

Optometry Insights on the Diagnosis and Referral of Patients With Geographic Atrophy

**A DISCUSSION WITH DR JULIE RODMAN,
A LEADING OPTOMETRY EXPERT.**

Sponsored by Apellis Pharmaceuticals

TOPIC HIGHLIGHTS

- Geographic atrophy (GA) is an advanced form of age-related macular degeneration (AMD).^{1,2} GA progression is relentless and irreversible³⁻⁹
- Best corrected visual acuity (BCVA) is poorly correlated with lesion size and changes in BCVA may not fully capture disease progression.¹⁰ Functional vision continues to decline as lesions grow^{3,6,11-13}
- GA is a disease that needs to be identified early and appropriately referred¹⁴

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IN MORE?**



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FEATURED EXPERT BIO

DR JULIE RODMAN is chief of the Broward Eye Care Institute and a professor of optometry at Nova Southeastern University in Fort Lauderdale, Florida. Her research interests include optical coherence tomography (OCT)/optical coherence tomography angiography (OCT-A) and vitreoretinal disease. Dr Rodman has authored more than 30 publications with an emphasis on retinal disease. She recently published *Optical Coherence Tomography Atlas: A Case Study Approach*, the first reference book on this topic written by an optometrist. Dr Rodman is a member of the American Optometric Association, the American Academy of Ophthalmology, the Florida Optometric Association, and the Optometric Retina Society. She has been the recipient of numerous teaching awards, and was recognized with listings in both the *Primary Care Optometry News* Top 300 Optometrists and *Newsweek* Best Optometrists of 2022.

This program was developed in conjunction with and sponsored by Apellis Pharmaceuticals, based on an interview with Julie Rodman, OD, MSC, FAAO.

Q1 WHAT IS GA, AND WHAT UNMET NEED EXISTS FOR PATIENTS DIAGNOSED WITH THE CONDITION?

DR RODMAN: GA is an advanced form of AMD, and we know it is a progressive and irreversible disease.^{1,2} It currently affects about 1 million people in the United States.¹⁵ GA and neovascular AMD (nAMD) are different manifestations of advanced AMD: nAMD involves bleeding and breakdown in the blood/retinal barrier, and effective treatments have been available. GA is characterized by age-related changes that cause atrophy of tissue and vision loss.^{1,2} Patients with GA can develop nAMD, and patients with nAMD can develop GA.¹

The complement system appears to play a role in GA, based on genetic and histopathology studies.^{3,16-19} In patients with GA, increased levels of complement activity have been found in areas in the lesion, as well as areas just outside the lesion; this increases the risk of further lesion growth.^{16,19,20} All 3 complement pathways converge at C3. C3 plays a central role in driving the downstream damaging effects of complement overactivation, including inflammation, phagocytosis, and cell membrane disruption, all thought to contribute to retinal cell death.^{16,18,19,21-24}

The overall prevalence of GA and nAMD are similar.^{15,25*} The prevalence of GA increases with age:

- Prevalence quadruples every **10 YEARS** starting at **AGE 50**²⁶

*Prevalence of GA and nAMD in the US are ~973,000 and ~1.2 million, respectively.¹⁵

While some clinicians perceive GA progression to be slow, disease progression is often constant and always irreversible.³⁻⁶ Some patients may have more rapid progression with vision loss and diminished quality of life, but each patient is unique.^{2,6,27} According to a prospective AREDS study (N=3640), of the 397 patients who developed central GA, the median time to foveal encroachment was only 2.5 years from diagnosis.^{4†}

Research suggests that AMD may be underdiagnosed in older adults. In a study of 644 older adult patients who received a dilated comprehensive eye examination in a primary eye care setting, 25% of eyes deemed “normal” actually had macular changes characteristic of AMD according to a clinical classification staging system.²⁸

Often, by the time of GA diagnosis, there is already meaningful atrophy, so we want to identify the patients early and identify factors that make them more prone to progression.²⁷ Optometrists should consider whether annual visits are frequent enough to evaluate patients at high risk for GA. It is important that optometrists develop confidence in their ability to appropriately identify the disease and understand what they can do to help, including using multimodal imaging, identifying the correct diagnosis, and making a referral for a retinal evaluation when appropriate.^{5,14,28,29}

†The Age-related Eye Disease Study (AREDS) #26 is a long-term, multicenter, prospective study examining progression of GA area in a cohort of 3640 patients with signs of early and more advanced forms of AMD.⁴

Q2 HOW CAN GA AFFECT A PATIENT’S QUALITY OF LIFE, AND WHAT IS THE EMOTIONAL BURDEN OF GA?

