Semiautomated Image Processing Method for Identification and Quantification of Geographic Atrophy in Age-Related Macular Degeneration

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PURPOSE. To determine intraobserver and interobserver longitudinal measurement variability of novel semiautomated software for quantification of age-related macular degeneration-associated geographic atrophy (GA) based on confocal scanning laser ophthalmoscopy fundus autofluorescence (FAF) imaging.

METHODS. Three-field FAF (excitation 488 nm, emission 500–700 nm), near-infrared reflectance (820 nm), and blue reflectance (488 nm) images of 30 GA subjects were recorded according to a standardized protocol at baseline after 6 and 12 months. At all visits, the GA area was analyzed on central FAF images by seven independent readers using semiautomated software. The software allows direct export of FAF images from the database and semiautomated detection of atrophic areas by shadow correction, vessel detection, and selection of seed points.

RESULTS. The mean size of atrophy at baseline and the mean progression rate were 5.96 mm² (range, 1.80–15.87) and 1.25 mm²/year (0.42–2.93), respectively. Mean difference of interobserver longitudinal measurement variability of novel semiautomated software for quantification of age-related macular degeneration-associated geographic atrophy (GA) based on confocal scanning laser ophthalmoscopy fundus autofluorescence (FAF) imaging.

CONCLUSIONS. The new image processing software offers an accurate, reproducible, and time-efficient identification and quantification of outer retinal atrophy and its progression over time. It facilitates measurements both in natural history studies and in interventional trials to evaluate new pharmacologic agents designed to limit GA enlargement. (Invest Ophthalmol Vis Sci. 2011;52:7640–7646) DOI:10.1167/iovs.11-7457

Geographic atrophy (GA) is the atrophic late-stage manifestation of dry age-related macular degeneration (AMD) and represents approximately 20% of all late-stage AMD cases.1–6 It is characterized by the development of atrophic areas that enlarge steadily over time and that are associated with a corresponding absolute scotoma.7–9 Severe visual loss results from foveal involvement. Although anti–vascular endothelial growth factor (VEGF) therapy represented a breakthrough in the treatment of neovascular AMD, there are yet no means to halt or reverse GA progression.10

Based on conventional fundus photographs, GA has been defined as a sharply demarcated area of apparent absence of the retinal pigment epithelium (RPE), larger than 175 μm, with visible choroidal vessels and no neovascular AMD.3,11 This definition is based on histopathologic studies that have characterized clinically visible areas of atrophy as areas with RPE and outer neurosensory layer cell death with occasionally visible choriocapillaris.3,11

Most epidemiologic and natural history studies that have addressed the enlargement of GA areas with time have used color fundus photographs.7–9,12,13 Although this technique can be used to detect the presence of GA, graders at reading centers have reported difficulty reproducibly measuring atrophic areas because of intersubject variability of fundus pigmentation, media opacities, and the presence of drusen and small satellites of atrophy.14–16

Fundus autofluorescence (FAF) imaging is a recently introduced noninvasive imaging method for metabolic mapping of naturally or pathologically occurring fluorophores of the ocular fundus.1,7,16 The dominant sources are fluorophores in lipofuscin granules that accumulate with age and in association with various retinal diseases in the post-mitotic RPE.19 Because RPE cells are lost, with concurrent depletion of lipofuscin, atrophic areas in GA exhibit a markedly reduced autofluorescent signal. The high-contrast of these hypofluorescent areas, compared with the nonatrophic retina, allows for easy and accurate determination of lesion boundaries, particularly compared with conventional fundus photography.

In 2002, we proposed using customized image analysis software for semiautomated quantification of atrophic areas in eyes with GA on images obtained by confocal scanning laser ophthalmoscopy (cSLO) FAF imaging.20 Compared with a method whereby GA area was outlined manually by a mouse-driven arrow, this approach resulted not only in superior intraobserver and interobserver agreements but was also less...
time consuming and allowed electronic data transfer for analysis. Subsequently, it was successfully applied for atrophy quantification in the FAM (Fundus Autofluorescence in Age-Related Macular Degeneration) Study, a multicenter, longitudinal, natural history study in GA patients. In 2005, a further development led to improved customized software for atrophy quantification that included a contrast enhancing tool that could be applied when uneven illumination occurred during recording of FAF, a sensitive threshold adjustment that facilitated fine-tuning of atrophy segmentation, and an algorithm for identification of interfering vascular structures. In addition, all images of follow-up visits were aligned to their corresponding baseline images using retinal vessels as landmarks to compensate for any differences in scaling, shifting, and rotation. This approach has been subsequently applied in another multicenter longitudinal natural history study, the Geographic Atrophy Progression (GAP) Study, and its intraobserver and interobserver agreements have been regularly documented (Holz et al. JOVS 2010;51:ARVO E-Abstract 94/A141; Herrmann et al. JOVS 2010;51:ARVO E-Abstract 313/D666).

