

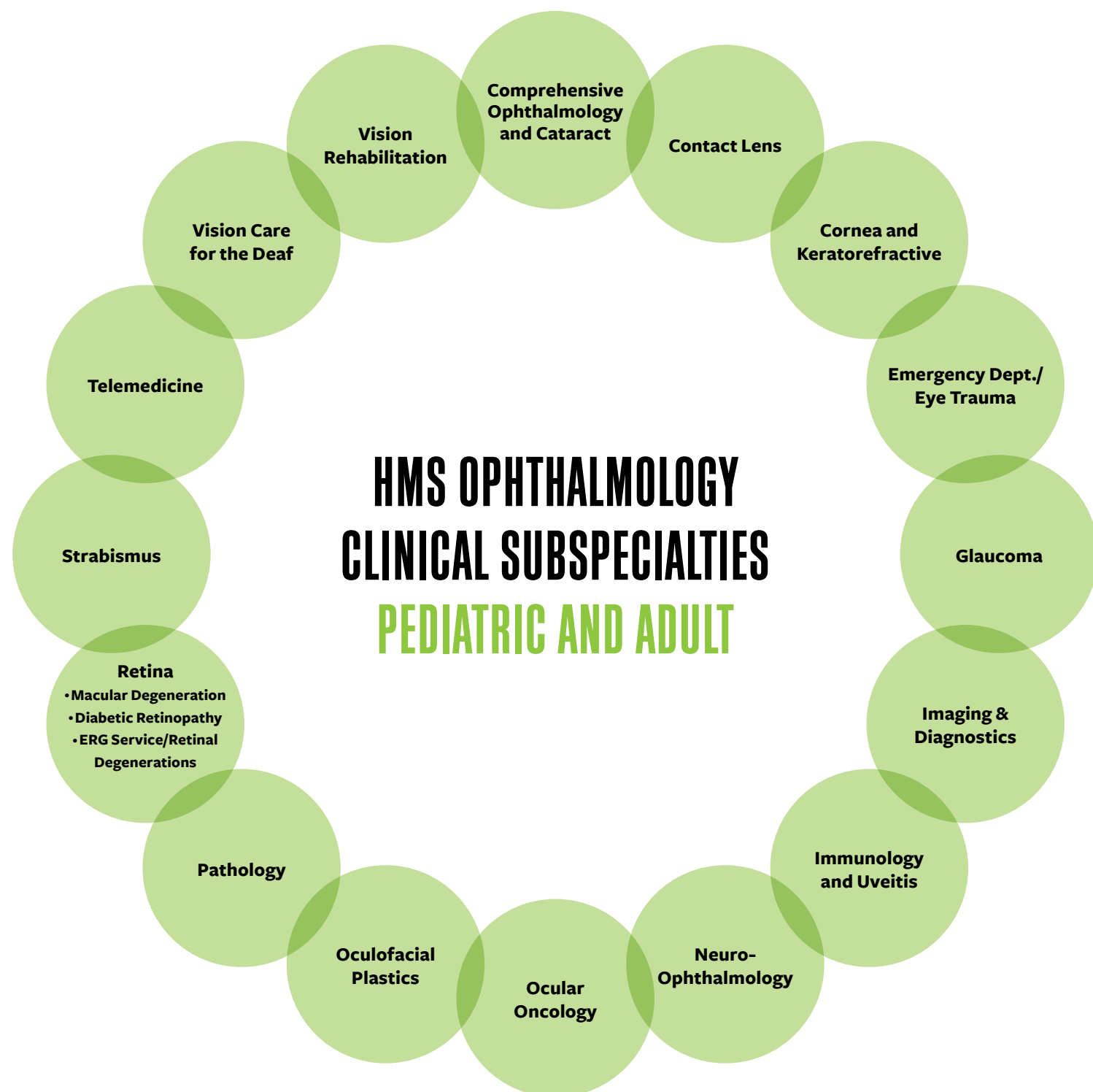
“I am still in awe of what I see every day! As a visual artist and photographer, everything I do is about light and the way it reflects off an object. This operation has given me my creative life back; my sight, I feel, is that of a newborn’s sight, but with a lifetime’s experience in which to use what I now see in artistic ways. I am forever grateful to Dr. Daly and her staff for the professionalism they have shown, and the follow-up care they have given me. Your system works amazingly well. Thank you!”

—JOSEPH PULEO, NAVY VETERAN, PHOTOGRAPHER  
AND VISUAL ARTIST

**TURNING INSIGHT INTO CURES**

**LIFE-TRANSFORMING CARE**





The brain receives more environmental input from the eyes than from any other sensory system. While most of us enjoy healthy vision, 314 million people around the world live each day with blindness or low vision. For many individuals, loss of vision can have devastating social and economic consequences, leading to a significant loss of independence, mobility, and productivity. In some cases, vision loss is accompanied by significant eye pain or discomfort.

In the United States, blindness or low visual acuity affects 1 in 28 Americans older than 40, or 3.3 million people, according to a 2004 study of age-related eye disease sponsored by the National Eye Institute (NEI). Authors of the study project a significant increase in age-related ophthalmic disease—including cataracts, macular degeneration (AMD), glaucoma, and diabetic retinopathy—as the population ages. By 2020, the number of blind persons in the U.S. is projected to reach 5.5 million—a 70 percent jump—with a similar projection for low vision.



Beyond individual suffering, the economic backlash of blindness and low vision on societies around the world is staggering. In April 2010, AMD Alliance International released a landmark report with the first-ever estimates of the global cost of vision loss—nearly \$3 trillion dollars (USD) in 2010 for the millions of people worldwide living with low vision and blindness. According to the study, these costs will rise dramatically through 2020, unless effective prevention and treatment strategies are adopted worldwide.

#### **Dedicated stewards of vision health**

Working the front lines of vision care every day, HMS Department of Ophthalmology physicians understand the extent to which blindness and low vision can compromise a patient's quality of life. Fueled by this knowledge, HMS clinicians practice exacting standards of care along the vision health continuum—from

well-visits to rehabilitation—combining their expertise with innovations that aim to prevent, mitigate or cure blinding eye diseases. Each year, the HMS network of physicians draws thousands of patients from around the country and the world seeking treatment for some of the most challenging and complex eye diseases. Collectively, they form a clinical ophthalmic powerhouse, offering an extensive array of the world's best tertiary and specialty care for patients of all ages and across every ophthalmic subspecialty.

The preceding section of this report, *People & Partners*, highlights the unique attributes, expertise, and strengths of HMS affiliates and partners. This section focuses on their inspiring clinical innovations and treatments, which have given hope and sight to millions of people around the globe, and credence to the possibility that one day blinding diseases will be relics of the past.

**“I recently have become some 20 years younger thanks to the remarkable skills of Dr. Mary Daly. I want to thank you and the VA Boston for giving me sight again.”**

*—First Lieutenant Theodore Scott Simpson, World War II and Korean War Air Force veteran*

Dr. Mary Daly checks the vision of patient, Mr. Edward Cahalane, a United States Air Force Veteran of the Korean War.



### Advanced Clinical Resources

The HMS Department of Ophthalmology continually invests in people, technology, and resources to facilitate a full spectrum of clinical services, advance quality of care, and enhance every patient's experience.

#### Clinical teams

Each clinical area is staffed by a team of highly skilled ophthalmic professionals, including dedicated faculty, fellows, residents, nurses, technicians, and clinical coordinators.

#### Dedicated eye emergency department

Mass. Eye and Ear's 24/7 Emergency Department is a unique Center of Excellence that offers unparalleled resources for emergency ophthalmic eye care and trauma.

#### Morse laser center

The center performs advanced laser procedures using state-of-the-art refractive, glaucoma, retinal, and anterior segment lasers.

#### Enhanced imaging and diagnostics centers

HMS Ophthalmology affiliates utilize highly sophisticated imaging and diagnostic equipment for precision diagnostic capabilities.

- At Mass. Eye and Ear, the Ocular Surface Imaging Center is equipped with confocal microscopes that enable rapid, non-invasive, corneal biopsies, and potentially earlier detection and treatment of disease. The

department's Electroretinography Service performs hundreds of high-tech evaluations annually for patients with retinal degenerative diseases who are referred for diagnosis, prognosis, genetic counseling, and treatment.

- Children's Hospital Boston uses child-focused, sophisticated diagnostic exams to test for a wide range of eye conditions and visual impairment.
- The Joslin Vision Network (JVN), the nation's foremost teleophthalmology program, utilizes unique custom software and a digital retinal imaging device to screen and evaluate diabetes patients for diabetic eye disease. To date, the service has evaluated nearly a million retinal images.

#### The David G. Cogan Laboratory of Ophthalmic Pathology

The Cogan Laboratory was the first ophthalmic pathology service in the nation, and provides enhanced diagnostic services and pools resources with Massachusetts General Hospital's Surgical Pathology service.

#### Biobank

Plans are underway to develop a centralized data registry and tissue repository of DNA samples that will be collected from patients and stored electronically. Genetic information will be merged with clinical information via electronic medical records, enabling clinicians to compare and contrast genetic differences for a

host of ocular diseases.

#### International programs

HMS affiliate hospitals offer extensive medical and non-medical coordination services to ensure a friendly and seamless experience for international patients. Services range from assistance with appointments, transportation and accommodations, to language translation assistance.

#### Contact lens services

Mass. Eye and Ear's full-service center specializes in therapeutic fits, bandage lenses, and a range of specialty contact lens uses that address numerous eye diseases and conditions, including astigmatism, bifocal, dry eye, and prosthetics. Children's Hospital Boston also provides complete contact lens care for newborns and infants, and specializes in fittings for children with cataract removal, keratoconus, astigmatism, and other conditions.

#### Around-the-clock pharmacy

Mass. Eye and Ear's 24/7 pharmacy specializes in ophthalmic medications.

#### Dedicated social work department

The Social Work and Discharge Planning Department at Mass. Eye and Ear is staffed by licensed clinical social workers and nurses registered in continuing care. Services are designed to help families cope with medical, psychological, social, and practical concerns related to their illness and treatment.

**\$3,000,000,000,000 (U.S. dollars) The estimated cost of global vision loss today.**

— *AMD Alliance*

#### FOCUS:

## AGE-RELATED MACULAR DEGENERATION

### Revolutionary AMD therapies reshape the landscape of patient care

Age-related macular degeneration (AMD) is the leading cause of blindness in adults over age 55 in the United States, and affects some 10 million Americans. The disease causes the macula, the central portion of the retina, to progressively deteriorate; left untreated, it eventually robs patients of their central vision.

There are two types of AMD. Dry AMD makes up about 90 percent of all cases, and involves the degeneration of the retinal pigment epithelium (RPE), which is a thin layer of supportive cells beneath the macular photoreceptors. This corresponds with atrophy of the macular photoreceptors and loss of central vision. Although dry AMD is a less common cause of significant vision loss, it is associated with an increased risk of developing the more severe "wet" form.

The process of new blood vessel growth in the body is called angiogenesis. "Wet" or neovascular AMD occurs when there is abnormal angiogenesis in the choroid, a layer of blood vessels that grows under and into the retina beneath the macula. The new blood vessels tend to be immature and leaky, which can rapidly destroy the photoreceptors. Wet AMD causes about 90 percent of vision loss in all AMD cases combined. In decades past, clinical interventions for wet AMD were limited to observation, laser photocoagulation (which often damaged surrounding healthy tissue), and sometimes surgery; however, none of these options offered patients long-term hope for arresting the disease's relentless march.

