postlaminar optic nerve invasion (PLONI). All cases had at least 3 mm of negative optic nerve posterior to the invasion with negative ON margin. Of those with PLONI 6 had less than 1.5 mm of invasion, 1 size couldn’t be measured and 7 had more than 1.5 of invasion and 2 had tumor impinging into the meninges but not visible tumor into the meninges. Of this last category one patient recurred and died of disease in spite of intense chemotherapy, radiation and bone marrow transplantation. We propose that the anatomic piercing of the meningeal vessels create a pathway for the tumor cells into the meninges without the tumor actually breaking through the meningeal collagenous tissue.

Conclusion: Examination of tumor characteristics in posterior laminar optic nerve invasion is highly recommended when considering adjuvant therapeutic strategies for high risk retinoblastoma.

Presentation Title: Large tumor size criteria for Group D and E eyes in the International Classification System for Retinoblastoma: effects on rates of globe salvage and high-risk histopathologic features.

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Abstract: Purpose: To determine the significance of large tumor size as a criteria for classifying advanced intraocular retinoblastoma, analyzing rates of globe salvage and high risk histopathologic features.

Methods: Retrospective chart review of 212 eyes diagnosed with Group D (111 eyes) or Group E (101 eyes) retinoblastoma in at least one eye from January 1, 2006 to December 31, 2016 using the Los Angeles (LA) Classification System. The 111 Group D tumors were then reclassified to Group E using 10,12,14,16,18 mm tumor size criteria.

Results: For eyes in the LA classification, 66.7% of Group D and 10.5% of Group E eyes which underwent globe preservation therapy avoided enucleation or radiotherapy (p<0.0001) (median follow-up of 33.0 months); 8.5% of Group D enucleated globes had high-risk histopathologic features while 26.3% of Group E globes had high risk features (p=0.0065). When Group D eyes with tumors meeting the size criteria were reclassified to Group E, 65.7-74.4% of Group D eyes and 16.1-36.7% of Group E eyes avoided enucleation or radiotherapy. Applying the tumor size criteria, 0-10.9% of Group D and 20.7-34.0% of Group E eyes had high-risk histopathologic features.

Conclusion: Our retrospective analysis suggests that large tumor size criteria for Group E retinoblastoma has no clinical basis, given that the LA classification system provided the greatest separation in globe salvage rates between Group D and E eyes. Similarly, the LA classification system was able to show a statistically significant difference in the rates of high-risk histopathologic features between Group D and E eyes.

Presentation Title: Clinically preventable causes of unfavourable retinoblastoma treatment outcomes

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Abstract: Purpose: The primary aim was to identify the frequency of unfavourable outcomes for retinoblastoma. The secondary aim was to determine if any unfavourable outcomes were preventable.

Methods: We conducted a
retrospective, non-comparative, single-institution review for children diagnosed with retinoblastoma and exclusively treated at SickKids (1/1/2000-13/7/2015). Unfavourable outcomes were defined as death, metastasis (including extraocular extension), use of external beam radiation therapy (EBRT) and enucleation. Preventable causes were factors that could have avoided an unfavourable outcome (e.g. by a change in practice). Causes were reviewed by a multidisciplinary committee. Main outcome measures were frequency of unfavourable outcomes and preventable causes.

Results: The study included 197 patients (120 unilateral, 77 bilateral, 274 eyes). There were 167 patients with at least 1 unfavourable outcome. Unfavourable outcomes included: 7 deaths (7/197, 3.5%); 8 patients with metastasis (8/197, 4.1%); 8 patients treated with EBRT (8/197, 4.1%) and 138 primary (138/274 50%) and 28 secondary (28/136, 20%) enucleations. Four patients had preventable causes of unfavourable outcomes. Two had metastasis leading to death; 1 had extraocular extension; and 1 underwent secondary enucleation. One death was associated with a failure of pathology to detect high-risk features of metastasis. One death was related to parental refusal of enucleation. The extraocular extension was related to scleral invasion, potentially facilitated by aggressive focal therapy. The enucleation was related to mismanagement of a treatment complication.

Conclusion: Comprehensive review of unfavourable outcomes for retinoblastoma can identify areas for practice change.

Presentation Title: Retinoblastoma: Do Shifting Treatment Trends Increase Metastatic/Mortality Risk in Advanced Retinoblastoma – An evaluation of 3 decades of advanced treatment

Authors: Timothy Murray
Miami Ocular Oncology and Retina, Miami, USA. Miami Children’s Hospital, Miami, USA

Abstract: Purpose: The purpose of this study was to evaluate shifting treatment trends at a major pediatric ocular oncology service focused on enucleation, metastasis, and mortality in advanced retinoblastoma treated by a single oncology practice (MOOR).

Methods: An IRB approved, retrospective review of 372 patients with Group D/E retinoblastoma (RE Stage Va/Vb) with outcomes analysis. All children had a minimum followup of 12 months. Patients were stratified by primary therapy and evaluated for need for supplemental treatment.

Results: Of the 497 eyes, 3/398 group D eyes were treated with primary enucleation while 22% of group E eyes were primarily enucleated (21/99 eyes). From 1991 to 2010 systemic multi-drug chemotherapy with CVE was the primary therapy. From 2011 to the present, eyes were treated with intra-arterial chemotherapy if vascular access was possible. IAC eyes were treated with 6 cycles. If tumor response was ongoing but tumor activity was present additional IAC was performed until tumor stability was documented. Two children with Group D advanced retinoblastoma developed metastatic disease and died (1/97, 1.03% IAC/1/275, 0.37% Systemic Chemotherapy). Secondary enucleation rates declined to approximately 3%, p<.01. Trilateral retinoblastoma occurred in 3/372 patients over the study window (3/372, 0.08%).

Conclusions: Advanced retinoblastoma treatment varies greatly within both the US and internationally. Retinoblastoma remains a life-threatening malignancy, but metastatic rates appear to be less than 1% in eyes presenting without evidence of extraocular disease. Shifting trends in treatment have lowered systemic treatment morbidity and decreased enucleation rates.
Presentation Title: Systemic adjuvant chemotherapy for advanced malignant ocular medulloepithelioma
Authors: Mandeep Sagoo1,2,3, Ibrahim Sheriff1, Esin Karaa1,4, Tanzina Chowdhury1,5, Irene Scheimberg1,4, Catriona Duncan1,5, M Reddy1,2
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Abstract: Purpose: Ocular medulloepithelioma (diktyoma) is a rare paediatric tumor of the non-pigmented ciliary epithelium, which can be teratoid and even malignant. Smaller tumors can be treated with brachytherapy but larger ones require enucleation or exenteration, and can invade locally and metastasise. Adjuvant chemotherapy can be given in advanced cases, but the indications and regimens remain to be defined.

Methods: This was a retrospective case series of advanced ocular medulloepithelioma treated with enucleation where brachytherapy was unsuitable for local tumor control and included those needing adjuvant systemic vincristine, etoposide and carboplatin. Outcomes were histopathology characteristics, chemotherapy regimen, recurrence, metastasis and survival.

Results: Between March 2010 and June 2017, four male patients (mean age 31 months) underwent enucleation for advanced ocular medulloepithelioma. Adjuvant chemotherapy was commenced in 3 patients (75%) due to malignant features on histopathology including rosettes (75%), numerous mitoses (75%) and extension into the choroid (50%), cornea (50%) or sclera (25%). Two patients (50%) received 4 cycles of chemotherapy and one patient (25%) received 6 cycles. Two patients (50%) suffered febrile neutropenia with positive blood cultures and one patient (25%) suffered chemotherapy-induced thrombocytopenia. With a mean follow-up time of 40 months (median 30 months, range 7-94 months), none of the patients have had recurrence, metastasis or death from the tumor.

Conclusion: This series reports the indications and management of advanced malignant ocular medulloepithelioma. The use of systemic vincristine, etoposide and carboplatin as an adjuvant for advanced tumors with malignant features is effective in preventing metastatic spread.

Presentation Title: Lessons Learnt In Management Of Advance Orbital Retinoblastoma
Authors: Shabana Chaudhry
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Abstract: Purpose: To identify the safe protocols in the management of advance orbital retinoblastoma

Method: Fifteen patients with age ranged from 2.5 years to 9 years presented in eye OPD in Mayo Hospital Lahore, Pakistan from 1st Jan 2018 till 30th September 2018, with proptosis or fungating ocular mass. Nine patients underwent enucleation, 4-patients had exenteration, 2-children with intracranial extensions sent for neurosurgical intervention. Three out of 15 children had completed chemotherapy in 2016. On presentation B-scan was done. EUA was planned in all patients. Pre-op assessment by pediatrician, MRI orbit & brain with contrast, Bone marrow biopsy & Bone scan was done where possible. 2-3 cycles of systemic chemotherapy was given before surgical intervention in all patients.

Result: Nine patients who undergone enucleation had wide range of histopathological involvement underwent post enucleation 6-9 cycles of chemotherapy depending on extension of orbital tissues involved. At time of exenteration 3 out of 4 patients had orbital wall erosion that was not been detected on MRI. Two patients who had bony erosion died of meningitis within one month of surgery. One patient abandoned therapy. One patient with intracranial extension develops lower limb paralysis & a phthisical eye. Any surgical intervention was withheld in this patient.

Conclusion: Lifelong follow-up criteria should be devised in
developing countries according to their local circumstances. CT-scan is a better option before planning exenteration to identify not only extension of orbital disease but to rule out bony erosion.

**Presentation Title:** Intensive Multi-Modality Therapy For Extra-Ocular Retinoblastoma (Rb): A Children’s Oncology Group (Cog) Trial (Aret0321)  
**Authors:** Ira Dunkel¹, Mark Krailo², Guillermo Chantada³, Anuradha Banerjee⁴, Sherif Abouelnaga⁵, Jeff Buchsbaum⁶, Thomas Merchant⁷, Meaghan Granger⁸, Rima Jubran⁹, Joanna Weinstein¹⁰, David Abramson¹, Jin Piao², Carlos Rodriguez-Galindo², Murali Chintagumpala¹¹  
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**Abstract:** Purpose: This prospective, multi-institutional, international trial studied whether intensified systemic chemotherapy +/- RT would improve outcomes in patient with extra-ocular RB. Methods: Patients with stage 2 or 3 disease received 4 cycles of chemotherapy (vincristine 0.05 mg/kg/day, cisplatin 3.5 mg/kg/day, cyclophosphamide 65 mg/kg x 2 days, etoposide 4 mg/kg x 2 days) followed by involved-field RT (4,500 cGy). Patients with stage 4a or 4b/trilateral disease also received 4 cycles of chemotherapy and those with ≥ partial response then received 1 cycle of high-dose carboplatin (Calvert formula with AUC=7/day, maximum 16.7 mg/kg/day) on days -8 to -6, thiotepa (10 mg/kg/day), & etoposide (8.3 mg/kg/day) on days -5 to -3 with autologous hematopoietic stem cell rescue on day 0. Patients with stage 4a or CNS RB who achieved an inadequate response to chemotherapy received RT. Results: Fifty-seven eligible subjects were included in the analyses (data current to 6-30-16). Toxicity was significant as expected and included 2 therapy-related deaths. EFS at 36 months was 87.7% (90% CI 65.4 to 96.0%) for stage 2 or 3, 79.3% (90% CI 54.2 to 91.6%) for stage 4a and 8.0% (90% CI 1.0 to 25.1%) for stage 4b/trilateral. The observed results significantly improved the EFS in each stratum compared with historical results used for planning the study. Conclusion: Intensive multi-modality therapy is highly effective for patients with regional extra-ocular RB and stage 4a metastatic RB. More effective therapy is required for patients with CNS RB.

