RETINA CONSULTANTS OF HAWAII

Retina Consultants of Hawaii Newsletter

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A Letter from the Medical Director

Revolutionary research with worldwide impact. This is the goal of the Hawaii Macula and Retina Institute, and the vision of our research program at Retina Consultants of Hawaii.

Recently, contributions from our research have led to incredible advances in our field. All of the biggest new treatments for the most common problems that we treat have come through multi-centered studies at Retina Consultants of Hawaii: Lucentis for Wet AMD, Lucentis for Diabetic Macular Edema, Eylea for Wet AMD, and Eylea for diabetic macular edema.

However, moving past these advances, we have designed and reported on prospective studies of treatment for polypoidal choroidal vasculopathy, including the use of regular dose ranizibizumb (0.5 mg, PEARL), high dose ranibizumab (2.0 mg, PEARL2) and aflibercept (EPIC). Because prospective trials are rarely available for polypoidal choroidal vasculopathy, the results of these trials have generated worldwide interest. Recently, results of these studies were presented at EURETINA in London by invitation in September 2014, and the EPIC results were recently presented in February 2015 at the Macula Society in Phoenix, Arizona. EPIC results lectures have now been invited in Asia in Taiwan and Korea, because the incidence of PCV is very high in these Asian countries, and the use of aflibercept is becoming important.

Additionally, the revolutionary ARGUS II procedure designed by Mark Humayun, MD, PhD, of the USC Eye Institute, will be implanted in the Asia-Pacific Region for the first time through our program. This is extremely exciting to allow patients who have developed blindness from hereditary retinal disease to see enough to make a difference in their lives. This has been one of the most impactful areas of research, where we make a true difference in patients' lives.

Thank you very much again for all of the support in the community of Hawaii and around the world for our research and education programs. These advances would not be possible without your help.

Sincerely,

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Gregg T. Kokame MD MMM Managing Partner Retina Consultants of Hawaii, Inc. Medical Director Hawaii Macula and Retina Institute



HAWAII MACULA AND RETINA INSTITUTE Revolutionary Research with World-Wide Impact



Retina Consultants of Hawaii Approved as first Argus II Implantation Site in the Asia Pacific Region

Retina Consultants of Hawaii has been approved to begin implantation of the Argus II for blind patients with retinitis pigmentosa. These patients will undergo surgery at the Eye Surgery Center of Hawaii, where the microelectrode implant will be placed in a 3 to 4 hour surgery. Postoperatively, vision training will be performed so patients can learn how to utilize the artificial vision. "These patients have loss of the outer retina or photoreceptors, but have an intact inner retina with the usual connections to the optic nerve and brain. The impulses from the camera mounted on the patients' glasses are then sent to the microelectrode array implanted on the surface of the retina, which then sends impulses to the retina. These impulses are then sent to the brain via the optic nerve," explains Dr. Gregg Kokame, head of the Argus II team at Retina Consultants of Hawaii. We are actively screening patients, and plan to start surgery in early 2015. This procedure will eventually draw patients with this condition from throughout the Asia Pacific region.

For referrals and more information, please call Sheila Chamian at our Research Department at (808) 380-8060, or email research@retinahi.com



Please visit our website: www.retinahi.com and our research website: www.hawaiimacula.com



Dr. Mark Humayun Inventor of the Electronic Implant for Blind Patients to See Speaking in Hawaii, March 24, 2015

Dr. Mark Humayun, Professor at USC Eye Institute, and inventor and leader in artificial vision for the blind, will be lecturing in Hawaii on the invitation of Dr. Gregg Kokame. Dr. Humayun developed the FDA-approved Argus II, which is the first Tech. We can now literally help the approved implant to allow blind patients with retinitis pigmentosa (hereditary lost outer retinal function) to see using artificial vision. The implant is a microelectrode array that receives visual signals from a camera mounted on the patients' glasses. The signals are then sent to the microelectorde array, which is implanted on other ground-breaking technologies, that the surface of the central retina with the elecrtodes touching the inner retina. The impulses from the camera are then utilized to stimulate the inner retina through the micorelectrodes, which then send the impulses through the inner retina and through the optic nerve to the brain. Dr. Gregg Kokame, director of the ARGUS II program in Hawaii, has known Dr. Humayun Momi in 2008." for many years, and spent time with Dr. Humayun while going to USC for his masters studies in 2004. Dr. Kokame notes,

"At that time this was still all just a dream – to help literally make the blind see, but now this is a reality through the leadership of Dr. Humayun and his great team both medically at USC and technologically at Cal functionally completely blind start to see again with artificial vision." The Argus II implant received FDA approval on February 15, 2013.

