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MD Research News

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Drug Treatment

BMC Ophthalmol. 2016 Aug 9;16:142.

Estimation of the need for bilateral intravitreal anti-VEGF injections in clinical practice.

Giocanti-Auregan A, Tadayoni R, Grenet T, Fajnkuchen F, Nghiem-Buffet S, Delahaye-Mazza C, Quentel G, Cohen SY5.

BACKGROUND: To estimate the need for bilateral intravitreal anti-VEGF injections in patients treated for neovascular age-related macular degeneration (nAMD), diabetic macular edema (DME), retinal vein occlusion, choroidal neovascularization (CNV) in high myopia, and other causes of CNV.

METHODS: All consecutive patients treated with intravitreal anti-VEGF injection over a 1-month period were included in a prospective multicenter survey. The reason for intravitreal anti-VEGF injection and the involvement of the fellow eye in the pathology requiring a treatment with intravitreal anti-VEGF were recorded. A time interval between bilateral injections longer than 1 month, within a 1-month period, and same-day bilateral injections were recorded.

RESULTS: A total of 1335 patients were included, corresponding to 1024 (76.7 %) patients treated for nAMD, 167 (12.5 %) for DME, and 144 (10.8 %) for other reasons. Four hundred and fifty-nine (34.4 %) patients were treated bilaterally with a time interval between injections longer than 1 month, 170 (12.7 %) were treated bilaterally within a 1-month interval, and 87 (6.6 %) had same-day bilateral injections. Bilateral injections were more frequent in diabetic patients than in nAMD patients (respectively 48 % vs. 36 %, p = 0.0033).

CONCLUSIONS: Patients with DME are more likely to be treated bilaterally with anti-VEGF injections. As the rate of second eye involvement requiring treatment increases progressively over time, a same-day bilateral injection strategy will become more common as it decreases the administrative burden on the healthcare system and treatment burden experienced by patients.

PMID: 27507298 PMCID: PMC4979182

Br J Ophthalmol. 2016 Aug 8. [Epub ahead of print]

Optical coherence tomography angiography of type 3 neovascularisation in age-related macular degeneration after antiangiogenic therapy.

Phasukkijwatana N, Tan AC, Chen X, Freund KB, Sarraf D.

BACKGROUND/AIMS: To assess the microvascular response of type 3 neovascularisation secondary to age-related macular degeneration (AMD) after antivascular endothelial growth factor (anti-VEGF) therapy using optical coherence tomography angiography (OCTA).

METHODS: Consecutive patients diagnosed with AMD and type 3 neovascularisation based on clinical examination, structural optical coherence tomography and fluorescein angiography when available were retrospectively evaluated. En face OCTA imaging (3×3 mm scans) with quantitative microvascular analysis was performed at baseline and after a single anti-VEGF intravitreal injection.

RESULTS: 17 eyes of 14 patients underwent OCTA before and after anti-VEGF treatment. OCTA demonstrated significant regression of small calibre type 3 neovascular tufts in all eyes. Median lesion area was 0.061 mm2 (range 0.003-0.198 mm2) at baseline and 0.009 mm2 (range 0-0.085 mm2, p=0.0003) at follow-up. Cystoid macular oedema and/or subretinal fluid resolved in all cases after treatment. The type 3 lesions became undetectable with OCTA post-treatment in 5 of the 17 eyes. However, in 11 eyes, large feeder vessels were identified and remained unchanged after treatment.

CONCLUSIONS: The microvascular morphology of type 3 neovascularisation secondary to AMD was assessed at baseline and follow-up and showed significant regression in response to anti-VEGF therapy by OCTA. Quantitative OCTA analysis was also performed and confirmed remarkable regression in response to a single intravitreal anti-VEGF injection.

PMID: 27503396

Int J Ophthalmol. 2016 Jul 18;9(7):1028-37. eCollection 2016.

