“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 Pulse, Navy Veteran, Photographer and Visual Artist
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.
Around the world, an adult goes blind every five seconds and a child goes blind every minute.

— National Eye Institute

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 layer of supporting 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 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 makes up about 10 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 angio genesis 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 (HMS ARG, see footnote on page 86), 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 commitment 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 research conducted under the auspices of the collaborative work pursued by HMS clinician scientists has established new paradigms merged with clinical care. Vi suudyne® 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.

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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 ophthalmologist to get reading glasses. During her exam, the ophthalmologist noticed accumulations of drusen (deposits) beneath the retina—an early finding of AMD. The ophthalmologist 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, two decades after her diagnosis, she noticed while playing golf one day that another person on the tee appeared to have “squir- glied” vision. Gloria 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 worsened 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—the procedure 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 JoAnn 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 20/120 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, “The number of patients showing 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 20/20 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 20/20 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 again.

“Lucentis®, Dr. Miller notes, “is the first treatment that, when properly given, can maintain the vision of more than 90 percent of patients with wet AMD.” This is good news for the 150,000 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 each treatment 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 of more treatments 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 at HMS, continue during the last two decades, mean that millions of people di- agnosed 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 the disease. Although studies have shown that vitamins 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 remains a top priority in the field. 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 model. Some exciting avenues of research and study include:

- Making current anti-VEGF treatments more “patient-friendly” by i) reducing the frequency of intravitreal treatments while optimizing their ef- fects, and ii) developing drugs ex vivo and direct injections into the eye, or developing new intravitreal therapies, thereby reducing or eliminating the need for intravitreal injections or eye drops.
- Developing new combination therapies that slow down 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 en- vironmental 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.
- “Robustness” or dead or damaged photoreceptors (rods and cones) through nerve regeneration tech- niques, as well as stem cell therapy, which has been shown to be promising.
- 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 degener- ation. 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 Diabe- tes Center, and the inaugural chair of the NIH-funded DRCR.net network. Nearly three decades ago, Dr. Lloyd P. Aiello’s grandfather, Wil- liam P. Beetham, MD, PhD, and father, Lloyd M. Aiello, MD, pioneered laser photoacoagulation, the first treatment shown to be effective at preventing or improving vision loss from proliferative diabetic retinopa- thy and diabetic macular edema, common complications of diabetes and a leading cause of vision loss in the working-age popu- lation. Since the introduction of laser photoacoagulation for diabetic eye complications, millions of people worldwide have benefited from this treatment, which can preserve vi- sion and reduce the risk of blindness in 90 percent of patients. Now, find- ings from the DRCR.net study dem- onstrate that anti-VEGF therapies may prove to be even more effective than the standard laser therapy by further re- ducing diabetic retinopathy-associated swelling in the retina.

Initially designed as a three-year study, involving 52 sites within the DRCR.net network, the trial—now in three years—has been extended to five years, and is supported by the National Institutes of Health and the National Institute of Diabetes and Digestive and Kidney Diseases.
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 2002, he first sought the help of Drs. Jennifer Sun and Lloyd P. Aiello, ophthalmologists at Boston’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 15 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.”

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. Uveal melanoma is a tumor 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, in a matter of decades, PBT has proven to have the lowest local recurrence rate of any radiation therapy. There are now 35 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 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 Varvavas 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 his colleagues may uncover innovative therapeutic and diagnostic methods for this prevalent and potentially deadly cancer.
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 at 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 1979, Dr. Gragoudas joined the full-time faculty at Mass. Eye and Ear. He was promoted to HMS Professor of Ophthalmic Pathology 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 aproven and safe alternative to enucleation. Along with refining proton beam therapy, Dr. Gragoudas has studied the epidemiology, genetics, and molecular biology of uveal melanoma for further improvement in 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 Verteporfin 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 Adams, Patricia D’Amore, and others in collaboration with the laboratory of famed anti-angiogenesis proponent, Dr. J. 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 Honor Award of American Academy of Ophthalmology, Retina Research Foundation prize of the Jules Gorin Lectureship, Senior Scientific Investigators Award from Research to Prevent Blindness, Senior Investigator of the American Academy of Ophthalmology, J. Donald M. Gass Medal of the Macula Society, and the Agora Award of the American Academy of Ophthalmology. Dr. Gragoudas’ mentorship has been recognized by numerous awards, including the Annual Poster Award 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 Vovas, Joan Miller, and Evangelos Gragoudas set out to find safer treatments for retinoblastoma.

