In vivo Fluorescein Angiography Quantifies Vascular Abnormalities in a Mouse Model of Oxygen-Induced Retinopathy – Clinical Implications for Retinopathy of Prematurity

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Purpose: Retinopathy of prematurity (ROP) is a disease of abnormal vascular development in premature infants that potentially leads to blindness. A finding of tortuous and dilated vessels or plus disease during dilated retinal exams indicates severe disease requiring treatment. However, it is difficult to distinguish arteries from veins. Treatment could be delayed due to the discrepancies in subjective diagnosis of ROP amongst experts. Using fluorescein angiography (FA), arterio-venous abnormalities were distinguished and quantified throughout vascular development in live OIR mice.

Methods: 48 newborn C57BL/6J mice were exposed to 77±2% oxygen from postnatal day (P)7 till P12. 48 mice were raised in room air (RA). In vivo FA was performed at early (P16 to P18), mid (P23 to P25), and late (P30 to P32) phases of retinal vascular development. Retinal artery tortuosity (RAT), retinal vein width (RVW), and retinal vascular area (RVA) were quantified. Values are given as mean ±SD.

Results: OIR mice had patchy areas of capillary vaso-obliteration unlike the uniform capillary network in RA mice, so that percent RVA in total image area was reduced in early phase (19.31±7.91, n=16) in OIR mice compared to RA (31.56±10.81, n=16, p=0.003). RVA in OIR mice increased from early to mid-phase (p<0.0001), but was smaller and sparser than RA at late phase (p=0.0249) despite full capillary coverage. RVW was higher in OIR (60.76±12.2µm, n=16) than RA mice in early phase (40.21±4.8µm, n=16 p<0.0001) and mid phase (p=0.041), but were equivalent by late phase (p=0.96). OIR mice were more tortuous arteries than RA mice in early (1.22±0.12 vs 1.00±0.03, p<0.0001), mid (1.1±0.06 vs 1.00±0.02, p<0.0001), and late (1.07±0.12 vs 1.00±0.03, p<0.004) phases of retinal vascular development. RA mice maintained uniform RVA, RVW, and RAT in all phases.

Conclusions: In vivo FA distinguishes arterial and venous abnormalities and reveals persistent retinal artery tortuosity in adult OIR mice. RAT may be a reliable, objective marker of ROP severity and progression during clinical diagnosis of plus disease. Clinical application of objective methods would facilitate earlier detection, more consistent diagnosis, earlier treatment, and closer monitoring of ROP to avoid adverse visual outcomes.
Topical Administration of Somatostatin to an Oxygen-Induced Retinopathy (OIR) Model of Retinopathy of Prematurity (ROP)

Hamzah Khalaf1, Jeffrey Dunkire1, Richard W. Hertle2,3, Berta Ponsati1, Jimena Fernandez1, Lluis Riera-Sans1, Rachida Bouhenni1.

Purpose: Currently, treatments for retinopathy of prematurity (ROP) are invasive and while topical applications for retinal delivery of medications have been successfully developed, there are none that have been shown to treat ROP. In this pilot study, we used an Oxygen-Induced Retinopathy (OIR) mouse model of ROP to test the efficacy of topical somatostatin in reducing retinal neovascularization, an approach that was proven effective in prevention of diabetic retinopathy in animal studies and is now undergoing human trials.

Methods: Neonatal mice (C57BL/6, n=9) were exposed to 75% oxygen from postnatal day (P)7 until P12 and returned to room air (21% oxygen). Somatostatin (0.1%, n=3 and 1.0%, n=3) or vehicle (n=3) was administered once daily to both eyes from P12 to P17. Mice with body weight less than 6g at P17 were excluded. Following enucleation on P17, whole retinas were dissected, mounted, and stained with isoelectin. The degree of vascular proliferation was examined by blinded observers using a fluorescent microscope and scored according to a well described retinopathy scoring system which assessed number of tufts, vessel tortuosity, vasoconstriction, and retinal hemorrhage. The total retinopathy score was compared qualitatively.

Results: Retinal mounts from the somatostatin treated eyes showed reduced average total retinopathy score compared to those treated with vehicle (4.8 vs 6.0 respectively). In addition, the average total retinopathy score of the somatostatin 1.0% group was slightly reduced compared to that of the somatostatin 0.1% group (4.67 vs 5.0).

Conclusions: These results support the hypothesis that topical administration of somatostatin once daily may reduce neovascularization in the OIR mouse model. This proof-of-concept study paves the road to add novel, obviously advantageous, topical treatments for ROP. We are continuing this research by increasing the sample size in order to test our hypothesis in a more statistically rigorous fashion.

Commercial Relationships: Hamzah Khalaf, None; Jeffrey Dunkire, None; Richard W. Hertle, None; Berta Ponsati, BCN Peptides; Jimena Fernandez, BCN Peptides; Lluis Riera-Sans, BCN Peptides; Rachida Bouhenni, None.

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Presentation Time: 11:00 AM–12:45 PM

A Novel Mouse Model of Hyperoxia-Induced Retinopathy that Mimics Pathognomonic Features of Severe Retinopathy of Prematurity (ROP) in Humans

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Purpose: The popular ‘oxygen-induced retinopathy’ mouse model (75% oxygen between postnatal days 7-12 [P7-12]) has been extensively used to study the vascular changes in the retina that result from exposure to hyperoxia followed by a return to room air. However, in this model the retina and its vasculature assumes normal morphology after 5-6 weeks. The aim of the present study was to develop a mouse model of hyperoxia-induced retinopathy that reproduced important key clinical, functional, histological and vascular features of untreated severe ROP in humans.

Methods: C57Bl/6J mice exposed to 65% oxygen from P0-7 mice (n=75) were investigated clinically using fluorescein angiography, optical coherence tomography (OCT), and electroretinography (ERG) at various time points between 3 weeks (w) to 40w. Histopathology, frozen section immunostaining and wholemount lectin staining of the retinal vasculature was undertaken at 3w, 5w, 8w and 40w. Controls (n=59) were exposed to normal air.

Results: At 3w, significant vitreous hemorrhages and persistence hyaloid vessels were observed in hyperoxia-exposed mice. Compared to controls, hyaloid and retinal vessels showed significantly increased tortuosity (p<0.05), which persisted until 40w. Following hyperoxia exposure retinal vascularization remained incomplete up to 40w and intraretinal capillary plexi were abnormal, particularly in peripheral zones. ERG studies showed a significant decrease in photoreceptor (a-wave), bipolar cell (b-wave), amacrine cell and ganglion cell function in P0-7 hyperoxia-exposed mice at 8w (p<0.01). All components of the ERG remain significantly attenuated at 20w of age (p<0.01); however, ganglion cell function was significantly more affected (p<0.05). Vitreal membranes associated with retinal detachments were collagen type IV and alpha smooth muscle actin. Abnormal hyaloid vessels and capillaries of the tunica vasculosa lentis persisted in hyperoxia-exposed eyes up to 40w of age.

Conclusions: Hyperoxia exposure between P0-7 resulted in several long-term changes that closely resembled severe ROP in humans. This model will prove useful in testing the safety and efficacy of potential interventions in humans such as anti-VEGF therapy.

Commercial Relationships: Paul G. McMenamin, None; Rachel Kenny, None; Cecilia Naranjo Golborne, None; Jeremiah Lim, None; Bang V. Bu, None.

Support: Jean and Julias Tahija Foundation, National Health and Medical Research Council of Australia.

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Presentation Time: 11:00 AM–12:45 PM

Risk Score for Predicting Development of Treatment-Required Retinopathy of Prematurity in the Telemedicine Approaches to Evaluating of Acute-Phase ROP (e-ROP) Study

Gui-Shuang Ying1, Deborah VanderVeen1, Graham E. Quinn1, Ebenezer Daniel1, Agnieszka Baumritter1.1 Ophthalmology, Scheie Eye Institute, Philadelphia, PA; 2Boston Children’s Hospital, Boston, MA; 3Division of Ophthalmology, The Children’s Hospital of Philadelphia, Philadelphia, PA.

Purpose: To develop a risk score for predicting treatment-requiring ROP (TR-ROP).

Methods: Secondary analyses of data among infants with birth weight of <1251g who had an imaging session ≥34 PMA weeks and at least one subsequent ROP examination for determining TR-ROP by study-certified ophthalmologists. Non-physician trained readers evaluated characteristics of ROP, posterior pole abnormalities, and hemorrhage in wide-field retinal images. Multivariate logistic regression modeling was performed to determine independent predictors of TR-ROP, and calculate the risk score points based on regression coefficients of statistically significant predictors.

Results: Among 771 infants, 85 (11.0%) developed TR-ROP. In a multivariate model, significant predictors [odds ratio (95% confidence interval)] for TR-ROP were: gestational age [5.7 (1.7 – 18.9) for ≤25 vs. ≥28 weeks], number of quadrants with preplus or plus [4.0 (1.4 – 11.4) for 3 preplus quadrants, and 3.8 (1.5 – 9.7) for 4 or more preplus quadrants].
In addition to bivariate and multivariate analysis, least absolute shrinkage and selection operator (LASSO) method was used to identify major risk factors, and restricted cubic splines (RCS) were used to formulate a risk calculator.

**Results:** Of the 20 variables examined, 13 conferred significant risk for severe ROP on bivariate analysis. The most influential risk factors on multivariate analysis included gestational age (OR=0.61 per week, 95% CI 0.47–0.81, p<0.001), birthweight (OR=1.00 per gram, 95% CI 1.00–1.00, p=0.08), average blood oxygen saturation at one month (OR=0.93 per percentage point, 95% CI 0.87–0.98, p=0.01), and transfer to the UCLA healthcare system (OR= 0.23, 95% CI 0.08–0.69, p=0.009) (table 1). A risk calculator based on these four major factors yielded an accuracy of 81.3%, sensitivity of 84.6%, and specificity of 77.9%.

**Conclusions:** Using the major risk factors of gestational age, birthweight, transfer status, and average oxygen saturation at one month of age, we formulated an easy-to-use risk calculator that predicts risk of severe ROP at tertiary care centers. This tool is useful for counseling families and informing a multi-disciplinary healthcare team of an infant’s vision care prognosis. Further refinement of the calculator may extend its applications to community settings or even guiding ROP management.

<table>
<thead>
<tr>
<th>Risk Score Points</th>
<th>OR (95% CI)</th>
<th>p-value (bivariate)</th>
<th>OR (95% CI)</th>
<th>p-value (multivariate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.96 (0.48–0.65)</td>
<td>&lt;0.001</td>
<td>1.00 (1.00–1.00)</td>
<td>0.08</td>
</tr>
<tr>
<td>1</td>
<td>0.88 (0.54–1.41)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>2</td>
<td>0.79 (0.47–1.33)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>3</td>
<td>0.71 (0.45–1.12)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>4</td>
<td>0.65 (0.41–1.03)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>5</td>
<td>0.59 (0.36–0.99)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>6</td>
<td>0.50 (0.29–0.89)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>7</td>
<td>0.41 (0.23–0.75)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>8</td>
<td>0.33 (0.19–0.57)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>9</td>
<td>0.25 (0.14–0.45)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>10</td>
<td>0.20 (0.12–0.33)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>11</td>
<td>0.15 (0.09–0.25)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>12</td>
<td>0.11 (0.05–0.21)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
<tr>
<td>13</td>
<td>0.07 (0.03–0.15)</td>
<td>&lt;0.001</td>
<td>0.88 (0.56–1.39)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Table 1: Risk factors for retinopathy of prematurity on bivariate and multivariate analysis. OR - odds ratio. CI - confidence interval. ¥ Variables with multiple clinical outcomes were treated as separate variables own p-value.

**Commercial Relationships:** Madeline Yung, Emily Tam, Sasha Hubschman, Irena Tsui, None; Deborah VanderVeen, None; Graham E. Quinn, None; Ebenezer Daniel, None; Agnieszka Baumritter, None

**Support:** U10EY017014, R21EY025686

**Program Number:** 6262 Poster Board Number: C0005

**Presentation Time:** 11:00 AM–12:45 PM

**Risk calculator to predict severe retinopathy of prematurity**

**Madeline Yung, Emily Tam, Sasha Hubschman, Irena Tsui. Stein Eye Institute, David Geffen School of Medicine at UCLA, Los Angeles, CA.**

**Purpose:** Although retinopathy of prematurity (ROP) is an important cause of vision loss, there are currently no data-derived risk prediction systems that are widely used in clinical practice. We conducted a prospective cohort study to examine the relationship of established ROP risk factors with the severity of ROP, with the goal of synthesizing a risk calculator to predict the risk for severe ROP.

**Methods:** This study included 282 infants (124 males and 158 females) who were hospitalized within the UCLA healthcare system between January 1, 2008 and December 31, 2014, screened for ROP based on published guidelines, and received care through at least 1 month of age. Patient charts were analyzed for established ROP risk factors and progression to severe ROP, defined as ROP requiring treatment with laser photoacoagulation or anti-VEGF therapy. In addition to bivariate and multivariate analysis, least absolute shrinkage and selection operator (LASSO) method was used to formulate a risk calculator.

**Results:** Of the 20 variables examined, 13 conferred significant risk for severe ROP on bivariate analysis. The most influential risk factors on multivariate analysis included gestational age (OR=0.61 per week, 95% CI 0.47–0.81, p<0.001), birthweight (OR=1.00 per gram, 95% CI 1.00–1.00, p=0.08), average blood oxygen saturation at one month (OR=0.93 per percentage point, 95% CI 0.87–0.98, p=0.01), and transfer to the UCLA healthcare system (OR= 0.23, 95% CI 0.08–0.69, p=0.009) (table 1). A risk calculator based on these four major factors yielded an accuracy of 81.3%, sensitivity of 84.6%, and specificity of 77.9%.

**Conclusions:** Using the major risk factors of gestational age, birthweight, transfer status, and average oxygen saturation at one month of age, we formulated an easy-to-use risk calculator that predicts risk of severe ROP at tertiary care centers. This tool is useful for counseling families and informing a multi-disciplinary healthcare team of an infant’s vision care prognosis. Further refinement of the calculator may extend its applications to community settings or even guiding ROP management.
Methods: We conducted cost analysis from the perspective of the Ministry of Health using retrospective data (2009-2014) from an existing telemedicine screening program. Follow up imaging and referral indications were according to current clinical screening guidelines. Referral was required for type 2 ROP or worse. All infants had final BIO examination by an ophthalmologist after discharge from NICU. Data on severity of ROP at each examination and at final in person exam was collected. Patient level data on costs was used for infants screened via telemedicine. We created a hypothetical control group that comprised of minimum number of in-person visits and inter-hospital transfers if the existing patients were screened by BIO. In total, costs consisted of cost of in-person exams, transfers, setting up and ongoing costs of telemedicine screening. Cost variables were compared using the Mann-Whitney U test.

Results: 102 infants were screened via telemedicine. A total of 223 telemedicine exams were performed. 34 infants were diagnosed with ROP. No cases of type 2 ROP were missed. 3 infants required laser treatment. Only 4 infants (3%) needed at least one transfer in the telemedicine group and 106 infants (90%) in the control group. Average total cost per examination was $4,855±$515 (2014 Canadian dollars) for the telemedicine group and $19,834±$13,814 for the control group (p<0.001). The main cost for the control group was inter-hospital transfer cost ($19,489±$13,605) compared to ($635±$3,968) for the telemedicine group (p<0.001).

Conclusions: Telemedicine appears to be a viable alternative for remote areas where access to ROP screening service is suboptimal. The telemedicine group reported significantly lower average total cost per visit compared to the hypothetical control group. Inter-hospital transfer was the main contributing cost. This information will be useful for planning similar ROP services for remote areas.