Comparison of the efficacy of anti-VEGF monotherapy versus PDT and intravitreal anti-VEGF combination treatment in AMD: a Meta-analysis and systematic review.

Tong Y, Zhao KK, Feng D, Biswal M, Zhao PQ, Wang ZY, Zhang Y.

AIM: To compare the effect of anti-vascular endothelial growth factor (VEGF) monotherapy versus photodynamic therapy (PDT) and anti-VEGF combination treatment in age-related macular degeneration (AMD).

METHODS: A computerized online search was performed using PubMed, Web of Science and the Cochrane Library. Studies that compared anti-VEGF monotherapy with PDT and anti-VEGF combination treatment of AMD and were designed as randomized controlled trials were included. The means and standard deviations of the best-corrected visual acuity (BCVA), central retinal thickness (CRT), number of treatments and proportions of patients who gained BCVA ≥15, 10, 5, or 0 letters at 12(th) month were extracted. A systematic review and Meta-analysis of the comparison of the two approaches was conducted using Review Manager 5.2. Subgroup. A sensitivity analysis was also performed.

RESULTS: Eight studies were included. When the subgroup and sensitivity analysis was conducted, the results indicated that in the findings that included the monotherapy group and PDT (standard fluence, SF) group of Kaiser's study, the patients in the monotherapy group had a better BCVA compared with the combination group at 12(th) month in the PDT (SF) subgroup [weighted mean difference (WMD): 3.54; 95% CI: 0.36 to 6.73; P=0.03], and there were more patients who gained ≥15 letters of BCVA in the monotherapy group compared with the combination group in the total result [odds ratio (OR): 1.41; 95%CI: 1.02 to 1.95; P=0.04]. The same conclusion was obtained in the total result that included the monotherapy group and PDT (reduced fluence, RF) group of Kaiser's study (OR: 1.56; 95%CI: 1.13 to 2.15; P=0.007). However, there were no significant differences in the other indexes between the two therapies.

CONCLUSION: We found that anti-VEGF monotherapy is more effective on the recovery of visual acuity than combination therapy and more researches with lager sample size should be performed to study on the effect of the two therapy approaches on CRT and number of injections.

PMID: 27500113 PMCID: PMC4951659

Curr Med Res Opin. 2016 Aug 5:1-32. [Epub ahead of print]

Real world evidence of use of anti-VEGF therapy in Denmark.

Vorum H, Olesen TK, Zinck J, Hedegaard M.

OBJECTIVE: This study evaluates real-world evidence regarding the frequency of anti-vascular endothelial growth factor (VEGF) injections during the first year of therapy of treatment-naïve patients with neovascular age-related macular degeneration (nAMD), diabetic macular edema (DME) and retinal vein occlusion (RVO) from the Danish National Patient Registry. There was a switch in anti-VEGF treatment for naïve nAMD patients during the study period, following the introduction of aflibercept, which was expected to reduce the injection frequency relative to ranibizumab due to a perception of prolonged treatment duration of aflibercept.

METHODS: All treatment-naïve nAMD, DME or RVO patients who received an intravitreal injection in Denmark from 1 January 2012 to 31 July 2015 were eligible for inclusion. Patients were required to have been treated for at least one year and, for nAMD, to have received at least three injections during the first four months of treatment. Patients were allocated to half-year groupings (2012/1 to 2014/1) based on registration of their first intravitreal injection. Injection frequency during the first year of treatment was calculated for each group and t-tests investigated whether injection frequencies changed over time.

RESULTS: In treatment naïve nAMD patients (n = 500), the mean (SD) number of anti-VEGF injections increased significantly from 6.04 (1.71) in 2012/1 to 6.73 (1.62) in 2014/1 (p = 0.001; 2012/1 and 2012/2 vs 2014/1) across all treatments. A similar trend was found for DME patients (n = 76) from 2012/1 to 2014/1 and RVO patients (n = 82) from 2012/2 to 2014/1, with mean injection frequencies increasing significantly from 5.14 (2.29) to 5.93 (1.98) (p = 0.007), and from 4.83 (1.21) to 6.08 (1.55) (p = 0.024), respectively. Post hoc sensitivity analysis also found a significant increase in injection frequency in nAMD patients who did not receive a loading phase (4.55 in 2012/1 and 5.05 in 2014/1; p = 0.006; n = 616).

