

Issue 319

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Drug treatment

Ophthalmologica. 2017 Mar 4. [Epub ahead of print]

One-Year Outcomes of a Treat-and-Extend Regimen of Aflibercept for Exudative Age-Related Macular Degeneration.

Yamamoto A, Okada AA, Nakayama M, Yoshida Y, Kobayashi H.

PURPOSE: The aim of this study was to investigate the 1-year outcomes of treat-and-extend aflibercept for exudative age-related macular degeneration (AMD) in Japan.

PROCEDURES: Clinical records of 67 patients (67 eyes) were reviewed. Monthly aflibercept was administered until resolution of exudation and maximal reduction of pigment epithelial detachment. Injection intervals were extended by 2-week units up to 12 weeks if no exudation was observed and shortened for recurrence.

RESULTS: Mean best-corrected visual acuity (logarithm of the minimum angle of resolution) improved from 0.29 to 0.14 at 12 months ($p < 0.0001$). Mean central retinal thickness decreased from 430 μm to 236 μm at 12 months ($p < 0.0001$). Fifty-nine eyes (88.0%) achieved a dry macula with a mean of 8.3 injections by study end. The injection interval was extended to 10 weeks in 44.8% and to 12 weeks in 17.9% of eyes.

CONCLUSIONS: At 1 year, good outcomes were obtained using treat-and-extend aflibercept for exudative AMD in Japan.

PMID: 28259869

Turk J Med Sci. 2017 Feb 27;47(1):40-46.

Intravitreal PRN ranibizumab treatment for macular edema due to branch retinal vein occlusion.

Çakmak HB, Arikan Yorgun M, Toklu Y, Mutlu M.

BACKGROUND/AIM: To evaluate the effect of intravitreal pro re nata (PRN) ranibizumab treatment from the start on the best-corrected visual acuity (BCVA) and the central retinal thickness (CRT) in macular edema (ME) due to branch retinal vein occlusion (BRVO).

MATERIALS AND METHODS: Patients with ME secondary to BRVO, who were treated on a PRN basis after a single intravitreal ranibizumab injection, were retrospectively evaluated. The main outcome measures were changes in BCVA and CRT as measured by optical coherence tomography.

RESULTS: The number of injections over 6 months was 2.43 ± 1.16 . The mean BCVA of the patients was 0.84 ± 0.10 logMAR at baseline and 0.41 ± 0.06 at the 6th month ($P < 0.001$). Mean BCVA of the ischemic

BRVO group was 1.06 ± 0.68 logMAR at baseline and 0.44 ± 0.30 logMAR at the 6th month ($P < 0.05$). Similarly, the mean BCVA of the nonischemic BRVO group was 0.77 ± 0.53 logMAR at baseline and 0.41 ± 0.36 logMAR at the 6th month ($P < 0.05$). Between groups, there was no significant difference in mean BCVA at any examination.

CONCLUSION: Intravitreal ranibizumab is a safe and effective treatment option for ME due to ischemic and nonischemic BRVO using PRN from the start.

PMID: 28263518

Clin Ophthalmol. 2017 Feb 22;11:403-408. eCollection 2017.

Prolongation of injection interval after switching therapy from ranibizumab to aflibercept in Japanese patients with macular edema secondary to branch retinal vein occlusion.

Tagami M, Sai R, Fukuda M, Azumi A.

PURPOSE: This study was conducted to investigate the outcome of switching therapy from ranibizumab to aflibercept in Japanese patients with macular edema (ME) secondary to branch retinal vein occlusion (BRVO) in daily practice.

MATERIALS AND METHODS: This retrospective study enrolled 15 eyes in 15 Japanese patients with ME secondary to BRVO who had been receiving a pro re nata regimen of ranibizumab and had provided written informed consent to switch to aflibercept therapy. The intravitreal injection interval, central retinal thickness, and visual acuity were evaluated before and after switching.

RESULTS: The mean period of ranibizumab treatment was 11.8 ± 4.2 months. The mean observation period after switching to aflibercept was 10.6 ± 3.4 months, and seven patients were observed for more than 12 months after switching. The mean intravitreal injection interval was prolonged by 23.6 days with aflibercept (68.2 ± 26.4 days with ranibizumab vs 91.8 ± 33.2 days with aflibercept; $P = 0.0011$). The mean intravitreal injection interval just before the switch was 81.3 ± 35.6 days and was significantly prolonged to 100.8 ± 34.2 days just after the switch to aflibercept ($P = 0.0309$). The mean central retinal thickness did not change before or after the switch to aflibercept (295 ± 55 μ m with ranibizumab vs 276 ± 25 μ m with aflibercept; $P = 0.12$). The mean visual acuity also remained at an improved level after the switch. No systemic or ocular side effects were evident during the study period.

CONCLUSION: Switching therapy from ranibizumab to aflibercept in Japanese patients with ME secondary to BRVO prolonged the intravitreal injection interval without anatomical or functional degradation.

PMID: 28260852 PMCID: PMC5328307

Clin Ophthalmol. 2017 Feb 21;11:393-401. eCollection 2017.

Anti-VEGF treatment of diabetic macular edema in clinical practice: effectiveness and patterns of use (ECHO Study Report 1).

Blinder KJ, Dugel PU, Chen S, Jumper JM, Walt JG, Hollander DA, Scott LC.

PURPOSE: To evaluate the efficacy, safety, and injection frequency of vascular endothelial growth factor (VEGF) inhibitors as used in clinical practice for the treatment of diabetic macular edema.

METHODS: Multicenter (10 sites), retrospective chart review in patients ($n = 156$) who received ≥ 3 anti-VEGF injections. Data collected for ≥ 6 months after the first injection included Snellen best-corrected visual acuity (BCVA) and central retinal thickness (CRT) by time-domain or spectral-domain optical coherence tomography (TD-OCT or SD-OCT).

RESULTS: Mean number of anti-VEGF injections (627 bevacizumab, 594 ranibizumab, 1 aflibercept) was 5.8 (year 1), 5.0 (year 2), and 3.4 (year 3). Percentage of patients with BCVA of 20/40 or better and CRT ≤ 250 μ m on TD-OCT or ≤ 300 μ m on SD-OCT at the same visit (primary endpoint) ranged from 16.4% to 38.9% after the first 10 injections; 51.9%-62.3% achieved $\geq 20/40$ BCVA and 26.2%-48.0% met CRT criteria. Therapy was well tolerated with 19 treatment-related adverse events (all ocular) reported.

CONCLUSION: Anti-VEGF injections were administered less frequently and were less effective than those in the ranibizumab registration trials. After each of the first 9 injections, $<25\%$ of patients achieved both BCVA of 20/40 or better and a dry macula. A substantial proportion of patients are suboptimal responders to anti-VEGF therapy; these patients may be candidates for other therapies, including intravitreal corticosteroid and laser therapy.

PMID: 28260851 PMCID: PMC5328320

Ann Anat. 2017 Mar 6. [Epub ahead of print]

Efficacy of aflibercept (EYLEA®) on inhibition of human VEGF in vitro.

Schicht M, Hesse K, Schröder H, Naschberger E, Lamprecht W, Garreis F, Paulsen FP, Bräuer L.

