# Does the Badal optometer stimulate accommodation accurately?

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**Keywords:** accommodation, Badal optometer, closed-view, instrument accommodation, open-view, real space

#### Abstract

*Purpose:* To study whether the accommodation response to Badal optometer is equivalent to the response for real space targets.

Methods: Accommodative responses were measured for 28 young eyes with the WAM-5500 autorefractometer in eight configurations for 0.17 D, 2.0 D and 5.0 D accommodation stimuli. Parameters that might contribute to differences in response were systematically isolated: stimulation method (real space vs Badal targets), field of view, instrument's cover proximity, the looming effect, and the peripheral interposition of objects in depth.

Results: Mean accommodative response differences between a natural view configuration and a configuration with a Badal Optometer were  $0.50 \pm 0.43$  D and  $0.58 \pm 0.53$  D for 2.0 D and 5.0 D stimulation, respectively (p < 0.001), with accommodation lags for the latter condition. Of the isolated parameters that might contribute to these differences, varying the interposition of objects in depth affected accommodation response more markedly.

Conclusions: It is likely that Badal optometers affect accommodation through a combination of some or all of the studied parameters. We conclude that accommodation response to closed-view Badal optometers is not equivalent to real space target response.

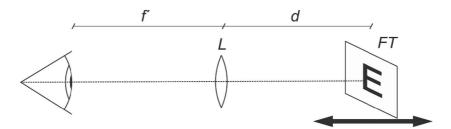
## Introduction

The Badal optometer has been used widely in ophthalmic instruments and in vision research as tool for presenting fixation targets at different stimulus vergences. Its basic configuration is a target and a lens (*Figure 1*), the latter being placed at its focal length from the eye. <sup>1,2</sup> This simple system has two characteristics that make it useful in visual optics: there is a linear relation between target position and vergence and there is angular size constancy of the target. Limitations of the basic configuration are reduced negative vergence range, target resolution and proximal accommodation effects (also called instrument myopia). <sup>1,3</sup> Some approaches have been proposed to minimise the first two limitations. <sup>1</sup>

One application of the Badal optometer is the study of accommodation.<sup>4–9</sup> However some authors have reported

difficulties accommodating to Badal targets. Some studies have found poorer responses to lens induced than to push-up stimulation, which is more pronounced for myopes than for emmetropes. <sup>10–12</sup> Stark & Atchison <sup>13</sup> studied whether the Badal optometer leads to accommodative responses different from targets in real space and concluded that responses were generally equivalent, but some participants had difficulty accommodating to the Badal optometer.

The Badal optometer system affects a number of parameters that might contribute to accommodation response. It removes or alters monocular depth cues to accommodation.<sup>13</sup> It maintains a constant angular size image, while in natural viewing this changes with object distance.<sup>14–16</sup> In a Badal system the scene is restricted to two dimensions, while under natural viewing conditions there is often a peripheral interposition of objects in depth, such as the



**Figure 1.** Scheme of the Badal optometer, consisting of lens L and moveable fixation test FT. The distance f' from the eye to the lens is the focal length of the lens and the distance d from the lens to the fixation test determines the stimulated vergence at the eye.

examiner, the rod for near targets and the background. The lens size of the Badal optometer may reduce the field of view. <sup>17</sup> In addition to effects on monocular depth cues, instrument 'accommodation' may occur due to the awareness of instrument proximity. <sup>3,17</sup>

From our understanding, the question of whether the Badal optometer stimulates accommodation similarly to real space targets remains unanswered. The objective of this study was to analyse the usefulness of a Badal optometer for accommodative stimulation. This was done by comparisons of accommodative responses with those for real space targets. Parameters that might contribute to differences in response were systematically isolated: stimulation method (real space targets vs targets viewed through a Badal lens), field of view, instrument's cover proximity, the looming effect, and the peripheral interposition of objects in depth.

