INTRODUCTION

The influence of contact lens wear on corneal integrity has been of interest to clinicians and researchers for decades. The potential lack of oxygen to the cornea, that is, corneal hypoxia, is considered a severe concern when assessing the influence of contact lens wear on the cornea.1 Traditionally, studies focused on investigating hypoxic corneal stress related to lens wear focused on macroscopic anterior ocular tissue changes, such as corneal oedema, evaluated by corneal swelling. Corneal thickness alterations after soft contact lens wear2,3 and scleral lens wear4,5 were repeatedly described. Most reported alterations in corneal thickness due to soft contact lens wear are minor and without clinical relevance, especially after the introduction of new soft contact lens materials with higher oxygen permeability (larger Dk), which will reduce corneal oedema.6

Corneal hypoxia is linked not only to corneal swelling but also to opacification due to neovascularisation and limbal stem cell deficiency.7,8 Thus, solely using corneal thickness as a biomarker for corneal hypoxia might be an oversimplification. Consequently, microscopic corneal changes (i.e., variations in intrinsic tissue properties), evaluated through corneal transparency, should also be...
investigated in contact lens wear as indicators of ocular health. Nowadays, corneal transparency is assessed objectively by estimating corneal densitometry from corneal Scheimpflug images using proprietary or custom-made software. The software uses the densitometry distribution analysis (DDA). The DDA is based on statistical modeling of the pixel intensity distribution of Scheimpflug images and correlates well with traditional densitometry (overall cornea, r = 0.89; p < 0.001). The DDA has proven to be platform-independent. Consequently, it can be used to investigate corneal densitometry from Scheimpflug-based tomographs even if those do not incorporate a detailed corneal densitometry module in their proprietary software. The DDA was already validated from Pentacam HR and Corvis Scheimpflug images.

Other than corneal transparency being repeatedly acknowledged as an essential indicator of ocular health, there are only a few objective studies on the influence of lens wear on corneal transparency. Recently, Ozek et al found a statistically significant difference in corneal densitometry between a group of soft contact lens wearers and control participants. In a further study using the DDA method, alterations in corneal tissue integrity, evaluated by two parameters: tissue transparency and homogeneity, were found as a consequence of a single 8-h period of scleral lens wear in noncompromised eyes. However, the potential influence of short-term soft contact lens wear on corneal tissue integrity is yet to be investigated.

This study aimed at investigating the effect of short-term soft contact lens wear on corneal tissue at both macroscopic and microscopic levels. Corneal thickness is used to quantify macroscopic changes, while a previously validated method, the DDA, is used to quantify microscopic changes within the corneal tissue through transparency and homogeneity. For the first time, the DDA method is applied to Galilei G2 Scheimpflug images. The potential effect of soft contact lens material on corneal tissue integrity will also be evaluated.

**METHODOLOGY**

**Subjects and protocol**

Twenty-two young healthy participants (17 female and 5 male) between 19 and 39 years old (mean age of 23.7 ± 4.7 years) with a narrow range of refractive errors (spherical equivalent between 0.00 and −1.00 D; mean − 0.50 ± 0.57 D) were recruited. Only one eye per participant (dominant motor eye) was chosen, providing a final sample of 22 eyes. The monocular visual acuity (VA), with correction, was >0.8 (decimal equivalent) in all cases. This study was approved by the Ethics Committee for Clinical Research of Aragon (PI20/377) and adhered to the tenets of the Declaration of Helsinki. All subjects gave written informed consent to participate after the nature and possible consequences of the study were explained.

Prior to the commencement of the study, all subjects were screened to exclude those with any contraindications to contact lens wear (i.e., significant tear film or anterior segment abnormalities). Regular contact lens wearers were excluded from participation. Occasional contact lens wearers were asked not to wear their lenses for at least 48 h prior to each measurement day. Occasional contact lens wearers were defined as those sporadically using contact lenses for sport or other leisure activities, and, as reported by the participants, for a maximum of 6 h of wear per day. Participants had no prior history of eye injury, surgery or current use of topical ocular medications. The sample size was derived from previously published data on the DDA as applied to lens wear. The same methodology applied to the current work suggested that a sample size of at least 12 participants would yield 90% power to distinguish corneal tissue changes as a consequence of lens wear at the 0.05 significance level.

