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Identifying Pigment Enclosure in Cosmetic Contact Lenses

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Objective: The presence of surface pigment in cosmetic contact lenses may influence possible ocular health issues and contact lens discomfort. Two in vitro test methods were developed to investigate whether a variety of cosmetic contact lenses are manufactured with a visible clear layer, indicating that the pigment bulk is enclosed within the lens matrix.

Methods: Two in vitro test methods using bright field microscopy and optical coherence tomography (OCT) were developed to assess whether a clear layer in a cosmetic contact lens could be identified. The OCT instrument in this study provided a limit of detection (LOD) of 2.4 μm in the identification of a clear layer. The cross-sectioning microscopy method described in this article requires a trained technician to execute; however, the LOD is smaller at 0.4 μm.

Results: Both test methods described were used to assess whether a clear layer could be identified on 19 commercially available cosmetic contact lens products across six manufacturers. Only one of the six manufacturers (5 of 19 products) produced lens images in which a clear layer was identified using either method.

Conclusions: Most of cosmetic contact lenses analyzed in this study contain the bulk of the pigment within 0.4 μm of the surface (beyond the limit of detection of the instruments used in this study) or on the surface itself.

Key Words: Tinted—Pigment—Contact lens—Printed—Cosmetic.

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The use of soft contact lenses containing pigments (cosmetic contact lenses) has grown dramatically in the past 10 years, predominantly in Asian countries. Different manufacturing processes are used for the commercially available cosmetic lenses resulting in different approaches to lens fabrication. If the pigment is located on the top or bottom surface of the lens, pigment particles have direct contact with the conjunctiva or cornea. If the pigment is enclosed in the lens matrix, pigment particles are not exposed on the surface. Most of commercially available cosmetic contact lenses tested in this study seemed to contain the bulk of the pigment on or closely located near one of the surfaces of the lens, as will be shown below.

Hotta et al.[1] showed that cosmetically tinted contact lenses have a wide variety of lens surfaces and colorants, which when deposited on the lens surface may consist of an element that has tissue toxicity. Chan et al. investigated 15 brands of cosmetic contact lenses and found that only two of the 15 brands had pigments that did not detach with the rub-off test. The 13 brands that failed the rub-off test showed higher *Pseudomonas aeruginosa* adherence, which may lead to a higher incidence of adverse events. The brands that had pigments that did rub-off showed at least 6 times more bacterial adhesion than the other 13 brands.[2] It has also been shown that surface roughness of lenses with surface pigments was greater than that of lenses with embedded pigments.[3,4] Ji et al.[4] reported that a rough lens surface increases microbial adherence. In addition, a case report found that direct contact between the corneal surface and bare pigments can cause corneal erosion.[5] Watanabe et al. found that the vendor claimed online to have pigment embedded within the lens, but a rub-off test indicated that pigment was coated on the lens surface. Jung et al.[6] studied the effect of the pigment location, and the results suggested that the presence of surface pigments in tinted contact lenses increases ocular inflammation and results in a poorer ocular surface status and greater discomfort compared with clear lenses and tinted lenses with an embedded pigment layer. This finding supported the theory proposed by Steffen and Barr,[7] which suggested that pigment particles exposed on the surface of a lens would alter the surface roughness and lens wettability, eventually decreasing the comfort. Alternatively, Rah et al.[8] performed a meta-analysis of Bausch & Lomb cosmetically tinted lenses and concluded that these lenses seemed to be safe when properly prescribed by an eye care professional and used in a compliant manner. It is worth noting that the studies used in the meta-analysis had varying second follow-up visit lengths and outcomes. Approximately 2.8% of the subjects who completed the study with the longest follow-up visit 2 (3 months) presented with grade 3 corneal staining, as compared with 0% of the subjects who completed the remaining studies with shorter follow-up visit 2 lengths (1 month).

