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Registration Number	☑ “KOU”　□ “OTSU” No.　*Office use only	Name	杨 丽珠 (Yang, Lizhu)

Thesis Title

Spatial Functional Characteristics of East Asian Patients With Occult Macular Dystrophy (Miyake Disease); EAOMD Report No.2

（東アジア人オカルト黄斑ジストロフィ（三宅病）患者における網膜機能の空間的特徴；東アジアオカルト黄斑ジストロフィ研究レポート第 2 報）

Thesis Summary

Occult macular dystrophy (OMD), first described by Miyake *et al*. in 1989, is a type of inherited macular dystrophy characterised by a progressive visual acuity loss but without the visible abnormality of the fundus or fluorescein angiogram. Patients with OMD typically present with an autosomal dominant inheritance, which is caused by pathogenic heterozygous variants in the *RP1L1* gene (i.e. *RP1L1*-associated OMD; Miyake disease).

Electrophysiological findings are key to the diagnosis of Miyake disease, which typically exhibits a normal full-field electroretinogram with abnormal macular function, as can be revealed by multifocal electroretinogram (mfERG). However, detailed functional assessments in a large cohort, including patients with various disease severities are still lacking, and the spectrum of functional phenotypes has not been established. Thus, this study aimed to determine the detailed functional characteristics of Miyake disease on the basis of a large East Asian patient cohort.

Twenty-eight participants (53 eyes) with Miyake disease who underwent mfERG recordings were enrolled at three centres in Japan, China and Korea. Comprehensive ophthalmological examinations, including spectral-domain optic coherence tomography (SD-OCT), were performed. Functional phenotypes based on the mfERG evidence of the spatial extent of posterior pole dysfunction were analysed. Patients were classified into three functional groups: Group 1, paracentral dysfunction with relatively preserved central/peripheral function; Group 2, homogeneous central dysfunction with preserved peripheral function; and Group 3, widespread dysfunction over the recorded area. Three functional phenotypes were compared in clinical parameters and the SD-OCT morphological classification (severe phenotype, blurred/flat ellipsoid zone and absence of the interdigitation zone; mild phenotype, preserved ellipsoid zone).

For the results, there were eight eyes in Group 1, 40 eyes in Group 2, and five eyes in Group 3. The patients in Group 1 showed significantly later onset ($P = .005$), shorter disease duration ($P = .002$) and preserved visual acuity ($P < .001$) compared with those in Group 2. No significant differences were revealed in age among the three groups, neither between Groups 2 and 3 or Groups 1 and 3 in all terms of clinical parameters. All eight eyes in Group 1 showed the mild morphological phenotype, while 43/45 eyes in Groups 2 and 3 presented the severe phenotype, which identified a significant association between the functional grouping and the morphological classification ($P < .001$).

In conclusion, a spectrum of functional phenotypes of Miyake disease was first documented, identifying three functional subtypes: paracentral dysfunction, homogeneous central dysfunction, and widespread dysfunction. Patients with paracentral dysfunction had the mildest phenotype, and those with homogeneous central or widespread dysfunction manifested overlapping clinical findings with severe photoreceptor changes, thereby suggesting various extents of visual impairments.