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Title:

The relationship between lid-parallel conjunctival folds and tear meniscus regularity along the lower eyelid

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Abstract

Purpose: To investigate the capability of a new, portable, digital meniscometer (PDM) to measure tear meniscus radius (TMR) and height (TMH) at different locations along the lower lid, and to evaluate relationships between tear meniscus regularity and the degree of lid-parallel conjunctival folds (LIPCOF).

Methods: Using the PDM, the TMR and TMH of 42 subjects were measured at three locations along the lower lid of one eye: central, perpendicularly below the pupil center (TMR-C; TMH-C); and temporal (TMR-T; TMH-T) and nasal (TMR-N; TMH-N), perpendicularly below the limbus. Nasal and temporal LIPCOF grades were recorded. Correlations between the measurements were analyzed using the Pearson coefficient (or Spearman rank in nonparametric data), and the differences evaluated by paired t-tests or ANOVA and post-hoc Fisher Least Significant Difference test.

Results: TMR-T was 0.041mm flatter ($p=0.002$) and TMH-T 0.063mm higher ($p<0.001$), while TMR-N was 0.026mm flatter ($p=0.038$) and TMH-N 0.046mm higher ($p<0.001$) than TMR-C and TMH-C. Temporal LIPCOF grades were significantly correlated to temporal alterations in TMH ($r=0.590$; $p<0.001$) and TMR ($r=0.530$; $p<0.001$), and nasal LIPCOF grades to nasal alterations in TMH ($r=0.492$; $p=0.001$) and TMR ($r=0.350$; $p=0.023$).

Conclusions: The PDM is able to non-invasively detect significant differences in TMR and TMH along the lower lid. The flatter TMR and higher TMH at the nasal and temporal locations are associated with increased LIPCOF. Since increased LIPCOF scores may affect tear film disruption along the lower lid, measuring TMR and TMH at the central position below the pupil may provide the best inter-subject reliability.

Key words: Tear film, tear meniscus regularity, portable digital meniscometer, reflective meniscometry, lid-parallel conjunctival folds, LIPCOF

In the diagnosis of aqueous-deficient dry eye, an evaluation of tear fluid volume is an important parameter. The tear menisci hold approximately 75-90% of the overall tear fluid volume and a tear meniscus reduction correlates to a decreased tear volume.[1-6] The measurements of tear meniscus height (TMH), tear meniscus radius (TMR) and the calculation of the cross-sectional area (TMA) are limited to one or, in the case of the area, to two dimensions. Since the meniscus is spread along the eyelid margins, the length of the lid is used to calculate the tear meniscus volume (TMV). As the eyelids are curved, the eyelid length measured on an image is adjusted by a multiplication factor of 1.294, according to Tiffany et al.[7]

In the published literature, the measurement of tear meniscus parameters is mostly performed at the center of the lower eyelid, directly under the pupil. Some authors report TMH to be greater at the center of the lid,[8] but others find no thinning of the inferior tear meniscus,[9] or even that the TMH is smaller at the center.[10] These differences might be explained by the different techniques used, the timing of such measures after a blink and the different areas of observation. At the same time, when calculating TMV, the meniscus is assumed to be equal along the lower lid,[7, 11] or a correction factor of ¾ is used to account for an unequal distribution.[8, 12, 13] ~~A insufficient or discontinuous lower tear meniscus, that can be classified by a grading system, indicates aqueous tear deficiency.[14-16]~~

Lid parallel conjunctival folds (LIPCOF) are folds in the lateral, lower quadrant of the bulbar conjunctiva, parallel to the lower lid margin. LIPCOF were described as a subtype that might represent a mild stage of conjunctivochalasis.[14] ~~LIPCOF can be observed with the slit-lamp or an OCT, and they were found to be an indicator of dry~~

eye symptoms.[17-23] Like conjunctivochalasis, LIPCOFs are located in the tear meniscus area and both are assumed to interfere with the meniscus.[15-18]

Recently, an iPod touch based system, named the Portable Digital Meniscometer (PDM), has been developed to measure TMR. It has been demonstrated as giving accurate and reliable measurements at the central position, which were significantly correlated to optical coherence tomography (OCT) and video-meniscometer values.[19, 20] It is not known how effective this new system is at assessing TMH and TMR at different locations along the lid margin.

The aims of this study are: (i) to investigate the capability of the new slit-lamp mounted PDM to measure TMH and, for the first time, TMR at different locations along the lower lid; and (ii) to evaluate any relationships between tear meniscus regularity and the degree of LIPCOF.

METHODS

Subjects

Forty-two subjects (male = 13, female = 29) were randomly selected from the staff and students of the Höhere Fachschule für Augenoptik Köln (Cologne School of Optometry), Cologne, Germany. Subjects were excluded if they were pregnant or breast-feeding; had a current or previous condition known to affect the ocular surface or tear film; had a history of previous ocular surgery, including refractive surgery, eyelid tattooing, eyelid surgery, or corneal surgery; had any previous ocular trauma, were diabetic, were taking medication known to affect the ocular surface and/or tear film, and/or had worn contact lenses during the preceding two weeks prior to the study.

All subjects gave written informed consent before participating in the study. All procedures obtained the approval of the Cardiff School of Optometry and Vision Sciences Human Ethics Committee and were conducted in accordance with the requirements of the Declaration of Helsinki.

Instrumentation and procedures

A newly developed, slit-lamp mounted, portable, digital meniscometer (PDM) was used to measure TMH and TMR along the lower eyelid. The PDM is based on an application that creates a grid of black and white gratings on the screen of an iPod touch or an iPhone (Apple Inc., Cupertino, CA, USA) (Figure 1). The tear meniscus acts as a concave mirror and creates an image of the grating that, when captured by a digital slit-lamp camera (BQ900 with IM900 digital imaging module, Haag-Streit, Koeniz, Switzerland), can be analyzed using ImageJ 1.46 software (http://rsbweb.nih.gov/ij). The detailed construction of the PDM has been previously described.[19, 20] Specular reflection with the slit-lamp was achieved by setting the incidence angle of the target grating equal to the observation angle of the microscope, which was set at 40x magnification. The PDM is mounted on a metal axis and fixed to the tonometer post of the slit-lamp and therefore the target can be rotated to avoid shadowing caused by the nose. Using the PDM, TMH and TMR was measured in a randomized order at three locations along the lower lid of one eye: central, perpendicularly below the pupil center (TMR-C; TMH-C); and temporal (TMR-T; TMH-T) and nasal (TMR-N; TMH-N), perpendicularly below the limbus (Figure 2). To minimize diurnal and inter-blink variation, images were recorded in the morning between 10 and 12 o'clock, and 3 to 4 seconds after a normal blink.

Each subject's symptoms were evaluated using the Ocular Surface Disease Index (OSDI) questionnaire and afterwards the total OSDI scores were calculated.[21]

Lid-parallel conjunctival folds were evaluated without fluorescein with a slit-lamp microscope (BQ900, Haag-Streit, Koeniz, Switzerland) using 25x magnification (Figure 3). The LIPCOF evaluation was performed in the area perpendicular to the temporal and nasal limbus on the bulbar conjunctiva above the lower lid, at the same location where TMH and TMR were measured. LIPCOF grade was classified using the optimized grading scale.[22, 23] Care was taken to differentiate LICPOF from micro-folds, which are less well organized and around three times smaller than LIPCOF.[24] To avoid any influence of blinking on the presentation of LIPCOF, the folds also were classified 3 to 4 seconds after a normal blink.

The study was conducted in a room with controlled temperature (20 to 23°C) and humidity (44 to 53%). All lower tear meniscus measurements and LIPCOF evaluations were taken on the right eye in primary gaze in a randomized order by a single observer. Analysis of tear meniscus parameters was masked against LIPCOF grading.

Statistical methods

Data were tested for normality using the Shapiro-Wilk test and appropriate statistical tests applied. Correlations were calculated with Pearson correlation (or Spearman rank in non-parametric data). The differences between the locations along the lower lid were calculated with a paired t –test. To detect the differences among the LIPCOF-groups, one-way ANOVA and post-hoc Fisher Least Significant Difference (LSD) tests were used ($p<0.05$). The data were analyzed using SigmaPlot 12 (Systat Software Inc., Chicago, USA).

RESULTS

The mean age of the subjects was 27.4 ± 8.2 (SD) years (range, 20 to 67 years). Mean OSDI score was 10.7 ±7.3 (SD) with a range from 0 to 32.5.