Given the potential influence of pigment location in cosmetic contact lenses on possible ocular health issues and discomfort, improved understanding of and recommendation on the pigment location is desired. The extent of pigment enclosure is currently not regulated in most countries by their regulatory agencies; yet, the evidence that the pigment location impacts cosmetic contact

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lens safety and comfort is growing. Larger clinical studies establishing a relationship between ocular health issues, discomfort, and in vitro pigment attributes such as pigment particle size, pigment composition, and pigment particle location would be extremely meaningful. The two measurement methods described in this article aim to address characterizing the pigment particle location from the bulk perspective, that is, whether the majority of the pigment is located on the surface of the lens or enclosed in the lens matrix.

Two in vitro test methods using bright field microscopy and optical coherence tomography (OCT) were developed to assess whether a clear layer in a cosmetic contact lens could be identified. Although in vitro scanning electron microscopy has been shown to image pigment particle location[1,3] and has the highest resolution of the available methods to image pigment location, it was not used in this study due to cost and timing constraints. The SEM field of view is generally limited to a few hundred microns, and this is a complex type of testing for labs to execute. Several other tests have also been developed, including a rub test,[2] subjecting the test article to high temperature in a liquid and quantifying pigment in the test solution, and centrifuging the lens immersed in solution and assessing any changes to pigment using bright field microscopy. These tests methods either have large sources of variation (e.g., force used to rub lens) or have limited physiological relevance (e.g., boiling or centrifuging). A single method to assess whether pigment is enclosed has not yet been standardized or widely accepted.

A similar bright field microscopy method to the method described below has been published[9]; however, the method described below images the cross-sectioned lens while it is immersed in solution which prevents sample dehydration. Disadvantages of using a microscopy to image cross-sectioned samples include the significant amount of training required to cross-section the lens such that the edges have clean cuts and do not bias the test result, and the field of view is limited to less than 1 mm with a ×20 objective lens, within one image. Multiple images would be required to analyze the entire diameter of the lens. The OCT method described below is novel and does not require rigorous training or skill to execute. The sample preparation includes a method to limit dehydration, and the area scanned within one image is the largest of the imaging methods. Finally, eye care providers, optometrists, and ophthalmologists are familiar with OCT, and some may even own an OCT instrument; therefore, they may be able to execute the method below and may find OCT images to be more intuitive than bright field microscopy.

METHODS

Cross-Sectioning With Bright Field Microscope Imaging Method

Contact lenses were cross-sectioned using 2 razor blades with a gap of approximately 300 μm between the blades to cut a sliver from edge to edge through the center of the printed lens. The sliver was placed in a cuvette filled with contact lens packing solution (borate buffer with 0.9% NaCl; JJVCI, Jacksonville, FL) and imaged using a Nikon ME600 with ×200 (×10 internal, ×20 objective lens) magnifying power. The resulting images had a resolution of 0.4 μm/pixel, which we consider to be the limit of detection (LOD) of this method, and were analyzed in Image J (software by National Institutes of Health).

Optical Coherence Tomography Method Development

An attribute method with a binary "yes/no" response was developed to identify the clear layer in an OCT image of an in vitro contact lens. The OCT instrument used was the Bioptigen R2310 with the 10-mm objective lens, and an axial optical and digital resolution of 2.4 μm in contact lens material (refractive index=1.4), which is considered to be the LOD. The OCT instrument was set up for in vitro imaging (Fig. 1) with the objective lens pointing down, onto a tip-tilt sample mount. Tilt was optimized to be ~10° in 2 planes such that a strong signal from the lens surface was present, but specular reflection artifacts were minimized. For the lens to mount flat, facing up, which provides optimal image quality, a quarter of the lens was cut with a razor blade and imaged. A quarter of the lens was used because it is large enough to capture pigment pattern variation intended by the printed lens design and small enough to be mounted flat. In addition, to obtain the best-quality image of the pigment, the surface closest to the pigment was mounted toward the OCT objective. For most products, this was the top surface; however, for lenses manufactured by Seed, the back surface was mounted up during imaging. During initial

