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Evaluation of clinical validity of the Rabin cone contrast test in normal phakic or pseudophakic eyes and severely dichromatic eyes

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ABSTRACT.

Purpose: **To evaluate the clinical validity of the Rabin cone contrast test (RCCT; Innova Systems, Inc.) in patients with normal phakic/pseudophakic eyes and severe dichromatic colour vision deficiency (CVD).**

Methods: **We evaluated age-related changes in the RCCT scores in 166 phakic eyes and 34 pseudophakic eyes and the RCCT sensitivity and specificity in 28 men with severe dichromatic CVD (10 with protanopia, 18 with deutanopia) and nine age-matched controls. All participants had 20/20 or better Snellen best-corrected visual acuity (BCVA). The RCCT was used to measure the L, M and S-CCT scores (range, 0–100).**

Results: **In normal phakic eyes, the mean L, M and S-CCT scores decreased gradually with ageing, with normal levels in patients in the second to seventh decades of life and some below normal in the eighth and ninth decades of life. In normal pseudophakic eyes, the mean L, M and S-CCT scores were normal in patients in the seventh to ninth decades of life. In eyes with severe CVD, the mean L, M and S-CCT scores were, respectively, 31.5 ± 18.3, 86.0 ± 12.6 and 98.0 ± 6.3 in patients with protanopia; 92.8 ± 10.5, 50.8 ± 19.6 and 97.8 ± 5.2 in patients with deutanopia; and 99.4 ± 1.7, 98.3 ± 5.0 and 99.4 ± 1.7 in controls. The RCCT sensitivity and specificity were 100% for diagnosing the CVD type.**

Conclusion: **The RCCT can be used in non-visually impaired patients up to the seventh decade of life and after cataract surgery in elderly patients. The RCCT is available for CVD screening and typing and the score has a wide distribution range even in patients with severe CVD.**

Key words: cataract – colour vision – cone contrast test – dichromatic colour vision deficiency

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Introduction

Representative conventional colour vision tests including pseudoisochromatic plates, the Farnsworth Panel D-15, lantern tests and anomaloscopy are time-consuming and do not consistently quantify the severity of congenital or acquired CVD resulting from dysfunctional L, M or S cones (Rabin 1996, 2004).

The RCCT is a novel colour vision test designed to diagnose rapidly and easily the type and severity of congenital CVD (Rabin et al. 2011). The RCCT also can be used to detect acquired CVD in eyes with glaucoma, optic neuropathy, vitreoretinal disorders and physiologic stress (Rabin et al. 2011; Niwa et al. 2014).

In a pilot study, Rabin et al. (2011) reported that the RCCT had high specificity and sensitivity for quantifying normal colour vision and diagnosing the type and severity of congenital CVD in young healthy pilot applicants during a military entrance physical examination. However, some issues have been identified in the clinical application of the RCCT. First, age-dependent changes in colour vision and contrast sensitivity should be considered (Boettner & Wolter 1962; Nomura et al. 2003). To use the RCCT clinically for various eye diseases, the availability of the RCCT in elderly subjects should be investigated. Second, Rabin et al. (2011) previously reported a mild correlation between the RCCT scores and matching range on anomaloscopy, which also is of interest. However, it is unclear whether the RCCT properly reflects the severity of congenital CVD. This study evaluated the clinical validity of the RCCT in normal phakic or pseudophakic eyes and in those with severe dichromatic CVD.

Patients and Methods

We evaluated the age-related changes in the RCCT scores in phakic eyes of patients 10 years of age and older and

pseudophakic eyes of patients 60 years of age and older. The phakic eyes included one eye of healthy volunteers or normal fellow eyes of patients treated for epiretinal membranes, idiopathic macular holes, rhegmatogenous retinal detachments and cataracts. Pseudophakic eyes included eyes implanted with yellow-tinted intraocular lenses without any ocular history except for cataract surgery. We excluded subjects with known CVD based on the medical interview. The main outcome measures in this analysis were the RCCT scores by age groups in phakic and pseudophakic eyes.

To evaluate the sensitivity and specificity of the RCCT in the diagnosis of dyschromatopsia, we evaluated the RCCT scores in men with severe dichromatic CVD, including 10 subjects with protanopia and 18 subjects with deutanopia, who were younger than 30 years. The type and severity of CVD were determined with pseudoisochromatic plates (Ishihara plates, Tokyo Medical College plates, and Standard Pseudoisochromatic Plates Part 1), the Farnsworth Panel D-15 and anomaloscopy (Anomaloscope OT-II, Neitz Instruments, Tokyo, Japan). Skilled orthoptists performed these colour vision tests under specific conditions. All dichromatic subjects met the failure criterion, that is two or more major crossings on the Farnsworth Panel D-15 and had a full matching range of 73 on anomaloscopy (Atchison et al. 1991). Nine age-matched male subjects without dyschromatopsia served as controls. The main outcome measures in this analysis were the RCCT scores in severe dichromatic CVD.