Regularity of Tear Meniscus Height

TMH-C (0.20 ± 0.04mm) was significantly correlated to TMH-T (0.27 ± 0.07mm; $r=0.561$, $p<0.001$) and nasal TMH-N (0.25 ± 0.06mm; $r=0.529$, $p<0.001$). TMH-T (0.063 ± 0.061mm, $p<0.001$) and TMH-N (0.046 ± 0.044mm, $p<0.001$) were both significantly higher than TMH-C (Figure 4). However, no significant differences were found between TMH-T and TMH-N ($p=0.118$).

Regularity of Tear Meniscus Radius

TMR-C (0.27 ± 0.08mm) was significantly correlated to TMR-T (0.31 ± 0.10mm; $r=0.653$) and TMR-N (0.30 ± 0.11mm; $r=0.770$) ($p<0.001$). TMR-T (0.041 ± 0.082mm, $p=0.002$) and TMR-N (0.026 ± 0.076mm, $p=0.038$) were both significantly flatter than TMR-C (Figure 5). No significant differences were found between TMR-T and TMR-N ($p=0.159$).

Relationship between LIPCOF Grades and Tear Meniscus Regularity

Temporal LIPCOF scores (1.43 ± 0.86) were significantly correlated to nasal LIPCOF scores (0.57 ± 0.79) ($r=0.317$; $p<0.05$). Temporal LIPCOF scores were significantly correlated to the difference between TMH-T and TMH-C ($r=0.590$; $p<0.001$) (Figure 6) and to the difference between TMR-T and TMR-C ($r=0.530$; $p<0.001$) (Figure 7), while nasal LIPCOF scores were significantly correlated to the difference between TMH-N and TMH-C ($r=0.492$; $p=0.001$) (Figure 8) and to the difference between TMR-N and TMR-C ($r=0.350$; $p=0.023$) (Figure 9).

However, with temporal LIPCOF grades of ≤1, the temporal TMH and TMR were similar to the central TMH and TMR, while for LIPCOF grades ≥2 they were significantly different (Figures 10, 11). Similarly, for the nasal LIPCOF grades of ≤1, the nasal TMH and TMR were not different from the central TMH and TMR, but were significantly different for LIPCOF grades of 2 compared to grade 0 (Figure 12,13).

DISCUSSION

This study has found that the PDM was able to detect variations of TMH and TMR at different locations along the lower lid. The results for the central TMH and TMR were within the range of previous values reported for central TMH: 0.15 ± 0.04 mm to 0.35 ± 0.11 mm, and central TMR from 0.24 ± 0.05 mm to 0.55 ± 0.26 mm, in healthy subjects.[25-28]

Temporal and nasal TMH were significantly higher than central TMH. This is in agreement with the observation of Garcia-Resua et al.[10], even though they reported slightly lower values. However they measured TMH as the distance between the darker edge of the lower eyelid and the upper limit of the brightest reflex of the meniscus, while in this study, the upper limit of the tear meniscus was measured. However, identifying the upper limit of the meniscus at the slit lamp is challenging unless sodium fluorescein is added to the tear film, which in turn renders the test invasive and will introduce errors. In contrast, TMR measurement is non-invasive and since the radius is measured, there is no need to detect the upper limit of the meniscus.

The PDM was also able to measure TMR, for the first time, at different locations along the lower lid. In previous studies a significant positive correlation has been reported between TMH and TMR at the central position, thus a steeper TMR can be expected in eyes with lower TMH, while a flatter TMR correlates with higher TMH.[29, 30] In this study, a flatter TMR was found at the temporal and nasal position compared to the central position, which concurred with the higher values TMH findings at these locations.

In contrast to these findings, Jones et al.[8] reported that central TMH was significantly greater than that found in the nasal and temporal areas 3mm from the nasal and temporal canthi. These differences may be principally explained by the different locations between the two studies. Furthermore, in this study the measuring time after a blink was controlled (3-4 sec after a blink) while it was not controlled in the study by Jones et al. However, Maki et al.[31, 32] has shown that, based on a mathematical model, the volume distribution of the tear film changes significantly over time between blinks. Jones et al. hypothesised that gravity forces a pool of tears to form at the center of the lower eye lid,[8] while Garcia-Resua et al.[10] hypothesised that tear fluid surface tension may explain the higher values of nasal and temporal TMH.

Harrison et al.[9] showed no significant thinning of the inferior tear meniscus at the limbus compared to the central cornea. However, since they visualised the meniscus with fluorescein and also measured TMH at the area where the lower lid contacts the limbus, it is inappropriate to compare their results with our findings.

Observed temporal and nasal LIPCOF degrees in this study are in concordance with previously reported LIPCOF .[15, 23, 33] LIPCOFs are small folds of the lower bulbar conjunctiva, parallel to the lower lid margin. LIPCOF scores have been reported to be increased in dry eye, but they are not age-related,[34, 35] while conjunctivochalasis has been defined as the redundant, loose, non-edematous conjunctival tissue found at the lower eyelid, typically in older people.[17] Since LIPCOF and conjunctivochalasis are both located in the area of the tear meniscus it is possible that they can influence the distribution of tear fluid along the lower eyelid. Huang et al.[18] found that the conjunctival folds in conjunctivochalasis obliterate tears not only in the meniscus, but also in the reservoir, and they assumed that the conjunctival folds could occupy and deplete the tear reservoir in the fornix. Conjunctivochalasis is often used to describe more prominent folds than described by LIPCOF, being around 0.08mm height.[24]

Using OCT images, Veres et al.[36] observed the coverage of LIPCOF by the tear meniscus and hypothesized that after a blink there is a coverage of the conjunctival folds by the tear film. However, in this study an irregularity of TMH and TMR was found with LIPCOF grades 2 and 3. Therefore one hypothesis may be that LIPCOF in the tear meniscus act as a barrier to the normal flow of tears along the lower eyelid (tear flows along the lower lid margin from temporal side towards the punctum and takes about 3 sec after blink[1, 9]), and that this impedance to the tear flow produces an increase in the tear volume at the temporal and nasal location of the LIPCOFs (Figure 14). A similar idea was previously described by Guillon.[37] He argued that LIPCOF might affect the morphology of the reservoir which loses its meniscus shape and follows the contour of the underlying conjunctiva.[37]

Holly and Lemp[38] reported that a scanty or discontinuous inferior tear meniscus was indicative of an aqueous tear deficiency or lipid abnormality. Taylor[39] described the inferior tear meniscus as “intact“, “not intact temporally“ or “not intact“ and found the marginal tear strip continuity to be a method of assessing the adequacy of the tear film. Guillon[37] reported that the reservoir may be interrupted and that this is one sign of potential dry eye symptoms. A subjective classification of tear meniscus profile was suggested by Khurana et al.[40] and modified by Garcia-Resua et al.[10] Grades 1 and 2 represent a healthy meniscus, whereas grades 3 and 4 represent an abnormal meniscus.

When comparing the change in central lower TMH immediately after a voluntary blink with TMH 3 seconds after the blink, Veres at al.[36] observed an almost 10-fold higher central tear volume decrease in patients with multiple conjunctival folds than in patients with single folds. They assumed that a sharp decrease in tear volume occurs after blinking in the neighborhood of the multiple folds. This seems to agree with this study showing that, in the presence LIPCOF scores greater than one, a smaller central TM is produced, compared to temporal or nasal TM, when measurement was performed 3-4 seconds after a blink. On the basis of this we can speculate that, following a blink, the tear flow may be driven from central to the temporal and nasal LIPCOF area, leading to a central decrease and temporal/nasal increase of TM. It may be hypothesized that the small distance between two conjunctival folds generate capillary forces drawing tear fluid towards the folds (Figure 15). This force might be more strongly generated if there is more than one fold, which would explain the alteration in TM with LIPCOF grades of ≥ 2 as analyzed in this study.

In summary, the PDM is able to non-invasively measure alterations in TMR and TMH along the lower lid. The flatter TMR and higher TMH at the nasal and temporal locations may be caused by the LIPCOF degree of the underlying conjunctiva. To avoid any interference by LIPCOF, it is recommended that TMR and TMH are measured along the lower lid margin below the pupil center.

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Figures

Figure 1. Patient positioned in front of the portable, slit-lamp mounted, digital meniscometer (PDM). The grid on the screen of the iPod touch is reflected by the cornea and the lower tear meniscus.

