

CANADIAN RETINA & VITREOUS SOCIETY

FRIDAY 13 JUNE

Paper #A-00067

Preliminary experience with gamma knife radiosurgery for the treatment of choroidal melanoma

Andrew A. Mis, Garry Schroeder, Anthony Kaufmann

Purpose: Conservative measures directed toward preservation of the globe are becoming more favorable in the management of choroidal melanomas. There are published series in the literature that show the favorable use of Gamma Knife Radiosurgery (GKS) in the treatment of choroidal melanoma. We would like to describe our experience in treating patients with choroidal melanoma using Gamma Knife Radiosurgery.

Methods: Seven patients were treated for choroidal melanoma using GKS from July 2004 to January 2006. Stereotactic frames were used for head immobilization and retrobulbar anesthetic blocks and scleral sutures were employed for eye immobilization. MRI images were used for tumor localization and treatment planning. Conformal plans were generated using Leksell GammaPlan and treatments were completed in a single day. Tumor response was assessed using clinical exam and B-scan ultrasonography while treatment toxicity was assessed with visual acuity measurement, clinical exam, and indirect ophthalmoscopy.

Results: All patients completed treatment. Prescription doses ranged from 30 to 35 Gy prescribed to 45 - 50% isodose lines (IDL) which encompassed the entire tumor. Median follow-up was 28 months. Five of 7 tumors regressed in size and the remaining two tumors did not change in size. Toxicities secondary to treatment were observed in all patients and included subretinal and vitreous hemorrhage, visual decline, cataract formation and neovascular glaucoma.

Conclusions: Gamma Knife Radiosurgery may have treatment results comparable to other globe sparing treatment modalities such as plaque brachytherapy and proton irradiation, however, further study is required.

CANADIAN RETINA & VITREOUS SOCIETY

FRIDAY 13 JUNE

Paper #A-00068

Radiation retinopathy secondary to iodine-125 brachytherapy of uveal melanoma

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Purpose: Since radiation retinopathy is a major long-term complication following brachytherapy of uveal melanoma, we report our experience with the incidence, pretreatment predictive factors and the outcome in patients who developed radiation retinopathy secondary to Iodine-125 brachytherapy.

Methods: A retrospective comparative case series analysis. Patients treated by Iodine-125 brachytherapy for uveal melanoma were divided into two groups to compare the data of patients who developed radiation retinopathy versus patients who did not. Electronic chart review, for demographic, clinical, tumor-related, and brachytherapy-related data were analyzed separately for each group.

Results: Included in this study were 300 patients with a mean follow-up period of 48 months after brachytherapy. The radiation retinopathy group was 107 patients (36%). No significant differences were detected in the demographic and the tumor dimensions related data between the two groups. In the radiation retinopathy group, however, the co-morbidity with diabetes mellitus was 12% and hypertension was 24%, in comparison to 6% and 5% respectively in the non-radiation retinopathy group. In the radiation retinopathy group, the mean posterior tumor edge distance from the fovea was 5.7 mm and from the optic disc was 6.8mm, in comparison to 8mm and 8.8 mm, respectively, in the non-radiation retinopathy group. Tumor-induced retinal or vitreous hemorrhage, before brachytherapy, was detected in 13% of cases of the radiation retinopathy group in comparison to 5% in the other group. The average plaque diameter used was 16 mm in both groups.

Conclusions: Radiation retinopathy affects more than one third of the patients treated by Iodine-125 brachytherapy for uveal melanoma causing significant visual loss. Diabetes mellitus and hypertension are risk factors for development of radiation retinopathy. Proximity of the posterior edge of the tumor to the fovea and the nerve may increase the incidence of the radiation retinopathy. Tumor dimensions were not found to represent a risk factor to develop radiation retinopathy.

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FRIDAY 13 JUNE

Paper #A-00069

Management of choroidal metastases with radiotherapy using a short fractionation schedule

Pedro Salazar, David Payne, Norman Laperriere, E. Rand Simpson

Purpose: To report the outcomes of treatment of choroidal metastases with a radiotherapy protocol delivered in 5 sessions over one week.

Methods: A retrospective case series was derived from patients referred to the Ocular Oncology and Radiation Oncology service of Princess Margaret Hospital, Toronto, a large comprehensive cancer hospital.

Results: This series confirmed breast and lung cancers as the most common primary neoplasias found to metastasize to the choroid. The diagnosis of suspected choroidal metastases was confirmed by indirect ophthalmoscopy, ultrasonography and expert clinical examination. Patients were then seen by a radiation oncologist and treated with palliative external radiotherapy. A total dose of 20 Gy was delivered in 5 sessions of 4 Gy each with simulator or CT-based planning. Most plans treated bilateral orbits and both choroids though some were unilateral. Total treatment lasted 1 week. The principal outcome measures were improvement of visual acuity, partial or total resolution of subretinal fluid, and reduction in the size of the choroidal lesion. The treatments were well tolerated with no immediate adverse effects.

