ARTICLE

Ocular-surface temperature modification by cataract surgery

Giuseppe Giannaccare, MD, Michela Fresina, MD, Luca Agnifili, MD, Piera Versura, BSD

PURPOSE: To analyze ocular-surface temperature changes after microincision cataract surgery and to correlate them with surgical, clinical, and laboratory parameters.

SETTING: Ophthalmology Unit, Saint Orsola-Malpighi Hospital, Bologna, Italy.

DESIGN: Prospective case series.

METHODS: Patients affected by monolateral senile cataract were examined preoperatively and 7 days and 28 days postoperatively. Infrared thermography was used to measure the temperature soon after eye opening, the temperature after 10 seconds of sustained eye opening, and the difference between these 2 values in the central cornea, nasal limbus, and temporal limbus. The Ocular Surface Disease Index (OSDI), Schirmer test, vital staining, tear breakup time (TBUT), conjunctival scraping cytology, exudated tear-serum albumin, and laser flare–cell meter examinations were performed.

RESULTS: The study comprised 26 patients (10 men, 16 women). The temperature changed significantly after surgery. The temperature soon after eye opening showed cooling in the central cornea and nasal limbus and heating in the temporal limbus. The temperature after 10 seconds of sustained eye opening minus the temperature soon after eye opening increased in all regions. The temperature after 10 seconds of sustained eye opening minus the temperature soon after eye opening in the central cornea was inversely related to the OSDI and directly related to TBUT. The temperature soon after eye opening increased in the temporal limbus and was directly related to inflammatory indices.

CONCLUSIONS: The ocular-surface temperature changed after cataract surgery depending on the region analyzed. The cooling in the central cornea could be related to the increased tear-film instability. The heating in the temporal limbus could be related to postoperative inflammation.

Financial Disclosure: None of the authors has a financial or proprietary interest in any material or method mentioned.

J Cataract Refract Surg 2016; 42:983–989 © 2016 ASCRS and ESCRS

The cornea possesses the richest sensory innervation of the body and is predominantly dedicated to nourish, induce the lacrimal reflex, and detect noxious stimuli. Most surgical procedures involving the anterior segment of the eye, including cataract surgery, disrupt the normal organization of corneal innervation, leading to reduced sensitivity in the affected area. At the same time, patients often have unpleasant sensations of itching, burning, dryness, and foreign-body sensation after cataract surgery. These sensations on the ocular surface are a result of abnormal activity and the responsiveness of the injured corneal nerve fibers.

Temperature is one of the fundamental characteristics of tissue metabolism and is a useful parameter for studying ocular physiology and pathology. Thermography is emerging as a potential tool for noninvasive diagnosis of ocular-surface diseases. It easily and rapidly enables noncontact mapping of thermal patterns of the entire ocular surface, and in particular of the cornea and conjunctiva. Infrared thermography has been used to noninvasively determine the temperature variations at the ocular surface in healthy subjects[1] and in patients with dry-eye syndrome,[2,3] contact lens wear,[4] refractive surgery,[5] or pterygium.[6]

Little information about the impact of cataract surgery on ocular-surface temperature is available in the literature.[7,8] Some studies were limited by the older instruments used and the design. To our knowledge, there are no studies in the recent literature of

Published by Elsevier Inc.
http://dx.doi.org/10.1016/j.jcrs.2016.04.023
0886-3350

ocular-surface temperature changes related to microincision cataract surgery (MICS). The purpose of the present study was to analyze ocular-surface temperature changes after surgery and to correlate them with surgical, clinical, and laboratory parameters.

PATIENTS AND METHODS

Patients with senile cataract having surgery at the Ophthalmology Unit of Saint Orsola-Malpighi Teaching Hospital were enrolled. All patients signed an informed consent form before any procedure, and the study strictly followed the tenets of the Declaration of Helsinki.

Inclusion criteria were age of 60 years or older, monolateral nuclear or corticonuclear cataract classified as grade 3 according to the Lens Opacities Classification System III scale,[9] and axial length between 22.5 mm and 25.5 mm. Patients who had a history of diabetes, autoimmune disease, atopy, allergy, contact lens use, ocular disease, or surgery in the operated eye and the contralateral eye were excluded because these factors are recognized to cause ocular-surface impairment.

Patients were examined a mean of 3 days $\pm$ 1 (SD) before surgery and 7 $\pm$ 1 days and 28 $\pm$ 2 days after surgery. The following clinical tests were performed according to the Dry Eye Workshop guidelines[10]: Ocular Surface Disease Index (OSDI) (pathological value score $>$12/100), Schirmer test type I (pathological value $<$10.0 mm length wet paper), fluorescein corneal staining (National Eye Institute [NEI] score range 0 to 15[11]), lissamine green conjunctival staining (van Bijsterveld score range 0 to 9[12]), and tear breakup time (TBUT) (pathological value $<$10 seconds).