The status quo began to change in the 1970s when angiogenesis pioneer, Judah Folkman, MD, first proposed the groundbreaking concept that angiogenesis is central to the development and growth of tumors. Dr. Folkman theorized that it was possible to identify specific factors that induce and inhibit angiogenesis, thus providing a way to arrest tumor growth and develop new treatments for cancer. In the decades to follow, Dr. Folkman and other scientists conducted intensive research to identify specific promoters driving angiogenesis. In particular, the efforts of the nine-member HMS Angiogenesis Research Group (HMSARG, see footnote on page 88), led to key studies that elucidated the role of vascular endothelial growth factor (VEGF) in ocular neovascularization, and its potential as a target pathway for treating neovascular AMD.

Studies directed by Joan Miller, MD, and Evangelos Gragoudas, MD, in the Mass. Eye and Ear Retina Research Institute and HMSARG led to the first FDA-approved drug treatment for neovascular (wet) AMD: photodynamic therapy (PDT) with Visudyne®. Now a decade in use, Visudyne® was a revolution in patient care. Injected systemically and activated by light, the drug targets and destroys pathogenic blood vessels in the eye. A relatively painless and quick treatment, Visudyne® marked a significant milestone in patient care by slowing and limiting vision loss without damaging surrounding healthy tissue.

Photodynamic therapy laid the foundation for the second wave of pharmacologic treatments that soon followed. Anti-VEGF drugs Macugen®, Avastin®, and Lucentis® represented a novel attack on the underlying cause of wet AMD. Given by intraocular injection, this class of inhibitors prevents specific VEGF proteins from binding to receptors, thus thwarting the growth and leakage of destructive new blood vessels

that can lead to the disease. These new therapies represent a quantum leap in patient care—not only saving but restoring vision in many patients. In particular, clinical trials of Lucentis®, approved by the FDA in 2006, showed nine out of 10 patients avoided moderate vision loss, while one-third of patients experienced gains of three lines or more on an eye chart. Forty percent of these patients achieved vision of 20/40 or better on a monthly treatment regimen lasting one year.

Today, these pioneering discoveries—coupled with a passion and persistence to translate them into vision-saving therapies—have ushered in a new era of patient care for treating wet AMD. Physicians now have powerful anti-VEGF therapies at their disposal that can slow or arrest vision loss in patients—or even markedly improve vision in some cases. In the last decade, nearly one million AMD patients around the globe have avoided vision loss thanks to these therapies.

The unprecedented and rich tapestry of angiogenesis and translational work pursued by HMS clinician scientists has established new paradigms of patient care. It has given hope—and sight—to millions of people, and set forth a promising precedent that is helping to shape the vision of the future. Research efforts continue at full throttle as the HMS Department of Ophthalmology continues the quest to solve some of the most complex genetic and epidemiologic puzzles in retinal science. "We've made some dramatic gains in AMD research and clinical care that gives us an exciting platform of discovery on which to forge ahead," said department chief and chair, Joan Miller, MD. "Our research mantra today of 'follow the biology' takes aim at several different AMD targets that potentially could lead to better therapies and preventive measures in the years ahead."

JOAN W. MILLER, MD



**Around the world, an adult goes blind every five seconds and a child goes blind every minute.**

— *National Eye Institute*



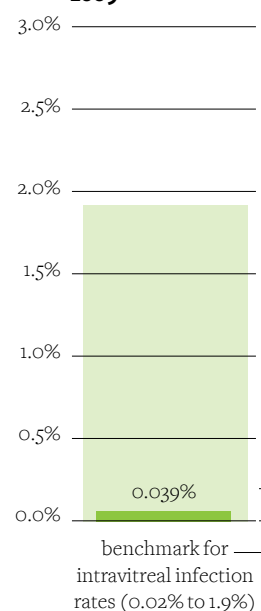
“I no longer feel handicapped,” says Gloria Cohen. “That’s a very good feeling.”



PATIENT  
PROFILE

## Transforming AMD treatment restores vision

Mass. Eye and Ear intravitreal injection infection rates July 2006 to June 2009



N=5,067

Gloria Cohen, an avid tennis player and golfer and now a youthful 72, was diagnosed with AMD at the age of 49. Reading one evening, she noticed that the words on the page were blurred. Gloria made an appointment with an optometrist to get reading glasses. During her exam, the optometrist noticed tiny accumulations of drusen (deposits) beneath the retina—an early finding of AMD. The optometrist referred Gloria to the Mass. Eye and Ear Infirmary for further examination, and she was diagnosed with dry AMD.

Thankfully, Gloria’s vision did not change for many years. Then, in 2004, some two decades after her diagnosis of dry AMD, she noticed while playing golf one day that another person on the tee appeared to have “squiggly” legs. Soon afterwards she realized that she was not seeing objects that were in her center of vision. “When I met with a retina specialist, I learned my condition had changed from dry to wet AMD,” Gloria said. This progression occurs only in 15 percent of all AMD cases. The retina specialist suggested that she undergo laser treatment to destroy the blood vessels and stop the leakage.

Uncomfortable with this suggestion, Gloria decided to research other options. She read an article in AARP Magazine about Dr. Joan Miller, a retina specialist who was working with a new drug called Lucentis®. In November, 2004, Dr. Miller examined Gloria and found that her visual acuity had decreased to 20/200 on the eye chart. Dr. Miller recalls, “When I met Gloria, I was conducting a clinical trial investigating Lucentis® here at Mass. Eye and Ear. Gloria was a good candidate for the treatment.” The studies found that Lucentis® slowed or helped prevent vision loss in patients. According to Dr. Miller, “A substantial number of patients showed significant vision improvement. In fact, 30 percent of the patients who were given Lucentis® gained three or more lines of vision improvement on an eye chart.

Forty percent of patients achieved driving vision of

20/40 or better.”

The U.S. Food and Drug Administration (FDA) approved the new drug in June 2006. Lucentis® is administered in small-doses, injected directly into the eye through the sclera (white coating) of the eye. Gloria remembers the procedure. “The treatment was quick and I didn’t feel a thing.”

“We haven’t seen any serious side effects with Lucentis®,” Dr. Miller says. Gloria was given three injections of Lucentis® over a three-month period. “When I saw Dr. Miller after the third injection, I had a wonderful surprise,” she said. “My vision had been restored to 20/25 with correction. I hadn’t noticed the vision improvement because it happened slowly.” Two months later, she had a fourth injection and her vision improved to 20/20.

“Lucentis®,” Dr. Miller notes, “is the first treatment that, taken monthly, can maintain the vision of more than 90 percent of patients with wet AMD.” This is good news for the 155,000 Americans who are diagnosed each year with the disease. However, Lucentis® is expensive and some people are not covered by insurance, or they are burdened with high co-pays. For others, getting to a doctor’s office for treatment each month can be difficult. “To make treatment easier,” Dr. Miller says, “we are looking at ways to slowly release Lucentis® into a patient’s eye without injections as well as combination therapies with other drugs that might lead to good results with fewer treatments. We’re also part of a multicenter trial (Comparison of AMD Treatments Trials) to compare Lucentis® and Avastin®, a less expensive anti-VEGF agent.”

Lucentis® treatments and excellent ophthalmic care from Dr. Miller have transformed Gloria’s life. “I no longer feel handicapped,” she says. “That’s a very good feeling.”

### HMS scientists forge ahead

Crucial gains in AMD research and treatment, pioneered by an eminent team of HMS scientists during the last two decades, mean that millions of people diagnosed with neovascular AMD will potentially retain their vision for life.

While this is exciting and remarkable progress, much work remains. In the United States, wet AMD is still the leading cause of blindness in older adults, and is expected to rise dramatically as the population ages and adults live longer. Also, there are currently no FDA-approved treatments for treating the atrophic or “dry” form of AMD, though studies have shown vitamin and mineral supplementation in certain patients can help to delay or prevent dry AMD from advancing to the neovascular form.

Thus, while important milestones have been achieved, AMD laboratory and translational research remain a top priority in the department. Efforts continue unabated with an aggressive, multi-pronged attack that aims to improve current therapies, refine diagnostic tools, and develop future therapies that “follow the biology” through epigenetics and gene-based models. Some exciting avenues of research and study include:

- Making current anti-VEGF treatments more “patient-friendly” by 1) reducing the frequency of intraocular treatments while optimizing their effects, and 2) developing drug-eluting contact lenses that may allow for topical delivery of anti-VEGF drugs, thereby reducing or eliminating the need for intraocular injections or eye drops.
- Developing new combination therapies that slow or reverse vision loss, including photodynamic therapy and steroids, or PDT in combination with current anti-VEGF drugs.
- Targeting new disease pathways for additional potential therapies by pinpointing genetic and environmental factors that make some people more susceptible to AMD.
- Developing neuroprotective agents in combination with anti-VEGF therapies to prevent photoreceptor death—the ultimate cause of vision loss in both wet and dry AMD.
- “Reawakening” dead or damaged photoreceptors (rods and cones) through neuro-regeneration techniques, as well as stem cell therapy, which has been shown effective in animal models.
- Refining diagnostic tools and optical methodologies for detecting early signs of AMD, so patients can be tracked and treated sooner to minimize or prevent vision loss.

### Anti-VEGF therapies redefining diabetic macular edema treatment

For the first time in 30 years, some people suffering from central retinal swelling, or diabetic macular edema (DME), may be able to substantially improve their vision thanks to novel pharmacologic therapies already FDA-approved for treating the “wet” form of age-related macular degeneration. A recent landmark clinical trial, sponsored by the Diabetic Retinopathy Clinical Research Network (DRCR.net), has shown that the anti-vascular endothelial growth factor (VEGF) medication ranibizumab (Lucentis®)—combined with either prompt or deferred laser treatment—significantly improved vision in many patients with DME, and is quickly emerging as a potential and powerful first-line treatment for people with the disease. The lead author of the study is Lloyd P. Aiello, MD, PhD, Director of the Beetham Eye Institute at Joslin Diabetes Center, and the inaugural chair of the NIH-funded DRCR network.

Nearly three decades ago, Dr. Lloyd P. Aiello’s grandfather, William P. Beetham, MD, and his father, Lloyd M. Aiello, MD, pioneered laser photocoagulation, the first treatment shown to be effective at preventing or improving vision loss from proliferative diabetic retinopathy and diabetic macular edema, common ocular complications of diabetes and a leading cause of vision loss in the working-age population. Since the introduction of laser photocoagulation for diabetic eye complications, millions of people worldwide have benefited from this treatment, which can preserve vision and reduce the risk of blindness in 90 percent of patients. Now, findings from the DRCR.net study demonstrate that anti-VEGF therapies may prove even more beneficial than standard laser therapy by further reducing diabetes-associated swelling in the retina.

The ongoing, five-year study involves a total of 854 eyes of 691 people diagnosed with type 1 or 2 diabetes and diabetic macular edema involving the center of the retina (macula). At one year of follow-up, participants who received anti-VEGF therapy gained an average of nine letters (nearly 2 lines) in

visual acuity—a three-fold improvement over laser treatment alone. The percentage of patients who achieved at least two lines of vision gain also jumped dramatically, from 28 to approximately 50 percent with anti-VEGF treatment (with prompt or deferred laser) compared to laser treatment alone. Conversely, the number of individuals treated with anti-VEGF medication versus laser alone who experienced two or more lines of vision loss also fell sharply from 13 percent to fewer than 5 percent of patients, representing a significant reduction in the number of people who experienced adverse effects.

