Clinical performance and “ex vivo” dehydration of silicone hydrogel contact lenses with two new multipurpose solutions

José Manuel González-Méijome*, Ana Carla da Silva, Helena Neves, Daniela Lopes-Ferreira, António Queirós, Jorge Jorge

Clinical and Experimental Optometry Research Lab, Center of Physics, University of Minho, Braga, Portugal

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ABSTRACT

Purpose: To compare the performance of two novel multipurpose disinfecting solutions (MPDS) in preventing silicone hydrogel contact lens dehydration, provide higher scores of subjective comfort and stable optical quality during a month of lens wear in neophyte volunteers.

Method: This is a prospective, double-blind, contralateral and randomised study involving the contralateral use of Complete RevitaLens® and Biotrue MPDS. Twenty-five neophytes wore Air Optix Aqua for 1 month. Volunteers were evaluated on day 1 and days 30 at 2 and 10 h after lens insertion. Tear film stability using Tearscope Plus (Keeler, UK), whole eye aberrations for 4.5 mm pupil size (IRx3, ImagingEyes, France) and subjective comfort (0–10 score) along with the dehydration values obtained with a gravimetric method were collected at each follow-up visit.

Results: NIBUT values decreased significantly with both care systems from baseline to 10 h visit on day 1 (p < 0.032 and 0.016, mean difference −6.7 s and −7.0 s, for Complete Revitalens and Biotrue, respectively). Dehydration rates and ocular aberrations did not change significantly over the month of follow-up (p > 0.05, ANOVA with Bonferroni post hoc corrections), nor between visits within the same day (p > 0.05, paired sample T-test). End-of-day dryness sensation worsened similarly with both MPDS after 1 month (p = 0.021 and 0.005, mean difference −1.4 and −1.3, for Complete Revitalens and Biotrue, respectively).

Conclusions: Regardless of their different chemical compositions in terms of moisture additives both MPDS solutions evaluated performed similarly regarding objective measures of dehydration, tear stability and optical quality but presented significant differences in subjective symptoms.

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1. Introduction

Dryness, discomfort and red eyes are among the primary causes of soft contact lens (CL) wear discontinuation [1]. All these symptoms and signs might be somewhat related to dehydration effects. Avoiding on-eye dehydration of soft CL is one of the major challenges for ophthalmic materials scientists and contact lens industry. On-eye dehydration of soft CL materials has been measured by different authors with conventional lenses dehydrating to a greater extent compared to silicone hydrogel materials [2,3]. Although in vitro dehydration tests do not predict in vivo lens performance [4], we have previously confirmed that worn silicone hydrogel lenses have a lower ability to retain bulk hydration compared to new silicone hydrogel lenses under in vitro conditions [5].

Some authors suggest that a lower dehydration rate might be an important factor to reduce dryness symptoms [6]. Moreover, a more stable tear film at the lens surface will contribute positively to the optical quality of the eye [7,8], thus potentially reducing volunteers symptoms. However, a direct relationship between objective measures of lens dehydration and increase in dryness symptoms is difficult to be established and the literature has been somewhat controversial in this regard [9].

CL care industry is also committed to develop more effective care systems in the form of multipurpose disinfecting solutions (MPDS) combining excellent antimicrobial efficacy [10] with an increased wetting effect to improve the interaction between the CL and the ocular surface. Recently, new MPDS that attempt to improve the safety, efficacy and comfort of soft CL have been developed with promising results, including the solutions assessed in this trial [10,11] as well as others [12].

The purpose of the present study was to evaluate the clinical performance of two new MPDS used contralaterally by neophyte volunteers wearing a silicone hydrogel contact lens during 1 month. Dehydration rates, whole-eye optical quality, tear film stability and symptoms were evaluated after 1 day and after 30 days of lens wear.
Table 1
Composition of MPDS used in the study.

