

News in Review

COMMENTARY AND PERSPECTIVES

Big Data at Work: FLACS Findings

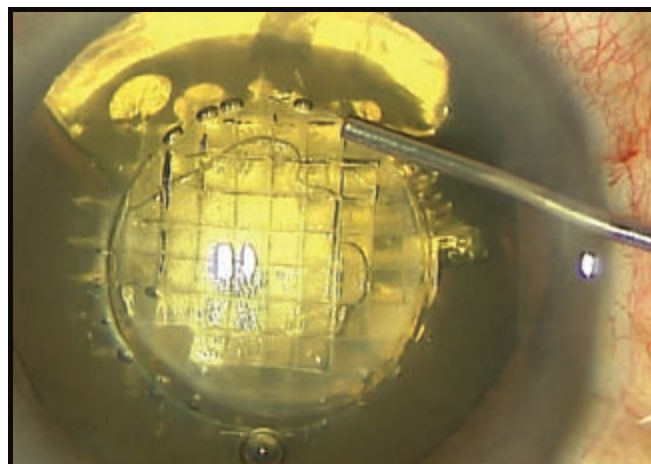
A European coalition of cataract surgery researchers put Big Data to work in a recent study comparing the results of cataract surgery performed with and without femtosecond laser assistance.

Making use of the EUREQUO, a registry of outcomes data on 1.5 million cataract surgeries, the researchers took barely five weeks to traverse the wide gulf between final data acquisition (on 7,014 patients) and reporting of the initial results. (See the Multimedia Extra at www.eyenet.org for study details.)

No commercial bias. This is the first large-cohort research effort on this topic that is completely free of commercial ties, said Peter Barry, FRCS. He reported the preliminary findings of the Femtosecond Laser-Assisted Cataract Surgery

(FLACS) study at the European Society of Cataract & Refractive Surgeons (ESCRS) 2014 congress.¹ Dr. Barry, a member of the study's steering committee, is also head of ophthalmology at St. Vincent's University Hospital and senior retinal surgeon at the Royal Victoria Eye and Ear Hospital, in Dublin.

ESCRS sponsored the study to try to inject reliable clinical evidence into the debate over whether femtosecond laser improves cataract surgery outcomes, Dr. Barry said. "There has been an enormous amount of hype, for lack of a better term, about laser cataract



LASER ASSIST. The FLACS study mined a database to assess whether the use of femtosecond laser improves outcomes compared with conventional cataract surgery.

surgery. There has been a subliminal message that because it is more expensive, it is better."

Similar outcomes on quality measures. But when the researchers compared the outcomes on several quality markers tracked by EUREQUO, differences were minimal between the 4,992 conventional surgeries (controls) and 2,022 laser-assisted surgeries performed in 10 countries. "In summary, femto currently matches but does not outperform phaco," Dr. Barry said.

The quality markers were postop visual acuity; biometry prediction error; surgically induced astigmatism; intraoperative surgical problems; and postoperative complications such as corneal edema, uveitis, and elevated intraocular pressure.

Highlights of the study's comparisons included:

- 70 percent of the laser group had postop best-corrected distance visual acuity (BCDVA) of 20/20 or better compared with 68.5 percent in the control group.
- Femto patients had lower

postop astigmatism (10.2 percent with 1.5 D cylinder or more vs. 22.9 percent for the standard surgery patients); however, the femto group had a higher rate of postop complications (3.2 percent vs. 1.8 percent).

Demographics and vision choices differed. Femto patients were younger (64.8 vs. 73.5 years); had a far higher rate of previous keratorefractive surgery (5.2 percent

vs. 0.2 percent); had better preop vision (41.7 percent BCDVA of 20/25 or better vs. 28.8 percent); and chose premium intraocular lenses at nearly 100 times the rate of the control group (46.7 percent vs. 0.5 percent).

Study pros and cons. Although the conclusions are limited because FLACS was neither a randomized controlled trial nor a strict case-control study, it has

one major advantage over a full-fledged clinical trial, Dr. Barry said: timeliness.