Commercial Relationships: Maram Isaac, None; Wanrudee Isaranuwatchai, None; Nasrin N. Tehrani, None

Program Number: 6264 Poster Board Number: C0007

Education for Retinopathy of Prematurity (ROP): Assessment of a Tele-education System to Enhance ROP Training Among International Trainees

Samir N. Patel1, Maria Ana Martinez-Castellanos2, David Berrones Medina1, Ryan Swan1, Michael Ryan1, Karyn Jonas1, Susan Ostmo2, Michael F. Chiang1,2, Robison V. Chan4, Ophthalmology, Weill Cornell Medical College, New York, NY; 2Asociación para Evitar la Ceguera en México, Mexico City, Mexico; 3Ophthalmology, Casey Eye Institute at Oregon Health & Science University, Portland, OR; 4Ophthalmology & Visual Sciences, Illinois Eye and Ear Infirmary, University of Illinois at Chicago, Chicago, IL; 5Medical Informatics & Clinical Epidemiology, Casey Eye Institute at Oregon Health & Science University, Portland, OR.

Purpose: The third epidemic of ROP has predominately affected middle-income countries and has been exacerbated by insufficient training in ROP diagnosis and management. Previously, we have demonstrated the utility of a web-based system to improve ROP education among trainees in the USA. The purpose of this study is to assess the effectiveness of a tele-education system for international trainees from a middle-income country.

Methods: A secure web-based educational system was developed using a repository of over 2500 image sets of ROP. 36 infants were used for 65 clinical cases (20 pretest, 20 posttest, and 25 chapter-based training) in the system. 58 trainees from a middle-income country were prospectively evaluated and randomized either to an educational intervention (pretest, ROP tutorial, ROP educational chapters, and posttest) or to a control group (pretest and posttest only). Accuracy and reliability of ROP diagnosis were determined using sensitivity, specificity, and the kappa statistic from the educational intervention and control group.

Results: Trainees completing the educational intervention had significant improvements (P<0.01) in the sensitivity of ROP diagnosis for plus disease, zone, stage, category, and aggressive posterior ROP (APROP) between the pretest and posttest. Compared to the control group, the educational intervention group had statistically significant improvements on the posttest for the sensitivity of presence of ROP (P<0.01), plus disease (P=0.04), and specificity for APROP (P<0.01), type-2 ROP or worse (P=0.04) and treatment-requiring ROP (P<0.01) (Table 1). Intra-grader agreement improved for identification of plus disease, zone, stage, and category of ROP after completion of the tele-education program (Table 2).

Conclusions: A tele-education system for ROP is effective in improving diagnostic accuracy of ROP by trainees from middle-income countries. This system has the potential to increase competency in ROP diagnosis and management for practicing ophthalmologists in middle-income countries to address the third epidemic of ROP.

Table 1 Sensitivity and Specificity of Retinopathy of Prematurity Diagnosis in the Posttest by International Trainees Participating in the ROP Tele-education Program.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sensitivity during posttest, % (SE)</th>
<th>Specificity during posttest, % (SE)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Educational Intervention (N = 29)</td>
<td>Control Group (N = 29)</td>
<td>Educational Intervention (N = 29)</td>
<td>Control Group (N = 29)</td>
</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1 or worse</td>
<td>96 (3)</td>
<td>94 (2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Stage 2 or worse</td>
<td>92 (3)</td>
<td>89 (3)</td>
<td>0.09</td>
</tr>
<tr>
<td>Stage 3 or worse</td>
<td>82 (4)</td>
<td>65 (3)</td>
<td>0.06</td>
</tr>
<tr>
<td>Zone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zone II or III</td>
<td>85 (3)</td>
<td>83 (1)</td>
<td>0.10</td>
</tr>
<tr>
<td>Zone I</td>
<td>55 (6)</td>
<td>59 (2)</td>
<td>0.10</td>
</tr>
<tr>
<td>Plus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-plus or worse</td>
<td>82 (3)</td>
<td>80 (1)</td>
<td>0.04</td>
</tr>
<tr>
<td>Plus</td>
<td>67 (6)</td>
<td>64 (3)</td>
<td>0.21</td>
</tr>
<tr>
<td>Category</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild or worse</td>
<td>95 (3)</td>
<td>94 (2)</td>
<td>0.01</td>
</tr>
<tr>
<td>Type-2 or worse</td>
<td>89 (3)</td>
<td>92 (2)</td>
<td>0.03</td>
</tr>
<tr>
<td>Treatment-requiring</td>
<td>71 (6)</td>
<td>64 (3)</td>
<td>0.01</td>
</tr>
<tr>
<td>Presence APROP</td>
<td>77 (8)</td>
<td>79 (5)</td>
<td>0.01</td>
</tr>
<tr>
<td>Presence ROP</td>
<td>96 (1)</td>
<td>91 (1)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*P value using paired t-test.

Table 2 Kappa Statistics for Intra-grader Agreement Among International Trainees in the Pretest and Posttest of the ROP Tele-education Program.

<table>
<thead>
<tr>
<th>Cohen’s Kappa (κ)</th>
<th>Trainees with Educational Intervention (N = 29)</th>
<th>Trainees in Control Group (N = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Prettest</td>
<td>Posttest</td>
</tr>
<tr>
<td>0.62</td>
<td>0.92</td>
<td>0.74</td>
</tr>
<tr>
<td>Zone</td>
<td>0.32</td>
<td>0.75</td>
</tr>
<tr>
<td>Plus</td>
<td>0.64</td>
<td>0.75</td>
</tr>
<tr>
<td>Category</td>
<td>0.41</td>
<td>0.56</td>
</tr>
<tr>
<td>Presence APROP</td>
<td>0.43</td>
<td>0.52</td>
</tr>
<tr>
<td>Presence ROP</td>
<td>0.64</td>
<td>0.86</td>
</tr>
</tbody>
</table>

APROP, Aggressive posterior retinopathy of prematurity; ROP, retinopathy of prematurity.
Commercial Relationships: Samir N. Patel, None; Maria Ana Martínez-Castellanos; David Berrones Medina, None; Ryan Swan, None; Michael Ryan, None; Karyn Jonas, None; Susan Ostmo, None; Michael F. Chiang, Clarity Medical Systems (Pleasanton, CA) (S); Robison V. Chan, None

Support: Supported by a Departmental Grant from Research to Prevent Blindness, Supported by the St. Giles Foundation, Supported by NIH EY19474, Supported by the Bernadotte Foundation for Children's Eyecare, Supported by the Novartis Excellence in Ophthalmic Vision Award (XOVA), Supported by the iNighnt Foundation, Supported by OSLER TL1 NIH Grant (Grant# 5TL1TR000129-10)

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Presentation Time: 11:00 AM–12:45 PM

ROPtool analysis of Pictor images in the assessment of plus and pre-plus disease
Marguerite M. Cullen, David K. Wallace, Sharon F. Freedman, Sasapin G. Prakalapakorn. Duke Eye Center, Durham, NC.

Purpose: Retinopathy of Prematurity (ROP) is a leading cause of preventable blindness in children. ROPtool is a semi-automated computer program used to objectively measure retinal vascular characteristics in retinal images and has been validated to assess plus disease in RetCam and video indirect ophthalmoscopy images. Pictor is a hand-held, non-contact retinal camera. Our aim is to evaluate if ROPtool can accurately identify plus and pre-plus disease in a large set of Pictor images of varying qualities captured by non-physician health care workers (HCWs). While previous studies have used ROPtool to analyze single retinal images, we combined quadrant-level data from multiple Pictor images of a single retina to allow more major vessels to be analyzed.

Methods: As part of an ongoing prospective study, HCWs obtained Pictor retinal images of infants at risk for ROP during routine ROP rounds. Imagers selected 1-3 images per eye, aiming to show vessels in all 4 posterior pole quadrants. A non-physician HCW analyzed these images with ROPtool. Six measures reflecting vessel tortuosity and dilation were obtained per quadrant: tortuosity index (TI), maximum tortuosity (MT), dilation index (DI), maximum dilation (MD), sum of adjusted indices (SAI), and tortuosity-weighted plus (TWP). The reference standard was the diagnosis at the time of the clinical exam. Receiver operating characteristic (ROC) curves were generated for the identification of plus and pre-plus disease using the second-largest quadrant value of each measure, because plus disease requires 2 quadrants to have sufficient vascular abnormality.

Results: Of the 124 eyes imaged, 484 (98%) of 496 quadrants were analyzable by ROPtool, meaning they had at least one vessel traceable for at least one optic disc diameter in length. Overall, 92% of eyes had 4 analyzable quadrants, 6.5% had 3, and 1.6% had 2. For plus disease, area under the ROC curves (AUCs) were: TWP 0.97 = TI 0.97 = MT 0.97 > SAI 0.94 > DI 0.87 > MD 0.80. For pre-plus or plus disease, AUCs were: TWP 0.99 > MT 0.98 = TI 0.98 > SAI 0.97 > DI 0.87 > MD 0.80.

Conclusions: Pictor retinal images of varying qualities of infants at risk for ROP can be analyzed with ROPtool with high accuracy for the identification of plus and pre-plus disease. It is feasible for non-opthalmologist HCWs to capture retinal images and analyze them for the presence of plus disease, furthering the available workforce for ROP screening.

Commercial Relationships: Marguerite M. Cullen; David K. Wallace, FocusROP (P); Sharon F. Freedman, Inotek (C), Pfizer (C), FocusROP (P); Sasapin G. Prakalapakorn, NIH (F)

Program Number: 6266 Poster Board Number: C0009
Presentation Time: 11:00 AM–12:45 PM
The effect of clinical patient information on the diagnosis of and decision to treat retinopathy of prematurity
Andreas Gschliesser1, Thomas Neumayer2, Elisabeth Moser3, Andrea Papp1, Isabel Oberacher-Velten1, Stefan Egger1, Nenad Vukojevic2, Guido Dorner1, Eva Stifter1. 1Department of Ophthalmology, Medical University of Vienna, Vienna, Austria; 2University Hospital Centre Zagreb, Zagreb, Croatia; 3University Hospital Centre Regensburg, Regensburg, Germany; 4Paracelsus Medical University of Salzburg, Salzburg, Austria.

Purpose: The internationally recognized retinopathy of prematurity (ROP) classification and treatment guidelines are based on morphologic disease variables found at examination for the condition. However, information about clinical variables associated with the development of ROP may influence the examiners’ grading and treatment decision. This cross-sectional agreement study evaluated the effect of clinical patient information on ROP experts’ diagnosis of ROP and decision to treat it.

Methods: Wide-field fundus photographs of eyes of 52 premature infants of <32 weeks’ gestational age or <1500 grams’ birth weight were presented on two consecutive days to seven recognized ROP experts for ROP diagnosis (stage, plus disease, aggressive posterior ROP) and the necessity for treatment. On assessment day 1 the experts were blinded to all clinical patient data whereas on assessment day 2 they were provided with information about the patients’ gestational age and birth weight. The complete study group was analyzed statistically followed by subgroup analysis of infants with a very low birth weight (1st quartile, 580 grams) and infants with a heavier birth weight (4th quartile, >850 grams). The McNemar test and the Wilcoxon signed-rank test were used for statistical analysis.

Results: A statistically significant shift in the experts’ rating towards a less aggressive ROP grading stage (p=0.006) and a less frequent decision for intervention (p=0.021) could be observed after providing clinical patient information. The subgroup analysis showed that this was more true for infants with heavier birth weights (ROP stage p=0.001, treatment decision p=0.013), than for those with very low birth weights (ROP stage p=0.774, treatment decision p=0.703). No statistically significant shift could be found for plus disease (p=0.366) and aggressive posterior ROP (p=0.136).

Conclusions: The results of this study suggest that knowledge of clinical patient information such as birth weight and gestational age has an effect on the grading of ROP disease and the decision for treatment. ROP staging and the decision for treatment seem to be set at a lower level for babies with heavier birth weights. These findings may have implications for further refinements of the ROP guidelines and recommendations for clinical practice.

Commercial Relationships: Andreas Gschliesser, None; Thomas Neumayer, None; Elisabeth Moser, None; Andrea Papp, None; Isabel Oberacher-Velten, None; Stefan Egger, None; Nenad Vukojevic, None; Guido Dorner, None; Eva Stifter, None

Program Number: 6267 Poster Board Number: C0010
Presentation Time: 11:00 AM–12:45 PM
Evaluation of Choroidal Thickness in Preterm Infants using Hand Held Spectral Domain Optical Coherence Tomography (HH SD-OCT)
Samira Amaward1,2, Mintu Nath1, Aarti Patel1, Frank A. Proudluck1, Irene Gottlob1. 1Neuroscience, Psychology and Behaviour, University of Leicester, Leicester, United Kingdom; 2Ophthalmology, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom; 3Cardiovascular Sciences, University of Leicester, Leicester, United Kingdom.

Program Number: 6268 Poster Board Number: C0007
Presentation Time: 11:00 AM–12:45 PM
Evaluation of Choroidal Thickness in Preterm Infants using Hand Held Spectral Domain Optical Coherence Tomography (HH SD-OCT)
Samira Amaward1,2, Mintu Nath1, Aarti Patel1, Frank A. Proudluck1, Irene Gottlob1. 1Neuroscience, Psychology and Behaviour, University of Leicester, Leicester, United Kingdom; 2Ophthalmology, University Hospitals of Leicester NHS Trust, Leicester, United Kingdom; 3Cardiovascular Sciences, University of Leicester, Leicester, United Kingdom.

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Purpose: Choroidal involution has been demonstrated during oxygen induced retinopathy of prematurity (ROP) in an animal model while choroidal thickness (ChT) is observed to be thinner in older preterm children using spectral-domain optical coherence tomography (SD-OCT).

We describe in vivo ChT during development in preterm infants with and without retinopathy of prematurity (ROP) using hand-held spectral domain optical coherence tomography (HH-SD-OCT).

Methods: Cross sectional and longitudinal HH SD-OCT retinal images (n=203) were acquired from 65 preterm infants with (n=20) and without (n=45) ROP at 1-2 weekly intervals from 31 to 42 weeks postmenstrual age (PMA). Participants were recruited from the neonatal unit while also undergoing ophthalmic screening for ROP. No infant had received treatment for ROP at the time of scanning. HH SD-OCT (Biopigen, 2.6μm axial resolution) scans were performed without sedation and after dilatation of pupils. Customised Image J manual segmentation of ChT at the fovea and up to 1500μm nasally and temporally was performed and quantified. Data were analyzed using a linear mixed model.

Results: The difference between the mean ChT in ROP (259.67μm SD +65.57) and no ROP (256.33μm SD +81.48) was not statistically significant (p=0.681). There was evidence of a complex relationship between the mean ChT with location and PMA. An elevation of the outer plexiform layer (OPL) at the fovea had a significantly reduced mean ChT (251.92μm SD +70.77) compared with no elevation (259.71μm SD+77.86) (p<0.001).

Conclusions: In preterm infants, ROP was not associated with significant differences in overall mean ChT compared to no ROP, but ChT varied according to location across the central retina and PMA. A disturbance of the OPL at the fovea appeared to significantly decrease mean ChT but the significance of this is not yet clear.

Supported by: None.

Program Number: 6269 Poster Board Number: C0012
Presentation Time: 11:00 AM–12:45 PM
Retinal Hemorrhages in Very Low Birth Weight (VLBW) Infants in the Telemedicine Approaches to Evaluating Acute-phase Retinopathy of Prematurity (e-ROP) Study
Eli Smith1, Wei Pan1, Ebenezer Daniel1, Gui-Shuang Ying2, Graham E. Quinn1,2. 1Ophthalmology, University of Pennsylvania, Philadelphia, PA; 2Children’s Hospital of Philadelphia, Philadelphia, PA.

Purpose: To describe the characteristics of hemorrhages in infants with BW <1251g as observed on grading of digital retinal images by two non-physician trained readers (TR).

