RECOGNIZING GEOGRAPHIC ATROPHY

A guide to identifying and monitoring patients with Geographic Atrophy

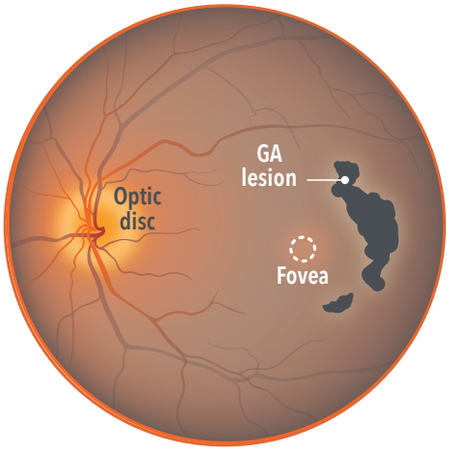
Apellis

GEOGRAPHIC ATROPHY:

An advanced form of age-related macular degeneration

Geographic Atrophy (GA) is an advanced form of age-related macular degeneration (AMD), a leading cause of significant vision loss worldwide and in Canada.[1-3]

GA is characterized by progressive loss of the photoreceptors, retinal pigment epithelium (RPE), and underlying choriocapillaris. Regions of atrophy typically start outside the fovea and expand to involve the fovea.[2,4]



It is critical to identify GA early because the damage is progressive and associated with irreversible vision loss[2,4]

4 STEPS TO DETECTING GEOGRAPHIC ATROPHY

1. Consider risk factors & symptoms
2. Use multimodal imaging
3. Assess lesion presentation
4. Monitor for progression

GA=geographic atrophy.

1 CONSIDER RISK FACTORS & SYMPTOMS

The pathogenesis of AMD is multifactorial, with many different genetic and environmental risk factors associated with its development and progression to more advanced forms like GA.[5]

Risk factors associated with development of AMD and/or progression to GA

Genetics

- **Family history*** of AMD[5-7]
- **Genetic predisposition*** (eg, complement gene variants associated with increased risk)[4-6]

Physiology

- **Age*** (greatest risk factor for AMD)[7]
- Obesity[5]
- Certain dyslipidemias[5]
- Cardiovascular disease/ hypertension[5]

Lifestyle/ environment

- History of **smoking**[5,7]*
- Diet[5]
- High alcohol intake[8,9]

Clinical factors & imaging findings

- Presence of GA in fellow eye[2]
- Drusen volume[10]

*Most significant risk factors.

Patient symptoms that may indicate GA

In the early stages of GA, visual symptoms may be minimal, as central vision is largely preserved until atrophy involves the fovea. Patients may experience some loss of peripheral, low-light vision, but it may only be noticeable under certain conditions or with designed tests. As the disease progresses, more severe deterioration in central visual acuity occurs.[4,11]

Visual symptoms[11]

- Delayed dark adaptation
- Reduced contrast sensitivity
- Distorted vision (eg, straight lines that appear wavy or crooked)
- Dull/washed-out colours
- Scotomas (characterized by blurry and/or blind spots)

Functional symptoms[11]

- Difficulty reading, driving, working, and with daily activities outside the home
- Particular difficulty in low light
- Difficulty recognizing familiar faces

AMD=age-related macular degeneration; GA=geographic atrophy.

2 USE MULTIMODAL IMAGING

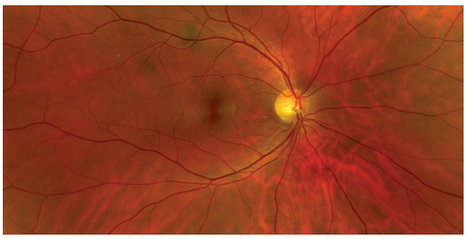
GA can be distinguished from other forms of AMD via imaging. It is characterized as cell layer loss with sharply defined borders.[2,12]