Figure 2. Reflected image of the portable digital meniscometer (PDM) lines on the concave temporal, central and nasal tear meniscus. The picture is a composition of the three single slit-lamp images with the red line marking the measuring location. The greater the line distance at the location the flatter tear meniscus radius.

Figure 3. Real slit-lamp image of lid parallel conjunctival folds (LIPCOF) grade 3 at the temporal position.

Figure 4. Tear meniscus height at the temporal, central and nasal position of the lower eye lid.

Figure 5. Tear meniscus height at the temporal, central and nasal position of the lower eye lid.

Figure 6. Correlation between temporal LIPCOF grades and alterations in temporal tear meniscus height.

Figure 7. Correlation between temporal LIPCOF grades and alterations in temporal tear meniscus radius.

Figure 8. Correlation between nasal LIPCOF grades and alterations in nasal tear meniscus height.

Figure 9. Correlation between nasal LIPCOF grades and alterations in nasal tear meniscus radius.

Figure 10. Mean difference between the temporal and central tear meniscus height in the four sub-groups with different lid-parallel conjunctival folds grades.

Figure 11. Mean difference between the temporal and central tear meniscus radius in the four sub-groups with different lid-parallel conjunctival folds grades.

Figure 12. Mean difference between the nasal and central tear meniscus height in the four sub-groups with different lid-parallel conjunctival folds grades.

Figure 13. Mean difference between the nasal and central tear meniscus radius in the four sub-groups with different lid-parallel conjunctival folds grades.

Figure 14. Barrier hypothesis for an irregular tear meniscus along the lower lid: The lid-parallel conjunctival folds in the tear meniscus act as a barrier, and tear flow from

the outer to the inner canthus is impounded at the temporal and nasal location of the folds.

Figure 15. Capillary hypothesis for an irregular tear meniscus along the lower lid: The small distance between two lid-parallel conjunctival folds generates capillary forces that draw the surrounding tear fluid towards the folds after a blink.

Figure 1

Figure 2

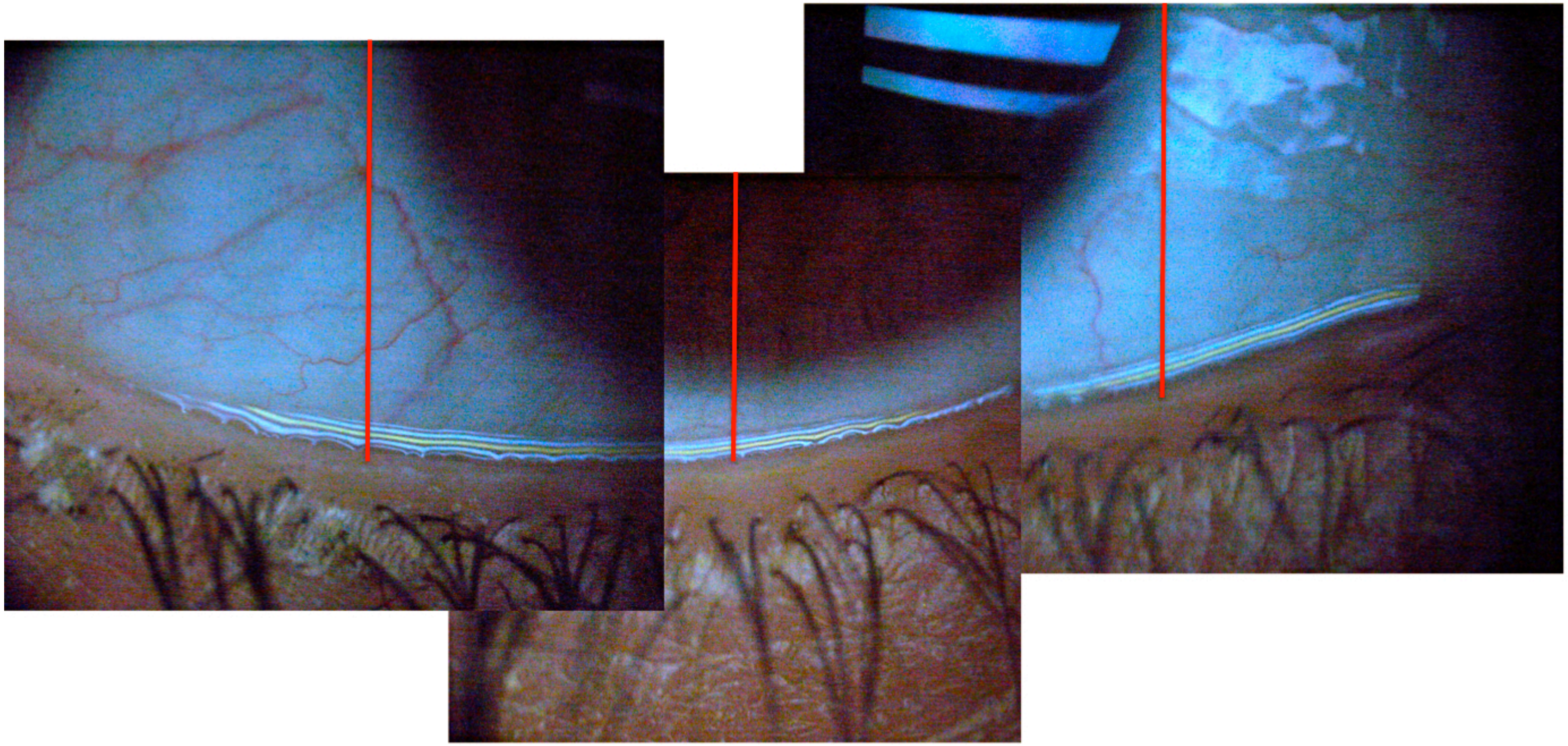
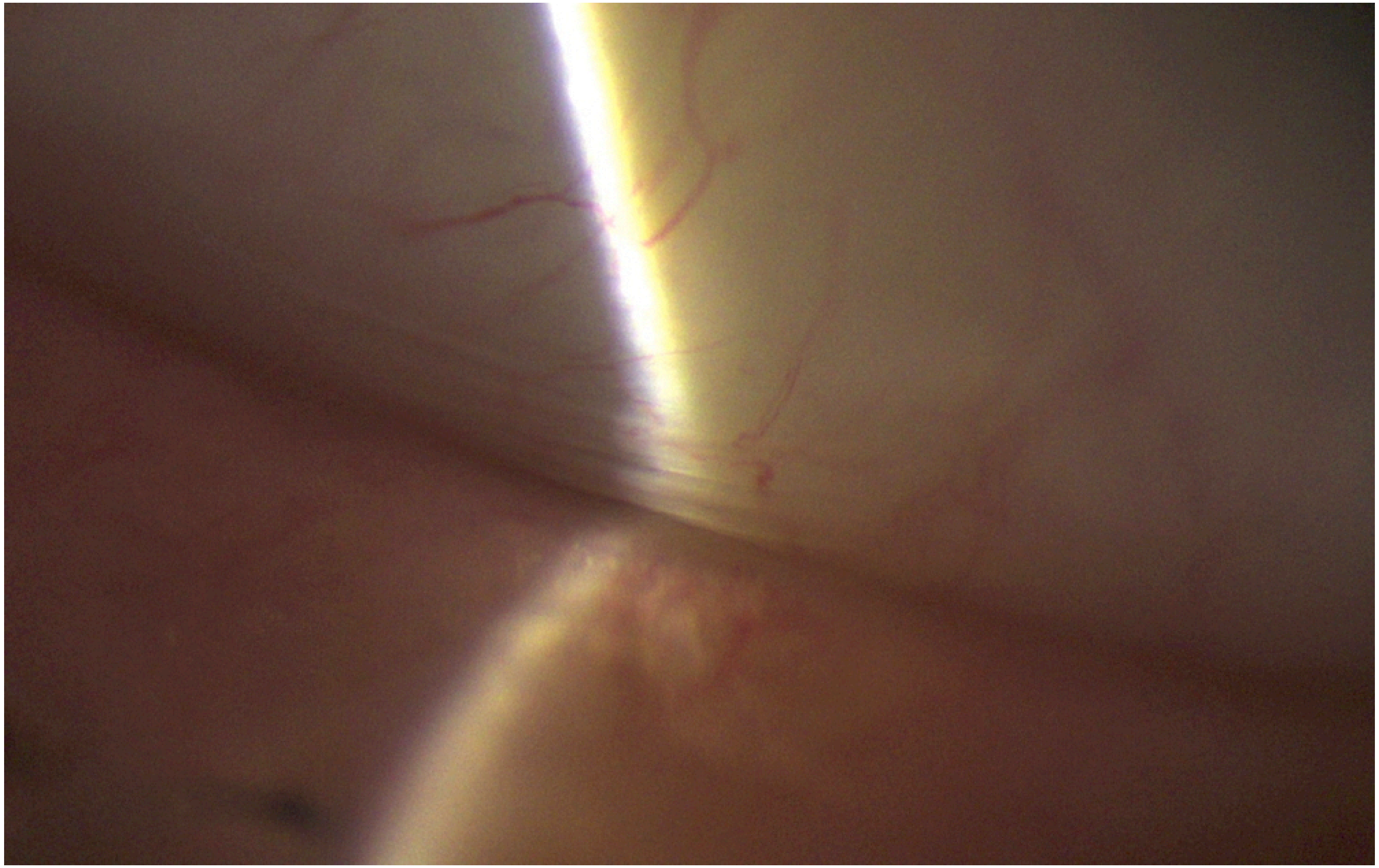