INTRODUCTION: Pathological formation of blood vessels plays a key role in the growth and metastasis of tumors and also in several serious ophthalmological diseases such as wet age-related macular degeneration (AMD) or diabetic retinopathy. In AMD treatment, aflibercept (tradename EYLEA®) is used to deactivate the underlying pathological neovascularisation. Aflibercept is a recombinant fusion protein which binds to vascular endothelial growth factor (VEGF) receptors, thereby inhibiting VEGF pathway activation. VEGF is one of the most important angiogenesis factors.

OBJECTIVE: This analysis investigates lasting efficacy of aflibercept in vitro for later application as therapeutic agent against macular degeneration (AMD).

MATERIAL AND METHODS: VEGF-ELISA assays were performed to investigate binding affinities at different aflibercept concentrations. The impact of VEGF on the proliferation of human umbilical vein endothelial cells (HUVEC) was investigated using proliferation assays. Moreover, time-dependent kinetic studies were performed to analyze different aflibercept storage durations with regard to its inhibitory capabilities on human VEGF.

RESULTS AND CONCLUSION: Our results reveal that aflibercept significantly lowers the amount of unbound VEGF as well as the proliferation rate of HUVEC. Moreover, in contrast to specifications given by the manufacturer, aflibercept retains its full inhibitory effect up to at least 120h after transference from the original vial into the injection syringe.

PMID: 28279730

Retina. 2017 Mar 7. [Epub ahead of print]

DEXAMETHASONE INTRAVITREAL IMPLANT VS RANIBIZUMAB IN THE TREATMENT OF MACULAR EDEMA SECONDARY TO BRACHYTHERAPY FOR CHOROIDAL MELANOMA.

Russo A, Reibaldi M, Avitabile T, Uva MG, Franco LM, Gagliano C, Bonfiglio V, Spatola C, Privitera G, Longo A.

PURPOSE: To evaluate the efficacy of an intravitreal dexamethasone (Dex) implant 0.7 mg compared with intravitreal ranibizumab (Ra) for the treatment of radiation maculopathy with macular edema secondary to plaque brachytherapy in choroidal melanoma.

METHODS: Eight patients were treated with intravitreal Ra, and eight patients received the Dex intravitreal implant. Visual acuity and foveal thickness were evaluated using spectral domain optical coherence tomography.

RESULTS: The mean calculated irradiation to the fovea and mean times from brachytherapy to maculopathy development did not differ significantly between groups. In the Ra group, a mean 7.8 ± 3.9 injections were given and the mean follow-up was 33 ± 15 months (range, 7-52 months). In the Dex group, a mean 2.1 ± 0.8 injections were given and the mean follow-up was 22 ± 7 months (range, 11-31 months). The mean visual acuity improved significantly from the baseline to the last follow-up visit in both groups. Foveal thickness decreased significantly in both groups from $459 \pm 81 \mu\text{m}$ to $243 \pm 58 \mu\text{m}$ and from $437 \pm 71 \mu\text{m}$ to $254 \pm 44 \mu\text{m}$ from the baseline to the last follow-up visit in the Ra and Dex groups, respectively. No patients developed significant cataract or ocular hypertension in both groups.

CONCLUSION: Both Ra and Dex are effective treatments for macular edema secondary to plaque brachytherapy for uveal melanoma. Dex-treated patients required fewer injections to achieve anatomical and functional improvement.

PMID: 28272283

Br J Ophthalmol. 2017 Mar 7. [Epub ahead of print]

Aqueous cytokine and growth factor levels indicate response to ranibizumab for diabetic macular oedema.

Shimura M, Yasuda K, Motohashi R, Kotake O, Noma H.

BACKGROUND/AIMS: To investigate the relations between aqueous humour levels of cytokines/growth factors and treatment response to intravitreal ranibizumab (IVR) for diabetic macular oedema (DME)

METHODS: Sixty-eight eyes of 68 patients with treatment-naïve centre-involved DME, central macular thickness (CMT) greater than $400 \mu\text{m}$ and visual acuity (VA) worse than logMAR 0.3 were recruited. Each patient received monthly IVR injection (0.5 mg/0.05 mL) until CMT was reduced to below $300 \mu\text{m}$. Additional IVR was given to maintain CMT below $300 \mu\text{m}$ during the clinical course of 6 months with monthly follow-up. Aqueous concentrations of cytokines/chemokines and growth factors were measured using samples obtained just before first IVR injection. CMT and VA were monitored monthly for up to 6 months. The number of monthly IVR injections given during the 6-month study period was also recorded.

RESULTS: Twenty-four eyes showed CMT $<300 \mu\text{m}$ soon after the first IVR injection (good responders), while 12 eyes did not reach the goal after six consecutive injections (poor responders). Baseline CMT and VA were not significantly different between the two groups. However, the good responders showed significant increases in baseline aqueous concentrations of vascular endothelial growth factor (VEGF), placenta growth factor, soluble VEGF receptor-1 (sVEGFR1), monocyte chemoattractant protein-1, intercellular adhesion molecule-1, interleukin 6 and inducible protein-10, but not of sVEGFR2, compared with poor responders.

CONCLUSIONS: Response to ranibizumab treatment for DME appears to be associated with aqueous concentrations of VEGFR1 family and certain inflammatory cytokines, but not with clinical parameters.

PMID: 28270488

Br J Ophthalmol. 2017 Mar 7. [Epub ahead of print]

Long-term safety and efficacy of ziv-aflibercept in retinal diseases.

Mansour AM, Ashraf M, Dedhia CJ, Charbaji A, Souka AA, Chhablani J.

AIMS: To investigate the long-term safety of intravitreal ziv-aflibercept in eyes receiving six or more intravitreal injections of ziv-aflibercept, an off-label substitute to the approved aflibercept.

METHODS: Consecutive patients with retinal disease receiving six or more of intravitreal 0.05 mL ziv-aflibercept (1.25 mg) injections were followed monthly in three centres. Outcome measures were best-corrected visual acuity (BCVA) (logarithm of the minimum angle of resolution (logMar)) and central macular thickness (CMT) on spectral domain optical coherence tomography and monitoring for ocular inflammation, progression of lens opacities and intraocular pressure rise. Paired comparison was done using Wilcoxon signed-rank test calculator.

RESULTS: Sixty-five eyes of 60 consecutive patients received a mean of 8.4 (6-17) intravitreal injections with a baseline mean logMAR BCVA of 0.98 ± 0.56 and CMT $432.7 \pm 163.0 \mu\text{m}$ and followed for a mean of 9.2 months (range 6-18 months). After the sixth injection, mean BCVA improved to 0.57 ± 0.36 ($p=0.001$) and CMT decreased to $274.8 \pm 117.8 \mu\text{m}$ ($p=0.0001$). At the 9-month follow-up, mean BCVA improved to 0.62 ± 0.37 ($p=0.0004$) and mean CMT decreased to $292.0 \pm 160.9 \mu\text{m}$ ($p<0.01$) in 19 eyes. At 1 year, mean BCVA was 0.73 ± 0.52 and CMT $311.6 \pm 232.5 \mu\text{m}$ in seven eyes. Intraocular pressures did not increase after injections. One subject developed transient mild iritis at the fourth injection but not on subsequent injections. No lens opacity progression or endophthalmitis was noted. Systemic adverse effects were not registered.

CONCLUSIONS: Repeated intravitreal injections of ziv-aflibercept appear tolerable, safe and efficacious in the therapy of retinal disease.

PMID: 28270485

Sci Rep. 2017 Mar 7;7:44020.

Incidence and risk factors of retreatment after three-monthly aflibercept therapy for exudative age-related macular degeneration.