IMAGING MODALITY

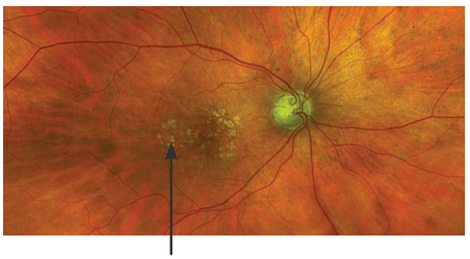
Colour fundus photography (CFP)[2,12]

- GA lesions are defined as sharply demarcated areas of RPE hypopigmentation
- Clear visibility of underlying choroidal vessels

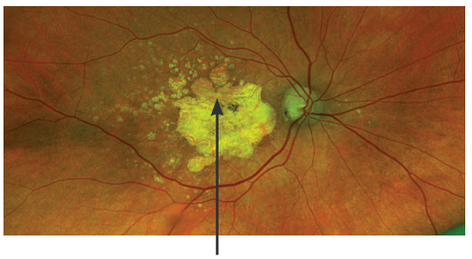
NORMAL EYE



EYES WITH GA



Choroidal vessels
Small multifocal non-subfoveal GA

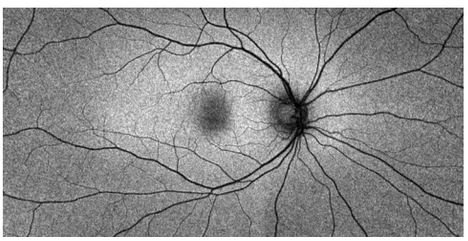


Choroidal vessels
Large multifocal subfoveal GA

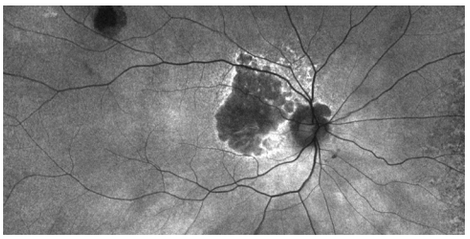
Fundus autofluorescence (FAF)[2,13]

- GA lesions appear as distinct areas of decreased autofluorescence due to loss of lipofuscin-containing RPE cells
- Hyperautofluorescence in the junctional zone indicates areas at high risk for atrophy

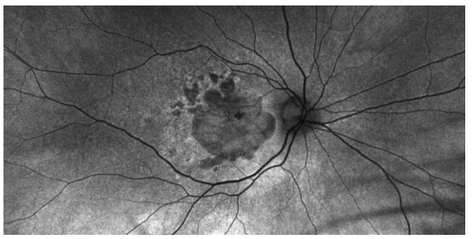
NORMAL EYE



EYES WITH GA



Medium unifocal subfoveal GA



Large multifocal subfoveal GA

FAF is the current standard imaging technology for morphological assessment of GA[13]

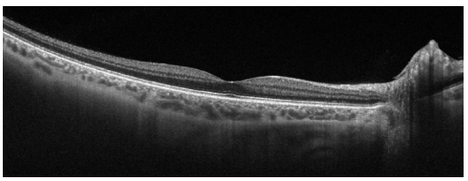
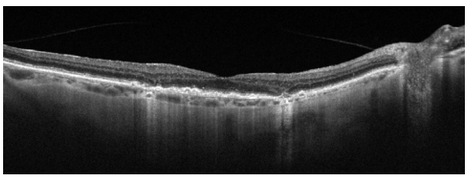
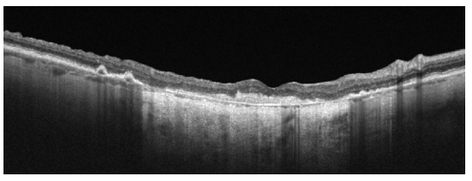
Images courtesy of Netan Choudhry, MD, FRCS(C), DABO, Vitreous Retina Macula Specialists of Toronto.
AMD=age-related macular degeneration; FAF=fundus autofluorescence; GA=geographic atrophy; RPE=retinal pigment epithelium.