DR RODMAN: GA progression can affect your patients faster than you may think.^{3,6-8} In my experience, even early in the disease, patients can experience significant burden due to reading difficulty, inability to drive, decreased health-related quality of life, and mental health concerns such as depression.²⁸

“I make an effort to educate patients on how GA can affect their visual function and how relentless it is because I want them to understand what to expect. I have had patients in my practice have difficulty completing many of their daily activities in just a few years. Of course, all patients progress at different rates, but at some point they will experience a decline in their functional vision.”

The Geographic Atrophy Insights Survey (GAINS) study demonstrates the many ways that patients are affected and confirms that GA is a significantly burdensome condition that may impact patients' ability to perform daily activities. The global GAINS study was sponsored by Apellis Pharmaceuticals and conducted by The Harris Poll between October 12 and December 10, 2021. To accommodate visually impaired respondents, the survey was conducted online and via the telephone among 203 participants aged 60 or over (mean age, 70 years) residing in the United States, United Kingdom, France, Germany, Italy, the Netherlands, Sweden, Canada, and Australia, who self-reported that they have been diagnosed with AMD and have dry AMD in at least one of their eyes. They must also have indicated that they have advanced

atrophic age-related macular degeneration, or advanced atrophic AMD, advanced/late/late-stage dry age-related macular degeneration, or advanced dry AMD, or GA in one or both of their eyes. Included patients must have been currently experiencing at least 3 GA symptoms and currently do/used to do/have been suggested by an eye care professional but have not done at least one of the following: take a high-dose formulation of antioxidant vitamins and minerals, stop smoking, maintain a healthy weight and exercise regularly, choose a healthy diet, manage other medical conditions, have check-ups of the retina regularly, or wear sunglasses with ultraviolet protection. Included patients must not have been diagnosed with glaucoma, Stargardt disease, or dementia, or be receiving regular injections into the affected eye every 4 to 6 weeks.⁹

Most patients in the GAINS study reported being surprised by the severity and speed of the disease's impact on their vision. In the survey⁹:



77% of patients said that the **IMPACT** on their vision happened **FASTER THAN THEY EXPECTED**



68% of patients said the **IMPACT** of the vision decline on their **QUALITY OF LIFE** and **INDEPENDENCE** was **WORSE THAN THEY EXPECTED**



Patients in the GAINS study started relying on caregiver support **AS EARLY AS 2.6 YEARS** following diagnosis, and **TWO-THIRDS (68%)** of patients felt dependent on others due to their vision loss



MORE THAN HALF (53%) of patients reported feeling uncomfortable asking for help

Many patients were impacted by GA in less than 2 years.* Two out of 3 patients with bilateral GA who were eligible to drive at baseline lost that ability in a median time of <2 years (n=523), according to a large, retrospective United Kingdom study.^{30†} Sixty-three percent of patients living with GA have difficulty reading for everyday tasks or for leisure, according to a qualitative United States study (n=8).^{31‡}

"I see the GAINS data reflected in my own practice. My patients are most challenged by losing their ability to complete their everyday activities, including driving."

Some choose to only drive under certain conditions, and others give up driving altogether—in either case, it represents a significant loss of independence. Public transportation is not always a viable alternative because it can be very intimidating for patients with poor vision. Patients also experience the loss of leisure activities they enjoyed, such as reading books and traveling. I often observe a significant emotional impact in my patients. They are fearful of what is to come and mourning what they have lost. They have gone from being independent to needing to rely on others for help. All of these factors can contribute to feelings of sadness and withdrawal that I see often in my patients with GA.