## Methods

## Participants

The study was approved by the Ethics Committee of Hospital Mutua de Terrassa (Terrassa, Spain), it followed the tenets of the Declaration of Helsinki, and all participants gave informed written consent. Participants were recruited from staff and students of the Faculty of Optics and Optometry at the Technical University of Catalonia (UPC, Terrassa, Spain). They were untrained in the use of the Badal optometer and thus can be considered to be naïve. Criteria for inclusion were best spectacle-corrected visual acuity of 0.10 logMAR (Snellen 6/7.5 or 20/25) or better and no history of any ocular condition, surgery and/or pharmacological treatment. Participants wearing spectacles were excluded to avoid measurement artefacts caused by reflections from lens surfaces. Consequently, only emmetropes and contact lens wearers were included, with spherical and cylindrical components of over-refractions within  $\pm 0.25$  D. The upper age limit was set at 27 years old to help ensure good amplitude of accommodation. Mean age  $\pm$  standard deviation of 28 participants was 24.3  $\pm$  2.1 years (range 18-27 years). One eye of each participants was included, with mean corrected visual acuity of  $-0.14\pm0.06$  logMAR (range -0.20 to +0.02 logMAR; mean Snellen  $\sim\!6/4.5$  or 20/15) and mean subjective amplitude of accommodation of 9.5  $\pm$  1.9 D (range 7.1–15.4 D).

## Instrumentation

The Grand Seiko WAM-5500 autorefractometer projects a target through a 2.3 mm diameter annulus onto the retina and determines refraction by measuring size and shape after reflection from the retina through the optics of the eye. Subjective refraction with high contrast targets, even in presence of spherical aberration, is mainly driven by the central part of the pupil and thus the small annulus of the instrument seems reasonable for measurements of refraction. It can measure in static mode (i.e. single shot) and in dynamic mode at a frequency of 5 Hz. The WAM-5500 allows binocular accommodative stimulation through an open-view, and it has been used for measuring accommodation. Of the state of the retinal state of the state

The setup consisted of the WAM-5500 autorefractometer and different configurations to stimulate accommodation. There was opaque black paper (2 × 2 m) surrounding the autorefractometer at 50 mm from the participant's pupil plane. The fixation target was a 2.0° black Maltese cross, which is suitable for accommodation studies due to its wide frequency spectrum,<sup>21</sup> surrounded by a white background of luminance 31  $\pm$  3 cd m<sup>-2</sup>, which provided the field of view. The colour temperatures of light sources were approximately 6500 K. Autorefractometer measurements were taken at target distances, or equivalent positions in a Badal system, of 6 m, 50 cm and 20 cm, corresponding to accommodation stimuli of 0.17 D, 2.0 D and 5.0 D, respectively. The refractions were converted to spherical equivalent refractions. Eight different configurations were used to investigate effects of stimulation method, field of view, instrument's cover proximity, looming effect and interposition of objects in depth. The configurations are summarised in Table 1.

Configuration 1 provided a closed-view autorefractor with a Badal optometer (Figure 2a). The Badal optometer consisted of a 150 mm focal length, 42 mm diameter lens

Table 1. The eight setup configurations

Configuration	Stimulation method	Field of view	Instrument cover?	Looming effect?	Interposition of objects?	Accommodation stimuli (D)	Angular size of the test (°)
1	Badal target	2.5°	Yes	No	No	0.17/2.0/5.0	2/2/2
2	Badal target	15.6°	Yes	No	No	0.17/2.0/5.0	2/2/2
3	Real space target	2.5°	Yes	No	No	0.17/2.0/5.0	2/2/2
4	Real space target	15.6°	Yes	No	No	0.17/2.0/5.0	2/2/2
5	Real space target	15.6°	No	No	No	0.17/2.0/5.0	2/2/2
6	Real space target	15.6°	No	Yes	No	-/-/5.0	<b>-/-/5</b>
7	Real space target	33.0° (WAM limited)	No	Yes	No	0.17/2.0/5.0	2/2/5
8	Real space target	33.0° (WAM limited)	No	Yes	Yes	0.17/2.0/5.0	2/2/5