The following diagnostic imaging techniques can be used to identify GA. Each modality provides insight into different aspects of GA lesions and disease progression.[4]

IMAGING MODALITY

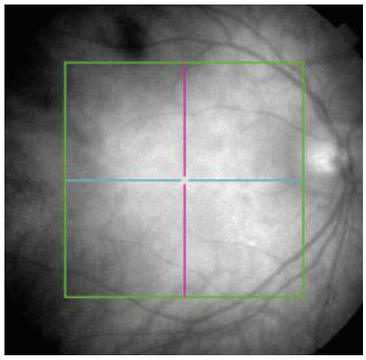
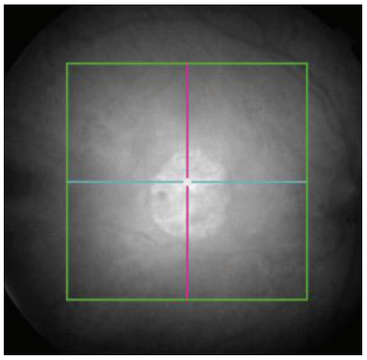
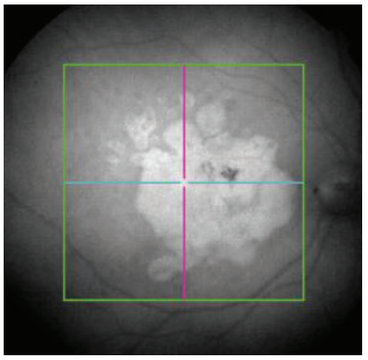
Optical coherence tomography (OCT) – structural B scan[2,13]

- GA appears as sharply demarcated region(s) of degradation in the RPE and photoreceptor layers
- Increased reflectivity from underlying choroid and choriocapillaris

NORMAL EYE	EYES WITH GA	
		
	Small multifocal non-subfoveal GA	Large multifocal subfoveal GA

Optical coherence tomography (OCT) – *en face*[12]

- Structural B scans can be combined with *en face* views of OCT scans to more easily identify lesion borders and measure lesion growth

NORMAL EYE	EYES WITH GA	
		
	Medium unifocal subfoveal GA	Large multifocal subfoveal GA

The earliest diagnosis of GA can be obtained using OCT imaging[12]

Images courtesy of Netan Choudhry, MD, FRCS(C), DABO, Vitreous Retina Macula Specialists of Toronto.
GA=geographic atrophy; OCT=optical coherence tomography; RPE=retinal pigment epithelium.

ASSESS LESION PRESENTATION

GA lesions can present in several different patterns. While the rate and nature of GA progression vary considerably among individual patients, some factors have been shown to be associated with rate of progression. Awareness of specific lesion features that could predict faster GA progression is important.[2]

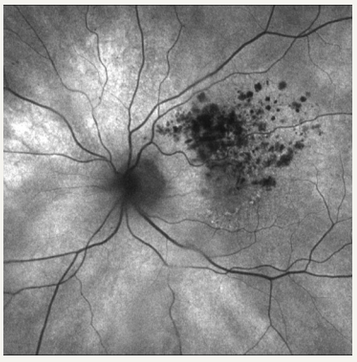
GA lesions grow at a rate of **~2 mm² per year** on average (~0.53 to 2.6 mm² per year)[2,14-16]

Lesion features associated with rate of GA progression[2,17,18]