Dr. Humayun has been featured around the world for his work in this area, as well as he continues to work on. He has been featured by the New York Times, BBC and the Huffington Post, and had wonderful news programs dedicated to his work shown around the world. "It is an honor to have Dr. Humayun join us again in Hawaii. He helped us celebrate the 15th Anniversary of The Retina Center at Pali

Working with the Future of Medicine and Ophthalmology University of Hawaii School of Medicine Students and Interns

The research and academic program at the Hawaii Macula and Retina Institute , and Retina Consultants of Hawaii's clinical practice have attracted many students, medical students and interns to our program. Our patients have been generous to allow the students to stay in the room with the doctors during their examinations. We want to thank them for their patience and generosity in allowing our students to examine them, and watch the research process.

To help our patients understand where our trainees have gone, we would like to update you on their present or future locations for study in medicine.

Dr. Michael Yim, who finished medical school and internship at the University of Hawaii School of Medicine, has now started his residency at the Bascom Palmer Eye Institute at the University of Miami School of Medicine (rated the #1 ophthalmology residency for the past 10 years by the US News and World Report). He reports that he is doing well, and is surrounded by excellent teachers and role models. Three of the senior medical students at the University of Hawaii School of Medicine decided to go into Ophthalmology, and worked with Dr. Kokame on research projects, and with Drs. Kokame, Lai and Wee in the clinics of Retina Consultants of Hawaii. Kyla Teramoto MSIV has matched at the University of Arizona School of Medicine for training in Ophthalmology in Tucson. Rajinder NIrwan MSIV has matched at the University of Rochester and the Flaum Eye Institute. Austin Nakatsuka MSIV has matched at the University of Texas at Galveston. We are very proud of our medical students, who will all join us as colleagues in ophthalmology in the future.

In addition, four recent employees of Retina Consultants of Hawaii, have entered medical school at the John A. Burn Scholl of Medicine (JABSOM) at the University of Hawaii. Christine Chan is now a 3rd year medical student, Kelsi Hirai is now a second year medical student, Julia Ayabe is now a first year medical student, and David Bailey is now a first year medical student. All four medical students helped with research and clinical care for Retina Consultants of Hawaii, and received significant exposure to medicine with us, which helped to prepare them for medical school.



Dr. Michael Yim



Kyla Teramoto





Rajinder Nirwan

Austin Nakatsuka

Please visit our website: www.retinahi.com and our research website: www.hawaiimacula.com

Clinical Trials- Enrolling Now!



Dry AMD: CHROMA Study- A study investigating the effectiveness of Lampalizumab injections every 30 or 45 days in patients with Dry Age-Related Macular Degeneration. There is no proven treatment for Dry AMD. Retina Consultants of Hawaii is the only clinical research site in Hawaii for this potential breakthrough treatment for Dry AMD. *Pictured above, an example of a CHROMA patient pre-enrollment.*

VMA: ORBIT Study- A study assessing patient outcomes after use of Jetrea to treat Vitreomacular Adhesion.

WET AMD: HAWK Study- A study investigating the effectiveness of RTH258 every three months, compared to two months, versus aflibercept to treat Wet Age-related Macular Degeneration.

Ongoing Clinical Trials- Enrollment Complete

PCV: EPIC Study— A study investigating the effectiveness of monthly or bimonthly injections of Eylea, for patients that have previously or not previously received treatment for Polypoidal Choroidal Vasculopathy.



DME: PALM Study— An evaluation of Abicipar Pegol injections in patients with decreased vision due to Diabetic Macular Edema.

For referrals and more information regarding our clinical trials, please contact our Research Department at (808) 380-8060, or email research@retinahi.com

Recent and Upcoming Lectures

10/21/14– Polypoidal Choroidal Vasculopathy (PCV). Gregg T. Kokame, MD, MMM. American Academy Course at American Academy of Ophthalmology Annual Meeting. Chicago, Illinois.

12/21/14– En Face OCT Imaging of PCV. Gregg T. Kokame MD, MMM, Kelsi Hirai MSII, Julia Ayabe MSI. Second International Congress of "En Face OCT Imaging." Rome, Italy.

2/25/15 -PCV. Is it really choroidal? Gregg T. Kokame MD, MMM. Macula Society. Annual Meeting. Phoenix, Arizona.

2/28/15 – Aflibercept for Hemorrhagic and Exudative Complication of PCV – Prospective 6 month Results of EPIC study. Gregg T. Kokame MD MMM, James C. Lai MD, Raymond Wee MD, Ryan Yanagihara BS. Macula Society. Annual Meeting. Phoenix, Arizona.

4/24/15 – 4/26/15 – Lectures on PCV and EPIC study throughout Taiwan. Gregg T. Kokame MD, MMM. Taiwan.

4/27/15 – 4/28/15 - Lectures on PCV and EPIC study throughout Korea. Gregg T. Kokame MD, MMM. Korea.