Conclusions: Palliative radiotherapy dose of 20Gy, delivered in 1 week (5 sessions) seems to be as effective as historically reported protocols lasting 4 weeks (20 sessions), for the management of choroidal metastases. Improving quality of life by reducing the number of hospital visits in patients with a short estimated survival is a major advantage of this approach.

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Paper #A-00070

Activation of the Renin-Angiotensin System (RAS) within rat retina is accompanied by upregulation of Receptor for Advanced Glycosylated Endproducts (RAGE) and its Ligand S100

Shelley R. Boyd, Farough Mohammadzadeh, Solomon Wang, Xu Zhao, Jim Tsoporis, Thomas Parker, Louis Giavedoni, Richard Gilbert, Filiberto Altomare, David Wong, Alan Berger

Purpose: Pre-clinical animal models and clinical trials confirm the importance of RAS to the onset and progression of diabetic retinopathy. However, the mechanism by which RAS promotes diabetic retinopathy is not understood. To address this question, we used the homozygous mRen2(27) rat, a transgenic model that carries a copy of the murine renin gene, and asked whether RAGE and its ligand S100 were upregulated. RAGE is known to upregulate VEGF in the rodent eye, and S100 can act as a neuroprotection or neurotoxic switch in the central nervous system. We additionally used the vitamin B1 derivative Benfotiamine to address, in part, the role of AGE/RAGE signaling.

Methods: Diabetes was induced in 6 week homozygous mRen2(27) transgenic rats by intra-peritoneal injection of streptozotocin (65 mg/kg); non-diabetic control Ren2(27) rats were injected with vehicle only. Non-diabetic Sprague Dawley (SD) rats, the background strain of the Ren2 rat, served as an additional control. At 1, 3 and 5 weeks after STZ injection, eyes were processed for immunohistochemistry, Western immunoblot analysis or quantitative real-time polymerase chain reaction (qPCR). Glycated albumin, fructosamine, was also evaluated. Tissue localization of RAGE and S100 was determined by epifluorescent IHC for retinal cell-specific markers, and with species-specific IgG negative controls. Total RNA was isolated using the Trizol method, and qPCR performed using SybrGreen (Applied Biosystems).

Results: By IHC, there was a clear upregulation of RAGE within Muller cells of the non-diabetic Ren2 rat compared against the non-diabetic SD rat. When made diabetic, RAGE increased further. Western immunoblot confirmed these data, and further demonstrate that S100 was simultaneously increased. Fructosamine levels were upregulated rapidly in the hyperglycemic, diabetic animals. Preliminary studies with Benfotiamine demonstrate a reduction in circulating glycated endproducts, and a shift in qPCR ratios. Analysis of the RAGE/S100 system with RAS blockade is underway.

Conclusions: This study demonstrates for the first time, that activation of retinal RAS is associated with increased RAGE expression. It also uniquely points to simultaneous S100 and RAGE upregulation. Studies are currently underway to determine the causal link between these molecules, and form the basis of novel theory of combined tissue protection with RAS and AGE/RAGE inhibition.

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Paper #A-00071

Increased apoptosis and glial reactivity in a rat model of serous retinal detachment

Filiberto Altomare, Graham Belovay, Xu Zhao, Solomon Wang, Qinghong Liang, Vinicius Saraiva, David Wong, Louis Giavedoni, Alan Berger

Purpose: Recurrent or persistent serous retinal detachments (SRDs) involving the macula can cause significant visual loss, and have limited therapeutic options. To better understand the pathophysiology of SRD, we developed an acute model in the rat. We asked if early cellular processes observed in rhegmatogenous RD, notably photoreceptor apoptosis and glial reactivity, also occurred in SRD. We extended these observations by developing quantifiable measures of the glial filamentary response and a sensitive ratio of pro- versus anti-apoptotic gene expression. We also asked if nestin, an intermediate filament often associated with neuroglial progenitor cell phenotype, could be detected.

Methods: Under direct visualization, acute SRDs were induced through superior transcleral injection of Provisc, with the goal of detaching 25% or 50% of the retina. At 24, 48 and 72 hours, whole eyes were fixed in formalin, and paraffin-embedded for H&E, TUNEL and immunohistochemical analysis. Same-species antibody controls were used. Other eyes were dissected, and the detached and non-detached segments of retina prepared for SybrGreen quantitative polymerase chain reaction (qPCR) or protein analyses. SHAM eyes served as further controls. Cell culture was used to confirm the utility of utility of Bcl-2/Bax ratios in determining the pro-survival and pro-apoptotic outer retinal response.