This study was conducted over two separate days, at least a week apart. The separation ranged from 7 to 10 days, with two visits being required during the day (i.e., four visits in total). The morning visit (baseline) occurred at least 2 h after the participant’s reported waking time, with the second visit (after contact lens wear) 8 h later. Each day, at the morning (baseline) session, a soft contact lens with a power of −0.50 D (so as not to affect the patient’s vision) was fitted. Participants needing vision correction were allowed to wear their spectacles between visits while wearing the contact lens. On the first day, different procedures were carried out, including those to ensure suitability for contact lens wear, that is, (1) determination of the dominant motor eye; (2) monocular visual acuity with correction (Snellen test at 6 m, and the SmarThings4Vision software, OptoTab, smarthings4vision.com); (3) objective refraction with an open-field auto-refractometer (WAM-5500, grand seiko.com); (4) assessment of the ocular surface (biomicroscopy). A silicone hydrogel soft contact lens (MyDay, coopervision.com) and a hydrogel contact lens (Biomedics 1 day extra, coopervision.com) were chosen for the study. On the first measurement day, each participant wore one of these soft contact lenses (randomly chosen), while on the second measurement day, they wore the other material contact lens, in the same eye as the first measurement day.
The main parameters of both soft contact lenses are shown in Table 1. Corneal Scheimpflug images were obtained from the selected eye of each participant using the Galilei G2 software (Ziemer Ophthalmic Systems, ziemergroup.com). This tomograph consists of two Scheimpflug cameras to decrease possible artefacts caused by movement. Consequently, the device captures two corneal images for each meridian under analysis, as shown in Figure 1a. The built-in Galilei G2 software superimposes both images to increase accuracy in estimating corneal parameters. Central corneal thickness (CCT) and corneal densitometry were extracted for each participant and session. Central corneal thickness (CCT) and corneal densitometry were extracted for each participant and session. The corneal densitometry module in Galilei G2 allows corneal densitometry estimation at a single point, manually selected and assisted by a pair of red lines, as indicated in Figure 1b. Corneal densitometry estimated by Galilei G2 ranges from 1 to 100 and is expressed in grey scale units (GSU).

On each of the two measurement days, Scheimpflug images were acquired before soft contact lens wear (during the morning visit) and immediately after lens removal, following 8 h of soft contact lens wear. Reliable Scheimpflug imaging of the corneal surface cannot be obtained with a lens on the eye due to the lens surface’s reflections. Thus, images were acquired immediately after lens removal. Three measurements of good quality, as indicated by the Galilei G2 software, were captured at each session to assess repeatability, using the 26-picture (i.e., 26 corneal meridians) scan mode.

**Image analysis**

In addition to extracting central corneal thickness and one-point corneal densitometry provided by the built-in Galilei G2 software, corneal transparency was estimated in the overall cornea by applying the DDA. Scheimpflug images corresponding to 26 corneal meridians (a fixed size of 1004 × 1004 pixels)—Figure 2a, b—were exported in .bin format for further analysis (i.e., 6864 images in total = 22 subjects × 2 measurement days × 2 sessions/day × 3 measurements/session × 26 images/measurement). Image analysis consisted of three main stages: (1) corneal registration, (2) corneal segmentation and (3) statistical modelling of the pixel intensity distribution. These steps are illustrated in Figure 2c–h and described below.

The Galilei dual Scheimpflug analyser obtains two corneal images per meridian, each captured with one of the two available Scheimpflug cameras (Figure 2c). Generally speaking, image registration is the process of transforming different sets of data into one coordinate system. Consequently, corneal registration is necessary to ensure that both corneal images captured per meridian share the same coordinate system. Corneal registration consists of corneal reorientation; thus, both corneal images captured in the same frame can be analysed independently.