Ocular-surface inflammation was evaluated before surgery and 28 days after surgery with conjunctival scraping cytology[13] (pathological score $>$4/20) and before surgery and 7 days after surgery with exudated tear-serum albumin[14] (pathological cutoff $>$10% versus total protein content). Anterior chamber inflammation was measured at all steps using a laser flare–cell meter[15] (500F, Kowa Co. Ltd.) and expressed as photon/ms. Evaluations were performed in both eyes, and data from the contralateral eye acted as the control.

Submitted: November 17, 2015.
Final revision submitted: April 11, 2016.
Accepted: April 13, 2016.

From the Ophthalmology Unit (Giannaccare, Fresina, Versura), Department of Experimental, Diagnostic and Specialty Medicine, Alma Mater Studiorum University of Bologna and Saint Orsola-Malpighi Teaching Hospital, Bologna, and the Department of Medicine and Aging Science (Agnifili), Ophthalmology Clinic, University G. d'Annunzio of Chieti-Pescara, Chieti, Italy.

Emmeci 4 S.r.l., Parma, Italy, provided the Tomey TG thermographer 1000 for research and training.

Corresponding author: Piera Versura, BSD, Ophthalmology Unit, Department of Experimental, Diagnostic and Specialty Medicine, University of Bologna, Saint Orsola-Malpighi Hospital, Pad. 1 Palagi, Via Palagi, 9 40138 Bologna, Italy. E-mail: piera.versura@unibo.it.

Thermography

Dynamic infrared noncontact thermal imaging (TG 1000 Thermographer, Tomey Corp.) was used to measure ocular-surface temperature in a 4.0 mm circular area. The instrument records images at a resolution of 320 pixels $\times$ 240 pixels with a pixel size of 23.5 µm $\times$ 23.5 µm and spatial resolution of 70 µm at 0.1°C. The monochromatic thermal images (65 to 536 grayscale increments) recorded by the thermographer were immediately transferred to a computer to be displayed on a monitor in up to 24-bit color and elaborated automatically by appropriate software. The image analysis took 10 seconds, and the results of a measurement were displayed immediately after.

The patient's head was positioned with a chinrest and headrest as at a slitlamp, and the patient was instructed to look straight ahead. The measurements were performed under previously described conditions.[16] The patient blinked normally and then closed both eyes for 5 seconds. The patient kept the eyes forcedly open up to 10 seconds while breathing normally with a closed mouth. The ocular-surface temperature was measured immediately after the eye was open and then every second during the 10 seconds of continuous eye opening. The temperature was recorded and averaged in the following 3 regions of the ocular surface: central cornea, nasal limbus, and temporal limbus (Figure 1). The following data were collected for each region: the temperature soon after eye opening, the temperature after 10 seconds of sustained eye opening, and the temperature after 10 seconds of sustained eye opening minus the temperature soon after eye opening. Data recorded with the thermographer were displayed on the screen and downloaded for further analyses.

Surgical Technique and Postoperative Treatment

The same surgeon (M.F.) performed all surgeries under topical anesthesia. The primary steps of the surgery were a self-sealing temporal limbal microincision (2.2 mm), phacoemulsification in the capsular bag using the phaco-chop technique, and implantation of a hydrophobic aspheric intraocular lens. Data regarding the microscope-light exposure time, the phacoemulsification time, the total volume of balanced salt solution used, and the cumulative dissipated energy (CDE) were recorded at the end of all surgeries.

The following standard therapeutic regimen was adopted for the operated eye in all patients: unpreserved combination of 2.0 mg dexamethasone and 5.0 mg chloramphenicol (Cloradex) slowly tapered from 5 times per day to once daily in the first postoperative month. None of the patients instilled eyedrops within 2 hours before the measurements were performed.

Statistical Analysis

The results were analyzed using the SPSS software (version 20.0, International Business Machines Corp.) and the Medcalc program (version 14.8, Medcalc Software). The Shapiro-Wilk test was used to evaluate the normality of the variables. The differences between the operated eye and contralateral eye were calculated with the Student t or the nonparametric Mann-Whitney U test. The differences between preoperative values and postoperative values were calculated with the Student t test or the Wilcoxon paired test. Results were expressed