CONCLUSIONS: In contrast to the decrease in injection frequency predicted with a switch to aflibercept treatment for nAMD, our study showed that injection frequencies increased significantly from 2012 to 2014 in patients initiating therapy across the three diseases.

PMID: 27494692 DOI: 10.1080/03007995.2016.1221803

J Ophthalmol. 2016;2016:7945619. Epub 2016 Jul 14.

Comparison of Perioperative Ranibizumab Injections for Diabetic Macular Edema in Patients Undergoing Cataract Surgery.

Yumuşak E, Örnek K.

PURPOSE: To compare the efficacy of perioperative ranibizumab injections on diabetic macular edema (DME) in patients undergoing cataract surgery.

METHODS: This study included 59 eyes of 59 patients. All patients had advanced cataract with DME and underwent an uneventful phacoemulsification surgery. There were 3 subgroups. The first group received intravitreal ranibizumab injection 2 weeks preoperatively, the second group received intraoperatively, and the third group received 2 weeks postoperatively. Follow-up examinations were performed at 1 week as well as at 1 and 3 months.

RESULTS: Baseline visual acuity showed a significant increase in all groups at 1 month. In group 1, compared to baseline value, foveal thickness (FT) increased significantly at 1 month and showed a significant decrease up to month 3. In group 2, FT increased at month 1 and this continued up to month 3. In group 3, FT increased at month 1 and was almost stable up to month 3. There were not any significant differences for visual acuity and FT between the groups.

CONCLUSIONS: Although intrapostoperative ranibizumab injection for DME seems to be more effective

than preoperative injections in patients undergoing cataract surgery, the treatment still needs to be continued following surgery.

PMID: 27493795

Other Treatment and Diagnosis

Br J Ophthalmol. 2016 Aug 8. [Epub ahead of print]

Prevalence and quantification of geographic atrophy associated with newly diagnosed and treatment-naïve exudative age-related macular degeneration.

Sikorav A, Semoun O, Zweifel S, Jung C, Srour M, Querques G, Souied EH.

OBJECTIVE: To identify and quantify geographic atrophy (GA) associated with neovascular age-related macular degeneration (AMD) at initial presentation using a fundus autofluorescence (FAF) semi-automated software and to correlate the results with demographic and clinical data.

DESIGN: Retrospective, observational study.

METHODS: The study population consisted of treatment-naïve patients with newly diagnosed neovascular AMD. Best-corrected visual acuity, fundus photographs, infrared reflectance, FAF and spectral-domain optical coherence tomography were performed, associated with fluorescein and indocyanine green angiographies. Identification of GA was independently performed by three readers. Quantification of atrophy areas was done using RegionFinder Software (RFA), a semi-automated software embedded in Spectralis device (Heidelberg Engineering, Germany).

RESULTS: We included 206 eyes of 173 consecutive patients (72% female, mean age: 79.7±9.1 years). Type I choroidal neovascularisation (CNV) was observed in 44.2% of eyes, type II CNV was observed in 20.9% and mixed CNV lesion was observed in 11.7%. Polypoidal choroidal vasculopathy was diagnosed in 7.7% and type III CNV was diagnosed in 15.5%. Analysis of FAF frames showed that GA was associated with nAMD in 46/206 eyes (22.3%). Taking into account data both from Region Finder and multimodal imaging, our results suggest that GA was present in 24.3% of eyes newly diagnosed with exudative AMD. Mean size of GA was 1.23±1.76 mm2 (range 0.03-7.39).