<table>
<thead>
<tr>
<th>Complete RevitaLens® MPDS</th>
<th>Biotrue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preservative</td>
<td>Polyquaternium-1 0.0001% + PHMB 0.00013%</td>
</tr>
<tr>
<td>Buffer</td>
<td>Boric acid; sodium borate</td>
</tr>
<tr>
<td>Chelating agent</td>
<td>EDTA</td>
</tr>
<tr>
<td>Surfactant</td>
<td>Tetronic 904</td>
</tr>
<tr>
<td>Wetting Agents</td>
<td>EDTA</td>
</tr>
<tr>
<td>Other</td>
<td>Rub-and-rinse</td>
</tr>
</tbody>
</table>

2. Methods

This is a prospective, single-center, double-masked, contralateral, randomised, daily wear clinical study. Twenty-five volunteers (7 males and 18 females) aged 19–33 years of age (mean 23 ± 4) participated in this study. Sample size was estimated to warrant 80% statistical power to detect differences of 2 s between MPDS systems on an independent samples comparison of means. The average refractive error was −1.74 ± 1.41D of spherical equivalent (range −0.50 to −6.00) with less than −1.00D of cylinder. Average keratometric readings were 42.77 ± 1.56D for steepest and 42.87 ± 2.1D for the flattest meridian. The experiments were conducted at the Clinical and Experimental Optometry Research Lab (CEORLab, Minho University, Braga, Portugal). An internal review board revised and approved the protocol of the study. Procedures followed the guidelines of the Declaration of Helsinki and all volunteers signed a Consent Form once the objectives and procedures of the study were fully explained and any doubt clarified appropriately.

Inclusion criteria were to be between 18 and 35 years of age, absence of ocular disease including amblyopia or optical media changes that could affect the optical quality of the eye, dry eye or dry eye symptoms as well as other conditions that could affect the tear film quality and stability including pregnancy or consumption of systemic or topical drugs, flat keratometry between 7.60 and 8.10 mm, refractive sphere between −0.50 and −6.00D, able to understand and sign Consent Form and attend scheduled visits. Volunteers were also required to have a pupil size of at least 4.5 mm without pharmacologic dilatation to participate in the clinical trial. Exclusion criteria were scores above 10 in McMonnies dry eye test performed before volunteer enrollment, taking topical or systemic medication, astigmatism above −0.75D and signs of ocular surface disease, even subtle (corneal/conjunctival staining) above grade 1 according to the Cornea and Contact Lens Research Unit (CCLRU) grading scales.

All volunteers wore bilaterally a silicone hydrogel soft CL (Air Optix Aqua, Ciba Vision, Duluth, GA) with 33% equilibrium water content, non-ionic material (FDA group I) made of DMA (N,N-dimethylacrylamide) + Tris (trimethylsiloxy silane) + siloxane copolymer (Lotrafilcon B). All lenses had base curve radius of 8.6 mm, overall diameter of 14.2 mm and spherical refractive power according to volunteer’s prescription corrected for vertex distance followed by objective and subjective overrefraction. Average thickness over the central 6 mm of the lens was 96 ± 14 μm for a −3.00 lens as measured with a Redner thickness gauge (Redner Developments, Castro Valley, CA).

Table 1 presents a general overview of the composition of both MPDS used in the study. Those principal constituents that might influence the clinical behavior of the MPDS and their interaction with the lens material and the ocular surface are reported. Volunteers received indications to rub-and-rinse their lenses with clean solution upon removal and to rinse before insertion. To warrant volunteers masking, before study starting, volunteers were informed about the contents of the package insert without any reference to the brand or manufacturer of each MPDS. The adhesive information in each bottle was removed before dispensing to volunteers. Each volunteer was dispensed with one bottle of each MPDS in the original containers. In order to minimize risk of interchanging the MPDS between randomly assigned eyes, a red or blue mark was done in the top of the bottle cap corresponding with the same color on top of “Right” and “Left” lens case container’s cap, respectively. Volunteers were not allowed to use rewetting drops during the period of study. We recognize that despite all this carefully protocol, the double making strategy might not be perfect because the volunteer might be somewhat influenced by the different design of the two containers.

