Dynamics of Macular Cysts in Retinitis Pigmentosa: A Longitudinal Optical Coherence Tomography and Adaptive Optics Study

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Purpose: Retinitis pigmentosa (RP), a genetic disorder marked by progressive photoreceptor degeneration, is frequently complicated by cystoid macular edema (CME), which is seen in 10–60% of patients. The precise temporal and spatial relationship between CME and the advancing front of photoreceptor degeneration, as well as the impact of cysts on underlying retinal structures, remains unclear. This study aims to characterize the dynamics of cyst formation and resolution in RP, testing the hypothesis that cysts emerge as the transition zone (TZ)—the demarcation of degenerating and healthy photoreceptors—encroaches upon the central macula, and subsequently resolve upon complete outer segment loss. Furthermore, we seek to identify optimal adaptive optics (AO) imaging techniques for concurrently visualizing both cysts and the integrity of the underlying cone mosaic.

Methods: We acquired and analyzed yearly longitudinal clinical Optical Coherence Tomography (OCT) data from a retinitis pigmentosa cohort (n=62) to determine the percentage of subjects with cysts (cyst prevalence) across different TZ eccentricities and track individual cyst dynamics over a four-year period. High-resolution enface confocal and non-confocal adaptive optics scanning laser ophthalmoscopy (AOSLO) was performed and analyzed to compare the efficacy of these detection modalities for cyst detection, visibility of cysts through various focal planes, and the visibility of cone photoreceptors within and around cystic areas. Individual AOSLO images, each covering a 2x2 degree field, were collected across the horizontal midline, extending from the fovea to +/- 8 degrees eccentricity, with acquisitions spaced by 2 degrees.

Results: Our findings demonstrate a relationship between cyst prevalence and TZ eccentricity (in µm), with peak prevalence reaching approximately 71% when the TZ is located within the central 1250 µm of the macula, compared to 50% at eccentricities beyond 1250 µm and 28% in the most advanced stages where no TZ was discernible. Overall, cysts were observed in 58% of the cohort, aligning with previously reported prevalence estimates for RP patients with CME. Longitudinal OCT data further revealed the episodic nature of cysts, showing their appearance in new areas as the TZ advances, followed by their resolution in regions of complete photoreceptor loss. In AOSLO, nonconfocal detection significantly enhanced the contrast and visibility of intraretinal cysts, identifying on average 55 cysts per 2x2 degree imaging area compared to only 34 cysts with confocal imaging (paired t-test, $p < 0.001$), and also exhibited a superior tolerance to system defocus, remaining highly visible across a range of 0.6 D. Conversely, when correctly focused, confocal AO imaging provided clearer visualization of individual cone photoreceptors

located directly beneath these cystic formations, revealing an average of 168 cones per cyst where offset modes showed only 103 cones (paired t-test, $p < 0.01$).

Conclusions: Our study suggests that intraretinal cysts in RP are dynamic features whose presence and resolution may be linked to the spatiotemporal progression of photoreceptor degeneration. For detailed investigation, a multi-modal AO approach is required: confocal AOSLO for visualizing underlying cone structure, and nonconfocal modes for enhanced cyst detection. This combined approach could offer a more comprehensive understanding of cyst-photoreceptor interactions in RP.