Intraocular lens technology has revolutionized cataract surgery. Cataract surgery is the most common intraocular surgery performed today; it provides dramatic improvement in quality of life and vision. Most patients undergoing cataract surgery do so without significant complications. Some patients, however, require secondary procedures such as intraocular lens exchange, which may be indicated when complications occur related to the primary cataract surgery, or after surgery related to the lens implant or pre-existing disease or trauma.

Most published reports of intraocular lens exchange outcomes originate from tertiary referral centers, preventing a true estimate of the incidence of this procedure in the general population. To identify a population-based incidence rate for pseudophakic intraocular lens exchange, Erick D. Bothun, M.D., Sanjay V. Patel, M.D., and a research team with Ophthalmology at Mayo Clinic’s campuses in Rochester, Minnesota, and Jacksonville, Florida, conducted a Rochester Epidemiology Project-based, retrospective study to determine the population-based incidence of pseudophakic intraocular lens exchange in Olmsted County, Minnesota. “The 148,201-member population of Olmsted County, Minnesota, as documented in the Rochester Epidemiology Project, allows a virtually complete ascertainment of all clinically recognized cases of intraocular lens exchange among county residents,” says Dr. Bothun.

The research team identified 80 people who received intraocular lens exchange, yielding an overall age- and sex-adjusted incidence rate of 28.4 per million (confidence interval, or CI, 22.1 to 34.7), which increased over the study period (P = 0.04). The 30-year cumulative probability of intraocular lens exchange among patients receiving cataract surgery was 1.5 percent (CI, 0.6 to 2.4 percent), and increased at a relatively constant rate.

Changes to incidence and indication

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The majority (72.5 percent) of intraocular lens exchanges were performed for dislocated lenses. More than half of these exchanges were associated with capsular tears that occurred at the primary cataract surgery, or from zonular weakness or corneal edema.

Two new indications emerged in the final decade of this study: unplanned refractive error and uveitis-glaucoma-hyphema syndrome. Intraocular lens exchange for unplanned refractive error typically took place within days of the primary surgery and was associated with the changing nature of cataract surgery, with patients and surgeons expecting specific refractive outcomes.

A uveitis-glaucoma-hyphema syndrome related to the increasing use of single-piece intraocular lenses with square-edged haptics was responsible for five intraocular lens exchanges in this study, all occurring after 2011. All five of these lenses were found to have been partially placed in the ciliary sulcus and were not exchanged until six to 15 years after primary cataract surgery. Study results were published in the American Journal of Ophthalmology in 2018.

“The population-based incidence of intraocular lens exchange has increased over the last three decades at a low and acceptable rate, but the overall increase in incidence was statistically significant,” says Dr. Bothun. “The explanation may include increasing complications of primary cataract surgery or increasing surgeon comfort with exchanging lenses — a lower threshold for intervention. The major contributing factor, however, is likely to be the increase in the population at risk.” The population-based incidence of cataract surgery doubled over the same period in Olmsted County.

Dr. Patel notes: “Surgeons should be aware of emerging indications of intraocular lens exchange, including unplanned refractive error and uveitis-glaucoma-hyphema syndrome from square-edged haptics in the ciliary sulcus, which reflect changes in lens design and increasing expectations of refractive outcomes.”

For more information


Fibrin Hydrogels Provide a Scaffold for Transplantation of RPE Monolayers

Macular degeneration is a class of diseases characterized by the loss of central, high-acuity vision. In most, if not all, cases, macular degeneration is the result of retinal pigment epithelium (RPE) dysfunction. RPE transplantation was a subject of much research as a treatment for macular degeneration starting in the 1980s. The discovery of processes for the differentiation of embryonic stem cells to RPE has renewed interest in RPE transplantation. That interest has been further revitalized by the discovery of methods to reprogram cells into a pluripotent state. Induced pluripotent stem cells (iPSC) can be generated from adult cells and thus are free of the ethical and legal issues that surround the use of embryonic stem cells. Another advantage of iPSC is that they can be generated from the patient in which the cells are to be re-transplanted.

Stem cell–derived RPE cell transplantation is currently in phase 1 clinical trials for macular degeneration. A major obstacle in these studies is the need to deliver the RPE as living, flat sheets without folding and clumping of the monolayer, or leaving behind foreign materials in the retina. Jarel K. Gandhi, Ph.D., and a research team led by Alan D. Marmorstein, Ph.D., in Ophthalmology Research at Mayo Clinic’s campus in Rochester, Minnesota, investigated the suitability of using hydrogels made from human blood-derived proteins for RPE transplant. Study results were published in Acta Biomaterialia in 2018.

Fibrin hydrogels as a scaffold
To overcome the issue of folding and clumping of the monolayer, the researchers investigated the use of hydrogels generated from human fibrin as a scaffold for RPE transplantation. Fibrin is a cross-linking fibrillar network formed spontaneously after the activation of fibrinogen. Fibrin forms the scaffold of the blood clot that physiologically occurs during wound healing, and has a well-established cascade of activation, formation, degradation and clearance.