**Presentation Title:** Cause-specific Mortality among 2053 Long-term Survivors of Retinoblastoma  
**Authors:** Ruth Kleinerman¹, Margaret Tucker¹, Byron Sigel¹, David Abramson², Johanna Seddon³, Lindsay Morton¹  
¹National Cancer Institute, Rockville, USA. ²Memorial Sloan Kettering Cancer Center, New York, USA. ³Tufts Medical Center, Boston, USA  
**Abstract:** Purpose Previous studies of hereditary retinoblastoma have reported a strikingly increased risk of subsequent cancers, especially sarcomas, compared with the general population. However, cause-specific mortality patterns for long-term survivors are poorly understood. Therefore, we investigated the cause-specific risk of death for a broad range of malignant and non-malignant causes in long term retinoblastoma survivors by hereditary status, treatment, year of diagnosis and time since retinoblastoma diagnosis. Method We analyzed a cohort of 2,053 retinoblastoma patients diagnosed 1914-2006 at two major US treatment centers and followed until 2016. We estimated cumulative mortality, standardized mortality ratios (SMRs), and absolute excess risks (AERs) for specific causes of death compared with the US general population. Results Most of the 690 deaths occurred in 1129 hereditary retinoblastoma patients (N=518 deaths, cumulative mortality 70 years after retinoblastoma=75.8%; SMR=8.5). Of these, 267 were due to subsequent cancers (SMR=27.4; AER=72.3 deaths/10,000 person-years), for which SMRs were highest 15-29 years after diagnosis (N=69, SMR=89.1, AER=38.0) but remained statistically significantly elevated at 60+ years (N=14, SMR=6.7, AER=328). Deaths due to bone cancer, soft tissue sarcomas and nasal cavity cancers were most common. For 924 patients with non-hereditary retinoblastoma, we noted a modestly increased risk of death for subsequent cancers (N=27, SMR=1.8) possibly due to treatment or misclassification of hereditary status. Conclusion Hereditary retinoblastoma survivors...
died mainly from an excess risk of subsequent cancers up to 6 decades later. These results highlight the need to develop clinical management guidelines for hereditary retinoblastoma survivors treated in the past.


Authors: Milo van Hoefen Wijserd, Armida Fabius, Flora van Leeuwen, Annette Moll

1Department of Ophthalmology, Amsterdam UMC location VUmc, Amsterdam, Netherlands. 2Department of Epidemiology, Netherlands Cancer Institute, Amsterdam, Netherlands

Abstract: Purpose: In high resource countries, because of the excellent survival from retinoblastoma (Rb) itself, second primary malignancies (SPMs) now are the leading cause of death in patients with heritable Rb. To properly inform Rb patients who transit from pediatric to adult care about their risks of developing a second cancer, we are interested in the SPM risks for 20-year survivors. Methods: The Dutch retinoblastoma cohort (n=1217) was extended to include 133 new Rb patients between 2006 and 2017 and was used to analyze risks of SPMs in Rb survivors. SPM follow-up was ascertained through the Netherlands Cancer Registry. Standardized incidence ratios (SIRs) and absolute excess risks (AERs) of subsequent cancers in patients with heritable and non-heritable Rb were calculated by comparison with Dutch sex-, age- and calendar year-specific rates. Results: In all 586 20-year survivors (median follow-up of 20.0 more years) the risk of SPMs after 20 years in heritable Rb patients (SIR 8.1, 95% CI = 6.3 – 10.3) far exceeded the risk of survivors of non-heritable Rb (SIR 1.3, 95% CI = 0.9 – 1.8). For heritable Rb patients, highest elevated absolute risks were observed for melanomas and for malignancies in bone, joints, soft tissue and urinary bladder. The AER of any SPM among 20-year survivors of heritable Rb was 167.3 excess cases per 10,000 person-years. Conclusion: Analysis of part of the Dutch retinoblastoma cohort shows that 20-year survivors of heritable Rb still have an eight times higher chance to develop any other malignancy compared to the general population.
**Presentation Title:** Chemoplaque (sustained-release topotecan episcleral device) for retinoblastoma: Opportunity for rapid clinical evaluation of toxicity and efficacy to support safe eye salvage.  

**Authors:** Brenda Gallie\(^1\,2\,3\), Sameh Soliman\(^1\,4\), Furqan Shaikh\(^1\,2\), Helen Dimaras\(^1\,2\), Ricardo Carvalho\(^5\), Dan Gombos\(^6\), Jesse Berry\(^7\), Jonathan Kim\(^7\), Rima Jubran\(^7\), Linn Murphree\(^8\)  
\(^1\)SickKids Hospital, Toronto, Canada. \(^2\)University of Toronto, Toronto, Canada. \(^3\)TECHNA Institute, UHN, Toronto, Canada. \(^4\)Alexandria University, Alexandria, Egypt. \(^5\)Targeted Therapy Technologies, LLC, Irvine, USA. \(^6\)MD Anderson/Texas Childrens Hospital/Baylor/The Methodist Institute (The Retinoblastoma Center of Houston), Houston, USA. \(^7\)Children's Hospital Los Angeles, Los Angeles, USA

**Abstract:** Purpose: To define a process to obtain rapid clinical evidence of the risk/benefit of a novel approach to treat retinoblastoma. Methods: After failure of chemotherapy (intravenous and/or intra-arterial, intravitreal), focal therapy, and brachytherapy, remaining options for last eyes are very poor: external beam radiation and enucleation. The chemoplaque is a novel concept in cancer treatment. The FDA approved chemoplaque for retinoblastoma contains 0.3–0.9 mg topotecan to diffuse into the eye over 40 days. Health Canada authorized compassionate First in Human use of the chemoplaque for a child with cT2b(cT2b)N0M0H1 refractory retinoblastoma with recurrence in the last eye from calcified tumor beside the optic nerve, vitreous seeds, dispersed laser-resistant tumors and serous retinal detachment of intact fovea. Results: In ONE patient, through the Special Access Program, toxicity was absent and vitreous seeds and dispersed small tumors disappeared by Day 28, the large tumor shrank and vision improved as retinal detachment resolved. The chemoplaque was removed at day 70 and at day 98 there was no recurrence. Two clinical trials (CT) in the US have not yet accrued: Phase I unilateral Group D and Phase I/II salvage refractory disease. A third CT is under development for low volume retinoblastoma, designed to have broad eligibility to support broad accrual. Conclusions: The chemoplaque delivered continuous chemotherapy over weeks, a novel cancer treatment approach. We seek an expedited but rigorous process to clinical evaluation of the chemoplaque, a novel potential therapy for retinoblastoma.

**Presentation Title:** Intracameral chemotherapy for spontaneous aqueous seeding in retinoblastoma: from proof of principle to current management  

**Authors:** Francis Munier\(^1\), Marie-Claire Gaillard\(^1\), Christina Stathopoulos\(^1\), Jessica Sergenti\(^1\), Maja Beck-Popovic\(^2\)  
\(^1\)Jules-Gonin Eye Hospital, Lausanne, Switzerland. \(^2\)Pediatric Onco-Hematology Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

**Abstract:** Purpose: to evaluate efficacy and toxicity of intracameral chemotherapy (ICC) in retinoblastoma (Rb) patients with non-iatrogenic aqueous seeding (AS). Method: all consecutive patients presenting with primary or secondary AS between November 2011 and October 2018 were reviewed. Results: A total of 11 patients presented during the study period, consisting of 8 secondary and 3 primary occurrences of AS. Five patients had unilateral Rb, including one anterior diffuse, one diffuse infiltrating, and one MYCN Rb. Six patients had bilateral Rb, including 5 only remaining eyes (one with anterior diffuse Rb). Bicameral injections of melphalan (9 eyes) or topotecan (2 eyes) were administered as previously described, with complete AS control in all cases after a mean number of 6.5 injections targeting a final aqueous concentration of 20μg/ml of either melphalan or topotecan. Concomitant anterior uveal involvement required appropriate therapy in 5 eyes. At mean follow-up of 17 months, eye preservation rate was 82% (9/11), including all 5 only eyes and the 3 eyes with anterior diffuse or diffuse infiltrating Rb. Mean visual acuity was 0.5 (range:0.03–1.0). Two eyes were enucleated for progressive disease, including the MYCN Rb. Histopathology revealed sclero-choroidal and retrolaminar infiltration in one of them,
supporting the indication for systemic adjuvant chemotherapy. There was no corneal toxicity post melphalan or topotecan injections, as assessed by stable endothelial cell counts. ICC-induced cataract occurred in one patient. All patients are alive without metastasis. Conclusion: ICC represents a new focal chemotherapy targeting AS in retinoblastoma with high efficacy and low toxicity.

Presentation Title: Intraocular surgery of retinoblastoma eye has dissemination risk but may be one option.
Authors: Shigenobu Suzuki, Hidetomo Izawa
National Cancer Center Hospital, Tokyo, Japan
Abstract: Purpose: to evaluate the risk of intraocular surgery after or during eye-preservation treatment for retinoblastoma. Method: Retrospective medical chart review was conducted. All patients with intraocular retinoblastoma treated in our hospital between January 2002 and December 2017 were included in this study. Laterality, initial tumor staging, procedures for eye-preservation treatments, procedure of intraocular surgery, period between tumor treatment and intraocular surgery, adjuvant treatment. result of the surgery, and extraocular dissemination. Results: 653 consecutive patients were included in this study: 344 were unilateral, 306 were bilateral, and 3 were trilateral retinoblastoma. 31 patients had received intraocular surgery (surgery group), and 622 patients had not received intraocular surgery (no surgery group). In surgery group 32 eyes of 31 patients had received intraocular surgeries: 17 eyes of 16 patients had received cataract extraction after 0 to 92 months of tumor treatment (median 19 months); 4 patients received scleral buckling during eye-preservation treatment: 9 patients received pars plana vitrectomy after 0 to 17 months of tumor treatment: 2 patients received anterior chamber tap to confirm the diagnosis of anterior chamber invasion. No extraocular recurrence or metastasis occurred in surgery group. On the other hand, 19 patients had suffered extraocular dissemination in no surgery group: CNS invasion (3), orbital recurrence after enucleation (10), and distant metastasis (6). Conclusion: intraocular surgery for retinoblastoma eye should be avoided or delayed as possible due to extraocular dissemination risk, but may be one option for selected eyes.

Presentation Title: Retinoblastoma treated by chemotherapy and PPV with 5 years follow-up
Authors: Junyang Zhao1, Qiyan Li2, Brenda Gallie3
1Beijing Children's Hospital, Beijing, China. 2Beijing Tongren Hospital, Beijing, China. 3The Hospital for Sick Children, Toronto, Canada
Abstract: Purpose: Attempted salvage eye with advanced retinoblastoma with systemic (IVC) and/or intra-arterial (IAC) chemotherapy can fail with drug-resistant recurrence. We reported 90% rescue eye salvage with 78% useful vision by pars plana vitrectomy (PPV) with/without tumor resection in 21 cases. We report outcomes of all PPV for retinoblastoma performed with 5-year follow-up. Methods: Patients with recurrent retinoblastoma after IVC and/or IAC, received PPV +/- tumor resection; PPV irrigation fluid contained 5 µg/ml melphalan; melphalan was injected subconjunctival at PPV port sites; during follow-up EUAs, extensive disease at PPV was treated for precaution with post-PPV intravitreal melphalan. Results: In the year 2013, 159 retinoblastoma patients (174 eyes) were treated by PPV. At 5 years follow-up, no extraocular extension was observed at the PPV port sites. Of 159 patients, 10 (6%) died with optic nerve and bone marrow metastasis (6 due to disease in the other eye); 6 (3.8%) patients with 7 (4%) eyes were lost to follow-up. Of the 174 eyes, 155 (89%) were evaluable for eye outcomes: 125 (81%) were saved; 30 (19%) were enucleated because cancer was not controlled or by the request of parents; 95/117 (81%) Group D and 17/25 (68%) E eyes were salvaged. Conclusion: PPV performed with safety precautions against tumor dissemination achieves a high rate of eye salvage despite recurrent drug resistance tumor. Optic nerve and blood metastasis were the main causes of death, due to delay removing eyes with advanced disease, and not related to the PPV surgical intervention.
**Presentation Title:** Intraocular surgery of treated retinoblastoma eyes – long-term results  
**Authors:** Eva Biewald¹, Norbert Bornfeld¹, Sabrina Schlueter¹, Klaus Metz², Selma Sirin³, Sophia Goericke³, Nikolaos Bechrakis¹  
¹University Hospital Essen, Department of Ophthalmology, Essen, Germany. ²University Hospital Essen, Department of Pathology and Neuropathology, Essen, Germany. ³University Hospital Essen, Department of Diagnostic and Interventional Radiology and Neuroradiology, Essen, Germany  

**Abstract:** Purpose: To analyze the results of intraocular surgery in pretreated retinoblastoma eyes. In particular, evaluation of the long-term results regarding local recurrences, secondary enucleation and metastases. Methods: Retrospective data collection of 39 bilateral retinoblastoma survivors. Results: From 1964 to 2006, a total of 39 treated retinoblastoma patients underwent intraocular surgery. All patients had bilateral disease, 31 of them were only eyes. The interval between last therapy and intraocular surgery was on average 9.5 years (5 months to 43.7 years). The most common procedure was lentectomy in 30 eyes. 12 cases showed the need for a vitrectomy, 3 of those combined with a lentectomy, in 4 cases several procedures were necessary. Reasons for vitrectomy were vitreous hemorrhage after EBRT in 9 cases, retinal detachment in 7 and a subretinal hemorrhage in another case. Seven patients have had cataract surgery in the traditional way. Fortunately, with one exception, no patient showed a recurrence or vital tumour cells in the vitrectomy fluid obtained. In one case active tumour tissue was found during the therapy of vitreous hemorrhage, so that enucleation of the last eye became necessary. No other patient had to be enucleated and no systemic metastases were observed. Conclusion: In our patient population no serious complications were observed after intraocular surgery of treated retinoblastoma eyes. In particular, lentectomy and cataract surgery did not lead to tumor recurrence with corresponding visual improvement. However, especially in the absence of fundus vision, the indication for surgery should be carefully considered to avoid tumor cell spread.
Presentation Title: Second and third courses of Superselective Intra-Arterial Chemotherapy for treatment of recurrence in retinoblastoma eyes.

