

News in Review

COMMENTARY AND PERSPECTIVE

RETINA

Grading Diabetic Eye Damage: Time for a New System?

THANKS TO RECENT STUDIES, OPH-thalmologists now know more about the molecular, neural, vascular, and systemic processes that contribute to diabetes-related retinal damage and disease progression. Yet the system for classifying and assessing these sight-threatening changes is lagging far behind, a group of researchers wrote in *Ophthalmology*.¹

Their proposed solution: A massive, coordinated, international effort to develop a new staging system that incorporates these advances. “We think that, by updating the severity scales relevant to diabetic eye disease, we will be able to revise the current staging system to help us better predict outcomes in the diabetic eye. And in doing so, we can drive advances that are much needed in both research and clinical care,” said Jennifer K. Sun, MD, MPH, at the Joslin Diabetes Center’s Beetham Eye Institute in Boston.

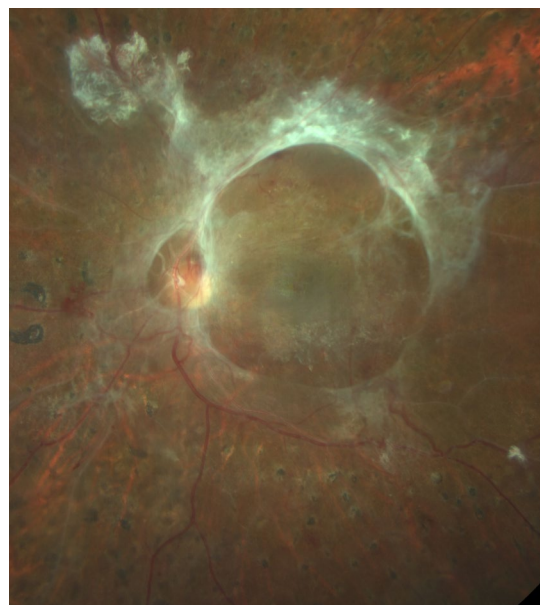
Say hello to DRD. One semantic signal of this new focus comes from the terminology the group has adopted, said coauthor Michael D. Abràmoff, MD, PhD, at the University of Iowa in Iowa City. “We don’t say ‘diabetic retinopathy,’ because that just addresses the vascular component of the retinal damage in diabetic eyes.” Instead, the preferred phrase is now “diabetic retinal disease,” and the narrow acro-

nym DR is being replaced by DRD, he said.

Developing the staging system. Six international panels are currently working on evidence-based recommendations for the metrics to incorporate into an updated staging system for DRD. “Ideally, an updated staging system will address retinal, neural, and vascular pathology and their contributions to visual function in the context of systemic influences such as diabetes type, glycemic control, blood pressure, renal disease, and anemia,” Dr. Sun and her coauthors wrote.¹

“As we learn more about diabetes [and its neural components], we have found that neural damage happens early,” Dr. Abràmoff said. While he believes that neural damage occurs earlier than vascular damage does, some of his colleagues think that the neural and vascular damage are “kind of interrelated,” he added. “Everyone in the group has a different view, but we all realize that it’s more than just vascular damage, especially in the macula and the periphery.”

Role for AI. A new system might include disease assessments made with advanced retinal imaging tools, such as ultra-widefield photography, spectral-domain optical coherence tomography (OCT), and OCT angiography, said Dr. Sun, who also serves as chair of diabetes initiatives for the DRCR Retina Network.



LATE STAGE. Ring fibrosis in a patient with proliferative diabetic retinopathy.

Artificial intelligence (AI) tools might be needed to integrate all this complex information into a system that clinical ophthalmologists could easily use, she added. “So much automated decision support is possible with computerized algorithms. That’s one way to potentially make a system that—in and of itself—is quite complex and contains a lot of nuanced information but is easy to use clinically.”

Three years in the making. The roots of the project were laid down in 2018, during an international colloquium cosponsored by the JDRF. That meeting led to the formation of this new initiative to re-envision DRD staging, Dr. Sun said. —Linda Roach

1 Sun JK et al. *Ophthalmology*. Published online Nov. 17, 2020.

Relevant financial disclosures—Dr. Sun: Adaptive Sensory Technology: S; Boston Micromachines: S; Genentech: C; Novartis: C; Novo Nordisk: C,S; Optovue: S; Roche: C,S. Dr. Abràmoff: Alimera: C; Digital Diagnostics: C,O,P; NovaGo: C.

Metastasis Update: Stage IV Uveal Melanoma

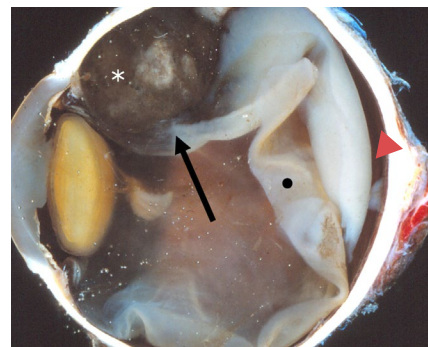
AN INTERNATIONAL TEAM OF researchers has concluded that all patients who present with stage IV uveal melanoma should be evaluated and staged for metastatic disease at initial presentation.¹ And because even small intraocular tumors may spread to multiple organs beyond the eye, the researchers recommend whole-body positron emission tomography/CT (PET/CT) imaging to avoid missing metastases, which are the leading cause of death due to uveal melanoma.