Corneal segmentation is necessary to discriminate corneal pixels from the image background. The protocol for

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Parameters of the contact lenses selected for the study: silicone hydrogel (MyDay, CooperVision) and hydrogel (Biomedics 1 day extra, CooperVision).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Silicone hydrogel (MyDay)</strong></td>
<td><strong>Hydrogel (Biomedics)</strong></td>
</tr>
<tr>
<td>Material</td>
<td>Stenfilcon A</td>
</tr>
<tr>
<td>Water content</td>
<td>54%</td>
</tr>
<tr>
<td>Modality</td>
<td>Daily</td>
</tr>
<tr>
<td>Dk/t (for a posterior vertex power of −3.00 D)</td>
<td>100</td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>14.2</td>
</tr>
<tr>
<td>Base curve (mm)</td>
<td>8.4</td>
</tr>
<tr>
<td>Power (D)</td>
<td>−0.50</td>
</tr>
</tbody>
</table>

**Figure 1** Corneal Scheimpflug tomography acquired by the Galilei G2 software for the horizontal meridian. (a) Corneal densitometry module in Galilei G2 to calculate densitometry at a single point. (b) The operator can freely move two red lines to the point of interest. Densitometry readings range from 1 to 100, as indicated in the upper and right panels, and are expressed in grey scale units (GSU).
corneal segmentation was described in detail in a previous
paper. In short, traditional image processing techniques,
including a median filter and Canny edge detection, were
used to remove the noise, extract the boundaries of inter-
est and segment the corneal tissue. Thus, in this stage, the
segmentation method automatically extracts the anterior
and posterior borders of the cornea (Figure 2d).

Following corneal segmentation, a region of interest
(ROI) was extracted automatically for statistical modelling,
as in our previous work. In short, the vertical (axial) ROI
dimension was delineated by the anterior and posterior
corneal boundaries. Regarding the horizontal (lateral) di-
mension, a moving ROI of 11 pixels, with a one-pixel step,
was applied across the cornea for each corneal image, as
illustrated in Figure 2e. The moving ROI covered approxi-
mately the central 10 mm of the cornea (Figure 2c). The
most peripheral cornea (beyond 10 mm) was not included
in the ROI to avoid undesired border effects (strong limbal/
scleral reflections).

Further, for the statistical modelling of the pixel in-
tensity distribution, pixels corresponding to a given ROI
were modelled using the Weibull distribution function
(Figure 2f), as described in previous work. From this
function, two parameters are extracted: \( \alpha \), scale param-
eter; and \( \beta \), shape parameter; which account for tissue
transparency and homogeneity, respectively. In general,
a change in scale parameter \( \alpha \) (transparency) causes
a shift in pixel intensity (x-axis), with higher \( \alpha \) values
Statistical analysis

Statistical analysis was performed using the SPSS software (ibm.com). The normality of all sets of data was not rejected (the Shapiro–Wilks test, $p > 0.05$). Paired $t$-tests and Pearson’s correlation coefficients ($r$) were used to assess relationships within the continuous variables under investigation. The coefficient of variance (CoV), coefficient of repeatability (CoR) and intraclass correlation coefficient (ICC) were used to assess the repeatability of the method. Additionally, Bland–Altman plots comparing baseline values of parameters $\alpha$ and $\beta$ on Days 1 and 2 are presented in Figure S1. The level of significance was set to 0.05.

RESULTS

Effect of short-term soft contact lens wear on corneal densitometry depending on lens material

Short-term soft contact lens wear had a significant effect on parameter $\beta$, that is, corneal homogeneity, increasing by 5% (paired $t$-test, $p < 0.001$). All corneal regions analysed were equally affected (all, $p < 0.01$), for both lens materials (Table 2). Regarding parameter $\alpha$, that is, corneal transparency, no significant difference was found due to short-term soft contact lens wear, independent of lens material (paired $t$-test, all $p > 0.05$, Table 2).

Regarding the different corneal annuli, significant differences were found between the central (0–2 mm) and midperiphery (2–6 mm) regions in all sessions, for both materials and $\alpha$ and $\beta$ parameters, as indicated in Table 2. Similarly, statistically significant differences were found between the midperiphery and periphery (6–10 mm) in all sessions, for both materials, but only for the $\beta$ parameter. No clear pattern was found when comparing other corneal annuli (Table 2).

