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Abstracts

0012

Clinical analysis of uveal melanoma in Japan

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Purpose: To clarify clinical features of Japanese patients with uveal melanoma.

Method: We analyzed 125 eyes of 125 patients diagnosed as uveal melanoma from 1992 to 2014 retrospectively.

Results: The mean age of the patients at the time of diagnosis was 58.1 ± 14.4 years. Tumor arose from choroid (93%), ciliary body (4%) and iris (3%). The main reason led to diagnosis included decreased vision (27%), visual field loss (17%), and no significant symptoms (16%). Average tumor size of the choroidal melanoma was 10.4 mm in largest basal diameter and 7.2 mm in height. Treatment included enucleation of eyeball (53 cases), local resection of the tumor (4 cases), heavy particle beam therapy (18 cases), and brachytherapy (4 cases). Extraocular metastasis was detected in 22% of the patients, 89% of them died within 5 years. Five-year survival rate was 20% in 6 cases (14%) who revealed extrascleral invasion in histopathologic study.

Conclusions: Prognosis of the patients with metastatic uveal melanoma is extremely poor. Early diagnosis and treatment, and establishment of follow-up system after local treatment are critical. Further development and dissemination of novel treatment for metastatic melanoma is desired.

0013

Comprehensive polymerase chain reaction assay for detection of pathogenic DNA in lymphoproliferative disorders of the ocular adnexa

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Purpose: To conduct an exhaustive search for pathogenic DNA in lymphoproliferative disorders (LPD) of the ocular adnexa.

Methods: From 2008 to 2013, a total of 70 patients diagnosed with LPD of the ocular adnexa were studied. Specimens were screened for bacterial, viral, fungal, and parasitic DNA by multiplex polymerase chain reaction (PCR) and quantitative real-time PCR.

Results: Among 19 cases of conjunctival mucosa-associated lymphoid tissue lymphoma, human herpes virus (HHV)-6 DNA was detected in 1 case, HHV-7 DNA in 1 case, chlamydia DNA in 1 case, Epstein-Barr virus (EBV) DNA in 3 cases, and bacterial 16S ribosomal DNA (bacterial 16S) in 2 cases. HHV-6 DNA was detected in only one case of orbital mucosa-associated lymphoid tissue lymphoma. Among 22 cases of IgG4-related ocular disease, HHV-6 DNA was detected in 5 cases, HHV-7 DNA in 8 cases, EBV-DNA in 7 cases, and bacterial 16S in 1 case. Multiple infections were detected in 7 of 22 cases. In 7 cases of orbital reactive lymphoid hyperplasia, HHV-6 DNA was detected in 2 cases, HHV-7 DNA in 3 cases, EBV-DNA in 2 cases, and bacterial 16S in 1 case.

Conclusions: Our comprehensive PCR assays detected various infectious antigen DNAs in tumor specimens, especially herpes viruses HHV6, HHV7, and EBV. Chronic stimulation or oncogenes from these infectious agents might be involved in the pathogenesis of LPD of the ocular adnexa.

0015

Optic Nerve Obscuration in Retinoblastoma: a Risk Factor for Optic Nerve Invasion?

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Purpose: Obscuration of the optic nerve is a common finding in advanced intraocular retinoblastoma, but there are no previous studies examining its risk for optic nerve invasion. The objective of this study is to evaluate the risk of optic nerve invasion associated with optic nerve obscuration either at diagnosis or that persists during treatment.

Methods: Retrospective review from 2011-2016 of patients with advanced retinoblastoma (Group D/E) that demonstrated complete obscuration of the optic nerve by the tumor at diagnosis and a second group of patients who had this finding persist through the course of therapy.

Results: Advanced retinoblastoma was diagnosed in 102 eyes of 86 patients. The optic nerve was obscured in 69 eyes (68%) at diagnosis. Of these, 30 (43%) underwent salvage therapy and 39 (57%) primary enucleation. On histopathologic analysis of primarily enucleated eyes with optic nerve obscuration at diagnosis, 41% had pre-laminar invasion and 15% post-laminar invasion. Four eyes in the salvage group had persistent optic nerve obscuration throughout treatment; 2 were subsequently enucleated without evidence of optic nerve invasion. Average follow up was 23.5 months (range 1-62 months)

Conclusions and Relevance: Optic nerve obscuration at diagnosis may be associated with post-laminar optic nerve invasion. While persistent obscuration of the optic nerve is a poor prognostic sign for both globe salvage and vision, it does not appear, to increase the risk of optic nerve invasion during or after treatment. As long as appropriate control of the intraocular tumor can be attained these eyes can be safely monitored.

0021

An unusual orbital case of intermittent double vision: Multidisciplinary patient care in an urban and rural setting

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A 77 year old man presented with intermittent and variable double vision over the course of a year. Early laboratory and radiological investigations yielded no clear diagnosis and his symptoms resolved. Repeat MRI some months later demonstrated a right orbital apex lesion which on biopsy yielded a histological diagnosis of orbital lymphoproliferative disease. Systemic lymphoproliferative disease was subsequently detected and further medical management involved six months of intensive chemotherapy. Our report highlights the multidisciplinary and multicentre medical and surgical management of an uncommon presentation of double vision.

Optical coherence tomography-angiography in differential diagnostics of small uveal melanoma and circumscribed choroidal hemangioma

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Purpose: To examine optical coherence tomography - angiography criteria in small uveal melanoma and circumscribed choroidal hemangioma in a comparative perspective.

Material and Methods: 23 patients with small uveal melanoma (n=13) and circumscribed choroidal hemangioma (n=10) were examined by optical coherence tomography - angiography.

Results: Optical coherence tomography - angiography in 13 patients with small uveal melanoma showed neovascular component bounding avascular zone corresponding to the slope of the tumor under retinal pigment epithelium. We also revealed a loop-like vasculature nature with numerous bends and weaves under retinal vessels.

We observed a neovascular component with the larger caliber of the vasculature with a tree character vascularization in a large barrel and extending from it multiple branches in 4 cases in circumscribed choroidal hemangioma under retinal pigment epithelium. In 6 cases a diffuse-type vascularization with many small tortuous vascular branches was presented.

Conclusions: Optical coherence tomography - angiography allows to reveal own tumor vessels in small uveal melanoma and circumscribed choroidal hemangioma with its own vascularization characteristics. Increasing the frequency of own tumor vessels neovascularization detection will make it possible to establish a timely diagnosis of malignant tumor and provide adequate eye-preserving therapy.

Aqueous Humor as a Surrogate Liquid Tumor Biopsy in Retinoblastoma

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Purpose: The aim of this study is to determine whether tumor-derived nucleic acids and tumor DNA copy number alterations can be detected in the aqueous humor (AH) of retinoblastoma (RB) eyes.

Methods: AH was analyzed for DNA, RNA and miRNA using Qubit HS kits. Circulating cell-free DNA (cfDNA) isolation and sequencing library protocols were optimized to retain cfDNAs from the AH and these optimized methods were applied to AH samples from RB patients. Shallow whole genome sequencing was performed on Illumina platform followed by genome-wide copy number variation (CNV) profiling to assess the presence of tumor DNA fractions in AH cfDNA.

Results: Eighteen AH samples from 8 patients (6 patients pre-intravitreal injection and 2 post-enucleation) were examined. All had measurable DNA, RNA and miRNA, with miRNA having the highest concentrations. Whole genome sequencing of AH cfDNA from 2 primarily enucleated eyes and sequential AH cfDNAs obtained from 2 eyes undergoing intravitreal melphalan injections for treatment of tumor seeding revealed tumor-derived cfDNA based on CNV profiles that demonstrated tumor copy number alterations.

Conclusions: This is the first study to evaluate AH from RB eyes undergoing salvage therapy with intravitreal injection of melphalan. We were able to assay quantifiable levels of nucleic acids in treated and untreated eyes and found that AH cfDNA had retinoblastoma-related DNA copy number alterations in all four tested RB patients. This suggests that AH can serve as a 'surrogate tumor biopsy' when tumor tissue is not available.

0042

Spontaneous subretinal haemorrhage from optic disc astrocytoma

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An otherwise healthy 49-year-old white man, originally diagnosed with a solitary left optic disc astrocytic hamartoma 15 years beforehand, was referred because of visual blurriness in the left eye. Visual acuity was 20/20 and fundoscopy confirmed the presence of a pale mulberry-like tumour adjacent to the optic disc and surrounded by an arc of subretinal haemorrhage. Fluorescein angiography failed to demonstrate a choroidal membrane or aneurysm. Observation after 2 months showed most of the bleed was gone. Subretinal haemorrhage is a rare astrocytoma-related complication. However, a conservative approach may be found beneficial.

0043

Use of adjuvant sub-tenons anaesthesia in primary enucleations in reducing pain and incidence of bradycardia from the oculo-cardiac reflex

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Purpose: To evaluate the benefit of adjuvant sub-tenons anaesthetic during primary enucleation surgery in reducing post-operative pain. Secondary target in reducing the incidence of bradycardia induced by oculo-cardiac reflex.

Method: 30 eyes of 30 patients were randomly allocated to either receiving early adjuvant sub-tenons anaesthesia or sub-conjunctival anesthesia at the end of surgery. Patients were excluded if the eye was painful before surgery. Patients' pain scores were recorded 2 hours following surgery and again the following morning using graphical pain scores and questionnaire. The incidence of bradycardia during surgery was recorded if this occurred with muscle manipulation.

Results: There was a mean reduction of 30% in pain scores using sub-tenons anaesthesia during surgery when recorded over 18-24 hours. There was a similar reduction in the incidence of bradycardia during surgery. There were no complications with giving the local an

Conclusions: The use of adjuvant sub-tenons anesthesia during primary enucleation surgery is beneficial in reducing post-operative pain for the patient as well as reducing the risk of bradycardia during surgery.

0045

Identification of RB1 Germline Mutations and the Inheritance Pattern of Retinoblastoma in Jordan

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Purpose: Retinoblastoma (RB) is a childhood cancer developing in the retina due to mutations in the RB1 gene. Herein we are trying to identify the oncogenic mutations in the RB1 gene and the inheritance pattern of RB in the Jordanian RB patients.

Methods: The peripheral blood of 50 retinoblastoma patients was collected, and genomic DNA was extracted. DNA sequencing was conducted by Next Generation Sequencing analysis, Sanger sequencing, Quantitative multiplex PCR (QM-PCR), and Allele-specific PCR.

Results: In this cohort, 50 affected patients were studied. Twenty (40%) patients had unilateral RB, and 30(60%) had bilateral RB. Overall, 36(72%) patients had germline disease, 17(47%) of them had the same mutation detected in one of the parents (inherited disease). In the bilateral group, all (100%) patients had germline disease, and 13(43%) had inherited mutation, and in the unilateral group, 6(30%) had germline disease and 4(20%) had inherited mutation. Of interest, in the inherited cases, paternal mutation was seen in 88% of the affected patients. Only one (2%) of the patients had mosaic mutation detected, and in one(2%) of the inherited cases the mother had mosaic mutation. Over the 17 inherited cases, 16(94%) of them had unaffected carrier parent.

Conclusions: Even all bilateral RB patients in our cohort had germline disease, 30% of unilateral disease were germline, and 47% of patients with germline disease had inherited disease from affected (6%) or unaffected carrier (94%). Therefore molecular screening is very important for the genetic counselling regarding the risk for inherited Retinoblastoma in both unilateral and bilateral cases.

0054

Merkel Cell Carcinoma of the Eyelid and Periocular region in the West of Scotland

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Purpose: Our **purpose** was to present the clinical course and treatment of patients with periocular MCC in the West of Scotland.

Methods: We identified patients with MCC through our pathology and oncology services. We retrospectively reviewed patient's records and staged the cancer.

Results: Out of 18 patient's tumour was located on the temple in 5, the eyebrow in 3, the upper eyelid in 3 and the upper cheek in 6 patients. The mean age was 82. The diagnosis of MCC was clinically suspected in only 2 patients. Most common clinical diagnosis was SCC. All patients were treated with surgical excision. Out of 15 patients, 11 had clear margins, excision was incomplete in 4 patients. Six received adjuvant radiotherapy after primary excision and 6 additional were offered radiotherapy but were unable to proceed, one patient received chemotherapy. Six were not treated with adjuvant radiotherapy at the time of primary surgical excision. There was recurrence in 7 patients, to the parotid in 3, to the cervical lymph nodes in 3 and local recurrence in 1 patient. Out of 7 those who had recurrence, all of them had complete primary excision but only 2 of them had primary adjuvant radiotherapy, none had chemotherapy. Out of 9 those without recurrence, 6 had complete primary excision, 5 had primary adjuvant radiotherapy and one had chemotherapy.

Conclusions: MCC had a high incidence of recurrence with 7 out of 16 patients. Radiotherapy as adjuvant treatment to primary surgical excision was associated with lower rate of recurrence.

0055

MultiColour Scanning Laser Imaging of choroidal nevi and small melanomas

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Purpose: To establish whether there is a correlation between the colour of reflectance of choroidal nevi and small malignant melanomas on MultiColor Scanning Laser Imaging and both the thickness of these lesions and the presence of retinal or sub retinal fluid.

Methods: We included 88 lesions, 81 lesions were nevi and 7 lesions were melanomas thinner than 3mm. Images were divided into Group 1 with 39 lesions which were of mostly infrared reflectance and Group 2 with 49 lesions which were of mostly green reflectance. Lesions were further divided into those thicker than 1mm, thinner than 1mm, with the presence of fluid and without the presence of fluid. The correlation between the colour reflectance, thickness and the presence of the fluid was assessed.

Results: In Infrared group 87% of lesions were thinner than 1 mm and 81% of lesions had no presence of fluid. In Green group 61% of lesions had the presence of fluid and 69% of lesions were at least 1 mm thick. Lesions flatter than 1 mm tend to appear pink and lesions 1 mm thick or thicker tend to appear green. Lesions without retinal or sub retinal fluid tend to appear pink and lesions with the presence of fluid tend to appear green.

Conclusions: MultiColor Scanning Laser Imaging may help to distinguish between benign nevi that are small and the lesions with an increased blood, and blood vessels and therefore could the increased blood flow be an indication of possible progression to malignancy?

0056

Immunophenotypic profiles of inflammatory cells in chalazion and pyogenic granuloma

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Purpose: The pathological mechanisms of chalazion and pyogenic granuloma remain unclear. There is no report on the profiles of inflammatory cells in these two inflammatory conditions. We used flow cytometry to analyze the patterns of surface antigen expression on infiltrating cells in order to identify the specific immunophenotypic profiles of the inflammatory cells in chalazion and pyogenic granuloma.

Methods: Thirteen patients with chalazion and seven patients with pyogenic granuloma who underwent surgical resection in our department were studied. Flow cytometry was used to analyze the specimens obtained at surgical removal for the expression of T cell surface antigens (CD3, CD4, CD8, CD25, CD30), B cell surface antigens (CD19, CD20, CD23), plasma cell surface antigens (CD138), natural killer cell surface antigens (CD16, CD56), macrophage surface antigens (CD11b), dendritic cell surface antigens (CD11c), and stem cell surface antigens (CD34).

Results: In both chalazion and pyogenic granuloma, the proportion of cells expressing T cell surface antigen (CD3) was significantly higher ($p < 0.05$) than those expressing other cell surface antigens. The proportion of CD4 positive T cells was significantly higher than that of CD8 positive T cells ($p < 0.05$).

Conclusions: Although various inflammatory cells are involved in the pathology of chalazion and pyogenic granuloma, this study suggests that a significantly higher proportion of CD4 positive T cells may be closely related to the pathological mechanisms of chalazion and pyogenic granuloma.

Rhegmatogenous Retinal Detachment after Intra-Arterial Chemotherapy for Retinoblastoma

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Purpose: To evaluate rhegmatogenous retinal detachment (RRD) in eyes with retinoblastoma treated with Intra-Arterial chemotherapy (IAC)

Methods: Retrospective case series.

Results: Of 167 eyes in 157 consecutive patients, mean patient age at diagnosis of retinoblastoma was 19 months. IAC was primary (75/167, 45%) or secondary (92/167, 55%). There were 10 eyes (10/167, 6%) that developed RRD after IAC. The RRD was mostly related to rapid tumor regression with atrophic retinal hole and occurred within 1 month of IAC in 8 cases and within 12 months in 2. RRD was found following primary IAC (6/75, 8%) or secondary IAC (4/92, 4%). Of primary cases, RRD was found in group D (1/38 (3%), $p=0.11$) or group E (5/30 (17%), $p=0.03$). For primary IAC ($n=75$ eyes), RRD was found in endophytic (5/22 (23%), $p=0.007$), exophytic (0/29 (0%), $p=0.08$), or combined endophytic/exophytic growth pattern (1/24 (4%), $p=0.66$). Primary RRD repair involved pars plana vitrectomy (PPV) in 3, scleral buckle without drainage in 1, laser barricade in 1, and observation in 5 eyes. After 24 months mean follow-up, the retina showed complete reattachment (3/10, 30%), partial reattachment (2/10, 20%), and persistent detachment in all observed eyes (5/10, 50%). Enucleation was necessary for tumor recurrence (4/10, 40%) or neovascular glaucoma (1/10, 10%). There were no tumor-related metastases or death.

Conclusions: Following IAC for retinoblastoma, RRD occurs in 6%, mostly in advanced eyes with extensive endophytic tumor and generally from atrophic retinal hole following rapid tumor regression.

Blood Flow In Monocular Retinoblastoma, A Doppler Imaging Study (CDI)

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Purpose: CDI of retrobulbar blood vessels prior to enucleation, aiming to study the flow pattern.

Methods: Prospective study CDI of previously untreated monocular retinoblastoma in stages D or E, prior to enucleation. Blood velocities were assessed in the central retinal artery (CRA) and central retinal vein (CRV) of the tumor-containing-eyes (tuCRAv and tuCRVv); resistivity index in CRA (RIa) and the pulse index in CRV (PIv) were calculated. These measurements were studied in relation to optic nerve invasion (ONi), prelaminar (preONi), postlaminar (posONi), choroid invasion (mChi), and with tumor volume. Indices were calculated also in the contralateral normal eyes (N-RIa and N-PIv) and studied in relation to ONi. Statistics: Windows SPSS17.0.

Results: In 25 patients (mean age: 30.8±16.84 months). The mean and pattern deviation for tuCRAv, tuCRVv, RIa and PIv are respectively 26.94±12.32cm/sec; 16.2±9.56cm/sec; 0.88±0.12 and 0.79±0.29. Significant correlations are: Male sex with higher tuCRAv (P=0.032 t-Student); tumor volume with higher tuCRAv (P=0.025 Pearson's) and higher RIa (P=0.032 Spearman). ONi (present in 19 eyes) with smaller IPv (P<0.001 t-Student), indicating that with ONi, PIv is reduced (cut-value: IPv<0.935 with 89.5% sensibility and 83.3% specificity). Using variance analysis, IPv was higher than N-IPv in the ONi group (P=0.009) and in group without ONi (P<0.001). Delta value significantly higher in the group without ONi (P=0,006).

Conclusions: In advanced monocular retinoblastoma, blood velocity in CRA is higher in male sex. Tumor volume is directly correlated to the resistivity index and blood velocity in CRA. IPv is higher in retinoblastoma than in normal eyes. Lower venous pulse is correlated to optic nerve invasion.

0072

***ANRIL* lncRNA triggers efficient therapeutic efficacy by reprogramming the aberrant *INK4*-hub in uveal melanoma**

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Purpose: Uveal melanoma is an extremely aggressive disease with rapid progression, high metastatic potential and recurrence. Simultaneous correction of multiple tumor-specific gene abnormalities has become an attractive approach for developing therapeutics to treat uveal melanoma. To potentiate anti-melanoma activity, we tested a “domino effect-like” therapeutic approach by uniquely targeting one defect and automatically triggering the endogenous corrections of other defects.

Method: Transwell assay, colony formation assay and xenograft model were used to determine the role of “domino effect-like” therapeutic approach in tumorigenesis of UM.

Results: Using this strategy, in a suspicious *INK4b-ARF-INK4a* gene cluster at chromosome 9p21, aberrant *INK4a* and *INK4b* defects were simultaneously endogenously auto-corrected after targeting the suppression of abnormal *ANRIL* lncRNA. In cell culture, this treatment significantly reduced the tumor metastatic capacity and tumor formation compared with absence of treatment. In animals harboring tumor xenografts, this therapeutic approach significantly inhibited tumor growth and reduced the tumor weight.

Conclusions: Our results reveal a novel therapeutic strategy that significantly potentiates anti-melanoma efficiency by reprogramming the aberrant *INK4*-hub.

Characteristics of Malignant Ocular Tumors in a Japanese Cohort: A Review of 194 Cases Managed at the Shizuoka Cancer Center

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Purpose: To report the clinical and histopathological features of malignant ocular tumors treated at our hospital.

Methods: We retrospectively examined the records of 194 cases of malignant ocular tumors that were managed at the Shizuoka Cancer Center over the last 8 years (2007–2014). Cases of secondary tumors from head and neck cancers were excluded from this analysis.

Results: The study population included 89 male and 105 female patients, with a mean age of 62.12 years (range, 0.5–97 years). With regard to tumor site, there were 82 cases of eyelid tumors (including sebaceous gland carcinoma [n=28], basal cell carcinoma [n=27], and squamous cell carcinoma [n=11]), 35 cases of conjunctival tumors (including malt type lymphoma [n=17] and squamous cell carcinoma [n=10]), 41 cases of intraocular tumors (including malignant melanoma [n=13], metastatic tumor [n=13], and diffuse large B-cell lymphoma [n = 10]), and 36 cases of orbital tumors (including malt type lymphoma [n=12] and metastatic disease [n=7]). Of the 194 patients, 27 died (13.9%); these patients had malignant melanoma [n=2], metastatic tumor [n=23], or primary intraocular lymphoma [n=2]. Adenoid cystic carcinoma of the lacrimal sac [n=2] were the rare tumors that were observed. Proton beam therapy or carbon beam therapy was administered for this carcinoma, however the clinical course following treatment was not good.

Conclusions: Sebaceous gland carcinoma accounted for most cases of eyelid tumors, in agreement with previously reported data on Asian populations. In addition, we should consider that the feasibility of proton or carbon beam therapy for lacrimal sac carcinoma.

0081

Sebaceous carcinoma of eyelid mimicking lymphoepithelioma-like carcinoma

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Purpose: To detail the clinical and histopathological findings of a sebaceous carcinoma of eyelid mimicking lymphoepithelioma-like carcinoma(LEC)

Methods: A case report

Results: A 71-year-old male with a left lower eyelid mass was referred to The Cancer Institute Hospital of JFCR (Japanese Foundation for Cancer Research). An incisional biopsy was performed, and the specimen revealed the diagnosis of LEC. We performed operation of tumor resection and reconstruction, and final pathological diagnosis was sebaceous carcinoma.

Conclusions: This case illustrates that sebaceous carcinoma may mimic LEC.

Clinical features of malignant eyelid tumors in Hokkaido University Hospital in Japan

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Purpose: The aim of this study is to explicate the clinical features of malignant eyelid tumors in Hokkaido University Hospital.

Methods: Forty-two patients with histologically confirmed malignant eyelid tumors in Hokkaido University Hospital, Japan, during the 7-year period from January 2010 to December 2016 were retrospectively analyzed based on medical records.

Results: Of the total, 18 (42.8%) patients were male and 24 (57.2%) were female.

Mean age of all patients was 73.0 years (39~97 years). Among the patients, the location of the tumor was at the lower eyelid in 24 cases (57.1%), and at the upper lid in 18 cases (42.9%). Tumors occurred at the right side of 23 cases, and at the left side of 19 cases. Histopathologically, the eyelid tumors consisted of sebaceous carcinoma in 21 cases (50%), followed by basal cell carcinoma in 13 cases (30.9%) and squamous cell carcinoma in 6 cases (14.2%). Adenoid cystic carcinoma, Merkel cell carcinoma, endocrine mucin-producing sweat gland carcinoma, and metastasis from the lung cancer were observed in one for each. Most cases could be treated with local resection and reconstruction; however, 6 cases needed orbital exenteration (4 sebaceous carcinomas, one squamous cell carcinoma, and one metastasis).

Conclusions: Various histopathology-proven malignant tumors were noted in the eyelid, where half of the tumors were sebaceous carcinoma in this study.

0099

Planned orbital wall reconstruction (POWR) to prevent orbital complication during sinus tumor excision

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Purpose: Defect of the orbital bone and periorbital membrane is a complication of sinonasal surgery. Inverted papilloma is a common benign tumor of the sinus should be surgically excised with bone at the tumor base because of its potential malignancy. To prevent possible diplopia after surgery, we reconstructed orbital wall prior to the wall removal by otolaryngologists.

Methods: The diagnosis of inverted papilloma and tumor base locating at the orbital wall are the indication of planned orbital wall reconstruction (POWR). The patients are examined visual function previously. At the surgery, otolaryngologists confirmed the indication, and then trans conjunctival sub periosteal approach POWR using biodegradable (LactoSorb) implant was performed prior to bone removal. Lactosorb is intended to completely be absorbed within 12 months. Retrospective chart review was done to assess the safety by CT images and Hess chart before and one year after surgery.

Results: In 3 patients (3 men, age ranged 61-79), POWRs were performed and followed-up greater than one year. One patient grew into undifferentiated carcinoma one year after surgery. He was treated with external-beam radiotherapy and chemotherapy. All 3 patients didn't complain any vision problems, and Hess chart showed no changes compared to baseline exam. CT images revealed slight changes in the orbital shape during absorbing process of the implant without functional and cosmetic problems.

Conclusions: POWR may help otolaryngologists to excise orbital wall safely in the procedure, and prevent patients from possible severe surgical complications, if they require.

0105

Nodulo-ulcerative ocular surface squamous neoplasia with ciliary body infiltration: A rare presentation

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A 57- year-old female presented with complaints of progressively increasing reddish lesion in her right eye (OD) associated with pain since one month. She had a history of excision of (OD) conjunctival lesion one year ago. On examination, there was a conjunctivo-scleral ulcerated lesion of 12x12mm in the temporal quadrant with surrounding thickened conjunctiva, feeder vessels, and surface keratin. A clinical diagnosis of nodulo-ulcerative variant of ocular surface squamous neoplasia (OSSN) with scleral infiltration was made. Anterior-segment optical coherence tomography confirmed the nodulo-ulcerative nature of the lesion with scleral thinning. Ultrasound biomicroscopy showed tumor extension into the ciliary body. In view of intraocular extension, extended enucleation with implant was done. Histopathology confirmed the diagnosis of moderate to well differentiated squamous cell carcinoma with ciliary body extension. At 3 months follow-up, the patient is doing well with no evidence of locoregional lymph node or systemic metastasis.

Conclusions: Nodulo-ulcerative variant of OSSN is rare and is commonly associated with intraocular tumor extension.

**Can the late effects of fractionated stereotactic radiotherapy for choroidal melanoma be reduced without compromising distant metastasis-free survival?
An open phase II clinical trial**

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Purpose: The principal objective to test the hypothesis that reduced-dose stereotactic radiotherapy (SRT) in standard fractionation can preserve visual acuity after treatment of choroidal melanoma (CM) without compromising 5 year metastasis free survival (MFS).

Method: Eligibility; a diagnosis of CM (small or medium-sized), no metastases on liver ultrasound (US). Visual Acuity (VA) ≥ 0.1 , age ≤ 70 , Eastern Cooperative Oncology Group performance status 0-2. Exclusion criteria; prior therapy for CM, diabetes mellitus, non-malignant eye disease that could affect VA, prior cancer diagnosis.

Treatment is 60Gy in 30 fractions of SRT, 5 days /week. A custom built 'eye-tracker' system is used for eye position and immobilisation at planning CT, planning MRI and each treatment (in press.) Planning target volume is the tumour plus 2-3mm. Radiation dose constraints for normal tissues apply. Follow-up is at 3, 6, 12 months, then annually for 10 years. Surveillance for metastases is annual liver US and LFTs. The sample size of 20 is pragmatic to be accrued over 5 years. The primary endpoint is MFS at 5 years. Secondary endpoints are VA, radiation toxicities by Common Terminology Criteria version 4, (CTCv4), freedom from local tumour progression, freedom from enucleation.

Results: At time of abstract submission, 11 patients are on study, eight have completed treatment. The commonest early side effect is fatigue. Highest grade toxicity is CTCv4 grade 2 in 1 patient. There have been no cases of tumour progression or metastases.

Conclusions: With short follow-up, fully fractionated SRT is well tolerated and appears active against CM.

Clinical characteristics and treatment outcomes of children with intraocular retinoblastoma: the Queensland experience

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Purpose: To present the characteristics and treatment outcome of patients with intraocular retinoblastoma in a Paediatric Ophthalmology tertiary referral centre servicing the state of Queensland, Australia.

Method: In this retrospective study, 90 eyes of 63 consecutive patients with retinoblastoma were included, treated over 15 years from January 2001 to January 2016. The International Classification of Retinoblastoma (ICRB) staging system was noted for each patient. The patient data were reviewed for demographics, as well as the laterality, clinical manifestations, genetics and management outcomes.

Results: Of 63 cases, there were 33 (53%) female and 30 (47%) male, ranging in age from 0 to 69.5 months at presentation (median 16.1; mean 13.5 months). There were 28 bilateral cases (44%). Twenty-eight cases were found to have germline mutations (44%), and 4 of these had positive family histories. Leukocoria was the most common presenting symptom. Three eyes with unilateral Retinoblastoma were salvaged (8%), and 8 pairs of eyes of patients with bilateral retinoblastoma were salvaged (29%). Thirty-eight patients received adjuvant chemotherapy (61%). Overall 37 (46%) of preserved eyes attained a visual acuity of 6/12 or better.

Conclusions: Demographic results were generally coincident with previous reports. The incidence of retinoblastoma in Queensland has not been reported since 1980, this study provides updated information for the local and wider medical community regarding important presenting signs, treatment strategies and outcomes in this state.

0139

Additional primary malignancy in patients with uveal melanoma at a Norwegian center

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Purpose: To investigate the occurrence of other malignancies in the years before, at and after the diagnosis of the uveal melanoma.

Method: The melanoma data base in Oslo includes about 2/3 of all melanomas in Norway. Using the data registered between January 1996 and April 2016 we could track additional primary malignancies in this period. We separated them into three groups according to the number of additional tumours. Basal cell carcinomas were numbered separately.

Results: The cohort of uveal melanoma consisted of 811 patients and 193 of them had another primary malignancy. In group 1, with one additional tumour, 89 had a cancer diagnosis prior to the UM diagnosis, 20 were diagnosed simultaneously and 43 in the years after UM diagnosis (152 cases). In group 2, with two additional tumours, 12, 5, 22 (39 cases) were found in the respective groups, and in group 3, with 3 additional tumours 0, 2, 0 (2 cases) were found respectively.

In this cohort, 51 of the patients were also diagnosed with BCC, 17 before, 5 simultaneously, 29 after UM diagnosis. In 11 cases, BCC was the only additional cancer.

Two patients had four different cancers; the first lady died after 15 years, the second is still living after 3 years. In this lady, all the tumours was detected simultaneously during workup for a uveal melanoma.

Conclusions: Patients with UM have a risk for non-ocular primary cancers both before, simultaneously and after the diagnosis. The prognosis with more synchronous tumours can be fair.

0141

Distribution of hematoporphyrin monomethylether in rabbit choroidal melanoma

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Purpose: To investigate the distribution of hematoporphyrin monomethyl ether (HMME) in rabbit choroidal melanomas by dye fluorescence angiography and fluorescence microscopy.

Methods: Pigmented choroidal tumors models were established by improved methods. Digital HMME and angiograms were performed in 28 rabbits (20 eyes for experimental choroidal melanomas, 4 eyes for normal choroids, and 4 eyes for irides). HMME ($10 \text{ mg} \cdot \text{kg}^{-1}$) was injected intravenously and images of tumor, normal choroid, or iris were obtained 5 minutes, 15 minutes, 30 minutes, 60 minutes, 180 minutes and 480 minutes, 24 hours, 48 hours and 72 hours after the injection. Fluorescence microscopy was performed in 20 rabbits to observe the distribution of HMME and the result was analyzed semi-quantitatively.

Results: The maximal hematoporphyrin monomethylether fluorescence was observed in tumorous tissues 3~4 hours after injection. Fluorescence photometry corroborated these results.

Conclusions: HMME is selectively accumulated in choroidal melanomas 3~4 hours after injection, which is suitable time for photodynamic therapy.

0157

Establishment of Orthotopic and Heterotopia Transplantation Liver Metastasis Tumor Model of Uveal Melanoma in Nude Mice

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Purpose: To establish a orthotopic and heterotopia transplantation liver metastasis tumor model of uveal melanoma in nude mice. To compare the UM tumor formation rate and hepatic metastatic rate of different transplanting methods and different UM cell lines.

Method: Respectively by method of orthotopic and heterotopic transplantation, 48 male BALB/c-nu nude mice were selected and randomly divided into 6 groups, two high invasion of human UM cell line mum-2b and M619 were inoculated in nude mice eyes (orthotopic) and subcutaneous (heterotopic), reared in the same conditions, regularly observed in health status and tumor growth and metastasis. Finally, HE staining and immunohistochemical were applied

Results: The tumor formation rate of subcutaneous group A (M619) was 75.0%; subcutaneous group B (MUM-2B) was 87.5%; intraocular group A (M619) was 62.5%; intraocular group B (MUM-2B) was 75.0%($P = 0.019$). Liver metastasis rate in the subcutaneous group A (M619) is 33.3% ;subcutaneous group B (MUM-2B) 42.9%; intraocular group A (M619) 20.0%; intraocular group B (MUM-2B) 28.6% ($P = 0.042$). The tumor cell showed positive expression in the detection of immunohistochemistry.

Conclusions: we established a orthotopic and heterotopia transplantation liver metastasis tumor model of UM in nude mice and also found the tumor formation rate and liver metastasis rate in MUM-2B cells were higher, in the subcutaneous transplantation group, the MUM-2B tumor grew faster. The tumor formation rate and liver metastasis rate of heterotopia (subcutaneous) transplantation group were higher .

0163

Outcome of children with bilateral retinoblastoma in Costa Rica according to globe preservation

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Purpose: To evaluate eye preservation in patients diagnosed with bilateral retinoblastoma in Costa Rica according to the initial classification and treatment provided.

Method: Retrospective interventional case series of 34 eyes of 17 patients diagnosed with bilateral retinoblastoma between January 2006 and July 2016. All eyes were classified according to the International Classification of Retinoblastoma (ICRB).

Results: The mean patient age at diagnosis was 12 months. Eyes were classified according to the ICRB as group A (n=2), group B (n=6), group C (n=4), group D (n=11), or group E (n=11). All patients received a mean of 6 cycles of systemic chemotherapy. Combined transpupillary thermotherapy and cryotherapy achieved globe salvage for group A (100%), group B (83%), group C (75%), group D (18%) and group E (27%). Second line treatments included external beam radiotherapy (EBRT), which achieved globe salvage in 25% of group C and 18% of group D eyes (36% eye preservation in group D eyes). A mean of 1 session of intraarterial chemotherapy (IAC) was used in 25% of group C and 18% of group E eyes, achieving globe salvage only in the group C eye. Intravitreal chemotherapy was successfully used in conjunction with EBRT in 9% of group D eyes. Mortality during the study was 5%, and 18% of patients underwent bilateral enucleation.

Conclusions: Children with retinoblastoma groups A-C have good eye salvage prognosis with the treatment options available in Costa Rica. Group D and E eyes have bad prognosis despite use secondary treatments.

0176

iTRAQ quantitative proteomics of uveal melanoma

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Purpose: Compared quantitative iTRAQ proteomic analysis was performed in uveal melanoma and normal uveal tissue collected as control to investigate the proteome profiles.

Methods: A total of 6 uveal melanoma samples and 4 normal uveal tissue samples as control were used, with 3 spindle cell uveal melanoma and 3 epithelial cell uveal melanoma.

Results: We identified a total of 121,891 unique peptides (< 1% FDR), representing 4,256 protein groups, in which 1671 with more than 2 peptides hits (95% FDR). In general, 435 proteins were considered as significantly differentially expressed proteins (DEPs, fold change > 2, P < 0.05), including 257 up-regulated proteins and 178 down-regulated proteins. The top 3 up- and down- regulated DEPs were ATP synthase subunit F, Ig lambda-3 chain C and F-actin-capping protein subunit alpha-1, as well as interferon-induced GTP-like protein Mx2, pterin-4-alpha-carbinolamine dehydratase and carbonic anhydrase 3, respectively. Gene ontology and KEGG pathway enrichment analysis showed that these DEPs were significantly (FDR < 0.001) enriched in biological process of p53 signal transduction, mRNA splicing, ribonucleoside triphosphate catabolic process, arginine catabolic process, ATP metabolic process, fatty acid oxidation and protein polyubiquitination.

Conclusions: Our data for the first time provides a comprehensive quantitative proteomic analysis of uveal melanoma, and indicates that p53 signal transduction pathway and related protein phosphorylation modification may play important roles in the development of uveal melanoma.

0188

Surgical resection of orbital neurofibromatosis using navigation system

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Purpose: To evaluate the results of surgical resection of orbital neurofibromatosis using navigation system.

Design: Retrospective case series.

Methods: Diagnosis of ossifying fibroma is based on medical history, clinical characteristic, and imaging appearance. All patients preoperative assessments were performed, 3-dimensional reconstructed computed tomography and photographs pre, post operation were taken. Lesion can be virtually repaired by mirroring of the intact orbit from the other side; complete resection was achieved and defect were fixed by titanium plates.