Results: TUNEL-positive photoreceptor apoptosis was observed in all SRDs, and was especially severe in large SRDs. By H&E, large SRDs demonstrated near full-thickness loss of the outer nuclear layer. Similar to RRDs, immunohistochemical analysis confirmed opsin redistribution in photoreceptor cells, and GFAP and vimentin upregulation in Mueller cells. Quantitative PCR of GFAP mRNA showed 5, 8 and 18-fold upregulation at the three time-points. Uniquely, we also noted upregulation of nestin within Mueller glia. Bcl-2/Bax qPCR ratios were shown to be a sensitive indicator of cell survival and cell death in vitro, and are currently under evaluation in the detached retina.

Conclusions: This study demonstrates that under acute conditions, SRDs, like RRDs, demonstrate protein redistribution in the photoreceptors, photoreceptor apoptosis, and glial reactivity. Uniquely we have developed a qPCR-based method to measure both the pro-survival/pro-apoptotic ratio, and the extent of glial cell reactivity. Both these measures will have utility in determining the relative effects of different drugs or dosing regimens for tissue protection in RD. The demonstration of nestin in the detached retina may also suggest de-differentiation or cellular plasticity that could be a potential target for novel therapies.

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Paper #A-00072

A comparison of the in vitro safety of intraocular dyes

Darana Yuen, John Gonder, Alain Proulx, Hong Liu, Cindy Hutnik

Purpose: Another group recently reported that brilliant blue G (BBG) was a safe dye for internal limiting membrane (ILM) peeling in vitreoretinal surgery based upon in vivo animal studies. In vitro toxicity was not reported. The purpose of the present study was to compare the in vitro toxicity of BBG to indocyanine green (ICG), the current gold standard, as well as to trypan blue (TB) and evans blue (EB). A demonstration of in vitro safety would further support a potential paradigm shift in the first choice of adjuvant dye for ILM peeling.

Methods: The toxicity of four dyes was tested in two different cell cultures. These were a commercially available human retinal pigment epithelial cell line known as ARPE-19 and a primary murine retinal ganglion/ glial mixed culture. The dose-dependent toxicity of the dyes was determined by exposing the two different cell cultures to each dye, at four different concentrations, for a short exposure time of 3 minutes, which is an approximation of the maximal clinical exposure during surgery. In another experiment a medium exposure time of 30 minutes was performed. Cell viability was measured using the MTT assay. Time-dependent toxicity of the dyes was also studied. All four dyes, each diluted to 1/500th of stock concentration, were applied to the ARPE-19 cells for a prolonged exposure, simulating the possible long-lasting persistence of dye in the vitreous cavity after surgery. Cell viability was measured at the 2, 24, 48 and 72 hour time point using the MTT assay. Finally, the possible influence of osmolarity was assessed.

Results: After 3 minutes of dye exposure, only BBG caused significant loss of ARPE-19 cell viability. Longer exposure times of 30 minutes resulted in toxicity from both BBG and TB, with the toxicity of BBG being greater than that of TB. Prolonged exposure at 1/500th of stock concentration of either BBG or ICG produced equivalent loss of cell viability. None of the dyes produced any significant loss of retinal ganglion/ glial cell viability after 3 minutes of exposure. However after 30 minutes of exposure, BBG, TB and EB demonstrated toxicity, with the toxicity of BBG being greater than that of TB and EB. Osmolarity was not a factor in any of the experiments.

Conclusions: Overall, BBG was the most toxic of the four dyes in vitro. In contrast, ICG was found to be relatively safe at the concentrations and exposure times tested. Based upon this study, ICG is still recommended as the gold standard adjuvant dye in ILM peeling.

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Paper #A-00073

The AMD Telescreening Project: impact on wait times and health care costs

Adnan Pirbhai, Tom Sheidow, Greg Zaric

Purpose: To evaluate the effectiveness of screening patients deemed high risk for wet AMD and establish benchmark data for time to treatment through the use of teleophthalmic screening over usual care in a tertiary retinal referral practice. To develop and describe an economic model used to establish total health care costs and cost effectiveness of telescreening compared to conventional referral methods.

Methods: Data was collected prospectively on patients screened through the AMD Telescreening Project to determine wait times to consultation and treatment, as well as association between final clinical diagnosis and telescreening diagnosis. Wait times were compared between a historical retrospective cohort of all AMD referrals within a 6 month period prior to telescreening and the telescreening group. A societal perspective was used to establish base cost of evaluation +/- first treatment only of all AMD referrals per year through telescreening and through conventional referral, separately. Expected cost per patient referred was also calculated and compared between both systems. A time/cost model was also developed to determine theoretical overall difference per patient between each system.

Results: The mean wait time to clinical evaluation from time of referral (i.e. image upload vs conventional fax/phone referral) was 19.45 ± 1.56 days and 51.69 ± 7.81 days, respectively, showing a difference of 32.24 ± 6.78 days ($p < 0.0001$). The mean wait time from telescreening referral and conventional referral to treatment was 18.93 ± 2.03 days and 30.95 ± 4.56 days, respectively. The difference was 12.02 ± 4.67 days ($p = 0.0164$). Using telescreening, the average cost per patient referred was \$705.87 vs \$1355.48 per patient referred conventionally (difference of \$649.61 per patient referred). Incremental cost effectiveness ratio (expressed as \$ per patient day waited saved) of telescreening over conventional referral methods from referral to intervention was \$14.66.