Regarding the soft contact lens material, no significant differences were found after lens wear for the $\alpha$ and $\beta$ parameters (Table 2). There is a subtle but statistically significant difference ($p = 0.04$, Table 2) in parameter $\alpha$ when comparing materials in the corneal periphery (6–10 mm); in this region, $\alpha$ was smaller with the silicone hydrogel ($42 \pm 3$ arbitrary units [a.u.]) than with the hydrogel ($44 \pm 4$ a.u.), as indicated in Table 2. As expected, no significant differences were found in the baseline session, that is, before soft contact lens wear, when comparing the two experimental days (Table 2). Graphical representation of the distribution of the $\beta$ and $\alpha$ parameters in the cornea depending on the imaging session and soft contact lens material worn by the 22 participants is shown in Figures 3 and 4, respectively.

Individual differences in corneal densitometry as a consequence of short-term soft contact lens wear

Even though no statistically significant differences were found in the $\alpha$ parameter for both types of materials when considering the group means (Table 2), it was observed that in half of the participants (11 out of 22) a change in at least 5% with respect to the baseline value was observed in the $\alpha$ parameter when using one material, but not with the other, as exemplified in Figure 5. The $\alpha$ parameter in the cornea of participant 02, represented in Figure 5, increased by 8% with respect to baseline when wearing contact lens 1, but not when wearing contact lens 2 (increment of 2% with respect to baseline). Among those participants whose corneas registered a change in the $\alpha$ parameter depending upon the material used, one material was not found to be more likely to cause those corneal changes; this depended on the participant.

Likewise, as mentioned in the previous section, 8 h of soft contact lens wear produced a significant effect on the $\beta$ parameter (paired $t$-test, $p < 0.01$, Table 2). $\beta$ increased by at least 5% with respect to the baseline corneal value in over 70% of participants (16 out of 22). Once again, these changes were independent of the lens material used.

Looking more closely at the individual differences and considering corneal alteration as variability $\geq 5\%$ with respect to baseline, from the pool of 22 participants, six showed such a change in both the $\alpha$ and $\beta$ parameters. In five subjects, the change was only registered in the $\alpha$ parameter, while in 10 people, the alteration was solely registered in the $\beta$ parameter. Finally, no change in either $\alpha$ or $\beta$ was observed in only one out of 22 participants. These changes were independent of the soft lens material. Some participants were more affected by the hydrogel...
Densitometry distribution analysis repeatability

Three Galilei G2 measurements were acquired in each session to assess the repeatability of the DDA method. Repeatability results per material, parameters ($\alpha$ and $\beta$), session and region are shown in Table 3. Considering both materials together, that is, investigating the repeatability before and after lens wear, it was observed that the repeatability was slightly better at baseline ($\alpha$: CoV = 2.72%, CoR = 2.26, ICC = 0.94; $\beta$: CoV = 2.75%, CoR = 0.25, ICC = 0.94) than after contact lens wear ($\alpha$: CoV = 3.09%, CoR = 2.47, ICC = 0.89; $\beta$: CoV = 3.35%, CoR = 0.33, ICC = 0.90).

Comparison of corneal densitometry between the DDA method and Galilei G2 readings

Corneal densitometry readings acquired from the Galilei G2 built-in software are shown in Table 4. No changes in corneal densitometry were observed before and after 8 h of soft contact lens wear for both types of material (Table 4). Moreover, there was no significant correlation between corneal densitometry values estimated with the Galilei G2 and the $\alpha$ and $\beta$ parameters ($r = 0.18$ and 0.09, respectively; both $p > 0.05$).
Effect of short-term contact lens wear on corneal thickness

Central corneal thickness (CCT) was affected by 8 h of soft contact lens wear. A statistically significant thinning of the CCT was observed after silicone hydrogel lens wear (paired t-test, $p = 0.02$), while a significant thickening of CCT was recorded after hydrogel lens wear (paired t-test, $p = 0.03$; see Table 4).

No significant correlation was found between CCT and baseline $\alpha$ (silicone hydrogel: $r = 0.26$, $p = 0.12$; hydrogel: $r = 0.21$, $p = 0.17$) nor after lens wear (silicone hydrogel:...
FIGURE 5  Distribution of $\alpha$ (transparency) in the cornea of a participant (female, 22 years old) whose cornea was affected when wearing a soft contact lens of a given material (CL 1, silicone hydrogel), but was not affected when wearing the other material (CL 2, hydrogel). Note that this is a single example (participant 02) and not representative of others. Left: before contact lens wear; right: immediately after 8 h of CL wear. The coloured bars ($\alpha$) are expressed in arbitrary units (a.u.). CL, contact lens.