The stimulation method, field of view, instrument cover, looming effect, interposition of objects in depth, accommodation stimuli and angular size of the test of each configuration are detailed. The angular size of the test corresponds, in order, to the three accommodative stimuli (0.17, 2.0 and 5.0 D).

and a moveable fixation target, both attached to a calibrated rod mounted on the WAM-5500. The field of view was limited to 2.5° by a 6.5 mm diameter aperture at the front of the Badal lens. The first surface of the autorefractometer was covered with opaque black cardboard, called the 'instrument cover', with a 22.5 mm diameter circular aperture at 50 mm from the participant's pupil plane. The instrument cover was used to study the possible effect of instrument 'accommodation' due to the awareness of instrument proximity.

Configuration 2 was similar to Configuration 1, but the aperture at the front of the Badal lens was removed so that the field of view increased from 2.5° to 15.6° as limited by the Badal lens diameter. Comparison between configurations 1 and 2 isolated the field of view as a variable.

In Configurations 3–8, the Badal lens was absent, but Configurations 3–7 retained some characteristics of a Badal system. Configuration 3 was similar to Configuration 1, but the Badal lens was removed from the system (Figure 2b) and accommodation was stimulated by real space targets. As in Configuration 1, the field of view was 2.5° by means of the aperture where the Badal lens had been, the angular size of the Maltese cross was constant for all the accommodative stimulations (2.0°) and the instrument cover was retained. Comparison between configurations 1 and 3 isolated stimulating method (Badal optometer or real space targets) as a variable.

Configuration 4 was similar to Configuration 3, but field of view was increased from 2.5° to 15.6° by changing aperture size to 42 mm. Comparison between configurations 2 and 4 isolated the stimulating method as a variable, and comparison between Configurations 3 and 4 isolated field of view as a variable.

Configuration 5 was similar to Configuration 4, but the instrument cover was removed so that the participant saw through the WAM's window. Comparison between Configurations 4 and 5 isolated instrument cover as a variable.

Configuration 6 was similar to Configuration 5, but the Maltese cross's angular size was increased 2.5 times and testing was only for 5.0 D stimulation. Unlike previous configurations, the participant saw the fixation test moving towards the eye (push-up method) from 2.0 D to 5.0 D stimulation. Comparison between Configurations 5 and 6 isolated the looming effect as a variable.

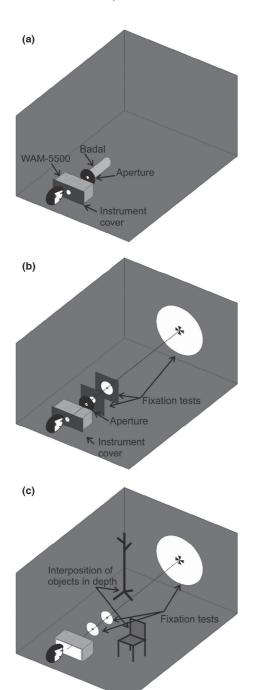
Configuration 7 was similar to Configuration 6, but the aperture was removed so that the field of view was limited by the WAM-5500 window of  $\approx 33.0^{\circ}$ .

Configuration 8 was the control condition. It mimicked a conventional open-view accommodation measurement by means of a push-up target (Figure 2c). This configuration was similar to Configuration 7, but with objects at different distances from the accommodative stimulation plane: a coat rack (at 1.50 m from the observer's pupil plane and 8° leftwards), back of a chair (0.33 m, 9° rightwards) and a pen (0.18 m, 15° rightwards). Comparison of Configurations 7 and 8 isolated interposition of objects in depth.