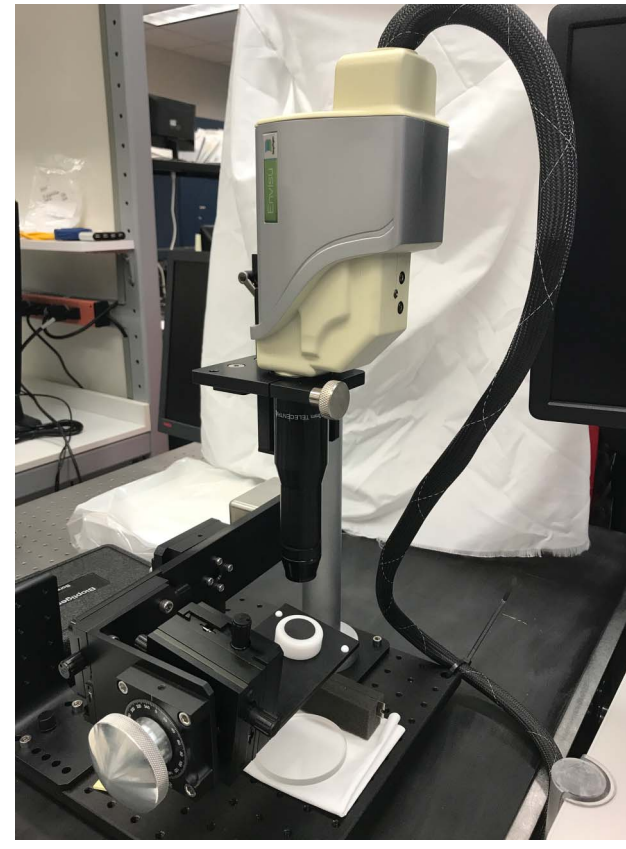

FIG. 1. Bioptigen R2310 with the 10-mm objective lens set up for in vitro imaging. Objective lens points down onto a sample mount on a tip-tilt stage. full color online

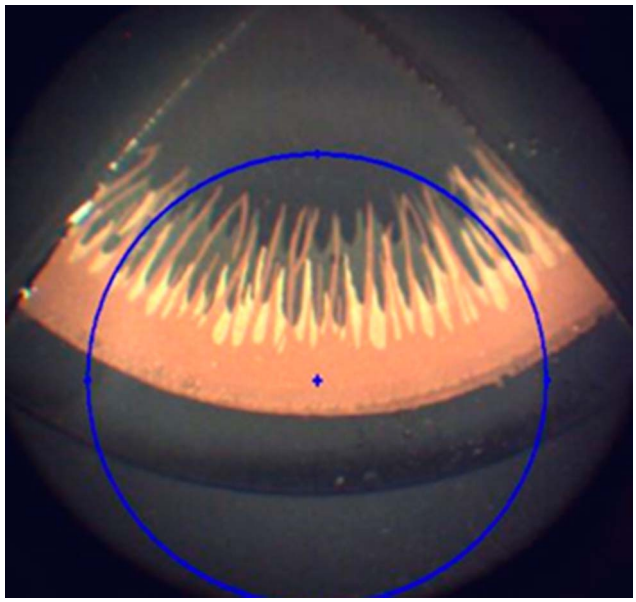

FIG. 2. Optical coherence tomography alignment camera image of a quarter of a cosmetic contact lens mounted on the sample stage. The cross is the center of the radial scan pattern, and it was placed in the limbal ring region where the print is most uniform. full color online

imaging, it was observed that excess solution on top of the lens could be mistaken for a clear layer. Therefore, a lens preparation step was added to the procedure to remove excess solution from the contact lens surface, but to prevent dehydration before imaging, described as follows. Thirty-five grams of contact lens packing solution (borate buffer with 0.9% NaCl; JJVCI) was poured on 20 blotting wipes (Berkshire DURX 670 $4'' \times 4''$; Berkshire Corporation, Great Barrington, MA). The lens was placed half way between the 20 blotting wipe stack, and a weighted press plate (Lodge Cast Iron Flat Grill Press $8.25''$; Lodge Cast Iron, TN) was placed on top of the blotting wipe stack for at least 1 min. A dehydration robustness study was performed to assess how a contact lens would change over time while mounted in open air on the OCT fixture. No visually noticeable changes, such as lens curling or warping, changes in image artifacts, or changes in strength of backscattered signal, were observed within the first 4 min. Dehydration was observed starting at 4 min and continued as time advanced. For this reason, all subsequent imaging was performed within 2 minutes of a contact lens being removed from its moist environment between the blotting wipes. After the cut lens was placed on the sample mount, a moist Foamtec International CleanWIPE Swab was used to gently roll the lens flat to remove any wrinkles or air gaps between the lens and the mount. Every 18° radially, a scan was acquired (Fig. 2), resulting in 10 total scans. Since the