CONCLUSION: GA is associated with nAMD in 1/4 of cases at initial presentation. Combined imaging, including RFA is an effective tool to identify and quantify GA at diagnosis.

PMID: 27503391

Microsc Res Tech. 2016 Aug 10. [Epub ahead of print]

Label-free optical detection of age-related and diabetic oxidative damage in human aqueous humors.

Woong Moon S, Kim W, Choi S, Shin JH.

ABSTRACT: In this study, we investigate the biochemical characteristics of oxidative stress in age-related macular degeneration (AMD) and diabetic retinopathy (DR) by analyzing aqueous humors. Nondiabetic cataract aqueous humor was used as the control. The level of oxidative damage was evaluated based on changes in Raman spectral intensity. Seven prominent peaks were detected at 1002, 1043, 1062, 1352, 1419, 1454, and 1656 cm-1 . We proposed four multimodal biomarkers to distinguish these peaks based on the ratios of Raman intensities in two wavelengths, including CHO (C-O stretching or C-O-H bending modes), AG (adenine and guanine), PRO-AG (protein and AG), and PHEα (phenylalanine symmetric ring

breath and amide I α-helix) markers. The presence of oxidative damage was detected by CHO and AG markers associated with C-O stretching, C-O-H bending modes in carbohydrates (1043 cm-1), and the nucleic acids adenine and guanine (1352 cm-1), respectively. DR-related oxidative damage was identified by PRO-AG and PHEα markers associated with adenine, guanine, and protein components (1419 and 1454 cm-1) and amide I α-helix protein structure (1656 cm-1), respectively. AMD-related oxidative damage was identified by four biomarkers. Four multimodal biomarkers with simple linear threshold values achieved high sensitivity of 100% and high specificity of 100% for classifying oxidative stress-induced AMD and DR diseases. Therefore, Raman-based label-free optical detection is effective for detecting the presence of age-related or diabetic oxidative damage in aqueous humor.

PMID: 27507597

Comput Med Imaging Graph. 2016 Jul 26. [Epub ahead of print]

Volumetric image classification using homogeneous decomposition and dictionary learning: A study using retinal optical coherence tomography for detecting age-related macular degeneration.

Albarrak A, Coenen F, Zheng Y.

ABSTRACT: Three-dimensional (3D) (volumetric) diagnostic imaging techniques are indispensable with respect to the diagnosis and management of many medical conditions. However there is a lack of automated diagnosis techniques to facilitate such 3D image analysis (although some support tools do exist). This paper proposes a novel framework for volumetric medical image classification founded on homogeneous decomposition and dictionary learning. In the proposed framework each image (volume) is recursively decomposed until homogeneous regions are arrived at. Each region is represented using a Histogram of Oriented Gradients (HOG) which is transformed into a set of feature vectors. The Gaussian Mixture Model (GMM) is then used to generate a "dictionary" and the Improved Fisher Kernel (IFK) approach is used to encode feature vectors so as to generate a single feature vector for each volume, which can then be fed into a classifier generator. The principal advantage offered by the framework is that it does not require the detection (segmentation) of specific objects within the input data. The nature of the framework is fully described. A wide range of experiments was conducted with which to analyse the operation of the proposed framework and these are also reported fully in the paper. Although the proposed approach is generally applicable to 3D volumetric images, the focus for the work is 3D retinal Optical Coherence Tomography (OCT) images in the context of the diagnosis of Age-related Macular Degeneration (AMD). The results indicate that excellent diagnostic predictions can be produced using the proposed framework.

PMID: 27507326

Med Image Anal. 2016 Jul 12. [Epub ahead of print]

Quantitative analysis of retinal OCT.

Sonka M, Abràmoff MD.