## **Examination protocol**

An optometric examination was performed. The refraction was measured by streak retinoscopy and subjective refraction, with the endpoint criteria of maximum plus power consistent with best vision. Monocular visual acuity with the usual correction was measured and the eye with better visual acuity was selected. Monocular amplitude of accommodation was measured by the push-up method. The fixation test was moved towards the participant at an approximate speed of 5 cm s<sup>-1</sup> with the endpoint criteria of reported blurred vision.

The participant was blindfolded and moved to the dark experimental room. The participant was not aware of the dimensions of the setup nor the room, which could have biased the accommodative response as suggested elsewhere. The blindfold remained in place for 5 min after



**Figure 2.** (a) *Configuration 1* in which the Badal lens is used for stimulating accommodation with small field of view, instrument cover and no depth cues; (b) *Configuration 3* with real space targets, but with small field of view, the instrument cover kept in place, and the angular size keep constant by varying physical size for different object distances; (c) *Configuration 8* with real targets in free space and with interposition of peripheral objects in depth.

being seated. In each configuration, the examined eye was uncovered (while the contralateral was occluded) and the refraction measured in ascending level of accommodative stimulation (i.e. 0.17 D, 2.0 D and 5.0 D) to minimise difficulties relaxing accommodation.<sup>13</sup> The participant was instructed to look at the centre of the cross and carefully focus it. The participant was blindfolded between different accommodative stimuli in order to avoid accommodative cues, except for Configurations 6 and 8 when the participant was allowed to watch while the target distance was changed. For the same reason, the examiner paid special attention to not interfere in the field of view of the participant, except for Configuration 8. The WAM-5500 was used in static mode, 10 consecutive readings per measurement were taken, the sensitivity was set at 0.01 D and vertex distance was set at 0.0 mm. The average of the spherical equivalent of the 10 consecutive readings per measurement for each fixation test distance were considered as the autorefractometer refractions. The accommodation responses for 2.0 D and 5.0 D stimuli were determined by subtracting the refractions for the 0.17 D stimulus from the refractions for these stimuli. The accommodation responses were thus negative, in order to be consistent with refractions. Configurations were randomised except for Configurations 7 and 8 that were performed at the end. That was to avoid participant awareness of room and setup dimensions, which could influence the accommodative response. <sup>22,23</sup>

## Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics 22.0 (IBM; Armonk, NY). Normality of each variable was checked by applying the Shapiro–Wilk test and comparing the skewness and kurtosis statistics to the standard error.

Two different analyses of variances were conducted. On the one hand, a three-way repeated measures anova was performed for the lead/lag of accommodation with the following three factors: Field of view (2.5° or 15.6°), stimulation method (Badal or real space targets) and accommodative stimulus (0.17, 2.00 or 5.00 D). This analysis corresponds to the first four configurations and provides straightforward information about interaction effects among these three variables. On the other hand, since the remaining factors (i.e., interposition of objects in depth, instrument cover and looming effect) are not fully permutated, one-way repeated measures anova to compare the eight configurations were conducted for each of the three refractions and two accommodation responses.

In all cases significance was set at p < 0.05 and where the assumption of sphericity was violated, the Greenhouse-Geisser correction was used. Where significance was obtained, *post-hoc* comparisons of configurations were made by paired t-tests incorporating a Bonferroni correction given by the number of pairwise configuration comparisons, with significance p < 0.05/n (for refraction n = 21 for 0.17 and 2.00 D, and n = 28 for 5.00 D of

accommodative stimulation, for accommodative response n = 21 for 2.00 D and n = 28 for 5.00 D of accommodative stimulation).

## Results

*Table 2* gives descriptive statistics of refractions for 0.17 D, 2.0 D and 5.0 D stimuli.