Kikushima W, Sakurada Y, Yoneyama S, Sugiyama A, Tanabe N, Kume A, Mabuchi F, Iijima H.

Abstract: Though anti-vascular endothelial growth factor therapy has become the standard treatment for exudative age-related macular degeneration (AMD), retreatment after the initial loading injection is inevitable in most eyes with residual or recurrent exudative changes. In the present study, we studied 140 treatment naïve eyes with typical neovascular AMD ($n = 71$) or polypoidal choroidal vasculopathy (PCV) ($n = 69$) and investigated the incidence and risk factors of retreatment after 3-monthly intravitreal aflibercept injection for exudative AMD during the 12-month period. At 12 months, best-corrected visual acuity (BCVA) improved significantly from 0.45 ± 0.39 to 0.26 ± 0.33 ($P = 4.1 \times 10^{-11}$). Multiple regression analysis revealed that better baseline BCVA ($P = 3.6 \times 10^{-14}$) and thicker subfoveal choroidal thickness ($P = 0.039$) were associated with better BCVA at 12-months. Retreatment was required in 94 out of 140 (67.1%) eyes. Multivariate logistic regression analysis revealed that older age ($P = 7.2 \times 10^{-3}$) and T-allele of ARMS2 A69S (rs10490924) variants ($P = 1.9 \times 10^{-3}$) were associated with retreatment. Cox-regression analysis revealed that older age ($P = 1.0 \times 10^{-2}$) and T-allele of the ARMS2 gene ($P = 6.0 \times 10^{-3}$) were associated with retreatment-free period. The number of retreatment episodes was significantly different among the ARMS2 genotypes ($P = 8.1 \times 10^{-4}$). These findings might be helpful for physicians when considering the optimal treatment regimen for exudative AMD.

PMID: 28266609 PMCID: PMC5339812

Other treatment & diagnosis

Clin Exp Optom. 2017 Mar 7. [Epub ahead of print]

Self-reported optometric practise patterns in age-related macular degeneration.

Ly A, Nivison-Smith L, Zangerl B, Assaad N, Kalloniatis M.

BACKGROUND: The use of advanced imaging in clinical practice is emerging and the use of this technology by optometrists in assessing patients with age-related macular degeneration is of interest. Therefore, this study explored contemporary, self-reported patterns of practice regarding age-related macular degeneration diagnosis and management using a cross-sectional survey of optometrists in Australia and New Zealand.

METHODS: Practising optometrists were surveyed on four key areas, namely, demographics, clinical skills and experience, assessment and management of age-related macular degeneration. Questions pertaining to self-rated competency, knowledge and attitudes used a five-point Likert scale.

RESULTS: Completed responses were received from 127 and 87 practising optometrists in Australia and New Zealand, respectively. Advanced imaging showed greater variation in service delivery than traditional techniques (such as slitlamp funduscopy) and trended toward optical coherence tomography, which was routinely performed in age-related macular degeneration by 49 per cent of respondents. Optical coherence tomography was also associated with higher self-rated competency, knowledge and perceived relevance to practice than other modalities. Most respondents (93 per cent) indicated that they regularly applied patient symptoms, case history, visual function results and signs from traditional testing, when queried about their management of patients with age-related macular degeneration. Over half (63 per cent) also considered advanced imaging, while 31 per cent additionally considered all of these as well as the disease stage and clinical guidelines. Contrary to the evidence base, 68 and 34 per cent rated nutritional supplements as highly relevant or relevant in early age-related macular degeneration and normal aging changes, respectively.

CONCLUSIONS: These results highlight the emergence of multimodal and advanced imaging (especially optical coherence tomography) in the assessment of age-related macular degeneration by optometrists. Clinically significant variations in self-rated test competency and the understanding regarding nutritional supplements for different stages of age-related macular degeneration suggest that further work to up-skill optometrists may be required.

PMID: 28266060

Int Ophthalmol. 2017 Mar 7. [Epub ahead of print]

Changes in reticular pseudodrusen area in eyes that progressed from early to late age-related macular degeneration.

Kaszubski PA, Ben Ami T, Saade C, Nabati C, Kumar V, Santos AR, Silva R, Cachulo ML, Cunha-Vaz JG, Smith RT.

OBJECTIVE: This retrospective cohort study utilized 3 imaging modalities to analyze quantitatively reticular pseudodrusen (RPD) area changes in eyes that progressed from early to late age-related macular degeneration (AMD).

METHODS: Subjects with AMD, unilateral choroidal neovascularization (CNV), and early AMD with RPD in the fellow eye (the study eye) were included. The study eyes underwent indocyanine green angiography (ICGA), near-infrared reflectance (NIR-R), and short-wavelength autofluorescence (AF) imaging of the macula at baseline and at follow-up. Study eyes were analyzed for RPD and for the development of late AMD-CNV and/or geographic atrophy (GA). RPD area was measured at baseline and at follow-up as a

percentage of the 30-degree field.

RESULTS: During the study period (mean follow-up time 23.5 ± 5.0 months), 12/31 study eyes developed CNV and 4/31 developed GA. In the eyes that developed CNV, there was a statistically significant decrease in mean RPD area over the follow-up period as seen on AF ($P < 0.01$) and NIR-R ($P = 0.01$), and the decrease in mean RPD area approached statistical significance on ICGA ($P = 0.08$).

CONCLUSION: Using 3 en face imaging techniques, we demonstrate that RPD undergo dynamic spatiotemporal changes in eyes that progress from early AMD to CNV, namely a decrease in the area of lesions detected.

PMID: 28265823

Br J Ophthalmol. 2017 Mar 7. Epub ahead of print]

Polypoidal choroidal vasculopathy: a common type of neovascular age-related macular degeneration in Caucasians.

Yadav S, Parry DG, Beare NA, Pearce IA.

AIMS: To describe the prevalence of polypoidal choroidal vasculopathy (PCV) in a Caucasian population with neovascular age-related macular degeneration (NAMD).

METHODS: All patients referred to a city AMD service over a 2-year period underwent imaging including Indocyanine Green Angiography at baseline. A panel of experts confirmed the patients with NAMD and diagnosed the lesion type including PCV. The proportion of Caucasian patients with PCV was identified. Two authors independently reviewed clinical imaging and recorded data of patients with PCV on lesion characteristics. Further information including treatments received and visual acuity at different time points was analysed.

RESULTS: A total of 492 patients were diagnosed with NAMD during the 2-year study period. Of these patients, 204 had occult lesions (41.5%). PCV was identified in 45 patients (22.1% of occult NAMD and 9.1% of all NAMD). 23 patients received anti-vascular endothelial growth factor (VEGF) monotherapy, 8 received verteporfin photodynamic therapy (PDT) monotherapy and the remaining 14 patients were managed with combined PDT and anti-VEGF treatment.

CONCLUSIONS: The prevalence of PCV in Caucasians is higher than previously reported. Indocyanine Green Angiography should be a standard investigation for all new patients with NAMD, particularly those with occult NAMD, to avoid missing this important subset.

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Transl Vis Sci Technol. 2017 Feb 28;6(1):12. eCollection 2017.

Individual Drusen Segmentation and Repeatability and Reproducibility of Their Automated Quantification in Optical Coherence Tomography Images.

de Sisternes L, Jonna G, Greven MA, Chen Q, Leng T, Rubin DL.