Results: The main presentations are proptosis, global displacement, others include diplopia, eye movement restriction and visual acuity reduction. The mean size of lesion is 40.517cm³. Follow-up ranged from 10 to 34 months. Patients of follow up had good cosmetic results. No recurrences were shown. No patients had diplopia in primary gaze.

Conclusion: navigation guided complete resection seems to be safe and useful as an treatment of orbit neurofibromatosis

0191

A Case of Bilateral Conjunctival Lymphoma who are on Fingolimod Therapy for Multiple Sclerosis

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Purpose: Systemic fingolimod therapy is frequently used to treat relapsing multiple sclerosis. 1 However there is concern in both animal studies² and human case reports that long term treatment with fingolimod may lead to lymphoma. It has been shown that systemic fingolimod reduces immunosurveillance and killing of B-cell lymphoma cells by suppressing tumor-specific Th1 cells.² There have not been any reports as of yet of patients on fingolimod who developed ocular adnexal lymphoma.

Methods: We present a case report of a woman with relapsing multiple sclerosis treated with fingolimod for 2 years and developed bilateral biopsy-proven mucosal-associated lymphoid tissue (MALT) conjunctival lymphoma.

Results: A 39-year-old woman had an 8-year history of multiple sclerosis and had been on systemic fingolimod therapy for 2 years because of multiple relapses. She initially presented with blurred vision and foreign body sensation on both eyes. On slit lamp examination, she had salmon-colored subconjunctival tumors along both inferior conjunctival fornices. Otherwise, her examination was normal. Biopsy of the right conjunctival tumor showed MALT lymphoma. Her systemic work-up was negative. She discontinued fingolimod therapy and was treated with 4 weekly treatments of systemic rituximab (375 mg/m²). After 4 months of follow-up, her conjunctival lymphoma totally regressed.

Conclusions: This is the first report of a patient on systemic fingolimod who developed ocular adnexal MALT lymphoma. It is important for clinicians to have a high level of suspicion for lymphoma in patients on fingolimod.

0200

'Ciliary body epithelioid tumor of uncertain origin' in a 26-year-old Asian Indian female

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Purpose: To report a case of ciliary body tumor of uncertain origin managed with partial lamellar sclerouvectomy.

Methods: A 26 year-old-lady presented with gradually decreasing vision in right eye of 4 months duration. Vision at presentation was 6/18 (-14D spherical) and 6/9 (-12D spherical) in right and left eye, respectively. Examination revealed amelanotic ciliary body(CB) tumor with internal vasculature, extending from 3.30' to 7 o'clock meridian. Lens was displaced superotemporally with localized anterior capsular opacity. There was no extra-ocular extension of tumor, or retrolental neoplastic membrane. Ultrasound biomicroscopy (UBM) revealed iris-CB tumor 4.9x8.2mm. MRI revealed enhancing mass with intermediate signal in T1, and isointense signal in T2-weighted images. PET-CT ruled out primary malignancy, or systemic spread. Tumor excision with partial lamellar sclerouveactomy (PLSU), lensectomy, scleral patch graft, and vitrectomy was done.

Results: Histopathological examination showed features suggestive of PEComa. Immunohistochemistry was negative for HMB-45, Melan-A, and smooth muscle actin, and positive for cytokeratin, Vimentin, and S-100. A diagnosis of epithelioid neoplasm of uncertain origin was considered. Till 15 weeks follow-up, there was no tumor recurrence and vision improved to 6/12 (+6D Spherical).

Conclusions: A rare case of 'ciliary body epithelioid tumor of uncertain origin' is hereby reported in a young Asian female that was successfully managed with partial lamellar sclerouvectomy.

Status and significance of ZEB2 and miRNA-200 family in eyelid sebaceous gland carcinoma

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Purpose: Sebaceous gland carcinoma (SGC) is an aggressive eyelid malignancy common in Asian countries. Epithelial-mesenchymal transition (EMT) is a phenomenon by which epithelial cells acquire a mesenchymal phenotype. miRNA-200c and miRNA-141 suppress EMT by downregulating ZEB1 and ZEB2 resulting in inhibition of cancer progression.

Methods: Prospective analysis of 42 eyelid SGC patients, including staging (AJCC, 2009), and follow-up for 7-44 months (Mean 19.81 ± 9.59 months). Immunohistochemistry (IHC) on ZEB2, ZEB2 mRNA and miRNA-200c, miRNA-141 expression was done in all the cases and normal skin by qPCR. Results were correlated with high risk features and follow-up data.

Results: Mean age of patients was 58.7±13.9yrs (M: F ratio of 0.9:1). ZEB2 overexpression was observed in 29/42 (69%) and 30/42 (71%) cases by IHC and qPCR respectively. Low expression of miRNA-200c and miRNA-141 was seen in 36/42 (86%) and 28/42 (67%) cases respectively. ZEB2 overexpression showed significant association with advanced tumour stage, poor differentiation, pagetoid spread and tumour recurrence. While low miRNA-200c correlated significantly with large tumour size and poor differentiation, low miRNA-141 correlated with large tumour size and lymph node metastasis.

Survival analysis revealed patients with high ZEB2 immunoexpression and low miRNA-200c had shorter disease-free survival. Univariate and multivariate Cox's regression analysis revealed ZEB2 overexpression as the most important poor prognostic indicator. There was an inverse significant association of miRNA-200c and miRNA-141 with ZEB2.

Conclusions: ZEB2 overexpression emerged as a novel potential biomarker in eyelid SGC. Low levels of miRNA-200c and miRNA-141 facilitates tumour progression by promoting EMT.

Photodynamic Therapy (PDT) for Treatment of Circumscribed Choroidal Hemangioma: Functional and Anatomical Outcomes

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Purpose: To evaluate the safety and efficacy of photodynamic therapy (PDT) for treatment of circumscribed choroidal hemangioma.

Methods: This study is a retrospective interventional case series. Twenty four eyes of 24 patients from January 2006 to January 2016 were treated with full dose PDT.

Results: Mean age of the patients was 47.1 ± 11 year, range (10-68), Nineteen (72.2%) were male and 5(2.8%) were female. Mean follow up duration was 28.6 ± 24 , range (5-118) months.

Mean PDT session was 1.5 ± 0.7 (1-4). Mean PDT spot size was 5.5 ± 1.1 mm. The average tumor distance from fovea was 2.1 ± 3.1 (mm) and from optic nerve was 2.2 ± 2.5 (mm).

Mean pretreatment visual acuity in Log MAR was 0.64 ± 0.5 that was improved to 0.25 ± 0.3 after the treatment. ($P=0.03$). The average pretreatment tumor basal diameter was reduced from 7.5 ± 3.1 (mm) to 5.7 ± 2.6 (mm) after treatment ($P<0.0001$). Mean initial tumor thickness was 3.2 ± 1.1 that decreased to 1.01 ± 1 (mm) following PDT ($P<0.0001$). Subretinal fluid and CME was resolved 2.2 ± 0.7 months and 2.1 ± 0.7 months after the last session of PDT respectively. Fourteen patients (58.3%) had CME in the first visit; in these cases mean central foveal thickness before treatment was 437 ± 107 μ that decreased to 249 ± 44 μ . ($P<0.0001$)

No tumor recurrence or treatment related adverse events or complications were identified during or after treatment with PDT.

Conclusions: PDT is an effective and safe modality for treatment of circumscribed choroidal hemangioma.

Choroidal Metastases: clinical features, visual outcomes and patients' survival

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Purpose: To report the clinical aspects, visual outcomes and patients' survival in choroidal metastases at a major ocular oncology referral center.

Method: A retrospective chart review of all patients with choroidal metastasis was performed at an ocular oncology referral center.

Results: A total of 147 choroidal metastases were diagnosed in 96 eyes of 79 patients. There were 57 female (72.2%) and 22 male (27.8%) patients with a mean age of 51.96 ± 14.57 . At diagnosis time, positive history of cancer was evident in 47 patients (59.5%) and primary origin was unknown in 32 patients (40.5%). Following complete systemic workup, the choroidal metastasis source was breast in 36 (45.6%), lung in 15 (19%), other organs in 13 patients (16.5%) and remained unknown in 15 (19%). Management included chemotherapy alone in 44 (55.7%), chemotherapy plus focal therapy in 14 (17.7%), focal therapy alone in 10 (12.7%) and enucleation in 5 patients (6.3%). Median survival time in all patients was 36 months (CI: 25.3-46.7). Median survival time in patients with breast cancer, lung cancer and other type of cancer was 36, 48 and 24 months respectively ($P=0.104$). Mean visual acuity was decreased from 0.51 ± 0.67 logMAR at initial visit to 0.70 ± 0.90 logMAR at last visit.

Conclusions: In era of Increased survival of patients with choroidal metastasis due to recent advances in management of different cancers, ocular oncologists can also continue to improve the quality of life of these patients by timely diagnosis and appropriate management of ocular involvement.

0001

Comparison of Cytopathological Yield of FNAB of Melanocytic Uveal Tumors Diagnosed Clinically as Uveal Melanoma Using 25g versus 27g Needles

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Purpose: Evaluate whether FNAB of primary uveal melanomas (PUM) using 27 g needles yields aspirates that are similar to those obtained by FNAB using 25 g needles.

Methods: IRB-approved clinical investigation of FNABs of consecutive patients with PUM (n=31) in which needles of different gauges (25 and 27) were used to sample distinct tumor sites. Each tumor was sampled 3 times. The first site was sampled with a 27 g needle and sent for gene expression profile testing. The second and third biopsy sites were sampled consecutively with a 27 g and 25 g needles and were submitted for cytology. Main endpoints evaluated were sufficiency of needle aspirates from different calibre needles and melanoma cytopathology in the two aspirates.

Results: The 32 studied patients had a mean age of 65.2 yr. Eighteen patients were women. Seventeen tumors were exclusively choroidal. Tumors had mean largest basal diameter of 13.2mm and mean thickness of 6.4 mm. Aspirates obtained with different calibre needles were sufficient for cytopathology in 96.9% of cases. The single case with an insufficient aspirate yielded acellular specimens using 27 g and 25 g needles. Cytopathology from the 2 aspirates was identical in all cases. Main difference between the 25g and 27g aspirates was a greater amount of blood and fibrous debris among 25 g aspirates.

Conclusions: FNAB aspirates obtained using 27 g needles appear sufficient for cytopathology and GEP in most cases. 25 g needles appear to cause more bleeding and do not increase the yield of tumor cells.

0003

Frequency of germline BAP1 mutation in uveal melanoma (UM) patients at risk for a tumor predisposition syndrome (TPDS)

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Purpose: To determine the frequency of germline BAP1 mutation in patients with high risk for a UM-TPDS.

Method: Patients were evaluated under an IRB-approved protocol. Patients with UM diagnosed before age 30 or UM plus a personal history of cancer or family history of multiple cancers, including familial UM, were evaluated for germline BAP1 mutation by sequencing. A subset of these patients was evaluated for large deletion and duplication in BAP1 by Multiplex Ligation Probe Amplification analysis. Patient and family cancer histories were reviewed. Data from the literature was combined to estimate the overall frequency of germline BAP1 mutation in UM.

Results: A total of 161 UM patients were evaluated for germline mutation in BAP1. We identified 8/161 (5%) patients with germline mutations in BAP1 including one missense and 7 frameshift truncating mutations. The frequency of germline BAP1 mutation in young patients was 1/14 (7%), while the risk in patients with familial UM was highest at 6/32 (19%). To further assess the frequency in patients with familial UM our data combined with the literature revealed 13/63 (22%) positive for germline BAP1. In contrast, the frequency of germline BAP1 in unselected UM from the literature is 1-2%.

Conclusions: Familial UM has the highest frequency of germline BAP1 mutation in those at risk for UM-related TPDS. Studies are needed to evaluate additional candidate genes in these UM-TPDS patients negative for BAP1.

0007

Concomitant primary simple limbal epithelial transplantation after surgical excision of ocular surface squamous neoplasia prevents limbal stem cell deficiency: A case-control study

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Purpose: To compare the surgical outcomes of ocular surface squamous neoplasia (OSSN) following wide excisional biopsy with and without primary simple limbal epithelial transplantation (p-SLET), and study the extent of corneo-scleral limbal dissection causing LSCD.

Methods: Case-control study including 21 patients who underwent wide excisional biopsy of OSSN without p-SLET (controls) and 7 patients with p-SLET (cases)

Results: The statistically significant differences in tumor features between cases versus controls included mean number of limbal clock hours affected by OSSN (6 vs 3; $p=0.0005$), mean tumor basal dimension (13 mm vs 7 mm; $p=0.002$), and mean number of clock hours of corneo-scleral limbal dissection due to wide tumor excision (8 vs 6; $p=0.0005$). Partial LSCD was noted in controls ($n=11$; 52%) and none of the cases developed LSCD ($p=0.02$). The time interval between tumor excision and onset of LSCD was 8 weeks. The mean follow-up duration in cases vs controls was comparable (12 months vs 17 months; $p=0.28$). A sub-group analysis of controls revealed that the occurrence of LSCD was higher in patients with > 3 clock hours of involvement of limbus by the tumor ($p=0.03$), necessitating corneo-scleral limbal dissection of > 6 clock hours ($p=0.03$). The occurrence of LSCD was 0%, 45%, 60%, 100%, 100%, and 100% with corneo-scleral limbal dissection involving 4, 5, 6, 7, 8, and 9 clock hours respectively.

Conclusions: Corneo-scleral limbal dissection of > 5 clock hours can cause LSCD. Concomitant p-SLET after surgical excision of OSSN prevents LSCD in cases requiring extensive corneo-scleral limbal dissection.

0009

Intra-arterial Chemotherapy versus Intravenous Chemotherapy for Unilateral Retinoblastoma. Who wins?

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Purpose: To compare outcomes following intravenous chemotherapy (IVC) versus intra-arterial chemotherapy (IAC) for unilateral retinoblastoma.

Methods: Retrospective comparative interventional case series of patients with unilateral retinoblastoma managed with either IVC using vincristine, etoposide, and carboplatin versus IAC using melphalan with or without topotecan and with minimum 1 year follow up. The primary outcome measure was globe salvage.

Results: Of 91 patients with unilateral retinoblastoma, IVC was employed in 42 (46%) cases and IAC in 49 (54%). By comparison (IVC vs IAC), patients in IAC group showed statistical difference with greater mean tumor diameter (14 vs 18 mm, $p < 0.001$) and thickness (7 vs 10 mm, $p = 0.001$), greater percentage with active vitreous seeds (29% vs 55%, $p = 0.01$), and greater total retinal detachment (10% vs 43%, $p < 0.001$). There were no cases of Group A in either treatment arm. Regarding outcomes (IVC vs IAC), globe salvage was not significantly different in Groups B, C, or E, but there was significantly improved globe salvage with IAC for Group D (48% vs 91%, $p = 0.004$). Regarding specific tumor outcomes (IVC vs IAC), control was significantly better with IAC for solid tumor (62% vs 92%, $p = 0.002$), subretinal seeds (31% vs 86%, $p = 0.006$), and vitreous seeds (25% vs 74%, $p = 0.006$). There were no patients with pinealoblastoma, second cancer, metastasis, or death in either group.

Conclusions: For unilateral retinoblastoma, IAC provided significantly superior globe salvage (compared to IVC) for group D eyes. Additionally, IAC provided significantly superior control for solid tumor, subretinal, and vitreous seeds.

0010

Primary Enucleation for Group D Retinoblastoma in the Era of Conservative Systemic and Targeted Chemotherapy: The Price of Retaining an Eye

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Purpose: In this study we have quantified disease burden in terms of examinations under anaesthesia (EUAs) and compared the number of EUAs after primary enucleation versus conservative chemotherapy in group D retinoblastoma patients.

Methods: A retrospective analysis of 92 group D patients (104 eyes), of which 40 (40 eyes) underwent primary enucleation and 52 (64 eyes) were treated initially with systemic chemotherapy. Number, frequency and overall period of EUAs were compared using univariate and multivariate analysis.

Results: Primarily enucleated patients had an average 3-fold fewer (whole cohort) or 2.3-fold fewer (unilateral retinoblastoma) EUAs compared to the chemotherapy group ($P < 0.001$). Primary chemotherapy, young presentation age, bilateral disease, multifocal tumours, retinoblastoma family history and germline cases were found on univariate analysis to correlate with increased number of EUAs ($P \leq 0.019$). On multivariate analysis, however, only primary treatment type and age of presentation were found significant ($P \leq 0.001$). Primarily enucleated patients also had EUAs less frequently ($\times 1.4$; $P = 0.022$) and for a shorter period ($\times 1.5$; $P = 0.001$). Of the 55 unilateral-presenting patients, a new tumour developed in the fellow eye only in a single (2%) case with known family history. The median follow-up time was 61 months (mean: 66, range: 14-156), in which time no cases of metastatic spread or death were recorded.

Conclusions: Group D patients' families should be counselled regarding the significant 3-fold difference in number of EUAs following primary enucleation versus systemic chemotherapy when deciding on a treatment strategy. In this regard, primary enucleation would be most beneficial for older patients with unilateral disease.

Risk of Metastasis and Orbital Recurrence in Advanced Retinoblastoma Eyes Treated with Systemic Chemoreduction versus Primary Enucleation

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Purpose: To evaluate the risk of metastatic disease and orbital recurrence in advanced retinoblastoma treated with systemic chemoreduction versus primary enucleation.

Methods: Retrospective review of patients with Group D/E retinoblastoma from 1995 to 2015. Overall, 345 eyes (294 patients) were included (165 Group D and 180 Group E). Primary outcome measures were orbital recurrence and metastatic disease.

Results: Of 345 eyes, 139 were treated with systemic chemoreduction (102 Group D, 37 Group E) and 206 with primary enucleation (63 Group D, 143 Group E). In the chemoreduction group, 1 patient developed metastasis (0.7%) and 1 patient an orbital recurrence (0.7%). In the primary enucleation group, 2 patients developed metastases (0.9%) and 1 an orbital recurrence (0.5%). After systemic chemoreduction, 58 of 139 eyes (30 Group D, 28 Group E) were secondarily enucleated for treatment failure (41.7%). The median time to secondary enucleation from diagnosis was 8.1 months. None of the eyes in the systemic chemoreduction group had high-risk pathologic features. In the primary enucleation group, 56 eyes had high-risk pathology.

Conclusions: Over a 20-year period, 345 eyes were treated for advanced retinoblastoma at Children's Hospital Los Angeles. Incidence of orbital recurrence and metastatic disease was <1% and did not vary by treatment modality or Group Classification. None of the eyes enucleated for treatment failure had high-risk pathology, and none of these patients developed metastatic disease. Globe salvage therapy with systemic chemoreduction and subsequent enucleation for poor response does not increase the risk of metastatic disease or orbital recurrence.

Topical 5-Fluorouracil following surgery for ocular surface squamous neoplasia in Kenya: a randomised, double-masked, placebo-controlled trial

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Purpose: This study was conducted to determine whether post-operative 5FU 1% eye drops applied four times a day for one month reduce recurrence of ocular surface squamous neoplasia (OSSN) tumours following surgical excision.

Method: We conducted a multicentre, randomised, double-masked, placebo-controlled trial in Kenyan adult OSSN patients. Following standard surgical excision, and healing of the excision site, participants were randomly allocated to topical 5FU 1% or placebo four times a day for four weeks. Randomisation was stratified by surgeon. Follow-up was at 1, 3, 6, and 12 months. Participants and trial personnel were masked to intervention. The primary outcome was clinical recurrence by one-year (supported by histology where available), and analysed by intention-to-treat. The sample size was recalculated as events were more frequent than estimated, and trial enrolment was stopped early. The trial was registered with Pan-African Clinical Trials Registry (PACTR201207000396219).

Results: We randomly allocated 49 participants to 5FU and 49 to placebo. Four participants were lost to follow-up. There were 5 (10.6%) recurrences in the 5FU group and 17 (36.2%) in the placebo group (odds ratio 0.21; 95%CI 0.07-0.63, $p=0.01$). There was little effect of adjusting for passive smoking and antiretroviral therapy (adjOR=0.23; 95%CI 0.07-0.75, $p=0.02$). Adverse effects were transient, mild and more frequent with 5FU: ocular discomfort (43 [88%] vs 36 [73%]), epiphora (24 [49%] vs 5 [10%]), and eyelid skin inflammation (7 [14%] vs 0).

Conclusion: Post-operative topical 5FU substantially reduced recurrence of OSSN, was well-tolerated, and its use recommended.

0018

Mushroom shaped choroidal lesions other than melanoma

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Purpose: There is a general belief that a mushroom shaped fundus mass is highly suggestive, or even pathognomonic, of a uveal melanoma.

Methods: We reviewed the charts of patients referred to the Ocular Oncology Service with lesions that had a mushroom shape clinically and with ultrasonography in which melanoma was a diagnostic consideration, but who proved on further evaluation to have lesions other than uveal melanoma. We also reviewed the literature on other similar cases.

Results: A total of 14 conditions, other than melanoma, with a mushroom configuration were identified. Those seen personally by the authors included adenocarcinoma of the retinal pigment epithelium, metastatic lung cancer, late recurrence of retinoblastoma, ciliary body leiomyoma and a mycotic abscess. Those shared with us by colleagues and/or cited in the literature included metastatic lung cancer, metastatic thyroid cancer, ciliary body schwannoma, choroidal hemangioma, age related macular degeneration, mycotic fungal abscess, retinal vasoproliferative tumor, solitary fibrous tumor of sclera, and idiopathic fibrovascular proliferation.

Conclusions: There are well established cases of lesions other than uveal melanoma that can assume a mushroom configuration clinically and with ultrasonography. Clinicians should be aware of these mushroom shaped pseudomelanomas in order to make an accurate diagnosis and avoid inappropriate management.

0020

The Expanding Uses of Intravitreal Melphalan

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Purpose: To report on our experience with intravitreal Melphalan for retinoblastoma issues other than vitreous seeds

Methods: IRB approved retrospective review of retinoblastoma cases in New York and Shanghai who were treated with intravitreal Melphalan for conditions other than intravitreal seeds.

Results: 58 eyes of 55 patients received intravitreal Melphalan for conditions other than vitreal seeds. 25 patients were unilateral and 30 bilateral. No patient died and no second tumors developed nor was there extraocular extension in any eye. Two eyes came to enucleation and 2 required brachytherapy but no eye received external beam irradiation. More than half the treated eyes were ICRb (COG) D and E and Reese-Ellsworth Va and b. Toxicity of the New York patients was monitored by ERG's. Conditions treated included sub retinal seeds, retinal tumors (recurrent) and anterior chamber tumor.

Conclusions: Intravitreal Melphalan has been used successfully for intracocular retinoblastoma for conditions beyond just vitreal seeding, including recurrent retinal tumors, sub-retinal seeding, anterior chamber disease as both solitary treatment and in combination with additional modalities. Retinal and ERG toxicity are common but no systemic toxicity was found.

0022

A novel antiangiogenic therapy decreases tumor burden in a retinoblastoma mouse model

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Purpose: As a highly vascularized tumor, retinoblastoma appears to be a good candidate for antiangiogenic therapy. Such therapy might reduce or replace cytotoxic systemic or local chemotherapy, limiting the side effects of chemotherapeutic drugs. Although antiangiogenic therapies have been tested with some success in retinoblastoma preclinical models, surprisingly no agents have been delivered intravitreally, the current route for antiangiogenic drug administration in other retinal diseases. We developed the novel antiangiogenic compound SH-11037 that has specific antiproliferative effects against retinal endothelial cells and efficacy in murine ocular neovascularization models, making it a candidate for antiangiogenic retinoblastoma therapy as well as combination antiangiogenic/cytotoxic therapy. Here, we explored intravitreal SH-11037 as a treatment for retinoblastoma in the TAg-RB transgenic mouse model.

Method: We injected SH-11037 or vehicle intravitreally to a final vitreous concentration of 10 μ M and followed tumor progression with optical coherence tomography in vivo and histopathological analysis post-mortem. TAg-RB mice were injected weekly starting at 7 or 8 weeks of age with sacrifice and enucleation at 10 or 11 weeks. Percent tumor burden in each eye was compared between cohorts and treatments by two-way ANOVA.

Results: Single-agent SH-11037 significantly reduced tumor burden over vehicle (up to 26% reduction, $p=0.022$). No adverse effects were observed with weekly compound injections.

Conclusions: SH-11037 administered by intravitreal injection may be a candidate for antiangiogenic retinoblastoma treatment, and prompts revisiting the possibility of antiangiogenic retinoblastoma therapy using other intravitreal drugs and other preclinical models.

Optical Coherence Tomography Angiography Characteristics of Iris Melanocytic Tumors

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Purpose: To evaluate tumor vasculature with optical coherence tomography (OCT) angiography (OCTA) in malignant iris melanomas and benign iris lesions.

Methods: Cross-sectional observational clinical study. Eyes were imaged using OCTA systems operating at 1050 and 840 nm wavelengths.

Results: One eye each of eight normal volunteers and nine patients with iris melanomas or benign iris lesions including freckles, nevi, and an iris pigment epithelial (IPE) cyst were imaged. The normal iris has radially-oriented vessels within the stroma on OCTA. Penetration of flow signal in normal iris depended on iris color, with best penetration seen in light to moderately pigmented irides. Iris melanomas demonstrated tortuous and disorganized intratumoral vasculature. In two eyes with nevi there was no increased vascularity; in another, fine vascular loops were noted near an area of ectropion uveae. Iris freckles and the IPE cyst did not have intrinsic vascularity. The vessel density was significantly higher within iris melanomas ($34.5\% \pm 9.8\%$, $p < 0.05$) than in benign iris nevi ($8.0\% \pm 1.4\%$) or normal irides ($8.0\% \pm 1.2\%$). Tumor regression after radiation therapy for melanomas was associated with decreased vessel density. OCTA at 1050 nm provided better visualization of tumor vasculature and penetration through thicker tumors than at 840 nm.

Conclusions: OCTA may provide a dye-free, cost-effective method for monitoring a variety of tumors, including iris melanocytic lesions, for growth and vascularity. This could be helpful in evaluating tumors for malignant transformation and response to treatment. Penetration of the OCT beam remains a limitation for highly pigmented tumors.

0033

Intraocular metastases secondary to breast carcinoma: identification of a specific molecular subtype associated with choroidal involvement

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Purpose: To identify a specific molecular tumor subtype based on estrogen (ER), progesterone (PR), and human epidermal growth factor-2 (HER2) receptor expression in the primary tumor of patients affected by choroidal metastases from breast carcinoma (BC).

Method: Thirty-four consecutive patients affected by choroidal metastases from BC were included. ER, PR and HER2 positivity of the primary tumor were defined following standard guidelines. BC molecular subtypes were also identified (Luminal A, Luminal B, HER2-enriched and triple negative). Thirty-five consecutive patients affected by metastatic BC without choroidal involvement were included as a control group.

Results: The study group and the control group did not statistically differ for histopathologic classification of the primary tumor (ductal, lobular, others) and AJCC-TNM stage ($p>0.05$). Patients affected by choroidal metastases from BC were characterized as ER+ in 43 cases (98%), PR+ in 39 cases (88%) and HER2+ in 8 cases (18%). Patients affected by choroidal metastases from BC showed a significantly higher expression of ER ($p<0.01$) and PR ($p<0.01$) receptor in the primary tumor compared with non-choroidal metastatic BC. Across all patients, the Luminal B molecular subtype was related to the presence of choroidal involvement ($p=0.001$).

Conclusion: Choroidal metastases by BC were associated with ER and PR expression in the primary tumor and the Luminal B molecular subtype, suggesting that primary tumor receptor expression may influence the choroidal metastatic tropism of BC. The presence of ER and PR receptor expression could potentially influence the treatment of these patients based on the expected sensitivity to anti-hormone drugs.

0037

Patient-Reported Outcomes after Treatment of Choroidal Melanoma: a Comparison of Enucleation vs Radiotherapy in 1596 patients

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Purpose: To test the hypothesis that patients treated with radiotherapy for choroidal melanoma report better QoL (QoL) than patients undergoing primary enucleation.

Methods: In this prospective, non-randomized study, patients with choroidal melanoma treated between 1993 and 2013 at the Royal Liverpool University Hospital, UK, were included if they completed QoL questionnaires (EORTC-QLQ_OPT30, Hospital Anxiety & Depression Scale and Functional Assessment of Cancer Treatment). Patient-reported outcomes were correlated with: demographics; social factors; general health; tumor and ocular status at presentation; survival; local tumor control; ocular conservation and visual outcome.

Results: The 1596 patients were treated with radiotherapy (72.3%) or enucleation (27.7%). Enucleation was associated with male gender (Chi-square, $P=.004$), older age (t-test, $P<.001$), larger tumor diameter (t-test, $P<.001$), monosomy 3 (Chi-square, $P<.001$), depression (Linear regression, 95% Confidence Interval [CI], .17 to 1.01) and reduced physical and functional wellbeing (Linear regression, 95% CI, -1.14 to .12 & -1.96 to -.47 respectively). Over time, FACT-G score diminished more after enucleation than radiotherapy (Multilevel regression, $P=.039$). Poor QoL was attributed to the ocular disease by 21% and 20% of enucleated and irradiated patients respectively (Chi-square, $P=.073$).

Conclusions: Contrary to several previous studies, patients reported better QoL after radiotherapy than enucleation. This is probably because factors reducing QoL also increased the likelihood of enucleation and, conversely, enucleation outcomes made it more difficult for patients to cope with events and conditions reducing QoL. Special measures should be taken to predict, detect and treat psychological morbidity in patients with uveal melanoma.

0038

Management of choroidal neovascular membranes associated with choroidal nevi

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Purpose: To evaluate the management options of choroidal neovascular membrane (CNVM) associated with choroidal nevi

Design: Retrospective observational case series

Methods: Nineteen eyes who had CNVM associated with choroidal nevi were included. CNVM was managed with observation, intravitreal anti-VEGF injections alone, photodynamic therapy (PDT) alone, or intravitreal anti-VEGF injections combined with PDT. Main outcome measures were the final visual acuity, and CNVM status.

Results: CNVMs were classic in 16 eyes (84%) and occult in 3 (16%). Seven eyes (39%) were treated with intravitreal anti-VEGF injections alone. Complete regression of CNVM was observed in 5 eyes, while partial regression was obtained in 2 eyes. Eyes gained an average of 2.3 Snellen acuity lines. Two eyes (10%) were treated with PDT alone. CNVM was partially regressed in both eyes, and vision remained stable. Four eyes with non-vision threatening CNVM (21%) were observed. Complete regression was observed in 1 eye, while the CNVMs remained active but stable in 3 eyes. Six eyes (32%) were treated with PDT combined with intravitreal anti-VEGF injections. Complete regression was seen in 1 eye, partial regression in 1 eye, and active CNVM in 4 eyes. There was an average of 3.3 Snellen acuity lines decrease in visual acuity. All choroidal nevi remained stable in thickness and size after a mean follow-up of 34 months.

Conclusions: In our series, anti VEGF injections alone, or PDT alone were most effective in treating vision-threatening CNVM associated with choroidal nevi. Non-vision threatening CNVMs could be observed.

0044

Microincision, 27-Gauge Aspiration Cutter-Assisted Multifocal Iris Biopsy for Melanoma

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Purpose: To determine the effectiveness of the modified 27-gauge Finger Iridectomy Technique as a minimally invasive method for establishing the diagnosis of iris neoplasms.

Methods: Patients with suspected iris melanoma underwent multifocal full-thickness surgical iridectomy biopsy using the modified Finger Iridectomy Technique. In this technique, a 27-G inked trocar was used to create a clear corneal incision and the anterior chamber was filled with sodium hyaluronate 1%. A 27-G aspiration cutter probe was placed over the lesion, with the aspiration portal occluding the lesion. The aspiration (600 mm Hg) cutter (300 cuts per minute) was used to create full- and partial- thickness surgical iridectomy biopsies. After each biopsy the probe was removed from the eye and its contents were aspirated into a separate 3-mL syringe (labeled by clock hour location). After multiple biopsies were obtained, the sodium hyaluronate 1% was removed and the wound was checked for leakage.

Results: A total of 5 cases were included. Diagnostic specimens were obtained in all cases. There were three cases of malignant melanoma, one diffuse iris melanoma, and one melanocytoma. All corneal wounds were self-sealing. No intraocular pressure increase, infection, cataract, or vision loss were noted. One patient had a small transient hyphema postoperatively. Intraocular tumor dissemination was not observed.

Conclusions: Multifocal surgical iridectomy biopsy can be minimally invasive and effective, allowing for partial and full-thickness iris biopsy. Using a 27-G aspiration cutting probe allows for small incision surgery, rapid recovery, and no significant complications.

0046

Treating Vitreoretinal Lymphoma By Intravitreal Methotrexate, 20 Years Of Experience

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Purpose: To report our 20 years' experience in treating vitreoretinal lymphoma by intravitreal methotrexate injections.

Methods: A retrospective analysis of all the patients with vitreoretinal lymphoma that were treated in the ocular oncology service of Hadassah Hebrew University Medical Center since March 1997. All the patients were treated by intravitreal injections of 400mg of methotrexate in 0.05-0.1 ml according to protocol of up to 25 injections.

Results: During the 20 years we treated 108 eyes of 62 patients (39 females; 23 males). The age range 21-92 years (mean 61.5 years). In 46 patients (74.2%) both eyes were involved, and in 16 the disease was monocular (RE-7; LE-9) 58 patients had B-cell lymphoma and 4 T-cell lymphoma. In 47 patients (75.8%) the ocular disease accompanied primary CNS lymphoma. In 22 the ocular disease preceded the CNS lymphoma and in 25 the CNS lymphoma preceded the ocular disease. All patients responded fully to treatment after 2-16 injections and in only one eye was there a recurrence after completion of the treatment (was treated successfully by a full second course of methotrexate). The side effects were mostly superficial (conjunctival hyphemia and keratopathy) and temporary and were reduced when using the methotrexate injections to 0.05ml.

Conclusions: Intravitreal chemotherapy using methotrexate is a very effective way of treating vitreoretinal lymphoma with 100% success rate and rare recurrences, with only superficial and temporary side effects.

0049

Intravenous chemotherapy for retinoblastoma causes reduction in deep capillary density on optical coherence tomography angiography

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Purpose: To study microvascular anatomy using optical coherence tomography angiography (OCTA) after intravenous chemotherapy (IVC) for retinoblastoma (RB).

Methods: Ten age-matched normal eyes with no documented ocular pathology (control), 10 fellow eyes of patients with unilateral RB treated with IVC (RB fellow), and 10 eyes with extramacular RB in patients with bilateral RB treated with IVC (RB tumor) were included. All eyes were scanned using enhanced depth imaging optical coherence tomography and OCTA.

Results: Mean age in control, RB fellow, and RB tumor was 12 (median: 12, range: 6-17 years), 10 (median: 9, range: 8-17 years), and 12 years (median: 11, range: 7-16 years), respectively (all $p > 0.308$). Mean interval between last IVC and OCTA scan was 9 years (median: 8, range: 3-17 years) for RB fellow and 10 years (median: 10, range: 5-14 years) for RB tumor ($p = 0.642$). There was no significant difference in logMAR visual acuity (all $p > 0.150$), central macular thickness (all $p > 0.094$), subfoveal choroidal thickness (all $p > 0.066$), superficial foveal avascular zone (all $p > 0.618$), deep foveal avascular zone (all $p > 0.610$), and superficial capillary density (all $p > 0.638$) of controls vs RB fellow, controls vs RB tumor, RB fellow vs RB tumor, respectively. In contrast, mean deep capillary density was significantly greater in controls (51%), compared to RB fellow (49%, $p = 0.026$) and RB tumor (48%, $p = 0.028$), but no significant difference was found between RB fellow and RB tumor ($p = 0.515$).

Conclusions: Long term follow-up after IVC for retinoblastoma showed significant reduction in deep capillary density without visual compromise.

Clinical findings and clinical courses of IgG4 producing MALT lymphoma

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Purpose: IgG4 producing MALT lymphoma (G4/MALT) is a MALT lymphoma in which lymphoma cells produce IgG4 in their cytoplasm as the name suggests. G4/MALT is a border zone of IgG4-related orbital disease (IgG4-ROD) and MALT lymphoma. If we don't know this disease, we may waver in diagnosis and/or management. We experienced four cases of G4/MALT, and will describe clinical findings of the disease and clinical courses following the treatment.

Method: The subject was four cases of G4/MALT who consulted Okayama medical center from September 2006 to August 2016. We retrospectively reviewed the charts, investigated involved sites in the orbit, serum IgG4 level, treatment method and clinical course.

Results: 1, MR image showed that tumors infiltrated orbital fat in 3 cases out of 4 cases and major lacrimal gland in two cases. The orbital fat infiltration was dominant and this infiltrating pattern seems more similar to MALT lymphoma than IgG4-ROD.

2, Serum IgG4 values were 159 mg/dl, 40.5 mg/dl, 169 mg/dl, 94.9 mg/dl, respectively. In 2 of 4 cases, serum IgG4 level was mildly elevated.

3, Two patients underwent radiation therapy, and the tumor size decreased. In one case, the tumor was completely excised. Neither case had tumor recurrence during follow-up period. One case is under follow-up without treatment. It seems that we can manage G4/MALT according to MALT lymphoma.

Conclusions: We should be aware of the existence of IgG4 producing MALT lymphoma, correctly diagnose it, and treat it according to MALT lymphoma.

Clinical presentations and outcomes of Asian Indian patients presenting with retinoblastoma at one or less than one year of age

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Purpose: To study the clinical presentation and outcomes of retinoblastoma patients presenting at an age of one year or less.

