

## Factors Affecting GA Progression Rate

GA progression rates vary widely among patients. Mean growth rates of atrophic areas ranging from 1.2 to 2.8 mm<sup>2</sup> per year have been reported in longitudinal studies.<sup>1,2</sup> Several studies have identified specific factors associated with variations in GA growth rates:

**Size, configuration and location of atrophic areas** - GA progression rates vary according to lesion size. Faster GA lesion growth rates are observed in eyes with larger vs. smaller lesions at baseline.<sup>3</sup> The shape (configuration) of the GA lesion (i.e. 'single', 'multi-focal', or 'merged') has also been found to be predictive of progression rates. An analysis of the Blue Mountains Eye Study population revealed faster progression rates in eyes with multifocal versus classic GA lesion configuration. However, it is unclear whether the multifocal GA configuration is indicative of more widespread disease, which may have a faster rate of progression.<sup>4</sup>

Location of the GA lesions also affects progression rate, with one study reporting that eyes with GA lesions further from the fovea had higher growth rates, compared with GA lesions that were closer (0.14 mm/year for every millimetre further from the fovea).<sup>5</sup>

**Fellow eye status** - AMD status of the fellow eye at baseline is another indicator for disease progression rates in eyes with GA. A sub-analysis of patients diagnosed with GA in the Fundus Autofluorescence in Age-related Macular Degeneration (FAM) study, reported faster GA progression rates among patients with GA in both eyes, than in patients who had early/intermediate AMD in their fellow eye.<sup>6</sup>

---

<sup>1</sup> Holz FG, Strauss EC, Schmitz-Valckenberg S, van Lookeren Campagne M. Geographic atrophy: clinical features and potential therapeutic approaches. *Ophthalmology*. 2014;121(5): 1079-1091.

<sup>2</sup> Schmitz-Valckenberg S, Sahel JA, Danis R, Fleckenstein M, Jaffe GJ, Wolf S, *et al*. Natural History of Geographic Atrophy Progression Secondary to Age-Related Macular Degeneration (Geographic Atrophy Progression Study). *Ophthalmology*. 2016;123(2): 361-368.

<sup>3</sup> Sunness JS, Margalit E, Srikumaran D, Applegate CA, Tian Y, Perry D, *et al*. The long-term natural history of geographic atrophy from age-related macular degeneration: enlargement of atrophy and implications for interventional clinical trials. *Ophthalmology*. 2007;114(2): 271-277.

<sup>4</sup> Joachim N, Mitchell P, Kifley A, Rochtchina E, Hong T, Wang JJ. Incidence and progression of geographic atrophy: observations from a population-based cohort. *Ophthalmology*. 2013;120(10): 2042-2050.

<sup>5</sup> Grunwald JE, Pistilli M, Ying GS, Maguire MG, Daniel E, Martin DF, Comparison of Age-related Macular Degeneration Treatments Trials Research G. Growth of geographic atrophy in the comparison of age-related macular degeneration treatments trials. *Ophthalmology*. 2015;122(4): 809-816.

<sup>6</sup> Fleckenstein M, Schmitz-Valckenberg S, Adrion C, Visvalingam S, Gobel AP, Mossner A, *et al*. Progression of age-related geographic atrophy: role of the fellow eye. *Investigative ophthalmology & visual science*. 2011;52(9): 6552-6557.

## Factors Affecting GA Progression Rate

**Genetic factors** - Genetic factors associated with AMD susceptibility have also been linked to GA lesion progression in clinical studies.

A combined analysis of data from the FAM study and the Age-Related Eye Disease Study (AREDS) revealed significant and independent correlations between variants of at least two genes – ARMS2 (rs10490924) and C3 (rs2230199) – and the rate of GA lesion growth.<sup>7</sup>

A separate analysis of the Blue Mountain Eye Study cohort found that subjects with ARMS2 and CFH risk variants had faster GA lesion progression.<sup>4</sup>

**Other risk factors** - Analysis of the Blue Mountain Eye Study data identified several factors associated with faster GA progression rates including smoking and less frequent fish consumption (suggesting a beneficial effect of omega-3 fatty acids). Pseudophakic participants also had a higher rate of GA progression, indicating that sun exposure may also be a risk factor in GA development.<sup>4</sup>

---

<sup>7</sup> Grassmann F, Fleckenstein M, Chew EY, Strunz T, Schmitz-Valckenberg S, Gobel AP, *et al.* Clinical and genetic factors associated with progression of geographic atrophy lesions in age-related macular degeneration. *PLoS one.* 2015;10(5): e0126636.