Supplement 2

Supplementary material to Choroidal Structure in Late-Onset Stargardt Disease and Age-Related Macular Degeneration – An OCT-Angiography Study

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1. Compensation for signal attenuation

Three-dimensional OCT-A data were processed by a general sliding slab method in order to remove decorrelation tail artifacts within the volume (Fig. 1). OCT-A and structural OCT en face images were generated from the artifact-corrected volume using a maximum intensity projection for choriocapillaris slab (CC; defined at a [+10 µm, +40 µm; with positive sign indicating increase in depth] interval from the RPE-Fit segmentation). Then, a recent approach was adapted from Zhang et al. 2018 and applied to compensate for choriocapillaris signal attenuation resulting from media opacification (e.g. floaters) as well structural changes in the retinal pigment epithelium (RPE) / Bruch's membrane (BM) complex. The OCT-A en-face images were downscaled to 512 x 512 pixel. Thus, each pixel represented the average of 4 pixels. Since the noise in OCT-A follows a random pattern, while the absence of flow-signal exhibits high spatial correlation, a reduction of noise was apparent. Similar to previously described methods, the structural OCT en-face images were preprocessed to remove bright background noise using a rolling-ball-algorithm (radius of 100 pixel), smoothed using a Gaussian smoothing filter ($\sigma = 5$ pixel) to minimize speckle noise followed by normalization. The inverted structural OCT en-face images were then multiplied with the OCT-A en-face images to obtain a attenuation-compensated OCT-A en-face image.
Supplementary Figure 1. In the first row, the optical coherence tomography angiography (OCT-A) en-face images of the choriocapillaris (CC-slab, RPE-Fit segmentation [+10 µm, +40 µm], maximum intensity projection) and the corresponding B-scans (grayscale depicting the structural OCT data and red depicting OCT-A flow signal) are shown. These corrected cc-slab images underwent subsequently compensation of signal attenuation by taking into account the structural information as shown in the second row. Please note, the study subject with the most severe floater (white arrow head) in the study was chosen for visualization purposes.

1. Removal of decorrelation tail artifacts

2. Compensation for choriocapillaris signal attenuation
2. Conservative analysis

A second "conservative" analysis was performed to assess whether our results truly reflect differences between late-onset Stargardt disease (STGD1) and age-related macular degeneration (AMD) due to vascular changes rather than signal attenuation secondary to flecks or drusen. Hereby, all areas with measurable retinal pigment epithelium (RPE) elevation with respect to Bruch's membrane were excluded from the analysis (Supplementary Figure 2). The results are shown in Supplementary Figure 3.

Supplementary Figure 2. The first row shows the fundus autofluorescence (FAF), the optical coherence tomography angiography (OCT-A) en-face images of the choriocapillaris (CC-slab, RPE-Fit segmentation [+10 µm, +40 µm], the OCT-A CC-slab after removal of decorrelation tail artifacts and compensation for signal attenuation (OCT-A**) and the retinal pigment epithelium (RPE) elevation map. All analysis were carried out for the complete area outside of RPE atrophy as well as the area outside of the RPE atrophy excluding flecks and drusen as shown for the thresholded OCT-A images, which were obtained using the Phansalkar method (radius of 13 px [corresponding to 152 µm]).
**Supplementary Figure 3.** The results for the “conservative” analysis (i.e. excluding areas with drusen or flecks) were highly similar to the results shown in the main manuscript. Briefly, AMD exhibited a significantly smaller area-fraction of absence-of-flow-signal (AFS) than STGD1 outside RPE atrophy (upper left panel). Considering the ratio of AFS inside to outside of RPE-atrophy, this difference between AMD and STGD1 was even more pronounced. Of note, the effect of age on AFS area-fraction outside RPE atrophy was not significant anymore. The flow texture analysis revealed that log-log size-frequency distribution differs significantly between AMD and STGD1. Hereby, STGD1 exhibited more small flow voids than AMD indicated by the higher intercept (b) as shown in the lower right panel. However, the distribution is steeper in STGD1 than AMD as shown by the more negative slope (m) in the lower right panel. This indicates the presence of fewer large areas of AFS in STGD1 compared to AMD.
References


