


# Sensory Changes in the Ocular Surface After Pterygium Removal

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**Purpose:** We measure changes in ocular surface sensation after pterygium surgery with a conjunctival autograft.

**Methods:** This prospective, interventional study was carried out in patients, with nasal primary pterygium undergoing pterygium surgery with conjunctival autograft. Sensation was measured by applying the tip of the Cochet-Bonnet esthesiometer filament perpendicular to the ocular surface in the cornea and conjunctiva. Patients were tested preoperatively (baseline), and at 2 weeks, 2 and 4 months, postoperatively.

**Results:** Nineteen eyes of 18 patients completed the 4-month follow-up. Mean age was 61±10.1 (range 36–76) years. Corneal sensation returned to normal values in all at 2 and at 4 months. The central cornea was significantly more sensitive compared to the average of the four peripheral measurements pre- (59.2 mm vs 48.3 mm,  $p=0.000$ ) and postoperatively (59.2 mm vs 48.4 mm,  $p=0.000$ ). Conjunctival sensation was reduced significantly 2 months postoperatively in the inferior region ( $p=0.04$ ). Four months postoperatively, it was more sensitive in the superior area (13.9 mm vs 17.1 mm,  $p=0.01$ ) and the inferior area (13.7 mm vs 19.5 mm,  $p=0.003$ ). In each matching area, the cornea was significantly more sensitive than the conjunctiva pre- and postoperatively ( $p=0.00$ ). Sensation was not significantly different between the sexes or age groups.

**Conclusion:** This study demonstrates the presence of inferior and superior conjunctival hyperesthesia at conjunctival autograft sites after pterygium surgery. The healing process, sensory input, tear film instability and epitheliopathy of the ocular surface are possible explanations for these novel findings.

**Keywords:** pterygium, esthesiometer, Cochet-Bonnet, ocular surface, sensory changes

## Introduction

Pterygium is a common ocular surface disorder<sup>1,2</sup> characterized by proliferation of fibrovascular tissue from the bulbar subconjunctival tissue that primarily mainly grows along the nasal interpalpebral fissure. It may be associated with inflammation, ocular surface discomfort, increasing astigmatism, obstructed optical axis and an unfavorable cosmetic effect.<sup>2,3</sup>

Some theories attribute UV exposure as the leading cause for pterygium formation. Other risk-factors include chronic eye inflammation or reaction to irritation from dust, air pollution or smoking.<sup>4</sup>

Surgical excision is the definitive standard of care. Several approaches have been described.<sup>5</sup> The high rates of recurrence following simple bare sclera excision have been explained by the theory of corneal limbal stem cell deficiency and are reported to be as high as 24%–89%.<sup>5,6</sup>

The common use of MMC and conjunctival autograft fixed with Vicryl sutures or fibrin glue as an adjunctive treatment is to prevent the recurrence of pterygium after the surgery.<sup>7</sup> This technique is safe and effective, with comfortable postoperative period, and low recurrence rate.<sup>8,9</sup>

Sensory changes in the ocular surface have been studied extensively following keratoplasty,<sup>10</sup> laser-assisted in situ keratomileusis,<sup>11</sup> cataract<sup>12</sup> and epikeratoplasty.<sup>13</sup> However, a search of the literature found only a few studies that examined sensory changes after pterygium excision.<sup>14,15</sup>

The main purpose of the current study was to measure changes in ocular surface sensation after pterygium excision surgery.

## Materials and Methods

This prospective, randomized, interventional study was carried out in patients, with nasal primary pterygium undergoing pterygium surgery from June 2018 to July 2020. Exclusion criteria were patients with diabetes mellitus, dry eyes, systemic diseases like rheumatoid arthritis, facial paralysis, history of using contact lens, previous ocular surgery, ocular surface diseases or trauma. Pterygium was graded according to the system described by Benitez-del-Castillo et al.<sup>15</sup> All patients enrolled in the present study had grade T3 pterygium (episcleral vessels obscured by the pterygium body.)

The study was approved by the Meir Medical Center Institutional Review Board and conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all study participants.

## Surgical Technique

A single surgeon (AYN) performed all the surgeries under an operating microscope. Anesthesia of the ocular surface was induced by topical application of 2% esracaine gel (Rafa Laboratories, Jerusalem, Israel) and supplemented by 1.0 mL of 2% lidocaine and 1/100000 adrenalin injected subconjunctivally with a 27-gauge needle. This was inserted into the body of the pterygium to separate it from the underlying sclera. The head of the pterygium was dissected from the cornea using a Colibri Forceps. The sclera and cornea were then flattened with a crescent knife. A blunt dissection of the pterygium from the surrounding conjunctiva using Westcott scissors was performed. The tissue was excised, leaving bare sclera. A 3×4 mm sponge was soaked in a solution of 0.02% mitomycin C and applied directly over the bare sclera in contact with the tissue for 2 min, and then rinsed thoroughly using balanced saline solution.