Conclusions: Compared to conventional referral methods telescreening for AMD offers patients shorter wait times to vitreoretinal evaluation and treatment. Telescreening also represents a cost effective method of accepting referrals and evaluating patients with high risk AMD.

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FRIDAY 13 JUNE

Paper #A-00074

Visual acuity and visual function outcomes following cataract surgery in the Age-Related Eye Diseases Study

Farzin Forooghian, Elvira Agron, Traci Clemons, Emily Y. Chew

Purpose: The decision to perform cataract surgery on a patient with age-related macular degeneration (AMD), especially when the patient has advanced disease, can be difficult to make. Cataract surgery is often not considered for patients with more advanced AMD because of the guarded prognosis. In order to better understand the visual prognosis for AMD patients with cataract, we evaluated the visual acuity and visual function outcomes in AMD patients enrolled in the Age-Related Eye Diseases Study (AREDS) who underwent cataract surgery during this trial.

Methods: A retrospective review of all patients who had cataract surgery during AREDS was performed. A total of 1384 patients (2182 eyes) had cataract surgery during this trial. Eyes with missing data for all covariates and outcomes were excluded. Eyes were classified as having either mild AMD (small and/or intermediate drusen only, n=512), moderate AMD (large drusen and/or pigment abnormalities, n=510), or advanced AMD (choroidal neovascularization and/or central geographic atrophy, n=136). Multivariate models were used to examine the change in visual acuity and change in visual function (VFQ-39 questionnaire score, n = 422 eyes) following cataract surgery in the various AMD groups. Models were adjusted for multiple covariates, including type and amount of cataract.

Results: A statistically significant gain in visual acuity was seen in all AMD groups. Patients with mild AMD experienced a gain of 8.66 letters ($p < 0.0001$), while those with moderate AMD experienced a gain of 6.12 letters ($p < 0.0001$). Patients with advanced AMD gained 4.07 letters ($p = 0.0001$) of visual acuity. We did not observe a significant change in overall VFQ-39 score in any of the AMD groups following cataract surgery.

Conclusions: Patients with all levels of AMD can experience a gain in visual acuity following cataract surgery. This gain of visual acuity, however, was not reflected as a significant gain in overall VFQ-39 score following cataract surgery in any of the AMD groups. An analysis of the various VFQ-39 subscale scores is currently underway, and will hopefully more accurately assess the potential for gains in vision-related quality of life in AMD patients undergoing cataract surgery.

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FRIDAY 13 JUNE

Paper #A-00075

Multiple modality imaging of type-2 idiopathic macular telangiectasia: correlation of autofluorescence, optical coherence tomography, and microperimetry findings

Farzin Forooghian, Wai T. Wong, Emily Y. Chew

Purpose: Type-2 idiopathic macular telangiectasia (IMT) is a complex disease involving telangiectasis of the parafoveal vasculature, foveal atrophy, retinal pigment epithelium (RPE) hyperplasia, and subretinal hemorrhage. As its pathogenesis is poorly understood, the use of multiple new techniques to evaluate macular structure and function may improve our understanding of the pathological changes in type-2 IMT.

Methods: Retrospective, cross-sectional study of 12 patients with type-2 IMT seen at the National Eye Institute (NEI) over a three-year period. In addition to conventional fundus photography and fluorescein angiography, optical coherence tomography (OCT) images, fundus autofluorescence (FAF), and microperimetry (MP) testing were obtained.

Results: Twenty-two eyes from 12 patients were classified into 5 staged categories based on systematic findings in parallel imaging studies. We have classified the eyes of these patients into five categories (0-4), each with a distinct constellation of findings obtained using a multiple modality approach. Category 0 eyes were unaffected, whereas the only abnormality seen in category 1 eyes was foveal hyperautofluorescence. Eyes in category 2 had fundoscopic and angiographic features of type-2 IMT along with foveal hyperautofluorescence. Additional features of category 3 and category 4 included foveal atrophy and pigment clumping, respectively. FAF hyperautofluorescence increased from category 1 through category 3, whereas category 4 eyes demonstrated a mixed pattern of hyperautofluorescence and hypoautofluorescence. Visual deficit in category 3 and category 4 eyes was related to the location of scotomata on MP testing.

Conclusions: Clinical characterization of type-2 IMT, a bilateral but sometimes asymmetric disease, can be improved with multiple modality clinical imaging. FAF imaging indicates foveal hyperautofluorescence as an early diagnostic change that precedes clinical signs and symptoms of type-2 IMT. Increasing FAF hyperautofluorescence and the emergence of FAF hypoautofluorescence with increasing disease severity suggest a primary role of the RPE in the initiation and progression of this disease.