Methods: Two certified TRs evaluated the presence, type and location of hemorrhages in the digital color fundus photographs at baseline and at follow up visits (at PMA weeks of 32 to 40) from both eyes of infants enrolled in the e-ROP study. A sample of 41 image sets in which hemorrhages were noted by the TR and/or by the opthalmologist during a corresponding bedside exam were used to determine intra and inter grader agreement in identifying presence and type of hemorrhages.

Results: Hemorrhages were observed in 267 (22%) of 1239 infants, were unilateral (73%), dot 8.2%, blot 12.3%, flame 3.4%, pre-retinal 12.3% and vitreous 1.6%. In the majority of eyes (78%) there was only one type of hemorrhage, two types coexisted in 19%, and in 3% three or more types were observed. 41% of the hemorrhages were in zone I, 35% in zone II and 23% in both zones I and II. In zone I, hemorrhages were distributed widely: superior 45%, temporal 55%, inferior 36% and nasal 57%. In zone II hemorrhages tended to be more temporally located with superior 23%, temporal 69%, inferior 21% and nasal 30%. When hemorrhages were associated with ROP, 61% were anterior, 43% posterior and 42% at the retina.

Intra-grader agreement was 67% for dot, 76% for blot, 95% for flame, 57% were pre-retinal, and 62% for vitreous hemorrhages. Inter-grader agreement was 52% for dots, 52% for blot, 100% for flame, 80% for pre-retinal, and 100% for vitreous hemorrhages.

Conclusions: Approximately a fifth of <1251g infants had intraocular hemorrhages, mostly blot and pre-retinal, and generally unilateral. They were observed both in zone I and zone II and presented mostly as a single type. There was reasonable agreement between graders in identifying the different types of hemorrhages.

Supported by: NEI Grant U10 EY017014
**Program Number:** 6270 **Poster Board Number:** C0013  
**Presentation Time:** 11:00 AM–12:45 PM  
**Analysis of Discrepancies between Diagnostic Clinical Examination and Corresponding Evaluation of Digital Images in the e-ROP Study**  
**Graham E. Quinn**1, 2, Anna Ells3, Antonio Capone, Jr.3, Ebenezer Daniel1, 2, P L. Hildebran3d, G B. Hubbard4, Gui-Shuang Ying2  
1 Ophthalmology, Children’s Hospital of Philadelphia, Philadelphia, PA; 2 Ophthalmology, University of Pennsylvania, Philadelphia, PA; 3 Associated Retinal Consultants, Royal Oak, MI; 4 University of Oklahoma, Oklahoma City, OK; 5 Emory University, Atlanta, GA; 6 University of Calgary, Calgary, AB, Canada.  
**Purpose:** To characterize discrepancies in retinopathy of prematurity (ROP) status between results of clinical examinations and gradings of retinal images from the “Telemedicine approaches to evaluating acute-phase ROP - e-ROP” Study.  
**Methods:** A secondary analysis of an observational cohort study of infants with birth weights of <1251g. Consensus review by four ROP experts of discrepancies [in stage 3, zone 1 ROP or plus disease which are components of referral-warranted ROP (RW-ROP)] between results of clinical examination and remote evaluation of images by trained readers. For discrepancy categories with >100 cases, 40 cases were randomly selected. A total of 188 image sets were reviewed.  
**Results:** Among the 5350 image set and clinical exam pairs where RW-ROP status could be determined for both, there were 161 discrepant cases where image grading did not detect RW-ROP noted on clinical examinations (G-/E+) and 854 discrepant cases where grading noted RW-ROP when the examination did not (G+/E-). Among G+/E- cases, 56.3% (18/32) of consensus reviews agreed with clinical exam that ROP was present in zone I and 45.0% (18/40) agreed stage 3 ROP was present. Consensus reviewers noted trained readers were less likely to detect stage 3 ROP than the clinicians, as, when the clinician noted stage 3 ROP, only stage 2 ROP was noted on review in 32.5% of 40 image sets evaluated and 22.5% no ROP was noted. Review noted only 5% (1/20) agreement with clinical exam on presence of plus disease in G-/E- cases. Among G+/E- cases, 90.0% (36/40) of consensus reviews agreed with trained readers that zone I ROP was present when the clinical exam did not, 57.5% (23/40) agreed with stage 3 ROP, and 25% (4/16) for plus disease.  
**Conclusions:** This report highlights strengths and limitations of both remote evaluation of fundus images and bedside clinical examination of infants at risk for ROP. Despite extensive training, trained readers were less likely to detect stage 3 ROP than the clinicians. However, for more quantitative evaluations including zone of ROP and plus disease, reader gradings were superior to clinical assessments. These findings are of importance as ROP telemedicine becomes more widespread and highlight the need for more quantitative approaches.  
**Commercial Relationships:** Graham E. Quinn, None; Anna Ells, Antonio Capone, Jr., Focus ROP (I); Ebenezer Daniel, None; P L. Hildebrand, Inoveon (I); G B. Hubbard, None; Gui-Shuang Ying, None  
**Support:** National Eye Institute of the National Institutes of Health, Department of Health and Human Services. U10 EY017014  
**Clinical Trial:** NCT01264276

**Program Number:** 6271 **Poster Board Number:** C0014  
**Presentation Time:** 11:00 AM–12:45 PM  
**Inter-Eye Agreement of ROP Features in Image Evaluation in the Telemedicine Approaches to Evaluating of Acute-Phase ROP (e-ROP) Study**  
Wei Pan1, Gui-Shuang Ying2, Graham E. Quinn2, Ebenezer Daniel1, Agnieszka Baumritter1  
**Purpose:** To determine the symmetry of ROP features (stage, zone and plus disease) between paired eyes in the image evaluation of retinal images of premature infants.  
**Methods:** Secondary analysis of data from image evaluation in e-ROP. Infants with birth weight less than 1251g underwent a series of retinal imaging sessions in both eyes by non-physician certified imagers using the Retcam Shuttle paired with a diagnostic eye examination by certified ophthalmologists starting at 32 weeks of postmenstrual age (PMA). Two trained readers graded independently ROP characteristics in a 5-image set from each eye. At the image reading center, readers were masked to diagnostic examination results, previous grading results, the current grading results of the fellow eye, and demographic data. A reading supervisor adjudicated disagreement between readers. The inter-eye agreements of ROP features were assessed using percent of agreement and weighted kappa.  
**Results:** Among 1235 infants with images taken in both eyes at a session (total of 3918 image sessions), the percent of exact agreement (weighted kappa) was 75.3% (0.65) for stage of ROP (no ROP, stages 1 or 2, 3 or above, cannot grade), 78.7% (0.51) for preplus/plus disease (normal, preplus, plus, cannot grade), and 82.3% (0.68) for zone of ROP (no ROP, zone I, zone II, cannot grade), 84.7% (0.56) for RW-ROP (no ROP, mild ROP, type 2, type 1, cannot grade). Similar inter-eye agreements were found in the first image session, the last image session and PMA weeks. Based on image evaluations at all sessions, 412 (33.4%) infants had ROP stage 3 or above at some point, 70 (5.7%) had plus disease, 148 (12.0%) had zone I ROP and 419 (33.9%) had RW-ROP; the percent of presence of these features in both eyes at some point was 71.4% for ROP stage 3 or above, 50.0% for plus disease, 56.8% for Zone I ROP and 73.7% for RW-ROP.  
**Conclusions:** The masked image evaluations by trained readers showed good inter-eye agreement in ROP characteristics, consistent with the high inter-eye correlation in ROP from clinical examinations by ophthalmologist. This finding supports the utility of using images in the clinical management and research of ROP.  
**Commercial Relationships:** Wei Pan, None; Gui-Shuang Ying, None; Graham E. Quinn, None; Ebenezer Daniel, None; Agnieszka Baumritter, None  
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Program Number: 6272 Poster Board Number: C0015
Presentation Time: 11:00 AM–12:45 PM

The German ROP Registry: Association of demographic factors and the requirement for re-treatments of retinopathy of prematurity

Johanna Madeleine Walz1, 2, Sebastian Bennme1, Daniel Boehringer1, Amelie Pielen1, Sabine Aisenbreym, Helge Breuβ1, Anne F. Alex8, Lars Wagenfeld, Susanne Schiedel10, Tim U. Krohne11, Andreas Stahl11.

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Purpose: The German ROP Registry collects multicenter data on ROP treatment and epidemiology of treatment-requiring ROP in Germany.

Methods: Nine participating centers entered data from 90 treated infants into a central database. Logistic regression was used to analyze possible associations of demographic and neonatal factors with the need for repeated treatments of ROP. The demographic covariates sex, gestational age (GA), birth weight, and initial neonatal care (internal vs. referred for treatment) were analyzed. Furthermore, the neonatal covariates need for supplemental oxygen and presence of co-morbidities (bacterial sepsis, systemic mycosis, cerebral hemorrhage, necrotizing enterocolitis or persistent ductus arteriosus) were assessed.

Results: One or more re-treatments were necessary in 31 of 177 eyes (18%). In logistic regression analysis, lower birth weight was significantly associated with multiple treatments for ROP (p=0.04). Mean birth weight was 716±261 g in the subgroup with a single treatment vs. 567±113 g in the subgroup with multiple treatments. Every 100 g of additional birth weight reduced the odds for requiring multiple ROP treatments by 4.4%. Similarly, extended oxygen supplementation was significantly associated with multiple treatments for ROP (p=0.03). Mean duration of oxygen supplementation was 97 days in the subgroup with a single treatment vs. 79 days in the subgroup with multiple treatments. Every day of oxygen supplementation increased the odds for requiring multiple ROP treatments by 4.2%.

Conclusions: All included infants required at least one treatment of ROP. Within this cohort, low birth weight and extended oxygen supplementation were significantly associated with an increased risk of requiring multiple treatments for ROP. This information helps to assess individual risk for ROP recurrence following treatment and to schedule follow-up exams.

Commercial Relationships: Johanna Madeleine Walz, Novartis Pharma GmbH (F); Sebastian Bennme, Novartis Pharma GmbH, Novartis Pharma GmbH (R); Amelie Pielen, Novartis Pharma GmbH (C), Bayer Healthcare (R), Bayer HealthCare (C), Novartis Pharma GmbH (R); Daniel Boehringer, None; Susanne Schiedel, None; Lars Wagenfeld, Bayer HealthCare (R), Novartis Pharma GmbH (C), Bayer HealthCare (C), Alimera Sciences (C); Tim U. Krohne, Bayer HealthCare (R), Novartis Pharma GmbH (F), Heidelberg Engineering (R), Alcon (F), Novartis Pharma GmbH (C), Novartis Pharma GmbH (R); Andreas Stahl, Boehringer Ingelheim (C), Novartis Pharma GmbH (F), Novartis Pharma GmbH (C), Bausch & Lomb (C), Zeiss (C), Novartis Pharma GmbH (R)

Support: Retina.net, Jackstaedt Foundation, German Retina Society, German Ophthalmological Society

Clinical Trial: www.drks.de, DRKS00004522

Program Number: 6273 Poster Board Number: C0016
Presentation Time: 11:00 AM–12:45 PM

Comparison of transpupillary laser versus intravitreal bevacizumab treatment in posterior zone II ROP


Purpose: To report the outcome of laser treatment in acute retinopathy of prematurity (ROP) in posterior zone II, to compare it to treatment with intravitreal 0.312mg bevacizumab (IVB) and to describe the vascular development over time.

Methods: In this retrospective study, 25 infants with ROP stage 3+ in posterior zone II were treated between August 2009 and August 2015 either by transpupillary laser photocoagulation performed with a diode laser (Ocu-Light SL, Iridex Corp) and a 20 or 28 dpt lens (Volk Optical Inc) in a near confluent technique (exposure time: 100-150ms, power: 200-500mW) (n=20, 40 eyes) or by IVB (n=5, 10 eyes) were included. Infants were examined by digital fundus photography and fluorescein angiography (FA) using a Shuttle, RetCam II or III (Clarity Inc.) before and after treatment.

Results: Mean gestational age was 25.2w ±4d, and 24.3w ±4d, and mean birth weight, 659 ±183g and 653 ±90g for the laser treated and the IVB group, respectively. Mean time to treatment was 12.5w ±16d and 10.7w ±6d, respectively. Acute ROP regressed in all eyes (100%) treated by a single IVB, but only in 75% of eyes with one laser treatment. Mean time to retreatment was 4.4 weeks after first treatment, and included repeated laser photocoagulation (1 infant o.u.), cryo-coagulation (3 infants o.u.) and IVB (1 infant o.u.). Repeated rescue treatments were necessary in 2 infants /4 eyes. No eye developed cataract or macular dragging. The overall success rate in the laser treated group was also 100%. Before treatment, most eyes showed leakage at the junction of the vascularized zone and capillary malformation. Vessel outgrowth into the periphery was observed in IVB treated eyes as well as in laser treated eyes, where the vessels continued to grow over the laser scars.

Conclusions: A single intravitreal dose of 0.312mg/eye bevacizumab was sufficient to induce regression of ROP in posterior zone II, in contrast to laser treatment, where 5 infants (10 eyes, 25%) needed at least one further treatment.

Commercial Relationships: Birgit Lorenz, None; Marie Neumann, None; Monika Andrassi-Darida, None; Melanie Jäger, None; Knut Stieger, None

Program Number: 6274 Poster Board Number: C0017
Presentation Time: 11:00 AM–12:45 PM

Laser Alone in Pre-Threshold Retinopathy of prematurity (ROP) and Combination Therapy in Threshold ROP: Anatomics results


Purpose: To describe the anatomic results after treatment with Laser alone in infants with Pre-Threshold ROP and a Combination Therapy of

Commercial Relationships: Carlos A. Abdulra, None; Maria A. Zuevondo, None; Cesar Atencia, None;
of Laser and Intravitreal Injection of Bevacizumab in infants with Threshold ROP in Barranquilla – Colombia between 2008 and 2014

**Methods:** Materials and Methods: Cross sectional study with case control analysis. Data collected from secondary sources.

Inclusion criteria: Infants ≤32 weeks and / or ≤ 1750 gr. Patients with incomplete medical records were excluded. The variables were: gestational age, birth weight, gender, chronological age, twin pregnancy, sepsis, oxygen, respiratory distress, perinatal surgeries, intraventricular hemorrhage, blood transfusions, distribution of ROP by stage, areas and type, distribution according to treatment and the relationship with weight and gestational age. Laser photocoagulation treatment in patients with Pre-Threshold ROP Type 1 and a Combined Treatment of Laser and Intravitreal Bevacizumab in patients with Threshold Disease was performed. Pogression or involution of ROP after treatment was also evaluated

**Results:** We studied 1038 eyes. Pre-Threshold ROP Type 1 was diagnosed in 88 eyes with a prevalence of 8.7% and Threshold ROP was diagnosed in 80 eyes with a prevalence of 7.7%. The largest proportion of patients with ROP by gestational age were ranged from 27 to 28 weeks group with 37.8%, followed by range of 29-30 weeks. 32.9% of patients with ROP were in 751-1000 g group, followed by 1001-1250 g group with 30.7%. A statistically significant difference was found between low birth weight, gestational age between 26 and 28 weeks, oxygen and respiratory distress. 96.6% of Pre-Threshold ROP infants treated with Laser had a completed resolution of ROP. 3.4% required a Rescue Therapy 15 days after initial treatment with Intravitreal Injection of Bevacizumab (0.65 mg/0.05 cc) and a second Laser treatment. 93.7% of Threshold ROP infants treated with Laser had a completed resolution of ROP. 73% of infants required a single dose of intravitreal bevacizumab and 26.6% required a second dose.

