In the READ-3 study, patients with DME received monthly intravitreal injections of either 0.5 or 2.0 mg of ranibizumab for 6 treatments followed by as-needed injections until month 24. OCT images from patients who completed the month-24 visit of the study were analyzed at the baseline visit to identify the presence (VMA+) or absence (VMA-) of VMA. Patients with any degree of vitreomacular traction (VMT) were excluded from the analysis. Two independent graders graded all images. VMA was classified by size of adhesion into either focal (<1500 µm) or broad (≥1500 µm). Main outcome measures were mean change in best corrected visual acuity (BCVA) and central retinal thickness (CRT) at month 24. Student t-test was performed; statistical significance was set at p<0.05.

Results: 152 eyes (152 patients) were randomized in the READ-3 study. 95 eyes (95 patients) were found to be eligible for the study based on study criteria. 57 eyes did not meet study criteria and were excluded from the study; 17 patients had ungradable images, 39 patients did not complete the month 24 visit and 1 patient had VMT. At baseline, 20 patients were classified as VMA (+) and 75 patients were classified as VMA (-). The distribution of the two doses of RBZ (0.5mg and 2.0mg) in the two groups was similar. At month 24, the VMA (+) group showed a mean improvement of 13.45 ± 9.80 letters, whereas the VMA (-) group showed a mean improvement of 8.07 ± 9.58 letters. The difference between the two groups was statistically significant (p=0.039). Mean improvement in CRT was 173.42 ± 153.68 µm and 185.85 ± 140.88 µm in the VMA (+) and VMA (-) groups, respectively (p=0.548).

Conclusions: Diabetic macular edema patients with VMA have a greater potential for improvement in visual outcomes with long-term anti-vascular endothelial growth factor therapy. Therefore, the presence of VMA should not preclude patients with DME from receiving treatment.

Commercial Relationships: Mohammad A. Sadiq, None; Muhammad Hassan, None; Rubbia Afridi, None; Muhammad S. Halim, None; Diana V. Do, Genentech (C), Regeneron (F), Regeneron (C), Genentech (F), Allergan (C), Santen (C); Quan D. Nguyen, Santen (F), Regeneron (F), Bausch and Lomb (C), Santen (C), MacuSight (F), Ophthotech (F), Genentech (F), L-path (F); Yasar Jamal J. Sepah, None

Program Number: 1590
Presentation Time: 11:00 AM–11:15 AM
Effect of Vitreomacular Adhesion on Treatment Outcomes in the Ranibizumab for Edema of the mAcula in Diabetes-3 (READ-3)
Study –Month 24 Results
Mohammad A. Sadiq1, Muhammad Hassan1, Rubbia Afridi1, Muhammad S. Halim1, Diana V. Do1,2, Quan D. Nguyen1,2, Yasar Jamal J. Sepah1,2, 1Ophthalmology, Byers Eye Institute - Stanford University, Palo Alto, CA; 2Ocular Imaging Research and Reading Center, Menlo Park, CA.
Purpose: To evaluate the role of vitreomacular adhesion (VMA) in determining long-term visual and anatomic outcomes in patients with diabetic macular edema (DME).
Methods: In the READ-3 study, patients with DME received monthly intravitreal injections of either 0.5 or 2.0 mg of ranibizumab for 6 treatments followed by as-needed injections until month 24. OCT images from patients who completed the month-24 visit of the study were analyzed at the baseline visit to identify the presence (VMA+) or absence (VMA-) of VMA. Patients with any degree of vitreomacular traction (VMT) were excluded from the analysis. Two independent graders graded all images. VMA was classified by size of adhesion into either focal (<1500 µm) or broad (≥1500 µm). Main outcome measures were mean change in best corrected visual acuity (BCVA) and central retinal thickness (CRT) at month 24. Student t-test was performed; statistical significance was set at p<0.05.

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Conclusions: Diabetic macular edema patients with VMA have a greater potential for improvement in visual outcomes with long-term anti-vascular endothelial growth factor therapy. Therefore, the presence of VMA should not preclude patients with DME from receiving treatment.

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Program Number: 1592
Presentation Time: 11:30 AM–11:45 AM
Cost Evaluation of Pneumatic Vitreolysis in Treatment for Vitreomacular Adhesion
Gabriel M. Gordon, Robert L. Avery. Research, California Retina Consultants, Santa Barbara, CA.
Purpose: The purpose of this study was to determine which therapeutic option for treating vitreomacular traction (VMT) provides the most efficient cost per quality life-years (QALYS). A similar assessment was reported in 2014, but only compared saline treatments with ocriplasmin or vitrectomy (PPV). Since then a growing body of work has shown that treating VMT with pneumatic vitreolysis (PV) results in a higher success rate and a cheaper procedure. Our hypothesis is that PV will prove to be a significantly better option for treating VMT as compared to other options with regards to the cost per QALYS.
Methods: Calculations were based off of the paper published by Chang and Smiddy and used identical assumptions. For PV, we...
assumed an 85% success rate based on recent work published by our clinic; the cost of the gas is less than $1 so is calculated as $0. Markov analysis, with cost data from the Center of Medicare and Medicaid Services (CMS), was used to calculate imputed costs for each primary treatment modality in a facility setting with surgery performed in a hospital serving as the highest end of the range and non-facility setting with surgery performed in an ambulatory surgery center (ASC) serving as the lowest end of the range.