Method: Retrospective study of 714 eyes of 435 patients.

Results: The mean age at diagnosis of retinoblastoma was 7 months (median, 7 months; range, <1 to 12 months). There was no gender preponderance (males, n= 229, 53% versus females, n= 206, 47%). There was preponderance for bilateral presentation (n= 282, 65%) and 1% (n=5) cases had unilateral disease on presentation and eventually became bilateral. Family history of retinoblastoma was positive in 6% (n=25) cases. The most common presenting complaint was leukocoria (n=203, 47 %). Of the 714 eyes with retinoblastoma, 98% (n=701) had intraocular tumors, while 2% (n=13) had extraocular tumor extension on presentation. As per the International Classification of Intraocular Retinoblastoma, maximum cases were grouped under Group E (n=300, 42%). Systemic chemotherapy was the most common primary modality of treatment (n= 462, 65%). Globe salvage was achieved in 64% (n= 453) Of the 186 eyes in which the vision was recorded, vision of 20/40 or better was recorded in 46% (n=85) eyes. Over a mean follow-up period of 49 months (median 33 months; range, <1 to 270 months), disease-related death occurred in 2% (n=9) patients due to non-compliance to treatment.

Conclusions: Retinoblastoma at an age of 1 year or less is associated with excellent life salvage (98%) and moderate globe (64%) and vision (46%) salvage in Asian Indian patients.

0052

Local Failure after Episcleral Brachytherapy for Posterior Uveal Melanoma: Patterns, Risk Factors and Management

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Purpose: To evaluate the patterns, the risk factors and the management of recurrence following brachytherapy in patients with posterior uveal melanoma.

Method: A retrospective cohort study of 374 consecutive patients (375 eyes) treated with episcleral brachytherapy for posterior uveal melanoma from January 2004 to December 2014. Exclusion criteria included inadequate follow-up (< 1 year) and previous radiation therapy. Local control rate and time to recurrence were the primary end points. Kaplan-Meier estimation and Cox proportional hazard models were conducted to identify risk factors associated with recurrence. The patterns of recurrence (chronologic and anatomic) and their management were also assessed.

Results: 21 patients (5.6%) experienced recurrence (follow-up range: 12 to 156 months, median 47 months). The median time to recurrence was 18 months (range: 4 to 156 months). Five-year estimated local recurrence rate was 6.6%. The majority (90.5%) of the recurrences occurred within the first 5 years. The predominant site of recurrence was at the tumor margin (12 patients, 57.1%). Univariate analysis identified 3 statistical significant recurrence risk factors: advanced age, largest basal diameter and the use of adjuvant transpupillary thermotherapy (TTT). Recurrent tumors were managed by repeat brachytherapy, TTT and enucleation.

Conclusions: Local recurrences following brachytherapy are uncommon 5 years after episcleral brachytherapy. Follow-up intervals can be adjusted to reflect time to recurrence. Most of the eyes with recurrent tumor can be salvaged by conservative methods.

0057

Usefulness of flow cytometry in diagnosis of extranodal marginal zone B-cell lymphoma of the ocular adnexa

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Purpose: Flow cytometry (FCM) is a method to evaluate cell surface markers by population of various lymphocytes quantitatively. Nowadays, it is mandatory to examine FCM in diagnosis of systemic lymphoid malignancies; however, little is known about usefulness of FCM in extranodal marginal zone B-cell lymphoma (EMZL) of the ocular adnexa. The aim of this study is to disclose results of FCM, which were compared with EMZL and reactive lymphoid hyperplasia (RLH).

Methods: This is a retrospective observational study. 72 tumors comprising 41 RLH and 31 EMZL were enrolled in this study. All tumors, surgically excised, were diagnosed based on histopathology, immunoglobulin (Ig) heavy chain gene rearrangement as well as FCM. In FCM, the percentage of T-cell markers (CD2, CD3, CD4, CD7, CD8), B-cell markers (CD19, CD20, CD5, CD10), and NK cell marker (CD56) was searched based on medical records. Ig light chain restriction was evaluated from results in kappa/lambda deviation by FCM according to a previous report (Samoszuc et al. Diagn Immunol 1985).

Results: The percentage of CD2, CD3, CD4, CD7, CD8, CD5, CD10 and CD56 was significantly lower in EMZL than RLH ($P < 0.01$ in every factor). In contrast, CD19 and CD20 percentages were significantly greater in EMZL than RLH ($P < 0.01$). Three tumors (7%) in RLH and 14 tumors (45%) in EMZL revealed Ig light chain restriction.

Conclusions: Analyses of cell surface markers using FCM are useful in differentiating EMZL from RLH. Sensitivity and specificity of Ig light chain restriction were 0.69 and 0.82 in this study.

Prognostic significance of nuclear survivin (BIRC5) in retinoblastoma

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Background: Management of retinoblastoma is evolving. Yet, other than histopathologic high-risk factors (HHRFs), molecular tumor markers predicting outcomes have not been well characterised. Survivin, a member of inhibitor of apoptosis (IAP) family, has been associated with poor prognosis in several human tumors.

Purpose: To evaluate the expression of survivin in retinoblastoma and, correlate its expression with HHRFs and clinical outcomes.

Method: Presence of survivin was studied using immunohistochemistry. Differences in HHRFs and clinical outcomes between low and high survivin groups were analyzed. Similarly, differences in survivin expression were analyzed between primary and secondary (post-chemotherapy) enucleation.

Results: The study included 65 eyes of 63 patients in whom enucleation was performed; 39 were primary enucleations and 26 were enucleated post chemotherapy. Mean age at presentation was 28.2 + 25 months with a male: female ratio of 1.59:1. All tumors expressed survivin in the nucleus (NS). NS score was low in 31 (47.7%) and high in 34 (52.3%). Tumors with high NS score had significantly higher incidence of massive choroidal invasion (38% vs 10%, p=0.008), retrolaminar tumor spread (29% vs 10%, p=0.05), ciliary body and anterior chamber involvement. Clinical outcomes were similar between groups. Primary and secondary enucleated eyes did not differ in survivin expression.

Conclusions: Nuclear survivin correlates with HHRFs. Differential expression of survivin is a novel finding and is thus a promising prognostic and potentially therapeutic marker in retinoblastoma. Further studies with a larger sample are required to elucidate molecular mechanisms to explain the precise cellular role of survivin in retinoblastoma.

0061

Clinical presentation and treatment outcome of Retinoblastoma children in National Eye Centre Cicendo Eye Hospital, Indonesia 2012-2016

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Purpose: To study the clinical presentation and treatment outcome among children referred to National Eye Centre Cicendo Eye Hospital as government tertiary eye hospital in Indonesia.

Method: A retrospective review of children referred to Cicendo Eye Hospital, during 2012-2016, demographic, clinical characteristic and treatment outcome were studied.

Result: Total 166 patients with diagnose of Retinoblastoma were studied. Most of the patient came from our district in West Java (58%), most range age was 24-35 month old (41%), unilateral retinoblastoma was 70%. Most of the tumor were intraocular 97%, extraocular 3%, the most clinical sign were leucocoria 51% and proptosis 19%. Patients were examine with CT Scan head and orbita, the advanced state show destruction bone, invation to optic nerve or penetrated to surrounding tissue 33%. The grading using IIRC, most of them had advanced clinical stage, grade D + E (85%). The most common treatment of the patient were enucleation and adjuvant chemotherapy 37%. After treatment 37% retinoblastoma regressed, tumor penetrated to surrounding tissue/recurrent were 17%, patient loss to follow up were 32%, cause patient refused chemotherapy or enucleation, or try to a herbal medicine.

Conclusions: Retinoblastoma patients in Cicendo Eye Hospital most of them came from West Java district, with advance clinical stage. The most common treatment were combine enucleation and chemotherapy. After treatment tumor regressed but some patient loss to follow up or refused chemotherapy or enucleation.

0062

Uveal melanoma in the only seeing eyes

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Purpose: to analyze the frequency, clinical features, and challenges of treatment of uveal melanoma (UM) in the only seeing eyes (OSE).

Method: retrospective analysis. The eye was considered as the OSE if the best corrected visual acuity (BCVA) of the contralateral eye was 20/200 or worse.

Results: a total of 2100 patients with UM treated between 2002 and 2016 were analyzed. Forty three (2%) of them had UM in the OSE. Seven of them had bilateral UM. Tumor thickness was from 1.4 to 16 mm, mean 5.7 mm, basal diameter from 4.1 to 21.6 mm, mean 11.1 mm. Choroidal tumors were in 27 eyes, ciliary body was involved in 12 eyes, iris in 4 eyes. Eighteen eyes (42%) had BCVA lower than 20/200. The main causes of low vision of the fellow eye were corneal dystrophy (n=7), bilateral UM (n=7), ARMD (n=5), diabetic retinopathy (n=5), high myopia (n=4), trauma (n=2), other (n=13). The primary treatment included Ru-106 brachytherapy using both BEBIG and Russian plaques in 22 eyes (51%), brachytherapy with TTT in 4 (9%), TTT in 8 (19%), Gamma-knife radio surgery in 2 (4%), enucleation in 9 (21%). In 2 patients both eyes were primary enucleated. Follow up was from 9 to 139 months. After treatment 32 eyes (94%) were retained, 37% of them had BCVA 20/200 and higher.

Conclusions: UM in the OSE is a challenging condition which requires different treatment approaches including enucleation even bilateral.

High-Risk Histopathology Features in Primary and Secondary Enucleated International Classification of Retinoblastoma Group D Eyes

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Purpose: To evaluate the rate and identify risk factors for high-risk histopathology (HRH) features in group D retinoblastoma eyes enucleated as primary or secondary treatment.

Methods: Retrospective clinicopathologic correlation of consecutive group D eyes enucleated from 2002 – 2014. HRH features were defined as presence of anterior chamber seeds, iris/ciliary body/muscle infiltration, massive (≥ 3 mm) choroidal invasion, retrolaminar optic nerve invasion, or combined non-massive choroidal and prelaminar/laminar optic nerve invasion.

Results: There were 64 group D eyes enucleated, of which 40 (40 patients) were primary and 24 (22 patients) secondary to other treatments. HRH features were detected in 10 (16%) eyes in the entire cohort; in 5 cases in each of the primary and secondary enucleated groups (13% and 21%, respectively). Absence of vitreous seeds at presentation was the only predictive factor found for HRH features in the primary enucleation group ($P=0.042$), whereas none were found in the secondary group ($P\geq 0.179$). Anterior structures invasion (anterior chamber, iris, ciliary body/muscle) was found significantly more after secondary enucleation ($P=0.048$). All patients with HRH features were treated with adjuvant chemotherapy and no metastases occurred in a median follow-up time of 73.2 months (mean: 71.5, range: 13.7-153.0).

Conclusions: The choice of primary treatment for group D retinoblastoma should be carefully weighed, as 13% of eyes harbor HRH features at presentation, with absence of vitreous seeds being a potential risk factor. Secondary enucleated group D eyes with HRH features more commonly involved anterior structures. Meticulous clinical and histological examinations are warranted for this subset of patients.

0066

Primary and secondary cavitory retinoblastoma tumours: identification, management and genetic analysis

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Purpose: To assess phenotypic features of primary cavitory retinoblastoma tumours (CRBs) at presentation and secondary CRBs which are identified after systemic chemotherapy. Genetic analysis was also undertaken.

Methods: Patients with retinoblastomas having ophthalmoscopically visible cavities between

2004 and 2014 in whom 4-6 cycles of systemic chemotherapy were given.

Results: Eighteen eyes of 17 patients displayed CRBs. This represented 6.8% of 250 patients.

Mean age at diagnosis was 13 months; 5 unilateral (29%) and 12 bilateral (71%).

The mean (median, range) number of retinoblastoma tumors per eye was 2 (2; 1-6).

The number of cavities per tumor was 3 (2, 1-6). At presentation intra-tumoral cavities were seen in the superficial portion of the tumor in 10 eyes (55%): primary CRBs. 6/10 (60%) involved the foveola. The cavities became visible in 8 eyes (44%) after systemic chemotherapy (secondary CRBs): 6/8 (75%) were Group D. Two eyes required enucleation due to relapse of non-cavitory tumors. Germline mutations were detected in 14 patients (82%) of whom four demonstrated mosaicism (29%); only one had a low penetrant mutation.

The mean follow-up period was 40 (35, 6-120) months.

Conclusions: 1ry and 2ry CRBs are distinct entities with 1ry CRBs were more likely to involve the foveola and 2ry CRBs were more likely to present as Group D eyes. However, they share stability and do not require aggressive adjuvant therapy. The aetiology is uncertain and there was no evident phenotype-genotype correlation with mosaicism noted in 29% of all cases

0067

FNAB of Choroidal Melanoma: Cytopathological Analysis of the Needle Tract

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Purpose: To report cytopathological observations on the cells retrieved from the 25G cannula used during prognostic transvitreal fine needle aspiration biopsy (FNAB) of choroidal melanoma.

Methods: Transvitreal FNAB of choroidal melanoma was performed through a 25G valved cannula. 20 samples from 20 consecutive patients were obtained. Most tumors were treated with plaque radiation therapy (16/20, 80%) following standard clinical guidelines. Four enucleated globes (4/20, 20%) were subjected to a similar transvitreal biopsy prior to enucleation.

Results: Cytopathological analysis of the cells retrieved from the cannula revealed absence of any cells in 4 of 20 samples (20%). In the remaining 16 samples, definite melanoma cells and atypical cells (probable melanoma cells) were observed in 2 samples each (total 4, 25%). Histiocytes (4/16, 25%) and lymphocytes (1/16, 6%) were also observed. Thirteen samples (13/16; 81%) contained conjunctival epithelial epithelium. Prognostication could be performed on all FNAB samples (20, 100%).

Conclusions: 25G valved cannula offers potential advantage of isolating the needle tract and allowing retrieval of the contaminating tumor cells.

0071

Microenvironment Regulation of Inflammasomes in Uveal Melanoma Favors Metastatic Growth

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Purpose: Uveal melanoma (UM) is the most common primary intraocular malignancy in adults. UM cells disseminate hematogenously to the liver. Despite multiple advances in medicine, there are no anti-metastasis drugs and current adjuvant therapies for liver metastasis, including intra-hepatic chemotherapy delivery and/or resection, does not provide a cure. The events leading to disruption between tissue homeostasis and the microenvironment leading to metastasis, are not fully understood. Recent work suggests the inflammasomes can act either in anti-cancer immunosurveillance or could promote tumor growth, based on microenvironmental signals. In this study we investigated the presence of inflammasomes in the metastatic liver of a UM patient post mortem.

Methods: We received approval for the Institutional Review Board at the University of Tennessee Health Science Center to perform analyses on post mortem tissue of uveal melanoma patients and compared them to healthy livers. We performed Western blot analyses on the inflammasomes NLRP1, NLRP2, NLRP3, and NLRP12.

Results: Western blot analyses showed absence of most known inflammasomes in the metastatic UM liver compared to healthy liver. Multiple areas of the metastatic liver were examined and found similar results. Results were confirmed by protein analysis of the inflammasomes' downstream signalling components caspase-1 and IL-1 β production.

Conclusions: Our work suggests the liver inflammasomes may contribute to clearance of UM metastasis in the liver. Further work is being conducted using an UM orthotopic xenograft system to understand the components of the liver inflammasomes and define factors, which may serve as drug targets to reduce metastasis.

0074

Clinical outcome of Multi-modal Therapy in Extra-ocular Retinoblastoma with optic nerve invasion

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Purpose: The purpose of this study was to evaluate the outcome of multi-modal therapy in retinoblastoma patients who had tumour invasion of the optic nerve at the time of diagnosis

Methods: Patients of retinoblastoma who presented to our tertiary care centre and had evidence of tumour extension into the optic nerve on contrast MRI scans of the orbit and brain were included. The treatment protocol consisted of neo-adjuvant chemotherapy, enucleation, orbital external beam radiotherapy and adjuvant chemotherapy. Following neo-adjuvant chemotherapy, the optic nerve status was re-assessed on MRI scans prior to performing enucleation surgery. The drugs used for systemic chemotherapy consisted of vincristine, etoposide and carboplatin (VEC), repeated for a total of 12 cycles. Survival outcomes and cause of death were analysed following treatment.

Results: During the study period, a total of 48 children were evaluated (66.7% unilateral, 60% boys). The median age at presentation was 30 months. After neo-adjuvant chemotherapy, MRI scans showed a marked reduction in the extent of optic nerve invasion by the tumour. The median follow-up was 18.6 months. Of 48 children, 18 (38%) died. The most common cause of death was CNS metastasis (83%). The Kaplan Meier survival probability was 79% and 59% at one year and four years respectively.

Conclusions: The management of extra-ocular retinoblastoma is challenging. The use of a multimodal treatment protocol with systemic chemotherapy, enucleation and orbital radiotherapy showed encouraging results in cases of extra-ocular retinoblastoma with optic nerve invasion.

0076

Delivered dose uncertainty analysis for partially loaded and eccentrically placed 16 mm COMS plaques compared to fully loaded plaques for brachytherapy treatment of uveal melanoma

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Purpose: To determine the magnitude of the tumor apex margin required to provide full dosimetric coverage at the apex for ¹²⁵I ocular brachytherapy treatments using partially loaded and eccentrically placed 16 mm COMS plaques, by estimating total dosimetric uncertainty at the tumor apex.

Methods: Uncertainties were assessed for four different plaque loading patterns commonly used at our clinic with the 16 mm COMS plaque, utilizing between 4 and 9 seeds to treat small- to medium-sized tumors. Uncertainty assessment follows the methods outlined in Morrison *et al.* [1]. Uncertainties pertaining to seed construction, source strength, plaque assembly, treatment planning calculations, tumor height measurement, plaque placement, and plaque tilt were included. Doses along the tumor central axis calculated using Plaque Simulator treatment planning software were used to assess the sensitivity of the apex dose to each source of uncertainty and comparisons were made to a fully loaded plaque.

Results: Total uncertainties at the tumor apex for all partially loaded plaques were slightly larger than for a fully loaded plaque due to the steeper dose gradient when using fewer seeds, as well as higher sensitivity to plaque placement and tilt for eccentrically placed plaques. The required apex margins ranged from 1.3 to 1.75 mm, compared to 1.3 mm for a fully loaded plaque.

Conclusions: This analysis extends our previous work to more complex scenarios in which individualized and conformal plaque loading is used, demonstrating that larger apex margins may be required for such scenarios.

[1] Morrison *et al.* Med. Phys. 43, 4891-4902 (2016).

Identifying Invasion-Promoting Molecular Pathways in Retinoblastoma

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Purpose: Retinoblastoma is the most frequent malignant intraocular cancer in children. In advanced cases, dissemination in the CNS or metastasis to distant organs can lead to death. Our goal was to identify the molecular drivers and signalling pathways associated with tumor invasion into the optic nerve and choroid in order to develop new prognostic markers and therapeutic targets.

Method: RNA extracted from eleven snap frozen retinoblastoma specimens was analyzed by RNA-seq. Samples were divided between invasive (retrolaminar, n=4; intralaminar, n=1) and non-invasive (prelaminar, n=4, no optic nerve invasion, n=2). Four cases with optic nerve invasion and two without also showed focal (<3mm) choroidal invasion, but none had massive choroidal invasion.

Results: We found 267 genes whose expression was modified more than two-fold in invasive versus non-invasive retinoblastomas: 27 upregulated and 240 downregulated. In the invasive cohort, we observed about 28-fold induction of DLX6, a transcription factor known to enhance migration and invasion by upregulating Twist1, and 11-fold induction of the matrix metallo-proteinase MMP12, which promotes invasion by degrading the extracellular matrix. We also found 24-fold reduction in WIF1 (WNT Inhibitory Factor 1), a tumor suppressor epigenetically silenced in various cancers, 16-fold reduction in CLUSTERIN, associated with apoptosis, and 11-fold decrease in GLI3, an inhibitor of Sonic hedgehog signalling.

Conclusions: Several genes and pathways were differentially expressed in invasive versus non-invasive retinoblastomas. In particular WNT, Sonic hedgehog, and MMP signalling might be responsible for driving CNS dissemination in retinoblastoma. Functional studies are in progress to confirm these data in retinoblastoma lines.

Extracellular matrix remodelling in an Etoposide resistant subclone derived from WERI-Rb1

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Purpose: Retinoblastoma (Rb) is the most common malignant childhood eye tumor worldwide. Studies indicate that extracellular matrix (ECM) remodelling plays a crucial role in tumour growth, metastasis and angiogenesis. This study aimed to analyse the ECM of two human retinoblastoma cell lines, Etoposide sensitive WERI-Rb1 and a Etoposide resistant subclone (WERI ETOR).

Methods: Quantitative RT-PCR analyses were performed for the proteoglycans *Aggrecan*, *Brevican*, *Neurocan* and *Versican*, the glycoproteins *Fibronectin*, α 1-*Laminin*, *Tenascin-C* and *Tenascin-R*, *MMP-2*, -7, -9, *TIMP-1* and -2 and α 5-, β 1-, α v-, α 4- and α 6-*Integrin* receptors. Proliferation behaviour analyses via *video microscopy* were performed after cultivation on *Fibronectin*, *Laminin*, *Tenascin-C* and *Collagen IV*.

Results: Quantitative RT-PCR analysis showed a reduced *Brevican*, *Neurocan* and *Versican* mRNA expression in the resistant compared to the sensitive cell line ($p < 0.01$). Furthermore, reduced expression levels of α 1-*Laminin*, *Fibronectin*, *Tenascin-C* and *Tenascin-R* were observed in the resistant cell line ($p < 0.001$). A significant down-regulation was shown for *MMP-2*, -7, -9 and *TIMP-2* ($p < 0.001$). Lower levels of α 5-, β 1- and α 4-*Integrin* were observed, whereas an up-regulation was detected for α 6-*Integrin* in the resistant cell line ($p < 0.001$).

Interestingly, proliferation of resistant cells was enhanced on *Tenascin-C*, while an anti-proliferative effect was observed for *Fibronectin* ($p < 0.05$).

Conclusions: In sum, our results indicate a different ECM regulation and cell-substrate interaction of resistant RB cells. This mechanism might be a step towards chemotherapeutic resistance transformation in Rb patients.

Optical Coherence Tomography Angiography in differential diagnosis between choroidal nevus and melanoma

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Purpose: evaluate optical coherence tomography angiography (OCTA) characteristics of macular vascular details in eyes with choroidal nevus and melanoma, compared with unaffected contralateral eye.

Method: 70 patients with choroidal nevus and 36 with choroidal melanoma examined with OCTA. Measurements: central macular thickness (CMT), superficial (sFAZ) and deep (dFAZ) foveal avascular zone area, and superficial (sCVD) and deep (dCVD) capillary vascular density.

Results: In patients with nevus, CMT (affected vs. unaffected eye) was similar, whereas in patients with melanoma, CMT was greater in affected eye. In patients with nevus, sFAZ were similar in both eyes. This was also valid for dFAZ. In patients with melanoma, similar values for sFAZ were noted for both eyes, whereas dFAZ was larger in affected eye with macular melanoma and similar in eyes with extramacular melanoma. Regarding CVD, eyes with nevus showed similar sCVD and dCVD. Reduced dCVD was found in four eyes with nevus, all with three or more risk factors for growth. In eyes with melanoma, significant reduction was found in both sCVD (related to presence of subretinal fluid) and dCVD (regardless subretinal fluid presence and tumor location, but proportional to tumor thickness). Reduced dCVD was found in 11% of eyes with nevus versus 58% of eyes with melanoma.

Conclusions: Compared with contralateral eye, eyes with nevus demonstrate similar CMT, FAZ, and CVD. In contrast, eyes with melanoma show increased CMT, enlarged FAZ, and reduced CVD, particularly related to increasing tumor thickness. OCTA could be a useful tool in differentiating choroidal nevus from melanoma.

0083

CANT1 lncRNA triggers efficient anti-tumor efficacy by targeting aberrant lncRNA cascade in uveal melanoma

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Purpose: Recent studies have shown the roles of long non-coding RNAs (lncRNAs) in tumorigenesis, thus, targeting tumor-specific lncRNA abnormalities has become an attractive approach for developing therapeutics to treat uveal melanoma.

Method: RACE assay was used to identify the full-length of novel lncRNA. Transwell assay, colony formation assay and xenograft model were used to determine the role of CANT1 in tumorigenesis of UM. Genome-wide cDNA array was used to search for the target of CANT1. Chromatin oligonucleotide precipitation and chromatin immunoprecipitation were used to determine the CANT1-guided lncRNA cascade.

Results: Here, we identified a novel CANT1 lncRNA (CASC15-New-Transcript 1) and acts as a necessary UM suppressor. CANT1 significantly reduced the tumor metastatic capacity and tumor formation *in vitro* and *in vivo*. Intriguingly, XIST lncRNA serves as a potential target of CANT1, and JPX or FTX lncRNA subsequently plays a contextual hinge to activate a novel CANT1-JPX/FTX-XIST lncRNA pathway in UM. Moreover, CANT1 triggers the expression of JPX or FTX by directly mediating H3K4 methylation of their promoters.

Conclusions: These observations reveal a novel lncRNA cascade in which lncRNAs directly build a long non-coding cascade without coding genes, thereby specifying a novel "lncRNA-cascade renewal" anti-tumor therapeutic strategy in uveal melanoma.

0084

Oncolytic adenovirus H101 combined with knocking down GNAQ amplifies the destruction effect of UM cells

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Background: Active mutation in G protein alpha subunit q (GNAQ/GNA11) is the major trigger to the tumorigenesis of uveal melanoma. Oncolytic adenovirus H101 is the first oncolytic virus for cancer treatment in clinical work approved by the Chinese State Food and Drug Administration. We endeavored to demonstrate whether the combination of down-regulating GNAQ pathway with H101 therapy would present a synergistic effect in tumor therapy.

Methods: The cell toxicity to adenovirus infection was analysed by cell growth assay. Western blot was used to detect GNAQ, MEK1/2, YAP and p-YAP expression. Appropriate concentration of H101 infection and cell survival rate were measured by a cell counting kit-8 assay. UM cells were stained with Annexin-V and propidium iodide for apoptosis assay and cell cycle distribution.

Results: 92.1 cells were more sensitive to H101 infection than OCM1 cells. GNAQ expression was markedly decreased by siGNAQ. United treatment of siGNAQ and H101 induced inhibited proliferation and activated apoptosis of 92.1 cells through blocking MEK1/2 expression and phosphorylating YAP pathway.

Conclusions: Combination therapy of H101 and siGNAQ is feasible and could potentially serve as a novel targeted molecular therapy for UM.

A Comparison of Vitreous Seed Clouds (class 3) Treated with Ophthalmic Artery Chemosurgery With or Without Intravitreous Chemotherapy

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Purpose: Class 3 retinoblastoma vitreous seeds, or clouds, are distinct: older patients with unilateral disease and peripheral tumors. They receive the highest amount of intravitreous melphalan and take the longest time to regress. This study compares efficacy and toxicity between ophthalmic artery chemosurgery with or without intravitreous chemotherapy.

Methods: 40 eyes containing clouds (class 3 vitreous seeds) of 40 retinoblastoma patients (19 treated with OAC alone and 21 treated with OAC and intravitreous (OAC/IVit) were investigated. The outcomes measures of ocular survival, disease-free survival and time to regression of seeds were analyzed with Kaplan-Meier estimates. Ocular toxicity was evaluated by clinical findings and electroretinography (ERG). Continuous variables (age, follow-up time) were compared with a Students' t-test and categorical variables (laterality, disease status, etc) were compared with Fisher's Exact Test.

Results: There was no significant difference in the age, laterality or disease and disease status between the two groups. The time to regression was significantly shorter for eyes treated with OAC/IVit (5.6mos), compared to eyes treated with OAC alone (14.6 mos, $p < 0.001$). The 18-month Kaplan-Meier estimates of disease-free survival were significantly worse for the OAC alone group: 67.1% (95%CI 40.9-83.6), compared to the OAC/IVit group: 94.1% (95%CI 65-99.1), ($p = 0.05$). The 36-month Kaplan-Meier estimate of ocular survival 83.3% (95%CI 56.7-94.3) for the OAC alone and 100% for the OAC/IVit, $p = 0.16$.

Conclusions: Treating vitreous seed clouds with OAC *and* intravitreous chemotherapy, compared to OAC alone, results in a shorter time to regression and is associated with fewer recurrences requiring additional treatment.

0091

The incidence of visual impairment and blindness in retinoblastoma

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Purpose: To assess incidence of visual impairment in retinoblastoma in a cohort of young children

Methods: A retrospective case series of all patients with bilateral retinoblastoma presenting to the London Retinoblastoma Unit between 2010-2014. Visual impairment and legal blindness were defined using the Centers for Disease Control (CDC) guidelines. Demographic data and tumor characteristics were tested for correlation with incidence of visual impairment or legal blindness.

Results: A total of 44 patients met the criteria for inclusion. The median age of presentation was 9 months. Visual impairment was found in 38% of the children. Legal blindness was present in 19% children. The presence of bilateral macular tumors predicted visual impairment and legal blindness. While 39% of patients with bilateral macular tumors were found to be legally blind, no child with macula sparing disease in at least one eye was found to be legally blind. The presenting International Intraocular Retinoblastoma Classification (IIRC) group of the better seeing eye was also correlated with visual impairment and blindness, with increasing rates of each for more advanced disease. Grating visual acuities were able to predict visual impairment in pre-verbal children, providing them with early assistance.

Conclusions: It is essential to detect and provide intensive early support for visually impaired infants as development can be affected by severe visual impairment. Less than 20% of patients with bilateral retinoblastoma become legally blind and this correlates with IIRC group and bilateral macular tumors. Our results can help in counselling families and predicting vision impairment in infants

The PDGF-PDGFR signalling pathway as a potential targeted therapy to reduce retinoblastoma cell survival and increase apoptosis

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Purpose: The greatest challenge in treatment of retinoblastoma (Rb) remains the resistance of vitreous seeding to current therapies. In all major standardized Rb staging systems the presence of vitreous seeding is a poor prognostic indicator of ocular survival. Previously, our group identified the PDGF-PDGFR signalling as a signalling pathway that sustains angiogenesis in Rb. In this study we investigated how the PDGF-PDGFR signalling pathway regulates Rb cell proliferation and survival.

Methods: We performed in vitro cell culture assays using Y79 Rb cells, considered the metastatic model of the disease. Cells were cultured in different conditions, which included stimulatory (recombinant human PDGF) and inhibitory (imatinib mesylate) conditions of the PDGF-PDGFR signalling pathway. Cell proliferation studies were done using the CellTiter 96® Aqueous Solution colorimetric assay. Assessment of cell survival included measurement of the AKT signalling pathway and the anti-apoptotic molecule BCL-2 by Western blot analyses. Nuclear translocation of the p65 subunit of NFκB was measured by imaging flow cytometry using FlowSight®.

Results: Our results suggest that PDGF-PDGFR signalling regulates Rb cell survival through AKT. We found a significant reduction in the nuclear translocation of the p65 subunit of NF-κB, and a reduction of BCL-2 concomitant with an increase in caspase-3 activity.

Conclusions: The outcomes of this study reveal that PDGF-PDGFR signalling regulates cell survival in addition to the previously described sustainment of angiogenesis. Future pre-clinical studies will aim to target inhibition of PDGF-PDFGR signalling as a potential novel treatment against Rb that could increase the chances for ocular survival.

0095

Regression of Iris Melanoma after Palladium-103 (¹⁰³Pd) Plaque Brachytherapy

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Purpose: To evaluate the patterns of regression of iris melanoma after treatment with ¹⁰³Pd plaque brachytherapy.

Method: This is a retrospective interventional case series including 50 cases of iris melanoma who underwent ¹⁰³Pd plaque brachytherapy (mean prescription dose=84.5 + 3 Gy). The outcome measures include: changes in tumor dimensions, pigmentation, vascularity, incidence of iris neovascularisation and radiation related complications.

Results: The mean age in the case series was 61.2 + 14.9 years. The mean tumor thickness was 1.4 + 0.6 mm. The tumor was melanotic in 37(74%), amelanotic in 13 (26%), of these 13(26%) showed variable pigmentation. Tumor was nodular in 34(68%), flat in 10(20%) and diffuse in 6(12%) cases. Ciliary body invasion was seen in 24(48%). Post-brachytherapy, mean tumor thickness was diminished to 1.1 + 0.2mm. Pigmentation increased in 28(56%), decreased in 13(26%) and was unchanged in 9(18%). For intrinsic vascularity (n=20), 17(85%) showed decrease and 3(15%) showed complete resolution. Newly present correctopia was observed in 5(10%) cases and iris stromal atrophy was noted in 26(52%) cases. Cataract was noted in 38(76%), neovascular glaucoma in 1(0.02%) and there were no cases of corneal opacity. There was no clinical evidence (0%) of radiation induced retinopathy, maculopathy or optic neuropathy. Mean follow up in this series was 5.4 (range 0.5 to 17) years.

Conclusions: The most common findings related to iris melanoma regression after ¹⁰³Pd plaque brachytherapy included: decrease in tumor thickness, increase in pigmentation and decrease in intrinsic tumor-vascularity. Most common complications were cataract (76%) and iris atrophy (52%). No irreversible sight limiting complications were noted.

Analysis of Circulating Tumour Cells and Plasma Tumour DNA in Uveal Melanoma: Towards a Uveal Melanoma Liquid Biopsy

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Purpose: Prognostic testing has become standard of care in uveal melanoma (UM), but requires a tissue biopsy, with a risk of sight-threatening complications. Identification and characterisation of circulating tumour cells (CTCs) may offer a viable alternative by means of a non-invasive and safe 'liquid biopsy.'

Method: Whole blood specimens were drawn from patients undergoing plaque brachytherapy for UM. CTCs were enriched by targeting the melanoma associated chondroitin sulphate proteoglycan (MCSP) and stained from a cocktail of melanoma markers (S100b, gp100 and MART-1). Plasma ctDNA was detected by droplet digital PCR for the GNAQ/11 Q209L/P mutations. Single cell WGA was performed using the PicoPlex WGA Kit (Rubicon Genomics). Chromosomal aberrations were detected through whole genome sequencing using the Ion PMG System (Life Technologies) at an approximate depth of 0.1x.

Results: 5 of 27 (19%) patients had detectable ctDNA ranging from 2 to 28.5 copies/ml of plasma. Of 23 cases analysed for CTCs, 15 had detectable CTCs (70%) ranging from 1 to 37 CTCs per 8 mL of blood. . Cytogenetic features of prognostic value such as loss of Chr3 and gain in 8q were clearly distinguishable in all cells analysed.

Conclusions: Isolation of CTCs by a combination of immunomagnetic beads with PicoPlex WGA and low-pass sequencing may offer a method of prognostic testing in UM without the need to perform a tissue biopsy.

Resection of Refractory Intraocular Retinoblastoma

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Purpose: To evaluate the role of pars plana vitrectomy (PPV) in only remaining eyes that failed systemic (IVC) and/or intra-arterial chemotherapy (IAC), and focal therapy in children with bilateral retinoblastoma and one eye enucleated.

Method: Last remaining eyes had failed 3 or more cycles of IVC and/or IAC and focal therapy. Children with metastasis were excluded. Solid tumors first were surrounded by a laser barrier to stabilize retina. Tumor and seeds were removed by PPV (5 µg/ml melphalan in irrigation fluid) with silicon oil replacement, removed after 3-6 months. Melphalan 1 µg/0.2 ml was injected sub-conjunctival at entry points 2- 4 times subsequently with 2-4 cycles of adjuvant IVC were given after large, active tumors were resected. Intravitreal melphalan (20 µg/0.05 ml) was injected monthly 4 times following removal of active vitreous seeds. Post PPV EUA was done 1-2 month/first year, 3-4 months/second year, 5-6 months/third year.

Results: Between February and June 2013, 21 patients were treated. Median follow-up time was 41 months (range 24-108). One patient was lost to follow-up with recurrent tumor and no patient had metastases or died. Two eyes were enucleated because of intraocular tumor recurrence and 18 eyes were saved. Good vision was measured in 12 patients; 5 patients had functional vision; and 1 patient had light perception.

Conclusions: Tumor resection by PPV with melphalan irrigation is safe and effective for selected eyes with refractory retinoblastoma.

0103

Primary malignant neoplasms of the lacrimal gland: Clinical features and outcome in 66 patients

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Purpose: To study the clinical presentation and outcomes of primary malignant neoplasms of the lacrimal gland.

Method: Retrospective study of 66 patients (68 tumors) with biopsy proven lacrimal gland malignant neoplasm.

Results: The mean age at presentation of primary malignant neoplasm of lacrimal gland was 42 years (median, 42 years; range, 11 to 80 years). There were 42 (64%) males and 24 (36%) females. The tumor was unilateral in 64 (97%) cases and bilateral in 2 (3%) cases. Based on Tumor (T) category of American Joint Committee Classification, the tumors (n=68) were classified as T1 (n=13, 20%), T2 (n=41, 60%), T3 (n=12, 17%), and T4 (n=2, 3%). At presentation, regional lymph node metastasis was present in 10 (15%) and systemic metastasis in 1 (2%) patient. Of the 54 patients who underwent surgical treatment, en-bloc tumor excision biopsy was done in 50 (93%), and orbital exenteration in 10 (18%) patients. Based on histopathology, the diagnoses included adenoid cystic carcinoma (n=46, 68%), lymphoma (n=11, 16%), mucoepidermoid carcinoma (n=6, 9%), pleomorphic adenocarcinoma (n=3, 5%), ductal carcinoma (n=1, 2%), and myoepithelial carcinoma (n=1, 2%). Perineural (n=30, 45%) and perivascular invasion (n=30, 45%) were noted. Over a mean follow-up period of 39 months (median, 15 months; range, <1 to 190 months), tumor recurrence was noted in 10 (15%), lymph node metastasis in 12 (18%), and systemic metastasis in 13 (20%) patients.