**Conclusions:** Laser alone in Pre-Threshold ROP and a Combination Therapy of Laser and Intravitreal Radiation in Threshold ROP showed to be an effective treatment to involution in active forms of ROP

**Commercial Relationships:** Carlos A. Abdala, None; Maria A. Izquierdo, None; cesar atencia

**Program Number:** 6275  **Poster Board Number:** C0018  **Presentation Time:** 11:00 AM–12:45 PM

**Bilateral Retinal Vascularization after Unilateral Bevacizumab for Type 1 Retinopathy of Prematurity**

**Nasrin N. Tehrani, Maram Isaac, Kamiar Mireskandari. University Eye Hospital, Hospital for Sick Children, Toronto, ON, Canada.**

**Purpose:** To address the question of whether a single injection of intravitreal bevacizumab (IVB) for type 1 retinopathy of prematurity results in abnormal retinal vascularization, we compared fundus fluoresein angiography (FFA) between treated and untreated eyes in unilaterally treated infants.

**Methods:** This is a retrospective chart review of all infants treated with IVB in one eye from March 2012 - April 2014. Treatment was performed and structural outcomes defined according to the Early Treatment for Retinopathy of Prematurity study criteria. We measured the extent of temporal vascularization before and after treatment. A linear measurement in disc diameter (dd) was taken from the center of the temporal edge of the optic disc extending through the fovea to the border of vascular-avascular retina. Measurements were performed using Imagej software with line analysis tools. We also collected data on the presence or absence of leakage on FFA.

**Results:** Five infants were included. The fellow eyes did not meet treatment criteria at any time. All treated eyes responded to a single injection of 0.625 mg IVB and showed regression of disease activity. None had a recurrence or required further treatment. Vascularization extent between treated and untreated eyes was within 2.0 dd on FFA performed at a mean of 10.2±2.9 months post treatment. In two patients, there was leakage of fluorescein on images performed at 12 and 14.5 months post treatment in treated and untreated eyes at the vascular-avascular margin in the absence of neovascularization. All treated eyes vascularized to ora serrata nasally and none developed unfavorable structural outcomes at a mean follow up of 28.9±10.1 months. All but one untreated eye vascularized into zone III.

**Conclusions:** In this cohort, vascular growth was comparable between treated and untreated eyes of the same infant. Systemic absorption did not appear to impede retinal vascularization in the untreated eyes. Leakage from advancing retinal vasculature in the absence of neovascularization may be seen in both treated and untreated eyes without long-term unfavorable outcomes. These vascular abnormalities may be related to prematurity rather than treatment with bevacizumab.

**Commercial Relationships:** Nasrin N. Tehrani, None; Maram Isaac, None; Kamiar Mireskandari, None

**Program Number:** 6276  **Poster Board Number:** C0019  **Presentation Time:** 11:00 AM–12:45 PM

**Vitreous changes associated with regression of Retinopathy of prematurity after intravitreal injection of anti-vascular endothelial growth factor**

**Francisco Olguin, Maria Ana Martinez-Castellanos, Virgilio Morales-Canton, Raul Velez-Montoya, Andrea Arriola Lopez, Guillermo Salcedo, Miroslava Meraz-Gutierrez. Retina, Asociacion para evitar la ceguera en mexico, Mexico city, Mexico.**

**Purpose:** To evaluate the vitreous changes associated with regression of ROP after therapy with intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF)

**Methods:** Retrospective case series study. This study was conduced with Institutional Review Board approval at Asociación para Evitar la Ceguera en México(APEC), from January 2013 to September 2015. We have selected patients with type 1 ROP with prominent fibrovascular component in the ridge at the demarcation line treated with ranibizumab. All patients were diagnosed and monitored at each visit with wide-angle images using 130° lens. The main outcome measure was the vitreous changes associated with ROP regression in patients that shown a prominent ridge at initial evaluation.

**Results:** A total of 9 eyes of 5 patients were included. All patients were treated with ranibizumab monotherapy. The mean gestational age and birth weight was 29.28 ± 1.22 and 1267 ± 249.7, respectively. The vitreous changes observed in treated patients were a posterior vitreous detachment (PVD) at the demarcation line observed by digital photographs and confirmed by ultrasonography at 9.44 ± 4.66 weeks after treatment.

**Conclusions:** Some infants treated with anti-VEGF that showed regression of ROP, developed a PVD during the monitoring with wide-angle digital images. The vascular component of the fibrovascular membrane regressed and a PVD occurred at the demarcation line. Further analysis are needed in more patients to understand the behavior of the prominent ridge during the regression of ROP.

**Commercial Relationships:** Francisco Olguin, None; Maria Ana Martinez-Castellanos, None; Virgilio Morales-Canton, None; Raul Velez-Montoya, None; Andrea Arriola Lopez, None; Guillermo Salcedo, None; Miroslava Meraz-Gutierrez, None

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**ARVO 2016 Annual Meeting Abstracts**

**Program Number:** 6277 Poster Board Number: C0020

**Presentation Time:** 11:00 AM–12:45 PM

**A Proposal Of An Algorithm For The Diagnosis And Treatment Of Recurrence Or Failure To Treatment Of Retinopathy Of Prematurity (ROP) After Anti-VEGF Therapy Based On A Case Series Analysis**

Maria A. Martinez-Castellanos1, 2, Francisco Olguin1, 2, Retina, Asociacion para Evitar la Ceguera, Toluca, Mexico; 2Retina, Clinica de Enfermedades de los Ojos, Toluca, Mexico.

**Purpose:** The aim of this study is to propose an algorithm for the diagnosis of recurrence vs failure to treatment after intravitreal anti-VEGF therapy for ROP and the management of both conditions.

**Methods:** Retrospective review of all patients treated with intravitreal anti-VEGF therapy for ROP admitted to a teaching hospital from 2005 to 2015. The patient’s medical records were reviewed for clinical features, diagnostic work-up, treatment strategies and response to therapy. All patients underwent wide angle imaging. Failure to treatment was defined as persistence of pathological new vessels, elevation of the ridge in the demarcation line, worsening of plus disease or retinal crunch in the first week after treatment. Recurrence was defined as the appearance of plus disease, an elevated ridge, or pathological new vessels after an initial regression of ROP after treatment. Suspected cases of recurrence or failure to treatment had supplementary angiograms and in some cases ultrasound to guide the therapeutic modality to be offered. Conservative therapy included close observation by angiography, modify the oxygen scheme if the baby persisted under oxygen and performing a differential diagnosis to rule out oxygen induced retinopathy or other vascular diseases as FVER. Interventional therapy was either new injection of anti-VEGF agents, switch to a different anti-VEGF, laser, vitrectomy, or combined therapy.

**Results:** We included 576 patients treated with anti-VEGF therapy for ROP. 7 patients (1.21%) had failure to treatment, 6 (0.79%) developed a recurrence of ROP, and 37 (6.4%) were misdiagnosed as a recurrence somewhere else and sent for treatment. The therapeutic ladder for these patients ranged from observation, new injection of the same or different anti-VEGF agent, through laser or vitrectomy or a combined therapy.

**Conclusions:** Failure to treatment is a condition to distinguish from recurrence of ROP. Appropriate patient evaluation algorithms and treatment therapeutic ladders are proposed. This is a novel algorithm that has the capacity to grow and expand as more clinical evidence becomes available. It offers, for the first time, a summary of recommendations for the treatment of failure/reactivation of ROP.

**Commercial Relationships:** Maria A. Martinez-Castellanos, None; Francisco Olguin

**Clinical Trial:** NCT00346814

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**Program Number:** 6278 Poster Board Number: C0021

**Presentation Time:** 11:00 AM–12:45 PM

**Determination of optimal dosing of rhIGF-1/rhIGFBP-3 to establish and maintain physiological intrauterine serum IGF-1 levels in preterm infants**

Ann Hellstrom1, Boubou Hallberg2, Ingrid Hansen-Pupp1, Jou-Ku Chung1, Jyoti Sharma4, Gerald Fetterly6, Mary Ann Mascelli4, Nerissa Kreher2, Norman Barton1, David Ley1. 1Sahlgrenska Academy, Gothenburg, Sweden; 2Karolinska Institute and University Hospital, Stockholm, Sweden; 3Department of Pediatrics, Institute of Clinical Sciences Lund, Skane University Hospital and Lund University, Lund, Sweden; 4Shire, Lexington, MA; 5PKPD Bioscience Inc., Exton, PA; 6Roswell Park Cancer Institute, Buffalo, NY.

**Purpose:** rhIGF-1/rhIGFBP-3 is being investigated for the prevention of retinopathy of prematurity in preterm infants. A population pharmacokinetic (PK) model was developed using data from phase 1 and 2 (Sections A-C) studies of rhIGF-1/rhIGFBP-3 in preterm infants in order to predict optimal dosing to establish and maintain serum IGF-1 within physiological intrauterine levels. Section D of the phase 2 study, evaluating dosing/efficacy of rhIGF-1/rhIGFBP-3, was initiated using the predicted dose. We report serum IGF-1 levels for the first 10 infants treated in Section D.

**Methods:** The phase 2 Section D study is ongoing in infants with gestational age (GA; wk+d) 23+0 to 27+6 at birth, randomized to rhIGF-1/rhIGFBP-3 or standard of care; target enrollment is 120 infants. rhIGF-1/rhIGFBP-3 is administered at 250 µg/kg/d by continuous intravenous (IV) infusion from birth up to a postmenstrual age of 29 wk+6 d. A review of serum IGF-1 data was conducted once 10 treated infants completed the dosing phase of the study to assess suitability of the dose regimen to reach and maintain serum IGF-1 target levels of 28–109 µg/L (physiological intrauterine levels for GA 23–28 wk based on published literature).

**Results:** Serum IGF-1 data were reviewed for 10 treated (50.0% male) and 9 control infants (66.7% male). At birth, GA (wk+d) ranged from 24+4–27+5 for treated and 23+3–27+6 for control infants; birth weight ranged from 0.5–1.1 kg and 0.6–1.2 kg, respectively. Duration of therapy in treated infants ranged from 1–34 days. At baseline, mean (SD) serum IGF-1 was 19.2 (8.0) µg/L for treated and 15.4 (4.7) µg/L for control infants. Mean (SD) serum IGF-1 levels increased to 45.9 (19.6) µg/L at 12h in treated infants, and remained within target levels for all subsequent timepoints. In controls, mean serum IGF-1 remained below target levels for all timepoints. Overall, 88.8% of serum IGF-1 measurements were within target levels for treated infants (11.1% for controls).

**Conclusions:** Using the selected dose of rhIGF-1/rhIGFBP-3 (250 µg/kg/d by continuous IV infusion), serum IGF-1 levels were within targeted, physiological intrauterine levels for the majority of measurements in treated infants. This analysis validates the population PK model and confirms the appropriateness of the designed dosing regimen for Section D.

**Commercial Relationships:** Ann Hellstrom, Premalux AB (I), Shire (C); Boubou Hallberg, Premacure AB (C); Ingrid Hansen-Pupp, Premalux AB (I), Shire (C); Jou-Ku Chung, Shire; Jyoti Sharma, PKPD Bioscience Inc.; Gerald Fetterly, PKPD Bioscience Inc., Shire (C); Mary Ann Mascelli, Shire; Nerissa Kreher, Shire; Norman Barton, Shire; David Ley, Premalux AB (I)
Support: This study was funded by Premacure AB, a member of the Shire group of companies. The authors thank Valerie Boissel PhD, of Excel Scientific Solutions, who provided medical writing assistance funded by Shire.

Clinical Trial: NCT01096784

Program Number: 6279 Poster Board Number: C0022
Presentation Time: 11:00 AM–12:45 PM
Retinopathy of Prematurity in an Inner-City Predominantly Hispanic Population
Xihui Lin, Ashish Singh, Kim Le, Yu-Guang He. Department of Ophthalmology, UT Southwestern Medical Center, Dallas, TX.

Purpose: The survival rate of premature infants has increased significantly over the past 2 decades and consequently, retinopathy of prematurity (ROP) has become a more prevalent problem facing ophthalmologists. The inner city population is of particular interest due to the poor access to healthcare and multiple maternal comorbidities. The aim of this study is to analyze the characteristics and risk factors for ROP in this population in which more than 60% of the population is Hispanic; a cohort that has never been studied before.

Methods: All newborns delivered at Parkland Memorial Hospital between 1/2009 to 7/2014 who had a screening eye exam for ROP and met the screening criteria of weight under 1500 grams or age under 32 weeks were included. Factors analyzed included demographics, comorbidities, severity and treatment of ROP. Maternal factors and comorbidities were also reviewed. Chi squared test was used for categorical data and Student t test for quantitative data analysis. Odds ratio was calculated for potential risk factors. This study received IRB approval from University of Texas Southwestern Medical Center.

Results: 391 consecutive newborns were analyzed: 69.3% were Hispanic. The average gestational age at birth was 28.3 weeks and weight was 1176.6 grams, 45.3% of the patients developed ROP and of those with ROP, 27.1% were stage 3 or higher. Statistically significant risk factors for the development of ROP included bronchopulmonary dysplasia (OR 3.34), patent ductus arteriosus (OR 3.08), high grade intraventricular hemorrhage (OR 8.97), sepsis (OR 19.70), and major surgeries (OR 7.37). Maternal risk factors included advanced maternal age (OR 3.98), and pre-eclampsia (OR 1.88). At the 6 year follow up, those with ROP had a visual acuity of 20/36 with a +0.47 diopter refractive error. Laser treated eyes had worse myopia. 6.25% of the patients developed amblyopia.

Conclusions: The high rate of ROP in an inner-city underserved population was correlated with multiple risk factors including bronchopulmonary dysplasia, patent ductus arteriosus, high grade intraventricular hemorrhage, sepsis, and major surgeries. Maternal factors that increased the development of ROP included high parity, advanced maternal age, and pre-eclampsia. At 6 years, visual acuity was good but the rate of amblyopia was high and myopia rate increased with laser treatment.

Commercial Relationships: Xihui Lin, None; Ashish Singh, None; Kim Le, None; Yu-Guang He, None

Program Number: 6280 Poster Board Number: C0023
Presentation Time: 11:00 AM–12:45 PM
Retrospective analysis on the prevalence of Severe Retinopathy of Prematurity with a Change in Oxygen Supplementation at Yale New-Haven Hospital
Tiffany S. Liu, Matthew Bizzaro, Richard Ehrenkranz, Kathleen Stoessel. Yale New-Haven Hospital, New Haven, CT.

Purpose: Retinopathy of Prematurity (ROP), a disease of underdeveloped retinal vasculature in premature infants, was previously treated with high oxygen saturation limits until studies have shown this may shut down normal vascular development by down-regulating an essential vascular endothelial growth factor. Recent studies have shown using lower oxygen saturation targets closer to in utero for the first weeks of life and then liberalizing the oxygen saturation lessened the incidence of severe ROP requiring laser photocoagulation intervention. In this retrospective study we evaluate the incidence of severe ROP requiring laser intervention before and after a change in oxygen saturation from initial higher rates to lower saturation rates at the Yale New-Haven Neonatal ICU.

Methods: Charts of premature infants (n=679) <=1500 grams birth weight and/or <=30 weeks gestational age born at Yale-New Haven Children’s Hospital or transferred in within the first 48 hours of life that were screened for ROP between the dates of 1/1/2009 and 12/31/2014 were reviewed. Zone and stage of ROP, progression of ROP, timing of progression of ROP, and need for laser surgery were recorded. Results were analyzed using repeated measures analysis of variance.

Results: Of 679 premature infants screened for ROP from 2009-2014, 27 had severe ROP requiring laser (7.3%). Prior to changing to lower initial oxygen saturation rates, of the 369 infants examined, 22 infants required laser (6.0%). After changing to lower oxygen saturation rates, of the 310 infants examined, 5 infants required laser (1.6%). This demonstrated a statistically significant decrease in the incidence of severe ROP requiring laser after oxygen saturation change (OR=3.87; CI=1.45-10.34; p=0.0039).

