

Journal Watch by Sean Henahan

Vision science highlights from the world's leading journals of medicine and science

Gene therapy concerns

Some promising gene therapy approaches for eye disease involve the use of the adeno-associated virus, or AAV, vector. A new study adds to previous evidence that this viral vector could increase the risk for certain cancers, at least in mice. Researchers previously observed that mice treated with AAV developed a higher rate of liver cancer than control mice, but the potential causal role was unclear. Researchers now report that tumours from newborn mice treated with AAV found that the viral DNA had inserted itself at a specific site in the mouse genome, resulting in altered expression of surrounding genes. Because disruption of gene expression by site-specific integration is a feature of oncogenic viruses, the finding supports the idea that AAV actively contributes to cancer development. The researchers urge caution in the clinical use of these viral vectors.

A. Donsante et al., Science, "AAV Vector Integration Sites in Mouse Hepatocellular Carcinoma," 27 July 2007 317: 477.

Predicting myopic regression after LASIK

A new statistical model developed by Taiwanese researchers could help predict the risk of regression toward myopia after LASIK. The researchers analysed 615 eyes of 311 patients

derived from a retrospective cohort who underwent LASIK in 2003. They recorded refraction outcomes ranging from one day, to more than 12 months after refractive surgery. Using a cross-validated design they developed an interval-censored model to predict the probability of regression toward myopia and to assess the predictors including demographic features and pre-operative and postoperative variables. They observed myopic regression in 26.7 per cent of eyes over a period of at least 12 months. The risk of myopic regression increased rapidly within one month, slowed down between one and six months postoperatively and became steady after six months. Risk factors included pre-operative manifest spherical equivalent, mean pre-operative central corneal curvature, size of optic zone, undercorrection and age. The researchers believe that this interval-censored model may be useful not only for predicting the probability of myopia regression after LASIK, but also for identifying the evolution of patients within low, moderate and high-risk groups.

Yi Chen, et al. Ophthalmol Vis Sci Invest. "An interval-censored model for predicting myopic regression after laser in situ keratomileusis", 2007;48(8):3516-23.

Glaucoma-Alzheimer's link?

New research indicating the presence of amyloid-beta protein in dying retinal cells

suggests a new direction in glaucoma research. Amyloid-beta is a protein found in Alzheimer's plaques. Using a rat model of glaucoma, the researchers found that the dying retinal cells showed accumulation of amyloid-beta. Moreover, adding the protein to retinal cells in vivo induced cell death. Blocking the effects of amyloid-beta delayed the onset of glaucoma in the animal model. The researchers believe amyloid-beta is likely the mediator of retinal cell death, suggesting new avenues for glaucoma treatment research.

L. Guo et al., Proceedings of the National Academies of Science, "Targeting amyloid- β in glaucoma treatment", August 2007 10.1073.

Measuring success with amniotic membrane transplantation

While there is considerable excitement about the potential for amniotic membrane transplantation to treat ocular surface problems, different protocols make it difficult to assess results. A new British study evaluated the indications for treatment, the surgical procedures used and the results of a subset of the first amniotic membrane transplant cases carried out in the UK. Of the 233 transplants, 126 (54.1 per cent) were valid outcome returns. The outcome for persistent epithelial defects was a healed and stable surface in 11 of 35 (31.4 per cent); for

chemical/thermal injuries, a healed uninfamed eye with clear cornea in five of 18 (27.8 per cent); for bullous keratopathy a pain-free, stable surface without bullae in four of 18 (22.2 per cent); for ocular surface reconstruction, an epithelialised uninfamed conjunctiva without scarring in 12 of 23 (52.2 per cent); and for limbal stem cell deficiency, a corneal phenotype in four of seven (57.1 per cent). Use of a bandage contact lens at the end of the procedure was associated with better success. Previous treatment with topical steroids was significantly associated with failure. The results of this study were generally less favourable than those of previously reported case series. The authors believe that controlled clinical trials would improve the quality of evidence for use of amniotic membrane in ocular disease.

VPJ Saw et al., Br J Ophthalmology, "Amniotic membrane transplantation for ocular disease: A review of the first 233 cases from the UK user group", 2007;91(8):1042-7.