TABLE 1. *Summary of Contact Lenses Used in This Study*

Manufacturer Name and Location	Contact Lens Product	Material	Base Curve (mm)	Diameter (mm)	Power (D)	Number of Lenses Measured
Seed, Japan	Plus Mode 1 day Man for Private	2-HEMA, EGDMA	8.70	14.0	−1.00	1
			8.70	14.0	−3.00	2
Seed, Japan	Plus Mode 1 day Man for Business	2-HEMA, EGDMA	8.70	14.0	−1.00	1
			8.70	14.0	−3.00	2
Seed, Japan	Eye Coffret 1 day UV Rich Make	2-HEMA, EGDMA	8.70	14.0	−1.00	1
			8.70	14.0	−3.00	2
Seed, Japan	Eye Coffret 1 day UV Natural Make	2-HEMA, EGDMA	8.70	14.0	−3.00	1
Johnson & Johnson	1 Day-Acuvue Define Accent Style	Etafilcon-A	8.50	14.2	−1.00	1
			8.50	14.2	−3.00	1
			8.50	14.2	−6.00	1
Johnson & Johnson	1 Day-Acuvue Define Vivid	Etafilcon-A	8.50	14.2	−1.00	1
			8.50	14.2	−3.00	1
			8.50	14.2	−6.00	1
Johnson & Johnson	1 Day-Acuvue Define Natural Shine	Etafilcon-A	8.50	14.2	−1.00	1
			8.50	14.2	−3.00	1
			8.50	14.2	−6.00	1
Johnson & Johnson	1 Day-Acuvue Define Natural Sparkle	Etafilcon-A	8.50	14.2	−1.00	1
			8.50	14.2	−3.00	1
			8.50	14.2	−6.00	1
Johnson & Johnson	1 Day-Acuvue Define Natural Shimmer	Etafilcon-A	8.50	14.2	−1.00	1
			8.50	14.2	−3.00	1
			8.50	14.2	−6.00	1
Interojo, Korea	Clalen Iris Latin 1 Day	Methafilcon A	8.60	14.2	−1.00	1
			8.60	14.2	−3.00	1
			8.60	14.2	−6.00	1
Interojo, Korea	Clalen Iris Suzy Gray 1 Day	Methafilcon A	8.60	14.2	−1.00	1
			8.60	14.2	−3.00	1
			8.60	14.2	−6.00	1
Interojo, Korea	Clalen Iris Rhapsody 1 Day	Methafilcon A	8.60	14.2	−3.00	3
Interojo, Korea	Clalen Iris Soul Brown 1 Day	Methafilcon A	8.60	14.2	−3.00	3
Bausch & Lomb	Naturelle Black Daily	Hilafilcon B	8.60	14.2	0.00	1
			8.60	14.2	−3.00	1
			8.60	14.2	−6.00	1
Bausch & Lomb	Lacelle Sparkling Black Daily	Hilafilcon B	8.60	14.2	−3.00	3
Bausch & Lomb	Lacelle Crystal Brown Daily	Hilafilcon B	8.60	14.2	−3.00	3
Bausch & Lomb	Lacelle Twinkle Brown Daily	Hilafilcon B	8.60	14.2	−3.00	3
Alcon	FreshLook One-Day Green	Nelfilcon A	8.60	13.8	−3.00	3
Miacare, taiwan	CONFiDENCE Daily	Silicone Hydrogel	8.90	14.0	−1.00	1
			8.90	14.0	−3.00	2