Few participants experienced eye-related complications, and there were no serious systemic events such as heart attack or stroke associated with treatment. Results from the trial were published online April 2010 in Ophthalmology. Two-year follow-up data are available for 57 percent of study participants, and these results are consistent with the one-year findings.

“The results from this clinical trial demonstrate that anti-VEGF therapies for treating diabetic macular edema can be remarkably effective, providing substantial improvements in vision and substantial reductions in vision loss,” said Dr. Lloyd P. Aiello. “Anti-VEGF treatments represent a full bench-to-bedside cycle of translational research and, for the first time in more than a quarter-century, offer a new and powerful method for restoring sight to perhaps millions of people whose vision might otherwise be compromised by diabetic macular edema.”

Initially designed as a three-year study, involving 52 sites within the DRCR network, the trial—now in year three—has been extended to five years, and is supported by the National Eye Institute and the National Institute of Diabetes and Digestive Kidney Diseases.



## New diabetic macular edema therapy is saving sight

Kevin England, a 32-year-old participant in the DRCR.net-sponsored diabetic macular edema (DME) study, was diagnosed with type 1 diabetes at the age of five. In October of 2007, he first sought the help of Drs. Jennifer Sun and Lloyd P. Aiello, ophthalmologists at Joslin's renowned Beetham Eye Institute. At the time, Kevin already had lost sight in his right eye due to complications from diabetic retinopathy. Substantial retinal swelling in his left eye, caused by DME, had reduced his vision to 20/200, the legal definition of blindness.

Fortunately, Kevin's left eye met the criteria for study participation and he was enrolled in the clinical trial the following January. He was randomly assigned to the study group receiving up to once-monthly injections of the anti-VEGF drug ranibizumab (Lucentis®) in combination with prompt laser therapy. Kevin remembers feeling hopeful that the treatment would arrest the ravaging progress of the disease and save the sight in his left eye. "Even though there were no guarantees, I

was happy to be accepted," he said.

From the outset, participation in this study has involved rigorous evaluation and careful follow-up of patients. For the first 13 months of the study, Kevin traveled once or twice a month from his home in Connecticut to the Beetham Eye Institute to receive treatment and/or an eye exam to check his progress. In Kevin's case, Dr. Sun gave him intraocular injections during nine of his first 13 visits and Dr. Aiello performed laser treatment every four months.

Within two months of treatment, Kevin's vision began to improve. As the DME-induced swelling decreased in his eye, his vision continued to show dramatic improvement. Thirteen months into the study, Kevin's visual acuity had climbed an astonishing 15 lines on the eye chart giving him better than average "normal" vision of 20/16. According to Dr. Sun, his results mirrored overall results from the study – now in year three – with half the participants experiencing an average eight to nine letter gain. "Kevin's left eye has done

remarkably well in this study and, despite minor variations month-to-month, his vision has remained strong and intact," she said. "And he hasn't experienced any serious side effects, which is consistent with the results from his treatment group."

For Kevin, who works in construction, the treatments have opened up a whole new world – literally. "I don't even remember how I managed before," he says. "I struggled to read a newspaper, watch TV, or see any distance. Now, life is just a whole lot easier."

Dr. Sun adds, "Our ultimate goal for all of our patients, including Kevin, is to maintain vision so that they're not limited by diabetic eye disease. The results in Kevin's case are especially exciting because he is a young person with many years ahead of him. Saving the vision in his left eye, hopefully, will give him maximum quality of life so he remains independent and continues to have a bright, productive future."

### PATIENT PROFILE

## FOCUS OCULAR ONCOLOGY

Ocular oncology involves the study and treatment of tumors that occur in or around the eye. These tumors may cause vision loss or even loss of the eye itself; some ocular tumors are potentially fatal, while others are benign yet severely disfiguring.

The HMS Department of Ophthalmology provides unparalleled care for patients with various forms of ocular tumors. Ocular oncologists at Mass. Eye and Ear regularly perform life-changing procedures, and researchers throughout the department are actively pursuing new and improved ways to treat tumors of the eye.

### Proton beam therapy: the gold standard of treatment for uveal melanoma

Between the sclera (the "white" of the eye) and the retina lies the uveal tract, which consists of the iris, the ciliary body, and the choroid. Melanomas, which are tumors that arise from melanin-producing cells (melanocytes), sometimes develop in the uveal tract. Uveal melanoma is the most common type of eye cancer that affects adults, and about 25 percent of cases are fatal.

The earliest treatment for uveal melanoma was enucleation, or removal of the eye. Radiotherapy is now the standard of care, and can allow patients to retain their eyes as well as visual function. Proton beam therapy (PBT), a very precise form of radiation therapy that was developed by Dr. Evangelos Gragoudas at Mass. Eye and Ear, is particularly effective for treating tumors near critical parts of the eye, such as the optic disc (where the optic nerve joins the retina) or the macula (area of the retina that provides central vision).

Presently, with more than 30 years of follow-up, PBT has proven

to have the lowest local recurrence rate of any radiation therapy. There are now 20 proton beam facilities in North America, Europe, South Africa, and Japan. More than 15,000 patients have been treated worldwide. Not surprisingly, the Mass. Eye and Ear Retina Service has become a major center for the treatment of this tumor, as well as a center of investigation for related areas of study in epidemiology, diagnosis, treatment, experimental models, new therapies, and basic research.

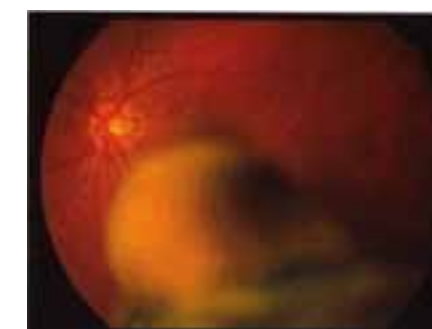
Dr. Gragoudas played a pivotal role in the development of PBT for uveal melanoma, and performed both preclinical studies and the first clinical studies in patients. For his invaluable contributions to the field of ocular oncology—as well to the development of vascular-targeting therapies for numerous eye disorders—Dr. Gragoudas received the esteemed Mildred Weisenfeld Award in 2006. In his Weisenfeld lecture entitled "Proton Beam Irradiation of Uveal Melanomas: The First 30 Years," Dr. Gragoudas describes the evolution of charged-particle tumor therapy from its conception in a Harvard physics laboratory in 1946 to its inaugural use for choroidal melanoma in 1975 at Mass. Eye and Ear. Despite the clinical success of this therapy, Dr. Gragoudas emphasized the need for further optimizing PBT—particularly for complicated tumors and for prevention of metastasis. Along with Drs. Ivana Kim and Demetrios Vavvas of Mass. Eye and Ear's Retina Service, Dr. Gragoudas continues to refine PBT, and has taken a multidisciplinary approach to developing new strategies for managing uveal melanoma. By investigating the epidemiology, genetics, and molecular biology of uveal melanoma, Dr. Gragoudas and colleagues may uncover innovative therapies and diagnostic methods for this prevalent and potentially deadly cancer.

**"I was diagnosed with an ocular melanoma in May of 1992...and was treated by Dr. Gragoudas in July, 1992. I am an 18-year survivor, and I still have good vision in my eye. I come to the Mass. Eye and Ear every year for checkups... Thank you so much for all you do and for adding years to my life."**

– Margaret Judy Poindexter

### Uveal melanoma registry

The HMS Department of Ophthalmology has stood at the forefront of uveal melanoma research and treatment since 1975, when proton beam therapy (PBT) was first used to treat choroidal melanoma at Mass. Eye and Ear. In the early 1980s, Mass. Eye and Ear established the Uveal Melanoma Registry, which contains detailed demographic and clinical data for most patients treated by PBT. Multiple published studies have shown PBT to be a safe and effective treatment for uveal melanoma. A serum, plasma and DNA archive was added to the registry in the mid-1990s, and houses specimens from more than 1,600 patients with uveal melanoma. This information is used as a resource for biomarker and genetic research, and has enabled Mass. Eye and Ear researchers to conduct several studies of cancer susceptibility genes and biomarkers.



Uveal melanoma before proton therapy



Uveal melanoma after proton therapy





## Evangelos S. Gragoudas, MD

Charles Edward Whitten Professor of Ophthalmology, Harvard Medical School

Director, Retina Service, Massachusetts Eye and Ear Infirmary

Dr. Evangelos Gragoudas completed his medical training in Athens, Greece and his ophthalmology residency at Boston University School of Medicine. He was a clinical fellow in diabetic retinopathy at the Elliot P. Joslin Research Laboratory at Harvard Medical School (HMS), and subsequently a retina fellow under Dr. Charles Schepens at Mass. Eye and Ear. In 1975, Dr. Gragoudas joined the full-time faculty at Mass. Eye and Ear. He was promoted to HMS Professor of Ophthalmology in 1994.

Director of the Retina Service since 1985, Dr. Gragoudas has helped transform the service into the preeminent academic and clinical service that it is today. Under his leadership, the service has grown from two clinicians to nine clinicians and clinician scientists pursuing vigorous research activities. The number of retina fellows also increased from two to six, and the fellowship expanded from one to two years. Dr. Gragoudas has trained more than 100 clinical retina fellows, many of whom have gone on to leadership roles in medicine, academics, and industry. The Retina Service also serves an important role in training the 24 residents in the Harvard Medical School Department of Ophthalmology Residency Training Program.

Dr. Gragoudas is an international authority in retinal diseases and intraocular tumors. His early translational work focused on uveal melanoma, for which he pioneered the use of proton beam irradiation—a highly successful treatment that has been used in over 15,000 patients to date as a proven and safe alternative to enucleation. Along with refining proton beam therapy, Dr. Gragoudas also has studied the epidemiology, genetics, and molecular biology of uveal melanoma to further improve diagnosis and treatment for this potentially fatal disease.

With a long-standing interest in retinal disorders, Dr. Gragoudas helped pioneer vascular-targeting therapies for neovascular diseases of the eye. In collaboration with Dr. Joan Miller, Dr. Gragoudas developed photodynamic therapy using the light-sensitive dye, Verteporfin (Visudyne®). He was instrumental in designing and executing the early clinical studies, and was an integral member of the study and writing groups for the large clinical trials. Based on these large clinical trials, photodynamic therapy using Visudyne® became the first FDA-approved treatment for AMD.

Dr. Gragoudas also was among the first to target vascular endothelial growth factor (VEGF) in the treatment of AMD. As a member of the HMS Angiogenesis Research Group, he worked with a group of ophthalmologists, including Drs. Joan Miller, Anthony Adamis, Patricia D'Amore, and others in collaboration with the laboratory of famed anti-angiogenesis proponent, Dr. Judah Folkman. This team first demonstrated the critical role of vascular endothelial growth factor (VEGF) in ocular neovascularization, and went on to develop therapies targeting VEGF.

Dr. Gragoudas has published over 200 articles in peer-reviewed journals, and authored more than 100 chapters, reviews, and books; he lectures nationally and internationally. His scientific discoveries in developing therapies for ocular malignancies and for retinal neovascular diseases have saved the sight and the lives of countless patients.