JCRS Highlights

by Associate Editor Thomas Kohlen

Phakic IOLs on trial

Phakic IOLs are being used increasingly in Europe and in the US, particularly for correction of higher refractive errors. However, neither the anterior chamber nor posterior chamber IOLs are without potential postoperative problems. Complications of the former include endothelial cell loss, pupil ovalisation, induced astigmatism, glaucoma, and chronic subclinical inflammation. Problems documented with the latter include cataract formation, pupillary block, pigment dispersion, and glaucoma. The situation became more serious with the recent demand by French health authorities for the withdrawal of angle-supported phakic IOLs, citing concerns about excessive endothelial cell loss. A number of articles in the August edition of the JCRS help to shed some light on issues surrounding these lenses.

Problems with hydrophilic acrylate phakic IOLs

Two articles demonstrate potential complications with hydrophilic acrylate lenses.

One, a report by Coulet and colleagues, describes severe endothelial decompensation after implantation of an I-Care pIOL. They report three eyes in which the same foldable angle-supported pIOL was implanted to correct high myopia. Rapid and severe postoperative endothelial cell loss occurred in all three cases. An over-sized pIOL that induced excessive vaulting into the anterior chamber was the main risk factor. The pIOL was explanted uneventfully in two cases but the third required Descemet's stripping automated endothelial keratoplasty. These cases illustrate the importance of accurate sizing of this lens type.

In a second study, Van Cleynenbreugel describes intrapupillary membrane and decreased endothelial cell density three years after backward implantation of a Vivarte pIOL. A 34-year-old patient underwent bilateral implantation to correct high myopia. Postoperatively, both pIOLs appeared to have been implanted backwards. The situation was corrected in the right eye. For unknown reasons, the left eye was not re-operated. Three years later the patient presented with a decrease in visual acuity from an intrapupillary membrane in the left eye.

Endothelial cell count of the left cornea showed markedly decreased endothelial cell density. The patient was successfully treated by removing the IOL and excising the intrapupillary membrane, leading to recovery of visual acuity.

Artisan and Artiflex

Iris-fixated phakic IOLs have been implanted successfully for two decades. The Artisan (Ophtec) known as the Verisyse (AMO) in the US is a rigid single-piece PMMA lens with a 5.0 or 6.0mm optic. It implanted through a 5.0 to 6.0mm incision. A new two-year study by Moshirfar and colleagues confirms that the lens provides accurate refractive results and acceptable safety over the longer term in highly myopic eyes. The researchers followed 85 highly myopic eyes (mean spherical equivalent -12.2 diopters) that received the lenses for two years. At six months seven per cent of the eyes lost one line of the best-corrected acuity; none lost two or more lines. Endothelial cell density decreased by 3.3 per cent and 6.5 per cent over the one-year and two-year intervals, respectively. Glare and halos, the most common complications of surgery, were reported by six per cent of patients at one month and by three per cent at two years.

A foldable version of the lens, the Artiflex, was designed to reduce surgically induced astigmatism. A foldable 6.0mm silicone optic and PMMA haptics makes implantation through a 3.2mm incision possible. While outcomes reported with the foldable version have been excellent, a report by Cisneros-Lanuza raises concerns about lenticular glistenings. The study of 20 eyes of 13 patients found lenticular glistenings ranging from grade 1+ to grade 4+ in four lenses over a two-year period. Although these did not affect visual function, the researchers call for continued, larger studies to assess the situation.

Coulet et al., JCRS, "Severe endothelial cell loss following uneventful angle-supported phakic intraocular lens implantation for high myopia", Vol 33, Issue 8, August 2007, 1477-1481.

H Van Cleynenbreugel, JCRS, "Late postoperative complications of backward implantation of a Vivarte phakic intraocular lens", Vol 33, Issue 8, August 2007, 1474-1476.

M Moshirfar et al., JCRS, "Two-year follow-up of the Artisan/Verisyse iris-supported phakic intraocular lens for the correction of high myopia", Vol 33, Issue 8, August 2007, 1392-1397

A Cisneros-Lanuza, JCRS, "Glistenings in the Artiflex phakic intraocular lens", Vol 33, Issue 8, August 2007, 1405-1408.