Conclusions: The most common primary malignant lacrimal gland neoplasm is adenoid cystic carcinoma and is associated with 15% tumor recurrence and 20% systemic metastasis.

Histopathology of enucleated retinoblastoma eyes prior intraarterial chemotherapy with focus on vascular treatment toxicity and tumour control

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Purpose: To demonstrate histopathologic features of retinoblastoma eyes enucleated after intraarterial melphalan with special focus on changes of the vascular system and the type of tumour recurrence if present.

Design: Retrospective histopathologic analysis of 11 eyes.

Method: From November 2010 to December 2015 eleven eyes were enucleated with prior intraarterial chemotherapy. Histopathological workup was done with special focus on vascular changes and the type of tumour recurrence if present.

Results: The main reasons for enucleation were poor treatment response in four cases, tumour recurrence in three cases in each group and an acute retinal necrosis in the remaining case. Histopathological evidence of ischemic atrophy was found in two eyes only, one showing a fibrosis of the central retinal artery and another one showing a perivascular inflammation. Another case should a severe scarring of the choroid. The last two cases also showed a slight vitreous bleeding.

Concerning tumour recurrence two cases showed a reactivation of a type II regression and one had multiple new tumours located in the peripheral retinal. Another three cases showed a localized infiltration of the choroid and/or a prelaminar opticus nerve invasion. So far none of our patients developed metastatic disease.

Conclusion: In our case series three eyes showed severe vascular changes following IAC making the treatment a relatively save procedure concerning vascular treatment toxicity. Nevertheless we found poor treatment response and recurrent tumours in 7 cases with a beginning optic nerve and choroidal infiltration with the potential risk to develop metastatic disease.

The Prognostic Value in Uveal Melanoma by Chromosome 3 and 8q testing is enhanced by adding AJCC staging

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Purpose: mRNA expression and chromosome status are important prognostic parameters in uveal melanoma. In addition, size is an important prognostic parameter. Size is used in the staging system of The American Joint Committee on Cancer (AJCC). We studied whether adding information on the AJCC stage enhances the prognostic value derived from knowing the chromosome 3 and 8q status.

Methods: We retrospectively studied a cohort of 522 patients, who had been treated for UM in two different centers between 1999 and 2015. The mean follow-up time was 47.7 months. Death due to UM metastases was chosen as the primary endpoint.

Results: When considering only patients with a tumor without monosomy 3 and without chromosome 8q gain, none with a stage I tumor died due to metastases, while patients with stage II and stage III showed a slightly higher incidence of UM death ($p=0.13$). When looking at tumors with either monosomy 3 or chromosome 8q gain, patients with a stage II or a stage III tumor showed a higher incidence of UM death than stage I cases ($p=0.03$). In tumors with monosomy 3 as well as chromosome 8q gain, more patients with stage III tumors died than with stage I or stage II tumors ($p<0.001$).

Conclusions: Adding information on size through the AJCC system improves the prognostic value of chromosome 3 and 8q testing. This supports the use of systems such as LUMPO that combine different prognostic factors to help provide prognostic information for individual patients, and it supports the integration of genetic information with the AJCC staging.

0107

Innovative use of intralesional interferon for chemoreduction of ocular surface tumours at first presentation

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Purpose: Ocular surface tumours require a variety of management strategies including surgical resection, radiotherapy, phototherapy, cryotherapy and topical chemotherapy. UK government cancer targets state there should be a maximum 31-day wait from the date of decision-to-treat to the first definitive treatment. Here we outline the safety and efficacy of an innovative use of intralesional interferon alpha for chemoreduction of ocular surface tumours at first presentation to Sheffield Ocular Oncology Centre.

Method: 6 patients seen in the ocular oncology clinic and clinically diagnosed with ocular surface cancers (3 squamous cell carcinomas, 2 malignant melanomas, 1 MALT lymphoma). Treatment was commenced on the same day by injecting 3 million international units (MIU) of interferon alpha into the lesion. Subsequent definitive management was also scheduled. Patients were followed up within the next 31 days for review and further treatment. Examination findings and slit lamp photographs were recorded on initial consultation and follow-up.

Results: Participants included 1 male and 5 females aged 51-86. On clinical examination and photography, 5 patients (83.3%) had reduced inflammation and size of lesion at subsequent visit. 1 patient (16.6%) had reduced inflammation but no change in size.

Conclusions: The use of adjuvant intralesional interferon injection at first presentation allows treatment to be commenced at diagnosis, thus meeting cancer targets. It aids the definitive surgical management with reduction in tumour size, improved definition of tumour margins, and reduced inflammation. We believe this improves the surgical success rate and long-term outcomes. Histopathological diagnosis of these surgically excised tumours is not altered and hence intralesional interferon can be safely used at first presentation.

A Phase II Study of Glembatumumab Vedotin for Metastatic Uveal Melanoma

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Purpose: Systemic treatment of metastatic uveal melanoma has been unsuccessful to date. Objective responses are rare, and improvement in survival even rarer. Targeted therapy, chemotherapy, and immunotherapy have been studied with little benefit. Antibody-drug conjugates (ADC) represent a way to deliver a chemotherapy payload preferentially to tumor cells. Glembatumumab vedotin (GV) is an ADC targeting the tumor protein GPNMB, which is expressed in 86% of primary uveal melanomas.

Methods: We performed a multi-center U.S. open-label, single-arm phase II study of GV in patients with metastatic uveal melanoma (NCT02363283). Patients received GV 1.9 mg/kg intravenously Day 1 of a 21-day cycle. Objective responses were measured every two cycles using RECIST 1.1. The study planned to enroll 18 patients in the first stage. If at least one objective response was noted in the first stage, an additional 14 patients would be enrolled for a total of 32 evaluable patients.

Results: In the first stage of enrollment, 17 of 18 patients went on to receive treatment. One patient demonstrated a partial response to treatment with 46% reduction in his target tumor burden in the liver, adrenal gland, and aortocaval lymph node.

Conclusions: Due to the presence of at least one objective response, the study's second stage is now open for full enrollment in the U.S. In addition to clinical responses, the study will examine impact on survival and pharmacodynamic change in GPNMB expression on metastatic tumors before and after one cycle of treatment.

0109

Exenteration and single stage repair of the orbital socket using a temporalis muscle flap in the management of ocular and eyelid tumors

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Purpose: To evaluate the outcomes of orbital exenteration and temporal muscle flap repair of the socket in the cases of ocular and eyelid malignancies

Methods: Retrospective single-center study. All the patients who underwent total orbital exenteration for a malignant tumor with temporal muscle flap repair were included. We report the oncologic outcomes and the complications of surgery

Results: 31 patients were operated using this technique between 2009 and 2016 (18 conjunctival melanomas, 3 choroidal melanomas, 7 squamous cell carcinomas, 2 sebaceous cell carcinomas and 1 basal cell carcinoma). Mean age at surgery was 71.5 years and mean follow-up time was 26.1 months. On histological analysis, tumor excision was complete in 26 patients, out of whom 3 had an orbital recurrence (3 conjunctival melanomas). 5 patients had incomplete excision of the tumor, out of whom 4 had postoperative orbital radiotherapy and no orbital recurrence occurred. Complete epithelialization of the socket was achieved in 4 to 6 weeks in all the patients except for one who had a persistent non-epithelialized area. Flap necrosis occurred in one patient after postoperative radiotherapy.

Conclusion: Following orbital exenteration, spontaneous epithelialization of the socket may take a long time. Temporal muscle flap can reduce the duration of wound healing after surgery, which allows early postoperative radiotherapy (if it is indicated). Local oncologic follow-up is done with orbital imaging. Esthetic results are acceptable using epithesis attached to glasses and local complications are rare.

0111

Fine Needle Aspiration for Suspected Ocular Metastases

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Purpose: We analyzed our experience with fine needle aspiration (FNA) for suspected ocular metastases to assess our technique's effectiveness.

Method: The study group of 30 aspirates from 28 patients with suspected ocular metastases derives from a Cleveland Clinic cytology data base computer search and a medical records review by the authors. The aspirates were prepared by the ThinPrep® (Cytoc, Marlborough, MA) method yielding at least one alcohol fixed Papanicolaou stained slide per case. One of the authors (CVB) interpreted all cytological slides and classified each sample as: positive, atypical, negative, or non-diagnostic.

Results: Interpretations included: positive (21 cases, 70%), atypical (2 cases, 7%), negative (4 cases, 13%), and non-diagnostic (3 cases, 10%). The positive cases included 17 metastases (16 carcinomas and 1 paraganglioma) and 4 uveal lymphomas. The atypical cases included 1 vitreoretinal lymphoma and 1 uveal lymphoma. The negative cases included 1 cryptococcosis, 1 inflammatory lesion, and 2 inflammatory aspirates that proved to be false negative aspirates of metastatic adenocarcinoma. The 3 non-diagnostic cases included 1 schwannoma, 1 uveal lymphoma, and 1 metastatic adenocarcinoma. FNA yielded information sufficient to treat in 24 (80%) of 30 aspirates. Six (20%) FNAs failed including 2 false negative inflammatory samples, 1 atypical (uveal lymphoma), and 3 non-diagnostic.

Conclusions: In our experience, FNA effectively confirms a clinical impression of ocular metastasis. Seventeen (85%) of 20 aspirates, from metastatic lesions, provided definitive diagnoses. Negative, but inflammatory aspirates should be interpreted with caution unless a specific cause is identified such as our case of Cryptococcosis.

0113

Long-term follow-up of a 24-month study of ranibizumab for the prevention of radiation vasculopathy

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Purpose: A pilot study of ranibizumab administered every 2 months for 2 years after proton beam irradiation in patients with small-medium choroidal melanomas near the optic nerve or fovea suggested visual benefit. Since high risk of radiation vasculopathy remains for at least 3 years after radiation, we evaluated longer-term outcomes of patients who participated in this clinical trial.

Methods: A retrospective review of 24 patients who completed the clinical trial was performed. Outcome measures included the proportion of patients with final visual acuity $\geq 20/200$, $\geq 20/40$, and the rates of radiation maculopathy/papillopathy at the last follow-up visit.

Results: Median follow-up for trial patients was 48.3 months. Nineteen patients (79.2%) had at least 3 years of follow-up; 12 patients (50%) had 4-years of follow-up. At the last follow-up visit, 54% (13/24) of ranibizumab-treated patients had visual acuity $\geq 20/40$ vs. 32% (19/59) of historical controls ($p=.054$). 83% (20/24) of treated patients had visual acuity $\geq 20/200$ vs. 59.3% (35/59) of controls ($p=.03$).

Six patients received anti-VEGF injections for radiation vasculopathy after trial completion. The proportion of patients with visual acuity of $\geq 20/200$ at the last visit was similar between patients who received subsequent treatment and those who did not (83.3%, both groups). However 66.7% of untreated patients vs. 16.7% of treated patients had acuity $\geq 20/40$ ($P=.05$)

Conclusions: The potential benefit of prophylactic ranibizumab extends for at least 1 year after discontinuation. A significant proportion of patients appear to retain good vision without continued treatment.

0114

Intraoperative monitoring of radical surgical excision of conjunctival and iris tumors

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Purpose: To estimate the value of intraoperative OCT (iOCT) imaging during surgical treatment of conjunctival and iris tumors.

Material and Methods: Surgical treatment was performed in 8 patients in the age of from 22 to 68 years. 5 patients were with conjunctival and 3 - with iris tumors. During surgery we used modern microscope Moller wedel iOCT with function of intraoperative OCT imaging.

Results: Histological analysis of excised tumors revealed that in all cases tumor's margins were clear of tumor cells that was also detected during tumor excision using iOCT.

Conclusion: Using of iOCT allows to precise the visualization of tumor's margins, to estimate the integrity of the surrounding tissues and to evaluate adapting of wound edges after plastic procedure.

0116

¹⁰⁶Ru – plaque radiotherapy for large uveal melanomas

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Purpose: To analyze the outcomes of ¹⁰⁶Ru-plaque brachytherapy for large posterior uveal melanomas.

Methods: 60 patients, 33 (55%) women and 27 (45%) men, aged from 24 to 83 years (mean – 52,4±11,9) with large UM underwent BT. Tumor thickness before BT was from 6,1 to 10 mm (mean – 7,5±1,0 mm), diameter – from 7,6 to 20 mm (mean – 13,4±2,9 mm). Second cancer was diagnosed in 4 (6,7%) patients. Mean follow up period composed 48 months (12-78 months).

Results: Local tumor control was in 57 patients. 7 (11,7%) patients underwent additional BT and 2 (3,3%) - TTT. Secondary enucleation was performed in 3 (5%) patients due to tumor regrowth and neovascular glaucoma. Metastatic disease developed in 6 (10%) patients in 18 to 39 months (mean – 24 months) after brachytherapy, one patient died of another condition.

Conclusion: Despite of using ¹⁰⁶-Ru radioactive plaques does not yield destruction doses to the tumor's apex in patients with large UM (thickness more than 6 mm), however in some cases it is possible to achieve good therapeutic effects, keep the patient eye without impairing the survival.

0119

Uveal melanoma-associated mortality within the Scottish Ocular Oncology Service

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Purpose: The Scottish Ocular Oncology Service (SOOS) manages all patients with uveal melanoma (UM) in Scotland. Our aim was to determine the long-term overall and cause-specific mortality of patients with UM, irrespective of treatment modality.

Method: A retrospective single-centre cohort study including all patients diagnosed with UM by the SOOS between 1/1/1998 and 31/12/2002. Data from the SOOS database was correlated with death records held by National Records of Scotland, accessed via the Scottish Cancer Registry (Information Services Division [ISD] Scotland), which provided the date, and all listed causes, of death for all deceased patients.

Results: 220 patients were diagnosed with UM between 1/1/1998 and 31/12/2002. 116 (52.7%) were female. The mean (median) age at diagnosis was 63 (65) years (range: 16-89).

Choroidal melanoma (n=185) (melanoma-specific) mortality was 7.5% (14.8% cancer-specific, 18.9% total) at 5 years, 12.9% (29.6%, 39.5%) at 10 years and 16.8% (40.1%, 55.1%) at 15 years.

Ciliary body melanoma (n=18) mortality was 17.5% (33.3%, 33.3%) at 5 years, 17.5% (50.0%, 50.0%) at 10 years and 17.5% (50.0%, 61.1%) at 15 years.

Iris melanoma (n=17) mortality was 0% (12.9%, 29.4%) at 5 years, 0% (12.9%, 29.4%) at 10 years and 0% (12.9%, 35.3%) at 15 years.

Conclusions: Correlation of SOOS and national records mortality data confirms 15-year melanoma-specific mortality of 16.8%, 17.5% and 0% for choroidal, ciliary body and iris melanomas respectively. This contrasts with frequently cited findings of 23.3-50% metastatic melanoma related mortality at 15 years. We can now provide accurate mortality data to our patients in Scotland.

Evaluation of the toxicity of Intravitreal carboplatin injection in a rabbit model

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Purpose: Carboplatin is widely used chemotherapy agent in the treatment of retinoblastoma via periocular, intravenous and intra-arterial delivery methods. The purpose of this study was to evaluate the toxicity of Intravitreal carboplatin injection in a rabbit model

Methods: Ten New Zealand male rabbits (1800-2000 gram) were injected with a single carboplatin intravitreal injection each, in decreasing dosage (8-3 µg)/0.1ml in one eye. The second eye was used as control.

The animals were evaluated clinically by Intraocular pressure (IOP) measurement, slit lamp examination and indirect ophthalmoscopic fundus examination, immediately post Injection, on day one, days 7,14,30 and before euthanasia (day 45).

Toxicity was evaluated using baseline and repeated (days 14,30, 45)

Electroretinogram (ERG), Optical Coherence Tomography (OCT) and Ultrasound (US) examinations.

After euthanasia the eyes were fixed and submitted for histopathological evaluation.

Results: All the eyes had normal repeated IOP, anterior segment and fundus examinations at all the examination points.

All the eyes had normal repeated OCT and US examinations at all the examination points in the study and the control eyes.

All the eyes were normal in histopathological evaluation in the study and the control eyes.

No significant ERG changes were noted under 3 and 4 µg carboplatin. ERG was decreased under 5-8 µg of intravitreal Carboplatin injections.

Conclusions: Intravitreal carboplatin injection appears to be safe in the dosage of 3-4 µg/0.1 ml in a rabbit model. Dosage of 5-8 µg/0.1 ml decreases the ERG reading but resulted in no anatomical ocular changes.

0121

The Use Of Gene Expression Profiling As An Adjunctive Measure To Guide The Management Of Indeterminate, High-Risk Posteriorly Located Choroidal Melanocytic Lesions

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Purpose: Our group has offered GEP assessment for juxtafoveal, subfoveal, and peripapillary indeterminate high risk melanocytic lesions that haven't demonstrated definitive growth to assist in making early treatment decisions. Our early experience with this algorithm is presented.

Methods: Ethics approval and informed consent were obtained and prospective databases were reviewed to co all clinical information. Our small sample size necessitated non-parametric analysis.

Results: 16 patients were included in this series. Eight (50.0%) had sub-retinal fluid and ten (62.5%) had orange pigment, 13 (81.3%) had absence of drusen, 12 (75.0%) were <3mm to the optic disc margin, and 6 (37.5%) were acoustically hollow. Six (37.5%) were class 1A, and ten (62.5%) were class 1B. Class 1A and 1B lesions had a median of 3.50 and 4 clinical risk factors, respectively ($p = 0.566$). Although a trend was noted, the difference in mean tumor height between the groups was not statistically significant (1A = 1.38mm, 1B = 2.21mm; $p = 0.128$). All class 1A patients have continued with close observation. None have shown definite growth or metastasis over a mean follow up period of 557 ± 731 days. All class 1B patients opted for plaque brachytherapy. None have developed metastasis or local treatment failure, and all are alive with a mean follow up of 742 ± 734 days (2.03 ± 2.01 years).

Conclusions: There may be a role for GEP in high risk, indeterminate, posteriorly located choroidal lesions to aide in the decision to proceed with early treatment, rather than close observation.

0122

Management of suspicious melanocytic lesions of the iris

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Purpose: To evaluate the natural history of indeterminate pigmented lesions of the iris.

Methods: We identified 260 patients evaluated at the Massachusetts Eye and Ear Infirmary for suspicious iris lesions between 2009 and 2015, and calculated rates of malignant transformation and metastasis. Melanoma-related mortality in these patients was compared to a group of patients diagnosed with iris or iridociliary melanomas originating in the iris (N=23) during the same period.

Results: Overall, median follow up was 5.7 years. Median VA at last follow-up was 20/25. Mean lesion height was 0.91 mm (0-3.5) for patients with suspicious lesions and 3.46 mm (1.2-6.5) for patients with melanomas. Thirteen (5.0%) lesions underwent malignant transformation; mean time from presentation to diagnosis was 76.4 months. These patients were treated with proton therapy using a light-field technique, and three (23.1%) developed complications (secondary glaucoma and NVG in one patient, rubeosis in one patient, and rubeosis and NVG in one patient). One patient (0.38%), followed for 98.4 months before being diagnosed with melanoma, developed metastasis 31.7 months after receiving proton therapy, and died of melanoma 1.5 months after metastasis diagnosis. Ten patients (43.5%) initially diagnosed with melanoma developed complications, including rubeosis (n=5), NVG (n=3), and secondary glaucoma (n=5). Four patients (17.4%) in the melanoma group died from malignant melanoma; time from treatment to metastasis was 26.8 months and time from metastasis to death was 1.3 months.

Conclusions: These data provide evidence that indeterminate melanocytic iris lesions have low malignant potential and that current conservative methods of follow-up are reasonable.

Superselective intra-arterial chemotherapy for retinoblastoma: first 5-year experience from two referral centers in Brazil

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Purpose: To evaluate the first 5-year experience using superselective intra-arterial chemotherapy (SIAC) for retinoblastoma in two referral centers in São Paulo-Brazil.

Method: Retrospective interventional study. From April 2011 to August 2016, 161 eyes of 138 patients with retinoblastoma were treated with SIAC as primary or secondary therapy. One to three different drugs were used (Melphalan 3,0-7,5mg; Topotecan 0,3-1,0mg; Carboplatin 20-40mg) as necessary.

Results: The mean patient age at SIAC was 26 months. Treatment was secondary in 121 eyes (75%) and primary in 40 eyes. Eyes were classified using the International Classification of Retinoblastoma before any treatment as group: A n=2(1%), B n=13(8%), C n=24(15%), D n=93(58%) and E n=29(18%). 537 infusions were performed, with a mean of three cycles per eye (median 3; range 1-10cycles). Melphalan plus topotecan and carboplatin (M+T+C) were used in 86 eyes (53%), melphalan and topotecan in 64 eyes (40%), melphalan alone in 10 eyes (6%). Intravitreal chemotherapy with M or M+T was used as adjuvant treatment in 32 eyes (20%). No eye received external beam radiotherapy. At a mean follow up of 23 months (median 19;3-67months) all patients are alive with no metastatic disease. No neurological complications were reported. 127 eyes (79%) were preserved. Important intraocular side effects found were globe ischemia n=2(1%), retinal and/or choroidal vascular ischemia n=7(4%), optic nerve ischemia n=8(5%) and persistent retinal detachment n=4 (2%).

Conclusion: The use of SIAC as primary or secondary therapy modality to treat naïve or recurrent- refractory retinoblastoma showed successfully results in our first 5-year experience.

Recovery of foveal microanatomy after intravenous or intraarterial chemotherapy for foveolar retinoblastoma: correlation with clinical features at presentation and visual outcomes in 104 eyes

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Purpose: To determine frequency for recovery of foveal microanatomy by optical coherence tomography (OCT) after intravenous or intraarterial chemotherapy (IAC) for foveolar-involving retinoblastoma.

Methods: Retrospective comparative case series including 104 eyes (90 patients) with foveolar-involving retinoblastoma and OCT determination of foveal microanatomy after treatment completion. Comparison of clinical features was performed between those with foveal recovery (FR) and those without (No FR).

Results: Overall 19 (18%) eyes had FR: 2 with complete foveal restoration to normal microanatomy, 10 with complete foveal restoration to abnormal microanatomy, and 7 with partial recovery (hemifovea) only. A comparison of clinical features (FR vs No FR) revealed significant differences in that FR demonstrated greater mean age at presentation (13 months vs 7 months, $p=0.003$), less advanced eyes (group B: 6/19 vs 6/85, $p=0.008$), and smaller mean tumor diameter (12.7mm vs 15.5mm, $p=0.026$). There was no difference regarding vitreous or subretinal seeds, extent of retinal detachment, and choice of primary therapy (IVC or IAC). Sub-analysis of visual outcome (Snellen visual acuity) in 74 eyes (FR=14, No FR=60) revealed eyes with FR showing better mean visual acuity (20/160 vs 20/400, $p=0.006$), greater number with visual acuity $\geq 20/40$ (3/14 vs 0/60, $p=0.006$), and lesser number with visual acuity $< 20/200$ (4/14 vs 41/60, $p=0.013$). Despite no FR, 32% (19/60) achieved visual acuity $\geq 20/200$.

Conclusions: Of 104 eyes with foveolar-involving retinoblastoma treated with chemotherapy, 18% demonstrated OCT-evidence of foveal microanatomic restoration, correlating significantly with better visual outcome. OCT can be useful for estimation of visual potential in preverbal children following chemotherapy for retinoblastoma.

0130

Breaching the Capsule; Biopsy in Lacrimal Gland Pleomorphic Adenomas and Risk of Recurrence

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Pleomorphic Adenomas of the lacrimal gland (LGPA) comprise approximately 20% of lacrimal masses. Whilst curable with complete surgical excision they are known to recur and potentially undergo metastatic transformation. Significant confusion exists regarding the role of biopsy in lacrimal masses that clinically & radiologically appear like LGPAs, with a causal link proposed between surgical biopsy and recurrence and metastatic change. This has resulted in a 'no-biopsy' approach to potential LGPAs. Given the invasive nature of surgical treatment and significant rate of false positive diagnosis members of the ophthalmic community have asked whether fine needle aspiration biopsy (FNAB) has a place in the management of LGPAs. We have systematically reviewed the evidence of incisional versus fine needle biopsy and the rate of LGPA recurrence and further appraise the evidence for the diagnostic accuracy of FNAB in salivary gland neoplasia. Using this information we propose a management protocol for LGPAs based on current evidence.

Benchmarking retinoblastoma service delivery: The Australasian experience

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Purpose: To report the benchmarking of retinoblastoma (Rb) management in Australasia including the development and introduction of new treatment modalities.

Methods: Collaboration with Australasian ophthalmologists identified the resources available at each centre for the provision of Rb treatment services.

Results: Six Rb treatment centres were identified across Australasia. Whilst all centres offer focal therapy, systemic therapy and plaque brachytherapy, only one centre currently offers intra-arterial chemotherapy (IAC). Interstate or international transfer of care for rescue therapy using IAC or ruthenium plaque brachytherapy is becoming increasingly more common.

Conclusions: Delivery of a comprehensive Rb treatment service including the complete suite of treatment modalities to a geographically dispersed, low-density population such as Australasia remains challenging. However, a collaborative, national approach in this geographic isolate could also provide significant opportunities for exploring longitudinal data for Rb survivors.

Retinoblastoma presenting as Preseptal and Orbital Cellulitis: A study of 80 consecutive cases

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Purpose: To discuss the clinical features and management outcomes of retinoblastoma (RB) patients presenting with preseptal or orbital cellulitis.

Method: Retrospective study of 80 consecutive patients of RB associated with preseptal or orbital cellulitis.

Results: Eighty (5%) of 1457 patients with RB presented with preseptal or orbital cellulitis. The mean age at presentation was 32 months and majority were males (n=42, 53%). Forty-five (56%) cases had unilateral RB. Solitary eyelid oedema (n=25, 31%) and eyelid oedema with leucocoria (n=25, 31%) were the most common presenting features followed by eyelid oedema with proptosis (n=22; 28%), red eye (n=7; 9%) and buphthalmos (n=1; 1%). The tumor was intraocular in 30 (38%) patients and had extraocular extension in 50 (62%). Of the 30 patients with intraocular tumor, 29 (97%) were classified as Group E by International Classification of Intraocular RB and one (3%) as Group D. Of the 50 patients with extraocular tumor extension, the tumor was classified as stage 2 (n=1, 2%), stage 3 (n=43, 86%) or stage 4 (n=6, 12%) based on International staging of RB. The primary modality of treatment was enucleation (n=17; 21%) and systemic chemotherapy (n=49; 56%), while 14 (18%) were lost to follow-up. Histopathological high-risk features were evident in 11 (65%) eyes that were primarily enucleated. At a mean follow up of 23 months, 8(10%) children died due to metastatic disease and morbidity.

Conclusions: Preseptal or orbital cellulitis is a rare presenting feature of retinoblastoma with high incidence of histopathological high-risk features and extraocular disease.

The Genetic Background of Iris Melanoma

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Purpose: Approximately 2-10% of all uveal melanomas (UM) arises in the iris. These iris melanomas are rare but account for 65-72% of all primary iris tumors. The aim of our study is to gain insight in the genetic background of iris melanomas.

Method: The genetic changes of 33 confirmed iris melanoma cases from Royal Hallamshire Hospital (Sheffield, United Kingdom), the Rotterdam Eye Hospital and Erasmus Medical Centre (Rotterdam, The Netherlands) were analyzed using next-generation sequencing (NGS). A panel of the known uveal melanoma genes including *GNAQ*, *GNA11*, *BAP1*, *SF3B1* and *EIF1AX* was used. *BAP1* immunohistochemical (IHC)-staining was performed as well.

Results: With NGS we detected for uveal melanoma a typical *GNAQ* (n=17) or *GNA11* (n=8) hotspot mutation. We also observed *EIF1AX* (n=4), *SF3B1* (n=1) and *BAP1* (n=13) mutations in our cohort. One sample contained both an *EIF1AX* and *BAP1* mutation. The *BAP1* IHC staining was negative or partially negative in 13 samples.

Conclusions: Uveal melanoma specific mutations in *GNAQ*, *GNA11*, *BAP1*, *SF3B1* and *EIF1AX* were also found in our iris melanoma cases. The frequency of these mutations in iris melanoma are lower than in uveal melanoma. We detected a *GNAQ* or *GNA11* mutation in 25 of the 33 samples. Furthermore, the genes *EIF1AX*, *SF3B1* and *BAP1* were mutated in about half of the cases and are (except one) mutually exclusive. The *BAP1* immunohistochemistry corresponds with the *BAP1* mutation analysis performed with NGS.

0135

Molecular classification of uveal melanoma subtypes using integrative mutational and whole-genome copy number analysis

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Purpose: Classification of structural and numerical chromosomal changes to elucidate the observed metastatic risk difference in uveal melanoma (UM) patients with mutually exclusive *BAP1*, *SF3B1* and *EIF1AX* mutations.

Methods: 280 UM patients from the Rotterdam Ocular Melanoma Study (ROMS) cohort were analysed. Unsupervised hierarchical clustering of genome-wide single nucleotide polymorphism (SNP) array data was used to identify molecular subclasses with distinct chromosomal patterns. Conventional karyograms were analyzed for the number and type of copy number variations (CNVs) and correlated with the different mutational statuses of UM. Results were validated using data from The Cancer Genome Atlas (TCGA).

Results: Unsupervised clustering identified five clusters with distinct copy number aberrations patterns, each of them was mainly comprised of UMs with a specific mutated gene. *BAP1*, *SF3B1* or *EIF1AX*-mutated UMs contained distinctive and specific chromosomal patterns. We show that *BAP1* negative UMs have the largest CNVs in size and *SF3B1*-mutated UMs harbored the most CNV events. Whereas *EIF1AX*-mutated UMs were characterized by the lack of CNVs. Isochromosomes occurred almost exclusively in *BAP1* negative UMs. Somatic mutation signature analyses generated different signatures for the clusters harboring mutations in either *BAP1*, *SF3B1* or *EIF1AX*.

Conclusions: UMs harboring mutations in *BAP1*, *SF3B1* or *EIF1AX* have distinct chromosomal aberration patterns that mainly differ by the affected chromosomes, the absolute number of CNVs and the type of CNVs. Mutations in these genes are strongly associated with distinct molecular subclasses. This highlights and reflects the biological difference between UMs on a genetic level.

A clinicopathological study on IgG4-related ophthalmic disease

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Purpose: IgG4-related ophthalmic disease (IgG4-ROD) basically has a good response to systemic corticosteroid; however, some cases relapse while PSL is tapered. The aim of this study is to investigate clinicopathological features of IgG4-related ophthalmic disease, and analyze the factors associated with recurrence following systemic corticosteroid administration.

Methods: Patients with IgG4-ROD underwent biopsy in the lacrimal glands. We retrospectively searched clinical features, laboratory and histological findings based on the medical records of 21 patients. We further investigated clinical and histopathological features of 15 patients who received systemic corticosteroid after biopsy. Histopathological diagnosis of IgG4-ROD was made according to the new diagnostic criteria published in 2015.

Results: The mean age was 60.7 years. Female cases were more predominant (67%). Serum IgG4 levels elevated in 95% patients. Extraorbital involvement was observed in 67%. Fourteen patients were diagnosed as definitive, and 2 and 5 patients were probable and possible, respectively. Systemic corticosteroids were administered to 15 patients after biopsy. All of the 15 patients showed remission of inflammation after treatment. Among them, 10 patients did not recur, whereas 5 patients recurred during tapering PSL. The dose of PSL when inflammation recurred was 0 mg in 4 patients, and 10 mg in 1 patient. Female gender and lymphoid follicles observed in the tissues were more likely in patients with recurrence than those without recurrence ($P < 0.05$).

Conclusions: Our study indicated that factors associated with recurrence after systemic corticosteroid administration are female cases and the presence of lymphoid follicles.

0137

Super Selective Intra-Arterial Chemotherapy In Retinoblastoma: Initial Experience From A Tertiary Care Institute Of North India

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Purpose: Retinoblastoma is the most common intraocular malignancy in children. Based on the International Grouping Classification various treatment modalities are available which include focal therapy, systemic intravenous chemotherapy, enucleation and radiotherapy. Intraarterial chemotherapy (IAC) is an emerging modality wherein chemotherapeutic agents are precisely delivered into the ophthalmic artery with the aid of interventional radiology, minimizing systemic toxicity.

Method: Retrospective and prospective analysis of six patients who presented between June 2013 to April 2016 and received intra arterial melphalan (4mg) in one eye, indicated for partially controlled tumor or those who refused enucleation. ICRB classification was used. Eyes were assessed for response of tumor mass, vitreous seeds, retinal detachment and subretinal seeds.

Results: Mean age of presentation was 16.66 months. Four underwent neoadjuvant therapy whereas two underwent primary intra-arterial chemotherapy (IAC). Five out of 6 underwent secondary IAC. Of the 6 eyes, 4 showed a favourable response and 2 underwent enucleation. Post IAC, none of the patients had any significant adverse reaction. Lid edema and chorioretinal atrophy was seen in 2 patients. Four eyes could be salvaged in (67%).

Conclusions: Our study finds that though technically challenging modality, IAC can be used for primary or secondary treatment of selected retinoblastoma eyes. It is precise and effective technique with minimal side effects.

0142

Retrospective analysis of the recurrence rate and complications associated with different topical mitomycin C regimens for the treatment of Ocular Surface Squamous Neoplasia

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Purpose: To audit the clinical safety and efficacy of a change in the cycling strategy of topical chemotherapy for ocular surface squamous neoplasia (OSSN)

Methods: 127 histologically proven cornea/conjunctival intraepithelial neoplasia (CIN) within clinical OSSN lesions underwent topical chemotherapy with 3 cycles of G. Mitomycin C 0.04% either for (Group 1) 3 weeks consecutively (Group 2) One week on-one week off (Group 3) one month on and one month off. Follow up was for up to 5 years

Results: 30% were graded as severe (Squamous carcinoma/Carcinoma in situ or high grade CIN). 70% of patients were in group 1, 10% in group 2 and 20% in group 3. Overall recurrence rates were 3% in group 1, 16% in group 2 and 11% in group 3. Recurrence rates for OSSN lesions with high and low CIN were not significantly different but more common in those with low CIN in group 3.

Conclusions: Significant differences in OSSN recurrence and other ocular side effects occurred between different treatment regimens. Increasing time between cycles of topical MMC was inversely related to ocular complications associated with the drug and directly proportional to the recurrence rate of OSSN clinically. Longer treatment cycling and lower grade of CIN appeared to carry the highest rate of clinical recurrence of OSSN and warrants further more rigorous investigation

Telephone (early) versus examination (late) disclosure of prognostic uveal melanoma Results: Associations with anxiety and depression

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Purpose: Molecular prognostic testing of the primary tumor predicts survival in uveal melanoma patients. Patients are typically informed of their prognostic test results by their ocular surgeon at a follow up appointment 4-6 weeks after surgery. Discussing prognostic results can be psychologically challenging, may decrease effectiveness of treatment planning, be time consuming and difficult for both surgeon and patient. We sought to demonstrate the benefit of prognostic test result disclosure by telephone from a medical professional, trained in counselling and genetics prior to surgical follow up appointment.

Method: A prospective study of anxiety levels, duration of anxiety and duration of follow up appointment were examined in two cohorts of patients. The first cohort (telephone cohort @ 3-4 weeks) included patients who had prognostic test results reviewed by telephone prior to their first follow up appointment. The second cohort (examination cohort @ 4-6 weeks) included patients who had not reviewed results of their prognostic test prior to their first follow up appointment. Anxiety and depression were measured using the Hospital Anxiety & Depression scale in both cohorts before and after each appointment. Duration of each appointment was measured.

Results: We found improvement in anxiety levels when prognostic results were delivered earlier with a genetic counselor compared to anxiety levels when results were given at follow-up appointment. Clinical follow up was shorter and could focus on post-operative clinical outcomes.

Conclusions: Delivering prognostic results by telephone prior to post-surgical follow up examination may improve anxiety levels in patients and improve patient satisfaction.

Correlation of COMS-based size categorization and gene expression profile (GEP) sub-classifications in uveal melanoma: a multi-center study

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Purpose: To study the relationship of clinical features and Collaborative Ocular Melanoma Study (COMS)-based size categorization of gene expression profile (GEP) sub-classifications in a multi-center cohort of uveal melanoma (UM) patients.

Methods: A retrospective, multi-center study was undertaken with patients entered from 9 major ocular oncology centers from across the United States. 379 ligible patients had UM and underwent I-125 plaque brachytherapy with concurrent tumor biopsy with GEP testing between January 1, 2010 and October 28, 2014.

Results: GEP class divided the cohort into three groups: Class 1a (n=186), Class 1b (n=77) and Class 2 (n=113). Class 2 tumors had a significantly larger baseline tumor height ($p<0.001$) and basal diameter ($p<0.001$) and were more likely to have ciliary body involvement ($p=0.007$) and exudative retinal detachment ($p<0.001$). Class 1a tumor patients, compared to Class 1b, were significantly older ($p=0.034$). Class 2 tumors, when compared to Class 1b, were associated with increasing patient age ($p<0.001$), larger tumor height ($p=0.010$), ciliary body involvement ($p=0.001$), exudative RD ($p=0.024$), and anterior tumor location ($p<0.001$). When the tumors were grouped by COMS size categories, increasing tumor size category was significantly associated with Class 2 status: 19% of Small tumors, 33% of Medium tumors and 46% of Large tumors were Class 2 ($p=0.009$).