Dr. Gragoudas holds honorary doctorates from the University of Athens and the University of Patras, Greece. Some of his major honors and awards include the Academy Honor Award of American Academy of Ophthalmology, Retina Research Foundation prize of the Jules Gonin Lectureship, Senior Scientific Investigators Award from Research to Prevent Blindness, Senior Achievement Award of American Academy of Ophthalmology, J. Donald M. Gass Medal of the Macula Society, HMS Distinguished Alumni Award, the Arnall Patz Medal of the Macula Society, and the Mildred Weisenfeld Award for Excellence in Ophthalmology from The Association for Research in Vision and Ophthalmology.

## Making treatments safer for retinoblastoma patients

Retinoblastoma is the most common primary ocular tumor that affects infants. This cancer develops in the retina, which is the light-collecting tissue at the back of the eye. In advanced cases, the affected eye must be removed; if the cancer spreads to other tissues, retinoblastoma can be fatal. If retinoblastoma is detected early enough, there is a good chance of survival, and it is often possible to save the eye as well as vision. Ongoing studies in the Department of Ophthalmology aim to improve existing approaches for retinoblastoma, as well as to develop new therapeutic strategies.

Chemotherapy is often used to treat retinoblastoma. Unfortunately, the existing chemotherapeutic treatments for retinoblastoma can be highly toxic, and may even increase the risks for other forms of cancer. Drs. Demetrios Vavvas, Joan Miller, and Evangelos Gragoudas set out to find safer treatments for retinoblastoma. They focused on a cellular protein called AMP-activated protein kinase (AMPK), which helps tumor cells grow and multiply. Along with colleagues, they found that they could inhibit retinoblastoma cells with a chemical that inhibits AMPK. This chemical, called 5-aminoimidazole-4-carboxamide-1-beta-4-ribofuranoside (AICAR), holds enormous potential in treating retinoblastoma because it not only inhibits cancer cell growth, but also has very low toxicity. This study, published August 2010 in *The FASEB Journal*, provides evidence that safer, non-toxic treatments for retinoblastoma may soon be possible.

Several ongoing collaborations between several HMS affiliates are also aiming to improve the methods of treating retinoblastoma. Dr. Shizuo Mukai, a pediatric retinal specialist at Mass. Eye and Ear, has helped develop collaborations with Mass General Hospital, Dana Farber

Cancer Institute, and Children's Hospital Boston to test combination chemotherapy and radiotherapy for retinoblastoma. In addition to fine-tuning proton beam therapy techniques, Dr. Mukai is also examining the possibility of inducing the body's own immune defenses to fight retinoblastoma. In a study led by Dr. Bruce Ksander of Schepens Eye Research Institute, Dr. Mukai and colleagues used the membrane-bound, pro-inflammatory form of Fas ligand (FasL) in a mouse model of intraocular tumors. FasL induced a potent inflammatory response in mice with tumors of the eye; this resulted in tumor rejection, reduced metastasis, and lower mortality. This study, reported July 2005 in the journal *Investigative Ophthalmology and Visual Science*, helped form the basis of potential immune-based therapies for retinoblastoma and other intraocular tumors.

## Life-changing surgery for patients with vascular malformations

About 10 percent of all babies have vascular birthmarks that develop either before birth or during the first few weeks of life. The most common vascular birthmarks are known as hemangiomas, which are actually non-cancerous tumors made almost entirely of abnormal blood vessels. Hemangiomas are generally not harmful, and many go away without treatment. However, some hemangiomas continue to grow and develop into life-long deformities that may cause significant complications. Such was the case with Alicia Loshkin, a young girl who developed a hemangioma near her eye when she was an infant. When Alicia came to Mass. Eye and Ear in 2009 as a 17-month-old toddler, her hemangioma had grown so large that it almost completely blocked her vision in one eye. Alicia was treated by Dr. Aaron Fay of Mass. Eye and Ear's Ophthalmic Plastic and Reconstructive Surgery Service.

In collaboration with the Vascular Birthmarks Foundation, Dr. Fay donated his consultation and services to remove Alicia's hemangioma—thus restoring her vision. “When we intervene, it's almost like—overnight—they're back to normal,” Dr. Fay says of the surgery. “You can't even put it in words; it's really a great feeling to be able to participate in that experience.”



## Dean Elliott, MD

Dr. Dean Elliott is Associate Director of the Mass. Eye and Ear Retina Service and a full-time clinical and research faculty member of the HMS Department of Ophthalmology. Dr. Elliott is an accomplished and nationally renowned vitreoretinal surgeon. He is active in clinical trials for retinal disease, with a strong interest in translational research on diabetic retinopathy, AMD, and non-diabetic retinal vascular disease. Prior to joining the department, Dr. Elliott was Professor of Ophthalmology, Director of Clinical Affairs and Director of the Vitreoretinal Fellowship Program at the USC Keck School of Medicine's Doheny Eye Institute in Los Angeles. Dr. Elliott has been awarded a Heed fellowship, an American Academy of Ophthalmology 2004 Achievement Award, and the Vitreous Society's 2003 Honor Award.



**FOCUS:****CLINICAL INNOVATIONS****Drug delivery: envisioning alternatives to eye drops**

Approximately 90 percent of ocular medications are delivered to the eye topically—often in the form of eye drops. Because drops are administered periodically, they do not provide sustained drug levels. Drops are also inefficient because reflexive blinking washes away much of the medication; typically, the eye absorbs less than 10 percent of each dose, and the rest may be absorbed by other tissues and result in unwanted side effects. Moreover, studies show that many patients often don't follow their medication schedules. This is of particular concern as the population ages and the frequency of age-related ocular disorders continues to rise.

Drug delivery is thus an increasingly intense focus of translational ophthalmology research—particularly for conditions that require repeated, long-term pharmacologic intervention. Two new methods of

drug delivery, currently in development in the HMS Department of Ophthalmology, may overcome many of the limitations of eye drops.

**Drug-eluting contact lenses**

Some research innovations have multiple therapeutic applications that may directly benefit a wide range of patients. This may very well be the case with a novel drug-eluting contact lens—developed in a collaboration between Children's Hospital Boston and MIT—that directly releases medications into the eye. Inspired in part by the needs of keratoprosthesis (KPro) patients, Drs. Joseph Ciolino, Daniel Kohane (MIT and Children's Hospital Boston), Claes Dohlman, and colleagues published a paper describing the development of a drug-eluting contact lens, which can potentially improve surgical outcomes by both protecting the ocular surface of the eye and by preventing post-operative infections. The prototype lens consists of a thin polymer film (containing the pharmaceutical agents) that is encapsulated within a hydrogel material that is used in standard contact lenses. The lens was char-

acterized using scanning electron microscopy and drug-release studies, and showed a steady release rate of an antibiotic (ciprofloxacin) that effectively inhibited bacterial growth for more than four weeks. The design and characterization of the drug-eluting contact lens was reported in July 2009 in *Investigative Ophthalmology and Visual Science*. Although the contact lens could benefit KPro patients, this technology may potentially also benefit a wide range of ophthalmic conditions. It also lays the groundwork for developing additional sustained ocular drug delivery systems.

**Implants for intraocular drug delivery**

More than three million people in the United States undergo cataract extraction each year. This procedure involves replacing a clouded lens with an artificial lens, and is the most common type of intraocular surgery. Patients usually require eye drops containing anti-inflammatory and antibiotic medications for at least one month after cataract surgery; however, inadequate dosing and patient compliance are regular concerns. Moreover, in some cataract surgery patients, an opaque membrane forms on the rear surface of the artificial lens—which often requires laser surgery as a follow-up intervention to optimize vision. To address these post-surgical issues, Dr. Joseph Rizzo, III has designed an implantable intraocular lens that may allow targeted, noninvasive, and controlled drug delivery to prevent inflammation and infection after surgery. The patented lens design may also be engineered to dispense anti-fibroblastic growth factors to prevent opaque membrane development, which may in turn reduce the number of follow-up laser surgeries. Other key benefits may include fewer complications post-surgery, reducing or eliminating the need for vision rehabilitation, and decreasing the need for medicated eye drops.

**New screening method identifies infants at risk for ROP**

Every year, according to the National Eye Institute, about 15,000 thousand infants in the United States are born prematurely. About 10 percent of these infants will develop retinopathy of prematurity (ROP), which, if left untreated, can lead to blindness. Traditionally, ophthalmologists have tracked the progress of at-risk infants (primarily those born before 31 weeks gestation) by conducting exams to check for signs of developing retinopathy. However, a new screening algorithm may offer a more accurate, efficient and less costly alternative to traditional screening methods.

Drs. Lois Smith of Children's Hospital Boston and Ann Hellström, a collaborator in Sweden, have developed an algorithm currently in trial called WINROP (Weight IGF-1 Neonatal ROP) that can predict ROP nine weeks before development of the disease based on postnatal weight gain indicative of postnatal IGF-1 (protein) levels. In prior research, Drs. Smith and Hellström identified IGF-1 levels as a key predictor of whether or not an infant would develop ROP. This simple surveillance model can eliminate the need for costly and stressful eye exams in infants by as much as 75 percent. Identifying children at-risk for the disease early on also can lead to more timely interventions, and possibly prevent loss of vision.

**Strabismus treatments benefit children and adults**

"It's hard enough to convince adult strabismus patients to get corrective surgery, because doctors may have told them it's too late," says Dr. David Hunter, Ophthalmologist-in-Chief at Children's Hospital Boston. "So imagine how hard it is to convince grown-ups to come to a hospital for kids!" he laughs.

Commonly known as "lazy eye"

**Detecting strabismus the easy way**

Dr. David Hunter has developed a Pediatric Vision Scanner that detects amblyopia and strabismus in children. The device is a quick 2.5 second test that can identify these eye conditions at their earliest stages when they are most amenable to treatment. The Pediatric Vision Scanner also has the potential to identify children with medical eye disease, including cataract and retinoblastoma. This means that the device will someday be used not just in the United States for detecting amblyopia, but also to improve medical care in developing nations by identifying most vision and life threatening eye conditions—instantly.

or "crossed eyes," strabismus occurs when a person's eyes are misaligned because the muscles or the nerves that control them are weak or don't function properly. Some people are born with strabismus, while others can develop the condition in adulthood as a result of illness or injury. People who develop strabismus as adults may also suffer from double vision, which can be severe enough to cause functional disability. Even so, many adults are hesitant to get corrective surgery for strabismus.