The experimental protocol is summarized in the diagram of Fig. 1. After recruitment and proper fitting of the study lenses, lenses were delivered to be worn during 1 month. Volunteers were
evaluated on day 1 and day 30, always in the morning after 2 h of lens wear and in the afternoon after 10 h of lens wear.

Upon arrival, the volunteers completed a questionnaire comprising 10 cm visual analog scales (VAS) to evaluate symptoms and comfort separately for right and left eye. This questionnaire was only applied after 10 h of lens wear, in the afternoon of day 1 and day 30. A sample of the questionnaire is presented in Appendix A.

Then, whole eye wavefront aberrometry was measured using a Harman–Shack aberrometer (IRx3, ImagInEyes, Orsay, France). Aberrometry was obtained between 2 and 6 s after blinking to standardize the conditions of data acquisition in order to minimize the effect of lens and tear instability on optical quality measures [13]. Values of spherical-like, coma-like, secondary astigmatism and total higher-order aberrations (HOA) were computed for a pupil size of 4.5 mm in all eyes without pharmacologic dilatation of the pupil. Then, a slit-lamp evaluation was conducted to assess ocular redness and pre-lens tear film stability using a Tearscope Plus (Keeler, UK) with the grid provided by the manufacturer projected on the corneal surface. The instrument and the slit lamp were adjusted in order to obtain a full coverage of the corneal area; three repeated measures of the tear film stability were obtained and averaged. Ocular redness and other signs observed in the ocular surface such as corneal staining were scored using CCLRU grading scales after 10 h of wear on day 1 and day 30.

After aberrometry and clinical inspection of the lenses and tear film, the lenses were removed using gloves to avoid lens contamination. Immediately after lens removal, lens was placed in a sterile holder and weighed in an analytical balance (model AT210, Metler Toledo, Giessen, Germany). Values obtained were recorded and compared against the values obtained before lens insertion for each given lens (baseline). Dehydration rates were derived according to previously described methodology [5,14] by the equation, Water loss = [(Worn lens mass – Baseline mass)/Baseline mass] × 100.

Statistical analysis was conducted using SPSS software v.18.0 (SPSS Inc., Chicago, IL). Descriptive statistics were obtained for the main outcome measures at each follow-up visit. Changes in the outcome measures over the follow-up period were assessed with ANOVA with Bonferroni correction. Comparison of means was conducted using independent samples T-test to evaluate differences between MPDS systems at a given follow-up period. Correlation between dehydration rates and subjective comfort scores were produced using Pearson correlation. Statistical significance was set for values of α < 0.05.

3. Results

Values of dehydration as percentage of weight loss from insertion (baseline) are shown in Fig. 2. There was not any statistically significant difference in the rates of dehydration at any given visit. The rate of dehydration was significantly lower for both lenses at the 2-h visit after 1 month (~2.4% for Biotrue and ~2.2% and for Complete Revitalens) compared with 2-h results on day 1 (~3.0%, p = 0.048 and ~3.2; p = 0.016 for Biotrue and Complete Revitalens, respectively.

Tear stability values measured with the Tearscope Plus (NIBUT) are presented in Fig. 3. There was a significant drop in tear stability after 10 h of lens wear on day 1 and day 30 (p < 0.05; Paired samples T-test for both MPDS). There is no significant differences between both MPDS care systems at any of the follow-up periods with the exception of day 30 after 10 h when a significantly higher NIBUT value for Complete Revitalens than Biotrue (15 vs 13 s; p < 0.05, T-test).

Changes in ocular redness and corneal staining throughout the day were not statistically or clinically significant, being less than 0.5 units on CCLRU grading scale for both MPDS systems. Average values did not reach 1.5 units and no volunteer achieved 2 units on CCLRU grading scale during the study thus not requiring any clinical intervention.

The optical quality of the lens front surface as expressed as spherical-like, coma-like, secondary astigmatism and total HOA RMS values remained unchanged during the whole period of the study as shown in Fig. 4. There was no significant difference between both MPDS at any of the four follow-up visits.