Authors: Luiz Teixeira¹,²,³, Sidnei Epelman³, Jose Roberto Fonseca⁴,², Marina Vilas Boas³, Monique Mangeon¹,², Márcio Marques⁵,³, Bruna Morales², Isabela Câmara³, Carla Renata Macedo²

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Abstract: Purpose To evaluate the use of second and third courses of superselective intra-arterial chemotherapy (SIAC) for retinoblastoma eyes that failed the first course. Method Retrospective interventional study in two centers in Brazil. All eyes treated with a second or third course of SIAC were analysed. Recurrence of tumor was considered after 3 months of the last cycle of the previous course. Results From 255 eyes treated with SIAC, 206 (81%) were saved with the first course. 45 eyes of the saved group eyes (22%) presented recurrence that needed more courses of SIAC. The eyes were classified before any treatment as group B n=3(7%), group C n=6(13%), group D n=30(67%) and group E n=6(13%). After the second course of SIAC 36 (80%) eyes were saved. From the 36 saved eyes 6 had a new recurrence and needed a third course. Only one eye was enucleated (17%). At a mean follow up of 31 months (median 29; range 6-76 months) all patients are alive with no systemic complications. 35 eyes (78%) were preserved. A mean of 5 cycles per eye (median 5; range 2-10 cycles) for the group with two courses of SIAC and a mean of 7 cycles per eye (median 6.5; range 5-12 cycles) for the group with three courses were used during all treatment time. Topotecan+Melphalan+Carboplatin combined were used in 62% of the eyes. Conclusion The use of second or third courses of SIAC for recurrent retinoblastoma after first course showed successfully results in our experience.

Presentation Title: The efficacy of alternate systemic intravenous chemotherapy and intraarterial chemotherapy for advanced retinoblastoma

Authors: Christopher Lee, Jung Hang, Seung Hahn, Dong Kim, Byung Kim, Chuyl Lyu, Sungchul Lee

Yonsei university College of Medicine, Seoul, Korea, Republic of

Abstract: Purpose: To determine the efficacy and safety of alternate intravenous chemotherapy (IVC) and intraarterial chemotherapy (IAC) for retinoblastoma patients. Methods: Retrospective, interventional case series of 42 patients with retinoblastoma treated with alternate systemic IVC (carboplatin, vincristine, and etoposide) and IAC (melphalan and/or topotecan) for 3 first cycles, followed by additional IVC and/or IAC. Results: Forty-two patients were classified by the International Classification of Retinoblastoma as Group D (n=19, 45%) and Group E (n=23, 55%). The mean follow-up duration was 27.3 months. The mean number of IVC was 11 and the mean number of IAC was 4. The overall globe salvage rate was 50.1%. There was no sign of life-threatening complication, metastasis, or death. Conclusion: Alternate IVC-IAC therapy provides globe salvage in 59.5% of retinoblastoma patients (Group D and Group E) with no metastasis.
Presentation Title: **Comprehensive Retrospective Evaluation of 6 years of Intra-arterial Chemotherapy for Retinoblastoma with case by case correlation of angiographic findings with RetCam imaging**

**Authors:** Stephen Chen1,2, Patricia Chévez-Barrios, MD1,2, Murali Chintagumpala, MD4,2, Frank Lin, MD4,2, Peter Kan, MD5,2, Cynthia Herzog, MD6,2, Dan Gombos, MD6,2  
1Baylor College of Medicine, Houston, USA. 2Retinoblastoma Center of Houston, Houston, Texas, USA. 3Houston Methodist Hospital, Houston, Texas, USA. 4Texas Children's Hospital, Houston, Texas, USA. 5Baylor College of Medicine, Houston, Texas, USA. 6The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

**Abstract:** Purpose: To find favorable anatomic characteristics and angiographic techniques for intra-arterial chemotherapy to improve retinoblastoma treatment. Method: Following multi-institutional IRB approval, a comprehensive review was performed on all our patients treated with intra-arterial chemotherapy. Images from the RetCam wide angle fundus camera utilized during exam under anesthesia after each treatment were reviewed retrospectively. Results: Anatomic variants between patients and catheter location and placement techniques are found to directly affect treatment outcomes seen on RetCam imaging. Conclusion: Evaluating blood flow patterns and anatomic variants can help improve outcomes through improving strategies during intra-arterial chemotherapy for retinoblastoma.

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**Presentation Title:** Ophthalmic artery chemosurgery with melphalan in the management of retinoblastoma: results of a prospective study.

**Authors:** Livia Lumbroso-Le Rouic1, Raphael Blanc2, Alexia Savignoni1, Caroline Saint Martin1, Christine Lévy-Gabriel1, Laurence Desjardins1, François Doz1,3, Isabelle Aerts1, Nathalie Cassoux1,3  
1Institut Curie, Paris, France. 2Fondation Ophtalmologique Rothschild, Paris, France. 3University Paris Descartes Sorbonne Paris Cité, Paris, France

**Abstract:** Purpose: To determine the efficacy of Melphalan Ophthalmic artery chemosurgery (OAC) as first-line treatment for retinoblastoma. METHODS: Phase II non randomized prospective study in order to evaluate globe salvage rates (without external beam radiation) patient survival and adverse events at 18 months after treatment with melphalan OAC. Patients with unilateral retinoblastoma group B, C or D (without massive vitreous seedings). RESULTS: Between February 2012 and December 2016, 39 patients (39 eyes) were included. IRC groups at diagnosis were: Group B 10.3%, Group C 33.3%, Group D 56.4%. Median age at diagnosis was 19.3 months (range 3.2-61.6). Two patients didn't receive the treatment (catheterization failure, and RSV bronchiolitis contra indicating general anesthesia) and were considered failures. Median number of OAC cycles was 4 (range 1-6). For 31 patients, OAC was associated to diode laser thermotherapy and/or cryotherapy. Twelve ocular adverse events were declared during treatment, including 4 retinal vascular occlusions. Six stopped treatment. Five other patients stopped treatment too: 2 due to catheterization failure, one for progressive disease, 2 for medical decision. At 18 months all patients are alive and well. Preservation ocular rate is: 76.9% [60.7-88.9%]. 4enucleation were performed for tumoral evolution and 3 for complications. CONCLUSION: OAC with melphalan alone as a first line treatment for retinoblastoma is efficient and well tolerated with no metastatic event, ocular preservation is 76.9%, but ocular ischemic complications can be observed.

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**Presentation Title:** Ten things you do not know about Intrarterial Chemotherapy (OAC) for Retinoblastoma

**Authors:** David Abramson1,2, Jasmine Francis1,2, Ira Dunkel1,2, Y. Gobin1,2  
1Weill/Cornell Medical School, New York, USA. 2Memorial Sloan Kettering Cancer Center, New York, USA

**Abstract:** Purpose: Almost every major retinoblastoma center worldwide has now performed or had experience with intrarterial chemotherapy for retinoblastoma. More than 200 peer reviewed papers worldwide have demonstrated that this technique saves eyes previously enucleated without increasing metastatic deaths or second cancers. For families worldwide who accept this approach but refuse enucleation it also saves lives. Although we introduced this technique 12 years ago and have the world’s largest experience we too are continuing to learn and the purpose of this presentation is to tell you about ten things related to intrarterial chemotherapy that
you do not know. Methods: Single center experience with >2,100 intrarterial infusions for retinoblastoma since 2006. Results: We will present 10 things about intrarterial chemotherapy for retinoblastoma that you don’t know. Conclusions: There are many things we all now know about intrarterial chemotherapy for retinoblastoma. Intrarterial chemotherapy is now both first line and second line therapy for advanced retinoblastoma worldwide (>45 countries) and has significantly changed management algorithms. It is used in developed and developing nations and has resulted in saving eyes that were previously enucleated. The time to cure is faster, the overall cost is less, it has fewer systemic side effects than primary systemic chemotherapy, is not associated with an increase in metastatic deaths nor second cancers and eliminates the short- and long- term side effects of external beam radiation and systemic chemotherapy. In this presentation we will tell you ten things about intrarterial chemotherapy that you do not know.

Presentation Title: Secondary neovascularization after intraarterial chemotherapy for retinoblastoma: incidence, features and outcomes
Authors: Christina Stathopoulos¹, Sabrina Chelbabi², Marie-Claire Gaillard¹, Francesco Puccinelli³, Maja Beck-Popovic⁴, Francis Munier¹
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Abstract: Purpose: To report incidence, clinical/angiographic features and outcomes of secondary neovascularization (SNV) in retinoblastoma eyes treated with intraarterial chemotherapy (IAC).Methods: Retrospective review of all retinoblastoma patients treated with IAC in Lausanne from November 2008 to December 2017. Included were eyes with SNV after first-line (n=68) or salvage IAC (n=114). Excluded were patients with SNV prior IAC in Lausanne (n=4). All were imaged with photography and fluorescein angiography.Results: 173 patients (182 eyes) were included. SNV occurred in 37 eyes (20%,n=37/182), among which 12 received first-line and 25 salvage IAC. Mean number of intraarterial injections to the complication was 3.3 (range 1-8); 25 eyes received intraarterial melphalan and 12 combined melphalan-topotecan. Mean interval to develop SNV since first IAC was 9.6 months (range 0.8-72.2). Clinical and angiographic features of the neovascularization included rubeosis iris (n=33), neo-vascular glaucoma (n=5), retinal neovascular membrane (n=16) and/or vitreous hemorrhage (n=11). Eye preservation was possible in 54% of eyes with no active tumor (n=14/26) at time of SNV with appropriate treatment including intravitreal anti-VEGF (mean follow-up:3.0 years, range 0.6-6.8) compared to 27% of eyes with active tumor at time of SNV (n=3/11). There are no metastases or death at a mean follow-up since SNV of 2.6 years.Conclusion: The incidence of SNV was higher after salvage compared to first-line IAC (22% versus 18%). Fluorescein angiography allows early recognition and follow-up of SNV, providing optimal conditions for adequate therapeutic decision and should therefore be part of routine post IAC assessment.
Presentation Title: Less is More - Minimally Invasive Conjunctival Approach to Orbitotomy

Authors: Santosh Honavar¹, Raksha Rao¹, Kaustubh Mulay²

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Abstract: Purpose: Orbitotomy conventionally involves skin approach and often osteotomy, and entails prolonged surgical time and postoperative morbidity. Minimally invasive transconjunctival approach, in contrast, offers scar-free outcome with minimal complications. We evaluated our results of transconjunctival approach to orbital lesions.