PURPOSE: To introduce a novel method to segment individual drusen in spectral-domain optical coherence tomography (SD-OCT), and evaluate its accuracy, and repeatability/reproducibility of drusen quantifications extracted from the segmentation results.

METHODS: Our method uses a smooth interpolation of the retinal pigment epithelium (RPE) outer boundary, fitted to candidate locations in proximity to Bruch's Membrane, to identify regions of substantial lifting in the inner-RPE or inner-segment boundaries, and then separates and evaluates individual druse independently. The study included 192 eyes from 129 patients. Accuracy of drusen segmentations was evaluated measuring the overlap ratio (OR) with manual markings, also comparing the results to a previously proposed method. Repeatability and reproducibility across scanning protocols of automated drusen quantifications were investigated in repeated SD-OCT volume pairs and compared with those measured by a commercial tool (Cirrus HD-OCT).

RESULTS: Our segmentation method produced higher accuracy than a previously proposed method, showing similar differences to manual markings (0.72 ± 0.09 OR) as the measured intra- and interreader variability (0.78 ± 0.09 and 0.77 ± 0.09 , respectively). The automated quantifications displayed high repeatability and reproducibility, showing a more stable behavior across scanning protocols in drusen area and volume measurements than the commercial software. Measurements of drusen slope and mean intensity showed significant differences across protocols.

CONCLUSION: Automated drusen outlines produced by our method show promising accurate results that seem relatively stable in repeated scans using the same or different scanning protocols.

TRANSLATIONAL RELEVANCE:

The proposed method represents a viable tool to measure and track drusen measurements in early or intermediate age-related macular degeneration patients.

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Graefes Arch Clin Exp Ophthalmol. 2017 Mar 9. [Epub ahead of print]

The role of pigment epithelial detachment in AMD with submacular hemorrhage treated with vitrectomy and subretinal co-application of rtPA and anti-VEGF.

Treumer F, Wienand S, Purtskhvanidze K, Roeder J, Hillenkamp J.

PURPOSE: To assess the incidence of pigment epithelial detachment (PED) in age-related macular degeneration (AMD) with submacular hemorrhage (SMH) and its response to treatment with pars plana vitrectomy (ppV), subretinal co-application of recombinant tissue plasminogen activator (rtPA) and anti-VEGF, and an intravitreal gas tamponade.

METHODS: Consecutive interventional case series of 132 eyes of 129 patients with neovascular AMD with SMH. All eyes underwent ppV with subretinal co-application of rtPA and bevacizumab followed by a gas tamponade. Postoperatively, two additional intravitreal anti-VEGF injections were applied monthly, followed by intravitreal anti-VEGF injections applied PRN thereafter. PEDs and SMHs were evaluated with SD-OCT pre- and postoperatively.

RESULTS: Preoperatively, 88 of 132 (67%) eyes were examined by OCT, and in 81 of these eyes the RPE could be visualised. A PED was found in 74 (91%) eyes, and no PED was found in five (6%) eyes. Median height of preoperative PED was 503 μ m (range 150-1242, $n = 65$) and reduced to 344 ($n = 62$) and 306 μ m ($n = 27$) after 3 and 12 months respectively. Two eyes showed a pre-existing rip of the RPE. Postoperatively, a rip was documented in 12 of 128 (9%) eyes. Median height of SMH was 762 μ m (range 217-1840), median diameter was 4.3 (1.5-15) disc diameter. A complete displacement of the SMH from the fovea was achieved in 112 of 129 (87%) eyes. Overall, median best-corrected logMAR visual acuity (BCVA) improved significantly from preoperative 1.6 (0.5-2.0, $n = 132$) to 1.0 (0.2-2.0) 3 ($n = 132$) and 12 months ($n = 74$) postoperatively. Excluding eyes with pre-existing macular scars ($n = 22$), BCVA 3 months postoperatively was 0.8. Height of PED or SMH did not correlate with postoperatively BCVA, while size of SMH showed a mild correlation ($\rho = 0.25$, $p = 0.005$).

CONCLUSION: PpV with subretinal co-application of rtPA and bevacizumab and an intravitreal gas tamponade effectively displaces SMH and improves BCVA. Preoperatively, PED is found in the majority of eyes. Height of PED or SMH did not correlate with postoperatively BCVA. Tears of the RPE occur as frequently as in exudative AMD without SMH.

PMID: 28280989

Klin Monbl Augenheilkd. 2017 Mar 10. [Epub ahead of print]

**[Choroidal Neovascularisation Other than Typical Neovascular Age-Related Macular Degeneration].
[Article in German]**

Sandner D.

Abstract: Choroidal neovascularisation (CNV) in the context of exudative age-related macular degeneration (nAMD) can be divided into type 1 (occult) and type 2 (classical) membranes. Retinal angiomatous proliferation (RAP) or polypoidal choroidal vasculopathy (PCV) are "rare subtypes" of chorioretinal neovascularisation and are distinguished by their distinct morphology and the sometimes worse response to therapy. Chorioretinal anastomosis, severe exsudates with serosanguinous pigment epithelial detachment and, in PCV, orange-red lesions in the papillomacular bundle can be diagnostic. Indocyanine green angiography (ICGA) is considered the gold standard for diagnosis of PCV and delivers important information for RAP too. Typical characteristics of PCV include foci of hyperfluorescence, with pulsatile filling in the early phase. This characterises choroidal polypoidal lesions, often in connection with an abnormal choroidal vascular network. In RAP, typical retino-retinal anastomosis can be identified, in particular in areas with pigment epithelial detachment. Optical coherence tomography (OCT) can complement diagnostic testing. In cases of RAP, early therapy initiation with intravitreal anti-VEGF is crucial for the prognosis of visual acuity. PCV can exhibit spontaneous regression. In active disease, photodynamic therapy (PDT) is efficient in the closure of PCV polyps. In association with CNV, it makes sense to combine PDT and intravitreal anti-VEGF medication. In spite of the initial increase in visual acuity, this state is normally "only" stabilised in the long term. In patients with idiopathic secondary CNV membranes (high myopia, post-inflammatory, post-traumatic changes or in hereditary connective tissue diseases), small "classical" type 2 membranes are mostly involved. Hence, these are strictly speaking not directly rare subtypes. Nevertheless, these patients are mostly younger, with less protracted illness and limited available regeneration ability of the retinal pigment epithelium (RPE): they may therefore differ favourably from the courses with nAMD, with earlier inactivation and with fewer required anti-VEGF injections. CNV with angioid streaks are a special case in this group. Unfortunately, these lesions have a recurrent, protracted and, in the end, mostly frustrating course.

PMID: 28282700

Biomed Opt Express. 2017 Jan 24;8(2):1056-1082. eCollection 2017.

Optical coherence tomography based angiography [Invited].

Chen CL, Wang RK.

Abstract: Optical coherence tomography (OCT)-based angiography (OCTA) provides in vivo, three-dimensional vascular information by the use of flowing red blood cells as intrinsic contrast agents, enabling the visualization of functional vessel networks within microcirculatory tissue beds non-invasively, without a need of dye injection. Because of these attributes, OCTA has been rapidly translated to clinical ophthalmology within a short period of time in the development. Various OCTA algorithms have been developed to detect the functional micro-vasculatures in vivo by utilizing different components of OCT signals, including phase-signal-based OCTA, intensity-signal-based OCTA and complex-signal-based

OCTA. All these algorithms have shown, in one way or another, their clinical values in revealing micro-vascularities in biological tissues in vivo, identifying abnormal vascular networks or vessel impairment zones in retinal and skin pathologies, detecting vessel patterns and angiogenesis in eyes with age-related macular degeneration and in skin and brain with tumors, and monitoring responses to hypoxia in the brain tissue. The purpose of this paper is to provide a technical oriented overview of the OCTA developments and their potential pre-clinical and clinical applications, and to shed some lights on its future perspectives. Because of its clinical translation to ophthalmology, this review intentionally places a slightly more weight on ophthalmic OCT angiography.