Along with the development of new therapeutic strategies and the initiation of several interventional trials for subjects with GA secondary to AMD, there is an increasing need for an imaging processing method that allows for rapid, easy, and reliable assessment of atrophic areas on FAF images. Particularly compared with existing methods, this software must be validated and must comply with US Food and Drug administration requirements. In collaboration with the GRADE Reading Center and the Duke Reading Center, the manufacturer of a commercially available cSLO system, Heidelberg Engineering, has developed the RegionFinder software. The aim of this study was to assess intraobserver and interobserver variability between independent, experienced readers of the RegionFinder software.

**Methods**

**Image Acquisition**

Retinal imaging was performed with a cSLO system (Spectralis HRA+OCT; Heidelberg Engineering, Heidelberg, Germany) and included the acquisition of near-infrared reflectance (IR 820 nm), blue reflectance (BR 488), and FAF (excitation 488 nm, emission 500–700 nm) using the high-speed mode. The field of view was set at 30° × 30° and was centered on the macula. For the current analysis, 30 eyes of 30 subjects with GA secondary to AMD with longitudinal imaging data over 1 year (baseline, month 6, and month 12) were randomly selected from the reading center imaging database and were uploaded in a dedicated Heidelberg Eye Explorer (HEYEX) database. Images from five subjects were uploaded twice to assess intraobserver agreement.

The study followed the tenets of the Declaration of Helsinki. Before inclusion, informed consent for additional imaging beyond routine clinical examination and use of retinal imaging data for additional research was obtained from each subject after explanation of the nature and possible consequences of participating in retinal imaging research. For the current analysis, subjects had to be 55 years of age and have a well-demarcated area of GA secondary to AMD in the study eye. The total GA lesion size had to be ≥20 mm² (approximately 8 disc areas [DA]) with a single lesion of at least 1.25 mm² (0.5 DA). Best-corrected visual acuity in the study eye had to be ≥25 letters using ETDRS (Early Treatment Diabetic Retinopathy Study) charts. Fluorescein angiography was performed at baseline to exclude any signs of choroidal neovascularization (CNV) or fibrosis in the study eye.

**Procedures**

Semiautomated atrophy detection and quantification were independently performed by seven readers using customized software (RegionFinder, version 1.5.0; Heidelberg Engineering) according to predefined grading instructions. The RegionFinder is novel dedicated software for semiautomated quantification of atrophic areas that allows FAF images in the HEYEX database to be directly processed. FAF images are digital images. The FAF intensity of every picture element (pixel) is given in a certain gray value. The dramatic decrease of the FAF signal in GA areas compared with nonatrophic retinal areas is used by the RegionFinder for the segmentation of atrophy areas. After the definition of the center of a region by the operator, the so-called region-growing algorithm tends to grow toward the borders of the region, taking into account all pixels with a signal intensity below a certain threshold. This threshold is defined by a parameter referred to as ‘growth power.’ The higher the growth power, the larger the enclosed area. The proper adjustment of this parameter allows for the precise measurement of the area of atrophy. For scaling, the individual scaling factor that is registered by the HEYEX during acquisition is used. Given the digital image resolution of 768 × 768 pixels of a 30° × 30° frame, one pixel roughly corresponds to 11 μm.