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Paper #A-00076

Combination treatment with intravitreal bevacizumab and PDT with verteporfin in exudative age-related macular degeneration: standard fluence versus reduced fluence

Tracey Wong, Luis Riveros, Yaping Jin, Michael Brent

Purpose: To determine whether reduced fluence PDT plus bevacizumab is as effective as standard fluence PDT plus bevacizumab for treating exudative age-related macular degeneration.

Methods: Retrospective, single centre, observational study. Consecutive cases of exudative age-related macular degeneration presenting to a retina clinic treated with reduced fluence PDT plus bevacizumab (RF) with 8 months follow-up were identified. Charts were retrospectively reviewed with respect to vision, OCT retinal thickness, number of treatments necessary to achieve lesion stabilization, duration of time for lesions to remain stable. These were then compared with a series of consecutive patients who had been treated with standard fluence plus bevacizumab (SF) with 8 month follow-up using the same parameters.

Results: Preliminary results at 8 months of follow-up for RF vs SF - lesion stabilization was achieved in 80% vs 100% respectively; the mean number of PDT treatments to achieve treatment stabilization was 1.28 vs 1.14 (1-2) and mean number of injections to achieve treatment stabilization in these groups was 3.8 vs 3.1 (2-6); once stable, mean duration of stability was 148 days vs 149 days.

Conclusions: Preliminary results indicate that reduced fluence patients required slightly more PDT treatments and injections of bevacizumab, but once stable had a comparable duration of stability with those treated with combination therapy using standard fluence. Ongoing follow-up data on these patients will be presented.

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Paper #A-00077

Sterile endophthalmitis/uveitis following multiple intravitreal bevacizumab injections for wet age-related macular degeneration

Pradeepa Yoganathan, Louis Giavedoni, Tom Sheidow, David R. Chow, Alan R. Berger, Shelley Boyd, Larissa Derzko-Dzulynsky, Bradley Kates, Filiberto Altomare, David T. Wong

Purpose: Three centers report 13 patients presenting with sterile endophthalmitis, vitritis, and/or iritis after multiple bevacizumab injections, with recurrence of inflammation when re-challenged with bevacizumab or ranibizumab.

Methods: Retrospective case series.

Results: Thirteen patients presented with acute uveitis between March and November 2007 in Ontario, Canada. All were treated with intravitreal bevacizumab 1.25-1.75mg for wet macular degeneration in the prior 1-8 days (average 2.5 days). Mean number of injections received was 6.0 (range 3-9) over a mean period of 10.3 months (range 3-18 mo). No patient had a history of or risk factors for uveitis. There was no change in technique or preparation. Ten patients (77%) complained of vision loss, 11 patients (85%) complained of pain or discomfort, and one (8%) was asymptomatic. Mean logMAR visual acuity prior to presentation was 20/177 (range 20/50-CF) and on presentation declined to 20/679, (range 20/200-CF). All patients had anterior chamber cellular reaction, 5 of which (38%) also had hypopyon, and 9 of which also (69%) had vitritis. Eleven patients (85%) had conjunctival injection. Five patients (38%) had diffuse corneal edema. Five patients (38%) with severe uveitis underwent aqueous and vitreous tap with injection of antibiotics and one also underwent vitrectomy. All cultures were negative. All patients received topical steroids. Six patients were subsequently re-injected with one or more bevacizumab, and two were re-injected with ranibizumab. All 7 patients who were examined following their re-injection (including one with ranibizumab) developed recurrence of iritis +/- vitritis. Mean last visual acuity was 20/183 (range 20/40-CF), not statistically different from the vision prior to inflammatory reaction. Each syringe of bevacizumab used was derived from a different batch from the compounding pharmacy.

Conclusions: Sterile endophthalmitis, vitritis, and/or iritis may occur following multiple bevacizumab injections. The uveitis in our case series recurred with subsequent bevacizumab or ranibizumab injections. Although the exact etiology remains unknown, a hypersensitivity to the drug or carriers is suspected. Further investigations are being conducted on these patients.

CANADIAN RETINA & VITREOUS SOCIETY

FRIDAY 13 JUNE

Paper #A-00078

Intravitreal bevacizumab in the management of central retinal vein occlusion

Aimee MacDonald, Arif Samad

Purpose: To determine safety and efficacy of intravitreal Bevacizumab (Avastin, Genentech) in patients with central retinal vein occlusion (CRVO).

Methods: A retrospective case series involving 16 eyes of 16 patients, 9 females and 7 males with a mean age of 73.1 years (range: 46-88), with macular edema and retinal hypoperfusion due to CRVO. No previous treatment had been administered to these patients including laser therapy or intravitreal triamcinolone acetonide. Patients underwent intravitreal injection of Bevacizumab 1.25mg at 6 week intervals for a total of 3 injections. Baseline assessment included Snellen visual acuity, intravenous fluorescein angiography (IVF) as well as, optical coherence tomography (OCT) to determine foveal thickness and total macular volume. These parameters were reassessed at 18 weeks, 6 weeks following the third injection.