Methods: This was a retrospective analysis of 102 consecutive cases of transconjunctival orbitotomy from January 2001 to December 2016. Results: Of 102 patients, 63 were male and 39 were female. Mean age was 46 years (range, 6 weeks to 82 years). All the patients manifested proptosis, 22 had extraocular motility restriction, 16 had diplopia, 8 had optic disc edema and 3 had optic disc pallor at presentation. The lesion was located predominantly in the mid and posterior orbit in a majority (92) patients; it was intraconal in 52, extraconal in 22, and both intra- and extraconal in 28. Maximum tumor diameter ranged from 12 - 58 (mean, 26) mm. Conjunctival incision was transcaruncular in 12, inferior fornicial in 32, inferior fornicial with transcaruncular extension in 18, and inferior fornicial with lateral canthotomy and inferior cantholysis in 40. Duration of surgery ranged from 20-120 (mean 70) minutes. In all, 90% of patients experienced recovery in 1 week (range, 1-4). Three patients had postoperative secondary bleeding that resolved with conservative measures. None of the patients had new onset functional problem. All the patients had aesthetically satisfactory outcome. Conclusion: Minimally invasive transconjunctival orbitotomy provides excellent access to most orbital lesions with faster surgery, quick postoperative recovery, minimal morbidity, and excellent aesthetic outcome.

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Presentation Title: MAP kinase and PI3K/mTOR pathways activity and inhibition in conjunctival melanoma

Authors: Alexandre Moulin¹, Ikram El Zaoui², Donata Rimoldi³, Michael Nicolas¹, Gurkan Kaya⁴, Ann Schalenbourg⁵, Leonidas Zografos¹, Carlo Rivolta ²

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Abstract: PURPOSE: To assess the activity of the MAP kinase and the PI3K/mTOR pathways in benign and malignant conjunctival melanocytic proliferations with or without BRAF V600E mutation. To determine whether specific inhibitors of RAS and PI3K cascades can suppress conjunctival melanoma growth in vitro.

METHOD: BRAF V600E mutation and activation of ERK, MEK, S6 and AKT were assessed by immunohistochemistry in 35 conjunctival naevi and 31 melanomas. The proliferation impact of a BRAF inhibitor (Vemurafenib), two MEK inhibitors (Trametinib, Selumetinib), a PI3K inhibitor (Pictilisib) and a dual PI3K/mTOR inhibitor (Dactolisib) were assessed in 3 conjunctival melanoma cell lines with either BRAF V600E mutation, NRAS Q61L mutation, or none of these mutations. Pathways activity was tested by western blots and apoptosis by caspase-3 immunostaining.

RESULTS: The BRAF V600E mutation was detected in 42.6 % of naevi and 35.5 % of CM. The activation of MEK and ERK as well as S6 was significantly higher in melanomas compared to naevi (90.3% versus 62.9% for MEK, 96.8% versus 45.7% for ERK and 90.3% versus 20% for S6). The BRAF mutant CM cell line was sensitive to all the drugs with apoptosis induction. The NRAS mutant CM cell line was only sensitive to Trametinib and Pictilisib with induction of apoptosis. The double negative cell line was resistant to all the drugs.

CONCLUSIONS: The activity of MAP kinase pathway is increased in conjunctival melanoma compared to
naevi. Targeted therapy may be useful for patients with CM and our results confirm the relative resistance of NRAS-mutated melanomas.

Presentation Title: Clinical features and outcomes of conjunctival melanoma with NRAS, BRAF, NF1 and ATRX mutations
Authors: Sara Lally, Marlana Orloff, Lauren Dalvin, Li-Anne Lim, Tatyana Milman, Takami Sato, Jerry Shields, Carol Shields
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Abstract: Purpose: We aim to evaluate clinical features and outcomes of conjunctival melanoma (CoM) associated with NRAS, BRAF, NF1 and ATRX mutations. Methods: Primary conjunctival melanoma was evaluated with next generation sequencing by Caris Life Sciences (Phoenix, AZ). Fisher’s exact test was used to investigate associations between tumor mutation and clinical features or outcomes, including patient race, tumor location, metastasis, and death. Spearman’s rho was used to test correlation between mutation and patient age, largest tumor basal diameter, thickness, involved areas, TMN staging, and number of surgeries. Results: Sufficient tumor cellularity for testing was available in 66 of 77 samples. The most common mutations were BRAF 24% (16/66), NRAS 24% (15/63), ATRX 34% (12/35) and NF1 42% (17/41). NRAS mutation was associated with metastasis in 40% (6/15) versus 8% (4/48) with no mutation (pp=0.01) and caruncle tumor location 31% (5/16) vs. 8% (4/50, p=0.03). BRAF was less frequently associated with superior quadrant tumor location 25% (4/16) vs. 58% (29/50, p=0.04) and negatively correlated to number of recurrences (R = -0.25, p=0.03). ATRX and NF1 mutations were not associated with any of the assessed parameters. Conclusion: This is the largest single institution report on CoM mutational status and clinical features and outcomes, with NRAS mutation imparting a higher risk of metastasis and BRAF mutation correlating with high-risk clinical features and frequent recurrence.

Presentation Title: Ulceration and sentinel lymph node biopsy status as prognostic factors in patients with conjunctival melanoma: Implications for the American Joint Committee on Cancer (TNM) Classification
Authors: Bita Esmaeli, Shiqiong Xu, Laura Rubin, Jing Ning, Christian El-Hadad, Joshua Ford, Phyu Aung, Michael Tetzlaff
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Abstract: Purpose: To validate AJCC 8th edition criteria and explore whether ulceration and sentinel lymph node biopsy (SLNB) status are of prognostic importance. Methods: Clinical and pathologic data (Age, gender, ethnicity, location, tumor thickness, ulceration, mitotic figures, TNM criteria) for 88 consecutive conjunctival melanoma patients were analyzed. Outcome measures: local recurrence, lymph node metastasis, distant metastasis, disease-specific survival (DSS). Results: 66 patients (75%) had invasive melanoma (median tumor thickness=1.56mm). Ulceration was present in 22 patients (25%). 31 patients had SLNB; 4 were positive. Overall 12 patients had nodal metastasis; 16 patients developed distant metastasis, 14 patients died of disease (median follow-up time=46 months). Ulceration had the most significant association with nodal metastasis, distant metastasis and death of disease (p<0.001); more significant than tumor thickness and AJCC T categories. In 31 patients who had SLNB, a positive SLNB was correlated with a significantly worse distant metastasis survival (p<0.001) and DSS (p=0.01). Conclusions: T category at presentation was not significantly associated with nodal metastasis or distant metastasis but was associated with DSS. Ulceration had the strongest association with nodal metastasis, distant metastasis and DSS. Consideration should be given to adding ulceration as a determinant of T category in future AJCC editions. A positive SLNB was significantly associated with DSS highlighting its important prognostic value.
Presentation Title: Conjunctival Melanoma: Checkpoint Immunotherapy Associated with Both Local and Systemic Melanoma Regression
Authors: Paul T Finger1,2, Anna C Pavlick3,2
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Abstract: Background: Current treatments for advanced local conjunctival melanoma typically result in poor local control leading to disfiguring orbital exenteration surgery. Regional and distant conjunctival melanoma metastases typically require either pre-audial and cervical lymph node dissection with post-operative adjuvant radiation therapy or unsuccessful treatment of metastatic disease. Methods: Herein, we describe a retrospectively analyzed clinical case series of 5 patients with biopsy proven conjunctival melanoma treated with checkpoint inhibition therapy. Of these, 3 were treated for residual ocular disease present after failing multiple local therapies and who refused orbital exenteration surgery as well as 2 who developed metastatic conjunctival melanoma despite local control. Both those with locally advanced disease and patients with metastatic disease received an anti-PD1 agent in combination with ipilimumab. All 5 were given multiple cycles of systemic anti-PD1 therapy and two received adjuvant topical interferon. As part of each ophthalmic examination, photographs of all conjunctival and eyelid surfaces were obtained. Systemic evaluations involved initial positron emission tomography/computed tomography staging as well as periodic re-staging scans. Results: All cases have shown durable responses. Of the 2 complete responses, 1 was a patient with systemic disease. No patients developed ocular toxicity or loss of vision. However, systemic adverse effects included adrenal insufficiency, Grade-III colitis, Grade-II dermatitis, Grade-II hepatotoxicity and Grade-II pneumonitis. Conclusions: This study suggests that systemic immunotherapy with or without topical interferon has an effect on locally advanced conjunctival melanoma, those who refuse orbital exenteration surgery and those with systemic metastasis.

Presentation Title: Immune Checkpoint Inhibitor Therapy for Metastatic Conjunctival Melanoma in 5 Patients
Authors: Marlana Orloff1, Sara Lally2, Tatyana Milman2, Takami Sato1, Jerry Shields2, Carol Shields2
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Abstract: Purpose: Conjunctival melanoma (CoM) is a rare and potentially fatal subtype of ocular melanoma. Though treatment with immune checkpoint inhibitors (ICI) has been effective in cutaneous melanoma there is limited experience with these agents in CoM. We describe our institutional experience with ICI in 5 adult patients with metastatic CoM. Methods: We conducted a retrospective review of 5 patients with metastatic CoM who were treated with ICI between September 2015 and October 2018. Results: Patient 1 received PD-1 inhibitor pembrolizumab but progressed after 6 months. Therapy was switched to CTLA-4 inhibitor ipilimumab in conjunction with nab-paclitaxel. There was further progression after four months and another therapy was started. Patient 2 received pembrolizumab and progressed after 6 months. Due to age and co-morbidities opted for no further treatment. Patient 3 received pembrolizumab but had unequivocal progression after 3 months and was switched to ipilimumab. There was progression after four months and followed by hospice. Patient 4 received combination ipilimumab and nivolumab, another PD-1 inhibitor, but due to toxicity after two combination treatments went on to receive nivolumab alone, and continues to have stable disease at 11 months. Patient 5 continues to receive nivolumab and has had stable disease now 8 months since initiation. Conclusion: ICI therapy for metastatic CoM did not provide disease control in the majority of patients in this series. This is contrary to a recently published report in JAMA Ophthalmology (Sagiv et al. 2018). A larger prospective study is needed to investigate the efficacy of ICI in CoM.

Presentation Title: Management of invasive melanoma of the conjunctival fornix or caruncle with external photon beam radiotherapy: a 27-year experience
Authors: Laurence Desjardins, Alexandre Matet, Christine Levy, Livia Lumbroso Le rouic, Nathalie Cassoux, valentin Calugaru, nathalie Algret, sylvain Dureau, remi Dendale
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Abstract: Invasive conjunctival melanoma requires adjuvant radiotherapy after local excision to avoid local recurrences. Caruncular or fornix localizations are not accessible to plaque brachytherapy or proton beam irradiation. We reviewed patients in this situation treated by external photon beam radiation (EPBR) in our institution over a 27-year period. Patients and Methods: Patients referred for primary treatment, adjuvant therapy or recurrence of invasive conjunctival melanoma and treated with adjuvant EPBR after complete surgical excision between 1987 and 2013, were retrospectively included. According to the size and local extension of the tumor, orthovoltage irradiation, low energy or high energy EPBR was administered. The initial localization and extension of the tumor, histopathological results, local recurrences and metastases were registered in our institutional database for conjunctival melanoma. Results: Fifty-five patients with invasive conjunctival melanoma were treated by EPBR between 1987 and 2013. The mean follow up was 9 years (range, 1 to 30 years). Twenty-six patients (47%) had primary acquired melanosis (PAM). No local recurrence was observed in the irradiation field, but local recurrences occurred outside the irradiation field in 20 patients with PAM and in two patients without PAM. Sixteen patients (29%) developed metastases, with a mean time since EPBR of 6 years (range, 1 to 18 years). Conclusion: Adjuvant EPBR is efficient for the local control of caruncular or fornix invasive conjunctival melanoma. After radiotherapy, local chemotherapy is warranted in case of PAM. Long follow up is essential since local recurrence and metastases can develop in affected patients.
Presentation Title: Conjunctival Squamous Neoplasia: Staging and Initial Treatment.
Authors: Claudine Bellerive1,2, Jesse Berry3, Ashley Polski3, Arun Singh1
1Cole Eye Institute, Cleveland Clinic, Cleveland, USA. 2Centre Hospitalier Universitaire de Quebec, Quebec, Canada. 3USC Roski Eye Institute, Keck School of Medicine, Los Angeles, USA
Abstract: PURPOSE:To evaluate the clinical relevance of the American Joint Committee on Cancer (AJCC) classification in the initial management of squamous neoplasia of the conjunctiva.METHODS:This retrospective study enrolled 95 histopathologically proven cases of treatment-naive conjunctival squamous neoplasia. Tumors were classified into 4 histological groups: conjunctival intraepithelial neoplasia (CIN) with mild dysplasia (grade 1/3), moderate dysplasia (grade 2/3), severe dysplasia (grade 3/3 or carcinoma in situ), and invasive squamous cell carcinoma (SCC). Clinical findings such as tumor location, largest basal diameter, growth pattern, and adjacent structures involved were recorded.RESULTS:CIN was observed in 74 cases (78%), and SCC was noted in 21 cases (22%). Based on the AJCC classification, all the 74 cases of CIN were classified as Tis (tumor in situ). Among the invasive SCC, there were 3 T1 tumors, 2 T2 tumors, and 16 T3 tumors. Complete excision with or without adjuvant therapy was selected as initial treatment in 80% of cases (76/95). Two cases of SCC with scleral invasion were treated using brachytherapy.CONCLUSION:The AJCC stage does not correlate with the initial treatment of CIN. The AJCC T3 category should be reviewed to differentiate diffuse SCCs with broad surface extension from tumors with deep scleral invasion.