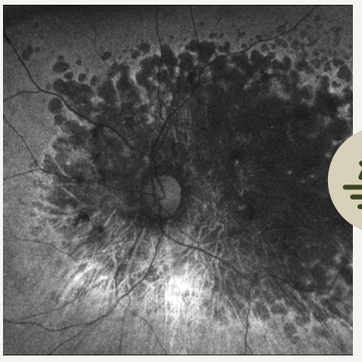
Predictors of faster GA progression

SIZE

Small

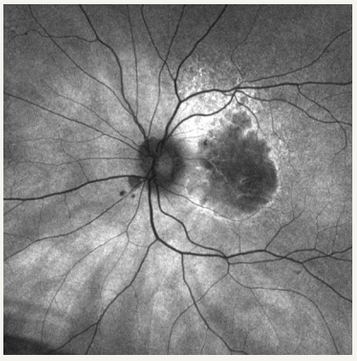


Medium/large

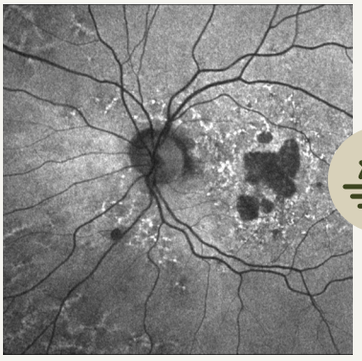


CONFIGURATION

Unifocal

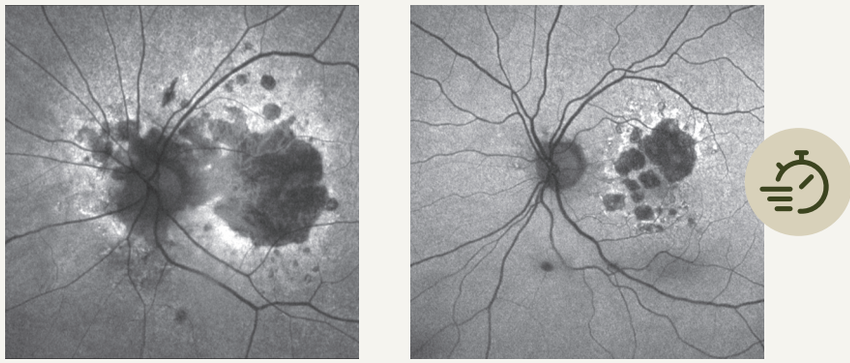


Multifocal

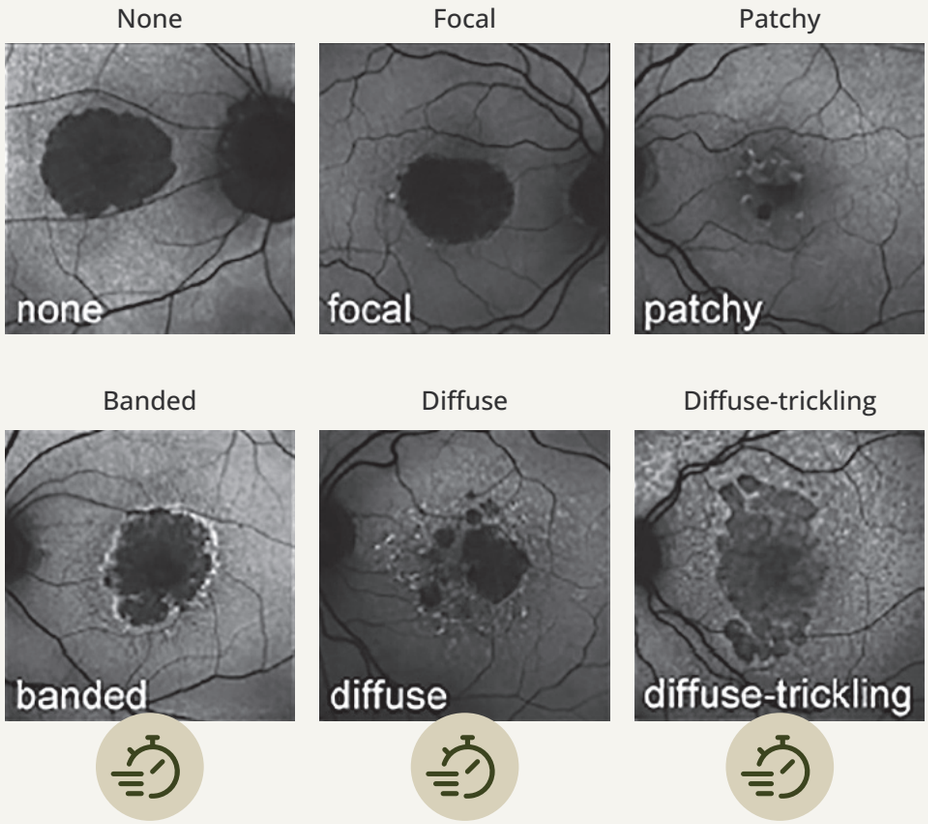


Images courtesy of Netan Choudhry, MD, FRCS(C), DABO, Vitreous Retina Macula Specialists of Toronto.
GA=geographic atrophy.