Conclusions: This is the first report to detail differences in clinical features between GEP sub-classes. When the tumors were grouped by size category, the distribution of the GEP sub-classes among the size groups was similar to reported time-to-metastasis data among the same size groupings.

Using droplet digital polymerase chain reaction (ddPCR) to confirm and validate copy number variants (CNVs) and low level mosaic single nucleotide variants (SNV) identified from *RB1* next generation sequencing (NGS)

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Purpose: NGS is a rapid and effective way to identify pathogenic variants in the *RB1* gene, including low level mosaic SNVs and CNVs. At present, given a moderate NGS error rate, it is important that all potentially pathogenic variants are confirmed by an orthogonal method. Here we present the utilization of ddPCR as a tool for confirmation and validation of low level mosaic SNVs and CNVs detected by NGS.

Method: The *RB1* gene coding sequence, flanking intronic regions and core promoter region were target captured using custom designed biotinylated DNA probes for hybridization and sequenced using the Illumina HiSeq4000. Sequencing data was aligned to the human genome reference (Hg19) and variant calling using customized bioinformatics. For ddPCR, dual-labeled locked nucleic acid (LNA) PrimeTime probes targeting the promoter region and each individual exon of *RB1* were designed for copy number analysis. For SNV validation, LNA probe pairs targeting the normal and variant allele were designed for each specific SNV. ddPCR reaction mix were partitioned by QX200 Droplet Generator, and analyzed individually on the Bio-Rad QX200 system.

Results: For this study, a total of 15 retinoblastoma patients identified by our targeted NGS panel to have either a mosaic SNV (range: 0.9-20%) or a CNV (ranging: 1 exon to full gene) were assessed by ddPCR. All previously identified changes were confirmed by ddPCR with confidence intervals well beyond NGS capacity.

Conclusions: ddPCR is a highly sensitive and reproducible method to confirm and validate *RB1* low level mosaic SNVs and CNVs detected by NGS.

0152

Novel laser photocoagulation of ocular surface squamous neoplasia

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Introduction: Ocular surface dysplastic squamous epithelial (OSSN) is a spectrum of disease involving abnormal cellular growth. Estimated OSSN prevalence is estimated <0.2 to 35 cases per million per year. Conjunctival intraepithelial neoplasia (CIN) and squamous cell carcinoma (SCC) are the most common benign and malignant conjunctival respectively.

Purpose: To evaluate the safety and short term result of a novel argon laser photocoagulation based treatment for OSSN.

Method: Patients with clinical diagnosis of ranging from conjunctival intraepithelial neoplasia (CIN) to squamous cell carcinoma (SCC) were recruited. Eleven were selected and underwent complete ophthalmologic exam including anterior segment photography, impression cytology and anterior optical coherence tomography (OCT). After topical anesthesia and toluidine blue 1% were instilled on the eye argon laser was applied to the lesion and surrounding conjunctiva with a 2mm margin. Patients were examined weekly with retreatment for lesions that were still present on biomicroscopy.

Results: Ten out of 11 lesions responded to treatment, with nine (81.8%) patients presented complete response after one to four laser treatments. One patient was treated with interferon despite major improvement and one patient submitted to surgery due to lack of response. Procedures were well tolerated with adverse effects including mild discomfort up to two days after treatment.

Conclusion: The argon laser photocoagulation of ocular surface squamous neoplasia to be a safe and effective treatment. Further studies with longer follow-up are necessary to confirm our findings.

0153

Radiation maculopathy and optic neuropathy risk associated to baseline clinical features of uveal melanoma prior to I-125 plaque brachytherapy

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Purpose: To determine the risk associated with development of radiation maculopathy and optic neuropathy after plaque brachytherapy for treatment of uveal melanoma.

Methods and Materials: All patients with primary uveal melanoma treated with iodine-125 plaque brachytherapy between August 1996 and December 2011 were included in the study. The primary endpoint was development of either radiation maculopathy or radiation optic neuropathy. Factors analyzed included age, gender, tumor size (largest basal dimension and apical height), tumor location, and brachytherapy plaque shape/size. Median follow-up time was 28 months (0 - 175.2 months). Univariate and multivariate Cox proportional hazards were used to associate clinical features at baseline to the risk of development of radiation maculopathy or optic neuropathy.

Results: The study included 551 eyes from subjects with uveal melanoma treated with brachytherapy. 41% (226) of subjects developed either radiation maculopathy or optic neuropathy. By univariate and multivariate Cox proportional analysis, increased tumor distance from the optic disc margin was found to be protective against the development of either radiation maculopathy or radiation optic neuropathy.

Conclusions: Shorter distance of the tumor margin to the optic disc is the most significant clinical predictor of radiation maculopathy and optic neuropathy following I-125 plaque brachytherapy for uveal melanoma.

Ultra Low Dose Radiation (4Gy) for Orbital and Ocular Adnexal Lymphoma

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Introduction: Ocular adnexal lymphomas (OAL) are historically treated with radiation doses ranging from 20-40 Gy, which are associated with ocular toxicity including dry eye, cataracts, and rarely radiation retinopathy. We report response and toxicity associated with "ultra-low" dose (4 Gy) radiotherapy (RT) for orbital and ocular adnexal lymphoma.

Methods: All consecutive patients with OAL low-grade B-cell lymphoma or mantle cell lymphoma treated with "ultra-low" dose (4 Gy in 2 daily fractions) orbital radiotherapy between 2013 and 2015 were included. Patients were retrospectively assessed at 2-4 month intervals after RT to assess response. Ocular toxicity was assessed using CTCAE v4.03 criteria.

Results: 22 patients had a median age of 64.5 years. 14 patients had mucosa associated lymphoid tissue (MALT) (64%), 5 patients had follicular lymphoma (23%), and 2 patients had mantle cell lymphoma (9%). 15 patients (68%) had stage IE disease; bilateral orbital disease was designated as stage IE. 7 patients (32%) had stage IV. The overall response rate was 100% [complete response in 86% (n=19) and partial response in 14% (n=3)]. With a median follow up of 15.2 months, only 1 patient experienced local relapse and 1 other patient developed contralateral orbital recurrence. Ocular toxicity was limited to one patient with grade 1 dry eye.

Conclusions: "Ultra-low" dose radiotherapy for OAL is associated with high response rates and minimal ocular toxicity. It is less expensive and associated with shorter duration of treatment. A prospective clinical trial using this treatment strategy is currently under way at our institution.

Ruthenium-106 Brachytherapy in the Treatment of Circumscribed Choroidal Hemangioma

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Purpose: To examine the efficacy and safety of Ruthenium-106 plaque radiotherapy in the treatment of circumscribed choroidal hemangioma.

Methods: Twenty-one eyes of twenty-one patients diagnosed with symptomatic circumscribed choroidal hemangioma who underwent Ruthenium-106 plaque radiotherapy were included in the study. Clinical response, ancillary tests findings improvement, and major side effects were evaluated.

Results: From the initial to the one-year follow-up visits, vision improved in 12 eyes (57.1%), was stable in 7 eyes (33.3%), and became worse in 2 eyes (9.5%). Based on fluorescein angiography and optical coherence tomography, subretinal fluid and cystoid macular edema resolved in all patients. Changes in LogMAR visual acuity ($P = 0.038$); tumor thickness ($P = 0.0001$) and largest diameter ($P = 0.007$) on ultrasonography; and subfoveal thickness on optical coherence tomography ($P < 0.0001$) were statistically significant between the initial and the one-year follow-up visits. Side effects as observed during the follow-up period included: radiation-related retinopathy in 5 (23.8%) eyes, radiation-related papillopathy in 1 (4.76%) eye, and subretinal fibrosis in 2 (9.5%) eyes. Subretinal fibrosis was the only permanent radiation-related side effect.

Conclusions: Ruthenium-106 plaque radiotherapy is an effective method of treatment for symptomatic circumscribed choroidal hemangiomas, with a low associated rate of permanent radiation-related side effects.

0159

Comparison of posterior lamellar resection versus non-posterior lamellar resection for localized tarsal conjunctival sebaceous carcinoma in 54 cases

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Purpose: Comparison of outcomes of localized tarsal conjunctival sebaceous carcinoma following posterior lamellar resection (PLR) versus (vs) non-posterior lamellar resection (non-PLR).

Methods: Retrospective, comparative, interventional case series of patients with tarsal conjunctival sebaceous carcinoma managed either by PLR or non-PLR.

Results: The mean age at presentation of PLR (n=26) and non-PLR (n=28) was 70 and 72 years, respectively. Patients managed by PLR had more extensive tissue involvement by the tumor as compared to those managed by non-PLR, with a greater mean tumor diameter (21 mm vs 12 mm, $p = 0.004$) and mean clock hours involvement (4 and 2, $p = 0.009$). For patients managed by PLR, each patient required only 1 surgery for complete tumor excision. Non-PLR treatment included excision biopsy plus cryotherapy (n = 14, 50%), wedge resection plus cryotherapy (n = 10, 36%), cryotherapy only (n = 3, 11%), and plaque radiotherapy (n = 1, 3%). At the final follow-up, the final mean visual acuity was better for the PLR group (20/50 vs 20/80, $p = 0.009$). Also the need for eventual orbital exenteration for tumor control was higher in the non-PLR group ($P = 0.029$). The number of patients who had positive lymph node metastasis was also higher in the non-PLR group ($P = 0.023$). A borderline significant difference between the groups was also noted for systemic metastasis, with non-PLR group having a higher systemic metastasis ($P = 0.052$).

Conclusions: PLR appears superior to LE in achieving local and systemic tumor control for localized tarsal conjunctival sebaceous carcinoma.

0160

Ophthalmic Screening of Children at Risk for Retinoblastoma: Consensus Statement from the American Association of Ophthalmic Oncologists and Pathologists (AAOOP)

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Purpose: To provide a set of surveillance guidelines for children at risk for development of retinoblastoma.

Method: A consensus group was chosen from members of the American Association of Ophthalmic Oncologists and Pathologists (AAOOP) with support from the American Academy of Pediatric Ophthalmology and Strabismus (AAPOS). The panel included representative ophthalmic oncologists, pathologists and geneticists from retinoblastoma referral centers located in various geographic locations with a variety of screening approaches for retinoblastoma. Patient "at risk" was defined as a person with family history of retinoblastoma in parent, sibling, or relative.

Results: Consensus statement from panel: 1. Dedicated ophthalmic screening is recommended for all children at risk for retinoblastoma above the population risk. 2. Frequency of examinations are adjusted based upon expected risk for RB1 mutation. 3. Genetic counseling and testing clarifies the risk for retinoblastoma in children with a family history of the disease. 4. Examination schedules are stratified based on high, intermediate and low risk children. 5. Children at high risk for retinoblastoma require more frequent screening which may preferentially be examinations under anesthesia (EUA).

Conclusions: Risk stratification with genetic counseling serves as the basis for screening of children at elevated risk for development of retinoblastoma.

Retinoblastoma in Thailand: Report from tertiary referral center

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Purpose: To report demographic data, clinical classification, and treatment outcome of retinoblastoma patients in Ramathibodi Hospital, Bangkok, Thailand.

Methods: Retrospective cases series.

Results: There were 69 eyes of 46 patients with retinoblastoma. Of 46 patients, 32 were treatment naive, and 14 had previous treatment. Twenty patients (43.5%) were male. The mean age at diagnosis was 12.2 months (range, 1 to 40 months). Twenty-three patients (50%) had bilateral retinoblastoma. Only one patient (2.2%) had familial retinoblastoma. Of 69 eyes, extraocular retinoblastoma was found in 4 eyes (5.8%). Of 65 eyes with intraocular retinoblastoma, the eyes were classified as International Classification of Retinoblastoma group A (n = 1, 1.5%), group B (n = 12, 18.5%), group C (n = 4, 6.2%), group D (n = 12, 18.5%), and group E (n = 36, 55.4%). Our treatment modalities included systemic chemotherapy, intraarterial chemotherapy (IAC), Ruthenium-106 plaque brachytherapy, external beam radiotherapy, cryotherapy, transpupillary thermotherapy, subtenon chemotherapy and intravitreal chemotherapy. At the mean follow up period of 44.9 months (range, 2.6 to 114.9 months), the overall globe salvage rate of intraocular retinoblastoma was 46.2%, with the globe salvage rate of 100% in ICRB group A and B, 75% in group C, 66.7% in group D, and 16.7% in group E. The overall survival rate was 95.7%. Two patients passed away due to brain metastasis and febrile neutropenia.

Conclusions: Treatment of retinoblastoma is challenging. With recent advanced treatment modalities available at our center, globe salvage is more promising. However, enucleation still required to save the patients life in advanced retinoblastoma.

Orbital Extra-medullary Granulocytic Sarcoma (Chloroma)

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Purpose: To document clinic-pathological features, immunohistochemical features, treatment and outcomes in patients with biopsy proven Orbital Extra-medullary Granulocytic Sarcoma (OEMGS).

Method: Retrospective review of a series of 10 patients diagnosed with OEMGS between February 2013 to September 2016.

Results: The study included 6 male and 4 female patients. The mean age at presentation was 12.3 + 10.0 (range, 5-33) years. Majority of the patients presented with rapidly progressive proptosis (90%). Initial clinical diagnosis was granulocytic sarcoma in 4 patients only. All patients underwent incisional biopsy. Myeloperoxidase, CD34, CD117 were positive in all cases and Ki-67 ranged from 40% to 70%. All patients had concomitant haematological malignancy, FAB AML-M2 in 6, and AML-M4 in 2. Disseminated disease was present in 2 patients. All patients were advised daunorubicin and cytarabine based chemotherapy for AML, including a two-part induction phase to achieve complete remission and a consolidation phase for maintenance (2 patients refused treatment). The mean follow up was 6.4 + 5.1 months (range, 7 days -18 months). Two patients had complete remission, 2 had partial remission, and 6 succumbed to the disease.

Conclusions: Granulocytic sarcoma is an uncommon and aggressive malignancy. It is a diagnostic challenge especially in patients with no prior history of hematologic malignancy, and who report to an ophthalmologist first. High index of suspicion in a child with acute proptosis, early diagnosis and prompt management confers better survival prognosis.

Rabbit Model of Intra-arterial Chemotherapy: Technique, Vascular Variations, Pharmacokinetics, and Toxicities

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Purpose: To describe a novel rabbit model of intra-arterial chemotherapy (IAC), determine anatomic variations in ocular blood supply, and determine the pharmacokinetics, tissue drug levels, and systemic and ocular toxicities of IAC melphalan.

Methods: Ocular vascular supply was determined angiographically in 79 eyes of 47 3.0kg-New Zealand white rabbits. The dominant ophthalmic artery (OA) of each eye was selectively catheterized. Melphalan 0.4mg/mL (up to 1.2mg/kg) was infused in pulsatile fashion. For pharmacokinetic studies, 18 rabbits were sacrificed at serial time-points. Retina, bilateral vitreous, and blood were collected.. Toxicity was assessed by fluorescein angiography, electroretinography, and histopathology, prior to and 5-weeks post-treatment. Complete blood counts were obtained weekly.

Results: The OA was successfully catheterized for 79/79(100%) eyes in 47/47(100%) rabbits. Melphalan was delivered successfully in 31/31(100%) eyes. External OA-dominant vascular variation was present in >75% of eyes. In treated eyes, maximum melphalan concentration (C_{max}) in retina was 4.95 μ M (30-minutes post-infusion) vitreous C_{max} was 2.24 μ M (1-hour), and areas-under-the-curve ($AUC_{0\rightarrow\infty}$) were 5.26 μ M*hr for retina and 4.19 μ M*hr for vitreous. Peripheral blood C_{max} was 1.04 μ M. Drug half-life was ~1 hour. Treated eye vitreous C_{max} was >100-fold higher, and $AUC_{0\rightarrow\infty}$ was ~50-fold higher, than untreated eye. No angiographic or histopathologic evidence of vascular occlusion, emboli, or retinal damage were seen, even with 1.2mg/kg melphalan. Electroretinographic reductions were not seen. With 0.8-1.2mg/kg melphalan, transient neutropenia occurred at 1-week.

Conclusions: This is the first small animal model of IAC. IAC melphalan delivery in rabbits leads to excellent ocular penetration and pharmacokinetics, without significant ocular, vascular, or systemic toxicities.

Case Series of Primary Orbital Sarcomas

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Purpose: To describe a case series of primary orbital sarcomas diagnosed between 2008 and 2016.

Methods: Retrospective review of case records.

Results: 1) A 24-year-old female with a history of treated metastatic alveolar rhabdomyosarcoma and posterior fossa meningioma was diagnosed with orbital low-grade spindle cell sarcoma. This was excised with globe preservation. Twenty-seven months post-surgery she has no residual disease, recurrence or metastasis. 2) A 45-year-old male with orbital spindle cell sarcoma extending intracranially was treated with exenteration, tumour resection and radiotherapy with curative intent. Recurrence was noted five months post-surgery. 3) A 50-year-old female with a recurrent liposarcoma underwent exenteration with clear margins & radiotherapy. Flap necrosis and fistula formation complicated post-operative recovery. Six months post-op she remains disease free and awaits a prosthesis. 4) A 50-year-old male presented with a history of left sphenoidal meningioma and childhood bilateral retinoblastoma treated with right enucleation and orbital radiation. He was diagnosed with left orbital rhabdomyosarcoma and underwent chemoradiotherapy and globe sparing tumour resection. Residual sinus and dural disease necessitated extensive surgery. Orbital recurrences were treated with palliative chemoradiation and the patient died of pulmonary metastasis. 5) A 61-year-old male with a recurrent malignant solitary fibrous tumour was treated with exenteration and radiotherapy. Residual disease was present at the orbital apex and the patient succumbed to the disease.

Conclusions: Post-irradiation sarcomas form a high proportion of our cases. Primary orbital sarcoma is a rare disease entity with a high risk of recurrence and death despite extensive surgery.

High-risk Histopathologic Features in RB: Analysis of 876 Primarily Enucleated Eyes from Beijing Tongren Hospital

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Purpose: To determine the true prevalence of high-risk histopathologic features present in the primarily enucleated eyeballs of the patients with advanced RB diagnosed in Beijing Tongren Hospital.

Method: Retrospective histopathologic analysis of 876 primarily enucleated eyes for advanced retinoblastoma during a 10-year period.

Results: Of 876 primarily enucleated eyes, high-risk histopathologic features were identified in 36.4%. Overall, retrolaminar optic nerve invasion was found in 77.9%, massive choroid invasion in 13.5%, and anterior segment invasion in 8.6%. Extraocular invasion was found in 3.8%. Of intraocular tumor invasion, 81.3% had 1 and 18.7% had at least 2 high-risk histopathologic features.

Conclusions: In our population, high-risk histopathologic features are present in a relatively higher percent of RB eyes. Since only primarily enucleated eyes were included, the distribution of high-risk histopathologic features in advanced retinoblastoma in China could be truly and objectively reflected.

0175

Simple Treatment for Circumscribed Choroidal Hemangioma

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Purpose: To share our results of 15 years experience treating circumscribed choroidal hemangiomas with transpupillary thermotherapy (TTT) with infrared láser.

Method: One to three sessions of infrared diode laser with 3 mm beam diameter for 60 seconds used at threshold power, looking for just a slight whitening in the last few seconds, applied away from the macula over the tumor.

Results: Complete reabsorption of the serous detachment in all of the relatively recent cases, with little response in older cases.

Conclusions: TTT for circumscribed choroidal hemangiomas was describes years ago, but the use of Photodynamic Therapy (PDT) was considered a better option by a majority of specialists. Now that Verteporfin is unavailable in most countries, we should consider TTT as a very good and inexpensive option.

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0179

Rabbit model of indirect photodynamic therapy for retinoblastoma

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Purpose: This study used the combination of the indirect ophthalmoscope laser delivery system and the 690 nm wavelength diode laser to perform photodynamic therapy (PDT) in a rabbit model.

Methods: The first phase of the study treated six rabbits with the Indirect PDT system, using a 690 nm laser unit delivered through a 810nm Indirect ophthalmoscope. Four rabbits received intravenous Verteporfin at doses of 0.43 or 0.86 mg/kg, and two rabbits did not receive Verteporfin (controls). The second phase of the study involved a retinoblastoma xenograft in 8 rabbit eyes, with six rabbit eyes being treated with the Indirect PDT system.

Results: There were a total of 20 laser treatments performed in the right eyes of 6 rabbits. In the 4 rabbits that received Verteporfin, focal retinal scars were noted at 40 mW/cm² while thermal burns were created in the 2 controls at 75 mW/cm².

Histopathology showed focal retino-choroidal scars at the site of PDT treatment without evidence of generalized ocular damage. The retinoblastoma xenografts in the rabbit eyes showed excellent growth, as demonstrated on Retcam photographs and histopathology.

Conclusions: The results demonstrate that Verteporfin can be activated in the rabbit retina with the indirect delivery system (i.e Indirect PDT). PDT was confirmed at 40-50 mW/cm², and fundoscopic and histopathologic examination showed circumscribed areas of retinal damage and a lack of ocular toxicity. The xenograft model of retinoblastoma in the rabbit eye provided additional evidence that indirect PDT may represent a new method to treat intraocular retinoblastoma.

Transpupillary Thermotherapy for Treatment of Tumor Edge Recurrence of Choroidal Melanoma post Brachytherapy

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Purpose: To report the efficacy and complications of Transpupillary Thermotherapy (TTT) in treating tumor edge recurrence of choroidal melanoma previously treated with ¹²⁵Iodine brachytherapy.

Method: Retrospective review of consecutive choroidal melanoma patients that were treated with TTT for tumor edge recurrence after plaque radiotherapy. All patients were treated with 810 nm infrared diode laser, spots of 3 mm diameter. The interval between treatment sessions was 4-6 weeks for the first 3 sessions; additional sessions were added according to the treatment response and treatment sessions were ceased when chorioretinal scarring developed.

Results: Twenty two patients met the inclusion criteria. Mean follow-up was 33 (6-59) months following the last TTT session. Mean thickness of the treated recurrent tumour edge was 2.1 (0.6- 2.6) mm; mean diameter was 4.2 (1.2- 5.9) mm. Mean power was 650 (450- 800) mW, mean duration was 70 (60-90) seconds. The mean number of sessions per patient was 4 (2-7) sessions, and the mean interval between sessions was 5 (4- 9) weeks. Tumor regrowth control was achievable in 12 (54%) eyes. Treatment complications included, petechial hemorrhages in 12 (75%) patients, and branch vascular occlusion in 4 (25%). No patient developed laser-induced retinal tears.

Treatment failure was associated with tumor thickness > 1.9, amelanotic lesion, and presence of subretinal fluid.

Conclusions: Transpupillary thermotherapy may be a useful treatment for selected tumor margin recurrence of choroidal melanoma post brachytherapy. The control rate is comparable to those reported for TTT as a primary treatment for small choroidal melanoma.

0183

Long-term results following intraocular surgery in unsuspected retinoblastoma eyes

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Purpose: To evaluate clinical long term results with a main focus on patient management, metastatic disease and overall survival after vitrectomy in unsuspected retinoblastoma eyes.

Method: Retrospective, noncomparative case series.

Results: We report on 8 patients referred to a national referral center after pars plana vitrectomy in unsuspected retinoblastoma (from 1992 to 2016). The main preoperative diagnosis included unilateral inflammation in 3 cases, vitreous bleeding after minor trauma in another 3 cases and retinal detachment with PFV and Coats' disease in the remaining 2 cases. The mean patient age was 4 years (14 months to 6.5 years). The mean interval between vitrectomy and referral was 15 days. All patients were affected unilaterally. Histopathological examination showed an infiltration of the vitrectomy ports in 2 eyes. Treatment consisted of enucleation and systemic chemotherapy of 4 to 6 cycles in all 8 cases. 6 out of 8 patients were treated with adjuvant radiotherapy including EBRT and proton beam irradiation. Of the 8 patients none experienced an orbital recurrence or metastatic disease during a mean follow up of 6.9 years.

Conclusions: Retinoblastoma may present as masquerade syndrome and vitreoretinal surgeons not trained in ocular oncology may mistake retinoblastoma as benign conditions like Coats' disease or endophthalmitis. If this happens aggressive treatment with enucleation, systemic chemotherapy and / or radiotherapy is the treatment of choice to prevent systemic tumor dissemination but results in severe systemic and orbital morbidity.

0184

Asymmetric loading of Iodine-125 radioactive plaques in the treatment of uveal melanoma

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Purpose: To report the indications and treatment efficacy of asymmetrically loaded episcleral plaques with variable energy Iodine-125 radioactive seeds for treatment of uveal melanoma.

Methods: A retrospective review of the brachytherapy database and medical charts of consecutive uveal melanoma patients treated with asymmetrically loaded I-125 plaques. Deeply-notched asymmetrically loaded plaques and patients treated with adjuvant laser thermotherapy were excluded. Patients were included between January 2010 and August 2016. Kaplan–Meier estimates were used to determine tumor control rates. Rates of complications were calculated using the cumulative incidence approach.

Result: Inclusion criteria were met in 124 uveal melanoma patients, mean follow up was 24 (12- 78) month. Indications for asymmetric plaque loading were: Juxtapapillary location (69%), small posterior tumours (16%), iris melanoma (9%), and irregular tumor profile (6%). Tumour control rate was 100% in irregular tumour profile melanoma, iris melanoma. Control rate was 98 % in small posteriorly located melanoma, and 92% in juxtapapillary melanoma.

Conclusions: Asymmetric loading of I-125 plaques permits manipulation of radiation dose distribution to provide superior radiation coverage for uveal melanomas in specific locations or have irregular configuration.

0189

Population cluster in uveal melanoma

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Purpose: to describe a possible population cluster in uveal melanoma.

Methods: there were 11 patients diagnosed with uveal melanoma who had some relationship with Huntersville, NC.

Results: 11 patients were diagnosed with uveal melanoma between 2006 and 2016; 7 were residents of Huntersville, NC, 3 were employed in this town and 1 was retired in the same town. Of these, 3 went to the same high school. From the 11 patients, 5 females were diagnosed at age of 20 years, 22, 24, 30 and 31 years, which represents earlier than average 55 year-old patients diagnosed with uveal melanoma.

Conclusions: Collaboration between ocular oncologist centers and tumor registry are necessary to better evaluate environmental causes of uveal melanoma.

0190

Uveal Melanoma Recurrence, Treatment and Outcomes

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Purpose: Review of treatments and outcomes of patients with uveal melanoma that received treatment and recurred locally.

Methods: Consecutive choroidal melanomas that had local recurrence following treatment were evaluated for treatment type, success of recurrence treatment, vision, and rate of metastasis. Recurrence was defined as persistent, progressive documented growth of the previously treated lesion.

Results: Forty patients were found to have local recurrence following standard treatment of uveal melanoma (plaque or proton beam). 53%(21) of patients were male, mean age was 59 years, all patients were Caucasian. Tumors were stage I (43%*n*=17), IIa (40%*n*=16), IIb (15% *n*=6), IIIb (2.5% *n*=1). AJCC classification was T1a (43%*n*=17), T1b (2.5% *n*=1), T2a (38% *n*=15) T3a (15% *n*=6), T3b (2.5% *n*=1). Mean time to recurrence was 3.4 (0.5-10) years following treatment, 28%(11) patients developed metastasis within a mean follow up of 3.4 (0-7.7) years from recurrence. Metastasis was seen 18% in the T1a group, and 55% in the T2a group. 66%(28) of eyes were salvaged with local treatment, (repeat radiation, or laser). Vision of 20/40 or better was preserved in 22% of patients at last follow up.

Conclusions: Local control of tumor recurrence can be achieved without enucleation in some cases. Recurrence of tumors following primary treatment may be associated with a higher rate of metastasis.

Treatment Outcomes of Focal Laser Consolidation during Chemoreduction for Group B Retinoblastoma

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Purpose: To evaluate the ocular treatment outcomes of focal laser consolidation during systemic chemoreduction for Group B tumors located in the posterior fundus.

Methods: Retrospective chart review of patients diagnosed with Group B retinoblastoma in the posterior fundus over a 20-year period. Primary outcome measures were: 1) change in the tumor size with treatment 2) association of the timing of laser consolidation to the horizontal and vertical diameters of the final chorioretinal scar.

Results: From 1995 to 2016, 40 Group B eyes (22 right eyes and 18 left eyes) were included in the analysis. The mean age at diagnosis was 6.4 months. Of the 40 eyes, 35 were treated with systemic chemotherapy and laser, 4 were managed with chemotherapy only. The mean number of laser session given over the course of treatment was 6. The overall globe salvage rate was 95%. The median reduction in the diameters of the tumors treated with chemoreduction and laser from diagnosis to the final visit was 13%. For tumors receiving chemotherapy prior to laser therapy, the median reduction in tumor area was 18%. Small tumors were found to have a 52% increase in size while larger tumors demonstrated a 37% decrease.

Conclusions: The size of the chorioretinal scar at the end of treatment was on average 13% smaller than the original tumor size, with greater reductions being noted when chemotherapy preceded laser treatment, and when the tumor size at diagnosis was greater than 4.5mm. A small subset of perifoveal lesions was treated successfully with chemotherapy alone.

0199

Genetic mutation analysis of retinoblastoma tumor cells and its relation with previous treatment

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Purpose: To analyze genetic mutations of retinoblastoma tumor cells and its relation with clinical data such as previous treatment.

Method: DNA was extracted from fresh frozen tissue (25 cases) or formalin-fixed paraffin-embedded samples (25 cases) enucleated in our hospital. Genetic mutations were analyzed using target sequencing technique with Illumina MiSeq® system and NCC oncopanel, which can detect 90 gene mutations including *RB1*. Clinical data were collected from medical chart, and divided into two subgroups: 24 cases had received no previous treatment (primary enucleation group), and 26 had received eye-preservation treatment before enucleation (secondary enucleation group).

Results: *RB1* gene mutation was detected in 40 cases, and one other case had *MYCN* amplification without *RB1* mutation. *NOTCH2*, *EP300*, and *CREBBP2* mutations were detected in more than two cases. In primary enucleation group (n=24), *RB1* mutation was detected in 17: 6 cases had only *RB1* mutation, and other had one or two other gene mutations. In secondary enucleation group (n=26), *RB1* mutation was detected in 23: 9 cases had only *RB1* mutation, and other had one to 21 gene mutations. 6 cases had more than three mutations. There was no relation between specific treatment such as radiotherapy or chemotherapy and specific mutation.

Conclusions: Many gene mutations were detected, but those differed respectively. Some tumors had specific gene mutations which may be candidate for targeted therapy. Some tumors in secondary enucleation group had many mutations, which may reflect genetic instability by *RB1* mutation.

0201

Endoresection technique and outcomes in the management of posterior choroidal melanoma

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Purpose: To evaluate the efficacy and safety of endoresection for recurrent posterior choroidal melanoma

Methods: Retrospective nonrandomised interventional case series. All patients who had pars plana vitrectomy and endoresection for choroidal melanoma at The Royal Victorian Eye and Ear hospital between August 2008 - August 2014 were included. All patients had previous brachytherapy. All patients had initial reduction in tumour size following brachytherapy with subsequent recurrence.

Surgery: All patients underwent small gauge vitrectomy (23 or 25 gauge) plus laser and/ or cryopexy and gas or oil tamponade.

Main outcome measures: Enucleation rate, local recurrence, post-operative surgical complications, metastasis, mortality

Results: Mean follow up time was 22 months. Range 7-72 months

Pre-op visual acuity (VA) ranged from 6/12-HM, Post-op VA range 6/15- HM

Visual outcomes: 1/7 VA improved, 1/7 patient VA reduced, 5/7 unchanged

Time from plaque treatment to endoresection surgery median: 42 months, range 19-96 months

Tamponade: Gas 6/7 patients, 1/7 silicone oil

No patients had evidence of recurrence in the post-operative observation period.

No patients required enucleation following surgery.

There was no reported metastasis. There were no deaths.

Post-op complications: 1 patient developed a post-operative retinal detachment following removal of silicone oil.

Conclusions: Endoresection of high posterior choroidal melanomas was not associated with a higher risk of metastasis, death or local recurrence than other reported techniques used to treat similar melanomas.

0205

Stereotactic Radiosurgery in the Management of Ocular Surface Tumours Invading into the Anterior Orbit

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Purpose: To identify the safety and efficacy of stereotactic radiosurgery in treating complex ocular surface tumours invading into the anterior orbit.

Method: Five patients with ocular surface squamous cancers invading into the anterior orbit were treated with stereotactic radiosurgery as the primary treatment after debulking/biopsy procedure.

Results: Follow up confirmed that tumour clearance was achieved clinically as well as radiologically at upto two years follow up with no systemic metastasis.

Conclusions: Ocular surface tumours rarely invade the anterior orbit. Management of these is complex as surgical clearance is difficult to achieve due to tumour invasion into the important structures of the socket. Exenteration surgery is quite often required. External beam Radiotherapy itself can be done as sight and socket saving procedure but carries a high risk of visual problems and socket and ocular surface complications. We used stereotactic radiosurgery successfully to treat the anterior orbital invasion from ocular surface tumours as a sight and globe saving procedure. Stereotactic radiosurgery can be used safely and effectively as a management strategy for complex ocular surface tumours invading into the anterior orbit and as an alternative to exenteration or external beam radiation surgery.

Brachytherapy for Diffuse Choroidal Hemangioma Exudative Retinal Detachment

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Purpose: Diffuse choroidal hemangioma is a rare, benign vascular eye tumor that usually presents as part of Sturge Weber syndrome. The tumor is clinically ill defined, with indistinct margins, and blends subtly with the choroid. Associated exudative retinal detachment is a reversible complication with management. Brachytherapy has potential advantages over external beam radiation therapy. Differentiating between the tumor and surrounding subretinal fluid for better target delineation is important for good outcome of this approach. There are few reports of method and outcome of brachytherapy for diffuse choroidal hemangioma.

Methods: We report our brachytherapy experience in a patient with diffuse choroidal hemangioma exudative retinal detachment. The report includes clinical and diagnostic studies features, imaging considerations in treatment planning for improved target delineation, the use of Eye Physics' plaque simulator software (Eye Physic, LLC, Los Alamitos, CA), and a review of the literature of brachytherapy for diffuse choroidal hemanagioma.

Results: Subretinal fluid in the macula improved within a month. Exudative retinal detachment completely resolved within six months.

Conclusions: Brachytherapy is a practical approach to treat exudative detachment from diffuse choroidal hemangioma. MR imaging to differentiate a tumor from surrounding subretinal fluid would optimize treatment planning.

0210

BAP1 germline mutations in Finnish uveal melanoma patients with and without family history

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Purpose: Germline pathogenic variants of BRCA-1 associated protein-1 (BAP1) gene predispose to uveal melanoma (UM) and other cancers, especially cutaneous melanoma, mesothelioma, and renal cell carcinoma. We report the frequency of such *BAP1* variants in consecutive Finnish UM patients with and without family history of UM.

Method: In Finland, UM is treated centrally in the Helsinki University Hospital. We collected genomic DNA from 284 of 417 consecutive patients diagnosed from January 2010 to June 2016. This included 10 patients with a family history of UM. The exons and exon-intron junctions of *BAP1* were sequenced. Copy number variants were excluded with MLPA in familial cases.

Results: We found a pathogenic germline *BAP1* variant, a T-insertion in exon 14 in three patients, each with 1-2 relatives with UM. The families also had other *BAP1*-related cancers, and probably share an unidentified ancestor. Three of the 7 patients affected with UM were younger than 40 years. We found another probably pathogenic variant, a donor splice site mutation in a conserved region after exon 2 in 57- and 65-year-old males, not known to be related. The former had relatives with other *BAP1*-related cancers, however. The frequency of germline mutations with and without a family history of UM was 30% (3/10) and 0.7% (1/137; 95% CI 0.1 to 2.6), respectively

Conclusions: The frequency of *BAP1* germline pathogenic variants in Finnish UM patients without family history was low. A family history of typical *BAP1*-related cancers was informative and should routinely be obtained to guide *BAP1* genetic testing.

Methods of regional chemotherapy, depending on the anatomical variants of the blood supply to the eye, at the selective ophthalmic arterial infusion (SOAI) at children with the intraocular retinoblastoma

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Purpose: describing of methodology of a SOAI in treatment of children with an intraocular retinoblastoma and demonstrating the various ways of alkylating agent delivery to a tumor.

Materials and Methods: 211 SOAI procedures to 95 children (103 eyes) have been performed from 2011 to 2016. 2 methods of a SOAI were applied: the microcatheter technique - superselective catheterization of an eye artery or collateral branches of an ECA at blood flow hemodynamic redistribution; the micro-balloon technique.

Results: technical success was 95,2% (201 procedures). From 175 procedures with using of a microcatheter infusion was carried out in: a. ophthalmica – 123 (70%), a.meningea media – 29 (17%), a.infraorbitalis – 20 (11%), a. temp. superficialis – 2 (1,2%), a.facialis – 1 (0,8%). From 28 procedures with using of micro-balloon 26 were successful. We didn't manage to put a balloon more distally than the place of an entry of an eye artery in 2 cases. Unsuccessful attempts – 10 cases: failure of catheterization of a femoral artery – in 2, a kinking/koyling of the ICA – in 2, a vascular collapse as a result of reaction to contrast agent and/or mechanical impact on ICA – in 2, lack of contrasting of a retina – in 3, an occlusion of an ICA – in 1.