**Results:** When PV was selected as the primary procedure, the overall imputed cost ranged from $2,913.62-$4,197.37 for facility and non-facility locations, respectively. These figures include the cost of vitrectomy for the patients who fail PV. The cost per line was $1,170.13-$1,685.69, the cost per line-year was $80.70-$116.25, and the cost per QALY was $2,689.95-$3,875.15.

**Conclusions:** In both a facility and non-facility setting, the PV cost per QALY is approximately half that of saline or PPV and one third that of occliplasm, irrespective of success rate. This analysis confirms the superior cost effectiveness of this simple office procedure over vitrectomy or occliplasm injection for VMT.

**Commercial Relationships:** Gabriel M. Gordon, None; Robert L. Avery, Novartis (I), Novartis (C), Regeneron (F), Alcon (C), Genentech (C), Regeneron (I), Genentech (F), Allergan (C)

**Program Number:** 1593
**Presentation Time:** 11:45 AM–12:00 PM

**Iron role in retinal detachment and neuroprotective effects of transferrin**


1. Centre de Recherche des Cordeliers UMR1138, INSERM, Paris, France; 2. CRC UMR1138, University of Paris 6 and 5, Paris, France; 3. Unit of Toxicology, CURML, Geneva University Hospitals, Geneva, Switzerland; 4. Department of Ophthalmology, University of Lauzanus; Jules-Gonin Eye Hospital; Fondation Asile des aveugles, Lausanne, Switzerland; 5. Department of Human Protein Science, Geneva University, Geneva, Switzerland.

**Purpose:** Retinal detachment (RD), characterized by the separation of the neuroretina from the retinal pigment epithelium (RPE), often leads to permanent visual impairment. Iron is known to be implicated in degenerative diseases and its excess enhances neural cells death. In models of retinal degeneration, we have previously demonstrated iron accumulation in the outer retina, and the neuroprotective effect of a natural iron chelator, transferrin (TF), after local administration. Here, we have investigated the involvement of iron in RD and the possible neuroprotective effect of TF treatment.

**Methods:** Iron status was assessed in ocular fluids from patients with RD and compared to controls. Iron was also detected on RD human retinal sections by Perl’s reaction and Inductively Coupled Plasma Mass Spectrometry. An organoculture system of murin retinas was created, on which the dose-dependent effects of iron were evaluated, and the protective effects of TF were screened. Rodent models of RD were produced by subretinal injection of sodium hyaluronate. Mice expressing human TF were used to evaluate survival of photoreceptors in detached neural retina.

**Results:** Elevated iron levels and fully saturated TF were found in the vitreous of RD patients compared to control ones. Iron was also detected in sub-retinal fluids (SRF). Iron level in SRF was significantly correlated to duration of RD, and associated with a worse post-operative visual recovery. Moreover, iron deposits were detected in the neuroretina and RPE. In organocultured mice retinas, addition of iron in culture media leads to its accumulation in the retina, cones death and decreases of rhodopsin protein level. After experimental RD in mice, intraretinal iron deposits and photoreceptors loss were observed. Expression of TF in RD mice model preserved against retinal edema, photoreceptor outer segments shortening and cone loss. Moreover, inflammation was decreased, iron metabolism was controlled and oxidative stress reduced.

**Conclusions:** Our results showed iron accumulation in the retina and ocular fluids during RD and the involvement of iron in the pathophysiology of retinal cell damage following RD. Moreover, we demonstrated the potential of TF as adjuvant therapeutic agent, preventing vision loss in RD and associated diseases.

**Commercial Relationships:** Emilie Picard, None; Alessandra Daruich, None; Quentin Le Rouzie, None; Laurent Jonet, None; Marie-Christine Naud, None; Laura Kowalczyk, None; Aurélien Thomas, None; Natacha Turck, None; Thomas J. wolvesberger, None; Alexandre Moulin, None; Jean-Antoine Pournaras, None; Yves Courtois, None; Francine F. Behar-Cohen, None

**Support:** ANR JCJC TRANSFIRON 2015

**Program Number:** 1594
**Presentation Time:** 12:00 PM–12:15 PM

**Retinal ischemia limits visual recovery in rhegmatogenous retinal detachment**

Junyeop Lee1, Jung Hwan Ahn1, Jehwi Jeeon1, Min Sagong1, Junhyuk Son1, Soocheol Cha1, Young Hee Yoor1

1. Department of Ophthalmology, Yeungnam University, Daegu, Korea (the Republic of); 2. Department of Ophthalmology, Asan Medical Center, Seoul, Korea (the Republic of).