“Our study is most specifically not a clinical trial. Because if we were doing a clinical trial, we wouldn’t be talking about it now; we’d be talking in five years’ time,” Dr. Barry said. “And then if the outcome weren’t favorable, we’d have the industry telling us the trial results were useless because

the technology had changed so much in five years.”

—Linda Roach

1 Barry P. Presented at: XXXII Congress of ESCRS; Sept. 14, 2014; London.

Dr. Barry reports no related financial interests.

MORE ONLINE. See a video interview with Dr. Barry at www.eyenet.org.

Genes, Environment & the Eye

Sun Exposure Is Key to Exfoliation Syndrome

Exfoliation syndrome (XFS), first described in a Scandinavian population, can occur anywhere the conditions are right. Though XFS has a genetic component, the triggering etiological factor appears to be a lifetime of exposure to light, especially when reflected off water and snow. Simply put, more time spent outdoors may increase the risk of XFS, according to a recent study by U.S. and Israeli researchers.¹

“XFS is not a Scandinavian disease,” said lead researcher Louis R. Pasquale, MD. “XFS is a disease of environmental risk factors among genetically predisposed people. If the conditions are right, the high prevalence seen in Scandinavian countries can be replicated just about anywhere.”

XFS (also called pseudoexfoliation) is the most common cause of secondary

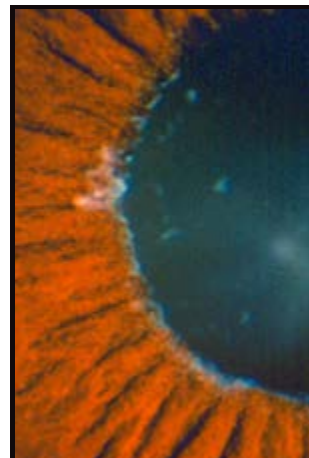
open-angle glaucoma. It is characterized by the production and accumulation of abnormal fibrillar extracellular material, which may clog the trabecular meshwork, leading to elevated IOP.

Study details. At study sites in the United States and Israel, XFS patients and XFS-free controls—all of whom were at least 60 years old and white—responded to a questionnaire that asked about solar exposure from ages 10 through 59.

They were asked about the number of hours they spent outdoors each week in the summer as well as time spent in leisure activities on water or snow. Other questions included residential history and the use of sunglasses and brimmed hats.

Results. The findings, reported as weighted lifetime averages, include:

- Time spent working near water or snow increased the odds of XFS nearly fourfold.



TELLTALE DEPOSITS. Gray-white pseudoexfoliative material is visible at the iris border and on the cornea.

- For each degree of latitude away from the equator, north or south, the odds of XFS increased 11 percent.
- Sunglass use decreased the odds by 2 percent in the United States, but not in Israel.
- Wearing brimmed hats did not reduce the risk.
- Time spent outdoors during teenage years and young adulthood was an important contributing factor.

The study is consistent with prior studies showing a high prevalence of XFS among indigenous people—Navajo Indians, Bantu tribes, and Australian Aborigines—who spend

considerable time outdoors, said Dr. Pasquale, director of the glaucoma service at Massachusetts Eye and Ear. “In these genetically disparate groups, there is a high burden of XFS, suggesting that there is something about their environment that contributes to the disease process.”

Looking ahead. Now Dr. Pasquale is investigating gene-environment interactions between *LOXLI* gene variants linked to XFS and time spent outdoors. (Variants of the *LOXLI* gene were present in 99 percent of the study’s XFS cases and in 80 percent of the controls.) He is also searching for animal models of XFS to provide proof of principle that solar radiation is important in XFS.

In the meantime, his advice is “invest in a good pair of wraparound sunglasses and protect your eyes from the sun, especially when you are young.”

—Miriam Karmel

1 Pasquale LR et al. *JAMA Ophthalmol.* Published online Sept. 4, 2014.

Dr. Pasquale reports no related financial interests.