5/15/15 – Prospective evaluation of subretinal vessel location in PCV and response of hemorrhagic and exudative PCV to high-dose antiangiogenic therapy. An American Ophthalmological Society Thesis. *Gregg T Kokame MD, MMM. Annual Meeting. American Ophthalmological Society Meeting. Newport, Rhode Island.*

New Treatment for Diabetic Macular Edema Ozurdex and soon Iluvien in March 2015

Diabetic macular edema (DME) is a common



cause of impaired vision in individuals with diabetes. DME is an accumulation of fluid in the macula, the central portion of the retina that is responsible for our detailed vision.

Historically, the gold standard for treatment

for DME was laser photocoagulation. More recently, intravitreal injections of anti-VEGF agents such as ranibizumab (Lucentis), bevacizumab (Avastin) and aflibercept (Eylea) have replaced laser treatment as the first line treatment for foveal involving DME. However, the pathway for DME development is multifactorial, and we know that certain patients do not respond well to anti-VEGF treatments. Intravitreal injections of steroids are an important and useful alternative treatment option in these patients.

Up until now, steroid options have included triamcinolone acetonide (Kenalog vs. Triesence) and dexamethasone intravitreal implant (Ozurdex).

On September 26, 2014, The US Food and Drug Administration approved Iluvien fluocinolone acetonide intravitreal implant (Iluvien) for the treatment of DME in patients who have been previously treated with a course of corticosteroids and did not have a clinically significant rise in intraocular pressure. Iluvien (pictured at left) is an injectable, non-erodible, intravitreal implant. The implant is a cylindrical tube (3.5 mm in length, 0.37 mm in diameter) that holds 190 µg of fluocinolone acetonide. Iluvien is designed to release a corticosteroid called fluocinolone acetonide for up to three years. Importantly, the device is small enough to be injected into the back of the eye with a 25 gauge needle creating a self-sealing hole.

Written by Dr. James Lai

Dr. Gregg Kokame Becomes Member of the Prestigious American Ophthalmological Society

After recommendation by Dr. Malcolm Ing, Chairman of Ophthalmology at the University of Hawaii School of Medicine, and Dr. Jose Pulido, Professor of Ophthalmology at the Mayo Clinic in Minnesota, Dr. Kokame was considered for the prestigious American Ophthalmological Society. This required a 3 year journey to complete a thesis, which would significantly impact the field of medicine on that topic. Dr. Kokame's topic was polypoidal choroidal vasculopathy (PCV), which is a leaking and bleeding condition in the back of the eye similar to exudative macular degeneration.

PCV is very prevalent in Hawaii, which is more common in Asian populations, but also occurs not infrequently in black and white populations. Dr. Kokame's thesis concentrated on understanding where the location of the PCV vessels are located. PCV was found to be below the retinal pigment epithelium and above Bruch's membrane. This is the same location as the majority of abnormal blood vessels associated with wet macular degeneration, so PCV is thus a subtype of wet macular degeneration.

Congratulations to Dr. Kokame!



Vitreous Surgery Incisions and Instruments Get Smaller



Dr. Gregg Kokame performed the first 27 gauge surgery in Hawaii using new technology being developed by Alcon Laboratories in October of 2014. This was successfully utilized to treat a patient with macular hole (a hole in the central

vision part of the retina). New instruments built specifically for 27 gauge allowed development of a good edge of the scar tissue for peeling of the epiretinal membranes. This patient had successful closure of the macular hole with improved vision following this 27 gauge surgery.

Dr. Yusuke Oshima from Japan has been the pioneer in 27 gauge surgery, being the first to publish on this technique (Oshima Y, Wakabayashi T, Sato T, Ohji M, Tano Y. A 27-gauge instrument system for transconjunctival sutureless microincision vitrectomy surgery. Ophthalmology. 2010;117:93-102). Dr. Oshima previously visited Dr. Kokame at Retina Consultants of Hawaii's Pali Momi office. Dr. Kokame noted that Dr. Oshima has helped many companies develop the technology necessary to go even smaller with 27 gauge surgery. "He has told me for years about the benefits of this surgery, and it is very exciting to finally be able to see the results of his work in my own hands. I think that this technology is very promising."

20 gauge vitrectomy has been utilized for decades, but recently smaller gauge surgery has become the standard of care utilizing 23 gauge and 25 gauge cannulas for surgery. 27 gauge vitrectomy took some time to develop because technology had to be developed to make the instruments that

small and to still function well for the vitreoretinal surgeon.