Conclusions: possession and use of various techniques for alkylating agent delivery to an eye tumor allows to achieve the maximum effect and doesn't depend on anatomy options and blood flow hemodynamic redistribution in the main vessels of an eye.

0212

OCT angiography evaluation of peripapillary vessel density following brachytherapy for uveal melanoma

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Purpose: To study peripapillary retinal capillary circulation using OCT angiography (OCTA) in eyes treated with brachytherapy for uveal melanoma.

Methods: Cross-sectional study of 20 subjects treated with I-125 plaque radiotherapy one to nine years prior to imaging with OCTA. Patients were prescribed 85Gy to the tumor apex over 100 hours using I-125 plaque brachytherapy.

Peripapillary retinal capillary circulation was measured by Angio Vue OCTA (Optovue Avanti RTVue XR) in both eyes using 4.5x4.5 mm optic disc scans. The peripapillary vessel density (PPVD) was calculated for the inner retina (inner limiting membrane to outer plexiform layer) in treated eyes and compared to fellow eyes. The relationship of the PPVD to the calculated dose to the optic nerve was evaluated.

Results: No significant difference was seen between PPVD in eyes with tumor and the fellow eye prior to radiation. Following treatment, the PPVD as measured by OCTA was significantly lower in treated eyes (58.0% +/- 22.6%) than in fellow eyes which did not receive radiation (73.9% +/-12.6%, $p = 0.002$). There was a correlation between radiation dose (D50, the dose to 50% of the disc) and the PPVD (Spearman nonparametric test; $\rho = -0.474$, $P = 0.041$).

Conclusions: Radiation optic neuropathy is a significant cause of morbidity in patients undergoing brachytherapy for uveal melanoma. OCTA provides a measure of the capillary changes following radiation, and may serve as a quantitative endpoint to address visual prognosis in individual patients. Study of a larger series of patients is warranted to further evaluate OCTA as a clinically significant endpoint.

0215

Intravitreal anti-VEGF enables globe salvage in retinoblastoma eyes developing secondary neovascularization

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Purpose: Primary and secondary neovascularization in retinoblastoma is considered an indication for enucleation. We investigated the use of anti-VEGF therapy in secondary vasoproliferative disease for globe salvage.

Method: Retrospective review of consecutive retinoblastoma patients with progression of proliferative retinopathy and/or rubeosis iridis despite cryo-phot- ablation of the ischemic retina, or inability to perform cryo-ablation due to hematovitreous and/or retinal detachment. Anterior and posterior segment was monitored under anesthesia by photography and fluorescein angiography, and intravitreal anti-VEGF administered using the safety-enhanced technique.

Results: From August 2008 to May 2016, 34 patients (36 eyes) with advanced retinoblastoma were included, 15 eyes following radiotherapy and 21 without radiotherapy. In the radiotherapy group all received systemic chemotherapy (IVC), 6 additional intra-arterial chemotherapy (IAC). In the group without radiotherapy, 17 received IVC with sequential IAC, one IVC alone, three IAC alone. Vasoproliferative complications were classified as: rubeosis with/without localized retinal neovascularization or extended fibro-vascular membrane. 64 injections were administered: 20 eyes with one injection; 16 eyes with multiple injections. 13/36 eyes were enucleated, 8 for progressive disease, of which 3 had intermediate histopathologic risk factors and received adjuvant chemotherapy. All patients are alive without metastases.

Conclusions: IAC is identified as a novel risk factor for secondary neovascularization related to ischemic retinopathy with/without retinal detachment. In our series, anti-VEGF enabled 23 (63.8%) eyes to be salvaged, by providing the conditions to continue conservative treatment, i.e. angiography-directed therapy of any ischemic retinopathy, subsequent retinal detachment surgery as necessary, and continued tumor-related management.

0217

Primary Photodynamic Therapy with Verteporfin for Small Pigmented Posterior Pole Choroidal Melanoma

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Purpose: To investigate the outcomes of primary photodynamic therapy (PDT) with verteporfin for small pigmented posterior pole choroidal melanoma.

Methods: Fifteen patients diagnosed with small, pigmented posterior pole choroidal melanoma were treated with 3 sessions of PDT with verteporfin. Risk factors for treatment failure were assessed and outcome measures at presentation, including subretinal fluid (SRF), vision and tumour dimensions, were compared to those at last follow-up visit.

Results: Tumour control was achieved in 12 (80%) patients with a median follow-up of 15 months (mean 14, range 8-18). Three patients failed treatment, diagnosed in a median time of 5 months (mean 4, range 3-6) after first PDT session. All failed cases were 100% pigmented, de-novo melanoma and showed a radial growth pattern rather than increased thickness. For the entire cohort, SRF was significantly reduced ($p < 0.001$), logMAR vision did not deteriorate ($p = 0.11$), and even improved significantly in a sub-analysis of patients with subfoveal SRF at presentation ($p = 0.018$), and tumour height significantly decreased ($p = 0.037$). No ocular or systemic complications were recorded after PDT or during follow-up.

Conclusions: Primary PDT was found to be a safe and efficient treatment modality for small, pigmented posterior pole choroidal melanoma, achieving short-term tumour control in 80% of patients. PDT resulted with significant reduction in SRF and tumour thickness. PDT with verteporfin offers patients the opportunity to preserve vision by avoiding radiation retinopathy/retinal ischaemia associated with conventional radiation treatments choroidal melanoma

Carrier risk for parents of children with non-familial retinoblastoma

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Purpose: The parents of children with non-familial retinoblastoma are concerned about the possibility that their other children are at risk to also develop retinoblastoma. We set out to find evidence for risk that parents could be carriers, from data on families of probands with defined RB1 gene mutations.

Method: The reports of genetic testing of parents of bilaterally and unilaterally affected probands carrying known RB1 mutations were reviewed. The mutations were characterized as "null" (no expected gene function) or reduced penetrance (published, predicted protein, promoter mutations) or mosaic in the parent.

Results: In 339 families with non-familial retinoblastoma, both parents or one parent found to be a carrier, were tested for the RB1 mutation of their child with retinoblastoma. Of parents of bilateral probands, 18/256 (7%) were found to be unaffected carriers of the RB1 mutation; 7/18 were mosaic for the RB1 mutation; 9/18 had a reduced penetrance mutations; and 2/18 had null mutations. Of parents of unilateral probands 16/83 (19%) were unaffected carriers; 3/16 were mosaic; 13/16 had a reduced penetrance mutations.

Conclusions: Overall risk for a parent of a child with retinoblastoma to be an unaffected carrier is 10%. However the risk is higher for unilateral probands, frequently with reduced penetrance mutations. A higher proportion of carrier parents of bilateral probands are mosaic: future offspring are at lower risk of inheriting the mutation, but if they do, are at risk for early bilateral disease.

0223

Minimal invasive biopsies with 27G vitrector in uveal melanoma advantages/inconvenient

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Purpose: in the era of conservative management of uveal melanoma there is less tumoral material available for researches. FNAB provide sufficient material for prognostication whatever the technique used but no tissue for tumor banking. Only the biggest enucleated tumors are tumor banking that not represents the panel of uveal melanomas.

Methods: A movie will show you the technique of UM biopsy using minimal invasive 27G vitrector during clip positioning that provides either sufficient DNA material for prognostication using a-CGH and a carrot of tumor for bank.

Results: This technique is successful for prognostication in 98% of the cases, for sampling the tumor in 75% of cases. Inconvenient are the increase of surgical time and vitreous hemorrhage, generally moderate, but requiring additional surgery in 15% of cases. We didn't observe severe complications (retinal detachment, endophthalmitis or seeding in the sclerotomies) to date. However we need more follow-up to be sure of this procedure safety.

Conclusions: This minimal invasive biopsy technique seems efficient for prognostication and tumor banking and was implemented for H2020 European grant project in order to obtain in our tumor bank UM and metastasis of the same patients for patient treated conservatively.

Neoadjuvant Cryotherapy for Periocular Sebaceous Carcinoma

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Purpose: To report the effective use of neoadjuvant cryotherapy in the treatment of periocular sebaceous carcinoma.

Methods: A retrospective case review of 4 patients with periocular sebaceous carcinoma in whom neoadjuvant cryotherapy applied at the time of treatment-staging map biopsies led to resolution of the lesion. The clinical, radiologic, histopathologic and surgical information from each case is reviewed.

Results: Mean age of the 3 reviewed cases was 76 (range 70-86) and all patients were women. Initial diagnosis was made by incisional biopsy in all 4 cases. Lesions ranged in size from 6.5 -14 mm. In all 3 cases, neoadjuvant cryotherapy administered at the time of treatment-staging mapping led to clinical resolution of the initial sebaceous carcinoma. Resolution of each lesion was confirmed histopathologically by repeat excision/biopsy. (Figure 1 and 2) Mean follow-up was 22 months (range 12-30), during which time there were no recurrences.

Conclusions: Neoadjuvant cryotherapy at the time of treatment-staging map biopsies can be of benefit in reducing tumor burden and improving tumor margins in periocular sebaceous carcinoma. This offers a new application of a well-established treatment modality in the management of this challenging disease.

0227

Ruthenium 106 (¹⁰⁶Ru) Plaque Brachytherapy in the Management of Ocular Surface Squamous Neoplasia (OSSN) with Scleral Invasion

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Purpose: Outcome of OSSN with scleral invasion managed by Ruthenium 106 (¹⁰⁶Ru) plaque brachytherapy.

Methods: This retrospective case series included 44 eyes with OSSN with scleral invasion managed by ¹⁰⁶Ru plaque brachytherapy. Plaque brachytherapy was used as an adjuvant therapy for residual tumor (excision base involvement on histopathology) or as primary or secondary treatment for OSSN with scleral invasion. Outcome measures were tumor regression, eye salvage, vision salvage and metastasis.

Results: Mean age was 48+4 years. Mean tumor diameter was 8.5 (range 4.0-18.0) mm and treated height was 2.4 (range 1.5-3.0) mm. Mean prescribed radiation dose was 5624 (range 4896-6736) cGy. Mean duration of follow-up was 24 (12-48) months. Forty (91%) eyes had complete tumor regression with eye and vision salvage. Four (10%) with local tumor recurrence were managed by extended enucleation (n=3) or orbital exenteration (n=1). None had metastasis.

Conclusions: ¹⁰⁶Ru plaque brachytherapy is safe and effective in the management of OSSN with scleral invasion.

Leaky Choroidal Nevi: A Clinical, Imaging and Therapeutic Analysis

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Purpose: To evaluate the clinical and imaging features as well as treatment offered to patients with Leaky Choroidal Nevi and their outcome.

Methods: The charts of patients with a choroidal nevus crossing the temporal arcades inwards and showing leakage on OCT were reviewed. We analyzed the clinical features, findings on ancillary tests (OCT, Color Fundus Picture, Fluorescein Angiography and Eye Ultrasound) and treatment methods used.

Results: Throughout the review of almost 12 years, 17 patients with the above diagnosis presented loss of at least one logMAR line in 57.14% of the cases; improvement in 28.57%, and stability in 14.29%. By Posterior Segment US, an increase of both mean tumor thickness and largest base was of 0.8mm. SRF was the most common finding on OCT. All lesions that required treatment received intravitreal Bevacizumab, with a mean number of injections of 5.41. 25% of these patients presented VA improvement. Although PDT was reserved as a 2-4 line of treatment, 3 out of 4 patients treated with this modality had an anatomical improvement and 1 out of 4 with a functional improvement. Intravitreal Ranibizumab, Focal LASER and TTT were also used.

Conclusions: Leaky Choroidal Nevi is a term proposed for borderline, suspicious lesions with deleterious effects on visual acuity. A short trial of Bevacizumab can be warranted initially and consolidated by PDT if needed. Close follow-up is suggested due to its morbidity and the risk of conversion to Choroidal Melanoma.

Clinical and genetic features of retinoblastoma

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Purpose: To show clinical-genetics peculiarities of RB in the Russian population.

Method: The study evaluates cohort of 393 Russian children from 351 families who were examined, treated and observed at a single center between 1994 and 2013 and who were referred for genetic evaluation. Molecular-genetic analysis was conducted for 75 patients and 137 their relatives. Peripheral blood was evaluated for *RB1* mutations, DNA typically extracted from white blood cells.

Results: RB patients with hereditary predisposition revealed at 44% patients. The second primary tumors were accounting for 3,1 % RB children. It is interesting that patients with unilateral RB have congenital malformations more frequently (4.6%) compared to bilateral RB (3.2%). Germline pathogenic variant of *RB1* among children with bilateral RB were found in 85% and with unilateral - in 14%. The most common germline mutations of *RB1* gene in patients were: a missense, nonsense, insertion, deletions variants. Children with nonsense, insertions and large deletions had significantly hard clinical picture of disease (bilateral, multifocal retinal lesion, early-onset RB, appearing new focus RB in spite of organ-saving therapy). Families harboring missense and site splice mutations in *RB1* shown a low-penetrance with reduced expressivity of the disease (unit foci of tumor, late clinical manifestation).

Conclusion: The patients with germline mutation in the *RB1* gene showed genotype-phenotype correlation. Some families with *RB1* pathogenic variants may be with reduced expressivity and incomplete penetrance. Therefore, genetic testing for *RB1* mutation should be offered to all patients, their first-degree relatives, including the unilateral cases.

0039

Evaluation of syk protein expression in treated versus untreated retinoblastoma

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Purpose: Spleen Tyrosine Kinase (SYK) is a proto-oncogene that is not related to normal eye development, but was found to be highly expressed in retinoblastoma. We studied SYK expression in retinoblastoma in relation to histopathologic high risk factors (HRF) while exploring the possible effects of chemotherapy on SYK expression.

Methods: Immunohistochemical staining of sections of paraffin embedded retinoblastoma tissue was carried out. The immuno-histochemical reaction for SYK was semi-quantitatively graded as: score 1+ (<1/3 tumor cells stained), 2+ (>1/3 but <2/3 of tumor cells stained) and score 3+ (>2/3 of tumor cells stained). Detailed study of histopathologic HRF in relation to SYK expression as well as difference in SYK expression between treated and untreated cases were statistically analyzed.

Results: Cytoplasmic expression of SYK was detected in 100% of retinoblastomas while sparing the native non-tumorous retina. No statistical relation between SYK expression and any of the histopathologic HRF (degree of differentiation, nerve invasion, choroidal invasion, necrosis) was detected. Further, there was no statistically significant difference in SYK expression between treated and untreated cases.

Conclusions: Expression of SYK in all retinoblastoma cases makes it a promising target for therapy. SYK expression was not correlated with any pathologic HRF. Systemic chemotherapy did not affect SYK expression.

0040

Meningioma and melanoma in patients with Turner syndrome

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Purpose: to highlight the increased risk of uveal melanoma and meningioma in Turner syndrome.

Methods: We report 2 cases: one with an uveal melanoma, one with sphenoidmeningioma and conducted a literature search.

Results: A 43 years old female with Turner syndrome was enucleated because of a large uveal melanoma. Genetic analyses showed anomalies in chromosome 8. A literature study did not revealed any overlap with the 45X/46 XY, partial /complete Turner syndrome.

A study of 3425 Turner patients revealed an increased risk for eye/orbital tumors (standard incidence ratio 10.5 and cerebral meningioma (SD ratio of 12.0(1), confirmed by Pier.(2).

Female 2 presented with bilaterally multiple meningiomas(middle fossa, parasellar, sphenoid). Neurosurgery was performed in 1994 and 2007 with irradiation. The Left Eye was blind, and the RE was deteriorating. Neither steroids nor Nolvadex did stop the progression. Since the tumor was positive for progesterone receptors, we suggested a progesterone antagonist. Unfortunately, complex surgery was performed after which the patient deceased.

Turner patients require live long hormonal replacement starting in early puberty,with estrogens and progesterone's. Growth of meningiomas can be induced by female hormones, and Turner patients have more melanocytic nevi.

Conclusions: Turner syndrome could be associated with an increased risk of melanoma and meningiomas. Whether their live-long hormonal substitution might be a causal factor, still remains to be determined. Regular ophthalmic check-up is necessary. If progression of the tumor is detected, multidisciplinary approach is mandatory.

1) Schoemaker M.J. Lancet oncology 2008,9-239

2).Pier D.P Eur j Gen 2014,57.269-274

0085

Uveal Melanoma: 5 Year Update on Incidence, Treatment, and Survival (SEER 1973-2013)

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Purpose: To analyze trends in incidence, treatment, and survival of uveal melanoma in the United States from 1973 to 2013.

Method: Systematic review of existing databases from the Surveillance, Epidemiology, and End Results Program in the United States from 1973 to 2013. Patients with primary uveal melanoma were identified using International Classification of Disease for Oncology codes including: C69.3 [choroid], C69.4 [ciliary body and iris], and C69.2 [retina]. Age-adjusted incidence, treatment, and 5-year relative survival trends were calculated using chi-square testing and 95% confidence intervals (CI). Age-adjusted incidence, treatment (surgery or radiation), and 5-year relative survival were analyzed.

Results: There were 4,999 patients with uveal melanoma identified. The majority (97.8%) were reported by hospital inpatient/outpatient clinics. Histopathologic confirmation was available in 67.8%. The mean age-adjusted incidence of uveal melanoma in the United States was 5.2 per million (5.0 -5.4; 95% CI). There was a decline in the percentage of patients treated with surgery alone (94.2% from 1973-1975 versus 24.7% from 2012-2013). A corresponding increase was observed in radiation as primary treatment (1.3% from 1973-1975 versus 68.3% from 2012-2013). No change in age-adjusted incidence (1973-2013) or 5-year relative survival (80.9%) was observed (1973 to 2008). When incidence was standardized for race, a small but statistically significant ($p < 0.05$) annual percentage change of 0.5% was detected in Whites alone.

Conclusions: The overall age-adjusted incidence of uveal melanoma (5.2 per million) has remained stable from 1973 to 2013. Despite a shift towards globe-preserving treatment, there has not been a concomitant improvement in survival.

Superselective intra-arterial chemotherapy for group D Retinoblastoma eyes

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Purpose: To evaluate the experience using superselective intra-arterial chemotherapy (SIAC) for retinoblastoma group D eyes in two referral centers in São Paulo-Brazil.

Method: Retrospective interventional study. From April 2011 to August 2016, 93 eyes of 87 patients with retinoblastoma Group D were treated with SIAC as primary or secondary therapy. One to three different drugs were used (Melphalan 3,0-7,5mg; Topotecan 0,3-1,0mg; Carboplatin 20-40mg) as necessary. Adjuvant therapy was used as needed to consolidate treatment.

Results: The mean patient age at SIAC was 24 months (median 17; range 7-119 months). The treatment was secondary in 67 eyes (72%) and primary in 26 eyes. 334 infusions were performed, with a mean of three cycles per eye (median 3; range 1-8 cycles). Melphalan plus topotecan and carboplatin (M+T+C) were used in 45 eyes (48%), melphalan and topotecan (M+T) in 43 eyes (46%), melphalan (M) alone in 4 eyes (4%) and topotecan and carboplatin in one eye. Intravitreal chemotherapy with M or M+T was used as adjuvant treatment for vitreous disease in 23 eyes (25%); in 11% of naïve retinoblastoma eyes and in 30% of rescue eyes. No eye received external beam radiotherapy. At a mean follow up of 25 months (range 3-64 months) all patients are alive with no metastatic disease, extra-ocular extension or secondary leukemia. No neurological complications were reported. 76 eyes (82%) were preserved.

Conclusions: The use of SIAC as primary or secondary therapy modality to treat group D eyes showed successfully results.

Selective Ophthalmic Arterial Injection Therapy for Refractory Retinoblastoma: A Two-Year Single-Center Study in China

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Purpose: To evaluate the effectiveness and complications of using selective ophthalmic arterial injection (SOAI) therapy for advanced refractory retinoblastoma (RB) in a large single-center cohort.

Method: From January 2009 to April 2011, 84 eyes of 62 consecutive patients with advanced refractory RB who received SOAI were included in the study. These patients failed to respond adequately to a standard systemic chemotherapy with or without local therapy. Clinical outcomes and complications of these patients were reviewed.

Results: All of the patients received SOAI of melphalan (5 mg) combined with carboplatin (20 mg). SOAI was successful in 189 procedures for 84 eyes. There were 36 eyes in Group D and 48 eyes in Group E according to the International Intraocular Retinoblastoma Classification. Each eye received between two and four SOAI treatment cycles. The mean follow-up period was 13.6 months after initial SOAI (ranging from 3 to 28 months). The rate of eye preservation was 41.67% in Group D and 20.83% in Group E of this study. Short-term ocular adverse events included eyelid edema, bulbar conjunctiva congestion and excessive tearing. Long-term complications included vitreous hemorrhage (n = 7, 8%), subretinal hemorrhage (n = 9, 11%), retinal vasculopathy (n = 6, 7%), and ophthalmic artery spasm with reperfusion (n = 11, 13%).

Conclusions: SOAI effectively saved eyes of retinoblastoma in group D and E which have failed in systemic chemotherapy and were destined for enucleation. The ocular and systemic toxicity of SOAI was within tolerance.

UM Cure 2020 - A Consortium of European experts in Uveal Melanoma to identify new therapies for patients with metastatic disease

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Purpose: Uveal melanoma (UM) is a rare intraocular tumour, with metastatic spread in up to 50% of patients, most often in the liver. Therapeutic options for metastatic patients are very limited, and little is known about the metastatic disease.

In UM Cure 2020, funded by European Union's Horizon 2020 programme, we will identify and validate at the preclinical level novel therapeutic approaches for the treatment of UM metastases (www.uncure2020.org). The Consortium comprises major EU experts in clinical, translational and basic research on UM, as well as patient representatives and innovative biotech companies.

Method: An ambitious multidisciplinary approach is proposed to move from patient tissue characterisation to preclinical evaluation of single drugs or combinations. We will characterise the genetic landscape of metastases and their microenvironment, perform proteomic studies to address signalling pathway deregulation and establish novel relevant in vitro and in vivo UM models. Underpinning this will be our virtual sample registry, linking existing biobanks into a harmonised network, which will prospectively collect primary and metastatic UM samples.

Results: In parallel, we are already evaluating in the first phase of the project the efficacy of a series of active compounds using partners' available models. In addition to the initiation of UM-dedicated clinical trials, dissemination of results includes initiatives to increase patient information and disease awareness, in particular by supporting the formation of a European UM patient network.

Conclusions: The UM Cure 2020 Consortium holds great potential to make significant advances in the treatment of metastatic UM, at present an incurable disease.

Management of Bilateral Retinoblastoma in the Intrarterial Era at MSKCC (2011-2016)

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Purpose: This study investigates the present day treatment of bilateral retinoblastoma at our institution over the past five years when both radiation and systemic chemotherapy have been replaced by intrarterial chemotherapy.

Methods: This study investigated 106 eyes of 53 patients with bilateral retinoblastoma who were naïve to treatment and managed at MSKCC between Sept 2011 and 2016. The outcomes measures of ocular survival, disease-free survival, metastatic disease and second cancers were analyzed with Kaplan-Meier estimates.

Results: 64% of patients were female and 23% of patients had a positive family history of retinoblastoma. The median age at diagnosis was 5 months, and the median follow-up was 34 months. 91% (48 of 53) patients received ophthalmic artery chemosurgery as primary treatment. The 2-year disease-free survival was 84.9% (95%CI 75.8-90.8). Of the 15 eyes necessitating additional treatment (11 for recurrence and 4 for persistent disease), 12 (80%) were treated with a second course of OAC. Nine eyes were enucleated as primary treatment, and among the remaining 97 eyes, the 2-year ocular survival was 97.7% (95%CI 85.2-99.4). There were no disease or treatment-related deaths.

Conclusions: In the present day at our institution, the majority of naïve patients are primarily treated with ophthalmic artery chemosurgery. Furthermore, the majority of patients with recurrent or persistent disease are treated with a second course of ophthalmic artery chemosurgery. This treatment paradigm results in ocular survival rates that surpass all historical numbers and has not resulted in an increase in disease or treatment-related deaths.

Magnetic resonance imaging features of the optic nerve in retinoblastoma patients after enucleation

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Purpose: The aim of this 8-year retrospective review was to determine the role of gadolinium-enhanced magnetic resonance imaging (MRI) in the assessment of the optic nerve in retinoblastoma patients after enucleation.

Methods: A total of 88 patients underwent 90 enucleations for retinoblastoma between January 2008 and December 2015, and 50 patients had post-enucleation scans available for review. The primary outcome measures were contrast enhancement along the cut end of the optic nerve after enucleation, abnormal optic nerve thickening, presence of orbital disease and/or trilateral retinoblastoma. Tumor extension into the optic nerve on histopathology was also assessed and categorized as pre- or post-laminar invasion.

Results: Overall, 41 out of 50 eyes (82%) of enucleated patients demonstrated post-operative contrast enhancement along the cut end of the optic nerve following enucleation at a mean interval of 10 months. Of these, 20 demonstrated mild enhancement and 7 moderate; the severity of enhancement wasn't graded for the remaining 14 patients. Post-enucleation optic nerve enhancement did not correlate with either chemotherapy administration or the presence of optic nerve invasion on histopathology. None of these patients were found to have subsequent orbital or metastatic disease at an average follow-up of 10 months (range 2 - 65).

Conclusions: Optic nerve contrast enhancement on follow up MRI post-enucleation for retinoblastoma is a common finding and appears to be consistent with normal post-surgical granulation tissue. The presence of post-enucleation enhancement did not correlate with pre-operative chemotherapy or the presence of optic nerve invasion on histopathology.

0202

Choroidal Melanoma metastatizing 19 years from the first diagnosis and EBR treatment and 14 years after enucleation for two metachronous tumors on the opposite side of primary site

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Purpose: Case report. Male 36 y.o. with a peripheral Choroidal Melanoma in his LE with secondary RD was treated by EBR. Good response to treatment but radiation side effects that did not prevent to examine the entire fundus. In 2002 two amelanotic choroidal masses were discovered in the opposite eye side of the affected eye. Enucleation was performed and general work-up excluded metastatic disease. In 2004 on echography and then on CT, some cysts appeared in the liver. Metastatic disease was excluded. At abdomen ultrasonographic control early (this year) 2016 one new mass was seen between liver and stomach. As abdomen NMR could not rule out GIST, a mass biopsy was performed. It confirmed liver metastasis so immune therapy was tried with no success. The patient died in three months.

Results: Metachronous CM is a rare event, three items only are cited in a .pubmed search. One paper cites three cases of out 139 patients. Late onset metastases are also known to occur and, in the long run, half of the patients are reported to die for metastatic disease

Comments: The age at diagnosis is considered a risk factor for late metastases and although promising immune therapy does not always succeed in prolonging the survival time as in this case.

In Vivo Confocal Microscopic Study With Histopathologic Correlation in intraepithelial conjunctival neoplasia

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Purpose: To describe the features and correlation between confocal microscopy and histopathology in the evaluation of suspected corneoconjunctival epithelial tumors.

Methods: Data and charts of 35 patients evaluated in Ocular Oncology Unit at Italian Hospital of Buenos Aires were analyzed in a retrospective study. Study patients with atypical-appearing non pigmented lesions underwent imaging by Confocal Microscopy performed with HRT II Rostock Cornea Module. Cases included primary lesions and possible recurrent and/or previously treated lesions. In 20 patients Confocal Microscopy and excisional biopsy were performed and included in the study to evaluate correlation. Features suggestive of epithelial malignant tumors in Confocal Microscopy were analyzed and compared with pathology features and in the patients who underwent topical treatment with chemotherapy we also evaluated follow up.

Results: Confocal microscopy and histopathology interpretations were highly concordant. The main outcome measures were confocal features and we evaluated sensitivity, specificity compared with the reference gold standard of pathology. The most important feature was the replacement of the normal corneal epithelium by large, irregular and pleomorphic, highly reflective epithelial cells with a sharp transition between normal and abnormal epithelium, consistent with neoplastic cells.

Conclusions: Cornea and conjunctival intraepithelial neoplasia is a low grade malignancy with high recurrence rate. Confocal microscopy provides excellent sensitivity for detecting atypical cells and highly correlates with histologic features. It is also useful to plan surgery treatment and to monitorate treatment after topical chemotherapeutic medication.

0209

Topical 5 Fluorouracil 0.5% for Ocular Surface Squamous Neoplasia: an study of efficacy and safety of treatment in Brazil

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Purpose: Evaluate the efficacy and safety of topical 5-FU 0.5% as a primary treatment for OSSN.

Methods: Retrospective study. Charts reviewed from August 2015 to November 2016 at the Department of Ophthalmology of University of Sao Paulo (FMUSP). Main outcome: complete resolution of the tumor and recurrence rate. Inclusion criteria: primary or recurrent OSSN, minimum of 2 months of follow-up, age \geq 18 years-old (yo). Exclusion criteria: invasive intraocular or orbital tumors.

Results: 27 patients were identified. Eighteen were included. Twelve were male. The mean age was 62 yo (range 21-87 yo). Fourteen had Conjunctival Intraepithelial Neoplasia (CIN), 10 primary/ 4 recurrent, and 4 Squamous Cell Carcinoma (SCC), 2 primary/ 2 recurrent. The TNM staging was: 14 TisN0M0, 1 T1N0M0, and T2N0M0. The mean follow up : 8 months (range 3-14 mo). Associated diseases: 5 immunosuppressed (1 HIV, 3 liver and/or kidney transplant, 1 systemic lymphoma) and 1 with Xeroderma Pigmentosum. Topical 5 - FU 0.5% was used 4 qid, in cycles of 7 or 14 consecutive days with 7 to 14 days intervals without medication. Complete resolution and recurrence rate were 83% (15/18) and 0%, respectively. Three patients (17%) had a partial response. Side effects observed: corneal epithelial defect (1 patient) and lid irritation (3 patients). No patient discontinued the medication.

Conclusions: 5 FU 0.5% is tolerable as a primary treatment for OSSN, with 83% of efficacy. The advantage is the low-cost (around U\$22/month) compared to other topical drugs. It should be considered as a treatment option for developing countries.

0214

Uveal melanoma and renal cell carcinoma in the same patient: 24 Finnish cases

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Purpose: Germline pathogenic variants of BRCA-1 associated protein-1 (*BAP1*) gene predispose to uveal melanoma (UM) and other cancers, especially mesothelioma and renal cell carcinoma (RCC). We report the characteristics of 24 Finnish UM patients who developed RCC before or after UM.

Method: In Finland, UM is treated centrally in the Helsinki University Hospital. We collected data on patients with UM and RCC, diagnosed with UM from January 1968 to June 2016. The exons and exon-intron junctions of *BAP1* were sequenced from those who were still alive and consented.

Results: The UM was diagnosed at the median age of 65 years (range, 48-90) and it was AJCC stage I, IIA, IIB, IIIA, IIIB, and IIIC in 5 (21%), 5 (21%), 8 (33%), 3 (12%), 2 (8%), and 0 cases, respectively. Of 956 patients diagnosed with UM after January 2000, 1.6% (95% CI 0.9-2.6) had RCC that was diagnosed a median of 1 month after UM (range, 10 years earlier to 14 years later). In four (17%) patients, the diagnosis was synchronous. Two patients had a breast cancer, and one had a cutaneous melanoma as a third cancer. One patient had a meningioma. Fourteen patients died, 8 (57%) of metastatic UM, 2 of nonmalignant disease, 1 of breast cancer, and 1 of RCC; one patient died of synchronous metastatic UM and RCC. So far, 3 patients have consented to *BAP1* sequencing, which did not show a mutation.

Conclusions: Germline mutations of *BAP1* do not always explain an association between UM and RCC.

0002

An alternative management for diffuse choroidal hemangioma in a child

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Report of a 9 year-old girl with Diffuse choroidal hemangioma OU and significant loss of vision in one eye. She has Glaucoma and history of multiple procedures to control her IOP. She did not respond to oral beta-blockers. We will briefly discuss management options, present 2-year visual outcome of this child, and potential long-term problems related to the treatment she received.

0008

Outer Space Tumor

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A 53 year-old pilot developed an intraocular tumor. A few years later he developed an orbital mass, suspected to be extrascleral tumor. But it was not. MRI imaging was instrumental in the diagnosis.

0011

Immune Response to Melanoma

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Case abstract: A case of VKH syndrome in a patient with metastases from skin melanoma treated with Yervoy
A case of large uveal melanoma rapidly regressing after fine needle aspiration biopsy.

0017

Rhegmatogenous retinal detachment in a patient with choroidal melanoma simulating choroidal detachment

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Purpose: Coincidence of rhegmatogenous retinal detachment (RRD) and choroidal melanoma (CM) is a rare phenomenon, accounting for less than 1 % among total CM cases. The aim of this study is to report a case of CM presenting with RRD, which needed to be differentiated from choroidal detachment (CD).

Methods: A 78-year-old female complained of blurred vision in her right eye. Visual acuity was 20/100 OD and 20/30 OS with normal intraocular pressure. Slit-lamp examination showed clear anterior chamber and mild cortical cataract OU. In her right fundus, there was a retinal detachment involving the inferior and nasal quadrants where a retinal tear exhibited measuring a half disc diameter in size. An orange choroidal elevation was noted behind the detachment mimicking CD. Fluorescein angiography revealed dye leakage from the detachment at a late phase, where indocyanine green angiography indicated hypofluorescence. MRI detected the choroidal elevation with enhancement by gadolinium. Clinically, she was diagnosed with CM and chose to receive X-ray radiotherapy; however, she suffered from ocular pain following radiation. Enucleation was eventually conducted in her right eye.

Results: Histologically, the choroidal lesion was diagnosed with spindle-cell type CM. She is well without local recurrence or distant metastases one year after enucleation.

Conclusions: If hypotony or inflammatory sign is absent, ophthalmologists should pay attention to the differential diagnoses of choroidal elevations observed in patients with RRD.

0019

Mystery Case

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A good start, but a sad outcome.

0023

Metastatic tarsal conjunctival placental site trophoblastic tumour (PSTT)

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Purpose: To describe the clinical aspects and histopathology of an unusual, rapidly expanding tarsal conjunctival mass in a 25 year-old female.

Method: A 25 year-old female with a history of a suspected tubal ectopic gestation, raised β -human chorionic gonadotropin (β -HCG) and a pneumothorax presented with a 4 week history of a rapidly enlarging mass on the tarsal aspect of the right lower lid. This was hemispherical, 7mm in diameter, pink, fixed, fleshy and vascular and encroaching the lid margin. The rest of the ophthalmic examination was unremarkable. There was no local lymphadenopathy. An incisional biopsy was performed.

Results: Histology revealed a malignant neoplasm within the substantia propria, composed of polygonal, pleomorphic eosinophilic to clear cells, alternating with zones of fibrinoid necrosis. Immunohistochemistry showed tumour cell positivity with cytokeratins, α -inhibin and focal positivity with β -HCG and human placental lactogen. The tumour was negative for lymphoid and melanocytic markers. The histology represented metastatic placental site trophoblastic tumour (PSTT) and was identical in nature to the previously biopsied lung that showed the same pathology.

Conclusions: Gestational trophoblastic disease comprises hydatidiform mole, invasive mole, choriocarcinoma and PSTT. PSTT generally presents a few months after pregnancy and while most cases follow an indolent course, some can disseminate aggressively. Metastases to the conjunctiva are rare and are rapidly growing and arise mainly from the breast and lung. In this case, the conjunctival metastasis occurred after chemotherapy for the previous lung disease, suggestive of the evolution of a chemotherapy-resistant, aggressive tumour subclone with a poor prognosis.

0027

Melanoma-associated vitelliform retinopathy: a clinical case

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Purpose: Melanoma-associated vitelliform retinopathy (MAR) is one of the manifestations of paraneoplastic syndrome associated with cutaneous melanoma. Our purpose was to describe the clinical case of MAR in 45 years old patient.

Method: All instrumental diagnostics, including ultrasound scan, fluorescein angiography (FA), spectral optical coherence tomography (SOCT) and autofluorescence, was performed.

Results: Clinically MAR was presented as bilateral multiple grey-yellow oval and round foci with smooth borders and surface in central and paracentral zone of fundus. FA revealed resistant hypofluorescence in arterial and choroidal phase, retinopathy on the back of hypofluorescence in venous phase and isofluorescence in later phase. Local thickening and hyperreflectivity of outer retinal layers with neuroepithelium detachment, which lifted intact inner retinal layers, small round hyperreflective foci in the outer retinal layers level were determined on SOCT tomograms. An uneven hyperautofluorescence of foci with hypoautofluorescent rim was visualized.

Conclusions: Diagnosis of MAR is rare, thus it should be taken in consideration when determining above mentioned symptoms.

0032

Selective intra-arterial embolization for advanced extrascleral uveal melanoma

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Purpose: To report a treatment approach for advanced extrascleral uveal melanoma.

Methods: Clinical examination including magnetic resonance imaging, computed tomography, angiography, and histopathologic analysis.

Results: A 49-year-old healthy woman presented with a seven-year history of an enlarging mass arising from the right eye. The right orbit had an exophytic, multilobulated pigmented mass with associated necrotic tissue measuring approximately 10 cm x 7.7 cm x 11 cm. No globe structures were present on physical exam or neuroimaging. Malignant melanoma was diagnosed after biopsy with immunohistochemical stains. Selective intra-arterial embolization was undertaken.

Conclusions: Significant reduction in tumor burden was seen 3 months after intra-arterial embolization. No complications were associated to treatment. Selective intra-arterial embolization may allow adequate palliative therapy in select cases of advanced extrascleral uveal melanoma.