PMID: 28271003 PMCID: PMC5330554

Biomed Opt Express. 2017 Jan 4;8(2):579-592. eCollection 2017.

Transfer learning based classification of optical coherence tomography images with diabetic macular edema and dry age-related macular degeneration.

Karri SP, Chakraborty D, Chatterjee J.

Abstract: We present an algorithm for identifying retinal pathologies given retinal optical coherence tomography (OCT) images. Our approach fine-tunes a pre-trained convolutional neural network (CNN), GoogLeNet, to improve its prediction capability (compared to random initialization training) and identifies salient responses during prediction to understand learned filter characteristics. We considered a data set containing subjects with diabetic macular edema, or dry age-related macular degeneration, or no pathology. The fine-tuned CNN could effectively identify pathologies in comparison to classical learning. Our algorithm aims to demonstrate that models trained on non-medical images can be fine-tuned for classifying OCT images with limited training data.

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Br J Ophthalmol. 2017 Mar 7. [Epub ahead of print]

Retinal pigment epithelial features indicative of neovascular progression in age-related macular degeneration.

Roberts PK, Baumann B, Schlanitz FG, Sacu S, Bolz M, Pircher M, Hagmann M, Hitzemberger CK, Schmidt -Erfurth U.

BACKGROUND/AIMS: To identify characteristic retinal pigment epithelium (RPE) changes in fellow eyes of patients with neovascular age-related macular degeneration (nAMD) using polarisation-sensitive optical coherence tomography (PS-OCT).

METHODS: Thirty-one fellow eyes of 31 patients with unilateral nAMD were evaluated in this cohort study of a prospective interventional trial. PS-OCT as well as conventional imaging including spectral-domain (SD)-OCT and fluorescein angiography (FA) were performed using a standardised protocol. Monitoring visits were performed continuously at 1-month intervals. Morphological RPE features associated with the development of choroidal neovascularisation (CNV) were systematically analysed.

RESULTS: Mean follow-up was 29 months (± 17 , SD). Thirteen (42%) of 31 eyes developed de novo CNV: 9 eyes type I CNV, 2 eyes type II CNV, 2 eyes a retinal angiomatous proliferation lesion. RPE thickening and reticular pseudodrusen (RPD) were observed significantly more often in eyes that developed CNV than in eyes without CNV development ($p < 0.01$). Monthly increase in drusen volume was higher in the CNV group with a median increase of +2.2% in area and +2.9% in volume compared with +0.8% and +0.6% in the non-progressing group. RPE migration within the neurosensory retina and at the level of the RPE resulting in RPE thickening was seen topographically and chronologically associated with CNV

development.

CONCLUSIONS: Conversion to CNV is associated with RPE-related changes such as RPE migration, RPE thickening, drusen volume or the presence of RPD. Early detection of these features may allow more efficient screening in risk eyes and timely vision-preserving treatment in eyes developing neovascular disease.

PMID: 28270492

Acta Ophthalmol. 2017 Mar 7. [Epub ahead of print]

Macular cystic changes as predictive factor for the recurrence of macular oedema in branch retinal vein occlusion.

Tilgner E, Dalcegio Favretto M, Tuisl M, Wiedemann P, Rehak M.

AIM: To evaluate the role of small cystic macular changes as a prognostic factor for the recurrence of macular oedema (ME) in patients with branch retinal vein occlusion (BRVO) treated with anti-VEGF drugs.

METHODS: We performed retrospective chart analysis of 116 patients treated with intravitreal injection of ranibizumab (IVR) or bevacizumab (IVB) for ME secondary to BRVO. At the baseline and monthly follow-up visits over a period of 12 months, a comprehensive ophthalmologic examination including best-corrected visual acuity (BCVA) and volume scan of macula using Spectral domain optical coherence tomography (SD-OCT) were performed. Patients without ME (CRT <250 µm) were screened for the presence of intraretinal cysts. In these patients, the changes in BCVA and CRT were evaluated over a period of 12 months and compared with the baseline.

RESULTS: In the IVR group (41 patients), 91 events of macular cysts, without a worsening of BCVA, were detected by OCT. In 89 of 91 events (97%), BCVA and CRT deteriorated significantly ($p < 0.0001$) within the next 4-11 (in mean 7.1 ± 2.0) weeks. BCVA decreased from 0.38 ± 0.25 to 0.49 ± 0.27 logMAR and CRT increased significantly from 223 ± 43 to 605 ± 244 µm. In the IVB group (19 patients), 54 events of cystic changes were detected. All of these patients showed significant worsening of BCVA from 0.40 ± 0.19 to 0.57 ± 0.22 logMAR and CRT from 251 ± 17 to 490 ± 147 µm within 4-10 (in mean 7.8 ± 2.8) weeks after the first presence of small macular cysts.

CONCLUSION: In BRVO patients treated with anti-VEGF drugs, the macular cystic changes may be used as an early indicator for impending recurrence of ME, with the decrease in BCVA in the following weeks. These patients should be scheduled for a next visit within 6-8 weeks.

PMID: 28266152

Acta Ophthalmol. 2017 Mar 8. [Epub ahead of print]

Association between pseudodrusen and delayed patchy choroidal filling in the comparison of age-related macular degeneration treatments trials.

Zhou Q, Daniel E, Grunwald JE, Maguire MG, Gewaily DY, Martin DF, Ying GS; CATT Research Group.

PMID: 28271612

Conf Proc IEEE Eng Med Biol Soc. 2016 Aug;2016:6006-6009.

Wearable diagnostic system for age-related macular degeneration.

Mohaghegh N, Zadeh EG, Magierowski S.

Abstract: This paper presents a novel head-mounted point-of-care diagnostic system for detection and continuous monitoring of Age-related Macular Degeneration (AMD). This wearable embedded open-source platform enables accurate monitoring of AMD by taking advantage of multiple standard graphical interface techniques such as Amsler Grid, Threshold Amsler Grid, Macular Computerized Psychophysical Test and Preferential Hyperacuity Perimeter (PHP). Here, we describe the proposed multi-Grid or so-called NGRID software and elaborate on the hardware prototype. This prototype includes a commercially available Oculus HMD incorporated with a single board computer. As the first step towards a fully integrated wearable system, this paper successfully proves the functionality of head-mounted graphical interface device ready for a live demonstration. Participants can experience this device and take a 10-minute AMD eye-exam. Furthermore, NGRID has been approved and permitted for an in-hospital clinical trial.

PMID: 28269621

Pathogenesis

PLoS One. 2017 Mar 10;12(3):e0173716. eCollection 2017.

Age-related macular degeneration phenotypes are associated with increased tumor necrosis-alpha and subretinal immune cells in aged Cxcr5 knockout mice.

Huang H, Liu Y, Wang L, Li W.