Figure 3



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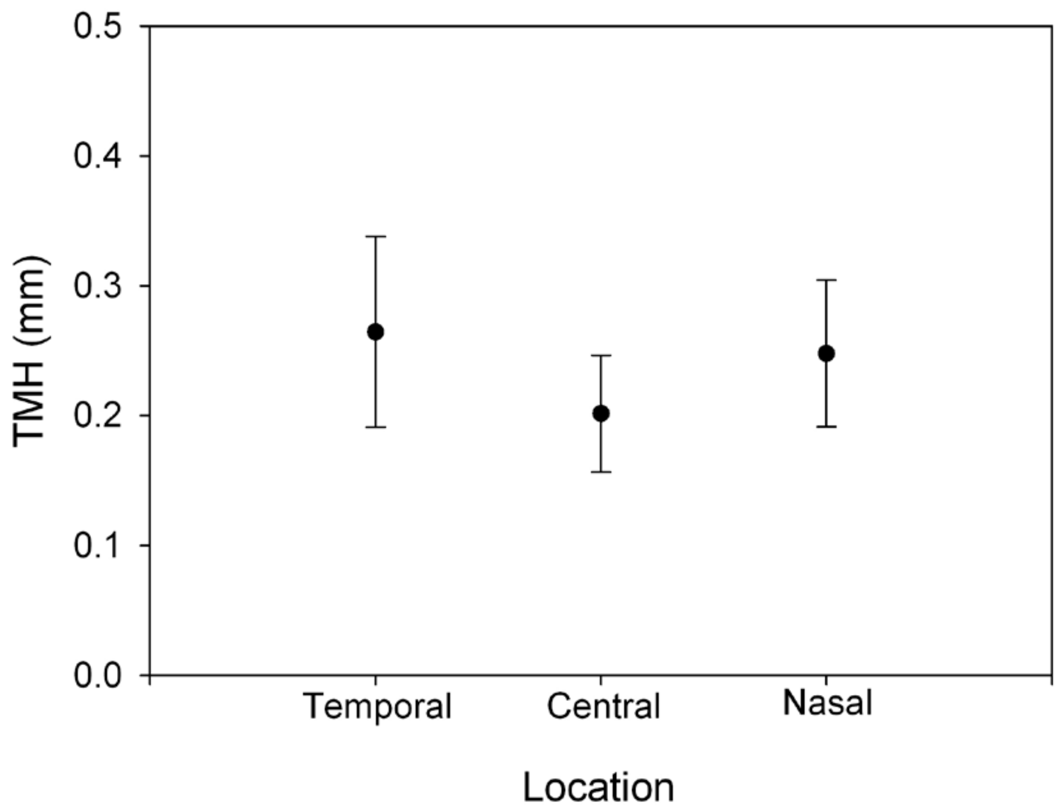