*Lesions encroached on the fovea in a median of just 2.5 years in AREDS #26, a long-term, multicenter, prospective study examining progression of GA area in a cohort of 3640 patients with signs of early and more advanced forms of AMD.⁴

†Retrospective cohort analysis (N=1901) of a multicenter electronic medical records database examining disease burden and progression in patients in the United Kingdom with bilateral GA secondary to AMD.³⁰

‡A cross-sectional qualitative study of patients with symptomatic GA, their caregivers, and eye care professionals who treat patients with GA (N=19) who were interviewed at United States sites to evaluate understanding of the disease, costs and burden of illness, use of vision aids or services, and impact on emotional or psychological well-being and on daily activities.³¹

Q3 WHAT SHOULD BE INCLUDED IN THE INITIAL OPTOMETRIST–PATIENT CONVERSATION AROUND GA?

DR RODMAN: As optometrists, we play a critical role at diagnosis. I start by explaining to patients that the retina is like the film in a camera: if it's damaged, they can't see. I show them images of their retina, their GA, and how their tissue is affected.⁴ I explain their risk factors and let them know what to expect as the disease progresses. I tell them that GA cannot be corrected with glasses or surgery. I find it is particularly important to be sure patients understand that glasses will not improve their condition because glasses will only magnify the area with missing vision.

"I encourage patients to get their family involved and explain that they will need support, and I empower them with suggestions for lifestyle modification."³²⁻³⁹

Informational brochures are helpful if patients are able to read them. Printed materials with QR codes that patients can scan to listen to information about GA are especially useful resources. The GAINS study showed us that patients wished they knew at the time of diagnosis the irreversible impact GA would have on their vision, and that they want more information and options about GA to feel empowered to take control of their disease.⁹ Optometrists can help address these needs.

Once GA is diagnosed, our job as optometrists is to help patients navigate the overall process. We have existing relationships with the patients, spend a lot of time with them during exams, and they trust us. But it is also important to make a timely referral for retinal evaluation to ensure optimal care. Optometrists, ophthalmologists, and retina specialists should reinforce with patients that regular check-ups are important, and encourage patients to mention any symptoms or any vision changes they notice to help monitor the progression of GA.^{14,40}

Visual function loss—the loss of vision that is used for reading, driving, household chores, and more—may happen even before the fovea is lost to GA.^{3,8} This may not be typically measured in the office, so practitioners should make it a priority by asking patients how GA affects their daily lives.¹⁴ Ask patients if they are experiencing emotional distress or fears after a GA diagnosis, and be prepared to offer resources for emotional support.^{14,40,41} It can be helpful to suggest that patients bring a checklist of their questions to ensure all their concerns are being addressed.

Q4 WHAT TRIGGERS REFERRAL OF A GA PATIENT? WHEN DOES THIS OCCUR, AND WHICH PATIENTS ARE TYPICALLY REFERRED? HOW DO YOU EXPLAIN THIS TO A PATIENT?

DR RODMAN: GA is a disease that needs to be identified, addressed early, and appropriately referred for a retinal evaluation.¹⁴ I refer patients with any signs of GA, given the irreversible nature of this condition, especially those who are at higher risk of progression. I certainly refer any patient with decreased vision that cannot be explained by a cataract, dry eye, or media opacity. If I observe a grayish-green area or similar abnormality on funduscopy or color fundus photography (CFP), I do additional imaging and consider a referral. I also refer any patient with fluid seen on OCT, and those with reticular pseudodrusen (RPD) with indications of atrophy or change.

"When referring a patient for a retinal evaluation, it is important to establish a plan for patient care after diagnosis.¹⁴ Which clinician will monitor for the development or progression of GA (in either eye)? How often should the patient follow up with the optometrist? This second question is especially crucial, as it is important to prevent any loss of follow up in your patient population."

When I refer a patient with GA, it is with the goal of co-managing the patient appropriately. I explain to my patients that I am a primary care physician for their eyes, while other eye care specialists have specific training in conditions like GA. My patients are often concerned about losing their relationship with me after referral, and I hear questions like, "Will I ever see you again?" I reassure patients that all of their eye care providers work together to make up their care team, and that I am always there for them. Similarly, it is important that optometrists not be concerned about losing the patient after referral.