All seven readers had previously trained and had graded for at least 1 year in a reading center setting cSLO images of GA secondary to AMD. For the current analysis, comparative grading using two computer screens was chosen. That is, all cSLO image data (including BR and IR) were available for the analysis of each single visit. By selecting the baseline FAF image in the HEYEX, the RegionFinder tool was activated for automated alignment of follow-up FAF images to baseline. If no automated alignment to the corresponding baseline image was possible (e.g., due to insufficient image quality), follow-up images were processed either with reference to the image of month 6 or, if not applicable or possible, individually with no image alignment. For each visit, total atrophy size was measured by a semiautomatic procedure. The minimum size of individual atrophic areas was predefined as 0.05 mm². Initially, the reader manually set a seeding point inside the atrophic region to start an automatic region identification algorithm that detects well-demarcated regions of severely decreased autofluorescence signal. The reader then manually changed the algorithm growth power and ‘growth limit’ to achieve further fine adjustments in lesion measurement. Readers were instructed to increase the algorithm growth power until the defined area exceeded the lesion boundaries. The growth power was then decreased by one increment below this threshold, which then defined the best-adjusted lesion area. Interfering retinal blood vessels that exhibited similar intensities as atrophic areas were excluded using the retinal blood vessel detection tool. In addition, a shadow correction tool was used when there was uneven illumination, and manual line, circles, contours or ‘free-hand’ constraints were applied to improve lesion boundary discrimination of atrophy patches. The two latter constraints were particularly helpful to manually adjust the region boundaries to exclude the fovea, when it was not involved by GA. Because of luteal pigment, blue-light FAF intensities are typically decreased in the fovea. Although atrophic patches exhibit an even lower FAF intensity than the central macula, foveal involvement can be challenging to identify. Readers were therefore instructed to use constraints while using the corresponding BR and IR images to improve foveal lesion boundary discrimination. When there was confluent peripapillary and central atrophy, standard operation procedures included the use of the line constraint tool to draw a vertical line at the most narrow part (the ‘bridge’) of the confluent atrophy. Any atrophy nasal to this line was disregarded for atrophy quantification. Once atrophic areas and constraints had been defined for the baseline visit, they could be easily copied to any subsequent image that belonged to the same follow-up series. Only a fine adjustment by the reader was then required. After processing every atrophic area, grading reports for each visit were automatically generated. These reports list, among other parameters, the name of the reader, time of analysis, total size of atrophy, number of spots, and sizes of spots. In addition, the defined lesion areas and any corresponding manually applied constraints are shown by the report.
Statistical Analysis

The intraobserver and interobserver agreements for total size of atrophy at each visit and atrophy progression rates over time were assessed using Bland-Altman statistics. Calculation of atrophy progression rates was performed by subtracting the total size of atrophy at month 12 from baseline (assuming a linear growth rate).

RESULTS

Confocal scanning laser ophthalmoscopy images of all 30 eyes were successfully processed at baseline by all seven readers using the RegionFinder software (Fig. 1). The results of each individual reading were directly exported and graphically displayed in a grading report that was printed and signed by each reader (Fig. 2). Automated alignment of images to baseline images was possible in 26 of 30 eyes for month 6 and in 26 of 30 eyes for month 12, respectively. Three of the month 12 images with no alignment to baseline could be aligned to the month 6 image. Therefore, it was not possible to align an image to any visit in just one eye. Reasons for unsuccessful alignment included low image quality and improper orientation of the image field at the time the FAF image was obtained. Because of the development of new CNV, two eyes were excluded from the analysis at month 12. The following data for the 1-year visit and the calculated 1-year progression rate are based on 28 eyes.

The mean total size of atrophy at baseline and the mean progression rate (given as the average measurement of all seven readers of each of the five eyes used for the intraobserver variability analysis) were 5.44 mm² (range, 3.28–8.13) and 1.46 mm²/year (0.66–2.43), respectively. No failures of automated alignment or CNV development were observed in these five eyes. The mean agreements for intraobserver variability with

![Figure 1](image-url)

**Figure 1.** Representative example for atrophy quantification over time. *First row:* near-infrared reflectance images at baseline, month 6, and month 12; *second row:* native fundus autofluorescence images; *third row:* results of reader 1; the detected areas of atrophic are highlighted in blue; *fourth row:* results of reader 2.
the Bland-Altman analysis were similar among the seven readers at baseline (mean agreements ranging from \(-0.02\) mm\(^2\) to 0.21 mm\(^2\)), month 6 (\(-0.08\) mm\(^2\) to 0.14 mm\(^2\)), and month 12 (\(-0.13\) mm\(^2\) to 0.32 mm\(^2\)) and for the calculated atrophy progression rates (\(-0.14\) mm\(^2\)/year to 0.11 mm\(^2\)/year) (Table 1).

For interobserver testing, the mean total size of atrophy at baseline and the mean progression rate (determined as the average measurement of all seven readers for each of the 30 test eyes) were 5.96 mm\(^2\) (range, 1.80–15.87) and 1.25 mm\(^2\)/year (0.42–2.93), respectively. Results of the Bland-Altman analysis for interobserver agreement are listed in Table 2 and are depicted in Figure 3, showing similar differences and 95% confidence intervals for the analyses of all seven readers to each other.