TABLE 2. *Summary of Clear Layer Identification Results*

Manufacturer	Contact Lens Product	Clear Layer Identified (Cross-Sectioned Microscopy), LOD 0.4 μm	Clear Layer Identified (OCT), LOD 2.4 μm
Seed	Plus Mode 1 day Man for Private	No	No
Seed	Plus Mode 1 day Man for Business	No	No
Seed	Eye Coffret 1 day UV Rich Make	No	No
Seed	Eye Coffret 1 day UV Natural Make	No	No
Johnson & Johnson	1 Day-Acuvue Define Accent Style	Yes	Yes
Johnson & Johnson	1 Day-Acuvue Define Vivid	Yes	Yes
Johnson & Johnson	1 Day-Acuvue Define Natural Shine	Yes	Yes
Johnson & Johnson	1 Day-Acuvue Define Natural Sparkle	Yes	Yes
Johnson & Johnson	1 Day-Acuvue Define Natural Shimmer	Yes	Yes
Interojo	Clalen Iris Latin 1 Day	No	No
Interojo	Clalen Iris Suzy Gray 1 Day	No	No
Interojo	Clalen Iris Rhapsody 1 Day	No	No
Interojo	Clalen Iris Soul Brown 1 Day	No	No
Bausch & Lomb	Naturelle Black Daily	No	No
Bausch & Lomb	Lacelle Sparkling Black Daily	No	No
Bausch & Lomb	Lacelle Crystal Brown Daily	No	No
Bausch & Lomb	Lacelle Twinkle Brown Daily	No	No
Alcon	FreshLook One-Day Green	No	No
Miacare	CONFiDENCE Daily	No	No

LOD, limit of detection.

images are acquired radially on a tilted stage in 2 planes, each image experiences a different amount of tilt with respect to the incident light beam. All the acquired images were visually inspected for specular reflection artifacts (these artifacts presented themselves as vertical streaks), and the scans that had did not have artifacts that interfered with clear layer identification were selected for analysis (7/10 scans). Each scan acquired produces an image of 8.0-mm-width, 2.4-mm-depth, 8.0-μm-lateral pixel resolution, less than 8.5-μm-lateral optical resolution, and 2.4-μm optical and pixel axial resolution. If the lens surface closest to the pigment was visibly separated from the pigment layer, a clear layer was identified between the lens surface and the pigment within the lens and recorded as "yes." If the lens surface closest to the pigment was not visibly separate from the pigment layer, a clear layer could not be identified within the lens—the test result was then a "no." This assessment was performed on three lenses of each product type, with seven test results per lens (one for each image).

To quantify the OCT method capability when test articles are greater than the LOD, the OCT method test result (binary test result of yes/no) was compared with the clear layer thickness measured using the cross-sectioning microscopy method (continuous test result). The assumption was made that the cross-sectioned test result was "truth," and a one sample proportion test was used to compare the proportion of an OCT yes/no outcome occurring in the population of cross-sectioned clear layer thickness measurements. The comparison of test methods was performed on seven research and development contact lenses designed to be a set of clear layer standards. These lenses were designed and manufactured by Johnson & Johnson Vision, Inc., Jacksonville, FL, to have varying clear layer thicknesses ranging from approximately 0 to 5 μm. Note that although the same lenses were evaluated between the measurement techniques, the exact same piece of the lens was not compared. The remaining pieces of the lens after cross-sectioning were evaluated on the OCT—different meridians of the same lenses were used for the comparison. To ensure the most consistent comparison, the yes/no OCT assessment and the cross-sectioned thickness measurement were performed in approximately the same location radially, at ~0.4 mm from the pigment edge. A single cross-sectioned thickness measurement was compared with 14 OCT scans that varied radially, acquired within the recommend 2 min. This resulted in 47 images of 4 lenses analyzed (observations) with 0 incorrect