Presentation Title: Stratification of conjunctival in-situ squamous carcinoma according to HPV16 gene expression: Evidence for higher detection rates in atopic patients and division into two pathogenesis groups.
Authors: Hardeep Mudhar1, John Doorbar2, Heather Griffin2, Ian Rennie3
1Dept of Histopathology, Royal Hallamshire Hospital, sheffield, United Kingdom. 2Department of Pathology, University of Cambridge, Cambridge, United Kingdom. 3Sheffield Ocular Oncology Service, Dept of Ophthalmology, Royal Hallamshire Hospital, sheffield, United Kingdom
Abstract: Purpose: To describe the HPV-16 landscape of conjunctival in-situ squamous carcinoma (in-situ SCC) and lower grades of dysplasia.Methods:In-situ SCC from atopes and non-atopes were screened for HPV by PCR and exposed to HPV DNA situ hybridisation, immunohistochemistry (proteins p53, Ki67, E4 and MCM) and HPV positive cases exposed to mRNA in situ hybridisation able to detect HPV-E6 and -E7 gene expression. Controls comprised normal epithelium, squamous metaplasia and lower grades of epithelial squamous dysplasia.Results: PCR only detected HPV16 in the in situ SCC cases. 79% of atopes and 20% of non-atopes were PCR HPV16+. 31% of lower grade dysplasias were HPV16+. HPV16DNA in-situ hybridisation was positive in HPV16+ tumour cases only. P53 reduced expression, MCM elevated expression and p16 block positivity was seen in HPV16+ tumour cases. The reciprocal pattern was observed in HPV16 negative cases and lower grades of dysplasia. E4 expression was absent in all cases (including controls). E6 and E7 mRNA transcripts were prominent in 67% of HPV16+ cases, but absent in the lower grade dysplasia.Conclusions: Atopes have a 4x higher rate of HPV-16 detection. The pattern of deranged protein expression and mRNA E6 / E7 transcript presence is strong evidence for causality for in-situ SCC. E4 absence indicates that the conjunctiva is a site of non-productive HPV infection, and that low grade dysplasia may not precede in-situ SCC development. This implies two pathogenesis pathways: In-situ SCC from inception associated with HPV16, or progression from lower grades of dysplasia when HPV infection is absent.
**Presentation Title:** A comparison of topical 5-fluorouracil and topical interferon alfa-2b as primary treatment modalities for ocular surface squamous neoplasia

**Authors:** Carol Karp¹, Nandini Venkataseswaran², Carolina Mercado³, Anat Galor²

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**Abstract:** Purpose: To compare the efficacy of topical 5-fluorouracil 1% (5FU) and interferon alfa-2b 1 MIU/mL (IFN) eye drops as primary treatment modalities for ocular surface squamous neoplasia (OSSN). Method: Retrospective study at a hospital-based eye center. 54 patients who received 5FU and 48 patients who received IFN as primary therapy for OSSN were included. Primary outcome measures were the frequency of clinical resolution and time to OSSN recurrence. Secondary outcome was the frequency of side effects with each therapy. Results: The mean age of patients was 68 years. More Hispanics were treated with 5FU. In a univariable analysis, frequency of OSSN resolution was higher with 5FU (96.3%, n = 52) than with IFN (81.3%, n = 39), p=0.01. In a multivariable analysis, treatment modality did not remain a significant predictor of resolution. In patients whose OSSN resolved, time to resolution was similar with both agents, (5FU - mean 6.6 months, standard deviation (SD) 4.5 versus IFN - mean 5.5 months, SD 2.9, p = 0.17). Of the 52 eyes which resolved with 5FU, 11.5 % of lesions (n=6) recurred while of the 39 eyes which resolved with IFN, 5.1% of lesions (n = 2) recurred, p=0.46. Kaplan Meier survival curves were similar between groups (log rank=0.16). Eyelid edema (p=0.04) and tearing (p=0.02) were more significant with 5FU. Conclusions: This is the first direct comparison study between 5FU and IFN eye drops as primary treatment for OSSN. Both modalities resulted in a high frequency of tumor resolution and low recurrence rates.

**Presentation Title:** Brachytherapy For Malignant Conjunctival Tumors

**Authors:** Svetlana Saakyan, Vladimir Valsky, Yriy Borodin, Marina Ziltsova

**Abstract:** Purpose: to evaluate efficiency of brachytherapy for conjunctival malignant melanocytic tumors, epithelial tumors and lymphomas of conjunctiva. Material and methods. 225 patients were treated with Stroncium-90 plaque brachytherapy for malignant tumors of conjunctiva in 2008-2016 yrs. 108 patients treated because of melanocytic lesions of conjunctiva: melanomas – 82 cases, primary acquired melanosis or nevus with malignant futures -22. 86 patients bear epithelial malignant tumors of conjunctiva: squamous cell carcinoma -57 cases, adenoid cell carcinoma – 13, Bowen’s disease – 13, andepithelial conjunctival dysplasia grade-2 – two cases. Lymphoma cases – 35 patients: marginal zone lymphoma – 24 cases, B-cell prolymphocytic leukemia– 8, diffuse large cell lymphoma – 3. Follow-up – 27±10,5 months for melanocytic lesions, 24±9,2 m. – in group of epithelial lesions and -- 31±8,2 m. in lymphoma cases. Results. Complete tumors regression achieved in 72 patients with melanocytic malignancies (69.2%), partial regression – in 11 (10.6%), treatment was not successful– in 21 (20.2%) cases. Metastases encountered in 8 patient. Among epithelial tumors – full response observed in 93% of patients (80), 4 tumors regrew and 2 –responded partially. In this group - lymph node metastases appeared -5. In lymphoma cases at the last examination there were no signs of disease in 30 patients, relapsed 3-2 – in the orbit and 1 -on another part of the same eye conjunctiva, in 2 cases residual tumors observed. Conclusion. Brachytherapy – is effective modality for treatment malignant conjunctival neoplasms of different origins. More prolonged term of observation needed for eventual conclusions.

**Presentation Title:** Assessment of superficial and deep vasculature in benign conjunctival and caruncle lesions with anterior segment OCTA

**Authors:** Iwona Rospond-Kubiak¹, Celina Helak-Lapaj², Magdalena Kozlowska², Wojciech Adamski³, Jaroslaw Kociecki³, Andrzej Marszałek⁴, Marcin Stopa²

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Abstract: Purpose: to evaluate the superficial and deep vasculature in benign conjunctival and caruncle lesions. Methods: This prospective study included a consecutive series of patients referred to the Ocular Oncology Service in Poznan, Poland, between August 2017 and September 2018 with benign pigmented and non-pigmented conjunctival lesions. All patients were examined clinically with the standard protocol including color photographs. Additionally, AngioVue OCTA (Optovue, Inc., Fremont, CA) with the anterior segment lens adapter was used to assess superficial and deep vasculature of the nevi (SSADA algorithm based firmware). If appropriate, the lesions were excised with dry no-touch technique. Results: There were 39 patients, 25 men and 14 women with the mean age of 47 years. Five (12.8%) patients were excluded due to non-interpretable data. Among analyzed cases, 20 (51.3%) lesions were pigmented, and 13 (33.3%) were non-pigmented. Mean deep vessel density in pigmented lesions was 1.30 +/- 0.2 (range: 0.15-1.63), mean superficial vessel density - 1.56 +/- 0.17 (range: 0.9-2.1). Mean deep vascular and superficial vessel density in non-pigmented lesions were significantly higher and reached 1.61 (range: 1.1-1.97) and 1.43 (range: 1.02 – 1.9), respectively (p=0.0192 vs 0.0354). 14 lesions were surgically removed, among them 12 were conjunctival nevi, 1 – papilloma and 1 haemangioma. Conclusions: OCT angiography was able to detect vascular density in bulbar conjunctival lesions although images of highly pigmented or thick lesions might be difficult to interpret. Furthermore, the caruncle lesions are more difficult for the OCTA assessment. The clinical significance of the superficial and deep capillary plexus vessel density requires further investigation.

Presentation Title: Documenting ocular surface lesions with digital imaging using fluorescein dye and filters to improved identification and visualization.

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Abstract: Purpose: to validate a novel method for documenting ocular surface lesions. Study design: randomized blind evaluation. Methods: 16 patients with ocular surface lesions were photographed using 2 different imaging methods: standard slit lamp digital camera imaging (DCI) and digital camera imaging filtering method with fluorescein dye (DCI-FD). All Photos were displayed randomly to 10 independent experienced reviewers. The reviewers were blind to the lesion photographing method. The following parameters were evaluated: lesion identification, presence of corneal involvement, lesion borders visualization and reviewer's preferred imaging method. The latter parameter was measured by simultaneously displaying the 2 methods for each lesion, comparing them in regard to the image quality and lesion borders visualization. Results: DCI-FD increased lesion identification rate (96.85% vs 81.8%, p value p<0.0001). Out of the 18.1% lesion identification failure with the DCI method, 82.7% were identified by DCI-FD method p<0.0001. Corneal involvement detection rate was 65.0% with DCI-FD vs 50.6% with DCI method (p<0.001). DCI-FD was graded as a preferred method by the reviewers in 65.6% vs 46.3% of the lesions (p= 0.01). Conclusions: DCI-FD is a simple and quick method for ocular surface lesions identification and visualization. In this study DCI-FD method was superior to the standard DCI method in documenting ocular surface lesions for follow up of the lesion size, lesion borders and corneal involvement. Future studies are needed for evaluation of the method contribution in lesion differential diagnosis and in surgery.
Presentation Title: Role of High Resolution Optical Coherence Tomography in Diagnosing Ocular Surface Squamous Neoplasia with Coexisting Ocular Surface Disease

Authors: Carol Karp
Bascom Palmer Eye Institute, Miami, USA

Abstract: Purpose: Coexistence of an ocular surface disease can mask the typical features of ocular surface squamous neoplasia (OSSN). The purpose of this case to illustrate the use of high resolution optical coherence tomography (HR-OCT) as an adjunct in the detection and differentiation of OSSN within coexisting ocular surface pathology. Method: As case of a 46 year old black male with longstanding, severe vernal keratoconjunctivitis, limbal stem cell deficiency, human immunodeficiency virus and diffuse opacification of the cornea will be presented. Results: HR-OCT was able to identify OSSN “hiding” within the diffusely abnormal corneal and conjunctival surfaces. HR-OCT images revealed classical findings of hyper-reflective, thickened epithelium and an abrupt transition from normal to abnormal epithelium. Biopsy confirmed the HR-OCT findings. The patient was treated with topical interferon with resultant dramatic clinical resolution of the corneal pathology and HR-OCT confirmed normalization of the epithelium. Conclusion: While histopathology is the gold standard in the diagnosis of OSSN, HR-OCT can be used to noninvasively detect the presence of OSSN in patients with coexisting ocular conditions.