A thin layer of conjunctival graft matching the bare sclera was harvested from the superior bulbar conjunctiva and the free graft was then placed on top of the bare sclera and rotated to limbus–limbus orientation. The graft was sutured to the recipient conjunctiva with continuous Vicryl 10/0 sutures, and 2 additional mattress stitches were used to secure the graft to the sclera at the limbal border. A therapeutic contact lens was worn, and topical steroids and antibiotic drops were applied. Postoperatively, maxitrol drops (Novartis, Israel) were applied 4 times a day and gradually tapered for 6 weeks.

## Sensation Measurement

The ocular surface sensation was evaluated by applying the tip of a Cochet-Bonnet esthesiometer filament perpendicular to the ocular surface (cornea and conjunctiva) until the filament bent slightly. This was performed by the same doctor (SE) according to the previously described technique.<sup>16</sup> Two positive responses in three attempts at each filament length were regarded as a positive result. We tested five anatomical locations in the cornea (superior, nasal, inferior, temporal and central) and four in the conjunctiva (superior, nasal, inferior and temporal). Each corneal measurement was taken 1–2 mm from the limbus, and conjunctival measurements were 3 mm from the limbus.

The measurements were performed preoperatively on the day of surgery, and then 2 weeks, 2 months and 4 months postoperatively. An average of three measurements at each point were recorded as touch threshold reading for that period. Each area was tested with a filament length, which was sequentially reduced in 5-mm steps starting at 60 mm. The longest filament length resulting in a positive response was considered the sensation threshold.

## Statistical Analysis

Data are expressed as means and standard deviations. Comparisons between mean values of preoperative sensation, 2 weeks, 2 months and 4 months postoperative were evaluated on Wilcoxon nonparametric test, as well as change in sensation between visits.

Mann–Whitney non-parametric test was used to find an association of demographic parameters change in sensation. Differences were considered statistically significant when  $P < 0.05$ . All statistical analyses were performed using SPSS-27 software (IBM Corp., Armonk, NY).

**Table 1** Sensation of Cornea and Conjunctiva Before and After Surgery

	Preoperative	2 Weeks	P-value	2 Months	P-value	4 Months	P-value
Cornea							
Central	59.17±2.57	46.39±18.69	0.01	56.67±8.4	0.26	59.17±2.57	1.0
Superior	44.44±15.52	33.89±15.3	0.031	46.39±12.58	0.66	48.33±13.5	0.39
Nasal	45.83±14.27	24.72±13.66	<0.001	40.56±13.05	0.23	44.72±8.66	0.75
Inferior	49.44±13.92	31.67±14.75	<0.001	46.11±11.95	0.41	47.78±10.18	0.62
Temporal	52.78±10.32	44.17±16.02	0.07	51.39±8.71	0.59	52.78±8.44	1.0
Conjunctiva*							
Superior	13.33±5.94	NA	NA	13.06±3.49	0.75	16.67±4.2	0.01
Nasal	13.89±11.32	NA	NA	11.67±3.43	0.68	15±4.54	0.67
Inferior	13.61±5.64	NA	NA	17.78±6.47	0.04	19.44±7.25	0.005
Temporal	18.89±12.55	NA	NA	13.06±3.49	0.17	19.44±7.25	0.41

**Notes:** Measurements are in mm. \*Conjunctiva sensitivity was not measured at the 2-week follow-up visit to avoid further irritation.

## Results

The study included 19 eyes of 18 patients (9 women and 9 men) with primary nasal pterygium, which completed the whole follow-up of 4-months. Ages ranged from 36 to 76 years (mean  $61 \pm 10.1$  years) and 9 were younger than 60. All the patients completed the follow-up.

The mean esthesiometry readings preoperatively and at the 2-week and 2- and 4-month postoperative follow-up visits are shown in [Table 1](#). There were no infections, significant inflammation or epithelial problems.

Re-epithelialization was completed within 2–3 weeks in the cornea and 2–8 weeks in the conjunctiva. The autografts healed with excellent cosmetic results. No recurrences were observed in the study period.

Sensation did not differ significantly based on sex or age.

## Corneal Sensation

Mean preoperative corneal sensations in the central, superior, nasal, inferior and temporal quadrants were  $59.17 \pm 2.57$  mm,  $44.44 \pm 15.52$  mm,  $45.83 \pm 14.27$  mm,  $49.44 \pm 13.92$  mm and  $52.78 \pm 10.32$  mm, respectively.