Conclusions: Our results demonstrate lower initial oxygen saturation rates in treatment of premature infants leads to a statistically significant decrease in the incidence of severe ROP requiring laser. Further analysis of the severity of ROP for premature infants including zone and stage before and after oxygen saturation change, as well as associated factors such as birth weight and gestational age, and comorbidities will need to be further explored to better elucidate the impact of the change in oxygen.

Commercial Relationships: Tiffany S. Liu, None; Matthew Bizzaro; Richard Ehrenkranz, None; Kathleen Stoessel, None

Program Number: 6281 Poster Board Number: C0024
Presentation Time: 11:00 AM–12:45 PM
Severe Retinopathy of Prematurity in Puerto Rico
Yousef Cruz-Inigo, Raoul Perez. Ophthalmology, University of Puerto Rico, San Juan, PR.

Purpose: To estimate the incidence of severe retinopathy of prematurity (ROP) for infants screened at the University of Puerto Rico Pediatric Hospital (HOPU) and, using our cohort’s baseline characteristics, to calculate the adjusted odds ratios (OR) for developing severe ROP.

Methods: Cross-sectional study of all infants born in Puerto Rico (PR) and screened for severe ROP between January 1, 2006 and December 31, 2006. Infants were either born at HOPU (inborns) or were transferred to HOPU from any of 19 Neonatal Intensive Care Units (outborns). According to the American Academy of Pediatrics guidelines from 2006, we included only infants that survived to 31 weeks chronological age and had a birth weight (BW) of less than 1500 grams (g) or a gestational age (GA) of 30 weeks (wks) or less. Severe ROP was defined by the Early Treatment for ROP Study (ETROP Type 1) for which prompt laser application had to be considered. This included zone 1 any stage ROP with plus disease, zone 1 stage 3 ROP with or without plus disease, or zone 2 stage 2 or stage 3 ROP with plus disease. Chi-square analysis was used...
Program Number: 6282 Poster Board Number: C0025
Presentation Time: 11:00 AM–12:45 PM

International publication trends of retinopathy of prematurity literature over 40 years
Paras P. Vakharia1, Natalie T. Huang1, Michelle Jankowski1, Benjamin J. Thomas2, Robison V. Chan1, Michael T. Trese3, Antonio Capone Jr.3, Yoshihiro Yonekawa1, Kimberly A. Drener2, 3
1Oakland University William Beaumont School of Medicine, Rochester, MI; 2Associated Retinal Consultants, Royal Oak, MI; 3Illinois Eye and Ear Infirmary, University of Illinois College of Medicine, Chicago, IL.

Purpose: The socioeconomic distribution of retinopathy of prematurity (ROP) has evolved, where middle-income nations are currently experiencing epidemics. We hypothesize that ROP research from middle-income nations has also increased. We therefore conducted a bibliometric analysis to evaluate the publication trends of ROP literature.

Methods: A search for indexed English abstracts using search terms of “retinopathy of prematurity” or “retrolental fibroplasia” was performed in PubMed from 1976 to 2015, and divided into 4 decades. Original research articles involving human subjects were included. Countries were grouped into high-, middle-, and low-income groups using World Bank criteria based on the population being studied, and impact factors (IF) were gathered from 2014 Thomson Reuters Journal Citation Reports.

Results: A total of 5,425 publications were identified, of which 2,045 referenced and the PMAs are compared statistically. High- (82.2%), middle- (17.7%), and low-income nations (0.1%) were increasingly producing more papers (p<0.01), but in lower IF journals overall (p<0.01) (Table 1). High-income journals overall (p<0.01) (Table 1).

Conclusions: Investigators from middle-income nations are increasingly contributing to ROP literature, but overall, may not be recognized in high-impact journals compared to literature from high-income nations.

Table 1. High-income vs. Middle-income vs. Low-income

<table>
<thead>
<tr>
<th>Year</th>
<th>High-income</th>
<th>Middle-income</th>
<th>Low-income</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articles</td>
<td>Mean IF (±SD)</td>
<td>Mean IF (±SD)</td>
<td>Mean IF (±SD)</td>
</tr>
<tr>
<td>1976-1985</td>
<td>N=105 (5.3%)</td>
<td>N=0</td>
<td>N=0</td>
</tr>
<tr>
<td>1986-1995</td>
<td>5.41 (10.21)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>1996-2005</td>
<td>N=317 (15.5%)</td>
<td>N=7 (0.3%)</td>
<td>N=0</td>
</tr>
<tr>
<td>2006-2015</td>
<td>2.83 (4.95)</td>
<td>1.06 (0.86)</td>
<td>N=0</td>
</tr>
</tbody>
</table>

Commercial Relationships: Paras P. Vakharia, None; Natalie T. Huang, None; Michelle Jankowski, None; Benjamin J. Thomas, Robison V. Chan, None; Michael T. Trese, FocusROP (S), FocusROP (I); Antonio Capone Jr., FocusROP (S), FocusROP (I); Yoshihiro Yonekawa, None; Kimberly A. Drener, FocusROP (S), FocusROP (I)

Support: Yoshihiro Yonekawa is partially funded by the Heed Ophthalmic Foundation and the Ronald G. Michels Foundation. The Foundations had no role in the design or conduct of the study. Dr. Robison Vernon Paul Chan is partially funded by the Departmental Grant from Research to Prevent Blindness. The grant had no role in the design or conduct of the study.

Program Number: 6283 Poster Board Number: C0026
Presentation Time: 11:00 AM–12:45 PM

A Retrospective Analysis of the Timing of Initial Treatment of Bedside Screened vs. Photographically Screened Retinopathy of Prematurity (ROP) Eyes
Akhila N. Alapati, Michael T. Trese. Ophthalmology, Oakland University at William Beaumont School of Medicine, Royal Oak, MI.

Purpose: We performed a retrospective clinical study to assess whether telemedicine screening for retinopathy of prematurity (ROP) allowed timely and accurate diagnosis for treatment warranted ROP compared to bedside examination.

Methods: We studied 130 eyes of 65 premature babies, comparing the postmenstrual age of patients with treatment warranted ROP determined by bedside examination (2006-2010) or telemedicine screening (2010-2014). Telemedicine screenings began during 2010 at Royal Oak Beaumont. All of the patients are in-born neonates at the Royal Oak Beaumont Neonatal Intensive Care Unit (NICU). Gestational age and birth weight are similar in both groups. All eyes received laser treatment. The data is sorted out to examine the number of eyes and postmenstrual age (PMA) of patients who had laser treatment for ROP. Both methods of diagnosis are cross-referenced and the PMAs are compared statistically.

Results: A total of 130 eyes of 65 infants meet the inclusion and exclusion criteria for this study. For the bedside examination infants, the range of gestational age (weeks) and birth weight (g) is from 23 to 29 1/7 weeks and 445 to 909g. For telemedicine-screened patients, the ranges are 23 1/7 to 26 3/7 weeks and 447 to 950g respectively. The p value of the gestational age between both groups is .46. There is a statistical difference in birth weight as bedside-screened neonates have an average of 618.9±115.9g and telemedicine screened have an average of 683±134 (p=0.043). From 2006 to 2010, 35 NICU patients
were screened through bedside examination. The average PMA at laser treatment for these infants is 36.50 weeks. From 2010 to 2015, a total of 30 infants were photographically screened. The average PMA at treatment for the telemedicine-screened patients is 36.42 weeks. There is no statistical difference in PMA of both groups after adjusting for birth weight (p = 0.58).

**Conclusions:** Previous studies have documented that photographic telemedicine ROP screening allows for accurate diagnosis and better documentation than bedside examination with drawings. This is the first study that confirms that telemedicine also allows for appropriately timed treatment for early retinopathy of prematurity.

**Commercial Relationships:** Akhila N. Alapati, None; Michael T. Trese

**Program Number:** 6284 Poster Board Number: C0027
**Presentation Time:** 11:00 AM–12:45 PM

A Model for Studying ROP in IUGR

Dallas S. Shi¹, Ashlie Bernhisel¹, Patrick Kamba¹, Ashley Brown², Camille Fung³, M Elizabeth Hartnett³. ¹School of Medicine, University of Utah, Salt Lake City, UT; ²Neonatology, University of Utah, Salt Lake City, UT; ³Moran Eye Institute, University of Utah, Salt Lake City, UT.

**Purpose:** Infants with intrauterine growth restriction (IUGR) are known to be susceptible to developing retinopathy of prematurity (ROP), yet no animal model mimicking the most common etiology of IUGR has been used to study ROP. Here, we use maternal infusion of a thromboxane A₂-analog in mice during the last week of gestation to mimic human pregnancy-induced hypertension, a common cause of IUGR. We test the hypothesis that IUGR pups would exhibit abnormal retinal vascular development after birth compared to pups from sham-operated dams.

**Methods:** Matings of C57BL6/J mice were set up. At E12.5, pregnant females were anesthetized with ketamine (40 ug/g) and xylazine (8 ug/g). Then, a 1-cm incision was made over the right hip. Micro-osmotic pumps (Durect Corporation) containing vehicle (0.5% ethanol for sham group) or 2000ng/h of U-46619 (Cayman Chemical) were implanted retroperitoneally through the incision. Dams were allowed to deliver spontaneously. On day 5, a cohort of sham and IUGR mice were weighed, euthanized, and retinas dissected. A separate cohort of animals was placed through the oxygen-induced retinopathy (OIR) model (Smith et al. 1994). All dissected retinas were fixed, stained with isolectin, flatmounted, and analyzed using student t-tests.

**Results:** IUGR pups weighed 12% less on postnatal day 5 compared to shams (n = 8, P = 0.04). At baseline on postnatal day 5, IUGR pups showed abnormal vessel development with a paucity of branched vessels but with further vessel migration. A 9-fold increase in neovascular tufts was observed in IUGR mice retinas on postnatal day 5 compared to sham controls (N = 3, P = 0.0061). Hyperbaric oxygen exposure similarly resulted in an increase in neovascular tufts in IUGR pups compared to controls (mean = 18.7% in sham vs. 28.9% in IUGR retinas, n = 5, P = 0.0127). Total avascular areas was not significantly different between the OIR groups but was decreased in baseline postnatal day 5 IUGR pups (37.2% in sham vs. 13.2% in IUGR retinas, n = 3, P = 0.0351).

**Conclusions:** Our results allows for animal interrogation into the molecular mechanisms of IUGR-induced ROP. We demonstrate that an *in utero* hypoxic environment produced by pregnancy-induced hypertension paves the way for pathological retinal vessel growth after birth. This abnormality is compounded by a secondary postnatal hypoxic challenge and reflects neovascular changes typically seen in human ROP.
media haze and development of treatment-warranted retinopathy of prematurity
Margaret Greven, Cassie A. Ludwig, Darius M. Moshfeghi.
Ophthalmology, Stanford University, Redwood City, CA.

Purpose: To describe the correlation between media haze on fundus photography and the development of treatment-warranted retinopathy of prematurity (TW-ROP).

Methods: A retrospective case control study. Fundus photographs of premature newborns enrolled in a teledermic screening protocol found to have TW-ROP and those of untreated controls within the same cohort at six neonatal intensive care units from December 1, 2005 to 2015 were reviewed to grade degree of haze based on modified NIH grading system at different time points. Statistical analysis was performed using McNemar’s chi-squared statistic for matched data to assess the relationship between media haze in newborns with TW-ROP compared with controls with non-TW-ROP.

Results: Images of 62 eyes of 31 newborns were analyzed for the TW-ROP group, and images of 62 eyes of 31 newborns were analyzed for the the non-TW-ROP groups. The TW-ROP and non-TW-ROP group were similar with respect to baseline characteristics including gender and multiplicity although there was a significant difference at baseline with respect to gestational age and birth weight. While there was a trend towards more haze in the TW-ROP group at baseline exam, this was not statistically significant (p=0.1206). When comparing degree of haze at all time points, there was no significant difference between the two groups (p=0.1947). There was strong inter-eye correlation in level of haze. In photographs from subsequent exams after the baseline exam, degree of haze improved in both groups.

Conclusions: In this exploratory analysis, presence of media haze on fundus photography of newborns undergoing ROP screening was not strongly correlated with development of TW-ROP. Media haze may preclude adequate fundus examination in infants at risk for TW-ROP, especially at baseline exam when it is most prevalent. Fortunately, the degree of haze decreases with time, thereby allowing better visualization of the fundus for adequate screening.

Commercial Relationships: Margaret Greven, None; Cassie A. Ludwig, None; Darius M. Moshfeghi

Quantification of VEGF-A in different blood samples of adults, term and pre-term infants
Claudia Carolina Lopez Tomayuzca, Knut Stieger, Birgit Lorenz.
Department of Ophthalmology, Justus-Liebig-University Giessen, Giessen, Germany.

Purpose: To quantify and compare the VEGF-A and platelet factor 4 (PF-4) concentrations in different blood samples of adults, term and pre-term infants. In this study, the VEGF-A status in blood samples, namely serum, plasma and other blood compartments, of healthy adults as well as term and pre-term infants was assessed.

Methods: Venous blood samples of healthy adults (n=10) and cord blood samples of term (n=13) as well as preterm (n=26) infants were collected. Serum, serum from recalcified citrate blood (rS), Citrate plasma (CB_P), Citrate-Theophylline-Adenine-Dipyridamol (CTAD) plasma (CTAD_P) and platelets suspensions were obtained. The VEGF-A and Platelet Factor 4 (PF-4) concentration was measured by Enzyme-linked Immunosorbent Assay (DuoSet ELISA, Fa. R&D Systems) or AlphaLISA immunoassay (Fa. Perkin Elmer). Additionally, citrate plasma and rS samples of 7 infants with ROP were also analysed, two of them before and after treatment with intravitreal bevacizumab (IVB).

Results: VEGF-A levels in CB_P samples of healthy adults as well as serum and plasma of pre-term infants were between below the detectable level and 220 pg/ml for both ELISA and AlphaLISA assays. PF-4 concentrations in the same samples were between 0,15 – 4,2 pg/ml. No significant differences between the concentrations of VEGF-A in CB_P and CTAD_P were found. VEGF-A as well as PF4 levels in serum and recalcified serum from citrate blood (rS) samples correlated significantly. In CB_P samples of infants with ROP VEGF-A values ranged from 6 to 200 pg/ml. Concentrations of PF-4 lay between

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Program Number: 6289 Poster Board Number: C0032
Presentation Time: 11:00 AM–12:45 PM
Pilot Study of a Tiered Approach to ROP Screening (TARP) using a Weight Gain Predictive Model and a Telemedicine System

Agnieszka Baumritter1, Jaclyn Gurwin1, Graham E. Quinn1, Gui-Shuang Ying1, Lauren Tomlinson1, Gil Binenbaum1.

Purpose: The e-ROP Study telemedicine system of remote fundus imaging and the CHOP-ROP postnatal-weight-gain predictive model are two approaches for improving the efficiency of retinopathy of prematurity (ROP) screening. Since current screening has low specificity for severe ROP, we sought to develop a tiered approach for identifying children who develop severe ROP (TARP) by using these two modalities synergistically.

Methods: Secondary analysis of data on premature infants with birth weight (BW)<1500g from the e-ROP and G-ROP studies. Four approaches to ROP screening were evaluated: ROUTINE (only diagnostic examinations), MODEL (BW, gestational age-GA, weight gain calculated weekly initiates examinations when risk cut-point surpassed), IMAGING (trained-reader grading of type 1 or 2 ROP initiates examinations), and TARP (CHOP-ROP alarm initiates imaging, image finding of severe ROP initiates examinations).

Results: The study included 242 infants, median BW 858g (range 690-1035). Sensitivity for type 1 ROP (32 (13%) infants) was 100% (95% CI 89.3%-100%) with all four approaches. With ROUTINE, 242 infants had 877 examinations. With MODEL, 184 infants had 730 examinations. With IMAGING, all 242 infants had 532 imaging sessions, with 94 having 345 examinations. With TARP, 182 infants had 412 imaging sessions with 87 having 322 examinations.