Children's Hospital Boston and Mass. Eye and Ear Infirmiry are home to a group of surgeons who specialize in evaluating, diagnosing, and treating all forms of adult strabismus, including Dr. Linda Dagi, Director of Adult Strabismus at Children's. The group's highly-skilled pediatric ophthalmologists perform delicate eye muscle surgery in patients of all ages, routinely handling difficult cases and correcting the condition in patients who have experienced failed surgeries

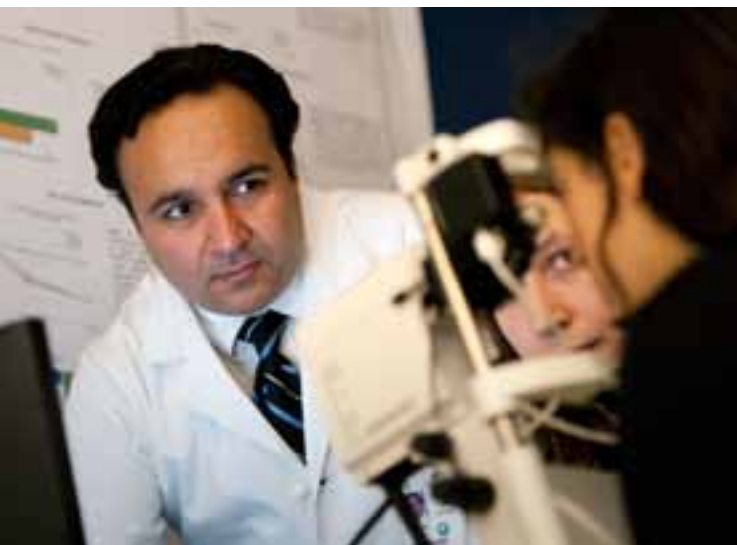
elsewhere. Dr. Dean Cestari, Neuro-ophthalmologist and adult strabismus surgeon at Mass. Eye and Ear, notes that there are many causes of the disorder, including very subtle medical or neurological disease. "Some people are under the false impression that strabismus correction is a vanity procedure," he said. "However, strabismus isn't just a cosmetic issue—it's a genuine medical condition that sometimes requires reconstructive surgery." Drs. Hunter, Cestari, and Gena Heidary, Children's Hospital's dedicated pediatric neuro-ophthalmologist, are currently preparing a case-based textbook on strabismus, which is slated for publication in early 2012.

With recent advancements like adjustable sutures and non-surgical alternatives, strabismus correction can be far less invasive and have greater long-term success than traditional procedures. Dr. Hunter has led efforts to improve the utility and surgical success of adjustable sutures. He developed an adjustable

Drug-eluting contact lens







PEDRAM HAMRAH, MD

suture procedure called the “short tag noose,” which allows physicians to wait up to one week after initial surgery to make final suture adjustments in the office if needed; prior to this, corrections were required within 24 hours of surgery. The short-tag noose procedure widens considerably the window of opportunity to ensure exact and proper positioning of the eye muscle(s) and, often times, eliminates the need for subsequent surgeries.

For some patients, Botox injections offer a viable, permanent, and non-surgical solution for treating strabismus. Physicians at Children’s Hospital Boston and Mass. Eye and Ear use Botox to successfully treat a variety of complex strabismus cases. Dr. Hunter and colleagues also have used Botox to correct residual strabismus in adults for whom previous multiple incisional surgeries have failed, as well as strabismus in children with cerebral palsy or developmental delays.

### Going live: new imaging techniques are patient-friendly

In routine ophthalmic practice, many standard diagnostic procedures are invasive, slow, and yield only limited insight into the pathology of corneal diseases. To

better understand the underlying mechanisms of corneal physiology and pathology, Dr. Pedram Hamrah has applied live corneal imaging techniques that may be used to examine nerves, vessels, and immune cells of the ocular surface. As director of the newly formed Ocular Imaging Center, Dr. Hamrah aims to standardize the use of in vivo confocal microscopy (IVCM) in clinical practice. IVCM is far less invasive than traditional biopsy tests, and may facilitate earlier detection and treatment for patients with corneal diseases—ultimately benefiting the quality of care given to patients and imposing less of a burden on the health care system. IVCM may also help shorten the treatment periods with medications (some of which can have harmful side effects), enable more targeted medical treatment, decrease the need for surgery, and delay disease progression—resulting in an overall improvement in visual acuity.

Recently, Dr. Hamrah, in collaboration with Drs. Deborah Langston and Reza Dana, used IVCM to measure corneal innervation, in patients with herpes simplex keratitis (HSK). Corneal innervation is a marker of disease severity in HSK and other corneal conditions, including dry eye syndrome and keratoconus. This study, and more recent studies, not only demonstrated that corneal innervation (as measured by IVCM) correlated with corneal sensation, but has also demonstrated that both corneal innervation and immune cells are altered bilaterally in unilateral corneal diseases. Prior to this study, clinicians could only measure corneal sensation using subjective and invasive methods. These prospective studies, the first of which was published September 2010 in the journal *Ophthalmology*, presents a rapid, noninvasive, qualitative, and reproducible method for measuring corneal innervation and inflammation, and assessing disease progression in clinical practice.

### Surgical advances benefit glaucoma patients

Glaucoma is the second leading cause of irreversible blindness in the United States,—affecting an estimated three million Americans—and the principal cause of blindness for people of African and Latino descent. This “silent thief of sight” progresses slowly and painlessly, leaving half the people affected by the disease unaware of it. Left untreated, glaucoma’s signature risk factor of high fluid pressure within the eye—known as intraocular eye pressure (IOP)—can eventually destroy the optic nerve, robbing people of their sight. There is no cure and early detection is critical; glaucoma can be controlled with eye drops, laser therapy, and surgery, but any vision lost to the disease is lost forever.

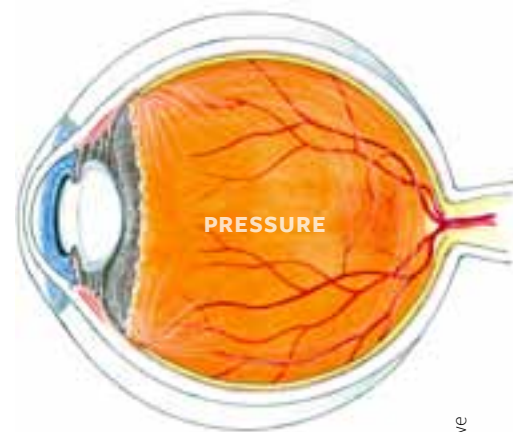


Illustration by Laurel Cook Lhowe

## Personalized glaucoma surgery saves sight

Fran Hall is one of the most active octogenarians you’ll ever meet. At 82, she still works professionally as a psychotherapist, skis in the winter, and plays tennis year-round. She also finds time to sing in a chorus, restore furniture, and participate in a book club. Amazingly, Fran maintains this lifestyle 15 years after she was first diagnosed with glaucoma, and just two and a half years after sight-saving surgery at Mass. Eye and Ear.

For ten years, Fran successfully controlled her glaucoma pressure with medicated eye drops and laser treatments. Over time, however, the pressure in both of Fran’s eyes continued to rise, and the treatments gradually became less effective. Fran sought the advice of glaucoma specialist Dr. Douglas Rhee at Mass. Eye and Ear. They discussed her busy lifestyle, and Dr. Rhee suggested they forego traditional trabeculectomy surgery in favor of a newer, less invasive procedure—trabectome surgery—that offers patients shorter recovery times and a lowered risk of complications.

Trabectome surgery works by treating the eyes’ primary “drain,” called the trabecular meshwork, which helps to remove fluid from the eye. The procedure is appropriate for patients with open-angle glaucoma, the most common form of the disease in the United States. Dr. Rhee was the first physician in New England to perform the trabectome procedure, and is currently one of the most experienced physicians in the world performing the procedure.

Dr. Rhee performed the surgery on both of Fran’s eyes. As expected, Fran’s recovery time was short and the pressure in both eyes is now under control. Aside from regular check-ups at the hospital’s Glaucoma Service, Fran is back to an active lifestyle, swinging her tennis racket and spending time with her grandchildren.

Besides trabectome surgery, Mass. Eye and Ear is also the first academic medical center in New England to offer canaloplasty—another new and innovative surgical option for pediatric and adult glaucoma patients. While the trabectome procedure utilizes an internal approach and removes part of the trabecular meshwork, canaloplasty utilizes an external approach without accessing the interior of the eye. During canaloplasty, surgeons dilate the canal behind the trabecular meshwork and place a suture to keep the canal open. As with trabectome surgery, canaloplasty helps to provide better drainage

“With a number of surgical procedures available under one roof, we can offer glaucoma patients options for the best, most individualized care, and ultimately, the best outcomes,” says Dr. Rhee.

PATIENT PROFILE



in the eye. It also speeds recovery time and lowers the risk of complications compared to traditional surgical interventions. “With a number of surgical procedures available under one roof, we can offer glaucoma patients options for the best, most individualized care, and ultimately, the best outcomes,” said Dr. Rhee. Fran agrees. “I’m one happy camper,” she says.

Years after having glaucoma surgery, Fran Hall is doing well. To celebrate her 80th birthday in 2007, Fran jumped from a wharf in Nahant, MA, with her three sons (left to right) David, Gordy, and Max.



**FOCUS:****KERATOPROSTHESIS****Boston KPro offers a second chance at sight**

There are an estimated eight million people in the world—including 1.5 million children—who are blind from corneal disease. In many severe cases of corneal disease, cornea transplants are the only hope for restoring vision. However, because transplantation facilities and suitable donor corneas are not always accessible, only a fraction of patients who need corneal transplants actually receive them. Moreover, standard corneal transplants are not successful in many corneal conditions—such as recurrent graft failure, congenital corneal dystrophies, ocular burns, or autoimmune diseases.

The Boston Keratoprosthesis (KPro), an artificial cornea developed at Mass. Eye and Ear, is an economically sustainable option for many cases that cannot be treated with classic donor-tissue corneal transplants. First conceptualized by Dr. Claes Dohlman in the 1960s, the Boston KPro received FDA clearance in 1992, and is now the most successful artificial cornea in the world with over 5,000 implantations to date. Dr. Dohlman, now working with Dr. James Chodosh and a number of research fellows, continues to lead advancements in Boston KPro design and postoperative management, and the device continues to grow in clinical success and worldwide demand.

The Boston KPro is made of medical grade poly(methyl methacrylate) or PMMA, a clear plastic with excellent tissue tolerance and optical properties. The three parts of the device form a collar-button shape when fully assembled. The device is inserted into a corneal graft and sutured into the patient's cornea using similar techniques to a standard corneal transplant.

Design innovations have greatly improved patient outcomes with the Boston KPro. Holes in the back plate now allow the donor corneal graft tissue to access nutrients from the aqueous humor, thus reducing complications such as stromal necrosis and corneal melt. Newer devices also incorporate a titanium locking ring, which prevents loosening of the device after implantation. Further updates include a threadless stem, which reduces the risk of damage to donor graft tissue during device assembly; this also reduces manufacturing costs, making the KPro more economically accessible. Mass. Eye and Ear researchers, including Drs. James Chodosh and Roberto Pineda II, are conducting ongoing studies of the Boston KPro in developing countries.

Improved postoperative care has been central to the clinical success of the Boston KPro. Common complications such as inflammation and infection are becoming more rare with new prophylactic drug regimens. Innovative devices also have significantly improved postoperative management of KPro. Soft contact lenses are now worn continuously to improve graft retention and prevent irritation and evaporative damage; with the current efforts of Dr. Joseph Ciolino, and colleagues at MIT and Mass. Eye and Ear, contact lenses may soon be used for drug delivery as well. Dr. Dohlman, with the help of Drs. Cynthia Grosskreutz, Teresa Chen, and Louis Pasquale, recently developed shunts that direct aqueous humor away from the anterior chamber to an epithelialized cavity (sinus, etc); these have been shown to reduce IOP after KPro surgery, and may effectively prevent glaucoma. Dr. Samir Melki is spearheading the development of a technique to insert a pressure transducer into the eye, which allows the intraocular pressure to be read from the outside via radio wave telemetry.