LOCATION



FAF PATTERN



4

MONITOR FOR PROGRESSION

Recommended monitoring schedule for patients with GA[6]:

- **Regular monitoring at least every 6 to 12 months** by an optometrist (OD) or ophthalmologist
- **Consider referral to a specialist** for patients at high risk of progression

Images courtesy of Netan Choudhry, MD, FRCS(C), DABO, Vitreous Retina Macula Specialists of Toronto (Lesion location).
Images reprinted from Fleckenstein M, et al. *Ophthalmology*. 2018;125(3):369-390. © 2018, with permission from the American Academy of Ophthalmology (FAF pattern).
FAF=fundus autofluorescence; GA=geographic atrophy.

You play a key role in early detection and ongoing monitoring of patients with GA

DISCOVER GEOGRAPHIC ATROPHY

Learn about lesion progression

Explore the patient burden

See the damaging effects of excessive complement activation

Visit GeographicAtrophy.ca

Apellis is a global biopharmaceutical company that leverages courageous science and compassion. We are committed to addressing the unmet needs of patients and eye care professionals worldwide.

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Developed in collaboration with Netan Choudhry, MD, FRCS(C), DABO
Co-founder and medical director of the Vitreous Retina Macula Specialists of Toronto

GA=geographic atrophy.

References:
1. Gehrs KM, Anderson DH, Johnson LV, et al. *Ann Med*. 2006;38(7):450-471. **2.** Fleckenstein M, Mitchell P, Freund B, et al. *Ophthalmology.* 2018;125(3):369-390. **3.** Noble J, Chaudhary V. *CMAJ*. 2010;182(16):1759. **4.** Boyer DS, Schmidt-Erfurth U, van Lookeren Campagne M, et al. *Retina*. 2017;37(5):819-835. **5.** Sobrin L, Seddon JM. *Prog Retin Eye Res*. 2014;40:1-15. **6.** Eye Health Council of Ontario. *Can J Optom*. 2015;77(1):1-11. **7.** Aldebert G, Faillie JL, Hillaire-Buys D, et al. *JAMA Ophthalmol*. 2018;136(7):770-778. **8.** Adams MKM, Chong EW, Williamson E, et al. *Am J Epidemiol*. 2012;176(4):289-298. **9.** Zhang J, Mitsuhashi T, Matsuo T, et al. *Curr Eye Res*. 2021;46(12):1900-1907. **10.** Nassisi M, Lei J, Abdelfattah NS, et al. *Ophthalmology*. 2019;126(12):1667-1674. **11.** Sacconi R, Corbelli E, Querques L, et al. *Ophthalmol Ther*. 2017;6:69-77. **12.** Sadda SR, Guymer R, Holz FG, et al. *Ophthalmology*. 2018;125:537-548. **13.** Sadda SR, Chakravarthy U, Birch DG, et al. *Retina*. 2016;36(10):1806-1822. **14.** Holekamp N, Wykoff CC, Schmitz-Valckenberg S, et al. *Ophthalmology*. 2020;127:769-783. **15.** Holz FG, Sadda SR, Busbee B. *JAMA Ophthalmol.* 2018;136(6):666-677. **16.** Heier JS, Pieramici D, Chakravarthy U. *Ophthalmol Retina*. 2020;4(7):673-688. **17.** Holz FG, et al. *Am J Ophthalmol*. 2007;143(3):463-472. **18.** Jeong YJ, Hong IH, Chung JK, et al. *Eye (Lond)*. 2014;28(2):209-218.

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