"The goal is teamwork, so knowing and communicating with eyecare professionals within your network is key. It is also important to clarify the role of each provider when you refer the patient to help optimize patient care because patients may not understand the differences between an optometrist, an ophthalmologist, and a retina specialist."



Q5 WHAT IS THE DISTINCTION BETWEEN BCVA AND VISUAL FUNCTION/QUALITY IN GA? WHY IS LESION GROWTH ONE OF THE MOST RELEVANT MEASURES OF DISEASE PROGRESSION IN PATIENTS WITH GA?

DR RODMAN: BCVA is widely accepted as a key measure of visual function. However, it is a measure of central acuity of the fovea and is poorly correlated with GA lesion size.^{8,10} Changes in BCVA may not fully capture disease progression, and BCVA does not assess all nuances of comprehensive visual function; therefore, we need to evaluate patients in a more comprehensive way.^{3,8,10-12} For example, sometimes I will simply hand a patient

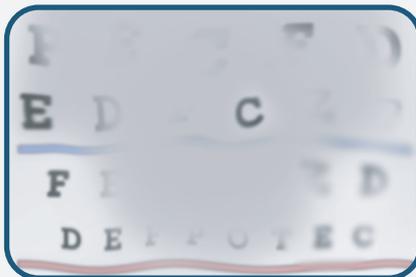
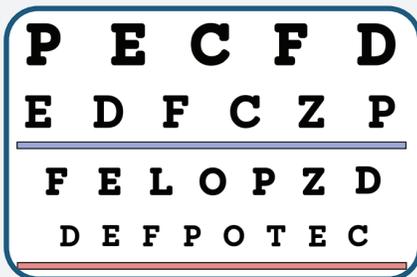
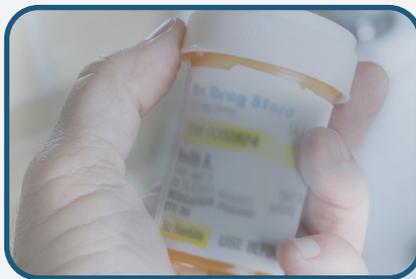
something to read and observe them to obtain an idea of their visual function. I also use low luminance testing to evaluate their visual function in dim conditions.

GA can grow in a unique, foveal-sparing pattern that tends to involve the fovea only late in the course of the disease.^{11,12} Even when BCVA remains relatively good, functional vision continues to decline as lesions grow (Figure 1).^{3,7,8}

Figure 1: Visual Impairment Associated With GA

NORMAL VISION

SEE THROUGH THE EYES OF A PATIENT LIVING WITH GA*



Some patients living with GA describe their visual impairment as blurriness, waviness, or areas that are missing. This may lead to difficulty reading or seeing faces.^{40,41}

BCVA is poorly correlated with lesion size. GA patients with relatively good visual acuity may still experience functional vision issues.¹⁰

*Vision loss from GA varies. Representations are for illustrative purposes only.

Because of the relentless nature of the disease, it is critical to diagnose and refer patients with GA as early as possible.^{2,3} Ask patients about changes in their vision beyond BCVA to help inform the initial diagnosis and to better monitor the progression of GA.^{40,41} My patients often report seeing a haze, or just having a sense that

something doesn't seem right. They may report difficulty seeing in the dark, blurred vision, straight lines appearing crooked or waviness in the visual field, colors seeming dull or washed out, blurry spots in the center of their vision, and missing areas of vision, all of which can lead to trouble doing tasks.⁴¹

PATIENT CASE: ANDREA

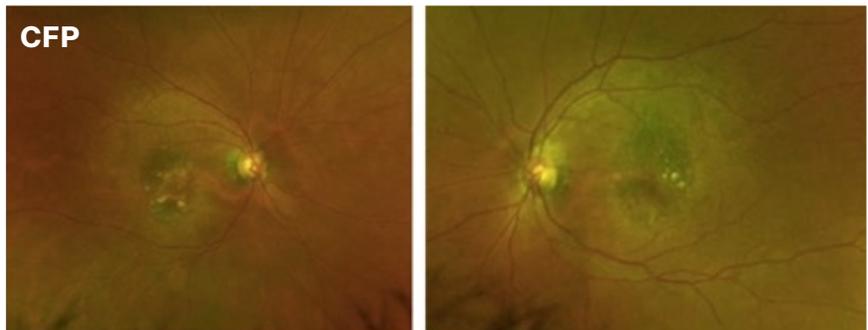
The following patient case profile provides a real-world example of how BCVA may not fully capture the extent of the disease. We will review the progression of the patient's GA over 3 years using multiple imaging modalities and see the impact on her BCVA and visual function.