Figure 5

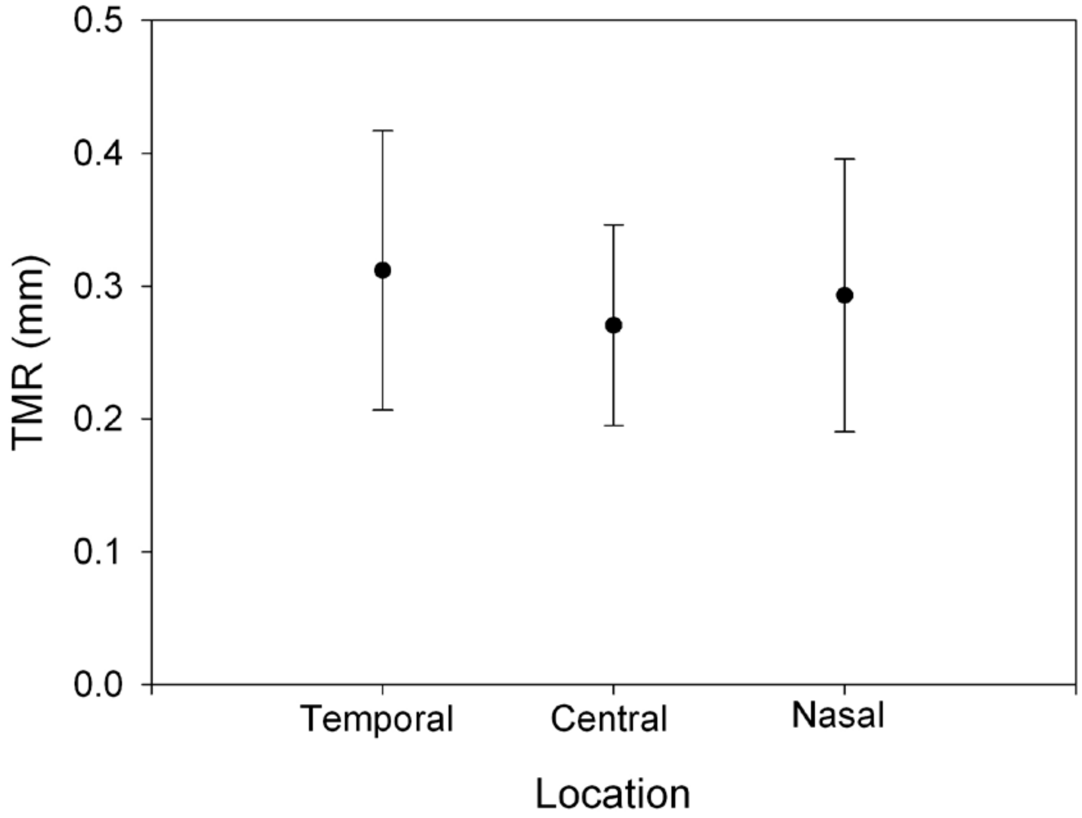
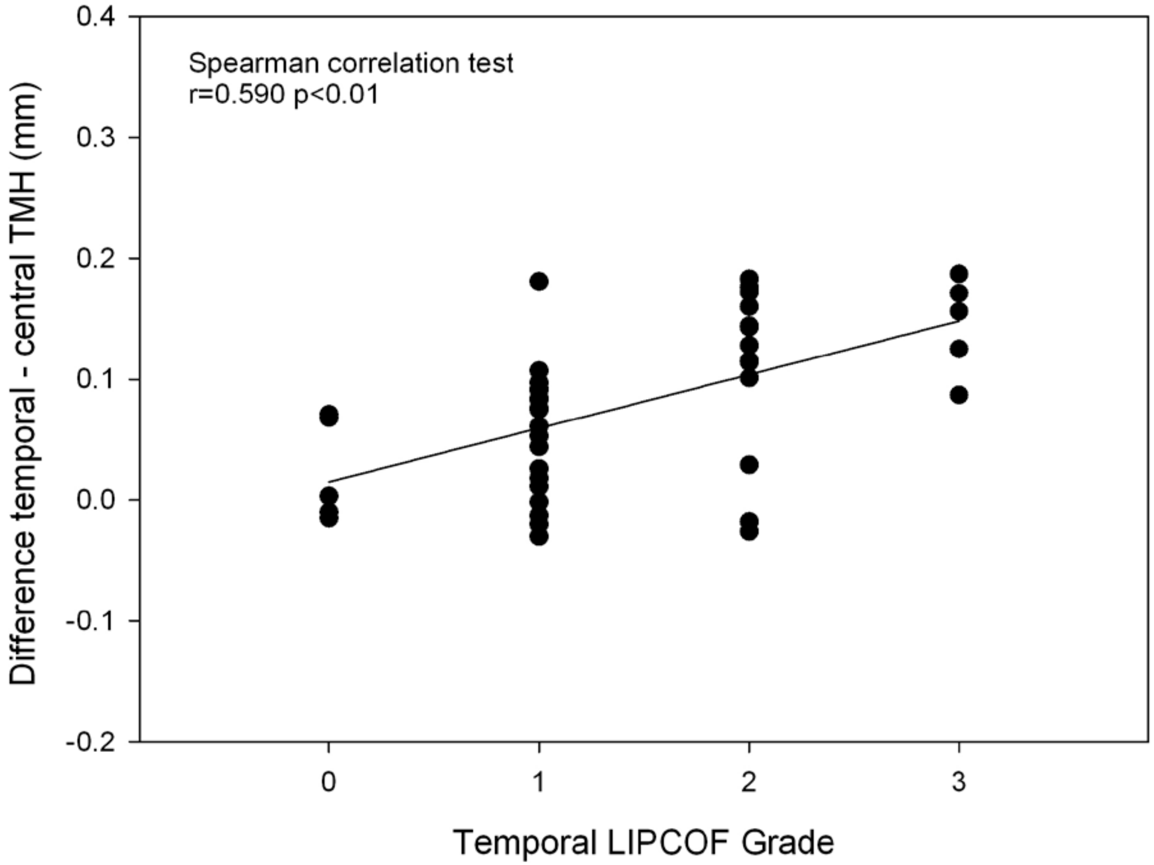
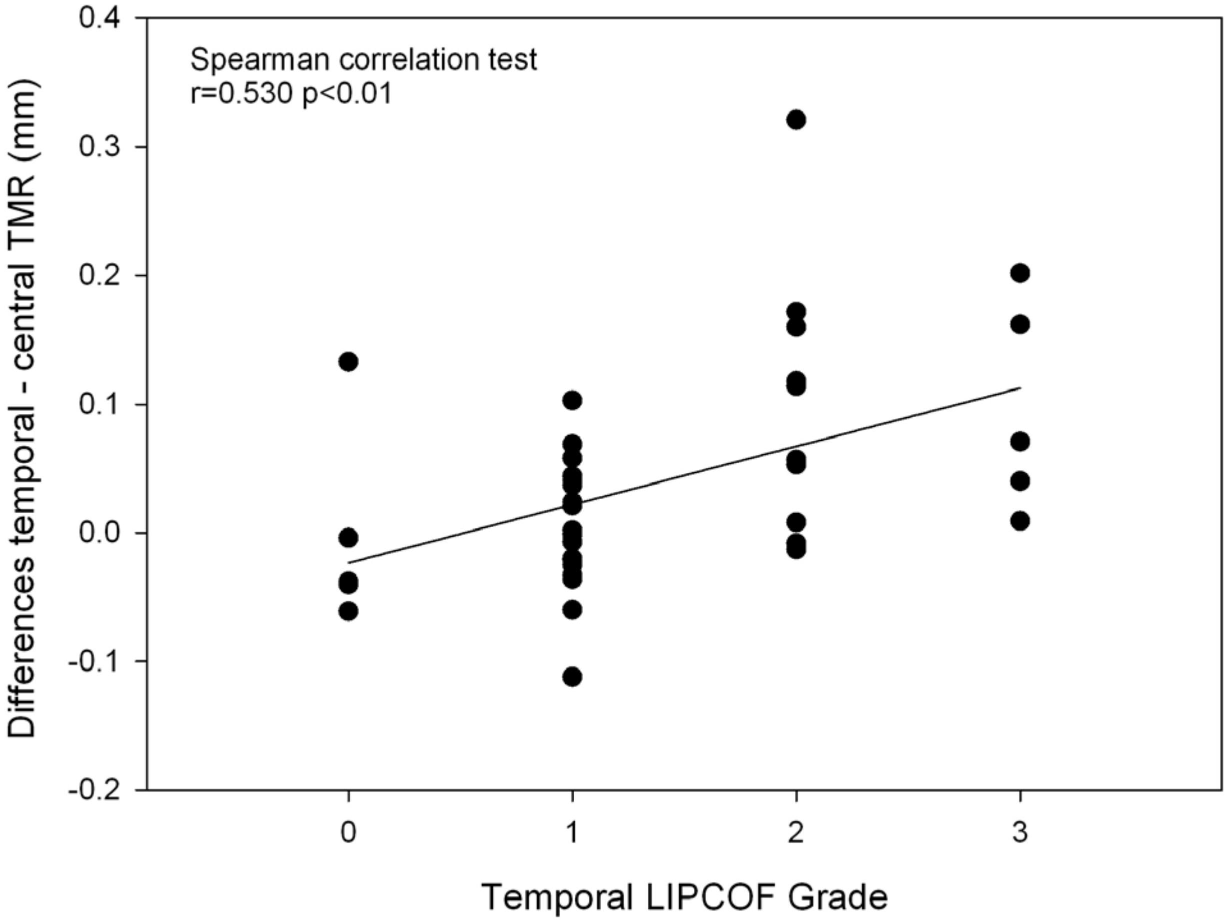


Figure 6



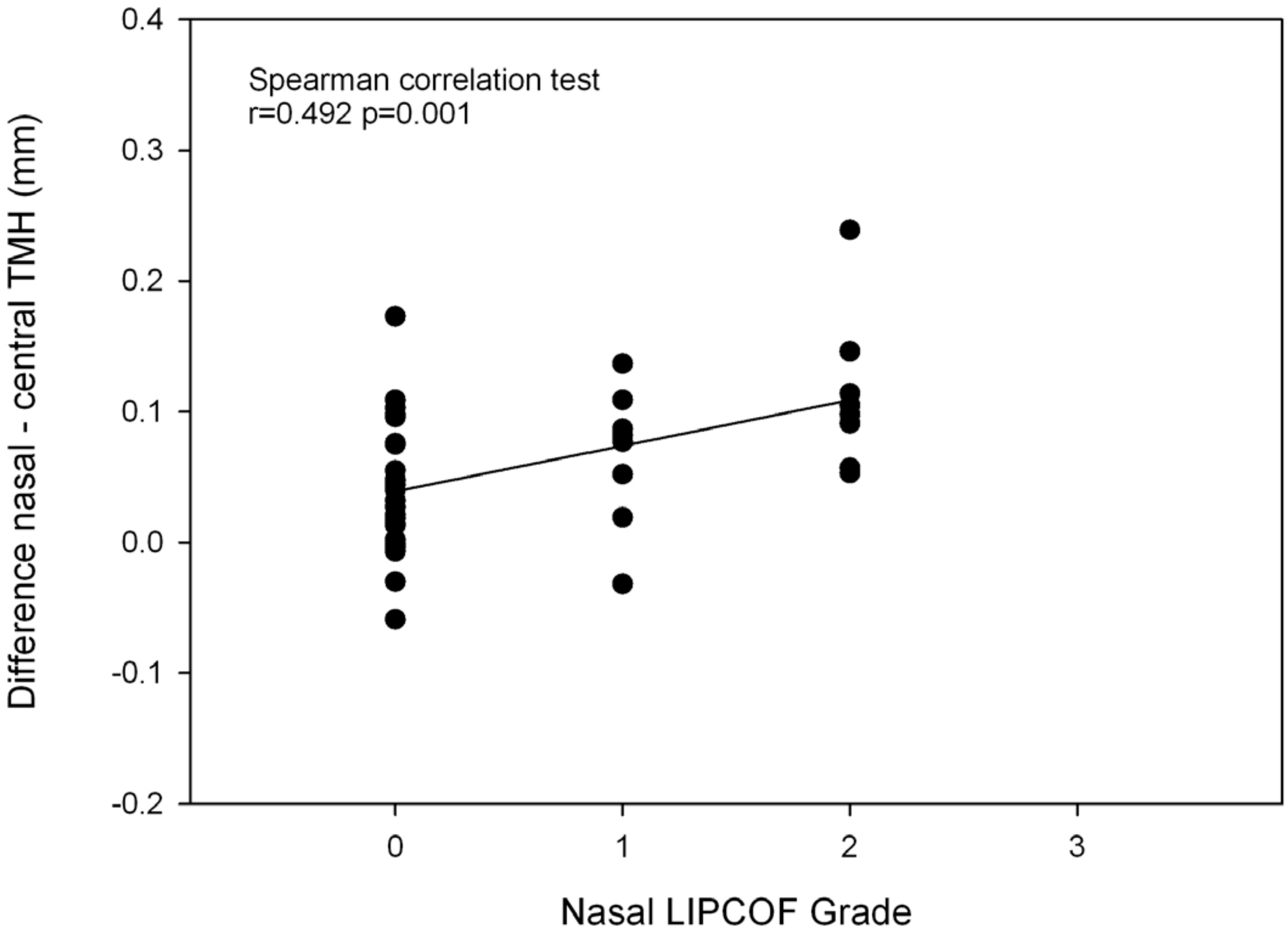
Spearman correlation test
r=0.590 p<0.01
Difference temporal - central TMH (mm)
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
0
1
2
3
Temporal LIPCOF Grade