The three-way repeated measures anova showed significant effects for the field of view ( $F_{1,27} = 9.0$ , p < 0.01), stimulation method ( $F_{1,27} = 5.7$ , p = 0.02) and accommodative stimulus ( $F_{1,1,29.7} = 65.8$ , p < 0.01). None of the interactions were statistically significant. The *post-hoc* test performed for each factor showed statistically significant differences in all pairwise comparisons. The stimulation method and field of view showed close to zero effects for 0.17 D of stimulation, while for 2.0 and 5.0 D of stimulation the Badal optometer (vs real space) and smaller

**Table 2.** Means  $\pm$  standard deviations of the refractions of different accommodation stimuli for different configurations

Config.	0.17 D stimulus	2.0 D stimulus	5.0 D stimulus
1	$-0.22\pm0.47$	$-1.11 \pm 0.36$	$-3.75 \pm 0.39$
2	$-0.17\pm0.46$	$-1.25\pm0.38$	$-3.83 \pm 0.37$
3	$-0.19\pm0.46$	$-1.27\pm0.35$	$-3.82 \pm 0.39$
4	$-0.22\pm0.44$	$-1.32\pm0.24$	$-3.97 \pm 0.35$
5	$-0.14\pm0.40$	$-1.37\pm0.30$	$-3.98 \pm 0.37$
6			$-3.87 \pm 0.35$
7	$-0.08\pm0.41$	$-1.35\pm0.30$	$-3.89 \pm 0.31$
8	+0.03 ± 0.35	$-1.37\pm0.28$	$-4.08 \pm 0.31$

(vs larger) field of view induced an approximate reduction in the response of 0.10 D. The one-way repeated measures anova for refractions showed highly significant differences between configurations (p < 0.001) for all accommodation stimuli: 0.17 D stimulus,  $F_{4.3,116} = 6.5$ ; 2.0 D stimulus,  $F_{3.9,104.6} = 5.0$ ; 5.0 D stimulus,  $F_{7,189} = 5.9$ . Also, the analyses of variance for accommodative responses showed highly significant differences between configurations (p < 0.001): 2.0 D stimulus,  $F_{6,162} = 10.9$ ; 5.0 D stimulus,  $F_{7,189} = 10.0$ .

Table 3 shows several post-hoc comparisons of configurations, with the differences being the values for the second specified configuration being subtracted from that of the first specified configuration. For 0.17 D stimulus, the refraction of Configuration 8 was significantly more positive (one-way ANOVA) that of the other configurations (except for Configuration 7), indicating more relaxed accommodation for the former. For 2 D and 5 D accommodation stimuli, the accommodation response of Configuration 8 was significantly greater than that of most other configurations (negative values in Table 3).

The other comparisons shown in *Table 3* are the ones isolating stimulation method, field of view, instrument's cover and looming effect: none were significant. Of the 60 comparisons not shown in the Table, the only ones with significance were the refraction comparisons of 5 vs 1 (p = 0.001) at 2.0 D stimulus and 4 vs 1 (p = 0.001) at 5.0 D stimulus and the accommodation response comparisons of 5 vs 1 (p = 0.001) and 7 vs 1 (p < 0.001) at 2.0 D stimulus.

In Figure 3, the Bland and Altman<sup>24</sup> plots are shown comparing the refraction of each configuration against the

Table 3. Differences between configurations for the three refractions and two accommodation responses