Dr. Yusuke Oshima, who was the first to publish on 27 gauge vitrectomy, recently retired from his academic position at Osaka University School of Medicine (see picture at left), and now has a thriving private practice. At his retirement party from the Osaka University, Dr. Oshima (pictured front row far right) is enjoying a celebration with friends from Asia and throughout the world. Far left is Dr. Fumi Gomi from Japan, a leader in research in polypoidal choroidal vasculopathy (PCV). In back row pictured from left to right are Dr. Timothy Lai from Hong Kong (leader of the PCV course at the American Academy of Ophthalmology with Drs. Kokame and Gomi), Dr. Wai-Ching Lam (retina fellowship director at Toronto, Canada), Dr. Gregg Kokame, Dr. Kourous Rezeai (Director of RETINAWS surgical video education series and FORMULA RETINA Eyetube educational series from Illinois Retina Associates in Chicago), and Dr. Lihteh Wu from Costa Rica.



Above, macular hole pre– 27 gauge surgery. **Below,** successful closure of macular hole after surgery.



The High Cost of Saving Vision

Retina Consultants of Hawaii has helped to pioneer the amazing new advances in treating wet macular degeneration, diabetic macular edema, and retinal vascular diseases. The pivotal studies leading to the approval of new medications were performed here in Hawaii as part of the multi-centered trials leading to approval of Lucentis for macular degeneration (MARINA study, FOCUS study), the approval of Eylea for macular degeneration (VIEW1 Study), the approval of Lucentis for diabetic macular edema (RISE study), and the approval of Eylea for diabetic macular edema (VISTA study). These drugs have led to marked improvement in visual outcomes for the patients that receive them by intravitreal injection. However, the cost of Lucentis on approval in 2006 was \$2000 per dose per patient, and the cost of Eylea on approval in 2011 was \$1850 per dose per patient. A compounded drug called Avastin with a similar mechanism of action is also available at a lower per dose price.

In the United States most injectable medications must be purchased by the doctor in order to administer to patients. This puts this very high financial liability on the physicians' office practice to buy the medications and pay the drug companies for the medications. Often times, the high cost of medications overwhelms the income that the doctors actually earn from clinical or surgical services. This requires the physicians' office to carefully require payment for all medications and co-pays immediately, as the physicians' offices are responsible for paying these large amounts to the drug companies. Amazingly, Medicare has attributed these drug costs to the doctors providing these medications in making financial payment information available to the public. Although the medicine costs become a financial liability to the retina specialist, Medicare attributes these dollars to the provider. In the meantime, insurers are trying to slow down payments of co-pays, and drug companies are requiring less and less time to pay for the medications. Because RCH has been at the forefront in the development of these important advances to save vision, we are dedicated to offering our patients the full complement of medications, but this requires that the drug costs be fully covered in order for RCH to pay for the drugs.



Our doctors are listed as **Best Doctors in Hawai'i** in Honolulu Magazine!



From left to right: Dr. James Lai, best MD for 7 years; Dr. Gregg Kokame, best MD for 14 years; Dr. Ray Wee, best MD for 2 years

Please visit our website: www.retinahi.com and our research website: www.hawaiimacula.com

Which Medication is Better for Retinal Swelling from Vein Blockage?

As the CRAVE research trial has successfully concluded, retina doctors have learned important information about the beneficial effects of two commonly used medications for the treatment of retinal swelling that occurs after blockage of the vessels that drain blood from the eye. CRAVE stands for Comparison of improving vision at both the 6 month and 12 Anti-VEGF Agents in the Treatment of Macular Edema from Retinal Vein Occlusion. Retina Consultants of Hawaii was one of ten research sites throughout the United States to participate in the study. I would like to thank and congratulate the community for their assistance in the project allowing the Retina Consultants of Hawaii to be the largestenrolling site outside of the home site of Saint Louis. I am not surprised by the eagerness and generosity of our local people to contribute to general medical knowledge, allowing doctors throughout the world to learn about two of the treatments for this condition. This aloha spirit makes me proud to live in Hawaii.

The study compares the use of ranibizumab (Lucentis) and bevacizumab (Avastin) to determine which medication results in the most improvement in retinal swelling after six months. Previous studies supported the



At left, a normal, healthy eye. At right, an eye with retinal vein occlusion.

beneficial effects of either of these medications, but a head-to-head comparison had not been performed in a randomized, prospective way. The CRAVE study demonstrated that both medications were effective in reducing retinal swelling and in month time-points. Neither medication was shown to be superior to the other. In practical use, there may be special circumstances where one medication may be preferable to the other.

A special aspect of this project was that it was not funded by a pharmaceutical company or government grant. Rather, the researchers involved realized that this was an important clinical question, and at their own expense, decided to spend time and effort to answer this question. Special acknowledgement should be given to Gaurav Shah, MD (Saint Louis, MO) for originating the project idea, Mike Altaweel, MD (Madison, WI) and his colleagues at the University of Wisconsin for reading the images, and Rithwick Rajagopal, MD (Saint Louis, MO), for compiling the data and preparing the scientific paper.

Written by Raymond Wee, MD



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