ABSTRACT: Clinical acceptance of 3-D OCT retinal imaging brought rapid development of quantitative 3-D analysis of retinal layers, vasculature, retinal lesions as well as facilitated new research in retinal diseases. One of the cornerstones of many such analyses is segmentation and thickness quantification of retinal layers and the choroid, with an inherently 3-D simultaneous multi-layer LOGISMOS (Layered Optimal Graph Image Segmentation for Multiple Objects and Surfaces) segmentation approach being extremely well suited for the task. Once retinal layers are segmented, regional thickness, brightness, or texture-based indices of individual layers can be easily determined and thus contribute to our understanding of retinal or optic nerve head (ONH) disease processes and can be employed for determination of disease status, treatment responses, visual function, etc. Out of many applications, examples provided in this paper focus on image-guided therapy and outcome prediction in age-related macular degeneration and on assessing

visual function from retinal layer structure in glaucoma.

PMID: 27503080

Am J Ophthalmol. 2016 Aug 2. [Epub ahead of print]

Choriocapillaris Flow Features Follow a Power Law Distribution: Implications for Characterization and Mechanisms of Disease Progression.

Spaide RF.

PURPOSE: To investigate flow characteristics of the choriocapillaris using optical coherence tomography angiography.

DESIGN: Retrospective observational case series.

METHODS: Visualization of flow in individual choriocapillary vessels is below the current resolution limit of optical coherence tomography angiography instruments, but areas of absent flow signal, called flow voids, are resolvable. The central macula was imaged with the Optovue RTVue XR Avanti using a 10 micron slab thickness in 104 eyes of 80 patients who ranged in age from 24 to 99 years of age. Automatic local thresholding of the resultant raw data with the Phansalkar method was analyzed with generalized estimating equations.

RESULTS: The distribution of flow voids versus size of the voids was highly skewed. The data showed a linear log-log plot and goodness of fit methods showed the data followed a power law distribution over the relevant range. A slope intercept relationship was also evaluated for the log transform and significant predictors for variables included age, hypertension, pseudodrusen, and the presence of late age-related macular degeneration (AMD) in the fellow eye.

CONCLUSIONS: The pattern of flow voids form a scale invariant pattern in the choriocapillaris starting in a size much smaller than a choroidal lobule. Age and hypertension affect the choriocapillaris, a flat layer of capillaries that may serve as an observable surrogate for the neural or systemic microvasculature. Significant alterations detectable in the flow pattern in eyes with pseudodrusen and in eyes with late AMD in the fellow eye offer diagnostic possibilities and impact theories of disease pathogenesis.

PMID: 27496785

Acta Ophthalmol. 2016 Aug 6. [Epub ahead of print]

A comparison of autologous transplantation of retinal pigment epithelium (RPE) monolayer sheet graft with RPE-Bruch's membrane complex graft in neovascular age-related macular degeneration.

Lu Y, Han L, Wang C, Dou H, Feng X, Hu Y, Feng K, Wang X, Ma Z.

PURPOSE: To compare the outcome after choroidal neovascular (CNV) membrane excision and retinal pigment epithelium (RPE) transplantation and make further evaluation of two types of RPE grafts on the visual function in patients with neovascular age-related macular degeneration (AMD), complicated by massive subretinal haemorrhage.

METHODS: We retrospectively reviewed 80 patients who underwent CNV membrane excision with or without RPE transplantation. Two types of RPE grafts were adopted, RPE-Bruch's membrane complex graft (subgroup 1) and RPE monolayer sheet graft (subgroup 2). Outcome measures included pre- and postoperative visual acuity score (VAS), clinical findings, complications and recurrence rates.