0047

Retinocytoma in a child with a large deletion in the RB1 Gene. A case report

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A 20-month-old baby girl was referred to our clinic with suspected monocular retinoblastoma. She was born after normal pregnancy in caesarean section at 39 weeks, weighing 2800 grams. As the age of 20 months she examined by an ophthalmologist and found to be myopic with astigmatism. A white retinal mass was seen in the fundus of the right eye with a feeder vessel. A diagnosis of monocular retinoblastoma was made in another medical center. The parents brought her to the Ocular Oncology Service at the Hadassah Medical Center for a second opinion. In examination under anesthesia we made the diagnosis of retinocytoma and recommended follow-up only. The child and her parents were referred to genetic counseling. She was found to carry a large deletion in chromosome 13 that included the RB1 gene (9 Mbp in chromosome 13q14.11q14.3). The parents were found not to be carriers of the deletion. In two years' follow-up examinations under anesthesia, the last one in July 2016, there was no change in the retinal lesion. The child shows a very mild motoric delay.

Mutations in the RB1 gene were described in patients with retinoblastoma and in patients with retinoblastoma who also have retinocytoma. To the best of our knowledge, deletion in the RB1 gene causing only retinocytoma has not been reported previously.

0048

Uveal melanoma in an indigenous Polynesian patient

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A short case of uveal melanoma in an indigenous Samoan is reported. Mention is made of other Polynesian patients the author has seen and treated, which indicates that it is not an unknown disease in such patients. An introduction to the genetic history of the South Pacific is given, illustrating both the variety of the region, its peoples and its rich history, which may provide an explanation for occurrence of uveal melanoma in this ethnic group.

0053

Limbal Stem Cell Preservation During Proton Beam Irradiation for Diffuse Iris Melanoma

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Purpose: To report the outcome after limbal stem cell preservation during proton beam irradiation for diffuse iris melanoma.

Method: This is a single-case report of diffuse iris melanoma that was managed with proton beam radiation (53Gy), wherein pre-emptively harvested superior and inferior limbal stem cells before radiation were replaced after irradiation. Regeneration of the palisades of Vogt and the limbal stem cells was documented by an optical coherence tomography-based imaging protocol.

Results: At 24 months after radiation therapy, best-corrected visual acuity was 20/25. The cornea was clear without evidence of limbal stem cell dysfunction. Clinical examination (including gonioscopy and ultrasound biomicroscopy (UBM)) indicative of local control, and systemic surveillance were negative for metastatic disease. At post-transplant (21 months), there were more palisade structures visible in both anterior and posterior regions of the superior and inferior limbus, and the linear presentation of the inferior palisades appears to have regenerated.

Conclusions: Diffuse iris melanoma can be managed successfully with proton beam radiation while preserving corneal limbal stem cells by harvesting them before radiation and then replacing them after irradiation. Regeneration of the palisades of Vogt could be documented by an optical coherence tomography-based imaging protocol.

0059

So-called 'malignant mesenchymoma' (composite sarcoma) of the orbit: a rare and perplexing pediatric tumor

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Background: Malignant mesenchymoma is an interesting but very rare tumor of mesenchymal origin in which malignant differentiation has occurred twice or more.

Purpose: To report a case of so-called malignant mesenchymoma in a 14-year-old girl child at an orbital location.

Methods: Case report

Results: A 14-year-old girl presented with rapidly progressive proptosis of the right eye. Biopsy confirmed a composite sarcoma with rhabdomyosarcomatous, osteosarcomatous and chondrosarcomatous components.

Conclusions: So-called malignant mesenchymoma is exceedingly rare and highly aggressive tumor. We report the first such case at an orbital location.

0060

6 Cases of Presumed Spontaneous Necrosis of Iris Melanoma: Clinical and Ultrasound Biomicroscopy Findings

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Purpose: 6 Cases of iris melanoma where tumour shrinkage and presumed necrosis occurred are discussed.

Methods: All patients underwent clinical evaluation, slit lamp photography, and ultrasound biomicroscopy. 4 Patients were aged 20 to 47 years when they presented to us. Patients were aged 27 to 56 when shrinkage was documented. Two other patients' are described separately.

Results: The group of 4 patients presented with suspected iris melanomas. In all cases it was elected to follow the lesion. In all cases tumour growth occurred and was documented clinically, with photographs, and with ultrasound biomicroscopy. Treatment discussions were initiated in 3 of 4 cases and all patients preferred ongoing follow-up. Tumour shrinkage was then noted. It was unassociated with inflammation or elevated intra-ocular pressure. Shrinkage involved a surface depression in the tumour (crater) with loss of volume. This was best demonstrated with ultrasound biomicroscopy. Follow-up after necrosis varied from 12 to 114 months and no patient demonstrated tumour growth.

The final two patient's presented elsewhere with melanocytic iris tumours at ages 10 and 17 and were followed. They were referred to our service at ages 37 and 55. The lesions at that stage demonstrated a large crater, we suspect prior necrosis. The lesions remained unchanged in 25 and 103 months of follow-up.

Conclusions: We present the phenomenon of spontaneous necrosis of iris melanoma. The presentations and growth of the lesions in these relatively young patients were consistent with iris melanoma. Further study may confirm loss of tumour volume implies a favourable prognosis.

Sympathetic ophthalmia associated with untreated choroidal melanoma

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Introduction: We report a case of sympathetic ophthalmia induced by an untreated choroidal malignant melanoma.

Purpose: A 41 year old man presented with reduced right eye vision. The left eye was pthisical and the patient gave a history of severe ocular trauma some years previously. Right eye vision was 20/30 with vitritis, optic nerve head oedema and phlebitis. Fluorescein angiography revealed multiple hyperfluorescent dots and OCT demonstrated subRPE lesions consistent with clinical Dalen Fuch nodules. Sympathetic ophthalmia was diagnosed.

Methods: The right eye subsequently developed steroid induced cataract and glaucoma and after phacoemulsification, achieved a vision of 20/40. The right eye required additional intravitreal steroids and oral immunosuppression for recurrent vitritis, cystoid macular oedema and active subRPE lesions. Four years after the diagnosis of sympathetic ophthalmia, the right eye vision was hand movements.

Results: The patient was lost to follow up and subsequently presented 5 years later with a painful left proptosis. CT scan showed a solid intraconal mass with retrobulbar extension and the patient underwent an eyelid sparing exenteration. Histopathology revealed a choroidal malignant melanoma. The clinical history provided, of significant previous ocular trauma, was discounted after further detailed enquiry. Previous medical records revealed an uninvestigated and untreated retinal detachment in the left eye.

Conclusions: Primary malignant melanoma could rarely trigger sympathetic ophthalmia in the other eye. Current reports suggest that treatment for choroidal melanoma could initiate sympathetic ophthalmia. This is the only contemporary account of untreated choroidal melanoma inciting uncontrollable sympathetic ophthalmia in the fellow eye.

0068

Surgical drainage of lymphangiectasia haemorrhagica conjunctivae

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Purpose: To report a case of non-resolving lymphangiectasia haemorrhagica conjunctivae (LHC) successfully treated with surgical drainage.

Methods: Retrospective case report.

Results: A 17 year-old Caucasian female presented with a history of a large red lesion affecting her right eye. Approximately one year earlier, she had noticed a small, painless “red spot” affecting the inferior aspect of the conjunctiva of her right eye. Three months prior to presentation, she noticed a sudden increase in the size of the lesion. There was no history of trauma and she was not a contact lens wearer. Her medical history was remarkable for a remote seizure disorder which had been stable on levetiracetam. MRI/MRA of the brain and orbits was unremarkable. Anterior segment fluorescein angiography did not show any flow in the lesion, indicating a lymphatic origin of the channels. Surgical drainage of the lesion was performed while sparing the affected conjunctiva resulting in an excellent cosmetic outcome. Incisional biopsy confirmed the diagnosis of lymphangiectasia haemorrhagica conjunctivae. The patient remained free of recurrence six months following the procedure.

Conclusions: Non-resolving lymphangiectasia haemorrhagica conjunctivae can be managed successfully with conjunctival sparing surgical drainage with an excellent cosmetic outcome.

0075

Multifocal Choroidal Melanoma in a Patient with Germline BAP1 Mutation

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Purpose: To report a case of unilateral multifocal melanoma in a patient with germline BRCA associated protein 1 (BAP1) mutation.

Methods: Case report.

Results: A 67-year-old Caucasian woman with a family history of lung and liver cancer developed blurred visual acuity of 20/30 in the left eye. She was discovered to have 2 independent pigmented choroidal melanomas in the macula and superotemporally, both demonstrating overlying subretinal fluid and orange pigment. Both melanomas were treated with a single custom-designed Iodine-125 brachytherapy device. Upon systemic evaluation, asymptomatic renal cell carcinoma was found, and blood lymphocyte testing for germline BAP1 mutation was positive.

Conclusions: Multifocal choroidal melanoma is exceedingly rare. Patients with uveal melanoma, especially if multifocal, and those with other systemic malignancy or family history of cancer should be tested for germline BAP1 mutation. Lifelong monitoring for other systemic malignancies is advised.

Preferred Retinal Locus (PRL) in a child with retinoblastoma and a macular tumour

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Purpose: We attempt to describe the assessment of visual function in a child with macular retinoblastoma in their remaining eye by fundus-driven perimetry and determine the position of the PRL.

Method: All children with bilateral retinoblastoma, in whom one eye had been enucleated or had severely visually impaired (visual acuity < LogMAR 1.0) were identified. Patients underwent ophthalmic clinical examination and were posteriorly tested with MP-1 Microperimeter (NIDEK Technologies, Padova, Italy)

Results: Five patients were thought suitable for this study. One patient aged 9 successfully completed microperimetry assessment. 21 months after enucleation, her vision was LogMAR 1.3 in her remaining eye and she was found to have a PRL above the superior border of her macular tumour in healthy looking retina. Two patients failed to complete the examination due to high-amplitude nystagmus and other two patients did not produce reliable results.

Conclusion: To our knowledge this is the first time microperimetry has been used in a child with retinoblastoma and a PRL identified. Applied to children with only one remaining eye, microperimetry offers clinicians a new approach in understanding the adaptive mechanisms after macular damage, and may have a role in future visual rehabilitative treatments.

A Suspicious Conjunctival Mass 27 Years after Iris Tumour Resection

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Purpose: To report a case of very late extraocular relapse with no concurrent intraocular component of a previously excised iris melanoma.

Methods: Retrospective case report.

Results: An 87-year-old white male patient presented with a left conjunctival mass 27 years after undergoing left iris tumour resection, performed elsewhere. Examination revealed a large amelanotic conjunctival vascularized lesion, with no concurrent intraocular component, and a large infero-nasal iris defect from his previous surgery. The patient underwent an excisional biopsy, adjuvant cryotherapy and placement of an amniotic membrane graft. Histopathology, supported by immunostaining, found the tumour to be a malignant melanoma, incompletely excised at the deep margin, with no junctional component and no evidence of melanosis with atypia, implying its origin was from a previously excised iris melanoma, rather than a primary conjunctival malignancy. The patient was offered adjuvant strontium plaque radiotherapy, but declined. On last follow-up visit, 18 months after first presentation with the ocular surface mass, the conjunctiva has healed-up, and no intra- or extraocular relapses were recorded. Systemically the patient remains clear from metastasis.

Conclusions: Extraocular spread of previously resected iris melanoma can occur even 27 years after primary iris tumour surgery, warranting long-term follow-up. In the absence of an intraocular component, diagnosis is challenging, as lesion may mimic a primary ocular surface tumour. In this respect, histopathology is a useful diagnostic tool to differentiate between uveal and conjunctival tissue origin.

0086

Mystery Case

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A 7-year old healthy Caucasian male child was seen in consultation for bilateral circumpapillary choroidal lesions. He had been evaluated by many prior eye care specialists and no diagnosis was given. Color fundus photographs, fluorescein angiography, enhanced depth imaging optical coherence tomography, and ultrasonography will be presented, along with a very brief discussion of a rare ophthalmic tumor of childhood.

0087

Conjunctival Tumor

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Purpose: to describe the management of an atypical amelanotic conjunctival tumor.

Method: a 76 year-old man presented with a conjunctival tumor initially diagnosed as OSSN. The patient initially responded to INF developing a relapse not responding to other forms of local chemotherapy (MMC and 5FU).

Results: patient underwent excision biopsy and amniotic graft placement. Pathology will be discussed at time of presentation.

Conclusions: diagnostic biopsy should be performed before recommending treatment in conjunctival tumors.

Isolated eyelid Rosai-Dorfman disease: A rare eyelid tumor

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A 16-year-old boy presented with right upper eyelid swelling which was gradually increasing in size associated with drooping of the eyelid since 5 months. He was being treated conservatively with a diagnosis of giant papillary conjunctivitis. On examination, there was right upper eyelid mechanical ptosis and the lesion was a 25x20x5 mm non-tender firm mass involving entire upper eyelid from the eyelid margin to the orbital rim. Posterior border of the lesion was palpable with smooth surface and no fixity to the overlying skin or the underlying conjunctiva. Entire eyelid margin was thickened with loss of lashes in the medial 2/3rd. The anterior and posterior segments of both eyes were within normal limits. Systemic examination was normal. With a clinical differential diagnoses of right upper eyelid Schwannoma versus juvenile xanthogranuloma, excision of the lesion was carried out. Intraoperatively the swelling was well defined with a pseudocapsule superiorly but was infiltrating the tarsus and the eyelid skin at the eyelid margin. Near total excision of the lesion was performed followed by eyelid reconstruction. Histopathology of the lesion showed characteristic features of histiocytes with emperipolesis with positive S 100 stain suggestive of Rosai-Dorfman disease. Rosai-Dorfman disease is a rare eyelid tumor and should be considered in the differential diagnosis of an atypical eyelid lesion.

0090

Bilateral Macula Uveal Melanoma

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A 65 yo woman was referred for evaluation of uveal melanoma located in the macula of both eyes. The mystery of this case will be revealed.

0097

Multimodal Management in a case of Primary Orbital Atypical Teratoid Rhabdoid Tumor

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Purpose: To report clinical, radiological, histopathological features and outcome after multimodal management in a rare case of orbital atypical teratoid rhabdoid tumor (ATRT)

Method: ATRT is an aggressive pediatric malignant neoplasm of the central nervous system. Primary and isolated orbital involvement is rare. Apart from surgical clearance, there are no established management guidelines. We present a case of a 3-year-old girl presenting to us with subacute proptosis of the left eye with features of compressive optic neuropathy. CT scan showed a large intraconal mass with variegated density in close association with the optic nerve, and extending to the orbital apex. An incision biopsy confirmed the diagnosis of extrarenal, noncerebral atypical teratoid rhabdoid tumor. Bone marrow examination and systemic evaluation ruled out metastasis. She underwent stereotactic EBRT (4600 cGy) sandwiched between 2 sessions of 3 cycles of chemotherapy with Vincristine, Adriamycin and Cisplatin.

Results: After 12 months of follow up, she remains stable with an inactive scar, with no metabolic activity detectable on PET scan and without any ocular or systemic complications.

Conclusions: Multimodal treatment involving chemotherapy and radiation can achieve eye as well as life salvage in atypical teratoid rhabdoid tumor.

0102

OCT Guided Sequential Targeted Laser Therapy in Juxtafoveal Retinoblastoma

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Purpose: Foveal pit conservation is important in potential for vision in juxtafoveal retinoblastoma, affecting choice of treatment modality (chemotherapy versus primary focal therapy), and laser technique and choice (532 nm versus 810 nm laser).

Methods: We present a child treated with 6 cycles of VEC chemotherapy regressing a large central tumor to be juxtafoveal; optical coherence tomography (OCT) showed an intact foveal pit. The residual tumor was treated with laser (532 nm) starting from the periphery from the edges away from the fovea and going inwards until no reaction is seen and avoiding the tumor nearest to the fovea. This was sequentially repeated on 3-5 week interval. A 1064 nm laser can be used in elevated areas with no response to 532 nm Laser at the last treatment session. We called this technique sequential (as it is performed on sequential sessions), targeted (as it targets tumor avoiding fovea) laser therapy (STLT).

Results: complete control of the tumor was achieved and the tumor was replaced by scar tissue. The fovea is maintained documented by OCT. the child is undergoing amblyopia therapy to improve the vision in this eye (currently <20/200)

Conclusions: STLT can be used to control juxtafoveal tumors to preserve the fovea and hence better visual potential. This is achieved if the papillomacular bundle is tumor free.

0110

Orbital melanoma in a patient with oculodermal melanocytosis: clinical, instrumental, morphological and molecular genetics examination (a case report)

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Purpose: To present a clinical symptoms, instrumental diagnostics features, histological and molecular genetic analysis in a patient with oculodermal melanocytosis with developed orbital melanoma.

Method: A 57 years old man was suffering from visual acuity impairment and periorbital pain during last 2 years. He was undergone both clinical and instrumental examinations due to revealed orbital mass. Surgical procedure was performed. The diagnosis of melanoma afterwards was confirmed histologically. Tissue blocks were used for molecular genetic analyses.

Results: The clinical examination revealed periorbital soft tissues oedema, light ptosis, proptosis with globe displacement inferior, eye motility disturbance to all directions. Eyelids, conjunctiva, episclera were hyperpigmented. Fundus examination had shown optic nerve disc swollen and hyperemic with uncertain margins, tortuous vessels, all over the fundus there were dystrophic foci and oedema. CT- scan revealed an oval lesion above the optic nerve with smooth margins, enlargement of superior and lateral extraocular muscles. B-mode echography demonstrated hypoechoic structure with certain margins. CDI revealed low vascularization of the lesion with very low blood flow velocity inside it. The histological examination confirmed a pigmented primary mixed cell orbital melanoma with large necrotic spaces and mitotic activity. Genetic analyses didn't revealed monosomy 3, but there was deletion in 8p12-p22.

Conclusion: Demonstrated features could help to diagnosis orbital melanoma. Despite of low risk of orbital melanoma development in patients with oculodermal melanocytosis, all these patients need to follow up to for early recognizing malignancy in the orbit.

0112

Bilateral diffuse and bilateral multifocal uveal melanoma

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A case report of 2 patients of bilateral diffuse (BD) and bilateral multifocal (BM) uveal melanoma (UM).

One 65 yo female patient had BD UM with diffusely thickened choroid and ciliary body and multiple nodules of the iris, ciliary body and choroid with maximum thickness of 4.2 mm. After bilateral biopsy patient agreed to enucleate both eyes. Histological investigation confirmed BD UM.

Another patient (male of 75 yo) had BM UM with 2 separate tumors in one eye and 2 separate tumors in the fellow eye. Patient was treated with enucleation of one eye (BM UM was confirmed histologically) and double Ru-106 brachytherapy of the fellow eye.

Systemic investigation of both patients did not reveal any oncological diseases.

Results: Follow up of these patients within 12 and 139 months is unremarkable. Histological and genetic analyses of enucleated eyes were fulfilled.

Conclusions: BD and BM UM is an extremely rare and challenging condition. Metastatic character of such tumors should be excluded. Successful management of multifocal tumors is possible.

0115

Protective eyewear in patients with retinoblastoma: Time to rethink

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It's not uncommon in children diagnosed with retinoblastoma, Rb, to find a large number of patients with one better-sighted eye or even with one remaining eye, due to the enucleation of more involved eye.

We are going to present a case of an 8-year old child with the history of blunt trauma to his right eye, who was a known case of bilateral retinoblastoma and consequent enucleation of left eye at the age of 2 months. He lost his vision of 20/20 to hand motions since the tractional rhegmatogenousretinal detachment developed at the site of old regressed (type 3, calcified and non-calcified regression) Rb lesion.

This case encouraged us to rethink about the importance of protective eyeglasses which have been strongly recommended in monocular individuals. We did a pilot study on a small group of monocular patients with retinoblastoma (35 Childs) in our referral ocular oncology clinic. Although 82% of cases were advised to use protective eye wear, only 17.6% of them were using this protective modality. It is of note that in 15% of cases, parents reported a history of facial trauma in the past six months.

Such case with visual loss in the remaining eye emphasizes how important safety glasses are in these patients. As we learn more about the better Rb management in recent years, it seems that revising the current safety protocols for monocular children with retinoblastoma is crucial, in order to find more effective approaches to protect the better-sighted or preserved eye.

0117

Sirolimus for treatment of large astrocytic hamartoma in a patient with tuberous sclerosis

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The management of a 20 yo male patient with tuberous sclerosis complex and a large retinal astrocytic hamartoma near the macula will be discussed. The tumor was initially treated with photodynamic therapy and intravitreal Avastin with minimal response. Addition of oral sirolimus resulted in significant regression of the tumor over the course of 1 year.

Choroidal melanoma with secondary orbital cellulitis

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Purpose: We present a case of secondary orbital cellulitis with angle closure from necrotic choroidal melanoma.

Methods: Retrospective case report.

Results: A 63 year old male was referred with presumed orbital cellulitis. Visual acuity was light perception on the right, and 6/5 on the left. There was periobital oedema and erythema, with massive indurated chemosis overlying the cornea. The pupil was mid-dilated with rubeosis and the anterior chamber was shallow with a 1mm hyphaema. Ocular motility was limited and the globe was tense to palpation. CT showed orbital cellulitis. US showed a choroidal mushroom-shaped lesion and subtotal retinal detachment. Subsequent MRI showed a heterogenous intraocular lesion with fluid levels, and restricted diffusion suggestive of high lesion cellularity. He was treated with intravenous and topical antibiotics, atropine and ocular hypotensive agents. Oral prednisone induced a rapid resolution of the chemosis and orbital inflammation. Enucleation was performed one week post-presentation. No metastases were identified.

Histopathology revealed choroidal melanoma (pT3NxMx) with clear margins, and evidence of acute on chronic panophthalmitis. Necrotic tumour in the vitreous had displaced the lens anteriorly.

Conclusions: Rarely choroidal melanoma can evade detection and cause orbital cellulitis. Our patient had a characteristic rapid response to oral steroids. Additionally he developed secondary angle closure from inflammatory change displacing the lens-iris diaphragm anteriorly and rubeosis.

This case demonstrates the diagnostic dilemma of choroidal melanoma presenting with secondary orbital cellulitis, and highlights the utility of imaging, and steroid sensitivity in helping differentiate neoplasia from other causes.

0123

Intratumoral oncolytic therapy for metastatic uveal melanoma

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Intratumoral treatment of metastatic melanoma is gaining in favor as a local therapeutic option with the possibility of distant bystander effect. The use of the oncolytic agent talimogene laherparepvec has not been studied in metastatic uveal melanoma. Here we present the case of two uveal melanoma patients treated with intratumoral oncolytic therapy using talimogene laherparepvec.

Patient A is a 69 year-old Caucasian gentleman status post enucleation in 2015 with metastatic uveal melanoma in 2016 to his liver (9 cm) and orbital cavity (6.7 cm). He received talimogene laherparepvec to his orbital tumor with good tolerance.

Patient B is a 31 year-old Caucasian woman status post brachytherapy in 2010 with metastatic uveal melanoma to her bilateral liver in 2015. As salvage therapy, she received talimogene laherparepvec to her dominant liver lesion (8.5 cm) in 2016. She tolerated the treatment without any adverse effects.

The clinical course of both patients will be updated at the ISOO 2017 meeting.

Concomitant orbital cavernous hemangioma and schwannoma in a patient: A rare presentation

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A 39-year-old female presented with painless, protrusion of the right eye associated with diminution of vision since 5 months. There was no significant systemic history. On examination, her best-corrected visual activity was 20/800 in the right eye and 20/20 in the left eye. Limitation of abduction by -2 and elevation by -1 were noted in the right eye. Right eye had early cortical cataract. Posterior segment was within normal limits in both eyes. Computed tomography of the orbits revealed a large well-defined homogenous solid mass with patchy enhancement in the right orbit inferotemporally pushing the optic nerve medially and causing globe indentation, and a smaller well-defined homogenous mass in left orbit inferotemporally pushing the optic nerve medially. A clinical differential diagnoses of bilateral schwannoma or cavernous hemangioma was made. The patient underwent transconjunctival orbitotomy with complete excision biopsy of mass in right orbit and subsequently in the left orbit 1 week later. Histopathology confirmed the diagnosis of cavernous hemangioma in the right orbit and schwannoma in the left. At 6 weeks follow-up, the patient is doing well with resolved proptosis, improved visual acuity and full extraocular movements.

Conclusions: Bilateral benign unrelated orbital lesions of varied pathology can occur, though rare.

0127

Uveal metastasis from prostate carcinoma: 3 cases in 6 months in a single institution

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Purpose: While prostate cancer is the most frequently diagnosed cancer in America, uveal involvement by metastatic prostate cancer (MPC) is rare. To date, the largest case series comes from Wills Eye Hospital with 9 cases collected over a 20-year period. Here we report 3 cases of MPC to the uvea within 6 months, the highest incidence of uveal metastases in a single institution to date.

Method: Retrospective case series and literature review

Results: A 63 year-old man presented with left eye choroidal mass 18 months after the diagnosis of visceral MPC. Fine needle aspiration biopsy confirmed prostatic metastasis to the choroid. External beam radiation therapy (EBRT) decreased the size of the mass but without improvement in vision. Another man, 58 years old, developed simultaneous multiple choroidal masses in both eyes with rapidly decreasing vision in the setting of MPC diagnosed 11 years prior. He died six weeks later. A third patient, a 66 year-old man with prostate cancer diagnosed 16 years earlier, developed acute painful vision decrease and was found to have a large anterior chamber mass with secondary ocular hypertension to 40mmHg. The mass and ocular hypertension resolved with EBRT. None of the three patients had a second extraocular primary.

Conclusions: Uveal metastasis from prostate, while rare, is an important differential diagnosis in patients with MPC. The incidence of prostate metastasis to the uvea may be on the rise as suggested by this report of 3 cases that presented within 6 months, the highest incidence of these cases in a single institution.

0145

Review of the distribution of DNA alterations identified by our uveal melanoma (UM) prognostic assay

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Purpose: Nearly half of all UM patients develop metastasis. In addition to clinical features, distinct DNA changes arising in UM tumors can be used to prognosticate UM patients into low and high risk subgroups. In this review, we will summarize the distribution of DNA alterations we have identified using our clinically validated UM prognostic assay.

Method: Our UM prognostic assay detects copy number changes on chromosomes 1p, 3, 6, and 8, in DNA extracted from fine needle aspirate biopsies (FNAB), using multiplex ligation-dependent probe amplification (MLPA). Confirmation of chromosome 3 loss or identification of isodisomy 3 is assessed using microsatellite analysis (MSA). When no chromosomal alterations are detected by MLPA and/or MSA, sequencing for recurrent mutations in exon 5 of *GNAQ* and *GNA11* is performed.

Results: Since July 2014, 35% of cases show monosomy 3, 46% disomy 3, 5% partial monosomy 3 and 2% isodisomy 3. Of the cases with monosomy 3, 80% also have 8q gain, while only 19% of disomy 3 have 8q gain. Of the cases with disomy 3 and no additional chromosomal gains or losses, recurrent mutations in *GNAQ* or *GNA11* exon 5 were identified in 58% of the specimens, while no recurrent mutations were identified in 42%.

Conclusions: Overall, our distribution of DNA alterations is consistent with published cohorts. Of note, the proportion of UM cases without *GNAQ* or *GNA11* exon 5 mutations is at the high end of published frequencies, suggesting sampling issues and/or tumor heterogeneity and the importance of tumor confirmation.

0147

Ocular surface epithelial atypia mimicking squamous neoplasia in association with ulcerative colitis

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Purpose: Inflammatory bowel disease may be associated with extra-intestinal manifestations. Here we report a case of severe reactive epithelial atypia resembling ocular surface squamous neoplasia (OSSN) in a patient with ulcerative colitis (UC).

Methods: Case report.

Results: A 32-year-old woman presented with sequential, progressive keratoconjunctival lesions in the left and right eyes, and both lesions were excised. Anterior segment optical coherence tomography was consistent with OSSN while histological examination revealed severe reactive epithelial atypia mimicking severe dysplasia. Shortly following treatment of the second eye, the patient was diagnosed with UC. Residual disease improved dramatically in response to systemic corticosteroids.

Conclusions: Severe ocular surface epithelial atypia resembling OSSN may be seen in association with UC.

0148

***RB1* cDNA mutation screening in a hereditary case of unilateral retinoblastoma reveals aberrant mRNA splicing and facilitates detection of a deep intronic substitution**

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Purpose: Unilateral cases of retinoblastoma with a positive family history are expected to carry an *RB1* germline mutation. To date, our clinical sensitivity to detect a causative mutation in presumed germline cases is 96.7%. Undetected *RB1* mutations might include translocations, very low-level mosaic mutations, alterations in unidentified *RB1* regulatory regions, or deep intronic mutations. Here we describe the utility of complete *RB1* cDNA coding sequence analysis to detect a deep intronic mutation in a family with retinoblastoma that routine complete *RB1* screening failed to identify.

Method: We requested fresh blood samples from affected mother and child in order to extract RNA and investigate for intronic changes not identified using our customary DNA screening methods. The complete *RB1* cDNA coding sequence was analyzed using Sanger sequencing to characterize splicing at exon junctions.

Results: *RB1* cDNA analysis revealed that both patient's transcripts showed retention of 125 nucleotides of from intron 18. Targeted sequencing of the proband's original DNA sample in this region revealed a heterozygous deep intronic c.1814+1307C>G substitution within intron 18, which was also confirmed in the proband's pregnant mother. With the mutation identified, we were able to offer targeted prenatal testing and concluded that the fetus did not inherit the familial mutation.

Conclusions: RNA analysis can increase the sensitivity to detect germline mutations in retinoblastoma patients by revealing deep intronic changes.

0150

Case report of 2 patients with massive vitreous seeding in choroidal malignant melanoma: A rare presentation, treated with combined tumor endoresection and Ruthenium (Ru-106) brachytherapy as the alternative treatment to enucleation

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Purpose: To report 2 cases of choroidal malignant melanoma with massive vitreous seeding treated with combined tumor endoresection and brachytherapy as an alternative to enucleation.

Method: Case report

Results: Two male patients (age 26, and 61 years old) presented with pigmented choroidal mass with retinal invasion located at equator and massive pigment clumping dispersed in vitreous cavity. Initial visual acuity was 20/40 for both patients. The tumor size (basal diameterxthickness) of the first and the second patients was 7.7x10.3 millimeters, and 11.3x11.5 millimeters, respectively. Both patients denied enucleation. Patients were well aware of the risk of tumor recurrence and systemic metastasis. Pars plana vitrectomy, tumor endoresection with silicone oil tamponade, combined with Ruthenium brachytherapy was performed. At the time of operation, vitreous biopsy was performed initially, then main tumor biopsy was performed. Vitreous specimen and main tumor specimen were sent for pathological diagnosis in separate container. The pathological diagnosis were malignant melanoma in both vitreous and main tumor specimen. No postoperative complication, tumor recurrence or systemic metastasis was detected during the follow up period (16 and 9 months, respectively).

Conclusions: Massive vitreous seeding is a rare presentation of choroidal malignant melanoma, and may not be controlled with local brachytherapy alone due to dispersive nature of the tumor cells. In order to remove all tumor cells in vitreous cavity, we proposed tumor endoresection and brachytherapy as an alternative treatment to enucleation. Long term follow up is required to evaluate the risk of local recurrence and systemic metastasis of this surgical technique.

0151

Oral propranolol in the management of periocular Infantile capillary Hemangioma-initial results

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Purpose: The reported literature has shown a promising effect of oral propranolol on infantile hemangioma with minimal side effect. However no consensus are available for the dosage, clinical assessment of the lesions, or drug bio-availability. The purpose of this Interventional study was to evaluate the safety and efficacy of oral propranolol in the management of periocular Infantile Hemangioma.

Method: Total 11 patients were treated with oral propranolol. All were evaluated by paediatrician to rule out any systemic involvement. Complete ocular examination for all and imaging was done wherever indicated. Main outcome measures were the regression in size of the lesions and any side effects related to treatment with oral propranolol.

Results: There were 3 males and 8 females with an average age of 6 months (range 8 weeks-12 months). Ten had unilateral presentation. Clinical presentation was superficial in five, combined in two, deep in one, and complex in three. The average starting dose was 4.36 mg and maximum average dose being 10.45mg. The mean duration of treatment and follow-up was 6.2 and 7.6 months respectively. Excellent response (>50% regression) was seen in 63% of patients and initial response was seen as early as two weeks in majority (73%). No significant side effects were seen with the use of above dosage.

Conclusions: This study finds the use of oral propranolol in the management of periocular infantile capillary hemangioma as safe and efficacious, providing an alternative to intralesional steroids.

0154

Sonic Hedgehog Inhibitors for Treatment of Locally Advanced Basal Cell Carcinoma of Periocular Region

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Purpose: To report our experience with sonic hedgehog inhibitors in patient with locally advanced basal cell carcinoma of orbital or periocular region.

Methods: All patients with locally advanced orbital or periocular BCC or basal cell nevus syndrome treated with the hedgehog pathway inhibitor, vismodegib from 2009 through 2016, were retrospectively reviewed. Age; gender; AJCC designation; type and grade of drug-related side effects; response to treatment; follow-up, and status at last contact were recorded.

Results: 15 white men and 2 white women had a median age of 64.5 years. 15 patients had locally advanced BCC; 2 had basal cell nevus syndrome. Among the patients with locally advanced BCC, 10 had T3bN0M0 disease at presentation; 1 each had T3aN0M0, T3bN1M0, T2N1M1, T4N1M1, and T4N2cM1 disease. Overall, 5 patients had a complete response, 9 had a partial response, and 3 had stable disease at last follow-up. All patients developed grade I drug-related adverse effects, most commonly muscle spasms (12 patients), and weight loss (10). Five patients developed grade II adverse effects. Neoadjuvant use of drug followed by surgery to remove residual disease was carried out in 6 patients. At last follow-up, none of the patients who presented with locally advanced disease that would traditionally be treated with orbital exenteration had required this disfiguring operation.

Conclusions: Hedgehog pathway inhibition produces a significant clinical response in most patients with locally advanced orbital or periocular BCC or basal cell nevus syndrome and can obviate orbital exenteration in some patients. Drug-related toxicity is manageable in most patients.

Combined type I and type II neurofibromatosis in a case

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Purpose: Neurofibromatosis (NF) is a low-grade-differentiated neurinoma/schwannoma including NF type I and NF type II, which are an autosomal dominant inherited disease. However, patients with simultaneously combined NF I and NF II are very rarely seen. We present a case who suffered from NF of right eye, optic glioma of left eye and meningioma, while having bilateral acoustic neuroma.

Methods: Retrospective case analysis. The patient's medical history, symptoms, orbital imaging data of CT, MRI and the histopathological data were reviewed.

Results: The result of postoperative pathological examination was neurofibroma of the right orbit. The postoperative physical examination showed that the visual acuity was index/20 cm for right eye; the degree of exophthalmus was 15 mm>-110 mm-<14 mm.

Conclusions: The orbital NF I may have diverse clinical manifestations, often cause exophthalmus and optical nerve compressive lesions. The treatment of NF is largely surgery plus symptomatic management. Serious exophthalmus should be treated aggressively, and surgery is its treatment of choice.

0161

Isolated choroidal amyloidoma mimicking an intraocular tumour

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Purpose: To report a case of choroidal amyloidoma

Methods: Case report

Results: A 70-year-old white female presented with a 2-week history of scotoma and photospiae in the left eye. Examination revealed 6/9 visual acuity, no anterior chamber or vitreous cells, and a pale sessile choroidal mass in the left eye. Optical coherence tomography showed a choroidal tumour with irregular contour. Ultrasound B scan revealed 2 choroidal lesions of medium-high echogenicity and elevation of 3.5 and 1.2 mm. Internal blood flow was detectable and there was a suspicion of extrascleral extension. Orbital CT scan confirmed extraocular extension of the tumour, but there were no other orbital or intracranial lesions. Systemic evaluation and PET / CT scan were clear. Orbital biopsy and subsequently intraocular biopsy showed non-AA type amyloid.

Conclusions: We report an unusual case of a choroidal amyloidoma, with as yet no development of systemic amyloidosis or plasma cell dyscrasia.

0165

Atypical Teratoid Rhabdoid tumour

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Purpose: To report the use of eye-conserving multimodal management in a rare case Atypical Teratoid Rhabdoid tumour of the orbit.

Method: A 3-year-old female presented to us with proptosis of the left eye with features of compressive optic neuropathy. MRI showed a large intraconal mass with variable internal intensity and close to the optic nerve. Incision biopsy was performed for tissue diagnosis.

Results: Histopathology along with immunohistochemistry confirmed the diagnosis of extrarenal noncerebral atypical teratoid rhabdoid tumour. Bone marrow examination and systemic workup were negative for metastasis. The patient underwent stereotactic radiotherapy (4600 cGy) sandwiched between 2 sets of 3 cycles of chemotherapy with Vincristine, Adriamycin and Cisplatin. She remains clinically stable with PET proven inactive residual disease at 18 months follow-up without any ocular or systemic complications.

Conclusions: Multimodal treatment involving chemotherapy and radiation can achieve eye salvage in rare conditions such as Atypical Teratoid Rhabdoid tumour.

0166

Conjunctival Melanoma During Pregnancy

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Purpose: To describe the clinical and histopathological features of a conjunctival melanoma (CM) during early pregnancy.

Method: A 37-year-old, 20-week pregnant primigravida was referred to the Sheffield Ocular Oncology Service with a rapidly growing lesion arising from the right superior conjunctival fornix, noted from the first trimester of pregnancy. This was associated with pain and bloody discharge. Incisional biopsy confirmed the clinical suspicion of invasive CM. She was treated by primary surgical excision and cryotherapy under local anaesthesia.