Conclusions: The MODEL alone decreased the number of infants requiring exams by 24% and exams by 17%. IMAGING required image acquisition and grading, but reduced infants receiving exams by 61% and exams by 60%. TARP decreased infants imaged by 25%, imaging sessions by 23%, infants examined by 63%, and exams by 63%. Applying a postnatal-growth model and telemedicine system in a tiered approach may improve ROP screening efficiency more than either approach alone. Further validation is needed before clinical use.

Commercial Relationships: Agnieszka Baumritter, None; Jaclyn Gurwin; Graham E. Quinn, None; Gui-Shuang Ying, None; Lauren Tomlinson, None; Gil Binenbaum, None
Support: NEI Grant U10EY1017014 and NEI R01EY021137
Clinical Trial: NCT01264276

Program Number: 6290 Poster Board Number: C0033
Presentation Time: 11:00 AM–12:45 PM
Retinopathy of Prematurity (ROP) Prevalence and Risk Factors in King Abdulaziz Medical City (KAMC) in Riyadh

Abdulaziz Anazi A. Alshamrani1, Bader Al-Qahtani2, Faris Ahmad3, Mohammed Al-Otaibi4, Mohand Al-Zughaihi5, Aamir Omair5, Khalid Al-Jobair1. 1King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia; 2College of Medicine, King Saud bin Abdul-Aziz University for Health Sciences, Riyadh, Saudi Arabia; 3College of Medicine, King Faisal University, Al-Ahsa, Saudi Arabia.

Purpose: BACKGROUND: Retinopathy of prematurity (ROP) is an eye disease that affect premature infants. A small gestational age, low birth weight and high oxygen therapy considered as risk factors for ROP. It is one of the common causes of childhood blindness unless treated appropriately. OBJECTIVE: The aim of this project was to determine the prevalence of ROP in preterm infants in the Neonatal Intensive Care Unit, to identify the risk factors that predispose to ROP and to assess the outcome of those infants.

Methods: METHODS: This was a retrospective cohort study of premature infants with birth weight of ≤1500 grams or gestational age of ≤32 weeks. Those infants were admitted to NICU of King Abdul-Aziz Medical City in Riyadh between January 2010 to December 2014. The demographic data, perinatal risk factors for ROP and outcomes of those patients were assessed and analyzed by SPSS.

Results: RESULTS: Five hundred and ninety three infants were included in this study. Out of those, 224 infants (37.8%) had ROP. A percentage of 11.1% of those infants had stage 3, which means a severe ROP disease. The mean body weight of infants with ROP was 983 g and the mean gestational age at birth was 27 weeks. A significant relationship with a p-value <0.05 has been found between the occurrence of ROP and small gestational age at birth, low birth weight, low APGAR score at 1 minute and long duration of receiving O2 therapy. Among those infants with ROP, 3 infants had Laser treatment and 14 had Anti-VEGF. Based on charts review, no one of those infants had blindness.

Conclusions: CONCLUSION: The prevalence of ROP in our study beside other local studies fall in the range of the disease prevalence in the developing countries. It is recommended to control the duration of oxygen therapy.

Commercial Relationships: Abdulaziz Anazi A. Alshamrani, None; Bader Al-Qahtani, None; Faris Ahmad; Mohammed Al-Otaibi, None; Mohand Al-Zughaihi, None; Aamir Omair, None; Khalid Al-Jobair, None

Program Number: 6291 Poster Board Number: C0034
Presentation Time: 11:00 AM–12:45 PM
Diagnostic discrepancies in retinopathy of prematurity classification

J. Peter Campbell1, Michael Ryan1, Emily Lore2, Susan Ostmo3, Karyn Jonas3, Robison V. Chans, Michael F. Chiang4, 5Oregon Health & Science University, Portland, OR; 6University of Illinois Chicago, Chicago, IL.

Purpose: To identify the most common areas for discrepancy in retinopathy of prematurity (ROP) classification between experts and between image-based and ophthalmoscopic classification

Methods: 325 infants were recruited as part of a multi-center ROP cohort study from 8 participating centers. Each site had participating ophthalmologists who provided the clinical classification after routine ophthalmoscopic examination, and obtained wide-angle retinal images (RetCam; Clarity Medical Systems, Pleasanton, CA).
Images were independently classified by two study experts using a secure web-based module. Image-based classifications (zone, stage, plus disease, overall disease category) were compared between the two experts, and to the clinical classification by the examining ophthalmologist. Inter-expert image-based agreement and image-based vs. clinical diagnostic agreement were determined using absolute agreement and weighted kappa statistic.

**Results:** 1774 study eye examinations from 325 infants were included in the study. Experts disagreed with each other on the stage classification in 721/1774 (41%) of comparisons, plus disease classification (including pre-plus) in 334/1774 (19%), and zone in 147/1774 (8%). Disagreement in classifying presence of type 1 disease was between 3 and 5% for all comparisons. There were systematic differences between image-based classification clinical (ophthalmoscopic) classification for zone, but not for stage, plus, type 1 or type 2 disease. Among discrepancies in the diagnosis of type 1 disease, the majority of disagreements involved classification discrepancies in both stage and plus disease.

**Conclusions:** The most common area of disagreement in ROP classification between experts in this study is in diagnosis of stage. However, agreement about presence of type 1 and type 2 disease is high. There were no systematic differences between image-based classification and the clinical exam in detecting type 1 or type 2 disease. These findings are important in identifying potential areas for error during ROP diagnosis and education, and support efforts to incorporate telemedicine approaches using image-based classification either using human graders or automated computer based image analysis.

**Table 1. Distribution of retinopathy of prematurity (ROP) classification for image-based and clinical diagnosis by experts. ($n=1774$ study eye examinations)**

<table>
<thead>
<tr>
<th>ROP Classification</th>
<th>Expert 1 (Image-Based) No (% of classifications)</th>
<th>Expert 2 (Image-Based) No (% of classifications)</th>
<th>Clinical Diagnosis No (% of classifications)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone</td>
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<td>124 (7)</td>
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**Commercial Relationships:** J. Peter Campbell, None; Michael Ryan, None; Emily Lore, None; Susan Ostmo, None; Karyn Jonas, None; Robison V. Chan, None; Michael F. Chiang, Clarity Medical Systems (S)

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**Program Number:** 6292 Poster Board Number: C0036
**Presentation Time:** 11:00 AM–12:45 PM

**Correlation Between Retinal Vascular Parameters And High Risk Threshold Retinopathy in Very Low Body Weight Premature Infants**

Ferdinando Martini1, Enrico Grisan1, Silvia Bini1, Marianna Berton1, Stefano Piermarocchi1. 1Ophthalmology, University of Padova, Padova, Italy; 2Information Engineering, University of Padova, Padova, Italy.

**Purpose:** Retinopathy of prematurity (ROP) is still one of the main causes of childhood blindness. Plus disease has become the major criterion for laser treatment in ROP, but its assessment can be variable and subjective. We retrospectively investigated which vascular parameters are better correlated with necessity of laser treatment, time of treatment, and ROP progression rate, in a population of very low body weight (VLBW) preterms.

**Methods:** 434 RETCAM fundus eye examination (Clarity Medical System, Pleasanton, CA) of 59 VLBW preterms were analyzed with an ad-hoc semi-automated computer image analysis software developed in-house using Matlab (The Mathworks Inc.), that can also compare images with a superimposition tool. 27 of these patients did not require laser treatment due to spontaneous resolution of ROP (type 2 ROP); 32 patients required laser treatment in both eyes (type 1 ROP) and 3 patient of these required also posterior vitrectomy in both eyes. The parameters evaluated for both arteries and veins were: vascular tortuosity, vascular caliber ratio between vessels distal and proximal to the optic disc, number of vascular branches; other parameters evaluated were: ridge progression rate, distance between optic disc and ridge.

**Results:** Mean birth gestational age (GA, weeks) was not significantly different between groups for laser treated and not treated patients (25.5+1.6 GA and 26.2+2.2 GA respectively); eyes with type 1 ROP had a higher vascular tortuosity index, higher vascular caliber ratio (distal/proximal), higher vascular branches index versus eyes with type 2 ROP. The parameters that better correlate with ROP progression were: venous tortuosity (p<0.05) and vascular calibers ratio between distal and proximal vessel (p<0.05).

**Conclusions:** Computed based image analysis system for the evaluation of specific retinal vascular parameters can be useful for a standardized evaluation of ROP and PLUS disease. Dedicated programs that enable the superimposition of follow-up images can improve ROP progression evaluation. These observations give the basis for future criteria that can be useful also for telemedicine ROP screening.

**Commercial Relationships:** Ferdinando Martini, None; Enrico Grisan, None; Silvia Bini, None; Marianna Berton, None; Stefano Piermarocchi, None

**Program Number:** 6293 Poster Board Number: C0036
**Presentation Time:** 11:00 AM–12:45 PM

**Evaluating The Role of The Autonomic Nervous System Activity In The Development And Severity Of Retinopathy Prematurity**

Mohamed A. Hussein1, Deng Nanfu1, Craig Rasin2. 1Ophthalmology, Baylor College of Medicine, Houston, TX; 2Cardiology, Baylor college of medicine, Houston, TX.
Purpose: To evaluate changes in the autonomic nervous system activity associated with the development and severity of retinopathy of prematurity.

Methods: Heart rate variability, as an indicator of autonomic nervous system activity, was calculated in two groups of premature infants. The first group was a group of infants that had severe ROP requiring treatments. The second group was a control group of the same age, weight, and similar risk factors, including, same frequency of intraventricular hemorrhage, bronchopulmonary dysplasia, and sepsis. For the purpose of analyzing heart rate variability at different times during their hospital stay, three time points were selected including day 1 of life, day of first ophthalmology evaluation for ROP, and day of ROP treatment or discharge if patient did not receive treatment. The recorded EKG data, sampled at 240 Hz, was exported out of MATLAB and converted to ASCII format compatible with the analysis software package (Kubios HRV). Calculations were done for the high frequency value (HF m²), low frequency value (LF m²), and low frequency/high frequency value (LF m²/HF m²) of the heart rate variability components for all infants in the 2 groups. Trends of changes in the autonomic nervous system activity over time was compared between the two groups using analysis of covariance.

Results: The 2 groups demonstrated similar increase in the sympathetic activity between birth and the first ophthalmologic examination. Between the first ophthalmologic evaluation and the final evaluation, there was reduction in both the sympathetic and parasympathetic activity, more so for the parasympathetic activity, in the treated group, while in the control group there was increase in both the sympathetic and parasympathetic activity, more so for the parasympathetic activity. The difference in the parasympathetic activity between the two groups was statistically significant (t = 2.9, degree of freedom=12, p<0.01).

Conclusions: Disruption in the autonomic nervous system activity, particularly the parasympathetic activity, may play an important role in the development and severity of retinopathy of prematurity.

Commercial Relationships: Mohamed A. Hussein, None; Deng Nanfu, None; Craig Rusin

Program Number: 6294 Poster Board Number: C0037
Presentation Time: 11:00 AM–12:45 PM

Headband-mounted holder for hands-free indirect fundoscopy through a smartphone. Gabriela Saidman, M.D.¹, Guillermo Montelovia, M.D.², Julio A. Urretes-Zavalia, M.D., Ph.D.²
¹Ophthalmology section, department of Neonatology, Evita Pueblo Hospital, South Zone ROP net, Berazategui, Buenos Aires, Argentina. ²Department of Ophthalmology, University Clinic Reina Fabiola, Universidad Catolica de Cordoba, Argentina.

Disclosure: all the authors have no financial relationship with commercial interests

GABRIELA R. SAIDMAN. Neonatology, ROP, Hospital Evita Pueblo Berazategui, Berazategui, Argentina.

Purpose: Interest in smartphone fundoscopy has been growing unceasingly, and several strategies and accessory devices have been developed for that purpose. However, the examiner must hold the smartphone with one hand as the other hand holds the condensing lens, limiting the possibility of simultaneously performing scleral depression or globe rotation in order to reach the far periphery of the ocular fundus. Our purpose is to report the development of a simple homemade novel device for hands-free digital indirect fundoscopy through a smartphone.

Methods: A commercial flexible, malleable stainless steel and PVC stand holder for smartphone was attached to an adjustable headband. Any smartphone with a camera of 8 megapixels or greater with available continuous flash lighting is recommended.

Results: Ocular fundus was easily viewed through a +20D, +28D, or +40D lens, allowing the examiner to use the free hand for scleral indentation and globe rotation during examination. During examination, the fundus image may be observed simultaneously in a TV screen, and high quality fundus pictures and videos may be obtained at any moment during the examination.

Conclusions: The headband-mounted holder for a smartphone proved to be very useful and comfortable for smartphone fundoscopy.

Headband-mounted holder for hands free digital indirect fundoscopy through a smartphone. Use in a ROP screening.

Commercial Relationships: GABRIELA R. SAIDMAN, None

Program Number: 6295 Poster Board Number: C0038
Presentation Time: 11:00 AM–12:45 PM

Outcomes in Type I Retinopathy of Prematurity treated with intravitreal bevacizumab

Purpose: This study aimed to determine the efficacy and complications associated with the use of intravitreal bevacizumab (IVB) (Avastin®; Genentech Inc, South San Francisco, CA) for treatment of Type I Retinopathy of Prematurity (ROP).

Methods: In this retrospective study, 17 eyes of 10 patients with Type I ROP treated with IVB between 2012-2015 were analyzed. 3 eyes of 2 patients were not included due to inadequate follow-up. All patients included had at least 6 months of follow up after treatment. Records were reviewed for birth-weight, gender, gestational age, chronological age at time of treatment, ROP classification, and length of follow up. Main outcome measurements included dilated fundus exam at last visit, recurrence of disease, and refractive error. Dilated fundus examination was recorded as: attached with no macular dragging, attached with macular dragging, detached stage 4 or detached stage 5. Recurrences were defined as new or recurrent neovascularization...
with or without plus disease. The time to recurrence, subsequent treatment and results were recorded for each recurrence. Refractive error was also recorded.

**Results:** Of the 8 patients (14 eyes) included in the study, average birth-weight was 776.5g (Range 460-1190g), average gestational-age 24.50 weeks (Range 23-28 weeks), and average chronological age at time of treatment 36.79 weeks (Range 32-45 weeks). 4 patients (50%) were male. 2 eyes (14%) were injected for stage III, zone II, pre-plus disease with neovascularization of the iris; the remaining 12 (86%) had zone 1 with plus disease. Average length of follow up was 467 days. On follow up, all 14 eyes (100%) remained attached with no macular dragging. 13 eyes (93%) reached maturity without further complication. 1 eye (7%) experienced recurrence of neovascularization with plus disease requiring retreatment at 8 weeks. After retreatment, there was regression of disease and no further complication on 15 months of follow up. No significant refractive error requiring spectacle correction was identified in any of the patients included.

**Conclusions:** Findings suggest that IVB use is effective in treating type I ROP in this small series of patients. No evidence of significant refractive error or evidence of macular dragging was found, which has been shown with conventional laser therapy. Further trials are needed to assess long-term safety and complications.

**Commercial Relationships:** Adnan Mallick, None; Brian Savoie, None; Ronni M. Lieberman, None

**Program Number:** 6296 Poster Board Number: C0039

**Presentation Time:** 11:00 AM–12:45 PM

**RENERIN ANGIOTENSIN SYSTEM COMPONENTS IN VITREOUS HUMOUR OF RETINOPATHY OF PREMATURITY (ROP) PATIENTS**

Madhu Nath1, Atul Kumar2, Parijat Chandra2, Ashok Kumar Deorari2, Nabana Halder2, Baskar Singh4, Thirumurthy Velpandian2, OPHTHAMOLOGY, ALL INDIA INSTITUTE OF MEDICAL SCIENCES, New Delhi, India; 2Ocular Pharmacology, ALL INDIA INSTITUTE OF MEDICAL SCIENCES, Delhi, India; 3Pediatrics and Neonatology, ALL INDIA INSTITUTE OF MEDICAL SCIENCES, Delhi, India; 4Biophysics, ALL INDIA INSTITUTE OF MEDICAL SCIENCES, Delhi, India.