To test the suitability of fibrin as a substrate for RPE transplantation, the research team produced a variety of fibrin hydrogels by varying the concentrations of fibrinogen and thrombin to form a thin rigid hydrogel with defined parameters for degradation in the scale of hours in vitro. Subsequently, the optimized conditions were utilized to produce fibrin gels on which the researchers cultured iPSC-RPE, forming well-differentiated monolayers (Figure).
“This study demonstrates the ability to generate large surfaces of iPSC-RPE on fibrin hydrogels, such as a 60-mm-diameter (28-cm²) circle. Generating large surfaces out of a single gel, as demonstrated, has tremendous benefits for clinical applications,” says Dr. Gandhi. “Over 250 implants (1.5 mm by 5 mm) can be punched out from a single 60-mm-diameter gel. This enables quality testing on the same batch of cells that would be used for the clinical trial. This also provides a surgeon with many options to select which region of the culture to implant. It allows for the prospect of implanting multiple sheets to cover a larger area, theoretically the entire 5-mm-diameter macula with as little as three implants. Or multiple implants can be used to target peripheral RPE replacement in various locations, in diseases of the peripheral retina. In addition, it has the potential to reduce the overall cost of the transplant.”

Finally, the researchers degraded the fibrin support in vitro, and the effects of this degradation on the RPE monolayer were assessed. The RPE remained viable and pigmented. “While many groups have investigated a large variety of hydrogels for RPE culture and support, fibrin has not been reported for this purpose previously,” says Dr. Marmorstein. “We suspect that a key difficulty encountered by others in the use of fibrin may have been the tendency of the RPE to degrade fibrin on its own.

“Stem cell-derived RPE cells require months to differentiate fully in culture, but we found that RPE degraded fibrin hydrogels in a matter of days. As such, a key finding of our study is the use of protease inhibitors, such as aprotinin, to preserve fibrin during RPE culture. This preserves the gel throughout the differentiation process, but allows it to be degraded when the protease inhibitors are washed out. Again, even without the addition of exogenous fibrinolytic enzymes, the RPE is able to degrade the fibrin gel rapidly.”

“Our data suggest that fibrin hydrogels hold great potential for use as a long-lived scaffold for the differentiation of RPE from stem cells that can then be degraded under controlled circumstances following delivery to the subretinal space,” says Dr. Gandhi. “Fibrin hydrogels offer a promising solution to transplant RPE for patients with macular degeneration.”

For more information

Optic Disk Edema in GFAP Meningoencephalitis May Mimic Papilledema

Glial fibrillary acidic protein (GFAP) autoantibody-positive meningoencephalomyelitis is a newly described entity characterized by a corticosteroid-responsive meningoencephalomyelitis accompanied by immunoglobulin (GFAP-IgG). Some patients with GFAP autoantibody-positive meningoencephalomyelitis have been reported to have bilateral optic disk edema, which is often asymptomatic and was first recognized in this clinical phenotype of encephalomyelitis prior to discovery of GFAP-IgG.

John J. Chen, M.D., Ph.D., and a research team with Ophthalmology at Mayo Clinic’s campus in Rochester, Minnesota, performed an observational case series of Mayo Clinic patients to better define the optic disk edema seen in GFAP autoantibody-positive meningoencephalomyelitis. The results were presented at the American Academy of Ophthalmology meeting in November 2017, leading to an award for best research presentation in neuro-ophthalmology, and published in the Journal of Neuro-Ophthalmology in 2017.

The researchers reviewed all Mayo Clinic patients with GFAP-IgG meningoencephalitis from Jan. 1, 2000, until Dec. 31, 2016, and identified 10 patients with optic disk edema. The visual acuity was unaffected and the disk edema was bilateral in all cases. The optic disk edema resolved with corticosteroid treatment but resulted in mild optic atrophy in two patients. Nine of the 10 patients had radial perivascular enhancement on MRI. Other characteristics included the following:

• Median age was 39.5 years.
• Six patients (60 percent) were male.
• Mild vitreous cell was noted in three patients.
• Median lumbar puncture opening pressure was 144 mm H₂O (range 84 to 298 mm H₂O).
• All patients had inflammatory cerebrospinal fluid.
Fluorescein angiography was available for one patient with optic disk edema, which showed selective leakage from the venules. “The clinical presentation of this disorder is quite broad and can range from subacute to chronic encephalitis with or without accompanying meningitis or myelitis. Patients can have characteristic radial perivascular enhancement on MRI, although other enhancement patterns may be encountered (leptomeningeal enhancement), and most have inflammatory cerebrospinal fluid,” says Dr. Chen.

Although the optic disk edema was typically asymptomatic and mimicked papilledema, the opening pressure was normal in the majority of the patients. “Only two patients in our cohort of GFAP autoantibody-positive meningoencephalitis had a mildly elevated opening pressure, indicating that raised intracranial pressure is unlikely the primary cause for the optic disk edema in the majority of cases,” says Dr. Chen. “The characteristic radial perivascular enhancement on MRI supports a venular process, which suggests that the optic disk edema may be a papillitis from an inflammatory vasculopathy as opposed to papilledema from raised intracranial pressure.”

“In addition, the fluorescein angiogram had a similar appearance to frosted branch angiitis, which is caused by multiple etiologies — including infection, inflammation and neoplasm — where disk edema is the result of papillitis. The selective involvement of the venules on fluorescein angiogram (Figure) was striking and clearly indicates that the development of optic disk edema is a process that primarily affects the veins as opposed to the arteries.”

Dr. Chen notes that the clinical characteristics of GFAP autoantibody-positive meningoencephalitis are still being elucidated. “We recommend testing cerebrospinal fluid GFAP autoantibodies in patients with unexplained meningoencephalitis, particularly if they have bilateral optic disk edema, accompanying myelitis or radial perivascular enhancement on MRI,” he says. “The optic disk edema is likely due to an inflammatory papillitis affecting the venules as opposed to elevated intracranial pressure.”

For more information