Abstract: The role of chemokine receptor in age-related macular degeneration (AMD) remains elusive. The objective of this study is to investigate the role of chemokine receptor Cxcr5 in the pathogenesis of AMD. Cxcr5 gene expression levels (mRNA and protein) are higher in the retina and retinal pigment epithelium (RPE) of aged C57BL/6 wild type mice than younger ones. Vascular and glial cells express Cxcr5 and its ligand Cxcl13 in mouse retina. Aged Cxcr5 knockout (-/-) mice develop both early and late AMD-like pathological features. White and yellow spots, which look like drusen in humans, were identified with fundoscopic examination. Drusen-like sub-RPE deposits with dome-shaped morphology were characterized on the sections. RPE vacuolization, swelling, and sub-RPE basal deposits were illustrated with light and transmission electron microscope (TEM). TEM further illustrated degenerated and disorganized RPE basal infoldings, phagosomes and melanosomes inside RPE, as well as abnormal photoreceptor outer segments. Lipofuscin granules and lipid droplets in the subretinal space, RPE, and choroid were revealed with fluorescence microscope and oil-red-O staining. Increased IgG in RPE/choroid were determined with Western blots (WB). WB and immunofluorescence staining determined RPE zona occuldens (ZO)-1 protein reduction and abnormal subcellular localization. TUNEL staining, outer nuclear layer (ONL) measurement and electroretinogram (ERG) recording indicated that photoreceptors underwent apoptosis, degeneration, and functional impairment. Additionally, spontaneous neovascularization (NV)-like lesions develop in the subretinal space of aged Cxcr5^{-/-} mice. The underlying mechanisms are associated with increased subretinal F4/80⁺ immune cells, some of which contain RPE marker RPE65, and up-regulation of the multifunctional cytokine tumor necrosis factor-alpha (TNF-α) in RPE/choroid and retina. These findings suggest that Cxcr5 itself may be involved in the protection of RPE and retinal cells during aging and its loss may lead to AMD-like pathological changes in aged mice.

PMID: 28282423

Mol Med Rep. 2017 Mar 1. [Epub ahead of print]

Protective effect of mitochondria-targeted peptide MTP-131 against oxidative stress-induced apoptosis in RGC-5 cells.

Chen M, Liu B, Ma J, Ge J, Wang K.

Abstract: The retina of the human eye is extremely vulnerable to oxidative damage. Previous studies have demonstrated that oxidative stress is the predominant mechanism associated with the pathogenesis of age-related macular degeneration, diabetic retinopathy, glaucoma and retinitis pigmentosa. MTP-131, a novel mitochondria-targeted peptide, has been demonstrated to specifically concentrate in the inner mitochondria membrane and to exhibit remarkable antioxidant effects both in vitro and in animal models. In the present study, the protective effect of MTP-131 was evaluated in response to hydrogen peroxide (H₂O₂)-induced oxidative damage in a retinal ganglion cell line, RGC-5. Cell viability was measured by lactate dehydrogenase (LDH) assay. Changes of mitochondrial membrane potential and generation of intracellular reactive oxygen species (ROS) were measured by flow cytometry and confocal microscopy, respectively. Annexin V-fluorescein isothiocyanate/propidium iodide staining was used for assessment of apoptosis. Release of cytochrome c was analyzed by confocal microscopy. Pretreatment of cells with MTP-131 inhibited H₂O₂-induced cytotoxicity and reduced LDH release in a dose-dependent manner, compared with cells treated with H₂O₂ alone. Mitochondrial depolarization and ROS generation were also prevented by MTP-131 pretreatment. In addition, MTP-131 pretreatment inhibited cytochrome c release from mitochondria to cytoplasm, and significantly reduced apoptosis in RGC-5 cells, compared with cells treated with H₂O₂ alone. In conclusion, mitochondria-targeted peptide MTP-131 exhibited a protective effect against oxidative stress-induced apoptosis in RGC-5 cells, which may provide a novel approach for the treatment of age-associated retinal diseases.

PMID: 28260075

Mol Med Rep. 2017 Feb 28. [Epub ahead of print]

Wogonin protects human retinal pigment epithelium cells from LPS-induced barrier dysfunction and inflammatory responses by regulating the TLR4/NF- κ B signaling pathway.

Chen C, Guo D, Lu G.

Abstract: Inflammation in the retinal pigment epithelium is an important contributor to the pathogenesis of age-related macular degeneration. Wogonin is a flavonoid isolated from the root of *Scutellaria baicalensis* and has multiple pharmacological effects, including anti-inflammatory effects. The present study sought to determine if the pharmacological effects of wogonin were relevant to the treatment of AMD. ARPE-19 cells were pre-conditioned with different concentrations of wogonin (0-50 μ M) prior to induction of inflammation with LPS (2 μ g/ml). Transepithelial electrical resistance analysis demonstrated that 24 h treatment with 10 and 50 μ M wogonin ameliorated LPS-induced changes. Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) and immunofluorescence analyses revealed that wogonin restrained LPS-induced tight junction proteins, claudin-1 and ZO-1. LPS-induced upregulation of inflammatory mediators in ARPE-19 cells, including IL-1 β , IL-6, IL-8, cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS) and TNF- α was reduced after pre-treatment with wogonin. In addition, RT-qPCR and western blotting demonstrated that wogonin inhibited the expression of TLR4 in LPS-stimulated ARPE-19 cells. This is a novel mechanism indicating that pre-treatment with wogonin could attenuate the TLR4/NF- κ B-mediated inflammatory response in LPS-stimulated ARPE-19 cells, and thus could be a potential therapy for the treatment of AMD.

PMID: 28260013

Biochemistry (Mosc). 2016 Dec;81(12):1413-1428.

Possible Interventions to Modify Aging.

Libertini G, Ferrara N.

Abstract: The programmed aging paradigm interprets aging as a function favored by natural selection at a supra-individual level. This function is implemented, according to the telomere theory, through mechanisms that operate through the subtelomere-telomere-telomerase system. After reviewing some necessary technical and ethical reservations and providing a concise description of aging mechanisms, this work considers interventions that could lead to the control of some highly disabling characteristics of aging, such as Alzheimer's and Parkinson's syndromes and age-related macular degeneration, and afterwards to a full control of aging up to a condition equivalent to that of the species defined as "with negligible senescence". The various steps needed for the development of such interventions are described along general lines.

PMID: 28259119

Epidemiology

Eye (Lond). 2017 Mar 10. [Epub ahead of print]

Prevalence of age-related macular degeneration in an elderly UK Caucasian population-The Bridlington Eye Assessment Project: a cross-sectional study.

Wilde C, Poostchi A, Mehta RL, MacNab HK, Hillman JG, Vernon SA, Amoaku WM.

Importance: There is paucity of data on prevalence and disease asymmetry of age-related macular degeneration (AMD), particularly the earlier stages, in the UK population.

Objective and Purpose: To determine the prevalence of age-related macular degeneration in an elderly Caucasian UK population.

Design: Cross-sectional population study, 2002-2006.

Participants: Residents in the study area of Bridlington aged 65 years and older.

Methods: Full-ophthalmic examination was undertaken in 3549 participants, of eligible 6319 Caucasian population (response rate of 56%). Non-stereoscopic Colour fundus photographs (30°) were graded masked using a modified Rotterdam Classification for 3475 (98%) participants with gradable images. Prevalence for different AMD grades were calculated. Demographic details were analysed then integrated with the AMD gradings for full analysis. Prevalence rates for the different AMD Grades were calculated, as well as the age-specific prevalences.