**Purpose:** Role of renin angiotensin system (RAS) is not yet clear in the vasculogensis and angiogenesis of the retinal vessels. Till now no study has been reported about the presence of renin angiotensin system components in vitreous of ROP patients undergoing vitrectomy surgery. This study was carried out to analyse and quantify the renin angiotensin system component in the ROP patients.

**Methods:** The study was conducted after obtaining human ethics clearance. In this study 44 ROP patients and 8 age matched control were included, who were undergoing vitrectomy following laser or congenital cataract surgery respectively. The vitreous was collected in MCT and stored in -80°C till the analysis. The vitreous was subjected for the total protein concentration and total collagen concentration using Bradford assay and Sircol collagen assay. VEGF was then subjected for sandwich and competitive ELISA for the analysis of renin, angiotensinogen, angiotensin converting enzyme, angiotensin II, vascular endothelial growth factor (VEGF) and hypoxia inducible factor 1 alpha (HIF). All the expression of RAS components, VEGF and HIF were normalised as per mg of protein.

**Results:** The conc. of total protein was found to be approximately 0.6mg/ml and collagen was found to be 400 microgram/mg of protein in ROP and control group. No significant difference was found in collagen and total protein in both the groups. The concentration of renin, angiotensinogen, angiotensin II, angiotensin converting enzyme, hypoxia inducible factor and vascular endothelial growth factor were quantified using sandwich ELISA and competitive ELISA technique. There was 12, 7, 6.3, 9.5, 8 and 5 fold increase was observed in VEGF, HIF 1 alpha, angiotensinogen, angiotensin converting enzyme, angiotensin II and renin respectively. The increase in fold change VEGF, HIF, Angiotensinogen, angiotensin II and angiotensin converting enzyme in ROP group was found to statistically significant in comparison with control group.

**Conclusions:** The presence of RAS components in the vitreous of normal control suggest that the retinal renin angiotensin system might be playing an important role in the normal vasculogenesis of the retinal vasculature. The increased expression of RAS components, VEGF and HIF in ROP vitreous are suggestive of pathological consequences by over activated RAS system.

**Program Number:** 6297 Poster Board Number: C0040

**Presentation Time:** 11:00 AM–12:45 PM

**Validating impact of temporal changes of adiponectin in relation to ROP development**

Chatarina Lolqvist1, Gunnel Hellgren1, Eva Engström1, Lennart Sigström1, Lois E. Smith1, Anna-Lena Hård1, Karin Sävman1, Ann Hellström1, 1Institute of Neuroscience and Physiology, Department of Ophthalmology, University of Gothenburg, Gothenburg, Sweden; 2Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden; 3Department of Ophthalmology, Harvard Medical School, Boston Children’s Hospital, Boston, MA.

**Purpose:** To validate earlier found physiologic response patterns explaining retinopathy of prematurity (ROP) development in infants born very preterm. Generally adiponectin production is up-regulated by weight loss and down regulated by weight gain, oxidative stress as well as pro-inflammatory cytokines. Disturbed homeostasis, impaired growth and inflammation are factors closely related to ROP development. This study assessed the longitudinal postnatal development of serum adiponectin levels and ROP development in a new cohort of very preterm infants.

**Methods:** A study was performed in 90 infants with gestational age (GA) < 28 weeks with a mean (SD) gestational age at birth of 25.2 (1.4) weeks and mean (SD) birth weight of 882 (220) g. Cord blood samples and thereafter venous blood samples were obtained at

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postnatal day 1, 7, 14, 28 days and at postmenstrual age 32, 36 and 40 weeks. Serum adiponectin levels were assayed using a human adiponectin ELISA kit (E091M, Mediagnost, Germany). The intra-assay CVs were 3.8% at 3.9 µg/mL and 4.7% at 13.1 µg/mL and the inter-assay CV was 16.3% at 9.9 µg/mL. ROP was determined according to the International ROP classification.

**Results:** Thirteen infants died before completing 40 weeks. ROP stages were assessed in 77 infants and grouped as ROP stage 0 (n=16), ROP stage 1 (n=11), ROP stage 2 (n=20) and ROP stage 3 (n=30). The temporal pattern showed that mean adiponectin concentrations increased steeply during the first 14 days after birth from 2.7 ± 3.7 (mean ± SD) µg/mL at day 1 to 47.3 ± 25.6 µg/mL at 14 days (P < 0.001). From 28 days after birth to 32 weeks postmenstrual age mean adiponectin levels gradually decreased. Mean adiponectin levels were consistently significantly lower in infants who developed proliferative ROP compared to infants with no ROP from birth up to postmenstrual age 32 weeks. During postmenstrual weeks 36 to 40 weeks mean adiponectin gradually increased to levels comparable to levels seen at 14 days after birth. Interestingly no significant difference in mean adiponectin levels were seen between ROP stages at this period.

**Conclusions:** Serum adiponectin levels exhibit an interesting biphasic response pattern in very preterm infants with a rapid increase during the first weeks after birth followed by a decrease and then a new increase. Persistent lower adiponectin levels were found in infants developing ROP at a time point preceding ROP development.

**Commercial Relationships:** Chatarina Loqvist, None; Gunnel Hellgren, None; Svetlana Najm, None; Eva Engström, None; Lennart Stigson, None; Lois E. Smith, None; Anna-Lena Härd, None; Karin Sävman, None; Ann Hellström, None.

**Support:** This study has been supported by the Swedish Medical Research Council (# 2011-2432), the European Commission FP7 project 305485 PREVENT-ROP, Swedish government grants (#ALFGB2770)

**Program Number:** 6298 **Poster Board Number:** C0041
**Presentation Time:** 11:00 AM–12:45 PM
**Poster Session:** Retinopathy of Prematurity

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**Severe Retinopathy of Prematurity**

Cassie A. Ludwig, Margaret Greven, Darius M. Moshfeghi.

Ophthalmology, Stanford University School of Medicine, San Francisco, CA.

**Purpose:** The Stanford University Network for the Diagnosis of Retinopathy of Prematurity (SUNDROP) initiative—an ongoing telemedicine-based community initiative for in-hospital screening of high-risk infants for treatment-warranted ROP (TW-ROP)—has been shown to be a safe, reliable, and cost-effective supplement to the efforts of ROP specialists. We utilized data collected in the SUNDROP initiative to determine whether posterior segment characteristics differ in newborns meeting threshold criteria for ROP treatment. We hypothesized that peripapillary atrophy and fundus pigmentation might differ in newborns with TW-ROP and non-TW-ROP.

**Methods:** A retrospective case control study. Participants included premature newborns requiring ROP screening at six neonatal intensive care units from December 1, 2005, to November 30, 2011 who underwent retinal ablative therapy and untreated controls within the same cohort matched for date of first exam. We reviewed fundus photographs from newborns enrolled in a telemedicine ROP screening protocol who developed TW-ROP compared to a control cohort to grade fundus pigmentation and peripapillary atrophy. We used McNemar’s chi-squared statistic for matched data to assess the relationship between peripapillary atrophy and fundus pigmentation in newborns with TW-ROP and with non-TW-ROP.

**Results:** When compared to 31 subjects with non-TW-ROP, 31 infants with TW-ROP were more likely to have peripapillary atrophy (McNemar’s chi-squared, p = 0.0113). As previously reported, there was also an increase in presence of a light fundus in those with TW-ROP as compared to those with non-TW-ROP (McNemar’s chi-squared, p = 0.0500). There was no difference between cases and controls in gestational age at the time of the first screening, gender, or multiplicity. However, there was a statistically significant difference between cases and controls in birth weight and gestational age at birth.

**Conclusions:** This study demonstrates a difference in the posterior segment exam with wide-field digital imaging of newborns with TW-ROP as compared to those with non-TW-ROP. Peripapillary atrophy and lightly pigmented fundi may help to predict need of retinal ablative therapy in newborns with ROP.

**Commercial Relationships:** Cassie A. Ludwig, None; Margaret Greven, None; Darius M. Moshfeghi, Clarity (R), Visunex (C), Clarity (I)
**Support:** TL1 Clinical Research Training Program: NIH TL1 TR 001084

**Program Number:** 6299 **Poster Board Number:** C0042
**Presentation Time:** 11:00 AM–12:45 PM
**Incidence of Asymmetrical Disease in Patients with Moderate to Severe Retinopathy of Prematurity**

Ru-ik Chee1, Samir N. Patel2, Mrenali Gupta1, Karyn Jonas1, Susan Ostmo1, Michael F. Chiang2, Robison V. Chan1.

1Ophthalmology, Weill Cornell Medical College, New York, NY; 2Ophthalmology, Casey Eye Institute at Oregon Health & Science University, Portland, OR; 3Ophthalmology and Visual Sciences, Illinois Eye and Ear Infirmary, University of Illinois at Chicago, Chicago, IL.

**Purpose:** To examine the incidence of asymmetrical disease in infants with moderate to severe retinopathy of prematurity (ROP).

**Methods:** 228 infants were recruited in this multi-center, prospective, cohort study from 7 centers. Bilateral wide-angle retinal images were captured after routine exam, and a consensus reference standard diagnosis (RSD) was determined from the color fundus images by three experienced readers in combination with the clinical diagnosis. For each exam session, the RSD (presence of ROP, zone, stage, plus disease, disease category) was compared between eyes. Attention was paid to identifying the findings in the fellow eye of eyes with moderate to severe ROP, defined as type-2 disease (zone I, stage 1 or 2 ROP without plus disease or as zone II, stage 3 ROP without plus disease) or worse.

**Results:** 607 exam sessions from 228 infants (mean 2.66 sessions per infant, range 1-13) were included. Of 72 sessions with a RSD of stage 3 or worse, the fellow eye had a diagnosis of stage 3 or worse in 46 sessions (64%) (Fig 1B). Of 78 sessions with a RSD of Zone I, the fellow eye had a diagnosis of Zone I in 70 sessions (90%) (Fig 1D). Of 25 sessions with a RSD of plus disease, the fellow eye had a diagnosis of plus disease in 12 sessions (48%) (Fig 1E). Of 149 sessions with a RSD of type-2 or pre-plus, the fellow eye had a diagnosis of type-2 or pre-plus in 95 sessions (64%) and treatment-requiring ROP in 12 sessions (8%) (Fig 1C). Of 48 sessions with a RSD of treatment-requiring ROP, the fellow eye had a diagnosis of treatment-requiring ROP in 31 sessions (65%), type-2 or pre-plus in 12 sessions (25%), mild ROP in 4 sessions (8%), and no ROP in 1 session (2%) (Fig 1A).

**Conclusions:** We report concordance rates of clinically significant ROP diagnoses in moderate to severe ROP, which was highest for
zone I disease and lowest for plus disease. The incidence of bilateral treatment-requiring ROP was lower in our cohort compared to previously published rates in the Cryotherapy for ROP and Early Treatment for ROP trials. This data may be relevant to the planning of clinical trials and may furnish guidelines for study design. Our findings may also have implications in screening and management of ROP, especially if we continue to evaluate our algorithm for treatment-requiring ROP.

Figure 1. Distribution of Retinopathy of Prematurity Diagnosis between each eye using a consensus reference standard diagnosis.

Commercial Relationships: Ru-ik Chee; Samir N. Patel, None; Mininali Gupta, None; Karyn Jonas, None; Susan Ostmo, None; Michael F. Chiang, Clarity Medical Systems (S); Robison V. Chan, None

Support: Supported by a Departmental Grant from Research to Prevent Blindness. Supported by the St. Giles Foundation. Supported by NIH EY19474.

Program Number: 6300 Poster Board Number: C0043
Presentation Time: 11:00 AM–12:45 PM

Causes of Severe Visual Impairment and Blindness in Children in Lima, Peru

Arjun Sood1, Luz Gordillo1,2. 1Ophthalmology, Emory University, Atlanta, GA; 2Instituto Damos Vision, Lima, Peru; 3Ophthalmology, Hospital Nacional Edgardo Rebagliati Martins EsSalud, Lima, Peru.

Purpose: To determine the causes of severe visual impairment and blindness (SVI/BL) in children in Lima, Peru, and to compare the prevalence of retinopathy of prematurity (ROP) to previous reports.

Methods: Children attending schools for the blind in Lima, Peru were examined in 2013. Data was collected using the WHO Childhood Blindness Software.

Results: 63 children were identified with SVI/BL. The major anatomical site of SVI/BL was the retina (43.5%). The major underlying etiology of SVI/BL was undetermined in 58.7% and perinatal factors in 31.7%. ROP accounted for 28.5% of SVI/BL.

Conclusions: More than one-third of causes of SVI/BL are potentially avoidable, with ROP being a leading cause. The prevalence of ROP in Lima has increased as compared to studies conducted in 1999 (16%) and 2005 (24%).

Commercial Relationships: Arjun Sood, None; Luz Gordillo, None

Program Number: 6301 Poster Board Number: C0044
Presentation Time: 11:00 AM–12:45 PM

How heavy are you today? - Predicting Retinopathy of Prematurity from regained birth weight

Madhurya Mallavarapu1, Anand Vinekar1, Chaitra Jayadev1, Shwetha Mangalesh1, Bhujang Shetty1,2,3. 1Pediatric Retina, Narayana Nethralaya Eye Hospital, Bangalore, India; 2Ophthalmology, Narayana Nethralaya Eye Hospital, Bangalore, India.

Purpose: Poor postnatal weight gain after the initial physiological loss of birth weight is a well known risk factor for developing retinopathy of prematurity (ROP). Estimating weekly weight to predict the risk score is difficult in developing countries. We report the correlation of the ‘age of regaining birth weight’ (ARBW) as a predictor of ROP.

Methods: 68 Asian Indian infants born <2000 grams at birth or <=34 weeks of gestation were enrolled. The number of days taken for these infants to regain their baseline birth weight (the ‘ARBW’ value) was recorded. This measure was correlated with the eventual ROP outcome categorized as ‘no’, ‘mild’ or ‘treatment requiring ROP’ respectively. A risk score is proposed to predict which babies could develop the disease based on this measure.

Results: The mean birth weight of the cohort was 1270.44 grams and mean gestational age was 31.13 weeks. 33 developed ‘no’ ROP, 20 had ‘mild’ and 15 had ‘treatment requiring’ ROP respectively. The mean ARBW was 11.9, 17.9, 26.6 days for the ‘no’, ‘mild’ and ‘treatment ROP groups respectively. (P<0.0001) (one-way ANOVA and Post Hoc test using Bonferroni correction). Using the “ARBW” measure and the overlapping standard deviations between the groups, we developed a risk score to predict ROP. There is a low risk if they regain their birth weight in <11 days, mild risk if it is between 11-14 days, moderate risk if it is between 14-20 days and high risk if it is >21 days.

Conclusions: The ‘day of regaining the birth weight’ is easily recalled by mothers and physicians alike, making it a useful tool in estimating ROP risk. The risk score allows us to predict which baby may develop ‘treatment requiring ROP’ even before 21 days of life, which is the first mandated screening visit in India. This could allow a prudent approach for prognostication and follow-up of these infants.