Results: Twelve patients were diagnosed with ischemic and five with non ischemic CRVO based on visual acuity, afferent pupillary defect and IVF. Mean visual acuity at baseline was 1.6 +/- 0.7 logMAR (range: 0.7 - 2.6) and improved to 1.0 +/- 0.6 at 18 weeks. ($p = .0014$) Mean foveal thickness was 531.3 u +/- 180.5 u at baseline and decreased to 279.9 u +/- 152.7 u at 18 weeks ($p = .0000056$). Mean total macular volume decreased from 12.0 mm³ +/- 3.17 mm³ at baseline to 7.9mm³ +/- 0.25 mm³ at 18 weeks ($p = .000018$). Intravenous fluorescein angiography (IVF) revealed decreased venous calibre, retinal hemorrhages and vascular leakage. No adverse events were observed, including clinically evident inflammation, endophthalmitis, increased intraocular pressure, retinal detachments or thromboembolic event.

Conclusions: Intravitreal bevacizumab appears to be safe and effective in reducing macular edema and retinal ischemia in patients with both ischemic or non-ischemic CRVO. This study is limited in the duration of follow-up; long term outcomes remain to be determined.

CANADIAN RETINA & VITREOUS SOCIETY

FRIDAY 13 JUNE

Paper #A-00079

Treatment of refractory diabetic macular edema: triamcinolone vs bevacizumab and “switch-over” treatment

Navapol Kancharanya, Wai-Ching Lam

Purpose: 1) To evaluate the visual outcomes associated with intravitreal injection of triamcinolone acetonide versus bevacizumab for the treatment of refractory diabetic macular edema (DME).
2) To evaluate the efficacy of switch-over treatment of triamcinolone to bevacizumab or bevacizumab to triamcinolone in patients who had no improvement with the first treatment.

Methods: The authors conducted a retrospective study of patients with refractory DME who were treated with at least one intravitreal injection of triamcinolone acetonide 4mg 0.1mL or bevacizumab 1.25 mg 0.05 mL and a “switch-over” group. Ocular history, adverse events, Snellen visual acuity testing, intraocular pressure, slit-lamp biomicroscopy, and fundus examination were assessed at baseline and at a post-treatment follow-up visit. Fifty-two consecutive patients with a minimum follow-up of 3 months and mean age of 65.08 \pm 10.03 years were included in this analysis.

Results: The mean follow-up period was 9.1, SD \pm 4.9, months. The mean number of injections was 2.1 \pm 1.2. Twenty-seven eyes received intravitreal triamcinolone injection and, twenty-five eyes were treated with intravitreal bevacizumab injection. The mean logMAR visual acuity statistically improved from 0.86 \pm 0.33 at baseline to 0.73 \pm 0.29 at the last follow-up time in triamcinolone group ($p=0.007$) and from 0.72 \pm 0.28 to 0.66 \pm 0.28 in bevacizumab group ($p=0.028$). There was a trend for best-corrected visual acuity improvement to be higher in the intravitreal triamcinolone group when compared with the bevacizumab group but this was not statistically significant ($p=0.143$). Four of five patients who had no improvement from bevacizumab and switched treatment to triamcinolone improved vision from 0.97 \pm 0.19 to 0.63 \pm 0.07 ($p=0.016$). Three patients experienced significant cataract progressions and three experienced increased intraocular pressure in the triamcinolone group. No adverse event was found in bevacizumab group. No injection-related complications occurred.

Conclusions: Both triamcinolone and bevacizumab injections resulted in a significant improvement in visual acuity. Triamcinolone caused more adverse events. Switch-over treatment had the potential for improvement in vision, especially in patients switched from bevacizumab to triamcinolone. Further larger prospective studies are needed to confirm these preliminary findings.

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Paper #A-00080

Ultra-widefield angiography in the diagnosis of diabetic macular edema secondary to peripheral nonperfusion: clinical characteristics and a novel treatment strategy

Ivan J. Suner

Purpose: Characterize and describe a subgroup of patients with diabetic macular edema (DME) secondary to peripheral nonperfusion. This subcategory of DME is predominantly VEGF driven.

Methods: Patients with diabetic macular edema secondary to peripheral nonperfusion were diagnosed with ultra-widefield angiography. Their treatment consisted of angiographically-directed scatter laser and anti-VEGF treatment.

Results: Resolution of macular edema was achieved with this novel treatment strategy. This regimen effectively promotes resolution of this subcategory of DME by reducing VEGF production by ischemic peripheral retina and by blocking available VEGF in the vitreous cavity.

Conclusions: Ultra-widefield angiography is a novel imaging technique that can effectively diagnose this previously poorly-characterized subgroup of patients with DME. Treatment with angiographically-guided peripheral scatter laser and anti-VEGF treatment is effective in this subcategory of patients with DME.