These conclusions, based on data from an internet-based retrospective registry representing eight countries and 10 oncology centers, were developed by the Ophthalmic Oncology Task Force of the American Joint

Committee on Cancer (AJCC). “Data sharing allowed us to compile significant medical evidence that answered a specific ophthalmic oncology question: What are the clinical characteristics of patients who presented with metastatic uveal melanoma?” said Paul T. Finger, MD, at The New York Eye Cancer Center in New York City.

Data collection. The data analysis, which characterized metastases to determine the amount and spread of disease, included site of origin, tumor thickness, largest basal diameter, extra-scleral extension, ciliary body involvement, and the AJCC’s classification system (stages T1-T4).

Findings on stage IV. Of 3,610 patients diagnosed between 2001 and 2011 with uveal melanoma, 69 (1.9%) presented with stage IV disease. Most of the primary tumors in this group of patients originated in the choroid (80%), followed by the ciliary body (16%) and iris (4%).



CILIARY BODY. This enucleation specimen shows a pigmented, nodular-shaped ciliary body melanoma (arrow) with extensive necrosis (*), a retinal detachment, and subretinal fluid (arrowhead). The retina is folded (*).

Significant predictors of metastasis included tumor thickness and largest basal diameter. Most tumors metastasized to the liver (91%), followed by lung (16%), bone (9%), and brain (6%). Multiple sites of metastases were noted in 24% of patients—and, Dr.

UVEITIS

Posterior Segment Involved in JIA-Associated Uveitis

TRADITIONALLY, UVEITIS ASSOCIATED WITH JUVENILE idiopathic arthritis (JIA) has been thought to occur in the anterior segment alone. More recently, however, some studies have detected inflammation in the posterior segment. Now, a retrospective evaluation with widefield fundus angiography (WFA) has confirmed the presence of posterior segment inflammation in more than 70% of eyes.¹

The clinical implications are significant, said Charles Stephen Foster, MD, FACR, FACS, in private practice in Waltham, Massachusetts. “JIA uveitis is a systemic vision-threatening disease that requires aggressive systemic therapy.”

Evaluating WFA characteristics. Dr. Foster and his coauthors culled the electronic records of their practice for patients who were diagnosed with JIA and underwent WFA with the Spectralis system (Heidelberg). The search yielded 20 patients (37 eyes) who were age 2 to 14 years at diagnosis.

All told, 27 eyes (73%) showed some evidence of posterior segment inflammation. Other WFA findings included optic disc hyperfluorescence in 19 eyes (51.4%), macular leakage in 10 eyes (27%), and retinal vascular staining/leakage at the posterior pole in

10 eyes (27%) and at the peripheral retina in 24 eyes (64.9%). In addition, capillary leakage was noted at the posterior pole in 14 eyes (37.8%), and peripheral capillary leakage was detected in 22 eyes (59.5%).

Additional findings. The researchers also quantified anterior chamber cells and severity of intraocular inflammation using standardized classification systems. Nine patients had quiet anterior chambers bilaterally, while seven had clinical anterior segment activity in only one eye. However, many of the patients presenting with few or no anterior chamber cells had the highest angiography scores—thus, significant inflammation would have been missed had the angiogram not been done, Dr. Foster said. A new course of treatment was prescribed for eight of the nine patients with bilateral quiet anterior chambers.

Going forward. The authors agreed that it will take larger, prospective studies to determine the exact role of WFA in JIA-associated uveitis. Nevertheless, the current findings suggest that subclinical posterior segment involvement may occur in many patients. “I strongly advise widefield angiography in the quest to understand as completely as possible what is going on,” Dr. Foster said. “The posterior segment must be considered, if one aims to cure the problem.”

—Miriam Karmel

1 Tripathy K et al. *Ocul Immunol Inflamm*. Published online Dec. 2, 2020.

Relevant financial disclosures—Dr. Foster: None.

Finger noted, “PET/CT [imaging] was significantly more likely to reveal multi-organ metastasis.”

Clinical impact. Dr. Finger noted that many centers only perform initial radiographic imaging of the liver—or a chest X-ray and blood testing—prior to treatment. But the results of this analysis suggest that “staging with liver imaging alone risks missing extrahepatic sites of metastasis,” said Dr. Finger, who routinely performs whole-body initial staging on his patients.

Overall, the findings support those of previous studies in suggesting that patients with higher T-category tumors should be more closely monitored for metastatic disease. They also provide a reminder that even small tumors can spread, as 11% of those with metastatic uveal melanoma belonged to the lowest AJCC category (T1).