Andrea is a 72-year-old Hispanic female. Her medical history is positive for stroke and hypercholesterolemia.

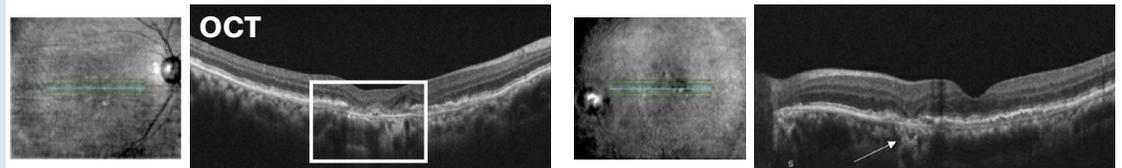
“With this patient, reviewing her imaging in multiple modalities over the years allows us to observe progressive enlargement of GA boundaries and reduction in choriocapillaris flow. These clinical signs align with her steady decline in both BCVA and functional vision.”

2018

- OD: 20/40
- OS: 20/20
- Despite large area of atrophy, BCVA is still relatively good due to foveal sparing
- Patient fails a DMV driving test
- She reports recent temporal metamorphopsia OD



“Because her fovea is still partially intact, Andrea’s BCVA is still relatively good. Despite this, she is complaining of symptoms, including metamorphopsia. Although Andrea’s BCVA meets legal criteria for driving, she failed her driving test.”



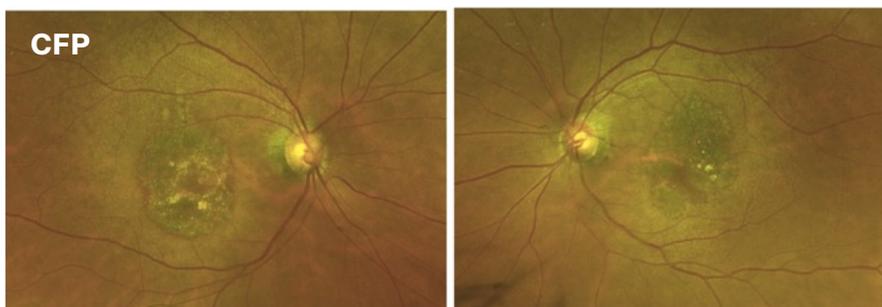
Despite significant atrophy, the fovea is still partially intact.

Hypertransmission defect outside the fovea; incomplete RPE and outer RPE atrophy.

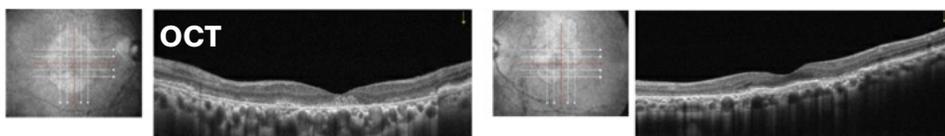
Images are courtesy of Dr Julie Rodman at the Broward Eye Care Institute.
DMV, department of motor vehicles; OD, right eye; OS, left eye; RPE, retinal pigment epithelium.

