Towards a normative spatio-temporal atlas of disease progression in intermediate AMD

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Purpose: To develop an atlas describing the typical topography of retinal disease progression markers and their change over time observed in SDOCT of patients with intermediate age-related macular degeneration (AMD).

Methods: We built a morphological atlas by aligning OCT scans automatically using a two-step registration, first within-subject alignment incorporating the vessel structure, followed by a between-subject alignment based on two landmarks, fovea and optic disc (OD) center-points (Fig. 1). For intra-subject registration we applied layer segmentation and motion correction on OCT scans, computed an en-face projection and performed an automatic segmentation of vessel shadows. Follow-up scans were aligned based on vessel maps and OCT en-face projections. For inter-subject registration we aligned the scans such that the fovea was placed at the center and the angle between fovea and the center of OD versus the horizon met the reported population mean of 5.6°. Fovea and OD center were automatically identified in the OCT and SLO scans. Finally, drusen and HRF were automatically segmented in OCT volumes using a deep learning approach, and were mapped into the reference system.

Results: A population mean atlas including drusen and HRF progression in the retina was obtained from 134 subjects with intermediate AMD and monthly visits over one year prior to conversion to choroidal neovascularization (CNV) (n=85) or geographic atrophy (GA) (n=49). HRF and drusen activity was mostly located in the central 3 mm (Fig. 2). A significant increase in disease activity, in terms of changes in drusen, was observed at time-points close to conversion, with a significant decrease in drusen at specific parafoveal areas for GA, indicating an increased amount of drusen regression before progression. Neovascular conversion was mostly drusen-centric, while atrophic conversion happened unrelated to drusen location.

Conclusions: The normative spatio-temporal atlas allows to establish anatomical correspondences between subjects and, thus, enables an analysis of disease marker progression in the retina, both on a population level, as presented here, as well as for an individual. It may also allow comparison of individual patients against a normative morphologic standard. Such an atlas is an important tool for longitudinal and cross-sectional analysis of disease progression in AMD, and furthermore for individual risk estimation and prediction.

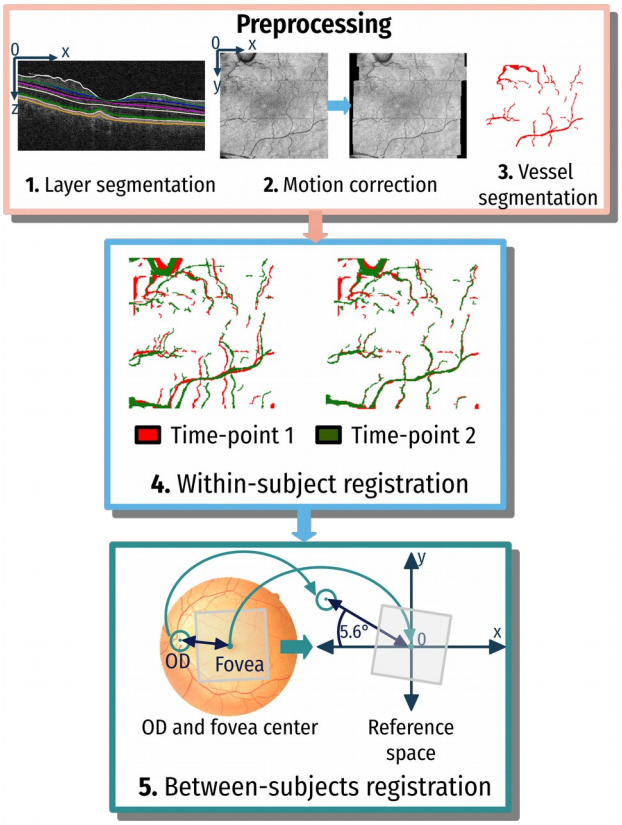

Figure 1: Steps to obtain a spatio-temporal atlas. **1.** Segmentation of layers. **2.** Correction of motion artefacts. An en-face projection before and after correction is shown. **3.** Automatic segmentation of vessels. **4.** Within-subject alignment using the vessel structure. **5.** Between-subjects registration by optic disc (OD) and fovea center identified in the SLO and OCT image. Fovea center is moved to coordinate origin and OD center is rotated to population mean angle.

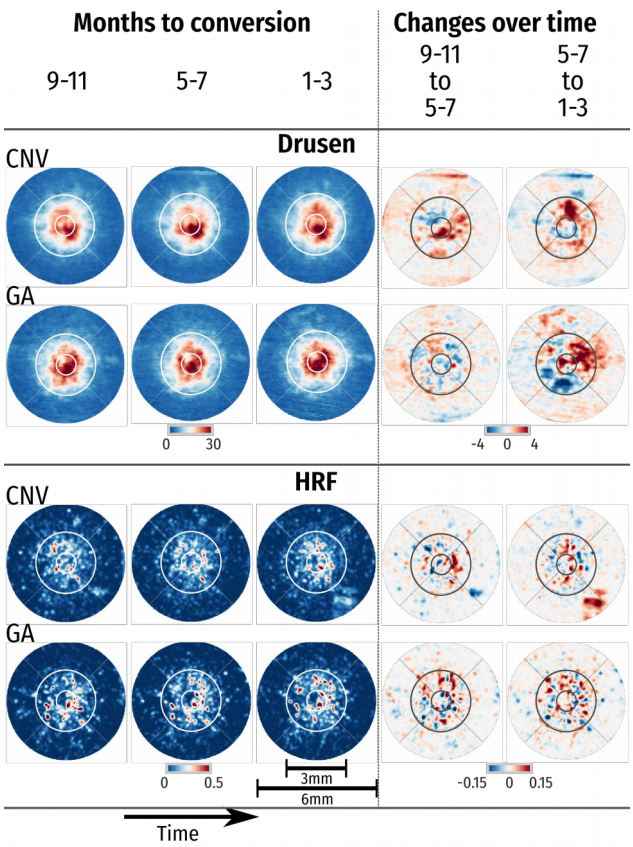

Figure 2: Atlas of drusen **(top)** and hyperreflective foci (HRF) **(bottom)** distributions observed at regular intervals from one year until conversion to choroidal neovascularization (CNV) or geographic atrophy (GA).
The two columns to the right illustrates changes between time-points as difference of means, with blue and red colors indicating areas with a decrease and increase in drusen and HRF over time.