Results: AMD prevalence in the worst eye were 38.5% grade 0, 41.4% grade 1, 12.8% grade 2, 2.8% grade 3, and 4.6% grade 4. Geographic atrophy (grade 4a) occurred in 2.5%, and neovascular AMD (grade 4b) in 1.8%. Prevalence increased with age such that grade 4 (advanced) AMD was 2.2% in the 65-69 years group, 15.8% for the 85-90, and 21.2% for over 90 years. There was significant asymmetry between the two eyes of individuals with advanced AMD ($P < 0.001$), such that vision loss was unilateral. Persons with more advanced AMD grades were more likely to be dissatisfied with their vision.

Conclusions: Advanced AMD occurs more commonly in the UK Caucasian population than previously reported. Significant asymmetry between the two eyes occurs in individuals with unilateral advanced AMD so that visual impairment statistics do not represent true prevalence of advanced AMD. Persons with more advanced AMD were more likely to be dissatisfied with their vision. Eye advance online publication, 10 March 2017; doi:10.1038/eye.2017.30.

PMID: 28282062

Genetics

Invest Ophthalmol Vis Sci. 2017 Mar 1;58(3):1570-1576.

Systematic Functional Testing of Rare Variants: Contributions of CFI to Age-Related Macular Degeneration.

Tan PL, Garrett ME, Willer JR, Campochiaro PA, Campochiaro B, Zack DJ, Ashley-Koch AE, Katsanis N.

PURPOSE: Genome-wide association (GWAS) and sequencing studies for AMD have highlighted the importance of coding variants at loci that encode components of the complement pathway. However, assessing the contribution of such alleles to AMD, especially when they are rare, remains coarse, in part because of the persistent challenge in establishing their functional relevance. Others and we have shown previously that rare alleles in complement factor I (CFI) can be tested functionally using a surrogate in vivo assay of retinal vascularization in zebrafish embryos. Here, we have implemented and scaled these tools to assess the overall contribution of rare alleles in CFI to AMD.

METHODS: We performed targeted sequencing of CFI in 731 AMD patients, followed by replication in a second patient cohort of 511 older healthy individuals. Systematic functional testing of all alleles and post-hoc statistical analysis of functional variants was also performed.

RESULTS: We discovered 20 rare coding nonsynonymous variants, including the previously reported G119R allele. In vivo testing led to the identification of nine variants that alter CFI; six of which are associated with hypoactive complement factor I (FI). Post-hoc analysis in ethnically matched, population controls showed six of these to be present exclusively in cases.

CONCLUSIONS: Taken together, our data argue that multiple rare and ultra-rare alleles in CFI contribute to AMD pathogenesis; they improve the precision of the assessment of the contribution of CFI to AMD; and they offer a rational route to establishing both causality and direction of allele effect for genes associated with this disorder.

PMID: 28282489

Acta Ophthalmol. 2017 Mar 7. [Epub ahead of print]

Dissecting microRNA dysregulation in age-related macular degeneration: new targets for eye gene therapy.

Askou AL, Alsing S, Holmgaard A, Bek T, Corydon TJ.

Abstract: MicroRNAs (miRNAs) are key regulators of gene expression in humans. Overexpression or depletion of individual miRNAs is associated with human disease. Current knowledge suggests that the retina is influenced by miRNAs and that dysregulation of miRNAs as well as alterations in components of the miRNA biogenesis machinery are involved in retinal diseases, including age-related macular degeneration (AMD). Furthermore, recent studies have indicated that the vitreous has a specific panel of circulating miRNAs and that this panel varies according to the specific pathological stress experienced by the retinal cells. MicroRNA (miRNA) profiling indicates subtype-specific miRNA profiles for late-stage AMD highlighting the importance of proper miRNA regulation in AMD. This review will describe the function of important miRNAs involved in inflammation, oxidative stress and pathological neovascularization, the key molecular mechanisms leading to AMD, and focus on dysregulated miRNAs as potential therapeutic targets in AMD.

PMID: 28271607

Zhonghua Yan Ke Za Zhi. 2017 Feb 11;53(2):144-147.

[The pharmacogenomics of CFH Y402H and wet age-related macular degeneration]. [Article in Chinese; Abstract available in Chinese from the publisher]

Chen LL, Chen YY.

Abstract: Age-related macular degeneration(AMD) is one of the main leading causes of irreversible vision damage in patients over 50 years old. Genetic factors play an important role in the occurrence and development of AMD. Since the significant correlation between complement factor H (CFH) gene and AMD was found, the pharmacogenomics of CFH polymorphism was paid close attention by academic circles. Among which, studies concerning CFH Y402H were more deeply. Studies have found CFH Y402H genotypes might lead to differences toward the outcome of PDT and anti-VEGF treatment. In this article, we review the researches on the pharmacogenomics of CFH Y402H in wet AMD treatment. (Chin J Ophthalmol, 2017, 53: 144-147).

PMID: 28260367

Stem cells

PLoS One. 2017 Mar 10;12(3):e0173575. eCollection 2017.

Generation of retinal pigmented epithelium from iPSCs derived from the conjunctiva of donors with and without age related macular degeneration.

Geng Z, Walsh PJ, Truong V, Hill C, Ebeling M, Kapphahn RJ, Montezuma SR, Yuan C, Roehrich H, Ferrington DA, Dutton JR.

Abstract: Fidelity in pluripotent stem cell differentiation protocols is necessary for the therapeutic and commercial use of cells derived from embryonic and induced pluripotent stem cells. Recent advances in stem cell technology, especially the widespread availability of a range of chemically defined media, substrates and differentiation components, now allow the design and implementation of fully defined derivation and differentiation protocols intended for replication across multiple research and manufacturing locations. In this report we present an application of these criteria to the generation of retinal pigmented epithelium from iPSCs derived from the conjunctiva of donors with and without age related macular degeneration. Primary conjunctival cells from human donors aged 70-85 years were reprogrammed to derive multiple iPSC lines that were differentiated into functional RPE using a rapid and defined differentiation protocol. The combination of defined iPSC derivation and culture with a defined RPE differentiation protocol, reproducibly generated functional RPE from each donor without requiring protocol adjustments for each individual. This successful validation of a standardized, iPSC derivation and RPE differentiation process demonstrates a practical approach for applications requiring the cost-effective generation of RPE from multiple individuals such as drug testing, population studies or for therapies requiring patient-specific RPE derivations. In addition, conjunctival cells are identified as a practical source of somatic cells for deriving iPSCs from elderly individuals.

PMID: 28282420

Diet, lifestyle & low vision

Acta Ophthalmol. 2017 Mar 8. [Epub ahead of print]

Plasma long-chain omega-3 polyunsaturated fatty acids and macular pigment in subjects with family history of age-related macular degeneration: the Limpia Study.

Merle BM, Buaud B, Korobelnik JF, Bron A, Delyfer MN, Rougier MB, Savel H, Vaysse C, Creuzot-Garcher C, Delcourt C.

PURPOSE: In numerous epidemiological studies, omega-3 polyunsaturated fatty acids (PUFAs) have been associated with a decreased risk of age-related macular degeneration (AMD). Beyond their structural, functional and neuroprotective roles, omega-3 PUFAs may favour the retinal accumulation of lutein and zeaxanthin and thus increase macular pigment optical density (MPOD). We examined the associations of MPOD with plasma omega-3 PUFAs in subjects with family history of AMD.

