

ADVANCES IN OPHTHALMOLOGY

George A. Cioffi, MD
 Ophthalmologist-in-Chief
 NewYork-Presbyterian/
 Columbia University Medical Center
 gac2126@cumc.columbia.edu

Donald J. D'Amico, MD
 Ophthalmologist-in-Chief
 NewYork-Presbyterian/
 Weill Cornell Medical Center
 djd2003@med.cornell.edu

SAVE THE DATE

Tele-Ophthalmology and Artificial Intelligence Conference

April 6, 2018

Philanthropy New York
 1500 Broadway
 New York, NY 10036

To Register or For More Information
www.columbiacme.org



New York's #1 Hospital
 17 Years in a Row.

The Rarefied World of Ocular Oncology

An estimated 3,000 adults in the United States will be diagnosed with primary intraocular melanoma this year. Relatively rare, cancers of the eye require the expertise of an ocular oncologist with experience in the diagnosis, treatment, and management of ocular tumors.

Brian P. Marr, MD, Director of Ophthalmic Oncology at NewYork-Presbyterian/Columbia University Irving Medical Center, is one of the few ocular oncologists in the country trained in all aspects of eye cancers and whose clinical experience in treating these diseases is among the most extensive. Dr. Marr's focus on ophthalmic oncology began during an eight-year tenure in the Ocular Oncology Service at the Wills Eye Hospital in Philadelphia. There, he gained extensive knowledge treating intraocular tumors, and tumors of the eyelid, orbit, and conjunctiva in adults, children, and infants.

Dr. Marr, who joined NewYork-Presbyterian in May 2017 from Memorial Sloan Kettering Cancer Center, is a world leader in the clinical development of therapies for ocular melanoma. He also helped



Dr. Brian P. Marr

pioneer the technique of delivering intra-arterial chemotherapy and other treatments for intraocular retinoblastoma, the most common malignant cancer of the eye in children, sparing them enucleation. The treatment regimen is now being performed in countries throughout the world.

(continued on page 2)

Retinal Detachment: Improving Outcomes with Technique and Technology

The incidence of rhegmatogenous retinal detachment, the most common type of retinal detachment, has been reported to be between 6.3 and 18 per 100,000 each year. The age-specific incidence increases to a peak in both sexes in the 60- to 70-year age group.

“The estimated lifetime risk is 3 percent at 85 years of age. The risk increases in patients with

high myopia, presence of lattice degeneration, trauma, or after cataract surgery. Retinal detachment is a major cause for universal vision loss if not treated quickly,” says **Thanos Papakostas, MD**, a retinal specialist in the Department of Ophthalmology at NewYork-Presbyterian/Weill Cornell Medical Center.

According to Dr. Papakostas, the surgical techniques and technology currently available today have greatly improved outcomes in the treatment of retinal detachment. In many cases, speed in treatment is critical. “Macula-on retinal detachment is, essentially, an emergency,” says Dr. Papakostas. “We operate as soon as possible, usually on the same day or next day so that we can preserve the patient's vision.”

(continued on page 3)

“The development of the small-gauge vitrectomy, wide-angle viewing systems, and the curved illuminated laser probe were key changes in the field.”
 — Dr. Thanos Papakostas

The Rarefied World of Ocular Oncology (continued from page 1)

“I was drawn to ocular oncology because it offers a diverse range of challenging problems where I feel I can make a difference,” says Dr. Marr, whose expertise spans the full range of treatment options, including intraocular tumor resection, as well as advanced laser, radiation, and chemotherapy. “Patients with ocular tumors are not your average patients. They require more resources and more time. That is one of the great aspects of our program at the Harkness Eye Institute at Columbia. We have a full-service eye hospital, a full-service oncology program, and access to multiple other subspecialists throughout NewYork-Presbyterian working together for the benefit of each patient with eye cancer.”