The Boston KPro is now the primary therapeutic option for a grow-

ing number of conditions. Studies using combined immunomodulatory therapy with the Boston KPro II, led by Drs. Chodosh, Stephen Foster, and George Papaliodis, may continue to improve the outcome in autoimmune disease in cases where the disease makes corneal allograft failure inevitable. A series of case reports by Drs. Dohlman and Deborah Langston demonstrated the Boston KPro's effectiveness in treating corneal damage caused by herpetic keratitis. At Mass. Eye and Ear, Dr. Kathryn Colby pioneered the use of the Boston KPro to treat corneal conditions in pediatric patients. Use of the Boston KPro has grown rapidly—from only 46 procedures in 2002 to 1,200 procedures worldwide in 2010—as corneal surgeons become increasingly aware of the device's numerous advantages.

The Boston KPro continues to evolve. A large number of research fellows are working with Dr. Dohlman to improve the device and its postoperative care. Ongoing research in collaboration with Dr. Eli Peli at Schepens Eye Research Institute is examining the optics in various Boston KPro models. Dr. Lucy Young and colleagues are studying ways to prevent postoperative retinal detachment, and Dr. Ilene Gipson is leading an effort to inhibit enzymes that can cause tissue melt and perforation around the Boston KPro. Dr. Irmgard Behlau and colleagues are examining antibacterial coatings for the device while, at the Kohane lab at MIT, Dr. Daniel Kohane is directing a large-scale effort in biointegration. Continued improvements will lead the Boston KPro ever closer to the goal of providing safe, economical, and effective treatments for corneal blindness.

**FOCUS:****VISION REHABILITATION****Technology and tools shaping the future of vision—today**

Despite many breakthrough treatments for eye disorders, millions of Americans suffer from irreversible vision loss that restricts their productivity, independence, and quality of life. By 2020, there will be an estimated 53 million Americans aged 65 and over who will suffer some form of visual impairment—a number that will rise as America ages. One of the goals of the HMS Department of Ophthalmology is to develop and implement new tools and technologies that can help patients make the best use of their remaining eyesight.

**Maximum impact**

It's 1968. Imagine that you've been diagnosed with advanced age-related macular degeneration (AMD) or diabetic retinopathy; a time when there are few vision-saving tools, technologies, and therapies to prevent you from going blind or slowing the progress of your disease. Medical options exhausted and facing an uncertain future, you're told by your doctor, "There's nothing more I can do." Fortunately, not all physicians—including Dr. Joel Kraut, a pioneer in Vision Rehabilitation at Mass. Eye and Ear—subscribed to this pessimistic but widely accepted mantra of the day. Instead, beginning in the 1960s, Dr. Kraut collaborated with social worker Dagmar Friedman and a dedicated group of trustees headed by Robert P. Storer. Together, they developed one of the nation's first comprehensive hospital-based Vision Rehabilitation Services at Mass. Eye and Ear.

Fast-forward fifty years. Much as Dr. Kraut envisioned, vision rehabilitation services have emerged as a separate subspecialty, and an integral and vital component in the



ophthalmologic continuum of care. Today, the Vision Rehabilitation Center (VRC) at Mass. Eye and Ear, under the direction of Dr. Mary Lou Jackson, utilizes leading diagnostic tools and therapies to evaluate remaining vision, and to provide comprehensive and sophisticated vision rehabilitation care for hundreds of patients every year. The center assists patients with a wide range of eye diseases and disorders, with the ultimate goal of teaching patients how to maximize their remaining vision and enhance their mobility, independence, and quality of life.

Expert staff members in ophthalmology, optometry, occupational therapy, and social work provide a patient-centric approach that aims to improve reading, activities of daily living, patient safety, community participation, and psychosocial well-being. During the last two years, the VRC has experienced significant growth in patient referrals, underscoring the value of the patient-centric nature of the program and highlighting the increasing

**Vision snapshot:**

This perimetry obtained with the Scanning Laser Ophthalmoscope provides a "map" of the patient's field of vision to assess, in this case, reading ability. Here, the word Mississippi was projected on to the central retina. The patient was unable to see several of the central letters (SSIS) because they fell into a scotomatous (degenerative) area of the patient's retina.

demand and need for services as the population ages.

Through a variety of tests, patients receive an in-depth clinical evaluation that enables VRC staff to determine which areas of the retina are affected by vision loss. The VRC houses one of New England's only scanning laser ophthalmoscope (SLO) with macular perimeters. Far more sensitive and accurate than the Amsler Grid, this unique tool produces a real-time, high-resolution map of the functioning areas of the patient's retina. VRC staff can instantly evaluate a patient's visual function, and develop appropriate interventions such as teaching the patient how areas of macular degeneration are affecting their reading.



## Determination and Diligence Mark the Career of HMS Ophthalmology Legend: Claes Henrik Dohlman, MD, PhD

Claes Henrik Dohlman, MD, PhD, Emeritus Professor of Ophthalmology at Harvard Medical School, was born in 1922 in Uppsala, Sweden. Dr. Dohlman earned his MD and a Doctorate of Medical Research (biochemistry) from the University of Lund in Sweden, and completed his residency in ophthalmology in the Eye Clinic of the University of Lund. In 1958, he was recruited to work at The Retina Institute of Boston by former mentor and world-renowned retina surgeon, Dr. Charles Schepens, founder of the Institute (now Schepens Eye Research Institute). He was also asked by Dr. Edwin Dunphy, then Chief of Staff at Mass. Eye and Ear, to establish a Cornea Service at the Infirmary. In 1974, the same year he achieved HMS professorial status, Dr. Dohlman was appointed Chairman of the Department of Ophthalmology of Harvard Medical School, Director of the Howe Laboratory of Ophthalmology, and Chief of Ophthalmology at Mass. Eye and Ear.

In a career that now spans six decades, Dr. Dohlman stands as one of the most highly honored ophthalmologists in the world. Recognized as the founder of modern corneal science, his work is considered “classic” literature on understanding corneal biology. His investigations of corneal physiology laid the groundwork for modern clinical practice in dry eye disease, management of corneal burns, wound healing, corneal transplantation, and keratoprosthesis.

His career reflects a remarkable number of firsts: Dr. Dohlman was first in the world to create an organized cornea subspecialty (Mass. Eye and Ear), first to create a formal structured cornea fellowship program (Mass. Eye and Ear and Schepens), first to recruit full-time cornea fellows to HMS, and first to pioneer surgical innovations in keratoplasty and keratoprosthesis. His most notable achievement is the Boston Keratoprosthesis (KPro), an artificial cornea he first conceptualized in the 1960s and is now the most successful artificial cornea in the world with over 5,000 implantations to date. During his career, Dr. Dohlman has trained first-hand over 200 cornea specialists—more than any other ophthalmologist in the world. His “real” contributions to ophthalmic


education are incalculable considering the hundreds of second- and third-generation cornea specialists who have trained under his protégées, and the thousands more who have benefitted from his prolific contributions to corneal literature and science.

In 2007, the American Academy of Ophthalmology named Dr. Dohlman recipient of the Laureate Award—the highest honor possible to bestow by the Academy—in recognition of his contributions spanning 50+ years of continuous service to the profession. The following year, he was again honored for his lifetime accomplishments in a named Harvard Professorship whose first incumbent is Dr. Reza Dana, famed for his pioneering science in corneal immunology and transplantation biology.

“Dr. Dohlman’s opus of research and clinical work set the stage for a world-class cornea center of excellence at Harvard,” remarked chief and chair Joan W. Miller. “His work has benefitted millions of people around the world, and his legacy of knowledge thrives today in the hundreds of fellows, students and colleagues he has trained and mentored over the years. Harvard Medical School—and indeed, the whole world—is a far better place today because of his remarkable talent, contributions, and character.”

Dr. Dohlman retired from formal administrative roles in 1989. Today, at the age of 88, he continues to advise and mentor students and colleagues, run a specialized KPro patient clinic, and pursue multi-disciplinary research to enhance clinical KPro outcomes. Despite a lifetime of achievement, Dr. Dohlman is remarkably self-effacing. While he acknowledges his numerous accomplishments, he prefers not to focus on what he has achieved, but rather what still needs to be accomplished—particularly in the area of KPro development. He continues to shape and set new standards for the field, and remains an inspiration to everyone in the Harvard community—and beyond.

*An interview with Dr. Claes Dohlman begins on page 160.*



“Dr. Dohlman’s work has benefitted millions of people around the world and his legacy of knowledge thrives today in the hundreds of fellows, students and colleagues he has trained and mentored over the years. Harvard Medical School—indeed the world—is a far better place today because of his remarkable talent, contributions and character.”

— Joan W. Miller, MD





## Mary Louise Jackson, MD

Assistant Professor of Ophthalmology, Harvard Medical School

Director, Vision Rehabilitation Center, Massachusetts Eye and Ear Infirmary

Dr. Mary Louise Jackson is a vision rehabilitation expert, committed to helping patients with impaired vision make the best use of their remaining eyesight. As Director of the Vision Rehabilitation Center (VRC) at Mass. Eye and Ear, Dr. Jackson aims to provide optimal treatment through rehabilitation techniques and visual aids. A graduate of York University in Toronto, Dr. Jackson completed her MD and internship at McMaster University in Hamilton, Ontario. She completed a residency in ophthalmology at the University of Toronto, and practiced in Victoria, British Columbia prior to joining the HMS Department of Ophthalmology in 2006.

One of Dr. Jackson's research interests is Charles Bonnet hallucinations, which are recurrent visual hallucinations seen by otherwise healthy individuals with significant vision loss. She is examining patients referred to the VRC to determine the frequency of these hallucinations, why patients experience them, and how they affect quality of life. She is involved with national research collaborations, and is currently conducting a trial of the impact of using a video magnifier on reading performance.

Dr. Jackson's focus is clinical practice and resident education. At Mass. Eye and Ear, she has restructured the multi-disciplinary VRC to follow a patient-centered model of rehabilitation. Under her direction, the VRC has seen significant growth in patient referrals, and is rapidly emerging as a national leader in the field. Dr. Jackson is the Secretary on the Executive Committee of the International Society for Low Vision Research and Rehabilitation. She serves on the American Academy of Ophthalmology's Vision Rehabilitation Committee; as Chair, she leads the development of a national vision rehabilitation residency curriculum and a web-based vision rehabilitation course for ophthalmology residents.