METHODS: The Limpia study is a double-blind, placebo-controlled, prospective randomized clinical trial performed in 120 subjects. Subjects with at least one parent treated for neovascular AMD, aged 40-70, with a best corrected visual acuity (BCVA) >20/25, free of late AMD and other major eye conditions and with no use of supplement containing lutein or zeaxanthin the preceding year were recruited in Bordeaux and Dijon, France. At baseline, MPOD within 1° of eccentricity was measured by modified Heidelberg retinal analyser (Heidelberg, Germany) and plasma omega-3 PUFAs by gas chromatography. Medical history and lifestyle data were collected from a standardized questionnaire. Associations of MPOD with plasma omega-3 PUFAs were assessed at the baseline examination, using mixed linear models adjusted for age, gender, centre, body mass index, smoking, plasma high-density lipoprotein (HDL) cholesterol and lutein+zeaxanthin.

RESULTS: After multivariate adjustment, high MPOD was significantly associated with higher level of plasma docosapentaenoic acid (DPA) ($\beta = 0.029$, 95% CI: 0.003, 0.055; $p = 0.03$). Plasma alpha linolenic, eicosapentaenoic and docosahexaenoic acids were not significantly associated with MPOD.

CONCLUSION: In the Limpia study, high MPOD within 1° was significantly associated with higher plasma levels of omega-3 DPA.

PMID: 28271618

Invest Ophthalmol Vis Sci. 2017 Mar 1;58(3):1514-1520.

Functional Outcomes of the Low Vision Depression Prevention Trial in Age-Related Macular Degeneration.

Deemer AD, Massof RW, Rovner BW, Casten RJ, Piersol CV.

PURPOSE: To compare the efficacy of behavioral activation (BA) plus low vision rehabilitation with an occupational therapist (OT-LVR) with supportive therapy (ST) on visual function in patients with age-related macular degeneration (AMD).

METHODS: Single-masked, attention-controlled, randomized clinical trial with AMD patients with subsyndromal depressive symptoms ($n = 188$). All subjects had two outpatient low vision rehabilitation optometry visits, then were randomized to in-home BA + OT-LVR or ST. Behavioral activation is a structured behavioral treatment aiming to increase adaptive behaviors and achieve valued goals. Supportive therapy is a nondirective, psychological treatment that provides emotional support and controls for attention. Functional vision was assessed with the activity inventory (AI) in which participants rate the difficulty level of goals and corresponding tasks. Participants were assessed at baseline and 4 months.

RESULTS: Improvements in functional vision measures were seen in both the BA + OT-LVR and ST groups at the goal level ($d = 0.71$; $d = 0.56$ respectively). At the task level, BA + OT-LVR patients showed more improvement in reading, inside-the-home tasks and outside-the-home tasks, when compared to ST patients. The greatest effects were seen in the BA + OT-LVR group in subjects with a visual acuity $\geq 20/70$ ($d = 0.360$ reading; $d = 0.500$ inside the home; $d = 0.468$ outside the home).

CONCLUSIONS: Based on the trends of the AI data, we suggest that BA + OT-LVR services, provided by an OT in the patient's home following conventional low vision optometry services, are more effective than

conventional optometric low vision services alone for those with mild visual impairment. (ClinicalTrials.gov number, NCT00769015.).

PMID: 28273318

Invest Ophthalmol Vis Sci. 2017 Mar 1;58(3):1560-1569.

A Comparison of Reach-to-Grasp and Transport-to-Place Performance in Participants With Age-Related Macular Degeneration and Glaucoma.

Pardhan S, Scarfe A, Bourne R, Timmis M.

PURPOSE: To compare visually guided manual prehension in participants with primarily central field loss (CFL) due to age-related macular degeneration and peripheral visual field loss (PFL) due to glaucoma. This study extends current literature by comparing directly "reach-to-grasp" performance, and presents a new task of "transport-to-place" the object accurately to a new location. Data were compared to age-matched controls.

METHODS: Three-dimensional motion data were collected from 17 glaucoma participants with PFL, 17 participants with age-related macular degeneration CFL and 10 age-matched control participants. Participants reached toward and grasped a cylindrical object (reach-to-grasp), and then transported and placed (transport-to-place) it at a different (predefined) peripheral location. Various kinematic indices were measured. Correlation analyses explored relationships between visual function and kinematic data.

RESULTS: In the reach-to-grasp phase, CFL patients exhibited significantly longer movement and reaction times when compared to PFL participants and controls. Central field loss participants also took longer to complete the movement and made more online movements in the latter part of the reach. During the transport-to-place phase, CFL participants showed increased deceleration times, longer movement trajectory, and increased vertical wrist displacement. Central field loss also showed higher errors in placing the object at a predefined location. A number of kinematic indices correlated significantly to central visual function indices ($P < 0.05$).

CONCLUSIONS: Significant differences in performance exist between CFL and PFL participants. Various indices correlated significantly with loss in acuity and contrast sensitivity (CS), suggesting that performance is more dependent on central visual function irrespective of underlying pathology.

PMID: 28282488

Conf Proc IEEE Eng Med Biol Soc. 2016 Aug;2016:4979-4982.

Inertial sensor based gait analysis discriminates subjects with and without visual impairment caused by simulated macular degeneration.

Kanzler CM, Barth J, Klucken J, Eskofier BM.

Abstract: Macular degeneration is the third leading cause of blindness worldwide and the leading cause of blindness in the developing world. The analysis of gait parameters can be used to assess the influence of macular degeneration on gait. This study examines the effect of macular degeneration on gait using inertial sensor based 3D spatio-temporal gait parameters. We acquired gait data from 21 young and healthy subjects during a 40 m obstacle walk. All subjects had to perform the gait trial with and without macular degeneration simulation glasses. The order of starting with or without glasses alternated between each subject in order to test for training effects. Multiple 3D spatio-temporal gait parameters were calculated for the normal vision as well as the impaired vision groups. The parameters trial time, stride time, stride time coefficient of variation (CV), stance time, stance time CV, stride length, cadence, gait velocity and angle at

toe off showed statistically significant differences between the two groups. Training effects were visible for the trials which started without vision impairment. Inter-group differences in the gait pattern occurred due to an increased sense of insecurity related with the loss of visual acuity from the simulation glasses. In summary, we showed that 3D spatio-temporal gait parameters derived from inertial sensor data are viable to detect differences in the gait pattern of subjects with and without a macular degeneration simulation. We believe that this study provides the basis for an in-depth analysis regarding the impact of macular degeneration on gait.

PMID: 28269386

Conf Proc IEEE Eng Med Biol Soc. 2016 Aug;2016:1348-1351.

Determining the difference in eyegaze measurements in individuals with age related macular degeneration.

Huiying Liu, Wong D, Ai Ping Yow, Yanwu Xu, Fengshou Yin, Laude A, Tock Han Lim.

Abstract: Age-related Macular Degeneration (AMD) is one of the leading causes of blindness in the elderly. Visual loss associated with AMD often results in a central scotoma which is an alteration in the central vision, leading to distortion or loss of vision. Current methods of detecting AMD are typically manual, require holding fixation and an external response trigger. In this paper, we propose the use of eyegaze tracking to detect for the presence of AMD, using a simple set of test patterns. Experimental results show that the derived eyegaze measurements can help to identify individuals with AMD from healthy individuals. This could lead to the detection of AMD using eye tracking data, and could result in a potential system device for screening.

PMID: 28268575

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