Finally, in a novel finding, 6% of uveal melanoma patients with metastatic disease belonged to subcategory T1a. —*Miriam Karmel*

1 Gang G et al. *Br J Ophthalmol*. Published online Jan. 15, 2021.

Relevant financial disclosures—Dr. Finger: Liberty Vision: O.

COMPREHENSIVE

Ongoing Damage From Cosmetic Iris Implants

THE ALLURE OF TURNING BROWN eyes blue is strong for some people—so strong that they sometimes balk at giving up the cosmetic iris implants that are imperiling their vision. And researchers at the University of California, Los Angeles (UCLA) have confirmed that ocular complications related to the devices occur not only before but also many months after explantation.¹

“Despite me telling them, ‘Your eye is not doing well, your cell count is down, you’re in pain, your pressure is 30, your eye is all inflamed, you need to get these things out,’ they say, ‘OK, I’ll

think about it.’ A year later, they come back, and their eye is totally decompensating. They just don’t want to let the implants go once they get them in their eyes,” said Kevin M. Miller, MD, at UCLA.

Dr. Miller made those observations while he and his coauthors treated implant complications and then studied postexplantation outcomes in 12 people (24 eyes) with brown irides. All wanted blue eyes and sought out the unapproved anterior chamber implants, which were inserted in France, Jordan, Mexico, Panama, and Turkey. (For more, including a discussion of body dysmorphic disorder in these patients, see Practice Perfect in the March issue, at aao.org/eyenet/archive.)

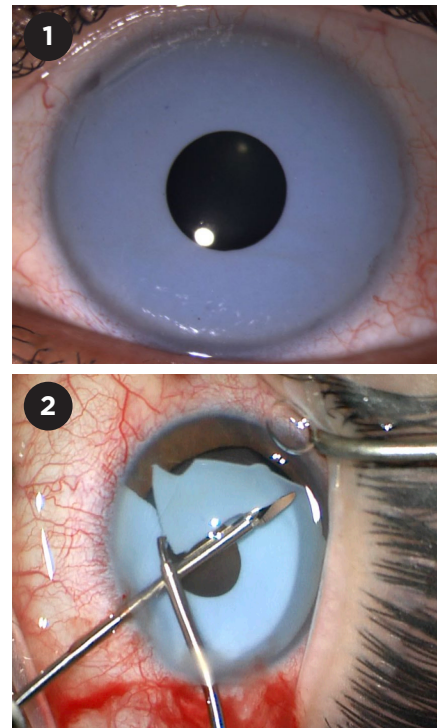
Before explantation. The mean interval from implantation to presentation was 61.7 ± 60 months. Complications at presentation included iris abnormalities (11 eyes, 45.8%), elevated intraocular pressure (eight eyes, 33.3%), corneal edema (six eyes, 25%), intraocular inflammation (five eyes, 20.8%), and cataract (four eyes, 16.7%).

Initial surgical interventions included cataract extraction, corneal transplantation, and glaucoma surgery.

These findings are similar to those from smaller case studies over the past decade, but the UCLA study expands on this literature by showing that ocular complications arise even after the implants are removed, Dr. Miller said.

After explantation. The mean follow-up after explantation was 35.5 ± 38.1 months. Complications observed during this time included native iris defects (11 eyes, 45.8%), persistent glaucoma (seven eyes, 29.2%), cataract (five eyes, 20.8%), corneal edema (four eyes, 16.7%), and intraocular inflammation (two eyes, 8.3%).

Secondary surgeries included cataract extraction, IOL exchange, pupiloplasty, corneal transplantation, tube shunt implantation, endoscopic cyclophotocoagulation, and implantation of a medically indicated artificial iris (HumanOptics). A few of the patients had to undergo multiple surgeries, Dr.



RELATIVELY LUCKY. (1) This patient—seen with the cosmetic implant in place—had a low endothelial cell count preoperatively, but he was fortunate in that his eye was otherwise unremarkable. (2) The intraoperative photo shows the segmentation and removal of the implant. During surgery, care must be taken to avoid further damaging the cornea and touching the native iris and crystalline lens.

Miller said. “The problems go on for the rest of their lives—and many of these patients are in their 30s and 40s when we first see them.”

A clinician’s frustration. It is frustrating that these invasive ocular devices can be sold as an aesthetic accessory despite the documented risks, Dr. Miller said. “These have not been tested in vigorous clinical trials. Not in the United States, not in Europe, not anywhere.”

—*Linda Roach*

1 Ghaffari R et al. *Am J Ophthalmol*. Published online Jan. 22, 2021.

Relevant financial disclosures—Dr. Miller: None.

MORE ONLINE. For additional images of an eye with more damage, see this article online at aao.org/eyenet.

See the financial disclosure key, page 8. For full disclosures, including category descriptions, view this News in Review at aao.org/eyenet.