All subjects had 20/20 Snellen or better BCVA without any ocular history except for cataract surgery. The exclusion criteria were the presence of diabetes mellitus, optic neuropathy and unilateral or bilateral glaucoma. The CCT scores were measured using a commercially available RCCT (Provideo CCT Plus System, Innova Systems Inc., Burr Ridge, IL, USA). The system firmware version was 14.2.6. The Rabin colour examination was performed from the right eye to the left eye at a distance of 70 cm with refractive correction if needed. The L, M and S-CCT scores were expressed in the range from 0 to 100. The liquid crystal display of the RCCT was calibrated before the examination. We used the results from the left eyes when both eyes met the criterion to minimize possible errors due to inexperience with the novel examination. Rabin cone contrast test (RCCT) scores of 75 or greater were defined as normal as previously reported (Rabin et al. 2011).

The institutional review board of Shiga University of Medical Science Hospital approved this study, which followed the principles of the Declaration of Helsinki. All participants provided written informed consent before the start of the study. Statistical analyses were performed using GRAPHPAD Prism 6 software (GraphPad Software Inc., La Jolla, CA, USA). Data are expressed as the mean ± standard deviation. $p < 0.05$ was considered significant.

Results

To evaluate the age-related changes in the RCCT, 166 phakic eyes of 166 patients (age range, 10–89 years) and 34 pseudophakic eyes of 34 patients (age range, 60–89 years) were included. The mean L, M and S-CCT scores in phakic eyes decreased gradually with age, with normal levels in patients from the second to seventh decades of life, but the mean S-CCT score was below normal in patients in the eighth decade of life. All mean L, M and S-CCT scores were below normal in patients in the ninth decade of life (Fig. 1). The L, M and S-CCT scores were significantly lower with ageing ($p < 0.0001$ for all comparisons by the Kruskal–Wallis test). In pseudophakic eyes, the mean L, M and S-CCT scores were normal in patients in the seventh, eighth and ninth decades of life ($p = 0.82$, 0.72 and 0.21 by the Kruskal–Wallis test; Fig. 2).

In the analysis in severe dichromatic CVD, the mean age and BCVA did not differ significantly among the patients with protanopia and deutanopia and the control subjects, ($p = 0.35$ and $p = 0.92$, respectively, by the Kruskal–Wallis test; Table 1).

Almost all L, M and S-CCT scores were 100 in the control group. The L-CCT scores in the patients with protanopia and the M-CCT scores in the patients with deutanopia were 75 or less with a wide distribution (Fig. 3). The mean L, M and S-CCT scores in the dichromatic and control groups are shown in Table 2. The mean L-CCT score in the patients with protanopia and the M-CCT score in the patients with deutanopia were significantly ($p < 0.0001$, for both comparisons by the Kruskal–Wallis test) lower than in the other groups. There was no significant ($p = 0.86$, by the Kruskal–Wallis test) difference in the mean S-CCT scores among the three groups. The mean L-CCT score in the patients with protanopia was significantly ($p = 0.013$, by the Mann–Whitney test) lower than the mean M-CCT score in the patients with deutanopia. Every L-CCT score in the patient with protanopia and every M-CCT score in the patient with deutanopia were the lowest in the individual RCCT scores among dichromatic patients.

Discussion

In the pilot study of Rabin et al. (2011), the 1,446 subjects were young applicants for pilot training (mean age, 24.3 ± 3.2 years). However, the RCCT should be performed in a wide age range of patients to establish its clinical usefulness.