Fig. 5 shows the average subjective scores on a visual analogue scale at the beginning and end of the study and the average differences in scores. While aspects of lens wear as hydration during the day or overall satisfaction did not change significantly from day 1 to day 30, symptoms related to end of day dryness and hydration dropped significantly during the month of lens wear. The only symptom that improved over the time of the study period was difficulty in lens removal. Overall, all subjective responses were rated lower after 1 month that on first day of lens wear except for handling difficulties at removal, which is related to learning effect. Burning sensation at insertion was significantly worse at 10-h visit after 1 month wear for Biotrue compared to 10-h visit on day 1 (p = 0.008, difference = −1.9). End-of-day dryness was significantly reduced with both MPDS by 1.4 (p = 0.020) for Complete Revitalens and 1.3 for Biotrue (p = 0.05). No significant differences did exist between MPDS regarding end-of-day dryness (p = 0.594) nor for end-of-day hydration (p = 0.591).

No significant correlation was present between dehydration after 10 h and subjective scores either on day 1 (r < 0.358 and p > 0.076) or on day 30 (r < 0.230 and p > 0.269).

4. Discussion

The values of dehydration measured in this study for a silicone hydrogel lens were very similar to the values reported by Morgan and Efron for Purevision (Balafilcon A) lens being 2.8% after 15 days in their study and 3.24 and 2.94 in the evening of day 1 to 2.49 and
In the same study, authors reported an absolute dehydration at the end of 15 days of daily wear of 6% for Acuvue 2 (Etafilcon A) lens [2]. The absence of statistically significant differences in hydration with both solutions might be somewhat surprising considering that one of the MPDS includes hyaluronan wetting agent that is supposed to increase the wettability of the CL for longer periods. Analyzing in detail the kinetics of release of fluorescein-tagged hyaluronan during 20 h period from Lotrafilcon B material, it is quite evident that after an initial period of 5 h where up to 40% is released, less than 10% is released during the following 5 h [15]. This will represent up to 50% of hyaluronan remaining within the polymer bulk or at the lens surface. Nevertheless, this seems not to contribute to keep neither the lens more hydrated nor the tear film more stable as measured with NIBUT compared to Complete Revitalens MPDS after 10 h of lens wear.

Beyond wetting agents, other factors might interact with the wetting properties of the contact lens, such as the different surfactants used in both solutions as these elements have showed to affect wettability of soft contact lenses [16]. Thus, the interaction of Tetronic 1107 in Biotrue and Tetronic 904 in Complete Revitalens might have a significant role in modifying Lotrafilcon B lens surface irrespective of the addition of different wetting agents or no wetting agents being present in MPDS. Further in vivo studies are needed to investigate the contribution of selective ingredients (wetting agents and surfactants) to the overall behavior of the lenses.

Despite a non-significant decrease in dehydration from day 1 in the afternoon to day 30, this might not be entirely attributed to an increased capability of the lens to retain water, but perhaps to the increased solid mass added by deposits adhered to the lens. One limitation of this study is that our dehydration estimates have been obtained without considering the amount of deposits on the lens as done in the Hall’s model to account for this factor [17]. However,
our clinical experience and the evidence provided by literature does not seem to support this hypothesis. Despite no gross deposits were observed on the lens surface, such instability might reflect an increase in hydrophobic deposits on the contact lens such as lipids, indeed, we have found in this study a significant decrease in the pre-lens tear film stability as measured non-invasively with Tearscope at the end of 1 month with both MPDS. However, previous in vitro studies have demonstrated that Lotrafilcon B material has the lowest affinity for major tear lipids such as nonpolar (cholesterol) and polar (phosphatidylethanolamine) lipids compared to other silicone hydrogel materials [18] after 20 days of incubation in artificial tear formulation. Similar results were found by Subbaraman et al. for lysozyme adsorption in lenses incubated for 28 days, with Lotrafilcon A and B family of lenses showing the lowest amount of lysozyme deposition [19]. Further, considering the values of deposits collected from lotrafilcon B in the previous studies (<5 μg lipids/lens and <10 μg lysozyme/lens), we can consider that the impact of deposits accumulated will not have any significant impact on dehydration rates. This assumption is based on the fact that the average lens weight in our sample was 0.030827 ± 0.001876 g. What makes the potential weight accumulated in the form of lipids and protein deposits to be in the order of 10⁻³ to 10⁻⁴ lower. Collection of cholesterol and lysozyme from Lotrafilcon B lenses worn by volunteers during 1 month showed even lower values that those obtained in vitro [20]. According to the same authors, the amount of deposits can vary between materials for a given solution, so our results might not be extrapolated to other materials different from Lotrafilcon B.