RESULTS: The mean VAS [Early Treatment of Diabetic Retinopathy Study (ETDRS)] in the CNV membrane excision group was 11.06 ± 18.28 at baseline and 14.41 ± 16.86 at follow-up (p = 0.12) in a mean follow-up period of 24.35 ± 9.31 months. While in subgroup 1, VAS increased from 22.62 ± 23.72 to

35.50 ± 24.46 (p = 0.02) in a mean period of 20.63 ± 6.25 months. The percentage of visual acuity (VA) improvement (at least two or more lines changed) in subgroup 1 is 62.5%, which is significantly higher than that in CNV excision group (23.5%), p = 0.02. In subgroup 2, VAS increased from 16.61 ± 27.98 to 29.16 ± 23.80 (p = 0.02) in a mean period of 21.72 ± 11.09 months. The percentage of VA improvement in subgroup 2 is 58.0%, which is also significantly higher than that in CNV excision group (23.5%), p = 0.02. Postoperative VA elevation was comparable between the two subgroups (p = 0.05). Complications including retinal detachment, proliferative vitreal retinopathy and CNV recurrence occurred in both techniques. Central fixation stability was observed in eight eyes in subgroup 1 and five eyes in subgroup 2.

CONCLUSIONS: The autologous RPE transplantation can increase the vision of patients with haemorrhagic AMD. Two types of autologous RPE grafts were both effective and comparable in restoring visual function and central fixation stability.

PMID: 27496526

J Tissue Eng. 2016 Jul 12;7:2041731416650838.

Methods for culturing retinal pigment epithelial cells: a review of current protocols and future recommendations.

Fronk AH, Vargis E.

ABSTRACT: The retinal pigment epithelium is an important part of the vertebrate eye, particularly in studying the causes and possible treatment of age-related macular degeneration. The retinal pigment epithelium is difficult to access in vivo due to its location at the back of the eye, making experimentation with age-related macular degeneration treatments problematic. An alternative to in vivo experimentation is cultivating the retinal pigment epithelium in vitro, a practice that has been going on since the 1970s, providing a wide range of retinal pigment epithelial culture protocols, each producing cells and tissue of varying degrees of similarity to natural retinal pigment epithelium. The purpose of this review is to provide researchers with a ready list of retinal pigment epithelial protocols, their effects on cultured tissue, and their specific possible applications. Protocols using human and animal retinal pigment epithelium cells, derived from tissue or cell lines, are discussed, and recommendations for future researchers included.

PMID: 27493715

Br J Ophthalmol. 2016 Aug 4. [Epub ahead of print]

Repeatability of swept-source optical coherence tomography retinal and choroidal thickness measurements in neovascular age-related macular degeneration.

Hanumunthadu D, Ilginis T, Restori M, Sagoo MS, Tufail A, Balaggan KS, Patel PJ.

BACKGROUND: The aim was to determine the intrasession repeatability of swept-source optical coherence tomography (SS-OCT)-derived retinal and choroidal thickness measurements in eyes with neovascular age-related macular degeneration (nAMD).

METHODS: A prospective study consisting of patients with active nAMD enrolled in the Distance of Choroid Study at Moorfields Eye Hospital, London. Patients underwent three 12×9 mm macular raster scans using the deep range imaging (DRI) OCT-1 SS-OCT (Topcon) device in a single imaging session. Retinal and choroidal thicknesses were calculated for the ETDRS macular subfields. Repeatability was calculated according to methods described by Bland and Altman.

RESULTS: 39 eyes of 39 patients with nAMD were included with a mean (±SD) age of 73.9 (±7.2) years. The mean (±SD) retinal thickness of the central macular subfield was 225.7 µm (±12.4 µm). The repeatability this subfield, expressed as a percentage of the mean central macular subfield thickness, was 23.2%. The percentage repeatability of the other macular subfields ranged from 13.2% to 28.7%. The intrasession coefficient of repeatability of choroidal thickness of the central macular subfield was 57.2 µm

with a mean choroidal thickness (±SD) of 181 μm (±15.8 μm).

CONCLUSIONS: This study suggests that a change >23.2% of retinal thickness and 57.2 μm choroidal thickness in the central macular subfield is required to distinguish true clinical change from measurement variability when using the DRI OCT-1 device to manage patients with nAMD.

PMID: 27491359

Genetics

J Vis Exp. 2016 Jul 14;(113).