Figure 7



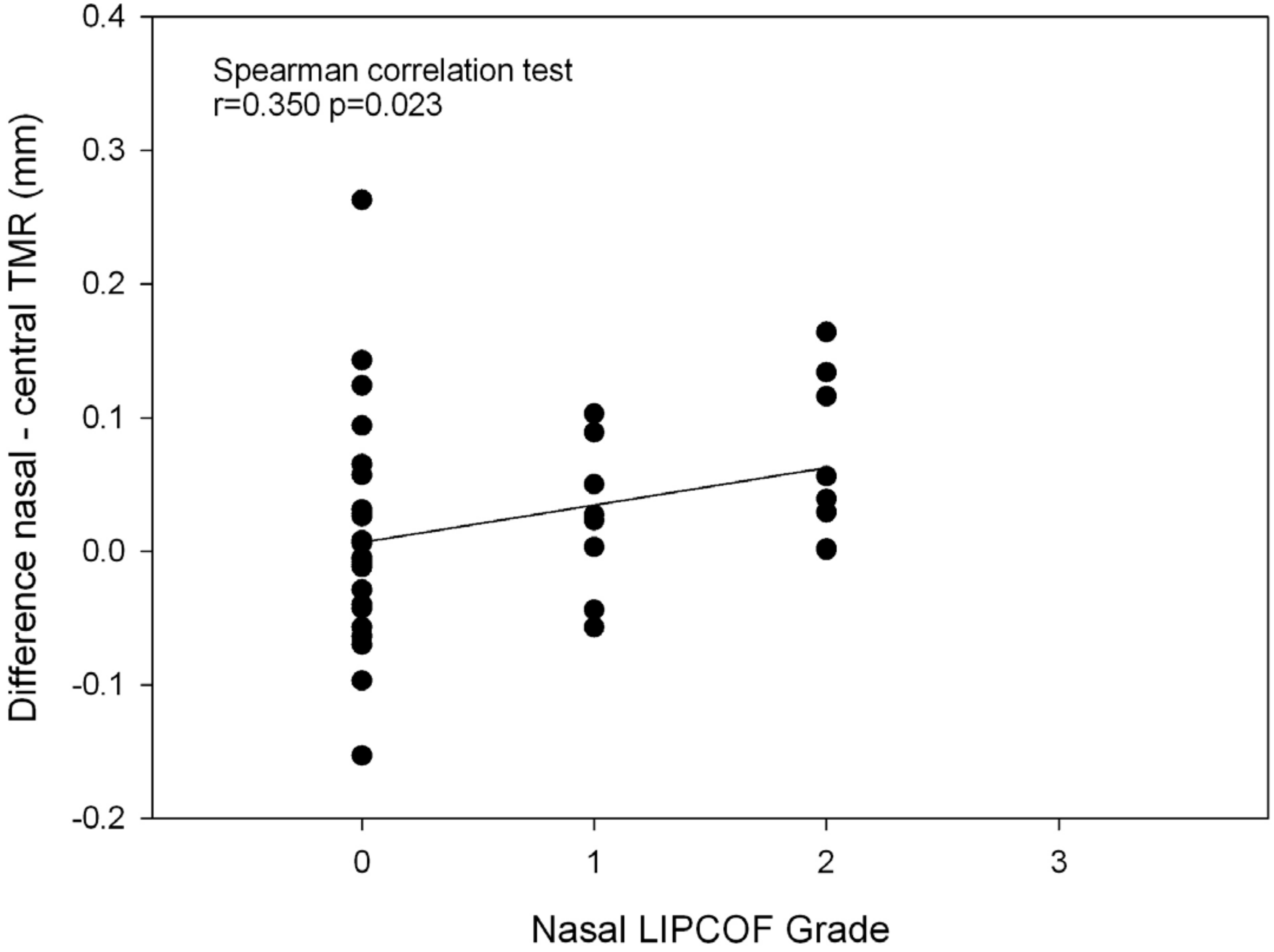
Spearman correlation test
r=0.530 p<0.01
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
Differences temporal - central TMR (mm)
0
1
2
3
Temporal LIPCOF Grade

Figure 8



Spearman correlation test
r=0.492 p=0.001
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
Difference nasal - central TMH (mm)
0
1
2
3
Nasal LIPCOF Grade

Figure 9



Spearman correlation test
r=0.350 p=0.023
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
Difference nasal - central TMR (mm)
0
1
2
3
Nasal LIPCOF Grade