Targeting Uveal Melanoma

Dr. Marr has developed a strong belief that the best research be used to help his patients, rather than his best patients be used to help his research. With that philosophy, he is pursuing clinical research in a number of areas, including uveal melanoma, the most common intraocular malignancy arising from melanocytes in the iris, ciliary body, or choroid. Early diagnosis and local treatment is critical, as survival correlates with the primary tumor size. However, approximately 50 percent of patients will develop metastatic disease, with a six- to 12-month survival from time of metastatic diagnosis.

Differential Diagnosis of Uveal Melanoma by Location

Iris Lesion	Posterior Lesion
Primary iris cyst	Choroidal nevus
Iris nevus	Disciform degeneration
Essential iris atrophy	Peripheral disciform degeneration
Foreign body	Retinal pigment epithelium hypertrophy
Peripheral anterior synechia	–
Secondary metastasis	Hemangioma

“There hasn’t been a new therapy for primary treatment of this disease for over half a century,” says Dr. Marr, who is currently the Principal Investigator for a multicenter phase 1b clinical trial for a first-of-its-kind, new class of drug treatment for primary uveal melanoma, collaborating with **Richard D. Carvajal, MD**, Director of Experimental Therapeutics and Director of the Melanoma Service at Columbia, and their colleagues internationally. “Uveal melanoma is considered rare – about 2,500 to 3,000 cases a year – but it is, in fact, the most common primary intraocular malignancy in adults. Biologically distinct from cutaneous melanoma, there are a number of underlying somatic gene alterations in uveal melanoma associated with a variable prognosis that are currently being investigated in clinical drug development.”

In February 2017, the FDA cleared an investigational new drug application for light-activated AU-011 in primary uveal melanoma. AU-011 is a targeted therapy administered through an intravitreal injection and consists of viral nanoparticle conjugates that bind to cancer cells in the eye. The drug is then activated with an ophthalmic laser, destroying the membranes of tumor cells. The clinical trial is evaluating the drug’s safety, immunogenicity, and preliminary

efficacy in two dose levels. Interim data reported in November 2017 showed that AU-011 was well-tolerated, patients had stable disease, and vision was preserved. The investigators hope that AU-011 will be able to be used for small primary melanomas early on.

“Early detection of ocular melanoma, combined with the administration of AU-011 as a potential vision-sparing therapy, could transform the treatment of patients with this devastating disease,” says Dr. Marr, who is the Principal Investigator for the AU-011 clinical trial nationally and at Columbia – the only site in New York participating in the trial. “Because these eye diseases are so rare, many times I end up trying to borrow other technologies to apply in treatment. That’s why I’m so excited about this clinical trial. It has potential and we’re fortunate to be able to offer it to our patients.”

Dr. Marr points to the dual goals of the new drug – to preserve both life and vision. “The problem with my group of patients is that, pardon the vernacular, cancer sucks, right? But going blind sucks, too. I need to manage both simultaneously,” he says. “Some people would rather die than lose their vision and vice versa. So, I have a twofold challenge to address because of the sensitivity of the organ. I can cure a lot of cancer now, but then I end up blinding people. I’d like to be able to not do that. This new drug may avoid the long-term side effects typically seen with current treatments.”

Dr. Marr is also investigating immune markers within uveal melanoma that are specific to this diagnosis and that have already been explored in investigations of skin melanoma. “Uveal melanoma is genetic-specific and breaks down to about four subsets of this disease. Some of them have infiltrating lymphocytes. In skin melanoma, if this occurs it is a good sign. Uveal melanoma is the exact opposite in that it’s a bad sign. So, we are trying to discover what the discrepancy is. There are a few targetable processes within that immune pathway that have recently been published by colleagues at Columbia and elsewhere. We’re going to try to pick apart those areas to see if certain drugs can target that pathway and whether it makes a difference if we turn it on or off. If it does, then maybe we can subselect patients with this type of immune signaling to target their specific tumor makeup so that they might have a better likelihood of doing well.”