A Phenotyping Regimen for Genetically Modified Mice Used to Study Genes Implicated in Human Diseases of Aging.

Patterson VL, Thompson BS, Cherry C, Wang SB, Chen B, Hoh J.

ABSTRACT: Age-related diseases are becoming increasingly prevalent and the burden continues to grow as our population ages. Effective treatments are necessary to lessen the impact of debilitating conditions but remain elusive in many cases. Only by understanding the causes and pathology of diseases associated with aging, can scientists begin to identify potential therapeutic targets and develop strategies for intervention. The most common age-related conditions are neurodegenerative disorders such as Parkinson's disease and blindness. Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly. Genome wide association studies have previously identified loci that are associated with increased susceptibility to this disease and identified two regions of interest: complement factor H (CFH) and the 10q26 locus, where the age-related maculopathy susceptibility 2 (ARMS2) and high -temperature requirement factor A1 (HtrA1) genes are located. CFH acts as a negative regulator of the alternative pathway (AP) of the complement system while HtrA1 is an extracellular serine protease. ARMS2 is located upstream of HtrA1 in the primate genome, although the gene is absent in mice. To study the effects of these genes, humanized knock-in mouse lines of Cfh and ARMS2, knockouts of Cfh, HtrA1, HtrA2, HtrA3 and HtrA4 as well as a conditional neural deletion of HtrA2 were generated. Of all the genetically engineered mice produced only mice lacking HtrA2, either systemically or in neural tissues, displayed clear phenotypes. In order to examine these mice thoroughly and systematically, an initial phenotyping schedule was established, consisting of a series of tests related to two main diseases of interest: AMD and Parkinson's. Genetically modified mice can be subjected to appropriate experiments to identify phenotypes that may be related to the associated diseases in humans. A phenotyping regimen with a mitochondrial focus is presented here alongside representative results from the tests of interest.

PMID: 27500671

Pathogenesis

PLoS One. 2016 Aug 9;11(8):e0160887. eCollection 2016.

miR-17-3p Exacerbates Oxidative Damage in Human Retinal Pigment Epithelial Cells.

Tian B, Maidana DE, Dib B, Miller JB, Bouzika P, Miller JW, Vavvas DG, Lin H.

ABSTRACT: Oxidative stress has been shown to contribute to the development of age-related macular degeneration (AMD). MicroRNAs (miRNA) are small non-coding RNA molecules that function in RNA silencing and post-transcriptional regulation of gene expression. We showed miR-17-3p to be elevated in macular RPE cells from AMD patients and in ARPE-19 cells under oxidative stress. Transfection of miR-17-

3p mimic in ARPE-19 induced cell death and exacerbated oxidative lethality that was alleviated by miR-17-3p inhibitor. The expression of antioxidant enzymes manganese superoxide dismutase (MnSOD) and thioredoxin reductase-2 (TrxR2) were suppressed by miR-17-3p mimic and reversed by miR-17-3p inhibitor. These results suggest miR-17-3p aggravates oxidative damage-induced cell death in human RPE cells, while miR-17-3p inhibitor acts as a potential protector against oxidative stress by regulating the expression of antioxidant enzymes.

PMID: 27505139

Front Neurol. 2016 Jul 27;7:119. eCollection 2016.

Links between the Brain and Retina: The Effects of Cigarette Smoking-Induced Age-Related Changes in Alzheimer's Disease and Macular Degeneration.

Yu SS, Tang X, Ho YS, Chang RC, Chiu K.

PMID: 27512384 PMCID: PMC4961692

Metallomics. 2016 Aug 9. [Epub ahead of print]

Iron accumulates in the primate choroid of the eye with aging as revealed with synchrotron X-ray fluorescence microscopy.

Ugarte M, Geraki K, Jeffery G.