Commercial Relationships: Madhurya Mallavarapu, None; Anand Vinekar, None; Chaitra Jayadev, None; Shwetha Mangalesh, None; Bhujang Shetty, None

Program Number: 6302 Poster Board Number: C0045
Presentation Time: 11:00 AM–12:45 PM

Three-dimensional assessment of vascular changes secondary to neovascularization in retinopathy of prematurity

Shwetha Mangalesh, Xi Chen, Alexandria Dandridge, Du Tran-Viet, Christian Viehland, Francesco LaRocca, Joseph A. Izatt, Cynthia A. Toth. 1Ophthalmology, Duke University School of Medicine, Durham, NC; 2Biomedical Engineering, Duke University, Durham, NC.

Purpose: Neovascularization during retinopathy of prematurity (ROP) is hypothesized to be caused by increase in oxygen concentration with subsequent vasodilation and vascular budding. While microscopic study of the stepwise processes has been extensive in animal models, such data are lacking from infants. Our goal is to study physiologic and abnormal retinal vascular development in three-dimensions (3-D) in human infants using non-contact optical coherence tomography (OCT) imaging to better understand mechanisms of neovascularization in ROP.

Methods: Under an IRB approved protocol, using 840 nm wavelength SD-OCT system (Envisu, Bioptigen Inc.), we captured...
Volumes of the macula and the vascular-avascular (V-AV) junction in preterm infants at the time of ROP examinations (between 31-41 weeks postmenstrual age). 3D volume maps and en face images of SDOCT images were constructed to enhance visualization for analysis of retinal vascular patterns.

**Results:** Fourteen eyes from 8 preterm infants with ROP, with and without areas of neovascularization, were analyzed. On 3D-rendered volumes we found multiple morphologically different patterns of retinal microvasculature. We observed 3 stages of development of neovascularization. 1) retina is composed of a bland inner surface without focal elevation of vasculature. 2) vascular budding occurs both at the macula and posterior to V-AV junction. These vascular buds appear isolated or grouped along vessels (Fig 1) or tangentially along V-AV junction. 3) webs of neovascular tissue connect and elevate from retinal surface (Fig 2). Intravitreal traction is often observed with neovascular tissue. Elevated neovascular tissue is sometimes associated with inner retinal split, a schisis-like change anterior to V-AV junction.

**Conclusions:** We demonstrate for the first time, ability to document vascular budding and stages of neovascularization in preterm infants with ROP; not readily visible on clinical examination. Different patterns of buds could indicate possible difference in underlying mechanisms of neovascularization. Further studies are needed to demonstrate vascular flow within these structures and their clinical relevance in ROP.

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**Purpose:** Selection of individuals with traits of interest that fall to opposite extremes of a spectrum are important in order to maximize the power of small studies. In cases of rare diseases where multiple phenotypes contribute to the disease definition and where there may be few individuals at these extremes, it is useful to take into account multiple outlier categories. However, incorporation of additional categories can introduce heterogeneity into the study population. We consider the case of retinopathy of prematurity (ROP) and selection of traits from a set including birth weight, gestational age, disease burden, and twin status.

**Methods:** A multicenter database was generated prospectively from infants screened for ROP at one of 6 major ROP centers in the United States. The database was reviewed to identify infants treated for ROP. Database information included level of ROP progression, treatment required, physical factors (birth weight, postmenstrual age), demographic data, and presence of additional disease factors (sepsis, necrotizing enterocolitis, chronic lung disease, death during hospital stay). Percentile weight for gestational age was calculated using gestational age and birth weight. Expert clinicians were consulted to determine weights reflecting the importance of each trait in the determination of interest as a genetic study participant.

**Results:** 406 Caucasian infants representing 1603 exams were identified from the full database. A weighting matrix was applied to the data and a ranked list of infants according to genetic interest was generated from the weighted data. Permutations of the ranked data were visualized and reviewed by a panel of expert clinicians and genetic specialists to determine a combination of traits leading to ideal separation in sample and collinearity of existing traits. The ideal factors indicating outlier status were determined to be birth weight, level of treatment, and degree of ROP.

**Conclusions:** Complex models provide context about the sample population, but incorporation of competing additional traits limits the ability to sample population extremes. Therefore in studies of limited sample size where maximum power is required to detect an effect, it is often necessary to limit the number of factors contributing to phenotypic interest. In retinopathy of prematurity, the highest priority information for outlier status is captured using the three factors listed above.

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Comparison of tortuosity indices across software for retinopathy of prematurity (ROP)

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**Purpose:** Current methods used in screening for Retinopathy of Prematurity (ROP) are based on guidelines set forth by the International Committee for the Classification of Retinopathy of Prematurity in 2005. However, even amongst experienced pediatric ophthalmologists there is disagreement in the diagnosis of ROP suggesting subjectivity in these guidelines. ROP is a leading cause of childhood blindness and is rising in incidence in regions without readily available pediatric ophthalmologists thus establishing the need for more objective measures to evaluate ROP. Multiple software packages have been developed to automatically segment vessels and analyze tortuosity from fundus images. To our knowledge, their automated segmentation algorithms have not been compared on the same set of images. We performed a cross-sectional study comparing the tortuosity indices of three software packages with automated segmentation to manual segmentation.

**Methods:** 16 retinal vessels from five premature infants were analyzed from photos by the RetCam3 (Clarity Medical Systems, Inc.). Visible vessels were divided into quadrants and compared. Automated Retinal Image Analyzer (ARIA) (Peter Bankhead), Computer Aided Image Analysis of the Retina (CAIAR) (University College London) and the investigational Automated Vessel Analysis Suite (AVAS) (Vasoptic Medical Inc.), were used to analyze the same images and the tortuosity indices were calculated for each of four quadrants. We used a linear regression analysis to compare the algorithms of software to manually segmented images.

**Results:** We found no significant linear relationship between tortuosity indices determined by manual segmentation and any of the software packages: ARIA (R²=0.051, P=0.15), CAIAR (R²=0.0873, P=0.13), and AVAS (R²=0.0172, P=0.64). When comparing each software package to each other, there was no relationship between ARIA and CAIAR (R²=0.0096, P=0.89), AVAS and ARIA (R²=0.1531, P=0.79), or AVAS and CAIAR (R²=0.084, P=0.56).

**Conclusions:** The weak correlations among the different software packages underline the need for more consistent, sensitive methods to identify the retinal vessels and to calculate tortuosity. Poor image quality may also play a role in these weak correlations. More significantly, this data emphasizes the need for additional quantitative measures aside from vessel tortuosity for assessing disease stage in ROP.

Rate of High Frequency Oscillator Ventilation (HFOV) in Infants with Type 1 Retinopathy of Prematurity (ROP) versus Untreated Controls in a Level IV Nursery

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**Purpose:** The purpose of the study is evaluate if newborns meeting criteria for ROP screening have a difference in ROP outcomes if managed with standard ventilation versus high frequency oscillatory ventilation.

**Methods:** A control group of infants < 28 weeks gestational age admitted during the ROP screening period was randomly selected from the total set of infants screened from January 2011 to June 2015. A set of infants treated for Type 1 ROP during this time period was compared for summed days on HFOV, days on conventional ventilation (V), and days on non-mechanical ventilation (no-V) support with a denominator of total NICU days to show percentage of time spent on each respiratory support mode.

**Results:** In the control group of 45 infants, 8 (18%) received HFOV interspersed with days of conventional ventilation, 28 (62%) received only V, and 9 (20%) no-V. In 29 treated for ROP, 3 (10%) received HFOV, 22 (76%) V, and 4 (14%) received no V. Percentage of time spent on each respiratory support mode, control versus treated...
respectively, were: HFOV 2.5% vs 0.3%; V 20.7% vs 21.6%; and no-V 76.8% vs 78.1%.

Conclusions: HFOV was used more in infants that did not develop Type 1 ROP in a Level IV nursery. At our institution, HFOV is a rescue treatment for critically ill infants rather than a primary ventilation mode. Control infants without Type 1 ROP had more HFOV days in our NICU than did infants treated for Type 1 ROP.

Commercial Relationships: Kara Dolezal, Namratha Turlapati, None; Marijean Miller, None

Program Number: 6306 Poster Board Number: C0049
Presentation Time: 11:00 AM–12:45 PM

Subclinical macular findings in infants with retinopathy of prematurity treated with bevacizumab or laser photocoagulation

Ryan N. Vogel, Alana D. Trotter, Mara R. Goldberg, Deborah M. Costakos. Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, WI.

Purpose: Laser photocoagulation and intravitreal bevacizumab are frequently used in the treatment of retinopathy of prematurity (ROP), but the effect of these treatments on foveal development is not well established. We used handheld spectral-domain optical coherence tomography (SD-OCT) to compare subclinical macular findings in infants who underwent treatment for ROP and those who regressed spontaneously.

Methods: Handheld SD-OCT imaging was performed longitudinally on infants at Children’s Hospital of Wisconsin during routine ROP exams. Subjects were included in the study if they developed stage 3 ROP. Factors for analysis included presence of cystoid macular edema (CME), foveal pit depth (parafoveal/central foveal thickness ratio), inner retinal thickness, and outer retinal maturation at the fovea (distance of ellipsoid zone (EZ) from foveal center).

Results: Thirty-six eyes from 18 patients met study criteria. Of those, 4 underwent treatment with laser photocoagulation, 4 with bevacizumab, and 1 with both treatments. CME was found in 12 eyes (33.3%). Four eyes developed new CME following bevacizumab and two following laser treatment. Using within-subject analysis and excluding images with foveal CME, the foveal pit increased in depth by 4.05% per week (±2.76 SD). Inner retinal thickness at the foveal center decreased by 5.10% per week (±2.75 SD). The distance of the EZ from the foveal center decreased by 12.71% per week (±2.44 SD). There was no statistically significant difference between bevacizumab-treated and untreated eyes for any of these measurements (p=0.52, 0.78, and 0.64 respectively). There were no consecutive post-laser treatment images available for these analyses. Hyperreflective vitreous structures were found in 4 out of 8 eyes following bevacizumab treatment and 4 out of 6 eyes following laser treatment, but were not found in untreated eyes.

Conclusions: Treatment with bevacizumab or laser photocoagulation does not appear to be correlated with the presence of CME, foveal pit development, inner retinal thickness, or outer retinal maturation in infants with ROP. Hyperreflective vitreous structures were found exclusively in bevacizumab- and laser-treated eyes. Further research is needed to determine the clinical significance of this finding.

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Program Number: 6307 Poster Board Number: C0050
Presentation Time: 11:00 AM–12:45 PM
Current Trends and the Future of Retinopathy of Prematurity (ROP) Screening and Treatment in the United States

Cagri G. Besirli, Rebecca Vartanian, John Barks, Chris A. Andrews, David C. Musch. Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI; Pediatrics and Communicable Diseases, University of Michigan, Ann Arbor, MI.

Purpose: To determine the current practice patterns of ROP screening and treatment and the attitudes towards new screening and treatment modalities in level 3 and level 4 NICUs reported by medical directors.

Methods: Paper surveys were mailed to the medical directors of 840 level 3 and 4 NICUs identified in the 2011 American Academy of Pediatrics (AAP) directory. Categorical variables were summarized by counts, percentages, and bar graphs; continuous variables by means, standard deviations, and histograms. Responses were compared to AAP guidelines and previous reports. Within sample comparisons were made by level, setting, size, and academic status. Analyses were performed in R 3.2.2 (R Foundation for Statistical Consulting, Vienna, Austria).

Results: Responses were received from 393 (47%) of the survey recipients. Respondents indicated that ROP screening is performed in their NICUs by pediatric (61%) and/or retina (43%) specialists; retinal imaging devices are infrequently used (21%). Treatment is performed by pediatric (39%) and/or retina (69%) specialists in the NICU under conscious sedation (60%). The most common treatment modality was laser photocoagulation (85%), followed by anti-VEGF injection (20%). Some NICUs did not provide screening (2%) or treatment (28%) services, often due to lack of ophthalmologists (78%). Respondents showed slightly more agreement (35%) than disagreement (25%) that a retinal imaging device could replace indirect ophthalmoscopy (40% neutral). More respondents agreed (30% vs 15%) that telemedicine for ROP screening is safe, but most were neutral (55%). Only 15% agreed that a well-trained non-physician could reliably review telemedicine images, while 49% disagreed.

Conclusions: Ophthalmologists perform the majority of ROP screening examinations and treatment in the U.S, while telemedicine is infrequently used as the primary method of screening. Most NICUs reported that infants are treated primarily with laser ablation in the NICU under conscious sedation. While the decreasing number of ophthalmologists available for screening and treating ROP is expected to increase the use of telemedicine, only a minority of respondents agreed that telemedicine is a safe screening modality.

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Presentation Time: 11:00 AM–12:45 PM
Vascular Endothelial Growth Factor and Apelin in Plasma of Patients with Retinopathy of Prematurity

Jing Feng, Yanrong Jiang. Peking Univ People’s Hospital, Beijing, China.

Purpose: To investigate plasma vascular endothelial growth factor (VEGF) and apelin levels in infants with or without retinopathy of prematurity (ROP).

Methods: Fifty-five preterm infants with ROP and 12 preterm infants without ROP were enrolled. Infants with ROP were divided into mild group and severe group. Analysis included evaluation of basic
clinical conditions and measurement of plasma VEGF and apelin concentrations using enzyme-linked immunosorbent assays (ELISA).

**Results:** Plasma VEGF level was lower in infants with ROP (P=0.011), while plasma apelin level was higher in infants with ROP (P=0.008). Plasma apelin had negative correlation with plasma VEGF. Meanwhile, plasma apelin increased statistically significantly in severe ROP (P=0.018, r=0.319).

**Conclusions:** Plasma apelin level was increased markedly in infants with ROP, while plasma VEGF level decreased. Severe ROP has elevated plasma levels of apelin.

**Commercial Relationships:** Jing Feng, None; Yanrong Jiang, None

**Program Number:** 6309 **Poster Board Number:** C0052 **Presentation Time:** 11:00 AM–12:45 PM

**Demographics and Comorbidities of Subjects with Retinopathy of Prematurity Requiring Treatment**

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**Purpose:** While certain risk factors for retinopathy of prematurity (ROP) have become well established, numerous other factors have been studied with conflicting results in the literature. In a retrospective chart review, we evaluated the demographics and comorbidities of ROP patients who required treatment, in order to gain insight into potential risk and protective factors for this high-risk neonatal population.

**Methods:** All subjects from 1999-2014 with ROP who required treatment were included in this study. The subjects consisted of a cohort in a tertiary care facility in Chicago, Illinois who were evaluated and treated by one retina specialist. As the study spanned a time frame of 19 years, criteria for treatment were dependent on the guidelines that were available at the time that treatment was decided. Demographic data as well as various prenatal and postnatal comorbidities were evaluated.

**Results:** Our data included 94 subjects (186 eyes) who received treatment for ROP. 77 of these subjects underwent laser therapy, while the rest received either intravitreal injections (Bevacizumab or Ranibizumab) or a surgical procedure. Gestational age for the patient population varied from <24 weeks up to 29 weeks with 60% of subjects having a gestational age ≤24 weeks. All subjects had a very low birth weight (<1500 grams), and 75% had an extremely low birth weight (<750 grams). As expected, oxygenation rates were high with 84% of subjects receiving 76 or more days of oxygen supplementation. Interestingly, 33% of the subjects were exclusively formula fed. In comparison, when evaluating the very low birth weight neonatal patients in our institution, only 5% have been exclusively formula fed. For all formula-fed neonates in our institution, the incidence of developing ROP that requires treatment was 0.203. In comparison, for all neonates receiving at least a partial breast milk diet, the incidence of ROP requiring treatment was 0.022.

**Conclusions:** The incidence of ROP requiring treatment was nearly ten-fold higher in exclusively formula-fed infants compared to infants with a diet including at least partial breast milk consumption. This is suggestive of a protective effect of breast-feeding on the development of ROP.

**Commercial Relationships:** Tatyana Spektor; Jack Cohen, None; Robert Kimura, None; Joseph Santamaria, None; Tovah Schwartz, None

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