Presentation Title: Protuberant corneal mass: a case of mistaken identity

Authors: Miguel Materin, M.D., Wajiha Kheir, M.D.
Duke University Eye Center, Durham, NC, USA

Abstract: Purpose: To describe a case of a unilateral corneal mass, including presentation, imaging, surgery (video), management and histopathologic findings. Methods: A 74-year-old white man was referred to the Duke Ocular Oncology Service for a right protuberant corneal mass suspicious of a squamous epithelial neoplasm. Patient had a history of herpes keratitis. He reported a 6-month long history of growth of the lesion. On slit-lamp biomicroscopy, there was a large 9x9mm white, elevated, well-demarcated, vascular mass involving the entire central cornea. The anterior chamber (AC) was difficult to visualize but was formed. On ultrasound biomicroscopy (UBM), the lesion was dense with a maximal thickness of 1.5mm. No extension was noted posteriorly into the cornea and AC, and the iris and ciliary body were not involved. Results: Surgical excisional biopsy of the lesion was elected. After delineation with viscoelastic, the lesion was scraped off the cornea en bloc with a 57 blade. The underlying cornea was intact except for an epithelial defect. An amniotic membrane graft was used to cover the cornea. Histopathological examination revealed the diagnosis of a corneal keloid. Conclusion: Corneal keloid formation secondary to corneal pathology is a reported but uncommon complication. The keloid may be easily excised from the underlying cornea as long as there is no infiltration into corneal stroma, potentially avoiding penetrating keratoplasty. Relapses are common.

Presentation Title: Keratoacanthoma - An Unusual Location!

Authors: Santosh Honavar1, Mrittika Sen1, Ankit Tomar1, Kaustubh Mulay2
1Dept of Ocular Oncology, Centre for Sight, Hyderabad, India. 2Dept of Ophthalmic Pathology, Centre for Sight, Hyderabad, India

Abstract: Purpose: To report a rare case of a keratoacanthoma of the palpebral conjunctiva of the upper eyelid. Method: A case report with clinico-histopathological correlation Results: A 55-year-old lady presented with a
History of a rapidly progressing painless swelling in the upper eyelid of the left eye for 2 weeks. Her visual acuity was 20/20 in both eyes. On examination, there was mild mechanical ptosis. Eversion of the eyelid revealed a well-defined, mushroom-shaped pedunculated, leukoplakic mass measuring 10 X 8 X 5mm. The surface was irregular with a central umbilication filled with keratin. The surrounding conjunctiva was hyperaemic with dilated vessels. The eyelid margin was not involved. Due to the large size, rapid growth, significant keratinization and unusual location, keratoacanthoma and squamous cell carcinoma were considered as the differential diagnosis. An excision biopsy with 4 mm clear margin, cryotherapy to the margins and repair of the conjunctival defect with amniotic membrane graft was performed. Histopathology demonstrated features consistent with a keratoacanthoma. There was no recurrence in 3 months.

Conclusion: Conjunctival keratoacanthoma is a rare entity. All the previously reported cases have described the lesion of the bulbar conjunctiva adjacent to the limbus. This case questions the long standing hypotheses of actinic damage as a causal agent and the origin of this tumour from multipotent stem cells of pilosebaceous units. It highlights the need to have further studies on the underlying pathology of the development of this lesion.

Presentation Title: Dabrafenib and Trametinib for BRAF-Mutated Conjunctival Melanoma
Authors: Renelle Lim, Jenna Kim, Sarah Weiss
Yale University, New Haven, USA

Abstract: Purpose: To describe the novel use of targeted therapy for the treatment of unresectable conjunctival melanoma. Method: Case report of a 52-year old man with unresectable conjunctival melanoma. Results: BRAF-mutated conjunctival melanoma treated with BRAF/MEK inhibitor therapy resulted in complete regression without evidence of metastasis after 1 year of treatment. Conclusion: The case reported herein is the first in the literature to demonstrate a complete response to BRAF and MEK inhibitor therapy in unresectable CM. This case demonstrates that the combination therapy has the potential to be a globe-sparing treatment option for patients with recurrent and unresectable BRAF mutant CM.

Presentation Title: Usefulness of topical interferon alpha -2b eye drop in patients with conjunctival melanoma
Authors: Satoru Kase, Iku Kikuchi, Kan Ishijima, Susumu Ishida
Hokkaido University, Sapporo, Japan

Abstract: Purpose: The aim of this study is to examine the clinical course of patients with conjunctival melanoma treated with adjuvant interferon (IFN) α-2b eye drops following local tumor resection. Methods: Seven eyes of 7 patients were enrolled in this study. All patients underwent the local resection of tumors, and topical IFNα-2b eye drops were given 4 times/day until the complete disappearance of the pigmented lesions. Clinicopathological findings, and imaging modalities were retrospectively analyzed. Results: The age of the patients ranged from 65 to 84 years (mean: 73.9 years). Locations of the tumor were the bulbar conjunctiva in 5 eyes, multiple palpebral conjunctivias in 1 eye, and palpebral conjunctiva and caruncle in 1 eye. All patients received topical IFNα-2b eye drop treatment for 6-10 months. Follow-up periods after resection ranged from 18 to 84 months. All the excised conjunctival tumors were histologically diagnosed with malignant melanoma. Severe adverse effects related to IFNα-2b were not observed. Six out of 7 patients consequently achieved complete remission. One patient underwent orbital exenteration 12 months after local chemotherapy. Conclusions: This study highlighted safety and efficacy of topical IFNα-2b eye drops as adjunctive treatments following surgical resection for conjunctival melanoma patients.

Presentation Title: Intralesional Bleomycin is effective in local control of diffuse conjunctival and orbital melanoma
Authors: Ihab Othman
Cairo University, Cairo, Egypt. EyeWorld Hospital, Giza, Egypt
Abstract: Purpose: To evaluate the role of Bleomycin, a glycopeptide antibiotic, in local control of recurrent conjunctivo-orbital melanoma. Materials and Methods: Two cases presenting with recurrent diffuse superior tarsal conjunctival, and an inferior conjunctivo-orbital melanoma were injected intralesionally, weekly with a 15 IU of Bleomycin for six doses as an alternative to exentration. Results: Tumor control was achievable in the two cases over a 24 months follow up as evidenced by repeated MRI and PET-CT scans. The second case developed hepatic metastases with no local recurrence at 13 months follow up. Conclusion: Intralesional bleomycin may be a viable option in local tumor control in cases of recurrent/extensive conjunctivo/orbital melanoma and should be considered as an alternative to exentration.

Presentation Title: Unilateral conjunctival infiltration as first sign of pediatric B-cell leukemia/lymphoma.
Authors: CAROLINA ALARCON1,2, FRANCY ORTIZ1, DIANA RENDON 1, CARLOS NARVAEZ1
1CENTRO MEDICO IMBANACO, CALI, Colombia. 2UNIVERSIDAD DEL VALLE, CALI, Colombia
Abstract: Purpose: To describe a case with association of Unilateral conjunctival infiltration as first sign of pediatric B-cell leukemia/lymphoma. Case presentation: One patient presented of 5 days with red eye, ophthalmic pediatric evaluation one month before normal. Not pathologic background history. At the ophthalmic exam we found conjunctival ulcerative salmon lesion on the inferior bulbar conjunctiva. Orbital Magnetic Resonance showed bilateral anterior preseptal reinforcement. The mass was removed. The pathologic findings revealed conjunctiva with proliferation of cells with less cytoplasm and large hyperchromatic and pleomorphic nuclei. Small cells of lymphoid appearance are also observed. This lesion ulcerates the epithelium. Immunohistochemistry, The tumor cells are positive for CD20 and TDT. CD30 positive cells are also observed. CD3, CD5, CD7 and CD2 mark accompanying T lymphocytes. CD38 marks some plastics cells. CD34, Bcl2 and CD68 mark in focal form. CD23, CD10, Cyclin, Bcl6 and IgD are negative. The cell proliferation index measured with Ki-67 is 80%. Conclusion: The patient that we identified with this lesion was the first sign of pediatric B-cell leukemia/lymphoma. And without commitment of any other organ and this condition had not been documented as first sign.

Presentation Title: Primary sebaceous gland carcinomas of the bulbar conjunctival.
Authors: Juan Valenzuela, Arturo Irarrazaval, Martin Devoto, Mariel Flores Fernandez
Consultores oftalmologicos, Buenos Aires, Argentina
Abstract: Purpose: Sebaceous carcinomas are uncommon malignancies that commonly develop at the level of the eyelids, in the meibomian glands and less frequently in the zeiss glands, hair follicles, and caruncle. The primary sebaceous carcinomas of the bulbar conjunctiva are extremely infrequent. Procedures: We describe a 94 years old man with a suspicious lesion of intraepithelial carcinoma with substantial growth after one month treatment with interferon alfa 2 beta. Results: Patient presented a tumor of upper temporal bulbar conjunctiva with abundant vascularization, and limbus involvement with adjacent corneal ulceration. No involvement of the palpebral conjunctiva or eyelids. An excisional biopsy was performed with "no touch" technique and margins of 4 mm. Followed by triple cryotherapy of the tumor bed and epitheliectomy with alcohol of the corneal component. The anatomopathological examination showed an atypical epithelial proliferation with sebaceous differentiation, high mitotic count and necrosis sectors with epidermoid areas. Confirming the diagnosis of a high grade sebaceous carcinoma. On 10 months follow up the patient have not showed recurrence or metastasis. Conclusions: Although glandular carcinoma usually occurs in the eyelids, isolated involvement of the bulbar conjunctiva is possible. In this way, it must be maintained as a differential diagnosis in atypical cases.

Presentation Title: Risk Factors for Local Recurrence, Exenteration, Metastasis and Death from Disease for Conjunctival Squamous Cell Carcinoma
**Authors:** Christian El-Hadad, Joshua Ford, Shiqiong Xu, Bita Esmaeli

**UT MD Anderson Cancer Center, Houston, USA**

**Abstract:** Purpose: To investigate correlations between AJCC 8th edition TNM classification and local recurrence, nodal metastasis, distant metastasis and death from disease in patients with conjunctival squamous cell carcinoma. Methods: Clinical data including age, gender, ethnicity, previous exposure to radiation, immunosuppression, AJCC TNM criteria, type of treatment, local recurrence, nodal metastasis, and distant metastasis were recorded. Results: 44 patients (24 men, 20 women; median age: 63 years) had AJCC stage at presentation as follows: TisN0M0 (n=18; 41%), T2N0M0 (n=7; 16%); T3N0M0 (n=13; 30%); T4aN0M0 (n=5; 11%); T4bN1M0 (n=1; 2%). 5 patients had a history of chronic immunosuppression. 34 patients presented with primary tumors and 10 with recurrent tumors. Overall, 7 patients (16%) experienced local recurrence. The T categories for these patients were: Tis (n=2), T2 (n=1), T3 (n=4). Time to local recurrence ranged from 4-44 months after definitive treatment (median 17 months). None of the patients presented with nodal metastasis at presentation; 3 patients developed nodal metastasis during the follow up period (at 11, 26 and 75 months); all had presented with T3 tumors. 11 patients had an exenteration: 8, at presentation and 3, after recurrence. The T categories at presentation for these 11 patients were: Tis (n=1; diffuse involvement of anophthalmic socket), T2 (n=1; blind eye with diffuse conjunctival involvement), T3 (n=3), T4a (n=5), T4b (n=1). Two patients died of disease (T3N1M1 and T4aN1M1) Conclusion: AJCC T category of T3 or more advanced was associated with a higher risk of local recurrence, orbital exenteration, nodal metastasis, and death from disease.
Presentation Title: Adjuvant high-dose rate (HDR) brachytherapy for ocular tumours with orbital invasion
Authors: Monica Pagliara¹, Luca Tagliaferri², Maria Blasi¹
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Abstract: Purpose: To evaluate local control, functional and cosmetic outcome of postoperative high-dose rate (HDR) brachytherapy in patients affected by ocular malignant tumours with orbital invasion.
Methods: A retrospective study was conducted in 6 patients affected by malignant eye cancer infiltrating the orbit, treated with surgical excision and postoperative (HDR) brachytherapy between 2013-2017. The primary tumour was uveal melanoma with extraocular extension in 2 (33.3%) patients, conjunctival melanoma in 2 (33.3%), basal cell carcinoma in 1 (16.7%), squamous cell carcinoma in 1(16.7%). The surgical procedures consisted of modified enucleation in 2 patients (two affected by uveal melanoma with extra-scleral extension and two affected by conjunctival melanoma with globe invasion) and surgical excision of the primary tumour and orbital infiltration in the remaining patients. Within one month from the surgery each patient underwent adjuvant interstitial high doses brachytherapy with 192Ir. A target dose of 3400 cGy (range, 3000-3400 cGy) was delivered in 10-12 twice-daily fractions (range, 250-340 cGy per fraction) over 5-6 consecutive days. Data analysis included local tumour control and metastatic rate, acute and late toxicity, functional and aesthetic results.
Results: in all patients treatment was well tolerated, there was no orbital recurrence at a median follow-up of 36 months (range 12-60 months). Postoperative high-dose-rate brachytherapy resulted in an excellent disease control and functional outcome, without no significant acute or late side effects.
Conclusions: postoperative high-dose-rate brachytherapy is a promising feasible, successful and well tolerated option for selected patients affected by ocular tumours with orbital invasion.