TABLE 3  Repeatability study of the DDA method.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Silicone hydrogel</th>
<th>Hydrogel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>After CL wear</td>
<td>Baseline</td>
</tr>
<tr>
<td>CoV (%)</td>
<td>CoR</td>
<td>ICC</td>
</tr>
<tr>
<td>Centre (0–2 mm)</td>
<td>1.88</td>
<td>1.63</td>
</tr>
<tr>
<td>Midperiphery (2–6 mm)</td>
<td>2.03</td>
<td>1.70</td>
</tr>
<tr>
<td>Periphery (6–10 mm)</td>
<td>4.27</td>
<td>3.32</td>
</tr>
</tbody>
</table>

Note: The coefficient of variation (CoV), coefficient of repeatability (CoR) and intraclass correlation coefficient (ICC) are calculated for the estimated values of $\alpha$ (corneal transparency) and $\beta$ (corneal homogeneity) from the three measurements acquired in each session.

TABLE 4  Mean values of corneal densitometry ± standard deviation, expressed in greyscale units (GSU), and central corneal thickness (CCT) ± standard deviation for the 22 participants, at baseline and 8 h after CL wear, for each soft contact lens material, acquired from the Galilei G2 built-in software.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Silicone hydrogel</th>
<th>Hydrogel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Densitometry (GSU)</td>
<td>17 ± 1</td>
<td>17 ± 1</td>
</tr>
<tr>
<td>CCT (μm)</td>
<td>562 ± 27</td>
<td>559 ± 27</td>
</tr>
</tbody>
</table>

Note: A paired t-test was applied to investigate differences between sessions (baseline vs. after CL wear).
more affected by the silicone hydrogel lens. From the sam-
tissue alterations. While the cornea of some participants
ture of 22 participants, only one did not have any corneal
tissue changes at the microscopic level estimated from
the DDA method applied to Galilei G2 images. Parameter
increased significantly following soft contact lens wear
(Table 2, Figure 3). In addition to the alterations in CCT
(Table 4), corneal changes were observed for both mate-
rine abnormalities. Two parameters: \( \alpha \) (corneal transparency)
and \( \beta \) (corneal homogeneity) were used to quantify corneal
tissue alterations to the corneal transparency \( \alpha \) changed by at least 5% with respect to the
baseline value in half of the participants when using one
material (silicone hydrogel or hydrogel) but not the other,
as shown in Figure 5. There was no predominance of one
material over the other to cause more substantial corneal
tissue alterations. While the cornea of some participants
was more affected by the hydrogel material, others were
more affected by the silicone hydrogel lens. From the sam-
ple of 22 participants, only one did not have any corneal
tissue alterations for either of the two CLs worn.

Little is known about soft contact lens wear and corneal
densitometry. Recently, Ozek et al. studied corneal densi-
tometry using the Pentacam HR, after prolonged wearing
of soft contact lenses. These authors found a significant
increase in corneal densitometry in participants who had
worn soft contact lenses for 4.45 ± 2.15 years compared
with the control group. Corneal densitometry readings
obtained with the Pentacam HR are equivalent to the \( \alpha \) parameter
in the current work. In the present study, after
8 h of wear, changes in the corneal tissue had already been
seen. This may indicate that the \( \beta \) parameter provides
extra objective information regarding corneal tissue in-
tegrity. Ozek et al. detailed the increase in densitometry
by region. Significant differences were noted between the
regular contact lens wearers and the control group in the
central (0–2 mm) and midperipheral (2–6 mm) zones (cen-
tral: 23.2 ± 4.7 GSU vs. 17.3 ± 5.6 GSU and midperipheral: 22.4 ± 6.4 GSU vs. 17.8 ± 1.4 GSU, respectively). However,
there were no significant variations in corneal densitom-
etry values in the ring from 6 to 12 mm. In the current
research work, an analysis per corneal region was also car-
rried out. Statistically significant differences have been de-
tected when comparing different corneal regions (Table 2).