The major reason for disagreement and the few major outliers between the readers were caused by different assessments of the extent to which the fovea was spared. Even with the help of other CSLO modalities, including IR imaging, this task is challenging. Because of similar macular pigment grayscale values compared with atrophy in FAF images, it was necessary to manually define constraints to assist the automated region algorithm to identify the extent of the atrophic lesion boundaries in the foveal area (Figs. 1, 2). Another common cause for disagreement was the definition of the threshold of the parameter growth power for the quantification of single atrophic patches. An exact turning point (i.e., an abrupt change in the identified boundary) of the algorithms was not obvious in some cases, leading to slight variations in the intraobserver and interobserver agreements. In one test eye with confluent peripapillary atrophy, the placement of the vertical constraint at the bridge to central atrophy also resulted in only minor differences (Fig. 4). The vessel detection tool was helpful for
r rapid exclusion of interfering retinal blood vessels with decreased corresponding autofluorescence signal adjacent to atrophic patches. There was good agreement with respect to the definition of a minimum size of 0.05 mm² for single atrophic areas. In case of disagreement, such as if one reader included one small satellite while others disregarded it, this did not cause any major effect. Particularly, in case of multifocal lesions, the RegionFinder software allows for rapid quantification of total atrophy size. Uneven distribution of the FAF signal because of incorrect orientation of the laser scanning at the time of image acquisition could be successfully minimized with the shadowing correction tool. Moreover, the availability of other cSLO modalities, particularly IR images, was very helpful in the assessment of atrophic areas.

**DISCUSSION**

This study demonstrates that a novel imaging processing method can assist trained readers to accurately identify and measure atrophic areas on cSLO FAF images of patients with GA secondary to AMD in a reproducible and time-efficient manner. The intraobserver and interobserver agreements are within the expected ranges compared with previously developed semiautomated software tools that are superior to manual outlining methods.\textsuperscript{15,20,22} The annual mean rates of atrophy enlargement reported in different natural history studies range between 1.3 mm²/year and 2.6 mm²/year\textsuperscript{12,13,21,25} (Holz et al. IOVS 2010;51:ARVO E-Abstract 94/A141). Reasons for the slightly lower average progression rate of 1.25 mm²/year in this study may be related to lesion-specific phenotype features such as smaller baseline areas or different FAF patterns.\textsuperscript{12,21} Given the intraobserver and interobserver agreement of the RegionFinder software, these data strongly support the assumption that the spread of atrophy could be well quantified by this software tool within 1 year. In comparison with previous approaches, the RegionFinder markedly facilitates the analysis of atrophy quantification. Direct operation of the RegionFinder software from within the Heidelberg Eye Explorer ensures correct image scaling and alignment within a follow-up series, excluding at the same time any transcription errors. Grading reports automatically include date, time, and reader details.

<table>
<thead>
<tr>
<th>Reader</th>
<th>Baseline</th>
<th>Month 6</th>
<th>Month 12</th>
<th>Atrophy Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.05 ± 0.28</td>
<td>0.15 ± 0.50</td>
<td>0.02 ± 0.07</td>
<td>−0.05 ± 0.22</td>
</tr>
<tr>
<td>2</td>
<td>0.21 ± 0.15</td>
<td>0.07 ± 0.10</td>
<td>0.32 ± 0.22</td>
<td>0.11 ± 0.29</td>
</tr>
<tr>
<td>3</td>
<td>−0.02 ± 0.04</td>
<td>−0.08 ± 0.09</td>
<td>−0.13 ± 0.10</td>
<td>−0.09 ± 0.08</td>
</tr>
<tr>
<td>4</td>
<td>0.15 ± 0.16</td>
<td>0.10 ± 0.13</td>
<td>0.15 ± 0.14</td>
<td>0.01 ± 0.15</td>
</tr>
<tr>
<td>5</td>
<td>0.11 ± 0.06</td>
<td>0.14 ± 0.05</td>
<td>0.05 ± 0.16</td>
<td>−0.06 ± 0.17</td>
</tr>
<tr>
<td>6</td>
<td>0.05 ± 0.05</td>
<td>0.07 ± 0.10</td>
<td>−0.09 ± 0.19</td>
<td>−0.14 ± 0.21</td>
</tr>
<tr>
<td>7</td>
<td>0.09 ± 0.07</td>
<td>−0.08 ± 0.18</td>
<td>−0.02 ± 0.14</td>
<td>−0.11 ± 0.18</td>
</tr>
</tbody>
</table>