Considering the first two factors analyzed (dehydration and tear film stability), our results suggest that there is not a correlation between them. This is in agreement with results from Young et al. who found no relationship either between tear stability and lens dehydration [21]. Despite not related with dehydration, it is well known that pre-ocular tear film stability is lower in intolerant contact lens wearers [22].

When it comes to direct comparison between both MPDS, no significant differences in objective or subjective parameters were found along the follow-up period. It is particularly interesting how similar are the values of pre-lens tear film stability between both solutions, considering that they have quite different formulations. The study results suggest that PLTF stability seems to be more dependent on lens material surface and probably individual tear film characteristics than the MPDS solution used. Previous in vitro studies have confirmed the affinity of certain deposits for certain materials [18,19]. Furthermore, an in vivo study has showed that despite significant interaction between lens material and care system, the main contributor to the amount of cholesterol and lysozyme deposited on silicone hydrogel materials, including Lotrafilcon B is lens material [20]. This effect was particularly remarkable for Lotrafilcon B that deposited between 0.1 and 0.5 μg of cholesterol irrespective of the care system used.

Thus, considering that objective evaluations have been conducted at 2 and 10 h after lens insertion and subjective evaluations after 10 h in the present study, our results do not support the assumption that a potential beneficial effect introduced by the care system will remain significant 2 or more hours after lens insertion. Instead, the MPDS might play an important role in keeping the lens surface clean and in optimal conditions to promote tear film deposition and stability instead of continuing promoting lens hydration mediating a stronger interaction between tear film and lens material through wetting agents. On this regard, both MPDS warrant similar PLTF stability, being significantly decreased with both MPDS at the end of a month when compared to baseline values. Glasson et al. have concluded that non-invasive pre-ocular tear film stability is significantly lower by an average difference in the median values of 7 s in intolerant contact lens wearers compared with tolerant contact lens wearers [22]. We also found a reduction of 6.7–7.4 s in PLTF stability from baseline to 10 h after lens wear with Complete Revitalens and Biotrue MPDS, respectively. However, our results report to pre-lens tear film evaluation which is known to be significantly lower than pre-ocular tear film values. Thus, considering that even after 10 h of lens wear after 1 month of daily wear PLTF is about 15 s, this might be understood as a positive result. Despite this, on average there was a slight worsening effect in symptoms after 1 month of lens wear, but we could not relate directly such a drop with the reduction in PLTF as such differences were only significant in the burning sensation such that Biotrue worsen more at the end of the month compared with Complete Revitalens. The remaining symptoms changed similarly with both care systems. Again, the composition of both MPDS might be involved in this difference to make Biotrue eyes to report more burning at the end of the month upon insertion of the lenses, but we cannot hypothesize on the potential origin of such a relationship.

In the present study is the contralateral nature of the study. The use of both eyes of the same subject to be exposed to different treatments might induce some confounding effect as it could be difficult for the volunteer to differentiate the sensations from each eye. However, the use of the two eyes simultaneously from the same volunteers might also enhance the accuracy of comparability between both treatments and similar study designs have been used previously [23,24].