Presentation Title: CT guided core needle biopsy of orbital tumours
Authors: Sachin Salvi¹², Lindsay McGrath¹, Daniel Connolly³
¹Sheffield Ocular Oncology Service, Royal Hallamshire Hospital, Sheffield, United Kingdom. ²Department of Oncology and Metabolism, University of Sheffield, Sheffield, United Kingdom. ³Department of Radiology, Royal Hallamshire Hospital, Sheffield, United Kingdom
Abstract: Purpose: To present our novel experience in the use of core biopsy needle under CT guidance to biopsy orbital tumours.
Method: Patients presenting to Sheffield Ocular Oncology Service between November 2017-October 2018 with suspected orbital metastasis and meeting eligibility criteria as decided by MDT were included in the study. Patients had a peribulbar block prior to planning CT done to localise the tumour. Under asepsis a 6 cm 18G Temno Evolution semi-automated biopsy needle was inserted at reference point. The correct location was confirmed with a low dose CT scan prior to gaining biopsy.
Results: All four patients included in the study developed periorbital bruising but no sight threatening complications. Biopsy was successful in 3 patients where metastatic disease was confirmed. The patient in whom the biopsy was unsuccessful then had a biopsy via surgical approach which demonstrated the lesion to be a sphenoid wing meningioma rather than a metastasis.
Conclusion: CT guided core needle biopsy of orbital tumour is safe and provides adequate tissue sample to aid diagnosis in soft tissue tumours. It may not be successful in tumours associated with orbital bone. It may be a preferable in elderly patients with suspected metastasis as this avoids major surgery such as lateral orbitotomy which may have otherwise been required with its associated morbidities. Procedure can be done as a day case thus avoiding hospital stay and its associated hospital acquired infections risks. Also as there is no post op healing time; radiotherapy treatment can be immediately commenced if appropriate.
**Presentation Title:** Clinical Characteristics of IgG4-related Ophthalmic Disease  
**Authors:** Shunichiro Ueda, Rei Nemoto, Yoshihiko Usui, Kazuhiko Umazume, Hiroshi Goto  
*Tokyo Medical University, Tokyo, Japan*  
**Abstract:** [Purpose] IgG4-related ophthalmic disease (IgG4-ROD) has been noted to have several patterns of ocular adnexal involvement and symptoms. The aim of this study is to elucidate clinical manifestations of IgG4-ROD. [Methods] This is a retrospective study being performed in Tokyo Medical University Hospital between 2002 and 2014. We reviewed the medical charts of the 92 patients with diagnosis of IgG4-ROD. The patients' demographic, clinical, and laboratory findings as well as their management and outcome were investigated. [Results] Based on the diagnostic criteria of IgG4-ROD (H Goto et al, 2015), 48 patients were diagnosed as definite, 10 cases as probable, and 33 cases as possible. Patients were 48 women and 44 men. An average age was of 58.3 years, and an average IgG4 serum levels was 595.2 mg/dL at the time of initial diagnosis. Imaging studies showed infiltrative lesions in lacrimal glands (90.1%), extraocular muscles (12.1%), orbital mass (5.5%), orbital diffuse mass (9.9%), eyelid (27.5%), sclera (1.1%), and optic nerve (7.7%). Symptoms included vision loss (12.1%), visual field loss (5.5%), diplopia (12.1%), and dry eye (27.5%). Furthermore, during its clinical course, swelling of salivary glands (33.0%) and IgG4-related disease other than head and neck (64.8%) were observed. Patients received oral corticosteroids (68.1%) and/or corticosteroids injection (31.9%), however, 23 patients (25.3%) developed recurrence. [Conclusions] We clarified the clinical characteristics of IgG4-ROD. This study demonstrated that visual function may be affected in IgG4-ROD.

**Presentation Title:** Tissue and circulating plasmablasts in patients with IgG4-related ophthalmic disease  
**Authors:** Yoshihiko Usui, Marina Ogawa, Kazuhiko Umazume, Kinya Tsubota, Hiroshi Goto  
*Tokyo Medical University Hospital, Tokyo, Japan*  
**Abstract:** Purpose: Immunoglobulin G4-related ophthalmic disease (IgG4-ROD) is a fibroinflammatory disease characterized by enlargement of orbital tissues, infiltration of IgG4-positive plasmacytes, and elevated serum IgG4 levels. It is reported that circulating IgG4-secreting plasmablasts cells expressing CD19+CD24−CD38high was elevated in patients with active IgG4-related disease and decreased after glucocorticoid treatment (Arthritis Research & Therapy, 2017). Therefore, we elucidate the profile of plasmablasts in involved tissues and peripheral blood from patients with IgG4-ROD and compared to those to orbital mucosa-associated lymphoid tissue (MALT) lymphoma. Methods: From 2017 to 2018, surgical biopsies and peripheral blood from consecutive patients with newly diagnosed IgG4-ROD and orbital MALT lymphoma were recruited from Tokyo Medical University Hospital. A total of 22 tumors from 22 patients were analyzed in this study, including 12 with 10 with definitive IgG4-ROD (4 men and 6 women, mean age 56.8 ±11.5 years) and orbital MALT lymphoma (4 men and 8 women, mean age 70.3±10.8 years). All patients were immunocompetent Asian adults. Flow cytometry was performed with the following antibodies: CD19, CD24, and CD38. Results: CD19+CD24+CD38high plasmablasts cells were significantly increased in the tissue of patients with IgG4-ROD (16.3±11.7%) higher than that in patients with orbital MALT lymphoma (2.3±3.1%). There were no differences in the peripheral blood or in other B cell populations (memory B cells CD19+CD24−CD38- and naïve B cells CD19+CD24+CD38intCD38int) between two groups. Conclusion: The results of the present study indicate that IgG4-secreting plasmablasts are involved in the pathogenesis in tissues of IgG4-ROD.
Presentation Title: Lymphoma of the ocular adnexal region in Denmark: A nation-based study of 387 cases from 1980 to 2017
Authors: Steffen Heegaard, Frederik Holm, Lauge Mikkelsen
Department of Ophthalmology and Pathology, Rigshospitalet, Copenhagen, Denmark
Abstract: Purpose: This nationwide study of ocular adnexal lymphoma (OAL) sought to find information on incidence, distribution of subtypes, survival, prognostic factors, as well as clinical findings. Method: Patients diagnosed with OAL from January 1st, 1980 to December 31st, 2017 were found through Danish registers and clinical as well as survival data was collected. The data was analyzed with Kaplan-Meier plots and the log-rank test. Results: In total 387 patients were included in the study. The major lymphoma subtypes were extranodal marginal-zone lymphoma (EMZL) (55%), diffuse large B-cell lymphoma (DLBCL) (13%), mantle cell lymphoma (MCL) (11%) and follicular lymphoma (FL) (10%). OAL is a disease of the elderly with a median age of 69 years and has an even gender distribution. The incidence of lymphoma of the ocular adnexal region has increased significantly throughout the time period (Pearson test: r=0.65; p>0.001). In the period 1980-1984 the incidence was 0.086 per 100 000 which increased to 0.307 per 100 000 in the period 2013-2017. Low-grade, low-stage primary lymphomas were commonly treated with external beam radiation therapy, whereas patients with high-stage, high-grade and/or relapsed disease were treated with chemotherapy with or without immunotherapy. The low-grade subtypes EMZL (81%) and FL (56%) had better 10-year disease-specific survival than the high-grade lymphomas DLBCL (38%) and MCL (31%)(p>0.001). Conclusion: OAL is frequently a disseminated disease and a thorough examination with a bone-marrow biopsy and PET-CT is recommended. The subtype is the primary predictor of outcome and the different subtypes should be considered as distinct entities.

Presentation Title: Clinical features and outcome of sebaceous carcinoma of the eyelid
Authors: Hiroshi Goto, Kinya Tsubota, Shun-ichiro Ueda, Rey Nemoto, Kazuhiko Umazume, Yoshihiko Usui
Tokyo Medical University, Tokyo, Japan
Abstract: Purpose: Sebaceous carcinoma is a relatively common eyelid malignant tumor in East-Asia compared to Western countries. The aim of this study was to clarify the demographic profile, clinical features and outcome of Japanese patients with sebaceous carcinoma of the eyelid.Methods: One hundred and twenty-six patients with sebaceous carcinoma of the eyelid diagnosed at Tokyo Medical University Hospital between 1994 and 2017 were reviewed. The outcome of 114 patients who were treated and followed for at least 18 months in our hospital was also investigated. Results: The patients comprised 52 males and 74 females. Average age of the patients at diagnosis was 70.6±13.8 (31-96) years. Main lesion was located at the upper eyelid in 52%, lower eyelid in 38% and others in 10%. Average tumor size of 105 measurable cases was 9.6 mm × 6.7 mm. Treatment included surgical resection and reconstruction of the eyelid in 109 cases (93%), orbital exenteration in 5 cases (4%) and radiation therapy in 3 cases (3%). Local recurrence was noted in 10 cases (9%). Among these 10 cases, 4 cases recurred within 3 months and 6 cases recurred 30 months on average after treatment. Metastasis to regional lymph nodes was confirmed in 10 cases (9%). Four patients (3%) died due to direct intracranial invasion of the tumor. Conclusion: Appropriate treatment at optimal timing is critical to improve the outcome of sebaceous carcinoma of the eyelid. Long-term follow up is required because local recurrence and metastasis may occur several years after treatment.

Presentation Title: Eyelid Basal Cell Carcinoma in Saudi Arabia
Authors: Azza Maktabi1, Manar Al Wehaib1, Hind Alkatan2, Silvana Schellini1
1KKESH, Riyadh, Saudi Arabia. 2KSU, Riyadh, Saudi Arabia
Abstract: PURPOSE Data on basal cell carcinoma (BCC) from the Middle East are deficient. We present the features and management outcomes for BCC over the last 36 years in Saudi Arabia. SUBJECTS AND METHODS This retrospective chart review included BCC patients diagnosed and treated at Saudi Arabia between 1980 and 2016. Data were collected on patient demographics, clinical and histopathological characteristics of the lesions, management, and follow-up. RESULTS One hundred and twenty-six patients with BCC were included in this
study. The incidence of BCC in Saudi Arabia is 0.8 cases a year. The median age of the patients was 71 years. BCC affected 58.9% of males. The lower lid was the most common site of occurrence (52.7%). Clinically, BCC was most commonly recognized as a mixed lesion (41.1%) and 50.4% were histologically nodular. Risk factors for poor prognosis included tumor localization in the medial aspect of the lid, tumor size > 5 mm, histological subtype being ulcerative or morphea forms, affected margins, and recurrent lesions. CONCLUSION BCC is a rare condition in Saudi Arabia. The clinical features and histopathology of BCC in Saudi Arabia are similar to the patterns observed in other regions of the world. Early detection and timely management mitigates the extensive destructive ocular/orbital damage due to BCC and results in better patient outcomes.