Preoperatively, the central cornea was significantly more sensitive than the upper, nasal and temporal regions (Pearson correlations were 0.00, 0.003 and 0.007, respectively). The central cornea was significantly more sensitive compared to the average four peripheral measurements pre- ( $59.2$  vs  $48.3$ ,  $p=0.000$ ) and postoperatively ( $59.2$  vs  $48.4$ ,  $p=0.000$ ).

Two weeks postoperatively, the inferior and nasal areas of the cornea were statistically significantly less sensitive. The sensation returned to normal values in all patients by 2 and 4 months ([Table 1](#)) after surgery.

## Conjunctival Sensation

Conjunctival sensation was measured 2 and 4 months postoperatively. Sensation was not measured at 2 weeks to avoid any extra insult to the already injured tissue.

Mean preoperative conjunctival sensations in the superior, nasal, inferior and temporal quadrants were  $13.33 \pm 5.94$  mm,  $13.89 \pm 11.32$  mm,  $13.61 \pm 5.64$  mm and  $18.89 \pm 12.55$  mm, respectively ([Table 1](#)).

Conjunctival sensation was reduced significantly 2 months postop in the inferior region ( $p=0.04$ ) compared to the preop measurements. Four months postoperatively, it was more sensitive at the superior area ( $13.9$  vs  $17.1$  mm,  $p=0.01$ ) and the inferior area ( $13.7$  vs  $19.5$  mm,  $p=0.003$ ). There were no significant changes in the nasal and temporal regions.

Conjunctival sensitivity measurements ranged from 13.33 to 18.9 mm preoperatively and from 16.67 to 19.44, postoperatively, whereas the corneal measurements ranged from 44.44 to 59.17 mm and 44.72 to 59.17 mm.

Comparing each area of the cornea to its matching conjunctival area, the cornea was significantly more sensitive than the conjunctiva, both pre- and postoperatively ( $p=0.00$ ).

## Discussion

Ocular surface sensitivity is relevant in both normal and dry eyes. Therefore, it is important to evaluate conjunctival and corneal sensation following pterygium surgery.<sup>10,17</sup>

The goals of pterygium surgery are to remove the lesion, restore the conjunctival anatomy, leave the cornea as smooth and clear as possible and prevent recurrences. Scraping the tissue from the cornea completely to obtain a smooth cornea may damage the corneal nerves that penetrate the Bowman layer and enter the epithelium, which may diminish sensation in this area.<sup>18</sup>

The cornea is a highly innervated structure. Normal corneal sensitivity is essential to normal corneal function and maintaining the health of the ocular surface.<sup>19</sup> In addition to their important sensory function, corneal nerves provide protective and trophic functions, and they regulate corneal epithelial integrity, proliferation, and wound healing.<sup>15</sup>

The threshold of sensitivity, especially in the centre of the cornea, is exceedingly low, so pathological changes can be diagnosed early and precisely and corneal sensation can be used for diagnosis, follow-up and even for prognosis of various corneal disorders.<sup>20</sup>

Loss of normal corneal sensation may compromise the protective blink reflex, delay epithelial wound healing, decrease tear flow, and be associated with neurotrophic keratitis.<sup>14</sup> Clinical and histological studies have demonstrated reinnervation of the cornea after cataract<sup>21</sup> and corneal surgeries.<sup>11</sup>

Sensory denervation may lead to dry eye by dysesthesia induced by denervation,<sup>22,23</sup> reducing the blink rate, and by changing the production and release of neuromediators that warrant trophic support and regulatory action in the corneal epithelium.<sup>17</sup>

Few studies have specifically documented the presence of sensation effect of the ocular surface following pterygium surgery. Sakarya et al observed that the corneal sensation in the area where pterygium was scraped remained hypoesthetic for 2 months, as well as at the conjunctival autograft where they used glue.<sup>14</sup> Our study differed, as we used stiches (10/0 Vicryl) and mitomycin c. Zhao et al have shown that pterygium excision improves corneal sensitivity and increases corneal subbasal nerve density.