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Paper #A-00081

How long are patients waiting for retinal surgery in Calgary?

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Purpose: Wait-times for medical treatment in Canada have increased by 93% (1993-2007). Despite reports of lower (4 weeks) wait-times for retinal eye surgery (RES) in Alberta compared to Canadian average (5.5 weeks), there remains a perception of treatment delays for RES in the Calgary Health Region (CHR). To address this discrepancy, we will assess wait-times for RES in the CHR, and determine how Treatment-Status (emergency, urgent and elective) specifically contributes to treatment wait-times.

Methods: A retrospective chart review was performed on a sample of 2000 RES in CHR. Patients' treatment-status, surgery wait-time and factors responsible for longer than expected wait-times were identified.

Results: Data were evaluated for 1841 RES performed by 3 of the 4 surgeons in CHR. The wait-time was measured from the date of seeing the retinal surgeon to the surgery date. The average wait-time for Emergency cases was 1.6 days, with a standard deviation (SD) of 5.52 days and median wait-time (MWT) of 1 day. One outlier in this data (resident of a Penitentiary) waited 66 days for treatment. This may be due to the absence of protocol in the given situation. Urgent patients waited on average 10.6 days, with a SD of 11 days and MWT of 4 days. One patient who waited 81 days took some time to decide whether to undergo the required surgery. Elective cases waited on average 48 days for RES with the SD was 47 and MWT of 38 days. The range was quite large as it extended between 1 and 316. Initial yearly wait time analyses indicate steady increase in wait time in all three groups from the year 2002 to year 2006 especially for urgent cases (median wait time rose from 0 day in 2002 to 3 days in 2006), however wait time reduced in first half of year 2007.

Conclusions: Our results indicate that wait-times for elective RES in the CHR (7.2 wks) are less than those published by the Fraser Institute and Alberta Health and Wellness for the CHR (10.4 wks) and Alberta (8.5 wks). The results demonstrate wide variation in wait-time according to treatment status. While Wait-times for Emergency and Elective cases are generally within the acceptable time ranges, wait-time for urgent cases is not.

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FRIDAY 13 JUNE

Paper #A-00082

A prospective unicentre randomized double-blinded controlled clinical interventional trial comparing the efficacy of 3% chlorprocaine/marcaine versus 2% lidocaine/marcaine for retrobulbar anaesthesia in scleral buckling surgery

Efrem Mandelcorn, Colin J. McCartney, Mark S. Mandelcorn

Purpose: Scleral buckling surgery is commonly performed under conscious sedation with retrobulbar nerve block anesthesia using a mixture of lidocaine and bupivacaine. In other types of surgery using nerve block anesthesia, agents that act more rapidly than lidocaine, such as chlorprocaine, are often preferred over lidocaine because of their more rapid onset and offset of action, which may improve their effectiveness and safety profile. Since the ease of performing scleral buckling surgery, and, in some cases, the success of the procedure, depends upon satisfactory local anesthesia, we undertook this prospective study to compare the relative effectiveness of lidocaine and chlorprocaine for retrobulbar anesthesia during scleral buckling surgery.

Methods: We compared a lidocaine-bupivacaine mixture with a chlorprocaine-bupivacaine mixture for retrobulbar anesthesia in 136 cases of scleral buckling surgery performed by one surgeon during a 12 month period. A total of 31 variables comprising surgical, anesthetic, and patient-centered data were compared and analyzed to determine which drug was more efficacious.

Results: With the exception of akinesia, no statistically significant difference was found between the chlorprocaine and lidocaine mixtures for retrobulbar anesthesia in scleral buckling surgery from the point of view of the surgeon, anesthetist or patient.

Conclusions: We found no difference in effectiveness comparing bupivacaine with either lidocaine or chlorprocaine given by retrobulbar injection from the perspective of surgeon, anesthetist or patient, except for a slightly greater degree of rectus muscle akinesia with the lidocaine mixture. Whether or not the theoretically better safety profile using chlorprocaine, not proved in our study, justifies the higher cost of chlorprocaine is controversial.

CANADIAN RETINA & VITREOUS SOCIETY

FRIDAY 13 JUNE

Paper #A-00083

Incidence of infectious endophthalmitis after 25-gauge pars plana vitrectomy: a consecutive retrospective chart review

Rajeev H. Muni, Wai-Ching Lam, Robert Devenyi, Tiiu Hess, Varun Chaudhary

Purpose: Endophthalmitis is a rare but serious complication following pars plana vitrectomy (PPV). Numerous recent reports have indicated a higher incidence of endophthalmitis with 25-G PPV compared to conventional 20-G PPV. The purpose of this study was to document the incidence of infectious endophthalmitis after 25-G PPV.

Methods: We retrospectively reviewed the charts of all patients who underwent 25G PPV by two surgeons from 2006 to 2007 at a single institution. All cases of documented post-operative endophthalmitis were recorded to determine incidence.