Differences were observed in the \( \alpha \) and \( \beta \) parameters and
were especially pronounced when comparing the central
(2 mm diameter) with the midperipheral region (2–6 mm
annulus). Generally speaking, regional differences were not
affected by soft contact lens material (Table 2), except for a minor but statistically significant increment \( (p = 0.04) \)
observed in the parameter \( \alpha \) in the periphery (6–10 mm
annulus) when using hydrogel (44 ± 4 a.u.) versus silicone
hydrogel (42 ± 3 a.u.) lenses (see Table 2).

In previous research investigating corneal tissue prop-
erties after 8 h of scleral lens wear using the DDA meth-
ology, as in the current work, Consejo et al. reported
significant changes in both the \( \alpha \) and \( \beta \) parameters, as
well as corneal swelling. They also reported that the cor-
eal tissue of the 14 young, healthy participants was not
equally affected by short-term scleral lens wear. That is,
the corneas exhibited a different hypoxic response to lens
wear. Because the current study is based on soft contact
lens wear, the reported corneal tissue alterations were sub-
tler than those resulting from scleral lenses. However, the
overall results are consistent in both studies. In the previ-
ous work with scleral lenses, researchers concluded that
the corneal \( \alpha \) and \( \beta \) parameters might be a useful metric to
quantify subclinical corneal changes associated with low-
level hypoxia.

The present study shows that the light scattering prop-
certies of the cornea were altered as a consequence of soft
contact lens wear. Previous research has demonstrated
that short-term hypoxic corneal stress alters proteoglycan
metabolism, which can affect the arrangement of collagen
fibres within the stroma, thus modifying the light scat-
ttering properties of the corneal tissue. In particular, an
incremental change in \( \alpha \) translates to more corneal back-
scattering (i.e., a less transparent stroma), while an incre-
ment in \( \beta \) indicates an increase in tissue homogeneity.

Both traditional corneal densitometry and the DDA
method used in the current work are based on the back-
scattering of light at the cornea. The advantages of the
DDA over traditional densitometry are as follows: platform
independency (it can be applied to any Scheimpflug image,
independent of the instrument used), versatility (it allows
customisation depending on the clinical purpose) and
precision (it offers information about tissue transparency
and homogeneity). The DDA has already been validated
with rotating Scheimpflug cameras (Pentacam HR)
and Scheimpflug tonometry (Corvis ST), showing a good level of agreement between devices. The DDA
method has shown to be repeatable when applied to
Pentacam HR Scheimpflug images and Corvis ST Scheimpflug
images. This is the first time the DDA method has been
applied to Galilei G2 Scheimpflug images. In the current
work, three measurements per participant were acquired
in each session to investigate the DDA repeatability with
Galilei G2 Scheimpflug images. Both \( \alpha \) and \( \beta \) showed good
repeatability with a CoV <5.00% in all cases, as shown in
Table 3. It was also observed that CoV worsens towards
the corneal periphery. This worsening in repeatability towards
the periphery was expected because of the influence of the eyelids and limbal reflex, which might cause artefacts during image acquisition and consequently increase error probability. The ICC, a statistical measure of reliability, ranged between 0.78 (good reliability) and 0.96 (excellent reliability), as indicated in Table 3. Accordingly, the DDA is a reproducible and versatile method for investigating corneal tissue in detail and assessing tissue transparency and homogeneity, both objectively and automatically. The DDA can be applied to Scheimpflug corneal images, regardless of the source tomographer.

The Galilei G2 incorporates a module to estimate corneal densitometry manually at a single point (one pixel), assisted by a pair of red lines, as illustrated in Figure 1b. This is a rudimentary method to estimate corneal densitometry compared with the Pentacam HR or the DDA, which can automatically consider the whole cornea (thousands of pixels). Previous work has reported that the DDA method used here to characterise corneal tissue correlates well with traditional corneal densitometry readings estimated with the Pentacam HR, for both $\alpha (r = 0.89, p < 0.001)$ and $\beta (r = -0.60, p < 0.001)$.10 In the current work, contrary to the DDA results (Table 2), no statistically significant changes were found in corneal densitometry, either before or after contact lens wear, when estimated with the Galilei G2 densitometry module (Table 4). Densitometry estimated directly from the Galilei G2 software lacked objectivity and resolution to discriminate between before and after lens-wearing sessions. However, as the device allows image export, it is possible to estimate corneal densitometry objectively considering the whole cornea using alternative methods, such as the DDA.