Retina Report

From Skin Cells to RPE: First Human Implant

Eye surgeons in Japan recently performed the first successful implantation in a human patient of tissue derived from pluripotent stem cells. The recipient is a 70-year-old woman with age-related macular degeneration (AMD).¹ Masayo Takahashi, MD, PhD, created the retinal pigment epithelium (RPE) tissue by causing the patient's own skin cells to revert to induced pluripotent stem (iPS) cells and then coaxing them to differentiate into RPE cells and grow into a tissue sheet.

Dr. Takahashi is based

at the RIKEN Center for Developmental Biology in Kobe, Japan, next door to the Institute for Biomedical Research and Innovation, where a team led by Yasuo Kurimoto, MD, performed the implant surgery.

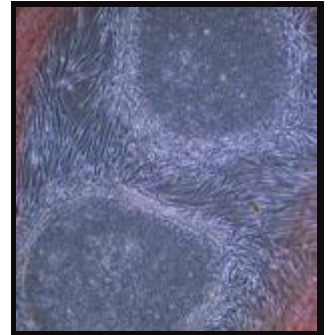
How it works. The RPE supports photoreceptor cells, which are destroyed by AMD, retinitis pigmentosa, and other blinding diseases. By implanting healthy tissue alongside photoreceptors that are alive but ailing, scientists hope to restore the cells to full function and thereby halt vision loss.

"This highly promising

approach could be particularly useful in combating atrophic AMD, the most common form of the disease," said Henry J. Klassen, MD, PhD, director of the Stem Cell and Retinal Regeneration Program at the University of California, Irvine.

Expectations. The researchers do not expect this first implant to restore the patient's vision. They are closely monitoring her progress, especially for any sign of immune response or cancer development. Regenerative medicine researchers are highly interested in iPS cells because they have the potential to differentiate into almost any type of tissue; moreover, their use raises fewer safety and ethical concerns than the use of embryonic stem cells.

"The next focus of our research will be to reduce



NOVEL CELLS. iPS cells derived from the first patient.

the costs of producing iPS retinal tissue and the implantation procedure so that this treatment will be affordable for many patients," said Dr. Takahashi.

—Mary Wade

1 Cyranoski D. *Nature*. Published online Sept. 12, 2014.

Dr. Klassen has intellectual property interest in an unrelated type of retinal stem cell technology.

Dr. Takahashi reports no related financial interests.

Cornea Outcomes

10-Year PK Graft Data

Although the number of penetrating keratoplasty (PK) procedures in the United States is declining with the rise of lamellar keratoplasty, tens of thousands of U.S. patients still undergo PK annually. Identifying factors that affect PK graft survival has important implications for their visual outcomes.

Long-term data. A recent publication from the Cornea Donor Study (CDS), which has followed 1,090 post-PK patients for up to 12 years, sheds light on some of those factors.¹

The study looked at both graft rejection (inflammatory episodes) and graft failure, defined as a regrant or a loss of central graft clarity that compromises vision for three or more months. Risk of ultimate failure is strongly linked with rejection and rises with multiple rejection events.

The glaucoma connection. While the study showed a 75 percent cumulative graft survival rate at 10 years, certain groups of patients did not fare so well—notably glaucoma patients. According to CDS

coauthor Christopher J. Rapuano, MD, chief of the cornea service at Wills Eye Hospital, this finding was not new. However, what had been unclear from past studies was whether the risk of rejection was higher in glaucoma, or only the risk of failure. Now, he said, this study offers strong proof that glaucoma—in particular, history of filtering surgery and use of glaucoma medications—is definitively linked with graft rejection.

A modifiable risk factor. This distinction has important clinical implications because rejection is a modifiable risk factor for graft failure. "How do we prevent rejection? More steroids. Of course, steroids are associated with glaucoma, so

that's the Catch-22," he said, noting that doctors may be tapering steroids earlier and more rapidly in post-PK patients with glaucoma than those without. This may add an independent risk factor for rejection.

He suggested that surgeons carefully reconsider their post-PK steroid regimen in light of this study: "I would encourage slower and more judicious tapering of steroids in glaucoma patients, keeping in mind that their pressure needs to be monitored and managed."

—Peggy Denny

1 Dunn SP et al. *Cornea*. 2014; 33(10):1003-1009.

Dr. Rapuano reports no related financial interests.