Dr. Gragoudas and colleagues focused on retino-5-aminoimidazole-4-carboxamide-1-beta-4-ribofuranoside (AICAR), which inhibits the enzyme cell growth and cell proliferation. Along with colleagues, they found that they could inhibit retinoblastoma cells with a chemical that inhibits AMPK. This chemical, called 5-aminomidazole-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 Mukaï, 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. Mukaï 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. Mukaï 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 of these vascular malformations are known as hemangiomas, which are actually non-cancerous tumors made of abnormally high numbers of 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 was pressuring her eye, and blocking her vision in one eye. Alicia was treated by Dr. Aaron Pay of Mass. Eye and Ear’s Ophthalmic Plastic and Reconstructive Surgery Service.

In collaboration with the Vascular Birthmarks Foundation, Dr. Fay dicated 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 recognized 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.
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 keratoplasty (KPro) patients, Drs. Joseph Ciclione, Daniel Kobane (MIT and Children’s Hospital Bos- ton), Glaes 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 pharmacological agents) that is encapsulated within a hydrogel material that is used in standard contact lenses. The lens is characterized 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. Dr. Srinivasan, in a collaboration with an ophthalmology group at the University of California, identified IGF-1 levels as a key predictor of whether an implant 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” 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 may develop the condition in adulthood as a result of injury or illness. 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 Infirmary 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 gentle 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.”

Dr. 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 a 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 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 at 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, inadequate control of and patient compliance are regu- lar 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 Bizio, 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-fibroelastic growth factors to prevent opaque membrane development, which may in turn reduce the number of follow-up laser surgeries. Other key features include fewer complications post-surgery, reducing or eliminating the need for vision rehabilitation, and decreasing the need for medicated eye drops.

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 condi- tions 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.
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 recent 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.

Surgical advances benefit glaucoma patients

Glaucoma is the second leading cause of irreversible blindness in the United States,—afflicting 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.

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 lower risk of complications.

Trabectome surgery works by treating the eye’s primary “drain,” called the trabecular meshwork, which helps to remove fluid from the eye. The procedure is appropriate for patients with open-angle innervation, 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 explained 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 trabeculectome surgery, Mass. Eye and Ear is also the first academic medical center in New England to offer canoplasty—an 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, canoplasty utilizes an external approach with a rapid, non-invasive, transcutaneous approach to the interior of the eye. During canoplasty, surgeons dilate the canal behind the trabecular meshwork and place a suture to keep the canal open. As with trabectuclidean surgery, canoplasty helps to provide better drainage 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,” says Dr. Rhee. Fran agrees. “I’m one happy camper,” she says.
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, corneal 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 actually receive them.