**Purpose:** Factors determining the reversibility of visual function in retinal detachment are yet to be clearly defined. We performed a retrospective study to evaluate the hemodynamic changes in the detached and reattached retina and its association with post-operative visual recovery in rhegmatogenous retinal detachment (RRD).

**Methods:** This study included 52 eyes with primary RRD which underwent successful vitrectomy or scleral buckling by a single surgeon. Pre- and post-operative ultra-widefield fluorescein angiography (UWF FA), spectral domain-optical coherence tomography (SD-OCT), and post-operative OCT angiography (OCTA) were obtained. The integrity of ellipsoid zone (EZ) was evaluated in post-operative SD-OCT. Using the OCTA, vascular flow density in the superficial capillary plexus (SCP) and deep capillary plexus (DCP) of the reattached retina were compared with those of the contralateral unaffected eye.

**Results:** In the UWF FA, all RRD eyes presented areas of capillary hypo- or non-perfusion at the detached periphery, venous stasis and diffuse paravascular leakage at the detached retina, all of which were
partially recovered after reattachment. In the 26 eyes with macula-off RRD, less flow density of DCP in post-operative OCTA was strongly correlated with longer duration of detachment ($r = -0.888$, $p < 0.001$), greater EZ disruption in SD-OCT, ($r = -0.923$, $p < 0.001$) and the poor visual recovery ($r = -0.935$, $p < 0.001$). In contrast, the flow density in SCP was not associated with post-operative visual outcome or duration of detachment.

**Conclusions:** RRD resulted in hypo-perfusion, venous stasis, and associated vasculopathies at the detached retina, which were restored after the reattachment. Because the low blood flow triggers the regression of capillaries, the longer duration of low-flow in the detached retina, the more capillary loss in DCP leading to greater photoreceptor damage and poor visual outcome in the eyes with macula-off RRD. This study suggests that retinal ischemia serves as a major cause of irreversible photoreceptor cell death in RRD. Thus, early reattachment and reperfusion are required for the prevention of visual impairment in the macula-off RRD.

**Commercial Relationships:** Junyeop Lee, None; Jang Hwan Ahn, None; Jehwi Jeon, None; Min Sagong, None; Junhyuk Son, None; Soonchol Cha, None; Young Hee Yoon, None.

**Program Number:** 1595
**Presentation Time:** 12:15 PM–12:30 PM

**A mathematical model of posterior vitreous detachment and generation of vitreoretinal tractions**

Rodolfo Repetto¹, Federica Di Michele², Amabile Tatone².

¹Department of Civil, Chemical and Environmental Engineering, University of Genoa, Genoa, Italy; ²Department of Information Engineering, Computer Science and Mathematics, University of L’Aquila, L’Aquila, Italy.

**Purpose:** Posterior vitreous detachment (PVD) can lead to strong tractions on the retina that are the most common cause of non-traumatic retinal tearing. We propose a mathematical model of the generation of retinal tractions induced by vitreous contraction, which is aimed at understanding the mechanics of the process.

**Methods:** The vitreous humor is modeled as a soft solid surrounded by a membrane that initially fills a spherical domain with rigid walls. We assume that the maximum adhesive force per unit surface between the membrane and the wall can be variable in space, which allows us to simulate cases of focal adhesions. We assume that the relaxed configuration of the solid progressively shrinks in time and, owing to the non-uniformity of the adhesive force, this generates detachment of the vitreous from certain regions of the boundary and localized tractions.

**Results:** In Figure 1(a,b) we show two examples of predicted configurations of the vitreous attained during the progression of the PVD. In (a) we show a “complete vitreous detachment”, in which detachment progressively proceeds from the back (right) towards the front (left) of the vitreous chamber. In (b) we show the case of a PVD in the presence of a focal vitreoretinal adhesion. In this case the model predicts that the vitreous deforms substantially during the contraction process, thus also generating large stresses.

**Conclusions:** The model can be used to identify shapes of the detaching vitreous that are likely to be associated with large tractions on the boundary and to the existence of particularly strong focal adhesions on the retina, which are risk factors for the generation of retinal tears.

Two examples of the shape taken by the contracting vitreous during PVD, as predicted by the model. (a) Complete PVD, (b) case in which there is a focal adhesion at the back of the vitreous chamber.

**Commercial Relationships:** Rodolfo Repetto, None; Federica Di Michele, None; Amabile Tatone, None.