Figure 10

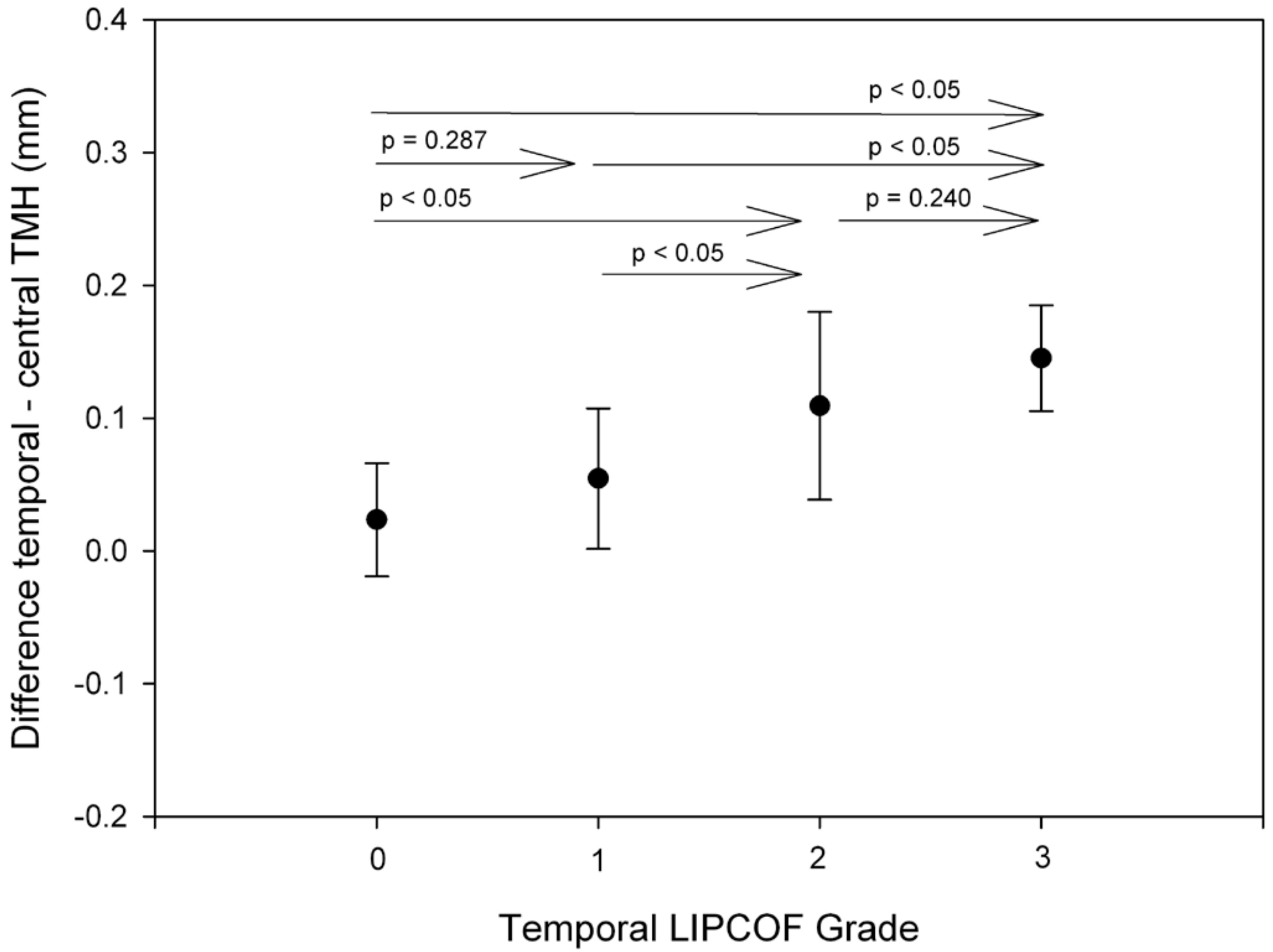
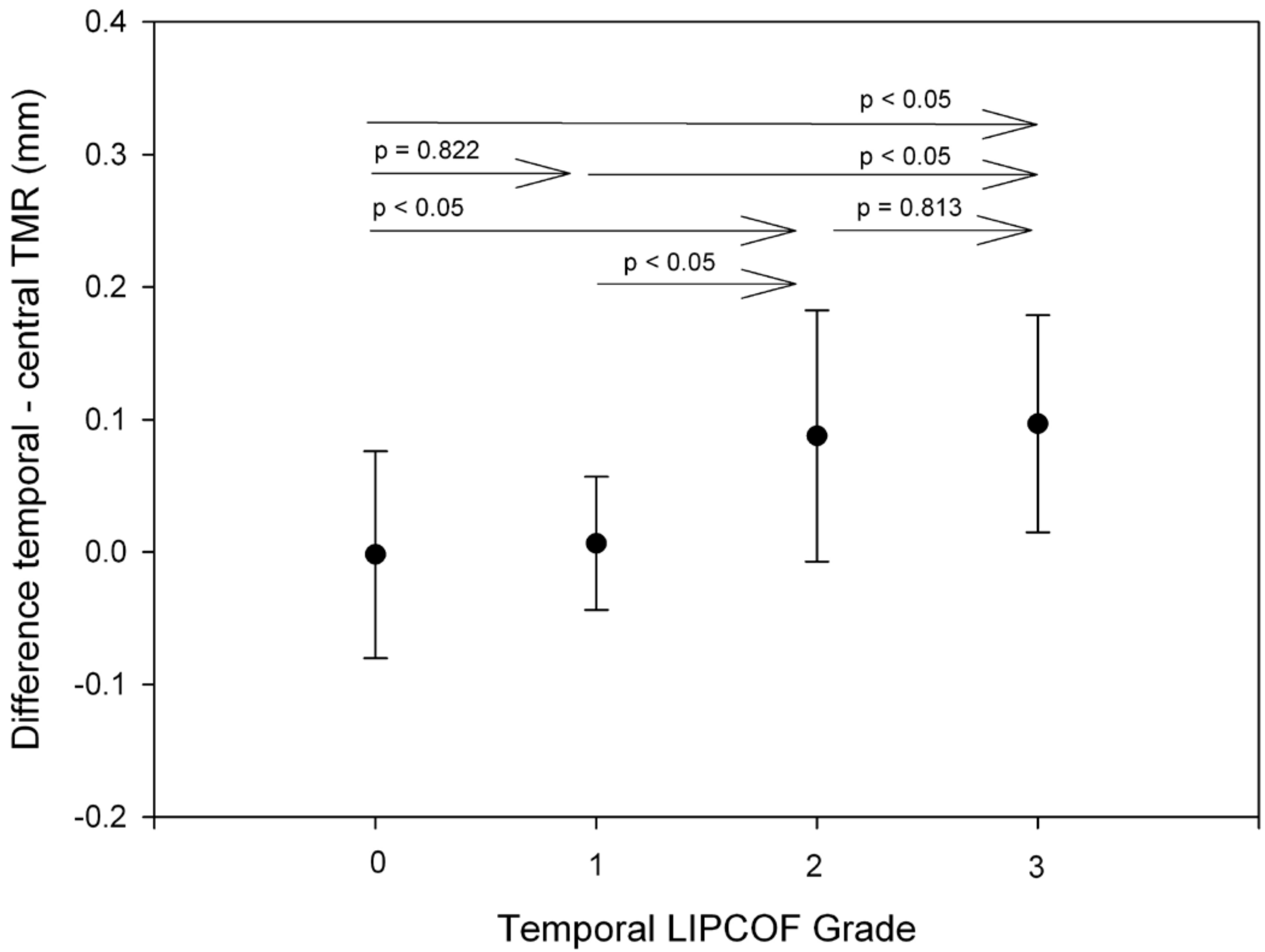
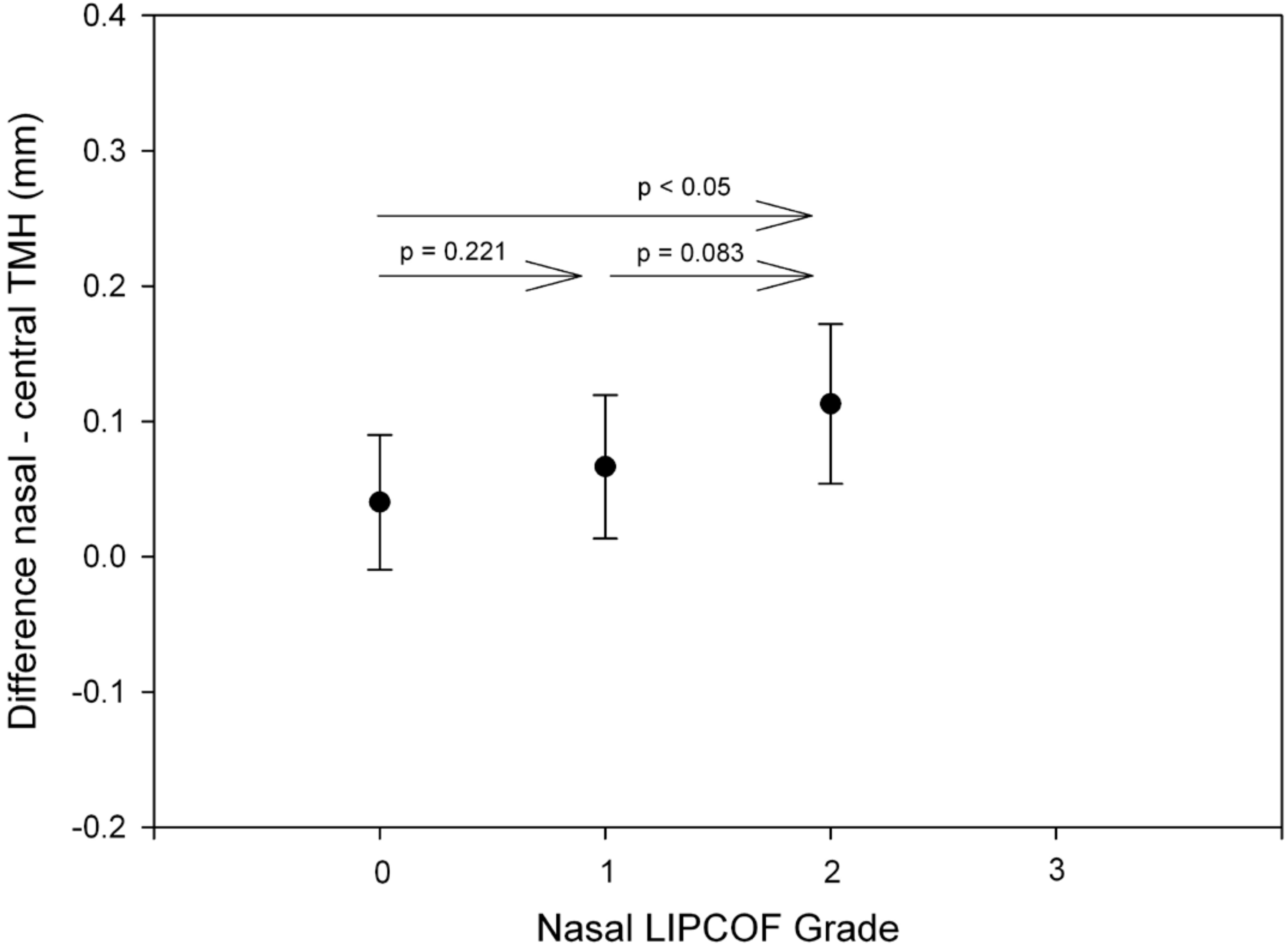

0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
Difference temporal - central TMH (mm)
p < 0.05
p = 0.287
p < 0.05
p < 0.05
p = 0.240
p < 0.05
0
1
2
3
Temporal LIPCOF Grade