Mean 0.09 0.05 0.04 −0.05
Minimum −0.02 −0.08 −0.13 −0.14
Maximum 0.21 0.14 0.32 0.11

**Table 2.** Mean Differences and 95% CIs for Interobserver Agreements for Total Size of Atrophy at Different Visits (in mm²) and for the Atrophy Progression Rates over Time (in mm²/year)

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Month 6</th>
<th>Month 12</th>
<th>Atrophy Progression</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1−R2\textsuperscript{a}</td>
<td>0.21 ± 0.18</td>
<td>0.15 ± 0.14</td>
<td>0.13 ± 0.19</td>
</tr>
<tr>
<td>R1−R3</td>
<td>0.14 ± 0.15</td>
<td>0.22 ± 0.17</td>
<td>0.25 ± 0.20</td>
</tr>
<tr>
<td>R1−R4</td>
<td>0.30 ± 0.17</td>
<td>0.27 ± 0.18</td>
<td>0.29 ± 0.20</td>
</tr>
<tr>
<td>R1−R5</td>
<td>0.03 ± 0.21</td>
<td>0.24 ± 0.30</td>
<td>0.04 ± 0.15</td>
</tr>
<tr>
<td>R1−R6</td>
<td>0.03 ± 0.14</td>
<td>0.05 ± 0.12</td>
<td>0.08 ± 0.16</td>
</tr>
<tr>
<td>R1−R7</td>
<td>0.27 ± 0.13</td>
<td>0.42 ± 0.16</td>
<td>0.44 ± 0.18</td>
</tr>
<tr>
<td>R2−R3</td>
<td>−0.01 ± 0.13</td>
<td>0.15 ± 0.12</td>
<td>0.13 ± 0.20</td>
</tr>
<tr>
<td>R2−R4</td>
<td>0.04 ± 0.19</td>
<td>0.14 ± 0.12</td>
<td>0.16 ± 0.17</td>
</tr>
<tr>
<td>R2−R5</td>
<td>−0.13 ± 0.29</td>
<td>0.09 ± 0.26</td>
<td>−0.09 ± 0.21</td>
</tr>
<tr>
<td>R2−R6</td>
<td>−0.13 ± 0.18</td>
<td>−0.07 ± 0.13</td>
<td>−0.05 ± 0.18</td>
</tr>
<tr>
<td>R2−R7</td>
<td>0.06 ± 0.20</td>
<td>0.29 ± 0.15</td>
<td>0.31 ± 0.20</td>
</tr>
<tr>
<td>R3−R4</td>
<td>0.11 ± 0.14</td>
<td>0.02 ± 0.20</td>
<td>0.05 ± 0.19</td>
</tr>
<tr>
<td>R3−R5</td>
<td>−0.12 ± 0.22</td>
<td>−0.12 ± 0.20</td>
<td>−0.20 ± 0.19</td>
</tr>
<tr>
<td>R3−R6</td>
<td>−0.15 ± 0.13</td>
<td>−0.16 ± 0.17</td>
<td>−0.14 ± 0.20</td>
</tr>
<tr>
<td>R3−R7</td>
<td>0.12 ± 0.14</td>
<td>0.21 ± 0.17</td>
<td>0.20 ± 0.17</td>
</tr>
<tr>
<td>R4−R5</td>
<td>−0.24 ± 0.24</td>
<td>−0.05 ± 0.27</td>
<td>−0.25 ± 0.17</td>
</tr>
<tr>
<td>R4−R6</td>
<td>−0.25 ± 0.09</td>
<td>−0.19 ± 0.12</td>
<td>−0.21 ± 0.15</td>
</tr>
<tr>
<td>R4−R7</td>
<td>−0.01 ± 0.16</td>
<td>0.16 ± 0.14</td>
<td>0.15 ± 0.14</td>
</tr>
<tr>
<td>R5−R6</td>
<td>0.00 ± 0.22</td>
<td>−0.15 ± 0.33</td>
<td>0.04 ± 0.15</td>
</tr>
<tr>
<td>R5−R7</td>
<td>0.24 ± 0.23</td>
<td>0.20 ± 0.26</td>
<td>0.40 ± 0.16</td>
</tr>
<tr>
<td>R6−R7</td>
<td>0.26 ± 0.10</td>
<td>0.39 ± 0.14</td>
<td>0.36 ± 0.14</td>
</tr>
</tbody>
</table>

Mean 0.04 0.11 0.10 0.07
Minimum −0.25 −0.19 −0.25 −0.12
Maximum 0.30 0.42 0.44 0.28

\(a\) R1−R2, results for the comparison between reader 1 and reader 2.
They can be printed and signed to serve as source document data in clinical trials and daily practice.