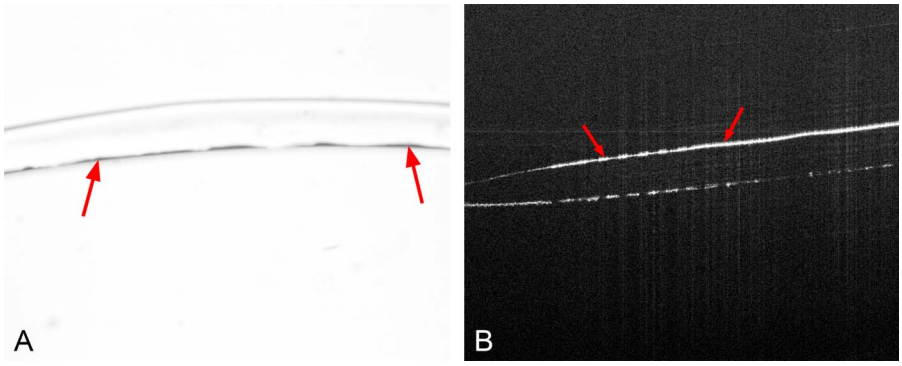

FIG. 3. (A and B) Microscopy and OCT images of Seed Eye Coffret 1-Day UV Natural Make. Pigment enclosure was not identified using either method. Arrows indicate regions of pigment. OCT, optical coherence tomography. full color online

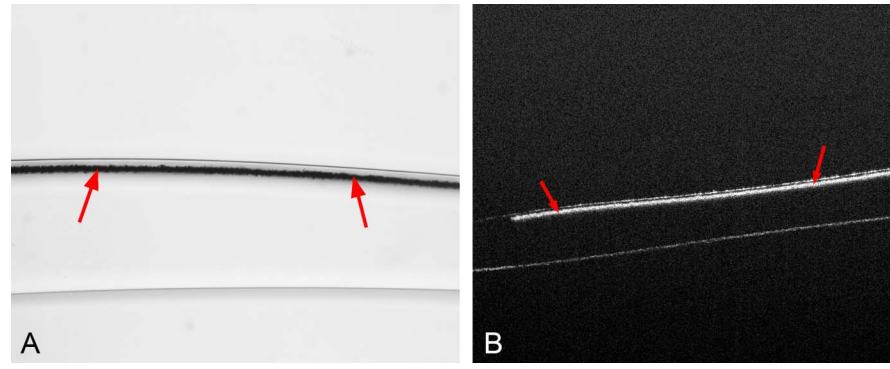

FIG. 4. (A and B) Microscopy and OCT images of Johnson & Johnson 1 Day Acuvue Define Accent Style. Pigment enclosure was identified using both methods. Arrows indicate regions of pigment. OCT, optical coherence tomography. full color online

assignment events—the resulting probability of correctly identifying when a clear layer is present when a test article has a 2.4 μm or greater clear layer is 93.8% with 95% confidence for the OCT assessment.

RESULTS

Optical coherence tomography and microscopy methods were used to assess whether a clear layer could be identified on 19 commercially available cosmetic contact lens products across six manufacturers. Three lenses from each product were tested. The three lenses were sampled from lots of varying sphere powers when the samples were available. Table 1 shows a summary of the lenses analyzed in this study. For each lens, one cross-section test and seven OCT test results were acquired. Although multiple test results were obtained per product at different locations and on different lenses, there were no instances of disagreement. Within each product, a clear layer was either identified in all 3 cross-section test results and 21 OCT test results, or in none of the test results. Table 2 summarizes the results of whether a clear layer could be identified per product. A clear layer was only identified in the products manufactured by Johnson & Johnson Vision, Inc. Figures 3A and B, 4A and B, 5A and B, 6A and B show representative microscopy and OCT images of Seed Eye Coffret 1-Day UV Natural Make, Johnson & Johnson 1 Day Acuvue Define Accent Style, Bausch & Lomb Lacelle Crystal Brown Daily, and Interojo Clalen Iris Rhapsody 1 Day, respectively. Pigment is indicated by arrows in both the microscopy and OCT images. In OCT images of lenses in which the pigment enclosure could not be identified, the pigment is visualized by an increase in back-scattered light, which seems to thicken the top lens surface. Due to the large number of products imaged, representative images of additional products are included as Supplemental Digital Contents (see Figures, http://links.lww.com/ICL/A127). All OCT images presented have been contrast enhanced in ImageJ by setting the minimum grayscale value to 85 and cropped to 849 × 700 pixels to present an optimized lens to background viewing ratio.