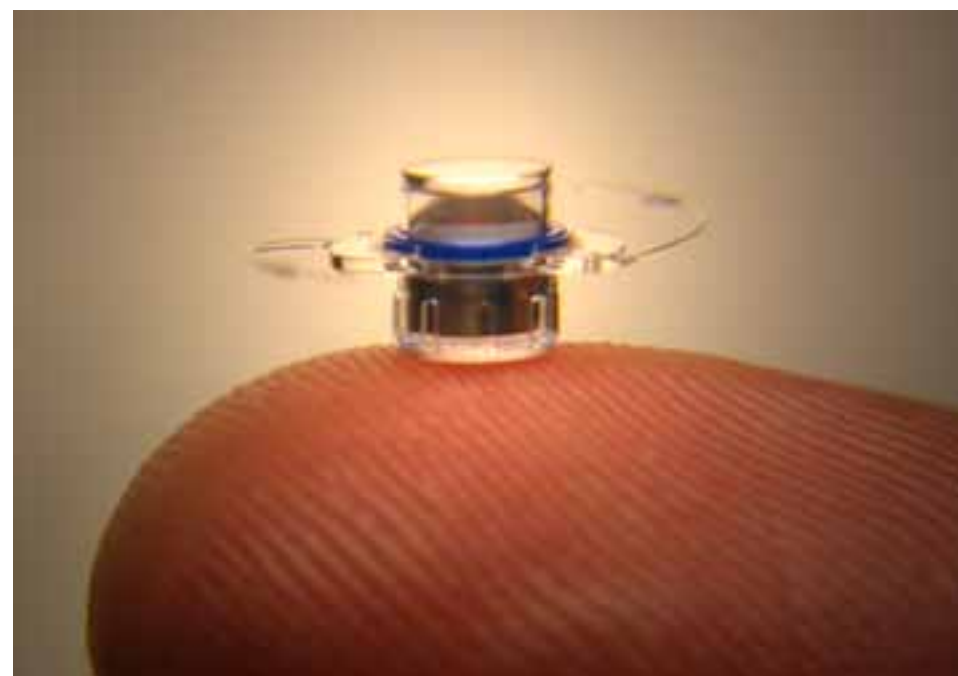
### Tiny telescope restores vision to some AMD patients

Jo Ann Preece has a spring in her step and a sparkle in her eye despite living with end-stage age-related macular degeneration (AMD). The vibrant 84-year-old had a miniature telescope implanted in her eye in 2003 during a clinical trial at Mass. Eye and Ear. At a recent check up, JoAnn peered out of a sixth floor window and saw the cars driving by below. Before the surgery, these cars—and everything else—would have appeared blurry. “It’s like you’re in a fog,” JoAnn explains. “I stopped driving and reading.”

The CentraSight® Implantable Miniature Telescope (IMT), a new option for some AMD patients, gave JoAnn a new outlook on life—literally—by restoring central vision to one of her eyes. This innovative device is surgically implanted in one eye, where it magnifies and projects central images onto a healthy portion of the retina. This enables patients to see objects in fine detail, and perform “near” activities like reading, watching TV and recognizing faces. The non-implanted eye is then used for peripheral vision.

Post-surgery rehabilitation helps patients develop the skills needed to make their eyes work together to achieve the best possible vision.

Dr. Kathryn Colby has played a key role in optimizing methods for implanting the miniature telescope in AMD patients, and described the surgical procedure in the August 2007 issue of *Archives of Ophthalmology*. Dr. Colby was also an investigator in a multicenter clinical trial that showed the IMT significantly improved vision in most patients who received the implant. She describes the pea-sized technology as a true “breakthrough” for millions of patients with end-stage AMD, whose treatment options, until now, have been limited. But she also cautions that the telescope, approved by the FDA in July 2010, will not work for everyone, and is geared specifically for patients 75 years and older with blind spots (bilateral central scotomas) associated with end stage AMD. For many of these patients, however, the device is life-changing. “Over 90 percent of patients in the clinical trial improved two lines in vision as measured in the doctor’s office, but what really matters is how this technology impacts quality of



life,” Dr. Colby said. “Can you write out a check? Watch TV? See your grandson’s face? That’s significant improvement.”

### Restoring peripheral visual function with prisms

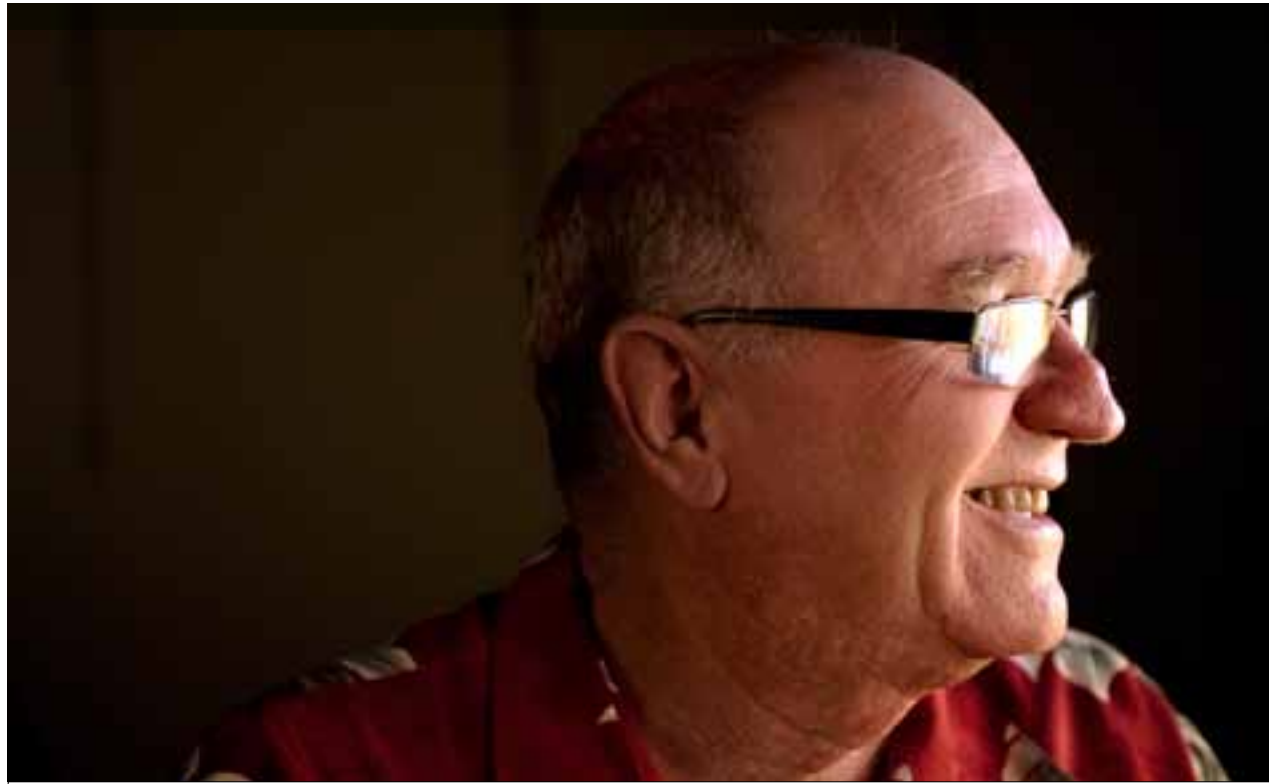
Peripheral vision loss makes it extremely difficult for patients to navigate safely around objects and other people. This occurs in retinitis pigmentosa, which causes gradual loss of eyesight starting from the outside edges of the visual field. Another condition that affects peripheral vision is homonymous hemianopia, which causes loss of half of the visual field on one side in both eyes—not due to a problem with the eyes themselves, but rather due to brain injury. Stroke, trauma, brain tumors, and surgery are com-

mon causes of this condition, which affects over one million people in the United States. Hemianopia can severely impact activities of daily living, such as driving or even walking.

Dr. Eli Peli, Co-Director of Research at Schepens Eye Research Institute and Professor of Ophthalmology at HMS, has devised a solution using prism lenses. Mounted on eyeglasses, the prisms redirect images from a blind side and project them onto functional parts of the visual field. This causes objects from the blind side to appear as “ghost images” in the remaining visual field. People wearing these special prism glasses can then be aware of objects in their blind side, and make adjustments to either examine them further or move to avoid collision. So far, the prism lenses have been

tested in two multi-center clinical trials directed by Dr. Peli, who is also an optometrist and Director of the Vision Rehabilitation Service at the New England Eye Center. In the first trial, published in the May 2008 issue of *Archives of Ophthalmology*, 43 patients with hemianopia reported that the prism glasses were “very helpful” in navigating around obstacles. These results were confirmed in a later randomized control study of 61 patients, presented at ARVO 2010. At around \$600 for glasses with permanently mounted prisms—and even less for temporary stick-on prisms—these lenses represent an affordable breakthrough for people with hemianopia and other conditions that cause peripheral vision loss.





## Eliezer (Eli) Peli, MSc, OD

Professor of Ophthalmology, Harvard Medical School

Senior Scientist, Co-Director of Research, and Moakley Scholar in Aging Eye Research, Schepens Eye Research Institute

Director Vision Rehabilitation Service, New England Eye Center

Dr. Eli Peli, trained as an engineer and optometrist, is a worldwide authority in low vision. Born in Tel-Aviv, Israel, Dr. Peli earned his BSc and MSc degrees in electrical engineering from the Technion-Israel Institute of Technology. Since 1983, when he received his DO degree from the New England College of Optometry, Dr. Peli has specialized in vision rehabilitation care. He has developed innovative clinical techniques and a variety of low vision aids, and continues to provide specialized patient care as Director of the Vision Rehabilitation Service at New England Medical Center Hospital in Boston. At Schepens, where he is Senior Scientist and Moakley Scholar in Aging Eye Research, Dr. Peli leads the Vision Rehabilitation Laboratory and the Mobility Enhancement Center; additionally, he serves as Co-Director of Research.

Drawing upon his multidisciplinary expertise, Dr. Peli consults for the National Institutes of Health, NASA Aviation Operations Systems, National Highway Safety Administration, Federal Motor Carrier Safety Administration, Natural Sciences and Engineering Research Council of Canada, and numerous high-tech and ophthalmic corporations. He holds various editorial board positions and co-founded TaperVision Inc., a manufacturer of fiber-optics-based magnifiers for the visually

impaired, and Visya, Inc., a manufacturer of adjustable spectacle lenses for presbyopia. He serves as Professor of Ophthalmology at HMS and Adjunct Professor at both New England College of Optometry and Tufts University School of Medicine.

Dr. Peli's work reflects his multifaceted background in engineering, optometry, and vision research. With over 150 scientific publications, two books, and nine patents, he has made significant contributions to the areas of eye movement analysis, image processing, image communications, and optics. In the last decade, Dr. Peli's work has concentrated on issues of mobility with impaired vision, including pedestrian mobility and driving. The Peli Lens, which Dr. Peli developed for a form of vision loss known as hemianopia ("half blindness"), represents a clinical breakthrough for individuals with peripheral vision loss.

During his career as a clinician scientist, Dr. Peli has received several notable and prestigious awards. These include the Pisart Vision Award from Lighthouse International, a worldwide organization dedicated to vision research, rehabilitation, and advocacy. Dr. Peli was co-recipient of the 2004 Alfred W. Bressler Prize in Vision Science (along with Robert Massof, PhD, of Johns Hopkins University) and received the 2009 Alcon Research Institute award. In 2009, Dr. Peli was also honored by the American Academy of Optometry with the William Feinbloom Award, which is given annually to individuals who have made distinguished and significant contributions to the advancement of visual and optometric service. More recently, he was awarded the 2010 Otto Schade Prize from the Society for Information Display and the 2010 Edwin H Land Medal by the Optical Society of America.

## PROSE treatment: for some people, simply a miracle

Astonishing. Miraculous. Life altering. This is how some patients have described the powerful and life-transforming impact of a small, plastic prosthetic device. More than two million people in the United States suffer from complex corneal disease, making their lives a painful, daily struggle. Dr. Perry Rosenthal, HMS Assistant Clinical Professor of Ophthalmology, is a pioneer and innovator in the field of contact lens and the treatment of eye disease. As Founding President and Vice Chairman of Boston Foundation for Sight, Dr. Rosenthal has spent the last two decades developing and refining this life-changing treatment, which has restored sight to thousands of people blinded or impaired by corneal disease, helping them to reclaim their lives.