We believe that the use of predefined grading criteria, the training of readers and the use of other corresponding cSLO imaging modes, and the strategy of comparative grading for follow-up visits were helpful in minimizing variability within and between readers. They are essential prerequisites for future studies and analyses. In particular, awareness of the influence of macular pigment on FAF intensities and the availability of IR images are of particular importance for reducing uncertainty in the delineation of the foveal-sparing extent.

The additional use of other ocular fundus imaging methods, especially optical coherence tomography (OCT), may further improve the accuracy and reproducibility of atrophy quantification. Recently, Yehoshua et al.26 and Baumann et al.27 have independently reported that planimetric measurements of atrophic lesions can be made on images obtained by spectral-domain OCT. Further studies are required to investigate whether this approach is applicable in multicenter trials. Furthermore, SD-OCT volume scans produce interpolated images with a resolution dependent on the number of vertical scans that make up the volume scan in the posterior pole. One additional advantage of FAF imaging is that increased autofluorescent intensity in the perilesional zone of atrophy can be visualized and may assist in predicting future atrophy progression.21,28 It may be speculated that the combination of both modalities in the future could represent the optimal approach to identify and quantify atrophy.29,30

Improvements in the accuracy and reproducibility of the determination of total size of atrophy compared with the approach used in this study would be of great value to better monitor disease progression and to evaluate new treatment strategies. Semiautomated measurement of GA based on FAF imaging may currently represent the most precise method; however, its sensitivity and interobserver agreements are still limited, which is particularly reflected by the size of the confidence intervals of the interobserver testing in this study. In the reading center setting, we have established the threshold of ±0.15 mm² as the maximum variance of two independent readings for the total size of atrophy. If the measurements of the total lesion size of the two graders differ ≥ ± 0.15 mm², a senior reader quantifies the total lesion size again. The measurement made by the senior grader along with the closer of the two graders’ measurements is averaged, as long as the deviation between these two measurements is within ±0.15 mm². If the senior grader measurement differs > ± 0.15 mm² from either of the grader measurements, a second senior grader reads the image, and the measurements made by the two senior graders are averaged. The senior grader measurements are the final measurements performed on the images, no matter the degree of discrepancy. In extreme cases, the senior graders may discuss the image, specify lesion boundaries, and then independently measure the lesion size again.

Outer retinal atrophy is a common downstream result of various complex and monogenetic retinal diseases. On FAF images, the appearance is uniformly associated with a markedly decreased signal. However, lesion boundaries may not be as well defined as in atrophic AMD. Despite the possibility of acquiring composite images over larger retinal areas using the confocal SLO system applied here, expansion of outer retinal atrophy beyond the regular 30° × 30° images area at the posterior pole may limit area quantification with accuracy and reproducibility similar to what we have shown here for GA. Further clinical evaluation may assess the use of the described image processing software for other retinal diseases such as...

![FIGURE 3. Results of statistical analysis (Bland-Altman design) for evaluation of agreement between the reader 1 (R1) and the other six readers (R2–R7) at the baseline visit.](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933248/)

![FIGURE 4. Quantification of central atrophy in the presence of confluent peripapillary atrophy is challenging. In this study, readers were instructed to use the constraint tool to draw a vertical line at the most narrow part (the bridge) of the confluent atrophy. Any atrophy nasal to this line was disregarded for atrophy quantification. The constraint was then automatically copied to the images of the following visits.](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933248/)
Stargardt’s disease, for which interventional clinical trials have already been initiated or planned.

Area measurements using the new imaging processing software require well-demarcated lesion boundaries. Accurate determinations of affected areas would depend on these criteria. Especially with concurrent exudative disease or fibrotic changes after a former neovascular process, lesions boundaries usually become ill defined. There are as yet no means based on FAF images to precisely outline the border zone. Therefore, the absence of well-demarcated lesion boundaries represents a significant limitation of the new software.

In summary, analysis of FAF images using a novel image processing tool allows reproducible and rapid semiautomated detection and measurement of the size and progression of atrophic GA areas. This software can be used in the context of large-scale multicenter studies in patients with GA. Effective and accurate tools for automated detection and quantification are indispensable for monitoring the effects of prospective therapeutic interventions to halt progression in patients with GA caused by AMD.

References

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