DISCUSSION

The OCT method in this study required minimal training to execute and provided an LOD of 2.4 μm in the identification of a clear layer. The cross-sectioning microscopy method described in this article requires a trained technician to execute; however, the LOD is smaller at 0.4 μm. Note that if a clear layer is present that is thinner than the limit of detection, the method would not be able to identify it.

Although the two methods described in this article aim to address the need to define the pigment bulk location, a standardized method that can additionally characterize the pigment particle size distribution, location, and composition is still desired. In addition to the articles referenced herein that indicate pigment location may impact the safety and comfort of cosmetic lenses, numerous case reports of adverse events have been documented due to cosmetic lens wear, primarily from purchases from unlicensed vendors.[10–17] Patients acquiring contact lenses from unlicensed vendors are unlikely to receive instruction on lens use, care, be informed possible side effects, or receive a follow-up examination, therefore

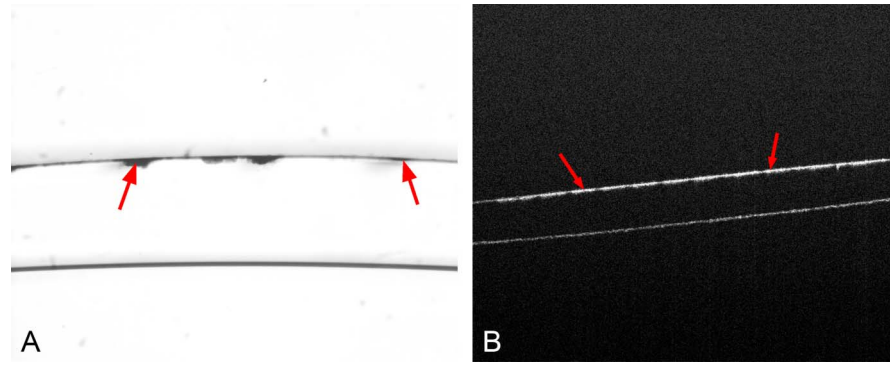

FIG. 5. (A and B) Microscopy and OCT images of Bausch & Lomb Lacelle Crystal Brown Daily. Pigment enclosure was not identified using either method. Arrows indicate regions of pigment. OCT, optical coherence tomography. full color online

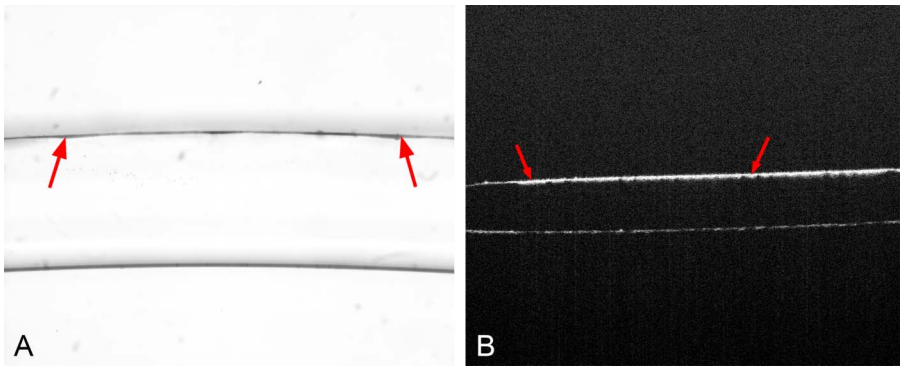

FIG. 6. (A and B) Microscopy and OCT images of Interojo Clalen Iris Rhapsody 1 Day. Pigment enclosure was not identified using either method. Arrows indicate regions of pigment. OCT, optical coherence tomography. full color online

increasing their safety risk. Readers of this article are encouraged to question whether the cosmetic lens is sold by a licensed vendor, whether the pigment in the lens complies with any local regulations (if any exist), and whether pigment is enclosed within the lens matrix as these factors may influence the safety and comfort of the cosmetic contact lens wear.

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