The concept behind this treatment is simple but groundbreaking: prosthetic replacement of the ocular surface ecosystem (PROSE) uses

a piece of gas-permeable plastic, about the size of a nickel, to replace or support the functions of the ocular surface system. Unlike contact lenses, which touch the cornea, PROSE devices are designed to "vault" over the cornea and rest on the sclera, the sturdy white of the eye.

The device is filled with sterile saline at the time of insertion. Once inserted, the device protects the cornea and conjunctiva from the environment and blink trauma, while creating a reservoir of fluid that continuously bathes the ocular surface with oxygenated artificial tears. A PROSE device creates a transparent, smooth optical surface over a damaged or irregular cornea, masking imperfections, and improving vision by transmitting a sharp image to the back of the eye.

PROSE devices are made using a proprietary CAD/CAM software system linked to a manufacturing lathe via the internet. The system uses mathematical functions, called splines, which allow physicians at Boston Foundation for Sight and its partner clinics to design and fit prosthetic devices to each eye to exacting specifications that maximize ocular surface system function. For patients with complex corneal disease—many of whom have suffered from blinding and painful ocular conditions for years—the devices are immediately transforming, capable of restoring vision and mitigating symptoms, including pain and light sensitivity.

Although this technology was initially developed for patients with irregular astigmatism from keratoconus, trauma, or cornea transplantation, the benefits became apparent for patients with ocular surface disease, including Stevens-Johnson syndrome, chronic ocular graft-versus-host disease (GVHD), Sjogren's syndrome, and neurotrophic keratitis. Continuous technological and clinical innovations have yielded a treatment approach

## Boston Foundation for Sight: restoring sight, reclaiming lives

Today, PROSE treatments for the majority of patients are covered by health insurance, although this was not always the case. Based on the principle that "sight should not be a gift—it should be a birthright," Dr. Rosenthal founded Boston Foundation for Sight (BFS) in 1994 as a nonprofit eye health care organization. The organization is dedicated to restoring vision and improving the quality of life for patients and their families, regardless of their ability to pay. Since its inception, the Foundation has provided free care to approximately 20 percent of its patients.

Under Dr. Rosenthal's stewardship, BFS has evolved into a renowned and innovative corneal research, education, and treatment facility. PROSE has become an invaluable, front-line tool for helping patients manage the debilitating effects of complex corneal disease—combining patient-centered medical care, advanced clinical research, professional education, and community outreach. To broaden its availability, the Foundation recently established PROSE clinics in partnership with top-ranked academic medical centers in the United States and abroad, including the University of Southern California's Doheny Eye Institute in Los Angeles, and Weill Cornell Eye Associates at Weill Cornell Medical College in New York. Dr. Deborah Jacobs, Assistant Clinical Professor of Ophthalmology and Director of the Core Medicine Clerkship at Mass. Eye and Ear, joined Boston Foundation for Sight in 2006 as Medical Director. "Boston Foundation for Sight plays a unique role in the rehabilitation of patients with complex corneal disease," she says. "My goal as Medical Director is to increase awareness, appreciation, and availability of our treatment and approach to patient care, which together produce life-changing results."

Twice monthly at Mass. Eye and Ear, Dr. Jacobs sees patients referred by other physicians for consideration of PROSE treatment. If needed, candidates for treatment are referred to BFS headquarters in Needham, MA. Additionally, Mass. Eye and Ear cornea fellows come to Boston Foundation for Sight for a rotation under Dr. Jacobs' supervision, where they learn about all facets of the BFS treatment model and collaborative, patient-centered approach to care. The fellows also participate in clinical research projects that have led to presentation at scientific meetings and publication.



PERRY ROSENTHAL, MD



with demonstrated clinical benefits and cost-effectiveness, as highlighted recently in publication in the *American Journal of Ophthalmology*. A recent study published in *Seminars in Ophthalmology* details the case reports of five patients who have a history of significant corneal disease and glaucoma surgery who benefited from this innovative approach to visual rehabilitation.

### Improving peripheral vision in AMD patients

For some, even the best available medicines for AMD can only delay the gradual loss of vision; for others, the treatments may not help at all. As a result, some people with AMD may be left with only peripheral vision—which makes it extremely difficult to read or to see complex images. Dr. Peter Bex, an Associate Scientist at Schepens Eye Research Institute, uses computational models to understand how the brain processes peripheral vision, and uses this information to explain why it is so difficult to see details in the peripheral field. Dr. Bex is studying a phenomenon known as crowding, an effect that makes magnified peripheral images very difficult to distinguish. Because people with AMD often use magnifying lenses to read, these studies may lead to new rehabilitation techniques to improve peripheral vision. Dr. Bex and colleagues also showed that when people try to read with their peripheral vision, the size or shape of the letters may not be as important as how stable the images are. These results suggest that vision therapy with fixation training may help people to stabilize images in their peripheral fields to best utilize their remaining vision.

### Emerging retinal prosthesis technology aims to restore sight to the blind

A state-of-the-art retinal prosthesis, designed to help some people blinded by retinal disease to regain a portion of their vision, may soon be within reach. In many retinal disorders, such as retinitis pigmentosa and age-related macular degeneration (AMD), the image-sensing photoreceptors (rods and cones) eventually die—resulting in vision loss. However, even in patients who become legally blind, cells in the optic nerve—which connects the retina to the brain—may still be alive and functional.

Hoping to take advantage of the surviving nerve cells, Dr. Joseph Rizzo III and scientists of the Boston Retinal Implant Project are developing an implantable microelectronic prosthesis that will deliver visual information to the brain through the remaining retinal circuits. This highly sophisticated “bionic eye” will consist of internal electronic components that will be implanted around and behind the eyeball. Users wear a small camera, mounted to eyeglasses, that captures visual scenes and converts them into electrical impulses. The impulses are transmitted wirelessly to the prosthesis which stimulates the healthy nerve cells. The nerve cells, in turn, carry the visual impulses to the brain for image processing—helping patients with macular degeneration or retinitis pigmentosa regain some vision. Special innovations to the prosthesis include an ultra-low power design and a geometric architecture that minimizes that amount of hardware that is placed into the eye. The team has also developed a minimally invasive surgical method

of implantation.

The retinal implant may not work for all blind patients—particularly those with significant optic nerve damage, or those who were born blind because the visual centers in the brain have not developed. Furthermore, it’s still too early to tell exactly how much vision can be restored by the retinal prosthesis. Nonetheless, many blind patients maintain that even the smallest improvements to their eyesight can dramatically improve their quality of life. This technology represents a major milestone toward restoring some vision in many patients blinded by retinal disease.

Dr. Rizzo, Director of the Center for Innovative Visual Rehabilitation at the Boston Veterans Administration and Director of the Neuro-Ophthalmology Service at Mass. Eye and Ear, founded the Boston Retinal Implant Project in the late 1980s. This collaborative effort of Mass. Eye and Ear Infirmery, Massachusetts Institute of Technology, U.S. Department of Veterans Affairs, Schepens Eye Research Institute, Boston University Medical Center, and the University of Alabama brings together experts with diverse backgrounds. This multi-disciplinary team hopes to treat many forms of blindness by overcoming both the biological and engineering challenges of creating an advanced retinal prosthesis. Drs. Rizzo and John Loewenstein performed the first surgery to insert microelectronic components onto the retina of a human eye in 1998, and have since performed successful short-term electrical stimulation studies in humans. Soon, Dr. Rizzo’s team will perform longer-term studies with the retinal implants, which could last longer than 10 years in the eye.



## Joseph Rizzo III, MD

Professor of Ophthalmology, Harvard Medical School

Director, Neuro-Ophthalmology Service, Massachusetts Eye and Ear Infirmery

Director, Center of Innovative Visual Rehabilitation, Department of Veterans Affairs, Boston, MA

Founder and Co-Director, Boston Retinal Implant Project

Dr. Joseph Rizzo III is a clinician scientist dedicated to understanding the mechanisms of vision loss, and his decades-long mission has focused on improving the diagnostic and treatment methods for blinding diseases. A native of New Orleans, Dr. Rizzo received his undergraduate and medical training at Louisiana State University. Following an internship in adult medicine at UCLA Medical Center, Dr. Rizzo completed both a neurology residency at Tufts University/New England Medical Center and an ophthalmology residency at Boston University. He completed a clinical fellowship in neuro-ophthalmology at Mass. Eye and Ear before joining the faculty of the HMS Department of Ophthalmology.

As a clinician, Dr. Rizzo specializes in visual disorders that result from damage to the eye or brain. He is Director of the Neuro-Ophthalmology Service at Mass. Eye and Ear, which houses three of only a handful of dually trained neuro-ophthalmologists worldwide. Dr. Rizzo evaluates roughly 40 percent of all patients referred to the service, and collaborates closely with neurologists at MGH to deliver high-quality care for patients with visual disorders. As Professor of Ophthalmology at HMS, Dr. Rizzo is directly responsible for training clinical fellows, residents, and medical students in neuro-ophthalmology. He regularly delivers lectures on diverse ophthalmic issues, and directs the neuro-ophthalmology section of the Lancaster Course, which is the oldest and largest training course for ophthalmologists.

Dr. Rizzo devotes a major portion of his professional focus to developing new therapeutic options for vision disorders. He is Director of the Center of Innovative Visual Rehabilitation at Boston Veteran’s Administration Hospital and Co-Director of the Boston Retinal Implant Project (BRIP), an initiative he founded in 1988 to develop a retinal prosthesis for patients with acquired blindness. This multidisciplinary and international research collaboration now includes scientists and clinicians from over 20 institutions worldwide. For his significant contributions to visual science, Dr. Rizzo was presented with the Senior Achievement Award by the American Academy of Ophthalmology in 2007.

“Developing a retinal prosthesis is an enormous challenge, but if you never dive in you’ll never have an option for treatment.”

—Joseph Rizzo III, MD, Co-Founder of the Boston Retinal Implant Project (BRIP)

### It takes vision...

to get vision, which is remarkably complex. Developing a retinal prosthesis requires sophisticated engineering technology aimed at stimulating electrodes on the retina while protecting the delicate prosthesis. Equally tasking is the physical challenge of implanting the device in and around the eye without harming the retina. The advent of micro-fabrication technology 15 years ago has enabled Dr. Rizzo and his team to embed wires and electrodes onto an ultra thin plastic “membrane” many times thinner than a human hair. This membrane is the only component of the prosthesis that comes in contact with the delicate retina.

### It takes a deep fund of knowledge...

and an understanding of how the brain interprets data coming from the retina to develop a functional and useful prosthesis. The BRIP is now focusing considerable effort to unravel some of these mysteries. “Despite the challenges,” said Dr. Rizzo, “we’ve made considerable progress on many fronts and I believe solutions are within reach.”

### It takes a village...

of collaborators with multidisciplinary talents to move a research project of this magnitude forward, and the BRIP enlists experts from a diverse array of fields. Today, the 36-member team is comprised of retinal surgeons, physiologists, biologists, rehabilitation specialists, material engineers, chip designers, wireless communication specialists, and metallurgists.

### It takes resources...

Now in its third decade of development, the bionic prosthesis has required continuing and substantial resources. Initially funded by private industry and some federal monies, the project received a financial boost in 2001 with a grant from the U.S. Department of Veterans Affairs.

To find out more visit:  
[www.bostonretinalimplant.org](http://www.bostonretinalimplant.org)