PATIENT CASE: ANDREA (continued)

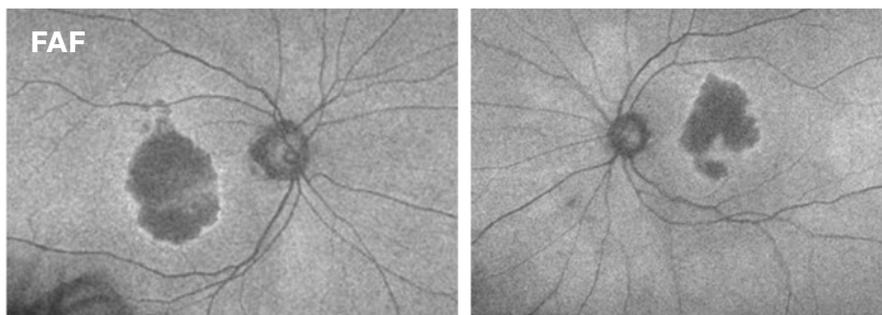
2020



- OD: 20/100
- OS: 20/25
- Patient reports seeing horizontal lines in inferior field while watching television OD

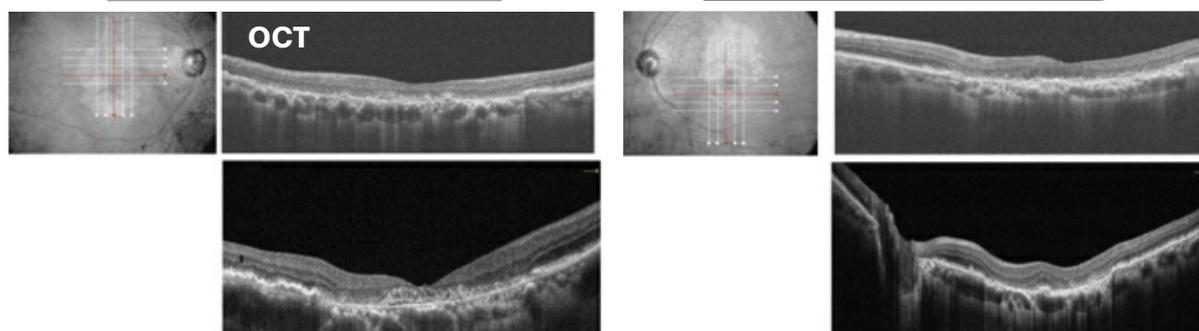


Complete outer retinal and RPE atrophy parafoveally.



2021

- OD: CF 5 FT
- OS: 20/30
- Patient reports increased light sensitivity OS, as well as “seeing a man in front of her” and visually hallucinating



Images are courtesy of Dr Julie Rodman at the Broward Eye Care Institute.

CF, count fingers; CFP, color fundus photography; FAF, fundus autofluorescence; FT, feet; OCT, optical coherence tomography.

Q6 WHAT IS THE IMPORTANCE OF MULTIMODAL IMAGING IN THE DIAGNOSIS OF GA?

DR RODMAN: GA can be diagnosed and monitored through multimodal imaging (Table 1).² It is especially important that the optometric community be well-versed in multimodal imaging because imaging is crucial for patient education and a key part of the referral process. Of course, not all practices have access to all of these imaging modalities. It is important to make the best use of the tools you have available to you.

CFP

CFP is a non-invasive option often used to detect a wide range of abnormalities in clinical trials. However, its reliability is limited due to reduced contrast.^{42,43}

“When using CFP, it is important to take a high-quality photo to be able to see evidence of abnormalities.”

OCT

Early signs of GA can be detected with OCT, which may help identify patients with the earliest signs of retinal cell loss, before there are definitive signs on fundus autofluorescence.⁴⁴ OCT B-scans can detect hyper-transmittance, produce high resolution images, and may not require dilation.⁴³

En face OCT is used in conjunction with B-scans to obtain a full picture of horizontal and transverse visualization. Interpretation can be challenging in some cases and may result in longer reading times.⁴³

“While the high quality of images from OCT allow us to pick up subtle changes and clearly see how much atrophy is present, its interpretation can be very nuanced. It is important to scan all the cuts when evaluating OCT to ensure nothing is being missed; if you have your technician bring you only one picture, it might result in a false negative. It is also important that optometrists know where to look for and how to measure hyper-transmission defects, as well as how to identify hyper-reflective foci and other indicators that can estimate how quickly a patient might progress. This is particularly true of OCT-A because this technology allows us to segment the retina and choroid into slabs, and then we can look at the vasculature at different levels of the retina. Specifically, if we look at the junctional zone, or the boundary between surviving and dead RPE, those patients that have more attenuation area typically go on to have higher progression rates.^{8,45} While we are still learning about OCT-A, it can provide a level of detail that may help drive clinical decision-making.”