Dr. Marr emphasizes that though he is among few specialists in the field of ocular oncology, he does not work alone. “There are so many nuances in eye cancers,” he says. “For example, if I am treating a primary tumor in the eye that starts to spread elsewhere, I bring in neurosurgery, ENT, plastic surgery, and others to help manage the patient’s care. I am like the quarterback who helps guide everything that is uncommon to most people, but common to me.”

Reference Articles

Carvajal RD, Schwartz GK, Tezel T, Marr B, Francis JH, Nathan PD. Metastatic disease from uveal melanoma: Treatment options and future prospects. *British Journal of Ophthalmology*. 2017 Jan;101(1):38-44.

Krantz BA, Dave N, Komatsubara KM, Marr BP, Carvajal RD. Uveal melanoma: Epidemiology, etiology, and treatment of primary disease. *Clinical Ophthalmology*. 2017 Jan 31;11:279-89.

Abramson DH, Marr BP, Francis JH. Intra-arterial chemotherapy for retinoblastoma. *JAMA Ophthalmology*. 2016 Oct 1;134(10):1202.

For More Information

Dr. Brian P. Marr • bpm2133@cumc.columbia.edu

Retinal Detachment: Improving Outcomes with Technique and Technology *(continued from page 1)*

While trauma is one cause for this form of retinal detachment, most happen spontaneously when the vitreous humor detaches from the retina. “As it detaches, it can cause a retinal break, the beginning of the detachment if left untreated,” says Dr. Papakostas. “The good news is that a retinal break can be addressed in the clinic with a minor laser procedure. But when it becomes a detachment, it is more involved. This is when you go to the OR.”

Dr. Papakostas performs one of several procedures to repair the detachment based on specific indications. Pneumatic retinopexy, performed in the office, involves injecting a gas bubble into the middle of the eye so that the bubble floats and presses against the retinal tear. The surgeon then seals the tear by applying cryotherapy or laser to the break.

“Other procedures include scleral buckling and vitrectomy; the indications for each is different depending on the unique characteristics of the retinal detachment,” says Dr. Papakostas. “Not all retinal detachments are the same. For example, a retinal detachment in a young patient is different than one in an elderly patient. We first consider the status of the lens in the eye. The patient can have a crystalline lens or an artificial lens, which happens with cataract surgery, or, in some cases, no lens.”

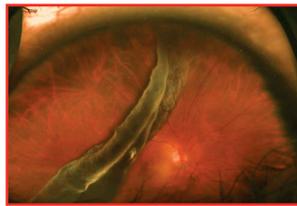
The status of the vitreous also plays a role. “If the vitreous is attached, there is a crystalline lens, and if the patient is young, we tend to do a scleral buckle,” says Dr. Papakostas. In this procedure, a piece of silicone band is sewn onto the sclera at the site of the tear to push the sclera towards the retina, thus relieving the vitreous traction on the retina.

“The scleral buckle has been performed for years and has a very high success rate,” says Dr. Papakostas. “In general, however, if the patient is older with a detachment of the vitreous and has an artificial lens, we tend to do a vitrectomy.” In a vitrectomy, the vitreous humor is removed, the subretinal fluid is drained, and then laser is applied around the retinal breaks and a long-acting gas bubble is injected in the eye. “Vitrectomy allows us to treat complicated forms of retinal detachments that involve scar tissue formation and also retinal detachments after open-globe injuries.”

Technology Paves the Way

“Successful outcomes with vitrectomy are due, in large part, to advances in instrumentation technology,” says Dr. Papakostas. “The instrumentation used in the 1970s when this technique was developed was crude. Nowadays, we use very small instruments to enter the eye – 23-gauge, 25-gauge, and 27-gauge – that are atraumatic. They do a good job of removing as much gel as possible without causing any damage to the retina. The eye has minimal inflammation after the surgery as well.”