In the current study, the mean L, M and S-CCT scores decreased gradually with age in phakic eyes, while they were normal in patients in the seventh, eighth and ninth decades of life in

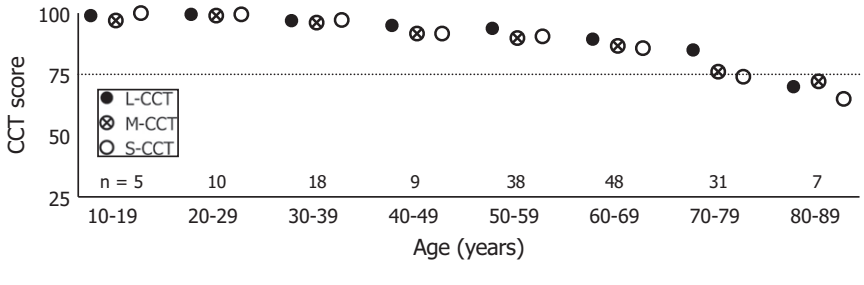

Fig. 1. The Rabin cone contrast test (RCCT) results in the phakic eyes of patients in the second to ninth decades of life. Each dot represents the mean L, M and S-CCT score, respectively. The mean L, M and S-CCT scores significantly decrease gradually with age to below the normal level ($p < 0.0001$ for all comparisons by the Kruskal–Wallis test). The dotted line indicates 75 points.

pseudophakic eyes. The presence of cataracts might cause an overall decrease in the L, M and S-CCT scores. Artigas et al. (2012) reported that the transmittance of visible light through the crystalline lens decreased with age especially for the short wavelengths, and it was apparent after 60 years of age because of yellowing of the crystalline lens. Nomura et al. (2003) reported that an age-dependent decrease in contrast sensitivity occurred even in phakic eyes in an elderly population with good BCVA (>20/20 or better Snellen equivalent), possibly due to cataracts. In the current study, age-dependent decreases in the RCCT scores in phakic eyes were comparable to previous reports. Yellowing of the crystalline lens with cataract formation may affect the RCCT scores even in eyes with good BCVA.

Age-dependent decreases in the mean CCT scores to below normal were found in the current phakic patients in the eighth and ninth decades of life. The decreases were marked in the M-CCT and S-CCT scores, that is, colour vision in the middle and short wavelengths, respectively. Age-dependent decreases in the transmittance of visible light have been reported to be particularly prominent in the middle and short wavelengths in phakic eyes (Boettner & Wolter 1962; Xu et al. 1997; Artigas et al. 2012). Therefore, the current results suggested that prominent decreases in the M-CCT and S-CCT scores in elderly phakic subjects, especially those older than the eighth decade of life, were affected mainly by cataract formation. It is also important to note that the CCT scores in the elderly could be affected by normal senescence changes including senile miosis, ganglion cell loss, any slight misalignment of cones and cognitive decline (Simunovic 2016).

All the mean CCT scores increased above the normal level after cataract surgery in the elderly subjects including those in the ninth decade of life. The RCCT might be clinically useful during colour vision examinations in elderly subjects if they obtained an improved BCVA after cataract surgery. Moreover, the RCCT could be clinically available for early qualitative and quantitative analysis of cataract formation like contrast sensitivity tests

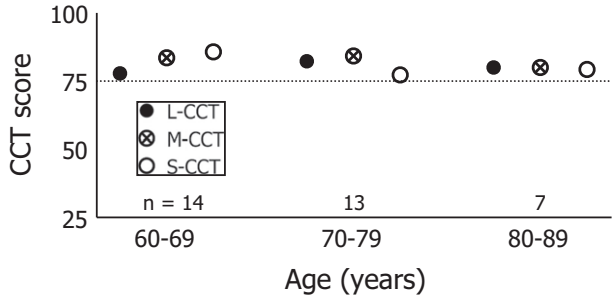

Fig. 2. The Rabin cone contrast test (RCCT) results in the pseudophakic eyes of patients in the seventh to ninth decades of life. Each dot represents the mean L, M and S-CCT score, respectively. The mean L, M and S-CCT scores are within the normal range in patients in the seventh, eighth and ninth decades of life (p = 0.82, 0.72 and 0.21, respectively, by the Kruskal–Wallis test). The dotted line indicates 75 points.

Table 1. Demographic data of the study groups.

	Control	Protanopia	Deutanopia	p value
No. patients	9	10	18	
Age (years)	17.1 ± 6.1	14.0 ± 5.9	14.2 ± 5.4	0.35*
BCVA, logMAR	−0.14 ± 0.07	−0.16 ± 0.04	−0.15 ± 0.07	0.92*

BCVA = best-corrected visual acuity, logMAR = logarithm of the minimum angle of resolution.
*By the Kruskal–Wallis test.

Table 2. Rabin cone contrast test scores of the study groups.