FAF

FAF gives a frontal view that allows for visualizing the extent of a lesion.^{45,46,47} FAF is valuable for detecting areas of atrophy, documenting baseline lesion area, and tracking lesion growth in GA.⁴⁵

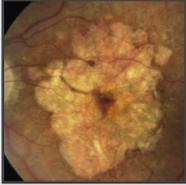
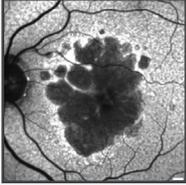
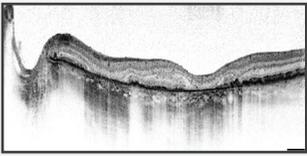
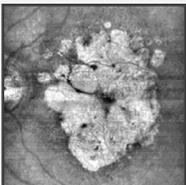
FAF detects the fluorescent signal coming mainly from lipofuscin, a naturally occurring compound in RPE cells. In healthy eyes, this autofluorescence appears uniformly gray, except for the fovea which appears dark due to macular lutein pigment blocking the fluorescent signal. In eyes with GA, where the RPE has degenerated, there is no fluorescent signal and the macula appears black, outlining the area of atrophy.⁸

FAF indicates the location and size of lesions at baseline and shows how lesions grow and change over time, allowing for determination of a patient's individual lesion growth rate.⁴⁵ For diagnosis, the contrast of surviving RPE versus absent RPE can offer a better delineation of the extent of the GA lesions compared with what is seen on clinical examination or on a color image.⁸ FAF is excellent at evaluating lesion type, which gives us information about progression risk. This predictive power is a key differentiating characteristic of FAF.^{8,48} In the junctional zone, bright areas of hyperfluorescence can often be observed, which are thought to indicate the cells most likely to next become atrophic. These areas of hyperfluorescence are likely to become atrophic as the patient's GA progresses.^{8,49}

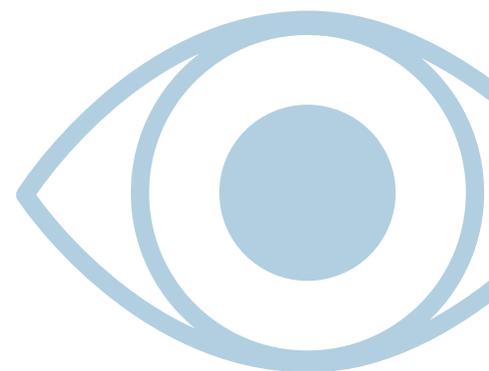
“In my practice, FAF is one of our most favored multimodal imaging techniques. We can compare images over time, and I find it helpful to view the images side-by-side on the screen. I find that patients can easily understand FAF images—they can see the black areas on the image and grasp that it is the atrophy that is causing their vision loss. By becoming familiar with using novel imaging techniques such as FAF, eye care professionals can help to identify GA early and better educate their patients about their condition.”^{39,45}

CFP, color fundus photography; FAF, fundus autofluorescence; OCT, optical coherence tomography.

Table 1:
Diagnostic Imaging Techniques Used to Identify GA^{2,42,43,47}

Imaging Modality	Pro(s)	Con(s)
CFP 	<ul style="list-style-type: none"> • Often used in clinical trials • Detect wide range of abnormalities • Non-invasive 	<ul style="list-style-type: none"> • Reduced contrast, limited reliability • Patient discomfort from bright light
FAF 	<ul style="list-style-type: none"> • High contrast to detect atrophy • Detection of small areas of atrophy 	<ul style="list-style-type: none"> • Hard to identify atrophy in the fovea • Requires high technical skill
OCT B-Scan 	<ul style="list-style-type: none"> • Detect hyper-transmittance • May not require dilation • High resolution images 	<ul style="list-style-type: none"> • Challenges in image interpretation can lead to longer acquisition/reading times
OCT en face 	<ul style="list-style-type: none"> • Visualize lesion contours • Detection of biomarkers (eg, reticular pseudodrusen) 	<ul style="list-style-type: none"> • Interpretation dependent on imaging quality