Today’s laser technologies also have enhanced surgical procedures. “The development of the curved illuminated laser probe was a key change in the field,” says Dr. Papakostas. “We can now treat the retina very safely without damaging the crystalline lens of the eye. Wide-angle viewing systems have also played a significant role in the development of vitrectomy surgery. These systems can provide



Retinal detachment associated with a giant retinal tear



Dr. Thanos Papakostas

wide-angle panoramic views of the retina that help the surgeon to identify all of the pathology, ensure a safe surgery, and decrease operating time.”

High-resolution, three-dimensional visualization is replacing direct optical viewing of the surgical field through a microscope. “The surgeon operates while wearing the 3-D fitted glasses and looking at a 4K high-definition monitor,” says Dr. Papakostas. “The monitor facilitates the involvement of the whole operating room team. Everyone can see exactly what the surgeon is seeing. In addition, we can use significantly lower levels of illumination in the retina. We know from experimental data, as well as human data, that prolonged strong illumination on the surface of the retina can be toxic. And being able to sit comfortably through the surgery improves ergonomics for the surgeons, who are notorious for getting back and neck problems.”

A Closer Look at Complications

In addition to clinical practice, Dr. Papakostas is pursuing research focused on proliferative vitreoretinopathy (PVR). “Proliferative vitreoretinopathy is abnormal scarring inside the eye after retinal detachment repair and also the main reason for failure,” he says. “Currently, meticulous surgery is the standard treatment of PVR. Better understanding of the biology of this disease will lead to new drugs that will improve outcomes.”

Although scleral buckles can lead to high success rates in retinal detachment surgery, they can be associated with certain complications, such as change in the refractive error of the eye, diplopia, infection, and buckle extrusion, among others.

Most recently, Dr. Papakostas reviewed the postoperative complications of scleral buckling, the results of which were published in the November 2017 issue of *Seminars in Ophthalmology*. “Careful planning, appropriate patient selection, and good intraoperative technique can reduce the rate of these complications,” says Dr. Papakostas.

Reference Article

Papakostas TD, Vavvas D. Postoperative complications of scleral buckling. *Seminars in Ophthalmology*. 2017 Nov 29:1-5.

For More Information

Dr. Thanos Papakostas • thp9034@med.cornell.edu

ADVANCES IN OPHTHALMOLOGY

NewYork-Presbyterian Hospital
 525 East 68th Street
 New York, NY 10065

www.nyp.org

NON-PROFIT ORG.
 US POSTAGE
 PAID
 STATEN ISLAND, NY
 PERMIT NO. 169

AMAZING ADVANCES IN RESEARCH, TECHNOLOGY, AND PATIENT CARE

NewYork-Presbyterian's new clinical innovations site for professionals

nyp.org/amazingadvances

On the Move to Prevent Blindness

NewYork-Presbyterian/Columbia University Irving Medical Center recently unveiled an advanced mobile testing unit in an effort to reduce blindness-causing eye diseases in underserved neighborhoods. The Tele-Ophthalmology Unit – the first such mobile unit in the country – reaches out to communities where residents are most vulnerable to four major sight-threatening conditions: glaucoma, cataracts, macular degeneration, and diabetic retinopathy. “You can treat these eye conditions and prevent blindness if they’re caught early,” says **Lama Al-Aswad, MD**, Director of the initiative. “Unfortunately, many people in underserved communities don’t have access to proper eye care, and by the time these diseases progress, it’s often too late. This project leverages technology and mobility to help these patients get the care they need, when they need it.”

The Tele-Ophthalmology Unit expects to conduct up to 2,000 free screenings each year at locations in the Bronx, Washington Heights, and Harlem. Dr. Al-Aswad and her team use an array of diagnostic equipment in the mobile testing station, which



includes highly secure, Wi-Fi-based data transmission that allows clinicians in NewYork-Presbyterian/Columbia’s reading center to evaluate data in real time. Screening participants are then given instructions or referrals to clinics for follow-up care.