Figure 11



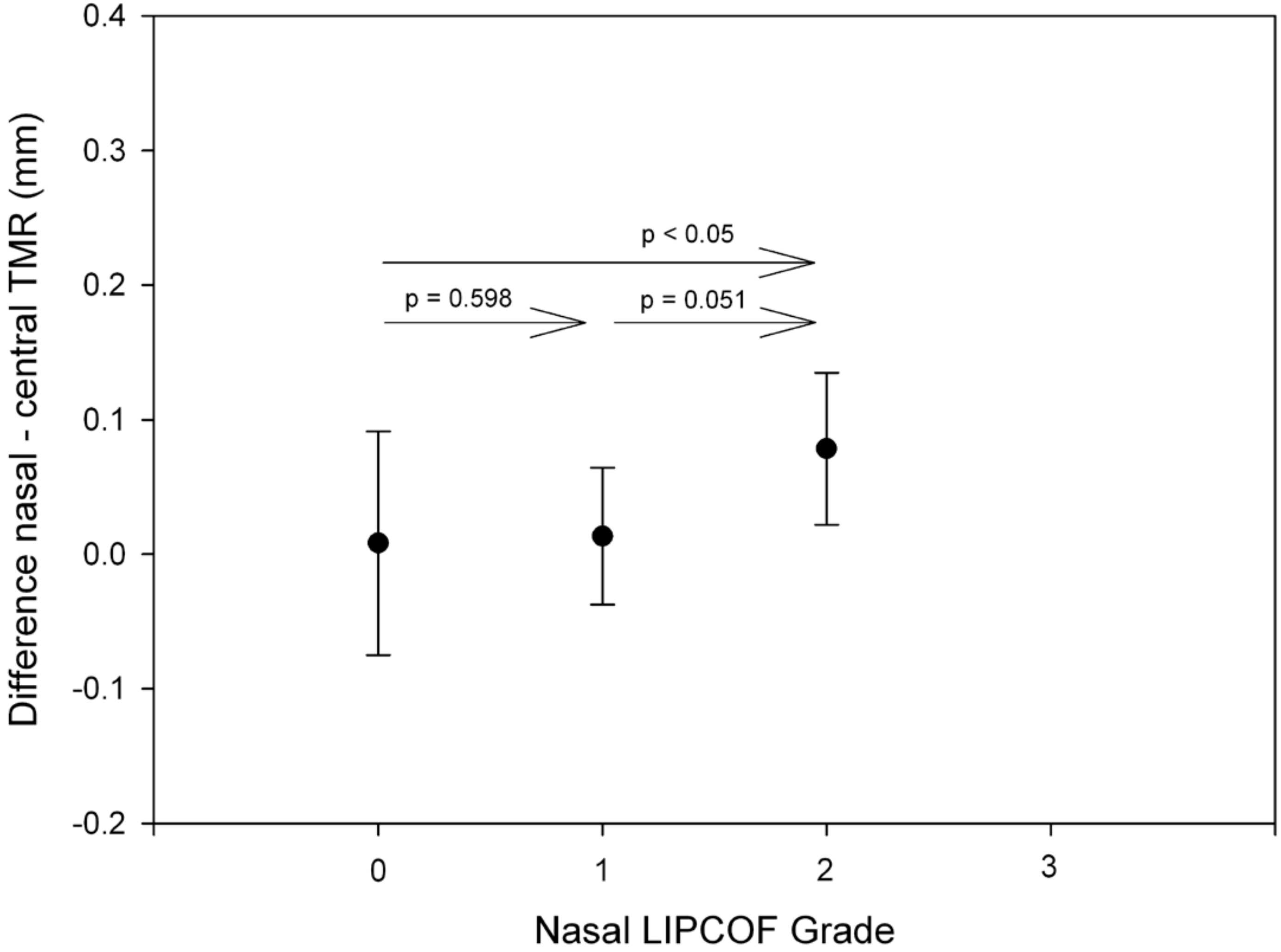
0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
Difference temporal - central TMR (mm)
p < 0.05
p = 0.822
p < 0.05
p < 0.05
p = 0.813
p < 0.05
0
1
2
3
Temporal LIPCOF Grade

Figure 12



0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
Difference nasal - central TMH (mm)
p < 0.05
p = 0.221
p = 0.083
0
1
2
3
Nasal LIPCOF Grade

Figure 13



0.4
0.3
0.2
0.1
0.0
-0.1
-0.2
Difference nasal - central TMR (mm)
p < 0.05
p = 0.598
p = 0.051
0
1
2
3
Nasal LIPCOF Grade

Figure 14

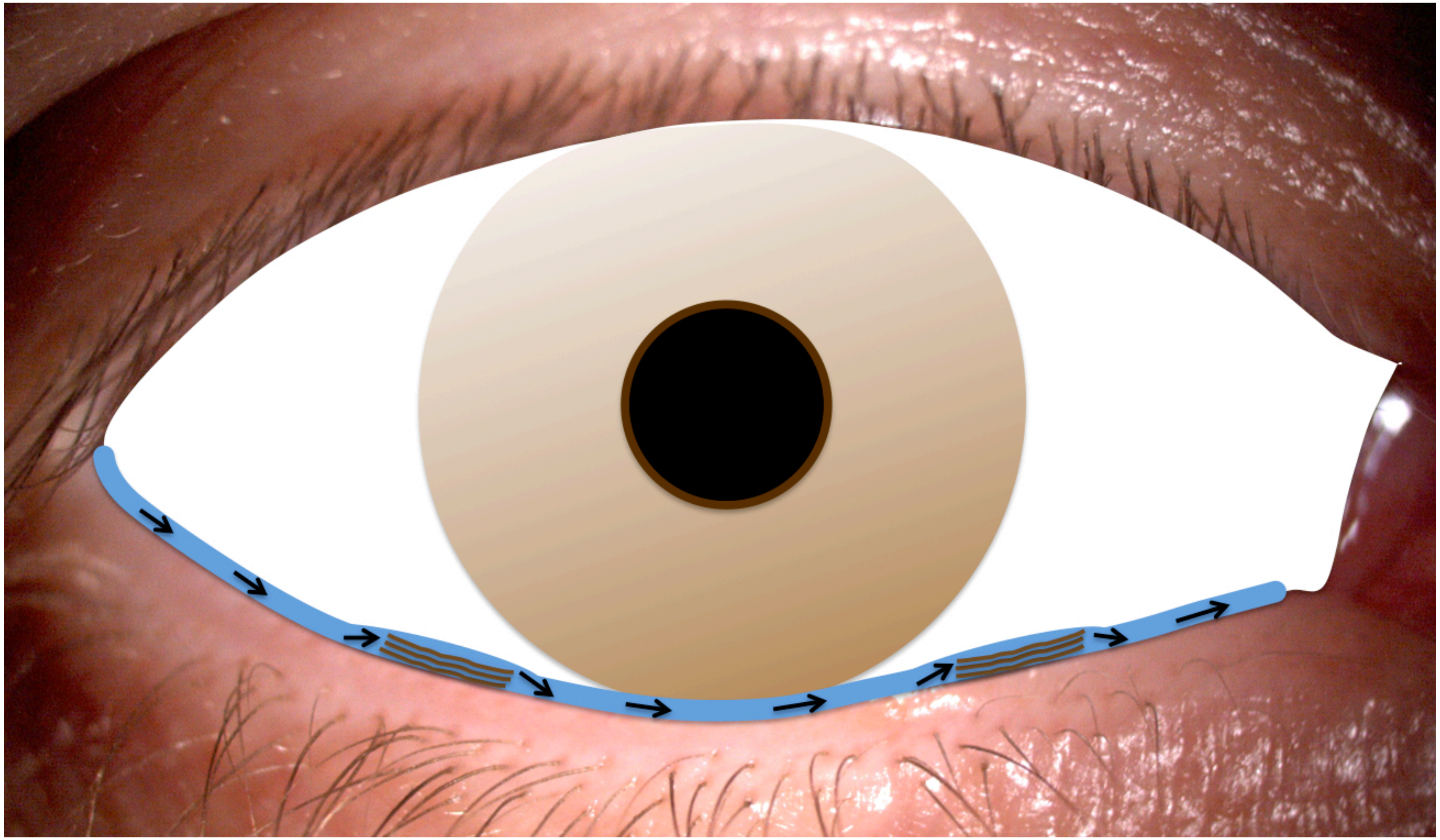


Figure 15