Presentation Title: Accuracy of Imaging in Predicting Tissue Diagnosis of Orbital Neoplasms: Past and the Future
Authors: Zeynel Karcioglu
University of Virginia, Charlottesville, Virginia, USA
Abstract: Purpose/Background: Currently, imaging is considered to be the gold standard for the diagnosis and management of orbital neoplasms. However, the predictive potential of imaging in terms of specific diagnosis varies substantially among tumor etiologies and tissue types. So, the question is what is the degree of predictability of tissue accurate tumor diagnosis by orbital imaging?
Methods: We investigated retrospectively, the correlation between the specific imaging diagnoses (IDx) cited in the radiology reports and the final histopathologic diagnosis (FHDx) in 119 patients with orbital mass lesions.
Results: Approximately half of patients had a biopsy performed based on clinical information alone while 59 had imaging (28% had an MRI, 53% had a CT and 17% had both) done prior to biopsy. Only 40% had FHDx correlating with the diagnosis listed as “most likely” by the radiologist.
Conclusion: Although the imaging data was accurate in characterizing the orbital lesions in a categorical fashion (neoplastic vs. inflammatory, benign vs. malignant etc.) and revealed detailed topographical information, our series revealed low yields of correlation between the imaging and histopathologic diagnoses. Clearly a more accurate testing method is needed for tissue specific diagnosis and that appears to be coming from the direction of molecular MRI research. When a receptor is selected that binds to a specific neoplastic cell, tumor specific imaging and hence the “in vivo biopsy” will be possible, similar to antibody specific staining in histopathology.
Presentation Title: Malignant Rhabdoid tumor mimicking optic nerve glioma in a 6 month old infant.
Authors: Jonathan Kim1,2, Jesse Berry1,2
1Children's Hospital Los Angeles, Los Angeles, USA. 2USC Roski Eye Institute, Los Angeles, USA
Abstract: Purpose: To describe a case of an infant initially diagnosed with an optic nerve glioma which on orbital biopsy was diagnosed as a malignant rhabdoid tumor.Method: A 6 month old boy presented with left proptosis of 3 mm as well as hypoglobus, hypotropia and a left RAPD. Fundus exam showed left optic nerve edema and evidence of a central retinal artery occlusion. CT scan in the emergency room showed a fusiform enlargement of the left optic nerve. MRI scan showed enlargement of the left optic nerve as well as infiltrative changes of the anterior clinoid process. Findings were consistent with an aggressive, hypercellular tumor with probable bone marrow involvement.Results: Urgent orbital biopsy was performed, and the pathology was confirmed as a malignant rhabdoid tumor with a homozygous deletion of SMARCB1. Patient was started on systemic chemotherapy with minimal tumor regression. Left orbital exenteration was then performed to decrease tumor load, using a lid-sparing, conjunctival-sparing technique with a silicone implant. Postoperatively, the patient received additional cycles of chemotherapy and radiotherapy. The patient is currently doing well although neurosurgical resection of the skull base component is being considered.Conclusion: Malignant rhabdoid tumor of the orbit is a rare entity which can present in young children with findings similar to optic nerve glioma although the clinical course is much more rapid and aggressive. Clinicians should be aware of this life-threatening malignant tumor and perform an urgent orbital biopsy when the presentation and radiographic findings are not typical for a benign neoplasm.

Presentation Title: Orbital retinoblastoma- complete resolution with 6 cycles of chemotherapy
Authors: Sumeet Lahane Dr, Ankit Tomar Dr, Santosh Honavar Dr
Abstract: Purpose: To report a case of orbital retinoblastoma showing complete resolution with 6 cycles of high dose chemotherapyMethods: Retrospective case studyResult: A 5-month-old presented with both eye retinoblastoma. Neuroimaging revealed large intraocular mass with calcification with extraocular extension and optic nerve extension in LE. Staging bone marrow and CSF examination were negative. He was diagnosed as LE orbital RB and planned for multimodal management in form of 6 cycles of neoadjuvant high dose chemotherapy, enucleation, followed by adjuvant chemotherapy and external beam radiotherapy. However, on completion of 6 cycles of neoadjuvant chemotherapy, there was complete regression with chemotherapy alone. Repeat neuroimaging showed complete resolution of extraocular extension with total calcification of the tumor. EBRT in this heritable case would increase the risk of second malignant neoplasm. So we have opted to carefully observe the eye, after having explained to the family about the risks and benefits. He has been on monthly follow-up for last 10 months and lesions in both eye are completely regressed. 3 monthly repeat neuro-imaging have shown completely regressed tumor.Conclusion: Orbital retinoblastoma requires multimodal management. In this unique case, we found complete regression of orbital RB with 6 cycles of neoadjuvant high dose chemotherapy

Presentation Title: A Case Report of Xeroderma Pigmentosum with Ocular Involvement in a 4 year old Boy
Authors: Thonnie Rose See1,2,3, Charmaine Ang2, Fatima Regala2
1Emory Eye Center, Atlanta, USA. 2East Avenue Medical Center- DOH Eye Center, Quezon, Philippines. 3St. Martin Eye Clinic, Candon, Philippines
Abstract: Xeroderma Pigmentosum (XP) is a rare autosomal recessive disorder of the nucleotide excision repair leading to a defective repair of DNA damaged by UV radiation. This is characterized by mucocutaneous and ocular hypersensitivity to UV radiation. It is more common in populations where marriage of close blood-relatives is common. There is no sex or race predilection. Purpose: To present a case of xeroderma pigmentosum with involvement of the periocular tissue and anterior segment of both eyes. Methods: A case report of a patient with xeroderma pigmentosum Case Summary: We present a case of a 4-year-old Filipino boy who started to have erythematous plaques all over sun exposed area starting 5 months of age. By two years old, lesions progress to mottled pigmentation and ulceration affecting more than 80% of the total body surface area. A skin biopsy was done and was found to be squamous cell carcinoma. On presentation he was found to have extensive ulceroproliferative lesion on the whole face and extremities. Ophthalmological examination revealed ulceration of both lower eyelids with bilateral diffuse corneal opacity and neovascularization. The conjunctiva was congested and a conjunctival mass extends to both cornea. Patient underwent multiple excision of skin lesions with skin grafting. Conclusion: Our case was unique one, as there was no family history or consanguineous marriage. This case is presented to create awareness among treating physicians and surgeons about this rare condition and importance of early detection and prevention of UV rays induced skin damage.

Presentation Title: Rare Malignant Sweat Gland Tumor of Eyelid - A Case Series

Authors: Fairooz Manjandavida1,2,3, Smitha Shambhu2, Kaustubh Mulay4
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Abstract: Purpose: To report 2 cases of syringocystadenocarcinoma papilliferum of the eyelid, which is a rare malignant eyelid tumor. Method: Consecutive case series of a rare malignant eyelid tumor with clinicopathological correlation. Two cases were included in the report; clinical characteristics, histopathological features and immunohistochemistry was studied in detail. Results: Two patients presented with large rapidly growing eyelid mass in the lower eyelid. Both underwent complete anterior lamellar excision with margin control. Immunohistochemistry differentiated the lesion from other benign and malignant sweat gland tumors. Differential diagnosis included metastatic breast and gastrointestinal adenocarcinomas. Systemic evaluation was within normal limits in both. One of the patient had histopathologically proven syringoadenoma in the contralateral eye. At a mean follow up of 12 months and 9 months there is no recurrence or regional and systemic metastasis. Conclusion: Syringocystadenocarcinoma papilliferum of eyelid is a rare malignant neoplasm rarely reported in eyelid. There is only a single reported case so far.

Presentation Title: Molecular genetics of primary orbital melanoma. A case report and analysis of 5 further cases.

Authors: Hardeep Mudhar1, Rachel Doherty2, Sachin Salvi3, Zanna Currie4, Jennifer Tan4, Karen Sisley2
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Abstract: Purpose: To report the molecular genetics of a case of primary orbital melanoma and an analysis of 5 further cases. Method: A 76y old male presented with left reduced visual acuity and pain for 2 weeks. Examination showed ocular melanocytosis, affecting the episclera without skin involvement, an RAPD, 4 mm proptosis and slight upward globe displacement. An MRI revealed a 22 mm fusiform mass abutting the medial rectus in the posterior medial orbit, with optic nerve compression. A body PET scan was clear. An incisional biopsy showed malignant melanoma. Clinically, there was no evidence of conjunctival, uveal, eyelid, remote mucosal or cutaneous melanoma. A skin-sparing exenteration was performed, followed by radiotherapy. Results Histology confirmed the presence of a necrotic mixed spindle and epithelioid primary orbital melanoma, with background
melanocytosis of the orbit soft tissue, episclera, and uvea. There was no evidence of active or regressed uveal melanoma. Array comparative genomic hybridisation and Sanger sequencing showed monosomy 3, partial 8q gain and a mutation in SF3B1. The patient died of miliary liver metastases 36 months after surgery. We further analysed 5 cases from our files and found 1 case with GNA11 mutation, 1 with SF3B1 mutation and 3 further cases displayed chromosomal changes reported in conjunctival melanoma, 2 of which showed NRAS and pTERT mutations. Conclusions: Primary orbital melanomas show chromosomal changes and point mutations known to occur in uveal and conjunctival melanomas. Whilst the numbers are small, this study suggests 2 molecular genetic subgroups worthy of further study.

**Presentation Title:** Clinical and Pathological Features Of 19 Eyelid Pilomatrixoma

**Authors:** Charles Eberhart, Sepideh Siadati

*Johns Hopkins University, Baltimore, USA*

**Abstract:** Purpose: To present clinical and histological data from 19 eyelid pilomatrixoma. Methods: Cases diagnosed at our institution since 1981 were identified, slides reviewed, and both demographic and clinical data obtained. Results: Patient ages ranged from 2 to 63 years (median 14 years), including 12 (63%) females and 7 (37%) males. Eight (42%), and 4 (21%) cases arose in the first and second decades of life, respectively, with 14 and 5 tumors in the upper and lower lids, respectively. All tumors presented as solitary lesions, although one patient had a second pilomatrixoma in the left temple. Initial clinical diagnoses included chalazion suspicious for sebaceous carcinoma (1 case), sebaceous cyst (2 cases), dermoid cyst (1 case), cystic lesion (4 cases), and suspicious nodule (11 cases). Tumors varied from 2 mm to 12 mm in maximum dimension. Microscopically, the tumors were relatively typical with basaloid and shadow cells accompanied by calcification and foreign body giant cells. However, mixed acute and chronic inflammation was noted in 1 case, acute inflammation in 3, hemosiderin laden macrophages in 1, and in 4 cases (21%) basaloid cells were absent. All tumors were located in the lower dermis or subcutaneous tissues, except for 1 case centered in the upper dermis. Conclusion: Eyelid pilomatrixoma are uncommon, with approximately 60% of cases presenting in the first two decades of life. They are rarely suspected clinically, and can be mistaken for cyst, chalazion, sebaceous carcinoma and other tumors. Complete excision is curative and diagnosis can generally be established by histopathological examination.

**Presentation Title:** Two cases of Warthin’s tumor

**Authors:** Koh-ichi Ohshima, Youko Shin-nou

*Okayama Medical Center, Okayama, Japan*

**Abstract:** A Warthin’s tumor is a benign tumor sometimes arising in salivary gland. It occupies about 4 to 11% of all salivary gland tumors. However, a Warthin’s tumor is quite rare in ocular adnexa. We experienced two cases of Warthin’s tumor and will present them. The first case was 53 year-old female. She came to our clinic for the treatment of right upper eyelid tumor that was gradually increasing since one year ago. The tumor size was 15 x 13 mm by the magnetic resonance imaging (MRI). The tumor showed low signal intensity in both T1-weighted images and T2-weighted images. We extirpated the tumor by superior palpebral sulcus incision. During the surgery we could find that the tumor had adhered to the tarsal plate. The histopathological finding showed that medium-sized tumor cells with eosinophilic cytoplasm and oval nucleus proliferated forming papillary or glandular structures. The second case was 89 year-old male. He came to us for the treatment of left lower eyelid marginal tumor that was gradually increasing since six months ago. The tumor size was 5 x 3 mm and the tumor surface was dark red. We totally removed the tumor keeping 1-mm safety margin. The pathological finding was almost same as that of the case 1.