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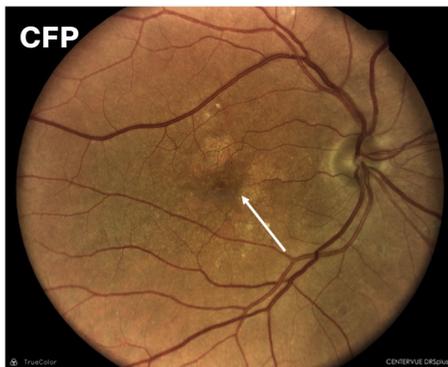


PATIENT CASE: MORRIS

In the following patient case, we'll compare CFP, OCT, and FAF images used in the diagnosis of GA. This case helps illustrate the difference between imaging modalities and demonstrates how it is possible to underestimate the severity of GA if imaging is not of sufficient quality.

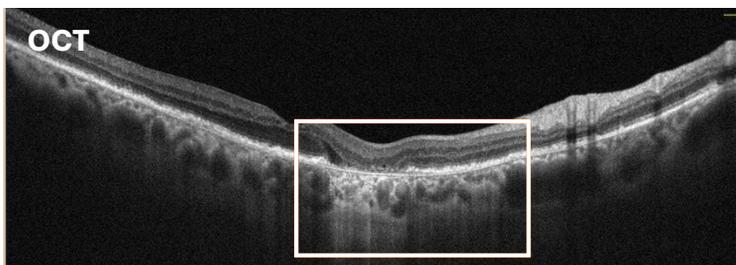
Morris is a 71-year-old Caucasian male. He has been a smoker for 40 years and still smokes 1 pack/day; his medical history is otherwise unremarkable. His grandfather had macular degeneration.

BASELINE VISIT

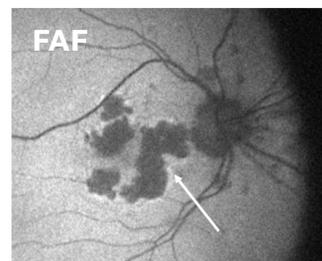


- BCVA: 20/30
- Patient at baseline has RPE mottling, drusen, and parafoveal patches of atrophy with minimal foveal involvement on CFP OD (arrows)
- Visual function: Patient reports decreased vision particularly at night. He also reports “pinhole” black spots in center vision

“These images provide a good example of how CFP cameras can be very different. The contrast is different from image to image. The image on the right is the same eye taken on the same day as the image on the left, but the GA is less apparent.”



Complete RPE and outer retinal atrophy with increased hypertransmission into choroid.



Extrafoveal lesions; hyperfluorescent border around the GA lesions indicates areas that are at risk for further progression.

“When we look at the same eye using OCT and FAF, the GA is apparent. On the OCT, there is hypertransmission and an area of complete atrophy. On the FAF, there are clear lesions and hyperfluorescence. If I had only used CFP to evaluate this patient, I would not have realized the extent of his disease. There are a lot of red flags present in this patient, but I would have underestimated the severity based on CFP alone.”

Images are courtesy of Dr Julie Rodman at the Broward Eye Care Institute.

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Q7 IN SUMMARY, WHAT IS THE CRITICAL ROLE OPTOMETRISTS PLAY IN RECOGNIZING GA AND ENSURING A TIMELY AND APPROPRIATE REFERRAL?

DR RODMAN: GA progression is relentless and irreversible; the condition can lead to difficulty completing activities of daily living and have detrimental impacts on quality of life and emotional health.³⁻⁹ With life expectancy increasing, eye care professionals are likely to see more patients with GA in the future.⁵⁰ Therefore, there is a critical need for

the proper identification, referral, and monitoring of these patients.¹⁴ Optometrists play a key role in diagnosing and referring patients with GA, and in working together with other eye care providers to optimize patient care.^{14,29} As a team, we can hopefully improve the patient's experience of this terrible disease.

"If you suspect GA in one of your patients, review the case with a specialist, ask questions if you are uncertain, and make a timely referral."

ADDITIONAL WEB RESOURCES

RecognizeAndReferGA.com

INTERESTED
IN MORE?



Dr Rodman has been compensated for the presentation of this educational information.

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