ABSTRACT: Aging leads to an increase in iron-loaded cellular structures in the choroid of the eye. This study was carried out to determine the distribution and content of iron, zinc and copper in the macular retina, choroid and retrobulbar optic nerve of young (4-5 years, n = 3) and aged (15-16 years, n = 5) male non-human primates, Macaca fascicularis, whose ocular anatomy is similar to humans. Thirty µm-thick tissue sections were analysed with synchrotron X-ray fluorescence and stained histologically for iron deposition. Quantitative measurements showed high levels of iron, zinc and copper in the choroid and retinal pigment epithelium in the macular area and arachnoid layer in the retrobulbar optic nerve. In aged animals compared to young ones, there was an increase in iron in the choroid with larger deposits and iron-loaded cellular structures. Iron-accumulation within these cellular structures may contribute to choroidal function impairment in aging and age-related macular degeneration.

PMID: 27504972

Eye Brain. 2016;8:67-79. Epub 2016 May 20.

Revisiting the mouse model of oxygen-induced retinopathy.

Kim CB, D'Amore PA, Connor KM.

ABSTRACT: Abnormal blood vessel growth in the retina is a hallmark of many retinal diseases, such as retinopathy of prematurity (ROP), proliferative diabetic retinopathy, and the wet form of age-related macular degeneration. In particular, ROP has been an important health concern for physicians since the advent of routine supplemental oxygen therapy for premature neonates more than 70 years ago. Since then, researchers have explored several animal models to better understand ROP and retinal vascular development. Of these models, the mouse model of oxygen-induced retinopathy (OIR) has become the most widely used, and has played a pivotal role in our understanding of retinal angiogenesis and ocular immunology, as well as in the development of groundbreaking therapeutics such as anti-vascular endothelial growth factor injections for wet age-related macular degeneration. Numerous refinements to the model have been made since its inception in the 1950s, and technological advancements have expanded

the use of the model across multiple scientific fields. In this review, we explore the historical developments that have led to the mouse OIR model utilized today, essential concepts of OIR, limitations of the model, and a representative selection of key findings from OIR, with particular emphasis on current research progress.

PMID: 27499653

Diet Lifestyle and Low Vision

Acta Ophthalmol. 2016 Aug 8. [Epub ahead of print]

Precursors of age-related macular degeneration: associations with vitamin A and interaction with CFHY402H in the Inter99 Eye Study.

PURPOSE: To investigate associations of very early age-related macular degeneration (AMD) with daily intake of vitamin A, beta-carotene, vitamin E, vitamin C, zinc and copper and interactions with AMD-associated polymorphisms in complement factor H (CFHY402H) and ARMS2/LOC387715.

METHODS: Cross-sectional study of 848 subjects aged 30-60 years from the Inter99 Eye Study. Daily intake of vitamins and minerals was estimated from a 198-item food frequency questionnaire. Digital fundus photographs were recorded in red-free illumination and graded for macular drusen >63 μm and numerous (>20) small hard macular drusen as a mean of both eyes.

RESULTS: Higher intake of vitamin A increased the risk of having macular drusen >63 μm with odds ratio = 1.82 (CI95 1.02-3.24, p = 0.042) comparing participants in the highest quartile of vitamin A intake with participants in the lowest quartile, adjusted for recruitment group, age and sex. There was a significant interaction with CFHY402H (p = 0.038). Among 504 participants with CFHY402H, the relative risk of having macular drusen >63 μm was increased in participants in the highest quartile of vitamin A intake (odds ratio = 2.58; CI95 1.16-5.73, p = 0.020) and in the second highest quartile (odds ratio = 3.27; CI95 1.50-7.13, p = 0.0029) compared with the lowest quartile. Further adjusting for total fat intake, energy intake, plasma cholesterol, body mass index (BMI), smoking, alcohol intake, education and physical activity strengthened the association.

CONCLUSIONS: In this cross-sectional study, a higher intake of vitamin A increased the risk of macular drusen >63 μm in subjects with CFHY402H. The study supports that vitamin A may be a risk factor for early AMD.

PMID: 27502478