In addition to microscopic corneal tissue alterations, the present study also estimated macroscopic corneal changes by means of CCT estimates from the Galilei G2 software. Significant changes in CCT were observed as a consequence of soft contact lens wear (Table 4). However, the difference in CCT varied with the lens material (Table 4). In the case of the silicone hydrogel lenses, corneal thickness decreased by an average of 3 μm, whereas corneal thickness increased by an average of 2 μm for the hydrogel material. This is in agreement with previous research.2 Del Águila et al. evaluated the effect of daily disposable contact lens materials on corneal thickness.2 They reported that hydrogel and silicone hydrogel lenses caused the most and least increase in pachymetry, respectively, while for the latter material, even minor thinning was observed.2 While statistically significant changes in corneal thickness were observed in the current work, they were not clinically relevant. No significant correlation was found between CCT and corneal tissue transparency and homogeneity, in agreement with previous work.17,20,21,23 Corneal thickness quantifies macroscopic changes, while $\alpha$ and $\beta$ quantify microscopic changes within the corneal tissue. Several investigations have discussed the absence of a correlation between corneal macroscopic and microscopic parameters in both healthy and compromised corneas.17 In addition, by means of bootstrap analysis, it was noted that not only are macroscopic and microscopic parameters independent from one another, but also that corneal thickness is not a confounding factor affecting the calculation of $\alpha$ and $\beta$.20

This work does have important limitations. Only one eye was used to avoid correlation with the fellow eye,24 following previous work in contact lens research.17,18,25,26 Additionally, the eye not wearing a CL was not used as a control because diurnal variation in $\alpha$ and $\beta$ has already been investigated in previous work using the DDA method.17 The authors found that $\alpha$ and $\beta$ remained stable during the day, when assessed in morning and evening sessions, 8 h apart.17 It is expected that observed changes in corneal homogeneity and transparency as a consequence of 8 h of soft contact lens wear will be reversed after lens removal. However, it would be valuable to investigate how long these parameters take to return to their original values in future research. Similarly, applying the DDA method to investigate the long-term effects of soft contact lenses wear would also be of interest. In this study, there was no predominance of one material over the other (silicone hydrogel or hydrogel) to cause corneal tissue changes. However, some participants were more susceptible to one material than the other. The present work does not provide enough data to analyse why an eye behaves differently depending on the CL material. Future research, based on a mixed model, should consider other parameters such as demographics, the contact lens’s design, corneal biomeetry and biomechanics to predict subject-mater biocompatibility. In the current work, the corneal microstructure was analysed indirectly, using parameters ($\alpha$ and $\beta$) that have previously been linked with corneal tissue integrity.13,20 However, an analysis at the cellular level was not conducted. Future work, correlating cellular observations with the reported changes in $\alpha$ and $\beta$, would be helpful.

In conclusion, following 8 h of soft contact lens wear, significant changes in corneal tissue properties were observed. These results indicate the importance of biocompatibility with contact lens materials. Although the clinical implication of these changes requires further experimentation, these findings may provide a useful additional metric to monitor subclinical corneal tissue changes as a consequence of contact lens wear.

**AUTHOR CONTRIBUTIONS**

**Alejandra Consejo:** Conceptualization; data curation (equal); formal analysis (lead); investigation; methodology (lead); project administration (equal); resources (lead); software; supervision (equal); validation; visualization (lead); writing – original draft (equal); writing – review and editing.

**Irene Trillo-Moreno:** Formal analysis; investigation (equal); validation (equal); visualization; writing – original
draft (equal); writing – review and editing (equal). **Laura Remón:** Investigation (equal); methodology; project administration (equal); resources (lead); supervision (equal); validation (equal); writing – original draft (equal); writing – review and editing (equal).

**CONFLICT OF INTEREST**

All authors declare that they have no conflicts of interest.

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**REFERENCES**


**SUPPORTING INFORMATION**

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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