In many of patients who need corneal transplants, suitable donor corneas are hope for restoring vision. However, cornea transplants are the only option for treating blindness from corneal disease. In many cases, including 1.5 million children—who are blind from corneal disease—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 Drs. Claes Dohlman in the 1960s, the Boston KPro received FDA approval 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 Robert Pineda II, is 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 in the clinic. Contact lenses are now worn continuously to improve graft retention and prevent irreversible and evaporative damage; with the current efforts of Dr. Joseph Cibis 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 growing number of conditions. Studies using combined immunomodulatory therapy with the Boston KPro, 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 disease caused by herpetic keratitis. At Mass. Eye and Ear, and 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 expand its indications. Current research in collaboration with Dr. Eli Peli at Schepens Eye Research Institute, utilizes OCT imaging in various Boston KPro models to help clinicians determine how patients are studying ways to prevent postoperative retinal detachment, and Dr. Renee Gipson is leading an effort to inhibit enzymes that can cause tissue melt and perforation around the Boston KPro. Dr. Irmgard Behlaus and colleagues are examining anti-bacterial coatings for the device surface at the Keane lab at MIT. Dr. Daniel Kohn 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 55 million Americans aged 65 and over who will suffer some form of visual impairment—a number that will rise to 82 million by 2050. 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 were few vision-saving tools, technologies, and therapies to prevent you from going blind or slowing the progression of AMD. Four decades later, enhanced diagnostic tools and therapies to evaluate and treat 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 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 ophthalmoscopes (SLO) with macular perimeters. Far more sensitive and accurate than the Amsler Grid, this unique tool evaluates a patient’s visual field and helps to determine how large areas of macular degeneration are affecting their reading ability. In Boston, the Scanning Laser Ophthalmoscope (SLO) is a tool used for detailed examination of the retina. The patient is seated in a comfortable chair, and the examining doctor uses a special instrument called a slit lamp to shine a beam of light into the patient’s eye. The light is then reflected back to the doctor’s eye, allowing them to see the retina in great detail. The SLO allows the doctor to look into the eye and see the blood vessels, nerve fibers, and other structures that make up the retina. This information is used to diagnose and monitor conditions such as diabetic retinopathy, macular degeneration, glaucoma, and other diseases that affect the retina. The SLO is able to detect very small changes in the retina that cannot be seen with the naked eye or even with a regular ophthalmoscope. This allows for early detection and intervention, which is critical in preserving vision. The SLO is an important tool in the field of ophthalmology and helps doctors provide the best care possible for their patients.
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 protégés, and the thousands more who have benefited 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.

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

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
Tiny telescope restores vision to some AMD patients

JoAnn 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 70 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 common 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, Scheie 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 1985, when he received his OD 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 Eye Center Hospital in Boston. At Scheie, 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 Typervision 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 clinical scientist, Dr. Peli has received several notable and prestigious awards. These include the Pierscionk Vision Award from Lighthouse International, a national, 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 Ophthalmology 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 corneas and rest on the sclera, the sturdiest white of the eye. The device is filled with sterile saline at the time of insertion. Once inserted, the device protects the corneas 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 optimize performance specifications that maximize ocular surface system function. For patients with complex corneal disease—many of whom have suffered from blocking and painful ocular conditions for years—the devices are immediately transform ing, 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 corneas transplanted, 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 that has led to presentation at scientific meetings and publication.

**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. BFS 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 Well Cornell Eye Associates at Well Cornell Medical College in New York. Dr. Deborah Jacobs, Assistant Clinical Professor of Ophthalmology and Director of the Core Medicine Clinic at Massachusetts Eye and Ear, joined Boston Foundation for Sight in 2006 as Medical Director. “Boston Foundation for Sight fills a unique role in the rehabilitation of patients with complex corneal disease,” she says. “My goal as Medical Director is to increase awareness 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.
with demonstrated clinical benefits and cost-effectiveness, as high- lighted 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 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 be as important as how stable the image is. 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, the University of Alabama, and the University of Massachusetts Institute of Technology, U.S. Department of Veterans Affairs, Schepens Eye Research Institute, and the Department of Ophthalmology, Boston University, 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 believe solutions are within reach.”

Joseph Rizzo III, MD
Professor of Ophthalmology, Harvard Medical School
Director, Center for Innovative Visual Rehabilitation, Department of Veterans Affairs, Boston, MA
Founding Director, Boston Retinal Implant Project

It takes a village... of collaborator with multidisciplinary talents to move a research project of this magnitude forward, and the BRIP enlists experts from a diverse array of fields. The BRIP’s 11-member team is comprised of retinal surgeons, physicists, biologists, rehabilitation specialists, materials engineers, chip designers, wireless communication specialists, and metallurgists.

It takes resources... Now in its third decade of development, the bionic prosthesis has required continuous 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