Patients with pterygium have basically deteriorated corneal subbasal nerve fibers and unstable tear film in comparison with healthy eyes. The decreased corneal sensitivity was related to deteriorated corneal subbasal nerve fibers when compared with healthy controls in terms of nerve length, nerve trunks, and nerve branches. No nerve plexus could be detected using *in vivo* confocal microscopy.<sup>15</sup>

In the current study, the central cornea was significantly more sensitive compared to peripheral corneal measurements. A gradation appears to exist in the sensitivity of the cornea with sensitivity inversely proportional to the total number of corneal stroma nerve fibers present. Corneal sensitivity is most acute in the central cornea and along the horizontal meridian, least sensitive along the vertical meridian. The central and peripheral cornea may be driven by different neural circuitry, perhaps at higher levels of the sensory processing pathway.<sup>17</sup>

## Conjunctival Sensation Findings

To our knowledge, the finding that the temporal conjunctiva is the most sensitive conjunctival region has not been reported previously. The conjunctiva has been reported to be least sensitive in the perilimbal area and most sensitive along the marginal palpebral conjunctiva.<sup>17</sup>

The finding of increased conjunctival sensitivity postoperatively at the superior and inferior areas was surprising. A similar altered sensitivity, which was more prominent in the conjunctiva than in the cornea, has been reported in dry eye.<sup>20</sup>

Similarly, pterygia create an ocular surface irregularity and are associated with dry eye.<sup>24</sup> Situ et al also noted ocular surface hypersensitivity in a group of patients with dry eye symptoms, indicating changes in sensory nerve function.

Pterygium surgery and its healing process, alter sensory input, which is related to tear film instability and epitheliopathy of the ocular surface. Each is part of a cycle of interacting mechanisms: It has been shown that the induction of dry eye disease in mice by lacrimal gland excision, shown by decreased tear production, increased corneal epitheliopathy and the development of corneal mechanical hypersensitivity.<sup>23</sup>

An increased responsiveness and spontaneous activity to suprathreshold stimulation can be induced by certain inflammatory mediators.<sup>25</sup> Interleukin (IL)-1 was found in the tears and conjunctiva, in patients with keratoconjunctivitis sicca has been reported to induce hyperesthesia.<sup>26</sup>

The increased conjunctival sensitivity at the superior and inferior areas after surgery evitable if amniotic membrane transplantation is used instead of conjunctival autograft.

We found that the cornea was significantly more sensitive than the conjunctiva. Preoperative conjunctival sensitivity ranged from 13.33 to 18.9 mm, compared to corneal measurements ranging from 44.44 to 59.17 mm. Previous reports also showed the threshold for tactile conjunctival sensitivity was 100 times higher than that of the center of the cornea.<sup>17</sup>

## Corneal Sensation Findings

In the current study, the central cornea was the most sensitive. Corneal sensation is probably unsurpassed by any part of the body.<sup>27</sup> It varies from a maximum apically to a minimum at the periphery, with a considerable drop in sensitivity at the limbus. Corneal sensitivity decreases by a factor of 3 with age.<sup>27–29</sup> Sensitivity also varies with iris color, in that blue eyes are more sensitive than dark brown eyes.<sup>30</sup> Nerves penetrate the posterior two-thirds, move forward, divide, penetrate Bowman's membrane and enter the epithelium.<sup>27</sup> There are nerve networks within the stroma, under Bowman's membrane and in the epithelium where nerve endings are most numerous.

The density of nerve terminals is greatest centrally, corresponding to approximately 600 terminals / mm<sup>2</sup>, which results in large overlapping receptive fields.<sup>20</sup>

Ocular surface sensitivity can be measured by extending fine strands of a cotton swab touching the surface of the cornea and conjunctiva. However, an esthesiometer is more accurate and quantifiable.<sup>17,30</sup> The classic technique for performing esthesiometry is with a Cochet-Bonnet esthesiometer filament, which consists of a fine nylon filament, the length of which can be adjusted to apply different intensities of stimuli. Sensitivity is measured as the length of the filament, which gives a 50% positive response from a minimum of 4 stimuli.<sup>17</sup>

The most crucial deficiencies of Cochet-Bonnet esthesiometer are its truncated intensity range and difficulties with alignment, placement and replication of the force applied to the nylon filament, and damages the epithelial surface by the filament.<sup>31</sup>

Recently, a non-contact air jet esthesiometer has been introduced and tested with good tolerance, and no adverse effects. It has shown that good reliability and correlation parameters can provide a more comprehensive understanding of reinnervation and could be used as a non-invasive alternative to the Cochet-Bonnet esthesiometer.<sup>32</sup>

There are limitations to this study. The superior bulbar conjunctiva was harvested during the operation, which may cause a problem if the patient needs other surgery in future like glaucoma filtration surgery. The study sample was relatively small.

In conclusion, the current study demonstrates that temporary hypoesthesia at the nasal corneal and inferior conjunctival areas occurred after pterygium excision surgery, which become more sensitive than the preoperative measurements in the inferior and superior conjunctiva at 4 months. This is a novel finding and may be explained by the healing process. These findings may help set the framework for further research into postoperative ocular surface sensitivity.

## Disclosure

The authors report no conflicts of interest in this work.

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