Results: Histology of the excised specimen showed an invasive malignant melanoma with surrounding in situ conjunctival changes arising from a naevus. The melanoma was 10.5 mm thick, focally necrotic, and had a mitotic count of 11/mm² focally. The patient responded well to surgical treatment. She gave birth to a healthy boy, and the placenta showed no evidence of metastatic melanoma. There has been no recurrence or distant metastasis during 5 years of follow-up.

Conclusions: CM during pregnancy is extremely rare. Because of possible transformation to malignant melanoma, we recommend close monitoring of females known to have pigmented conjunctival lesions of the conjunctiva during pregnancy.

0167

Asymptomatic cerebral ischemic event following intra-arterial administration of chemotherapy for retinoblastoma

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Purpose: To describe a case of an asymptomatic cerebral vascular event in a child treated with intra-arterial chemotherapy for retinoblastoma.

Method: Single case report.

Results: A 24 month old Asian female presenting with bilateral retinoblastoma (Group D and E) was treated with systemic intravenous chemotherapy followed by consolidation with single agent melphalan administered by uncomplicated intra-arterial administration via the external carotid x 3. Routine post treatment MRI one month later demonstrated asymptomatic subacute ischemia of the CNS. Two and ½ years later the patient remains asymptomatic with no focal neurologic deficit and retention of the right globe.

Conclusions: Cerebral vascular events following intra-arterial chemotherapy for retinoblastoma are well described and a known treatment complication. These events may be clinically silent and asymptomatic. We recommend that all children treated with this modality undergo routine post procedure neuroimaging and receive long term neurologic and neuropsychologic assessment during follow up.

0171

Malignant transformation of a multi-operated divided nevus of the eyelids

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Purpose: To report the case of an exceptional transformation of a divided nevus into melanoma

Methods: A woman in her early fifties had regular follow-up in ocular oncology because of a persistent divided nevus of the left upper and lower eyelids. Multiple surgeries had been performed on the nevus during childhood.

Results: A pigmented lesion occurred at the inferior part of the divided nevus. A biopsy was performed and showed *in situ* melanoma. A full thickness removal of the whole inferior eyelid allowed tumor clearance. Reconstruction of the inferior eyelid was performed. At 3 years follow up there was no local tumor recurrence and no metastases.

Conclusion: Divided nevi have a low risk of malignant transformation therefore partial excisions are acceptable for cosmetic or functional issues. Lifelong follow-up is recommended.

0172

Choroidal metastasis from lung cancer treated by iodine-125 brachytherapy

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Purpose: To report a case of choroidal metastasis from lung cancer.

Methods: A 53-year-old women with known lung cancer noted reduced visual acuity in the right eye. She was found to have an choroidal tumor measuring 10.1×3.2mm. The choroidal tumor was treated by iodine-125 plaque brachytherapy(80Gy to apex).

Results: Tumor regression to 5.7×1.2mm was documented at the 12-month follow up.

Conclusions: Lung cancer metastasis to the choroid can be treated by plaque brachytherapy. Useful vision and quality of life can be well preservation.

0173

A young woman with an old person's tumor

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Purpose: To present an unusual finding in a young woman that is generally found in older patients.

Methods: Case report. A 42 year old woman with vision of 20/15 in both eyes was referred for a newly-discovered amelanotic tumor in her left eye.

Results: In the left eye, there was a yellow choroidal mass inferonasally with speckles of RPE hyperplasia on its surface. By ultrasound the mass was calcified, suggestive of choroidal osteoma, sclerochoroidal calcification, or osseous metaplasia of RPE. By OCT, we visualized the mass in the sclera with a slightly irregular surface compressing the overlying choroid. There was no sign of nevus or melanoma and we diagnosed sclerochoroidal calcification. Serum levels of calcium and parathyroid hormone were normal.

Conclusions: Most patients with sclerochoroidal calcification are elderly. Younger patients on calcium supplements or with underlying syndromes like Gitelman syndrome or Bartter syndrome can manifest this deposition. Checking the serum levels of calcium, phosphorus, magnesium, potassium, parathyroid hormone, calcitonin as well as urine for calcium, phosphorus, magnesium and potassium would be warranted.

0177

Annular ciliary body melanoma?

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Purpose: To present the evolution of a case diagnosed as annular ciliary body melanoma in which enucleation was indicated.

Method: Treatment and follow up of a woman diagnosed as having annular melanoma with angle spreading of the tumor in circular fashion.

Results: 1 year after brachytherapy and cataract surgery, there is no sign of active tumor.

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Conclusions: Annular melanomas are very unusual, and the thickening of the ciliary body with malignant cells in all the angle is not the same as annular tumor.

0180

Acute large proptosis in an African American female patient: Case Report

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Purpose: To present the clinical course, diagnosis and management of an orbital condition with atypical presentation

Method: Case review of a 64-years-old female referred to evaluate an acute and rapidly progressive proptosis with left upper eyelid swelling. Clinical findings, imaging, histopathology and treatment were reviewed.

Results: Patient exhibited unilateral, proptosis with upper eyelid firm mass, without signs of acute inflammation. Orbital imaging showed ill-defined anterior orbital mass with infiltration of lacrimal gland and extraocular muscles. Differential diagnosis included orbital metastasis, infiltrative, or lymphoproliferative disease. Orbital biopsy provided a definitive diagnosis. Patient was treated accordingly which yielded complete resolution of proptosis. Further systemic evaluation was necessary in this condition.

Conclusions: This patient showed an unusual presentation and course for this orbital condition. Orbital biopsy and subsequent systemic assessment provided a treatment plan that controlled her condition.

0181

Neoadjuvant Chemotherapy in Sebaceous Gland Carcinoma with orbital extension

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A 41-year-old female presented with an orbital extension of a caruncular mass, with a part of it located in the inferomedial eyelid. The patient gave a history of excision biopsy 8 months ago, which was histopathologically diagnosed as basal cell carcinoma. She also gave a history of tumor recurrence, which gradually progressed to assume the form of the presently visible caruncular mass. Computed tomography of the orbits showed the mass extending into the left orbit inferomedially. There was no evidence of metastasis. A histopathological diagnosis of an undifferentiated sebaceous gland carcinoma was made post incision biopsy of the caruncular lesion. Neoadjuvant intravenous systemic chemotherapy with Cisplatin and 5-Fluorouracil was initiated in an attempt to reduce the size of the tumor. At the completion of three cycles of tri-weekly chemotherapy there was total clinical resolution of the tumor thereby obviating the need for surgery. The patient subsequently underwent external beam radiotherapy to eradicate microscopic tumour remnants and was doing well at a follow up of 25 months. Thus, neoadjuvant chemotherapy causes significant tumour reduction, downstages the disease, provides excellent locoregional tumor control and prevents distant metastasis thereby improving tumour free survival.

0185

A slowly growing optic nerve mass in an adolescent: Case Report

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Purpose: To present the clinical course, diagnosis and management of a slowly growing optic disc mass in a 15-year-old male

Method: Review of a patient who was referred to evaluate an optic nerve head mass that has been slowly growing over 7 years and associated with recent decline in vision.

Results: The mass appeared white grey in color, with protrusion into the vitreous. Clinical differential diagnosis included astrocytoma, retinocytoma, or retinal hamartoma. Systemic examination and MRI showed no associated abnormality. Tumor biopsy and histopathology provided a diagnosis, which required repeating the MRI with a certain technique to confirm the definitive diagnosis.

Conclusions: This patient presents with unusual presentation of an optic disc tumor. The diagnosis was reached through histopathology and was confirmed with a specific MRI technique.

0192

Genetic Analyses of Multifocal Uveal Melanoma

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Purpose: To describe the genetic analyses of two independent choroidal melanomas, a malignant melanoma and a malignant melanoma arising from a nevus, in the same eye.

Method: A 52-year-old woman presented with a symptomatic, large pigmented choroidal melanoma in her left eye. Family cancer history was negative and the right eye was unremarkable. Best-corrected visual acuity was 20/150 OS and intraocular pressure was 16 mmHg OS. Ultrasonography detected a mushroom-shaped tumor measuring 10.6mm in diameter and 11.2mm in thickness with overlying subretinal fluid and intravascular pulsations, and no extrascleral extension (lesion 1). Further ocular examination revealed a 9mm ciliary body mass superiorly (lesion 2). Enucleation and was performed and specimens were sent for immunohistochemical and genetic analyses.

Results: The enucleated specimen revealed two primary lesions confirmed by serial sections. Lesion 1 was a malignant melanoma, predominantly spindle cell type with formation of cavitation within the herniated component. Genetic studies showed GNAQ mutation and copy number gain on Chromosome 17q21-25. Lesion 2 was a malignant melanoma, predominantly spindle cell type with pronounced vasculogenic mimicry, arising from a nevus. This tumor was positive for GNAQ mutation, and copy number gain on Chromosome 17q22-25 and loss on 14q23-32. Bap1 mutation was negative.

Conclusions: Cases of two distinct uveal melanomas in one eye, with one arising from a nevus, are extremely rare. Cytogenetic analyses of these types of cases may help us better understand the pathogenesis of uveal melanomas.

0194

A Puzzling Pale Choroidal Mass

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Purpose: A 42-year-old woman with no past medical history presented with decreased vision in the left eye of 2 weeks' duration. She was first seen in her local town and referred to the ocular oncology service at the University of Washington for a "choroidal mass". Her exam was significant for decreased vision of the left eye (20/30), and cells in the anterior chamber and the vitreous of both eyes. Dilated exam of the right eye was unremarkable. Dilated exam of the left eye revealed a large, pale choroidal mass with indistinct borders in the temporal macula.

Method: A panel of blood work and imaging were ordered for the potential diagnoses (primary intraocular lymphoma, metastatic disease, or inflammatory lesion). When the patient returned one week later her vision had decreased to 20/200 in the left eye and the pale choroidal lesion was progressing.

Results: The workup was negative other than a positive Bartonella Henselae (BH) IgG (1:256). Upon further questioning, the patient lives with 4 cats and has multiple recent cat scratches. The diagnosis of bartonellosis with choroidal granulomas was made. She was treated with a one month course of doxycycline and oral steroids. Within 4 weeks the granulomas had disappeared and the patient was seeing 20/40.

Conclusions: Though choroidal granulomas are common in diseases like tuberculosis, there are only rare reports of BH resulting in choroidal masses. BH should be considered on the differential of patients with pale choroidal masses, especially in cases where inflammatory causes are likely.

0197

Atypical presentation of bilateral retinoblastoma with vitreous floaters and sub-internal limiting membrane floccular deposits in an 11-year-old Asian Indian male

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Purpose: To report a case of bilateral retinoblastoma in 11 year-old-child presenting with floaters and sub-internal limiting membrane (ILM) floccular deposits

Method: An 11-year-old male child presented with floaters of 4 months duration. He was referred with a diagnosis of sarcoidosis. Examination revealed circumscribed collection of whitish, subhyaloid floccular nodules and fine deposits at posterior pole in both eyes, with occasional vitreous cells. No solid tumor was seen in either eye. Swept source Optical coherence tomography (SS-OCT) revealed moderately reflective dot-like echoes in sub-ILM space. Diagnostic vitrectomy of right eye with aspiration of sub-ILM deposits and cytopathological examination was suggestive of retinoblastoma. Intravitreal Melphalan (20 microgram/0.02ml) was injected in right eye on same day, followed by 6 monthly cycles of high-dose systemic chemotherapy (Vincristine, Etoposide, Carboplatin). Metastatic work-up (Bone-marrow biopsy and cerebrospinal fluid aspiration) was negative for malignant cells. Genetic testing for RB1 mutation was negative. Ocular lesions were completely resolved by 13 weeks of treatment. The patient developed brain metastases after 20 weeks of presentation and was successfully treated with external beam radiation therapy (EBRT). Vitreous seeds recurred in both eyes 44 weeks after presentation and was successfully treated with intravitreal chemotherapy (Melphalan 20 microgram/0.02ml and Topotecan 20 microgram/0.02ml). There was no extra-ocular spread from sclerotomy sites.

Results: Retinoblastoma and brain metastases resolved with multimodal treatment without recurrence at 59 weeks follow-up.

Conclusions: Atypical manifestation of retinoblastoma can be seen in older children presenting with 'floaters' and bilateral deposits of sub-internal limiting membrane (ILM) floccular aggregations without solid tumor.

0203

Presumed bilateral ICE syndrome diagnosed as bilateral iris melanoma

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Method: Case report: A 58 y.o. mild myopic caucasian lady was found to have a bilateral pupillary distortion by her son “a medical student” in December 2015. Bilateral iris melanoma was supposed. Her more recent ophthalmologic clinical history dated back to 2001 when a bilateral nerve cupping was noticed leading to a series of exams to rule out OU low pressure glaucoma (VFs, IOP, NFA analyzer, CCT measurements, diurnal IOP curves). Iris anomalies were never reported in all AS examinations, the cornea resulted always transparent and IOP was found to exceed 20 mmHg two times only at pneumotonometry. CCTs were always over 550 micrometers.

Results: From January 2016 she underwent several HF ultrasound examinations showing a bilateral asymmetrical shrinking with thick masses of PE and stretched thin peripheral iris. Due to the hypotension of a bilateral ICE she was also seen by one internationally known expert of corneal diseases, who excluded corneal signs of ICE at the moment but strict follow-up of the optic disk cupping.

Conclusion: Bilateral ICE is a rare event. Female gender and glaucoma are present in the literature although glaucoma is described as high pressure and probably due to the endothelium anomalies that are not present in this case. The present case has its beginning late last year and its behaviour at HF ultrasonography was never described before.

0208

Case report: retinoblastoma or Coats?

Junyang Zhao

Beijing Children's Hospital, Beijing, China

Purpose: 4 years girl, DOB is Oct 17, 2012; No family history.

Strabismus was found at Oct 2015, and vision decreased from Oct 3, 2016 for her left eye. Right eye is normal.

Examination:

B Scan:

CT:

MRI:

FFA:

EUA:

Diagnosis: Coats or retinoblastoma?

0219

Mystery Case

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¹*Eye Research Center, Rassoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran,* ²*Mahak Hospital, Mahak Charity, Tehran, Iran*

Purpose: To report an interesting case

Method: 11 year old boy was referred to our clinic with history of painless blurred vision (OU) from one month ago. No history of ocular or systemic disease was evident.

Results: BCVA was 10/10 (OD) and 3/10 (OS). Fundus examination revealed choroidal thickening, choroidal fold, some subretinal fluid and flame shaped hemorrhages in both eyes particularly in the left eye.

Conclusions: It will be presented as an unknown case for opinions from the audience. Diagnosis will be presented at the end.

0225

Case

Michael Seider

Northern California/Hawaii region of Kaiser Permanente, California, USA

This is the case of a 35 year old woman who presents with a slowly growing amelanotic (very) vascular mass in the anterior chamber associated with high IOP and ON cupping. On UBM, the mass in the AC shows cystic spaces and a ciliary body component is revealed. Because of some concern for medulloepithelioma, an open biopsy was performed (edited video to be shown).. Pathologic examination reveals spindle cells with +melanin stains (melanoma). Post-plaque photos also show atrophy of tumor vessels.

0226

Diffuse Choroidal Melanocytoma Masquerading as Diffuse Choroidal Melanoma

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Purpose: To report a rare case of diffuse choroidal melanocytoma masquerading as melanoma.

Method: Case Report. A 40-year-old Asian Indian male presented with a history of blurred vision LE for 12 months. He had been earlier diagnosed to have choroidal melanocytosis and had been advised observation by a retina specialist. He had acute loss of vision 6 weeks ago, following which he was noted to have definite growth in the size of the lesion and exudative retinal detachment, and was referred to the Oncology Service for further management. His visual acuity was reduced to only light perception. Anterior segment was normal. Fundus examination showed a diffuse placoid choroidal mass with maximum thickness of 2.7 mm, with intense orange pigment and diffuse subretinal fluid. Based on the documented growth and clinical features suggestive of diffuse choroidal melanoma, enucleation was performed. However, histopathology features of choroidal melanocytoma. There was no evidence of choroidal melanoma on serial sections through the entire tumor. HMB45 was negative, Melan-A was negative and Ki-67 <0.5%.

Conclusions: Diffuse choroidal melanocytoma can have overlapping features of and masquerade as choroidal melanoma.

0229

Venetoclax can cause central serous-like chorioretinopathy

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Hadassah-Hebrew University Medical Center, Jerusalem, Israel

A 44-year-old man with CLL (del 17p) who relapsed twice after complete remission and partial remission to the last line of treatment was started on venetoclax, a first-in-class BCL-2 inhibitor designed to treat relapsed or refractory CLL patients who have a 17p deletion (Del(17p)) chromosomal abnormality. Two days after the dose was increased to 50mg/d he started complaining of blurred vision and vision dropped from 20/20 in BE to 20/70 (RE) and 20/28 (LE). Changes in both retinas proved to be macular sub-retinal fluid (SRF) collections on optical coherence tomography (OCT). The findings matched the central serous-like chorioretinopathy (CSR-like retinopathy) seen with MEKi treatment. Treatment continued until the patient developed febrile neutropenia due to transformation into systemic and CNS DLBCL complicated by Cryptococcal CNS infection (neither of which share the ocular findings of CSR-like retinopathy) and vision improved within days. Life-extending treatments should not be stopped because of SRF and some reduction in vision. We call upon clinicians to follow the visual acuity and perform baseline and routine OCT exams for patients scheduled for venetoclax treatment.

Schneiderian papillomas of the lacrimal sac

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Purpose: To present 5 cases of Schneiderian papillomas originating from the lacrimal sac, and to review the management principles.

Methods: The medical records of all patients were retrospectively reviewed. Details of clinical presentation, histopathological analysis, surgical approach and postoperative outcomes were recorded.

Results: Five patients with proven Schneiderian papillomas on histopathological analysis were included in this review. Inverted papillomas were the most common morphologic subtype, and some cases demonstrated features of squamous dysplasia and carcinoma in situ. All patients presented with chronic epiphora and most had a palpable mass. External dacryocystorhinostomy was performed and a diagnostic tissue biopsy was obtained. Screening for focal human papillomavirus (HPV) activity was performed using immunohistochemistry (p16 staining). All patients underwent a combined external and endoscopic en bloc resection with the multidisciplinary expertise of Oculoplastics and ENT surgeons. Adjuvant radiotherapy was used occasionally. All patients remained tumour-free at last follow-up.

Conclusion: Schneiderian papillomas of the lacrimal sac are rare, and have the potential for malignant transformation. There is no universally accepted management algorithm. Screening for high-risk HPV subtypes with p16 staining is warranted. This case series demonstrates that an initial wide surgical resection offers the best chance of recurrence-free survival.

0231

Solitary isolated neurofibroma of the conjunctiva

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Moorfields Eye Hospital, UK

Purpose: To report an isolated conjunctival neurofibroma in a patient without systemic involvement.

Methods: Case report.

Result: A 59-year-old white male was referred because of a long-standing left bulbar conjunctival lesion with slow enlargement. On examination, a 5x 5-mm pink circumscribed, mobile conjunctival mass was seen, located deep in Tenon's layer of the inferior palpebral conjunctiva. Excisional biopsy was performed. Histopathology confirmed the diagnosis of neurofibroma. At last follow-up there were no signs of recurrence of the lesion or systemic involvement.

Conclusions: Solitary isolated neurofibroma of the conjunctiva without systemic neurofibromatosis is extremely rare, but should be considered as one of the differential diagnosis of conjunctival lesions.

0232

Partial lamellar sclerouvectomy for uveal tumors

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Purpose: To evaluate the results and complications of partial lamellar sclerouvectomy (PLSU) procedure for uveal tumors performed by one surgeon (AKG).

Methods: Medical records of 43 patients who underwent PLSU for uveal tumors (iridociliary, ciliochoroidal, and choroidal) between May 1999 through May 2016 were evaluated retrospectively.

Results: The mean patient age was 51 years (range: 21-83). The histopathologic diagnosis was uveal melanoma in 27 (63%) cases, uveal nevus in 7 (16%), uveal melanocytoma in 3 (7%), iris stromal cyst in 3 (7%), Fuchs adenoma in 1 (2%), metastatic cancer in 1 (2%), and foreign body in 1 (2%). Postoperative complications included cataract in 23 cases (54%), transient vitreous hemorrhage in 10 (23%), scleral thinning in 9 (21%), posterior synechiae in 7 (16%), hyphema in 4 (9%), and secondary glaucoma in 4 (9%). At a mean follow-up of 38 months (range: 12-156 months), there was no tumor recurrence and only one case of death attributable to uveal melanoma metastasis.

Conclusions: PLSU seems to be an effective treatment option in selected cases of iridociliary and choroidal tumors, especially in developing countries where radiotherapy options are limited. Several postoperative complications inevitably occur and require frequent patient monitoring.

Surgical navigation assisted endoscopic orbital surgery in the management of thyroid ophthalmopathy

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¹*Department of Ophthalmology, Ankara University Faculty of Medicine, Ankara, Turkey, 2 Department of Otorhinolaryngology, Head and Neck Surgery, Ankara University Faculty of Medicine, Ankara, Turkey*

Purpose: To demonstrate the use of surgical navigation and endoscopic surgery in the management of orbital pathology.

Methods: Two cases with thyroid ophthalmopathy underwent balanced medial and lateral wall decompression using surgical navigation and orbital endoscopic surgery in one eye. First, the anatomical region to be operated was scanned and uploaded into the computer system to create a virtual patient image.

Results: The CT based surgical navigation was then used to assess the extent and amount of bone removed on the medial and temporal orbital walls and to delineate the critical orbital structures. Endoscopic surgery, on the other hand, was found to provide better visualization of the orbital structures compared to standard headlight and operation room lighting conditions. Both cases had proptosis reduction of 5 mm and 6 mm respectively in the operated eyes 1 month postoperatively. There were no complications related to surgery.

Discussion: The advantages of using surgical navigation include that the position of a tracked instrument can be shown in relation to the patient's preoperative anatomy on CT images. Therefore, it is possible to navigate the location of a tracked instrument to visualize the proximity to critical structures and to define the extent of surgery such as the amount of bone removal as in our 2 cases. Endoscope assisted approach provides increased light intensity and increased magnification of the orbital structures.

0234

C-B Choroidal Malignant melanoma masquerading as granuloma in a young child

Vicktoria (Vicky) Vishnevskia – Dai

The Goldschleger Eye Institute, Yehud, Israel

Purpose: to report a rare case of malignant melanoma atypically presented at a very early age.

Case report:

A healthy 13 years old girl presented at the age of 3 years to another hospital with RE strabismus and leukocoria.

She was diagnosed there as uveitis with vitreous hemorrhage and a granuloma. Full uveitis revealed positive IGM antibodies to CMV and to Toxocara. Pars plana vitrectomy was performed - no cytology report was found in her chart. Due to persistent vitreous hemorrhage second vitrectomy was performed. B-mode US examination at that time demonstrated attached retina vitreous hemorrhage and a solid -hyper echogenic mass with membranes and high spikes on A mode. During the second pars plana vitrectomy the surgeon reported: when the VH was cleared, a large mass superior temporal in location was noted, adjacent to the superior temporal vitrectomy ports. The surgeon felt the port is touching the mass, there for the trochar was moved to 11`. No blood vessels were noted on the mass and no bleeding source was noted within the mass. No change of the mass were demonstrated on follow up US.

Six months later, she presented to our service with a darkly pigmented subconjunctival mas at 10-11` suspected to represent iatrogenic extraocular extension (EOE) of the tumor. Fine needle aspiration biopsy and I -125 brachytherapy plaque were performed. The tumor and EOE regressed the child is alive and well since.

Conclusion: Malignant melanoma can atypically present at all ages including very early age.

0235

Treatment outcomes for small uveal melanoma

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Purpose: To report the long term results of ocular radiotherapy (proton beam (PBR) or 125I brachytherapy, depending on tumor location) for T1 uveal melanoma (UM), defined according to the 7th edition of the American Joint Committee on Cancer TNM tumor staging system.

Methods: Retrospective analysis of patients treated in Institut Curie between 1987-2010 and included in a prospective database. Main outcome measures were: tumor control, eye retention rate, and disease-free survival. The effect of treatment on visual acuity (VA) were assessed on patients treated with proton beam radiotherapy (PBR), comparing tumors involving the macula or optic nerve to those located >3 mm from both structures.

Results: Among 5149 UM treated in the study period, 841 were T1. Treatment was PBR in 71% and plaque in 29% of cases. Median follow-up was 9.6 years (range 5-26 years). Tumour control was achieved in all but 5 cases (98,2%). Secondary enucleation was performed in only 3% of cases. Disease-specific survival at 10 years was 94%. In 424 eyes treated by PBR, initial VA was 6/10 and final VA was 3/10. Tumour located >3mm from macula or optic disc retained VA of 6/10 or better in 70% of cases.

Conclusion: Early treatment of small UM allows excellent tumour control and good visual acuity.

Melanocytic Lesions of the Conjunctiva: The 2017 Stallard Lecture

Ralph C. Eagle, Jr.

Ophthalmic Pathology Laboratory, Wills Eye Hospital, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, Pennsylvania, USA

Pigmented lesions of the conjunctiva include some of the most difficult neoplasms evaluated by ophthalmic pathologists. Most are melanocytic in nature and include constitutional melanosis, a variety of nevi, and the important spectrum of intraepithelial melanocytic proliferation that potentially can progress to fatal conjunctival melanoma. The clinical and histopathologic features of approximately 120 melanocytic lesions of the conjunctiva accessioned by the Wills Eye Pathology Laboratory during the past two years will be discussed.

The pathologist must answer several questions when evaluating pigmented conjunctival lesions: is the melanin pigment confined largely to the cytoplasm of squamous epithelial cells?, are increased numbers of melanocytes present?, are the melanocytes atypical? And are the atypical melanocytes confined to the basal part of the epithelium, involve more superficial layers, or invade the substantia propria? Assessment of melanocytic hyperplasia in routine H&E-stained sections may be difficult when pigment production is sparse. Immunohistochemical stains for melanocytic markers Melan-A and SOX10 using red chromagen are helpful adjuncts in the assessment of melanocytic lesions, as they can disclose melanocytic hyperplasia as well as cellular atypia and nuclear pleomorphism. HMB45 and proliferation marker Ki-67 typically do not stain the subepithelial component of nevi, and hence, serve as a putative marker for benignancy. Conjunctival nevi evolve over time. Compound nevi gradually lose their junctional component and become subepithelial nevi, and characteristic cystic rests of conjunctival epithelium often enlarge. Junctional nevi are exceedingly rare at any age, and persistence of the junctional component in an adult should be considered primary acquired melanosis with atypia until proven otherwise. Alternative nomenclature for that important precursor of conjunctival melanoma will be discussed.

Recent developments in intravitreal therapy in retinoblastoma - Judith Kingston Lecture

Francis Munier

Lausanne, Vaud, Switzerland

Until recently, retinoblastoma seeding was considered the main reason for failure of conservative management. Successful control of subretinal seeding was significantly advanced with the advent of intra-arterial chemotherapy as published by Abramson in 2008. Subsequently intravitreal chemotherapy (IViC), using the safety-enhanced injection technique we described in 2012, has led to the wipeout of vitreous seeding. In this lecture I will describe how we have subdued the final frontier, namely aqueous seeding, which has remained the ultimate resisting retinoblastoma sanctuary. IViC has excellent efficacy, with virtually 100% control of vitreous disease achieved. This has resulted in the eradication of EBR and has allowed unprecedented globe salvage rates. However, its potentially blinding toxicity and risk of tumor spread has raised serious concerns. In this lecture I will also address these concerns by demonstrating that provided strict guide-lines are adhered to, vision-threatening retinal toxicity of melphalan (grade 4 and 5) is not dose-related but rather technique-related. I shall also present the results of a highly sensitive method of assessing retinoblastoma RNA reflux, showing no risk of tumor spread.

Differences in genomic landscape of uveal and cutaneous melanoma: implications for targeted treatments

Nick Hayward

QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia

Significant progress has been made for the treatment of cutaneous melanoma (CM) both in terms of targeted therapies and immunotherapies. However, the success of such treatments does not translate to the less common melanoma subtypes. This is particularly clear for the second most common form of melanoma, uveal melanoma (UM), which has shown poor response to targeted therapies and also to immune checkpoint inhibitors. The poor performance of UM in clinical trials, especially for targeted therapies, is largely due to the fact that most clinical trials are based on therapies developed for CM and are not specifically tailored to UM, which is a genetically and mechanistically, distinct subtype. Indeed, despite UM being the most common primary ocular cancer, there is very little understanding of the cellular mechanism underlying UM development, crucial for the development of effective therapies.

Unlike CM, where *BRAF* and *NRAS* are the main driver oncogenes, the primary driver oncogenes in UM are *GNAQ* and *GNA11*, which encode the alpha subunits of heterotrimeric G-protein complexes. *GNAQ* or *GNA11* are mutated in a mutually exclusive manner in ~83% of cases. Little is known about how these genes act as drivers for UM, partly due to paucity of investigation and partly to the fact that these genes are towards the apex of their signalling cascade and have effects on multiple signalling pathways and thus far have not proved to be actionable therapeutic targets. *PLCB4*, which encodes phospholipase C beta 4 (PLC-β4), was recently found to be recurrently mutated in UM, with a hotspot mutation at amino acid D630 in ~2-4% of cases. These mutations are mutually exclusive with those in *GNAQ* and *GNA11*, suggesting that they provide a driver oncogenic role in UM acting in the same pathway. Indeed, PLC-β4 is proposed to function downstream of, and to directly interact with, *GNAQ* and *GNA11*. Additionally, the transcription factor Yes-associated protein (YAP) has been demonstrated to be activated independently of PLC-β and to be important for the proliferation and survival of UM cells *in vitro*. This activation instead seems to occur downstream of mutant *GNAQ/GNA11* via Trio, a guanine nucleotide exchange factor, and the downstream GTPases Rho and Rac, through their regulation of the actin cytoskeleton and angiomin. A better understanding of the functional consequences of the driver mutations in UM should provide much needed insight into the mechanism of UM initiation as well as highlight important signalling pathways to investigate for therapeutic intervention.

Melanoma and the Hippo pathway

Mark Shackleton

Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

New drug therapies have revolutionised treatment of melanoma over the last decade, offering patients with metastatic disease hitherto unheard of benefits in terms of survival and quality of life. Clearly, on the back of fundamental discoveries in molecular signaling pathways that drive cancer growth and immune regulation of tumors within patients, the age of therapeutic nihilism in melanoma is over. However, despite these developments, the vast majority of patients with metastatic melanoma still die prematurely because of their disease, and the search for new therapies remains as keen as ever.

We are focused on extending and exploiting remarkable progress in understanding biological functions of the Hippo molecular signalling pathway, which is the most recently discovered major tumor suppressor regulatory network. Hippo pathway proteins, which were only identified just over a decade ago as key regulators of organ size in *Drosophila* development, are also important mediators of initiation and progression in numerous cancers. One of the best characterised of these is uveal melanoma, in which canonical activating mutations in G protein-coupled receptor components GNAQ and GNA11 have been shown to drive oncogenic signalling via Hippo proteins, specifically by activating Yes-Associated Protein (YAP), a key oncoprotein in the pathway. Our and other studies show that targeting YAP, which is a major focus globally of pharma and academic drug development programs, has wide-ranging anti-melanoma effects, even in cutaneous melanoma. Progress towards YAP targeting in melanoma will be discussed.

Molecular characterisation of cutaneous melanoma

Richard Scolyer

Royal Prince Alfred Hospital, NSW, Australia

In recent years, whole genome and exome sequencing studies of cutaneous melanoma have demonstrated that these tumours have the highest mutation burden of any known malignancy.

The heavily mutated landscape of cutaneous melanoma involves both the coding and non-coding regions of the genome and novel and known ultraviolet radiation signatures of mutagenesis have been identified. These studies have also demonstrated marked differences in cutaneous melanomas compared to ocular as well as acral and mucosal melanomas. Acral and mucosal melanomas are dominated by structural chromosomal changes and mutation signatures of unknown aetiology, not previously identified in melanoma.

Lessons from cutaneous melanoma for the ocular oncologist

Hans Grossniklaus

Dept of Ophthalmology, Emory University, Atlanta GA, USA

Cutaneous melanoma of the eyelid is rare, accounting for <1% of all skin melanomas. The peak incidence is 50-80 years, and the lower eyelid is the most common site. These tumors may be only in the skin or may be contiguous with conjunctival melanoma. Eyelid melanoma may be suspected by the ABCDE signs. The pathologic classification of eyelid skin melanoma is: superficial spreading (most common), lentigo maligna (similar to PAM of conjunctiva), and nodular. Cutaneous melanoma of the eyelid is staged using the Breslow thickness and Clark level. Cutaneous melanoma evolves either sequentially via accumulation of mutations or from stem cells that acquire mutations. These mutations include BRAF, AKT, CDKN2A, NRAS-cKIT, CCND1, p16^{CDKN2A}, PTEN, PI3K, and MITF. Treatment depends on the stage of the melanoma: Stage 0-complete resection; Stages II and resectable III-excision and lymph node management; Stage III, IV and recurrent melanoma-immunotherapy, chemotherapy, targeted therapy or palliative local therapy. Targeted therapy includes BRAF and MEK inhibitors; immunotherapy includes CTLA-4 and PD-1 checkpoint inhibitors, and injectable immunotherapy includes T-VEC. Ophthalmic side effects of checkpoint inhibitors include uveitis, which may require topical and/or systemic corticosteroid therapy. Cutaneous melanoma from other sites may metastasize to the eyelid, orbit, or eye, including the retina/vitreous. Management of metastatic melanoma to the eye or ocular adnexa is individualized and done in conjunction with medical oncology.

Eyelid and conjunctival melanoma, crossing the grey line

Bitá Esmali

University of Texas MD Anderson Cancer Center

Conjunctival and eyelid melanomas are rare and important causes of ocular morbidity with a real potential for recurrence and metastasis. In this section the clinical and pathologic features that are associated with aggressive clinical behavior for ocular adnexal melanoma will be discussed. As well, the areas of overlap between conjunctival and skin melanomas, particularly histologic and clinical features defining the AJCC TNM criteria and prognostic factors for recurrence and metastasis will be reviewed. Surgical and new immunotherapy options for complex ocular adnexal melanomas will also be briefly mentioned.

Sentinel node biopsy in cutaneous melanoma

John Thompson AO

Melanoma Institute Australia, The University of Sydney, Sydney, NSW Australia

The outcome for patients with many types of primary malignant tumours is predicted with considerable accuracy by the presence or absence of metastatic disease in regional lymph nodes. The minimally-invasive technique of sentinel node (SN) biopsy provides accurate staging in these patients. Pioneering studies in patients with melanoma led the way, and were soon followed by studies in breast cancer patients, then in patients with a wide range of other cancers (including colorectal, gastric, thyroid, prostate, lung, gynaecological, SCC of skin, and Merkel cell carcinoma).

The SN concept is simple. Lymphatic drainage from any site in the body passes first to a "sentinel" lymph node, then onwards to other nodes before the lymph eventually flows into the blood stream. A SN is thus defined as any node that receives direct lymphatic drainage from a tumour site. SNs can be identified by lymphoscintigraphy, most reliably performed with radio-labelled small-particle colloids such as antimony sulphide (particle size 5-15 nm). Dynamic imaging allows lymphatic channels passing directly to SNs to be visualised, and identifies second tier nodes that do not receive direct lymphatic drainage. Large studies in melanoma and breast cancer patients have shown that if SNs are tumour-free, the remaining nodes in the draining node field very rarely contain tumour. In melanoma patients, knowledge of the regional node status allows rational treatment planning based on accurate staging, and is essential for stratification of patients in clinical trials. A large international melanoma trial (MSLT-I) has shown that treatment based on SN status (immediate radical lymph node dissection in SN-positive patients) substantially improves survival outcome compared with later lymph node dissection when metastatic nodal disease becomes clinical apparent.

Screening for metastatic uveal melanoma

Stefan Seregard

St Erik Eye Hospital, Karolinska Institutet, Stockholm, Sweden

Uveal melanoma metastasizes preferentially to the liver and hence screening for metastatic disease is largely confined to the liver, typically using liver imaging by ultrasonography or magnetic resonance tomography. Techniques used in experimental settings include serum biomarkers and detection of circulating tumour cells.

As there is till no effective method to treat metastatic uveal melanoma, the choice of screening technique, interval between screening procedures and duration of screening need to be carefully balanced for likelihood to detect metastases and patient morbidity caused by screening.

Management of metastatic uveal melanoma at Thomas Jefferson University

Takami Sato

Thomas Jefferson University, Philadelphia, PA, USA

Despite successful treatment of the primary uveal melanoma, up to 50% of patients will subsequently develop a systemic metastasis, with the liver involved in up to 90% of these individuals. Recognition of the poor prognosis associated with liver metastasis has led to the development of various loco-regional treatment modalities at Thomas Jefferson University, including surgical resection, transarterial chemoembolization (TACE), immunoembolization, radiospheres, drug-eluting beads, and percutaneous hepatic perfusion, which resulted in improvement of overall survival of uveal melanoma patients with hepatic metastasis.

Controversy of the Day: Retinoblastoma

David Abramson

New York, USA

In 2017 ICRB "D" eyes are managed with enucleation, systemic chemotherapy and intrarterial chemotherapy in our center. As a result of the success of intrarterial chemotherapy only 5% of "D" eyes are enucleated in our center. Systemic chemotherapy has been abandoned for all children older than 3 months of age and for all children with retinoblastoma. The decrease in enucleation rate and abandonment of external beam irradiation and marked diminution in the use of systemic chemotherapy has not compromised patient survival-which is >99% in our center.