,	Parameter studied	0.17 D stimulus $ \begin{array}{l} \text{Refraction} \\ \text{Mean}  \pm  \text{S.D.}  \text{(D)} \end{array} $	2.0 D stimulus		5.0 D stimulus	
Comparison			Refraction Mean ± S.D. (D)	Accommodation response Mean $\pm$ S.D. (D)	Refraction Mean $\pm$ S.D. (D)	Accommodation response Mean $\pm$ S.D. (D)
8 vs 1		+0.25 ± 0.26*	−0.25 ± 0.33*	-0.50 ± 0.43*	−0.33 ± 0.35*	-0.58 ± 0.53*
8 vs 2		+0.20 ± 0.28*	$-0.12\pm0.23$	$-0.32\pm0.35*$	$-0.25\pm0.27$ *	$-0.45\pm0.38*$
8 vs 3		+0.22 ± 0.28*	$-0.09 \pm 0.32$	$-0.31 \pm 0.33*$	$-0.25\pm0.39*$	$-0.47\pm0.41$ *
8 vs 4		+0.25 ± 0.21*	$-0.04 \pm 0.21$	$-0.30 \pm 0.31*$	$-0.11 \pm 0.25$	$-0.36 \pm 0.36*$
8 vs 5		+0.16 ± 0.15*	$-0.00 \pm 0.20$	$-0.17\pm0.26*$	$-0.10 \pm 0.24$	$-0.26\pm0.28$ *
8 vs 6					$-0.21\pm0.24^{*}$	$-0.37\pm0.29$ *
8 vs 7	IOD	$+0.10 \pm 0.24$	$-0.01 \pm 0.18$	$-0.12\pm0.30$	$-0.18 \pm 0.25*$	$-0.29\pm0.36$ *
3 vs 1	SM	$+0.04 \pm 0.29$	$-0.16 \pm 0.40$	$-0.19\pm0.45$	$-0.07\pm0.43$	$-0.11\pm0.48$
4 vs 2	SM	$-0.05\pm0.31$	$-0.07\pm0.32$	$-0.02\pm0.40$	$-0.14 \pm 0.27$	$-0.09\pm0.39$
2 vs 1	FOV	$+0.05\pm0.24$	$-0.13\pm0.36$	$-0.19 \pm 0.39$	$-0.08 \pm 0.35$	$-0.13\pm0.44$
4 vs 3	FOV	$-0.03\pm0.31$	$-0.05\pm0.33$	$-0.02\pm0.38$	$-0.14 \pm 0.35$	$-0.11 \pm 0.41$
5 vs 4	IC	$+0.09 \pm 0.17$	$-0.04 \pm 0.17$	$-0.13\pm0.24$	$-0.01 \pm 0.30$	$-0.09\pm0.38$
6 vs 5	LE				$+0.11\pm0.33$	$-0.11\pm0.33$

IOD, Interpositions of Objects in Depth; SM, Stimulation Method; FOV, Field Of View; IC, Instrument Cover; LE, Looming effect.

<sup>\*</sup>Statistically significant.

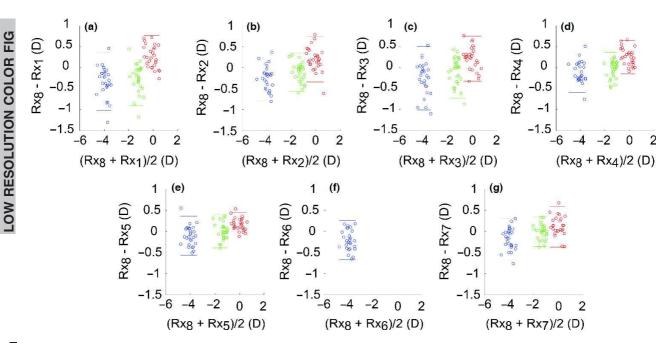


Figure 3. Bland and Altman plots of refractions (R×) when the different configurations are compared with Configuration 8: (a) Configuration 1, (b) Configuration 2, (c) Configuration 3, (d) Configuration 4, (e) Configuration 5, (f) Configuration 6 and (g) Configuration 7. Refractions corresponding to accommodative stimulation of 0.17 D are in red, those for 2.00 D are in green and those in blue are for 5.00 D. In (f) there is only data corresponding to accommodative stimulation of 5.0 D as for Configuration 6 refraction was measured only for this stimulation (see Table 1). The 95% confidence limits are shown by straight lines.

reference configuration (Configuration 8). The differences in the plot are calculated as the refraction for Configuration 8 minus the refraction of each configuration in the comparison. Thus, as in Table 3, negative differences correspond to greater accommodations for Configuration 8. As can be seen, there is a clear tendency to shift from positive to negative differences as the accommodative stimulation is increased.