Results: From 2006 to 2007 1110 25G PPV's were performed by the two surgeons. Two cases of endophthalmitis were documented. The incidence of endophthalmitis post-25G PPV was determined to be 1/555 or 0.18%. Both patients who developed endophthalmitis following 25G PPV did not receive subconjunctival antibiotics.

Conclusions: The incidence of endophthalmitis post-25G PPV in this consecutive retrospective chart review is 1/555. This rate is significantly higher than the documented rate of endophthalmitis following 20G PPV. Sub-conjunctival antibiotics at the completion of 25G PPV may be beneficial in reducing the risk of endophthalmitis.

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Paper #A-00084

Should lamellar holes be operated on?

Michael Butler, Raman Tuli

Purpose: To determine the effectiveness of macular lamellar hole surgical repair as determined by comparing pre- and postoperative visual acuity.

Methods: Case series of 12 patients who underwent surgical repair for lamellar holes in the macular region were reviewed.

Results: ANOVA statistical analysis revealed significant visual improvement postoperatively.

Conclusions: An operative approach to lamellar holes of the macular region appears to be a viable treatment option.

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Paper #A-00085

Visual performance and fixation location before and after macular hole surgery

Mark S. Mandelcorn, Luminita Tarita-Nistor, Esther G. González, Martin J. Steinbach

Purpose: This study examined changes in visual acuity, fixation stability and fixation location after macular hole closure following pars plana vitrectomy.

Methods: Seven patients (mean age = 65.1 years, SD = 12.3) with stage III and IV macular hole were tested before and three months after surgery. Best corrected visual acuity at 1 m was measured with the ETDRS acuity chart and with the Single E Optotype Acuity Test in reverse polarity (computerized version). Best corrected potential visual acuity at 1 m was measured with the Multiple E Optotype Acuity Test (González, Tarita-Nistor, Markowitz, & Steinbach, 2007). This test minimizes the effects of fixation instability while maximizing the likelihood of one of the optotypes falling on the most sensitive part of the retina. Fixation stability, fixation location and a fundus photograph were obtained with the MP-1 Microperimeter. Macular hole closure was confirmed by OCT examination.

Results: All but one patient improved their visual acuity after macular hole closure. The largest magnitude of change was shown by the Single E Optotype test (mean change = 3.96 arcmin, SD = 6.88). Fixation stability was estimated with a bivariate contour ellipse area (BCEA); its calculation is based on the standard deviation of the horizontal and vertical eye movements during fixation and it represents the area on which the eyes fixate for a certain proportion of the time. All but two patients improved their fixation stability (mean change in BCEA = 288 arcmin²). Fixation stability changes correlated highly with changes in visual acuity as measured with the Single E test ($r(5) = .77, p < .05$), marginally with changes measured with the ETDRS test ($r(5) = .64, p = .06$) and did not correlate with changes measured with the Multiple E test ($r(5) = .42, p = .17$). Fixation location shifted by an average of 1.5 deg.

Conclusions: Macular hole closure after pars plana vitrectomy leads to improvement in visual acuity and fixation stability. Changes in fixation stability are related to changes in visual acuity. Fixation location shifts after the hole closure.

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Paper #A-00086

Evaluating functional change following macular hole surgery

Stuart G. Coupland, Mandy Cheng, Bernard Hurley, Brian C. Leonard

Purpose: In the last 15 years there have been considerable advances in vitreoretinal surgical repair of macular holes with significant improvement in visual acuity seen in the majority of eyes. Microperimetry (MP) has shown to have significant effectiveness in the evaluation of focal retinal sensitivity in eyes before and after macular hole repair. Presently, MP has not been used to monitor the course and progression of visual recovery. The purpose of this study was to investigate and compare functional change in retinal sensitivity measured by MP with change in logMAR visual acuity and multiple-letter visual acuity (MLVA) in patients following macular hole repair. The natural progression of visual recovery was systematically investigated over an 8 week period following macular hole surgical repair.

Methods: To date, 6 patients with Stage 2, 3 or 4 hole who were undergoing three port vitrectomy with ILM peeling and air-fluid exchange with SF6 gas have been studied. Preoperative measures of visual acuity, macular hole size assessed by OCT and microperimetry were obtained and repeated at 1,3,5 and 8 weeks following macular hole repair.

Results: There was a significant increase in retinal sensitivity as measured by MP following macular hole repair ($p < 0.003$). There was significant correlation between 8 week postoperative visual acuity and preoperative retinal sensitivity ($p < 0.02$) suggesting that preoperative MP may have predictive value. Macular hole size was found to correlate with postoperative visual acuity at 8 weeks.

Conclusions: Microperimetry has benefit for patients undergoing macular hole surgery by predicting degree of recovery of visual acuity and monitoring improvement of retinal sensitivity following surgical intervention.