Regarding wavefront analysis, our results suggest that no significant differences do exist between the optical qualities of the eye when lenses have been exposed to different MPDS over a 1-month period. In a study evaluating the potential role of artificial tears on the optical quality of volunteers with dry eye, Montes-Mico et al. found that despite an immediate reduction of the wavefront error to half of the baseline error, 10 min later the optical quality of the eye worsened again, although remaining significantly lower than baseline [25]. As previously discussed it is not likely that any potential beneficial effect of either solution might remain significant after 2 or 10 h. Those studies reported the changes in optical quality in response to the application of artificial tears which have higher viscosity compared to MPDS, and were applied in clinical patients what could justify the presence of significant changes in optical quality not found in our study using MPDS in healthy patients.

In summary, despite the different composition of the MPDS used in this study, we were unable to find statistically significant different behavior in terms of objective and subjective performance between the two eyes of the same subjects when using different care systems. Thus, irrespective of the incorporation of wetting agents in the formulation of the solution, this might not warrant a clinically significant advantage in terms of comfort, dryness, the ability of the lens to remain hydrated or to keep its surface fully wettable at the end of the day and in the end of the month of lens wear. Previously published studies support the hypothesis that in the interaction of MPDS systems with contact lenses, the properties of the material might counterbalance the potential effect of different care system formulation. This might be the case for Lotrafilcon B that has shown to interact less with biological components of the tear film, resulting in a very low deposition index, either in vivo or in vitro experiments, not showing a significantly different performance when exposed to two different new MPDS solutions.

Acknowledgments

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Appendix A.

**QUESTIONNAIRE**

Name:

In the following scales mark a vertical line according to your level of agreement to the questions.

1- How comfortable do you feel with the contact lenses?

   | Very uncomfortable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Very comfortable |
---|-------------------|---|---|---|---|---|---|---|---|---|---|-----------------|

2- After inserting your CL you may feel some ocular stinging.

   2.1 How disturbing is this sensation in the right eye?

   | Very uncomfortable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Do not feel that sensation at all |
---|-------------------|---|---|---|---|---|---|---|---|---|---|----------------------------------|

   2.2 How disturbing is this sensation in the left eye?

   | Very uncomfortable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Do not feel that sensation at all |
---|-------------------|---|---|---|---|---|---|---|---|---|---|----------------------------------|

3- About contact lens hydration during the wearing time.

   3.1 How hydrated do you feel your contact lens in the right eye?

   | Low level of hydration | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | High level of hydration |
---|-----------------------|---|---|---|---|---|---|---|---|---|---|---|----------------------------|

   3.2 How hydrated do you feel your contact lens in the left eye?

   | Very Dehydrated | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Very Hydrated |
---|------------------|---|---|---|---|---|---|---|---|---|---|---|-------------------|

4- You may feel ocular dryness in the end of the day after wearing your contact lenses for several hours.

   4.1 How much dryness do you feel in your right eye?

   | Very Dry | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Do not feel that sensation |
---|---------|---|---|---|---|---|---|---|---|---|---|---|------------------------|

   4.2 How much dryness do you feel in your left eye?

   | Very Dry | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Do not feel that sensation |
---|---------|---|---|---|---|---|---|---|---|---|---|---|------------------------|
5. Regarding hydration of your lenses/des immediately before removing them from the eye.

5.1 How hydrated is your right eye lens?

<table>
<thead>
<tr>
<th>Low level of hydration</th>
<th>High level of hydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>

5.2 How hydrated is your left eye lens?

<table>
<thead>
<tr>
<th>Low level of hydration</th>
<th>High level of hydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>

6. About difficulties with lens removal in the end of the day.

6.1 How much difficulty do you experience removing your right eye lens?

<table>
<thead>
<tr>
<th>Very difficult</th>
<th>Very easy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>

6.2 How much difficulty do you experience removing your left eye lens?

<table>
<thead>
<tr>
<th>Very difficult</th>
<th>Very easy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>

7. Which is your overall satisfaction with your contact lenses?

7.1 Right eye contact lens?

<table>
<thead>
<tr>
<th>Dissatisfied</th>
<th>Very satisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
</tr>
</tbody>
</table>

7.2 Left eye contact lens?

<table>
<thead>
<tr>
<th>Dissatisfied</th>
<th>Very satisfied</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
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References