	Control	Protanopia	Deutanopia	p value
L-CCT	99.4 ± 1.7	31.5 ± 18.3	92.8 ± 10.5	0.0001*
M-CCT	98.3 ± 5.0	86.0 ± 12.6	50.8 ± 19.6	0.0001*
S-CCT	99.4 ± 1.7	98.0 ± 6.3	97.8 ± 5.2	0.86*

L/M/S-CCT = L/M/S cone contrast test scores, respectively.
*By the Kruskal–Wallis test.

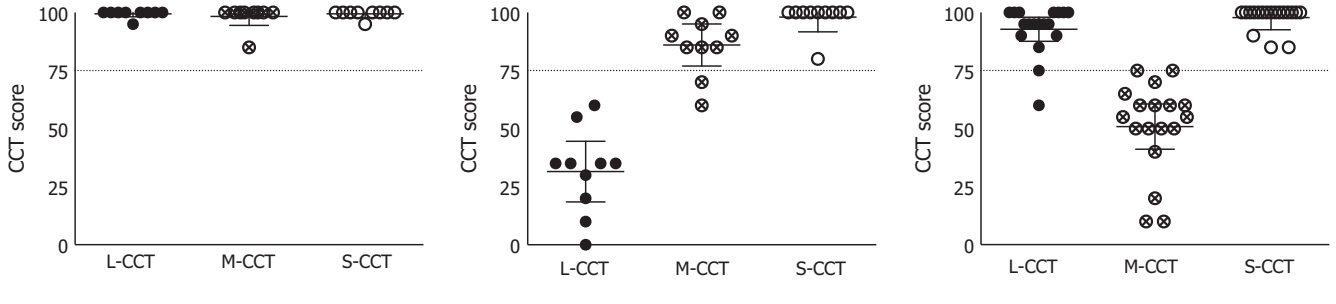

Fig. 3. Scatterplots of the Rabin cone contrast test (RCCT) results in the normal control group (left), protanopia group (centre) and deutanopia group (right). The mean L-CCT score in the protanopia group and the M-CCT score in the deutanopia group are significantly (p < 0.0001 for both comparisons by the Kruskal–Wallis test) lower than in the other groups. There is no significant (p = 0.86 by the Kruskal–Wallis test) difference in the mean S-CCT scores among the three groups.

(Chylack et al. 1993; Elliott & Situ 1998).

In a pilot study, Rabin et al. (2011) reported that the RCCT showed 100% sensitivity for detecting and categorizing CVD and 99.8–100% specificity for confirming normal colour vision. In the current study, the L-CCT scores in the patients with protanopia and the M-CCT scores in the patients with deutanopia were the lowest of the individual RCCT scores among all dichromatic patients. Moreover, the other RCCT scores except for the lowest RCCT score were not always within normal limits. Hence, the type of dichromatic CVD can be determined only by the lowest RCCT scores. It is noteworthy that some patients with protanopia might have M-CCT scores that are below normal and some patients with deutanopia might have L-CCT scores below normal. The specificity might decrease if patients develop cataracts.

In the current study, the mean L-CCT score in the patients with protanopia was significantly lower than the mean M-CCT score. Similarly, Rabin et al. (2011) reported previously that most patients with protanopia had greater decreases in the L-CCT score than in the M-CCT score in patients with deutanopia; in that study all subjects had anomalous trichromatism and none had dichromatism based on anomaloscopy results. In the current study, we included only patients with severe dichromatism. This result confirmed that patients with protanopia tended to have a lower RCCT score.

It is difficult to quantify the severity of dyschromatopsia using conventional colour vision tests. The severity of CVD was categorized as mild or severe based on the Farnsworth Panel D-15. The type of CVD was diagnosed by anomaloscopy in which patients adjust the red-green ratio and yellow test field luminance. A subject matching the entire 0–73 range is diagnosed as dichromatic. In the current study, we found wide distributions in the L-CCT scores in the patients with protanopia and M-CCT scores in the patients with deutanopia, although we included both severe and dichromatic subjects alone. The RCCT may sensitively reflect the extent of CVD in a different way from traditional colour vision tests and thus can make a quantitative diagnosis of dyschromatopsia including acquired CVD. Further investigation of the correlation between the RCCT scores and the severity of CVD is warranted in more patients with varying degrees of dyschromatopsia.

In conclusion, the RCCT can be used clinically in patients with good BCVA up to the seventh decade of life, but cataract formation may affect the RCCT score in phakic eyes of patients in the eighth and ninth decades of life with a VA of 20/20 or better. In pseudophakic eyes, patients in the eighth and ninth decades of life had normal RCCT scores. The RCCT is useful for screening and typing of CVD and might be able to quantitatively diagnose dyschromatopsia.

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