## Discussion

The Badal optometer is widely used for stimulating accommodation. We investigated whether accommodation can be similarly stimulated by means of Badal optometers and real space targets. Two variables were studied: the refraction obtained for each accommodation stimulation and the accommodative response, with the latter calculated as the near refraction minus the far refraction. We investigated the parameters that could contribute to accommodation differences, including stimulation method, field of view, instrument's cover proximity, looming effect, and interposition of objects in depth. The refractions and accommodation responses obtained when stimulated in closed-view with a Badal optometer (Configuration 1) differed from those obtained for an open-view real space stimulation (Configuration 8; Table 3). Interposition of objects in depth

was the 'stand-alone' parameter to induce more pronounced differences.

The binocular viewing is the natural viewing condition, including some cues, as vergence and disparity, which are missing in monocular condition.<sup>10</sup> In this study, which only considered monocular vision, Configuration 8 was considered as the closest to natural viewing condition since accommodation was stimulated by means of push-up targets in real space, in open-view and with depth cues. Despite the participants being in front of the WAM-5500 instrument, Rosenfield & Ciuffreda<sup>22</sup> stated that the open field design of such instruments avoid any extraneous stimuli to proximal induced accommodation. Configuration 1 can be considered as the situation found in closed-view autorefractors. When comparing these extremes for 0.17 D stimuli (Table 3), there was a myopic bias of 0.25 D in the Configuration 1 relative to Configuration 8. This is consistent with studies that have found the eye tends to overaccommodate when looking through closed-view optical instruments.<sup>3,25</sup> However, the accommodation response to 2.0 D and 5.0 D stimuli for Configuration 1 lagged behind those of Configuration 8 by 0.50 D and 0.58 D (Table 3). As previously mentioned, several authors have highlighted accommodative difficulties when stimulating with Badal optometers. 10,26,27 In contradiction with our results, Stark & Atchison<sup>13</sup> found that accommodation for real space and Badal targets is equivalent for practical purposes, but the only difference in their study was the stimulation method (real space or Badal lens) whereas we included other parameters. Some of these studies have referred to accommodation difficulties with Badal targets in a few participants, <sup>26,27</sup> and Stark & Atchison<sup>13</sup> found that some participants were unable to accommodate to Badal targets. We had no participants who were unable to accommodate. As can be seen in *Figure 3*, there is a general trend to poorer responses (negative differences) and this is not due to few participants unable to accommodate.

While the stimulation method (real space or Badal targets) might be considered to be the main difference between Configurations 8 and 1, when isolated in the comparisons 3 vs 1 and 4 vs 2 (Table 3), it did not explain by itself those differences. This suggests that there are factors beyond the Badal lens that affect accommodation response. Of the isolated parameters, the interposition of objects in depth was the one which induced more pronounced differences. These findings support the suggestion that a peripheral surround, at a different distance than the fixation target provides a cue for appropriate accommodation.<sup>22</sup> As there are few other effects of individual parameters, it is likely that Badal optometers affect accommodation through a combination of some or all of limited field of view, cover proximity, lack of looming effect and lack of peripheral interposition of objects in-depth.

The interposition of objects in depth has been the parameter with more marked effects and thus it could be used to improve accommodation response with Badal optometers. This could be further investigated by considering the relative depth at which the peripheral targets allow the most accurate responses. Using wider fields of view could also be a simple way to improve the accommodative response in Badal optometers.

In summary, this study investigated whether the accommodation response to Badal optometer is equivalent to real space targets. We conclude that accommodation stimulated by a Badal optometer embedded in an instrument is not as accurate as under the natural viewing condition. The Badal lens itself does not explain the differences. Introducing peripheral targets, at different distances away from participants than that of fixation targets, has limited influence on response. In isolation, neither field of view, instrument's cover, nor the looming effect, affects accommodation. It is probable that Badal optometers affect accommodation through a combination of some or all of these parameters.

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#### **Disclosure**

The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

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