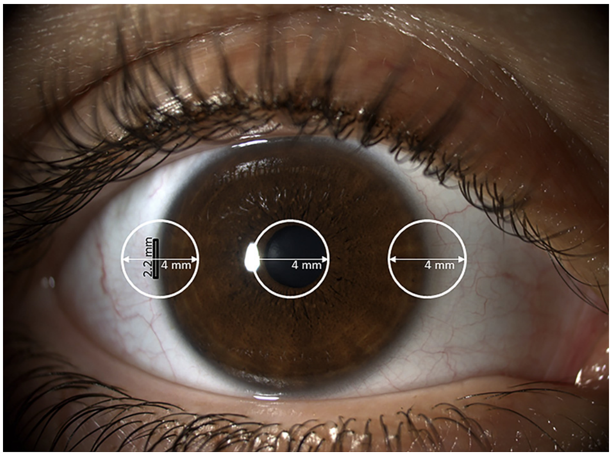

Figure 1. Representative image of the 3 analyzed regions of the ocular surface (circular area of 4.0 mm in diameter) in a right eye. The central cornea area is the circular region in the center of the cornea. The temporal and the nasal limbus areas are centered in the points of intersection between a horizontal line drawn through the center of the cornea and the temporal and nasal limbus, respectively.

as the median (minimum and maximum values; 95% confidence interval [CI]). A *P* value less than 0.05 was considered statistically significant.

The Spearman (ρ) correlation coefficient was calculated; correlations were considered statistically significant if the *P* value was less than 0.05 and a correction of *P* values for multiple testing was introduced. The strength of the correlation ranged from −1.0 to +1.0 and was estimated in absolute values as 0 to 0.29, weak; 0.30 to 0.69, strong; and 0.70 to 1.00, very strong.

RESULTS

The study comprised 26 patients (10 men, 16 women). The median age of the men was 78 years (range 65 to 90 years; 95% CI, 74.4-86.0). The median age of the women was 79.5 years (range 60 to 87 years; 95% CI, 74.2-81.3).

Surgical parameters had a low variance in the operated eyes. In particular, the median phacoemulsification time was 34.54 seconds (range 28.28 to 39.67 seconds; 95% CI, 32.76-35.89), the median balanced salt solution used was 97.87 mL (range 72.69 to 119.31 mL; 95% CI, 91.12-105.56), the median CDE value was 8.49 seconds (range 5.96 to 10.79 seconds; 95% CI, 7.13-9.65), and the median microscope-light exposure time was 11.03 minutes (range 8.76 to 13.75 minutes; 95% CI, 10.16-12.24).

No intraoperative complication occurred in the eyes under study. No postoperative complications occurred over the 1-month follow-up.

Figure 2 shows the results from clinical tests. In particular, tear-stability values were found in the pathological range as a median before surgery, whereas only light signs of surface damage and mild symptoms of ocular discomfort were recorded. No statistically significant difference was found between the 2 eyes of the same patient before surgery. The OSDI score (Figure 2, *A*), TBUT (Figure 2, *B*), corneal epithelial damage evaluated by the NEI score (Figure 2, *C*), and conjunctival epithelial damage evaluated by the van Bijsterveld score (Figure 2, *D*) significantly worsened in the operated eye 7 days after surgery, with a partial recovery at 28 days for all values except tear stability.

Figure 2 also shows the results of the laboratory analyses related to inflammation. No statistically significant difference was found between the 2 eyes of the same patient before surgery, with higher values recorded in the eye that had surgery. Flare values (Figure 2, *E*) significantly increased 7 days after surgery compared with before surgery, with a partial recovery toward baseline values 28 days after surgery. The percentage of exudate albumin in tears (Figure 2, *F*) and the conjunctival scraping cytology score (Figure 2, *G*) remained significantly increased 28 days after surgery as compared with before surgery.

All patients complied during thermography measurements. In all cases, it was possible to record reliable data in both eyes preoperatively and postoperatively.

The temperature changed significantly 7 days and 28 days after surgery compared with before surgery in all analyzed regions in the operated eye (Figure 3, *A* to *C*). In particular, the temperature soon after eye opening was significantly cooler in the central cornea and the nasal limbus 7 days after surgery than before surgery, with incomplete recovery toward preoperative values 28 days after surgery. In contrast, the temperature soon after eye opening increased in the temporal limbus 7 days after surgery, with complete recovery to preoperative values 28 days after surgery.

The temperature did not change significantly 7 days or 28 days after surgery compared with before surgery in all analyzed regions in the contralateral eye (Figure 3, *A* to *C*).

The temperature after 10 seconds of sustained eye opening minus the temperature soon after eye opening increased after surgery in the operated eye only. It increased in all analyzed regions, in particular, in the central cornea (Figure 4).

After surgery, in particular, in the operated eye, the temperature after 10 seconds of sustained eye opening minus the temperature soon after eye opening in the central cornea was significantly inversely related to the OSDI ($\rho = -0.648$, $P < .0001$) and directly related to the TBUT ($\rho = 0.510$, $P < .001$). Soon after eye opening, the temperature increased in the temporal limbus.

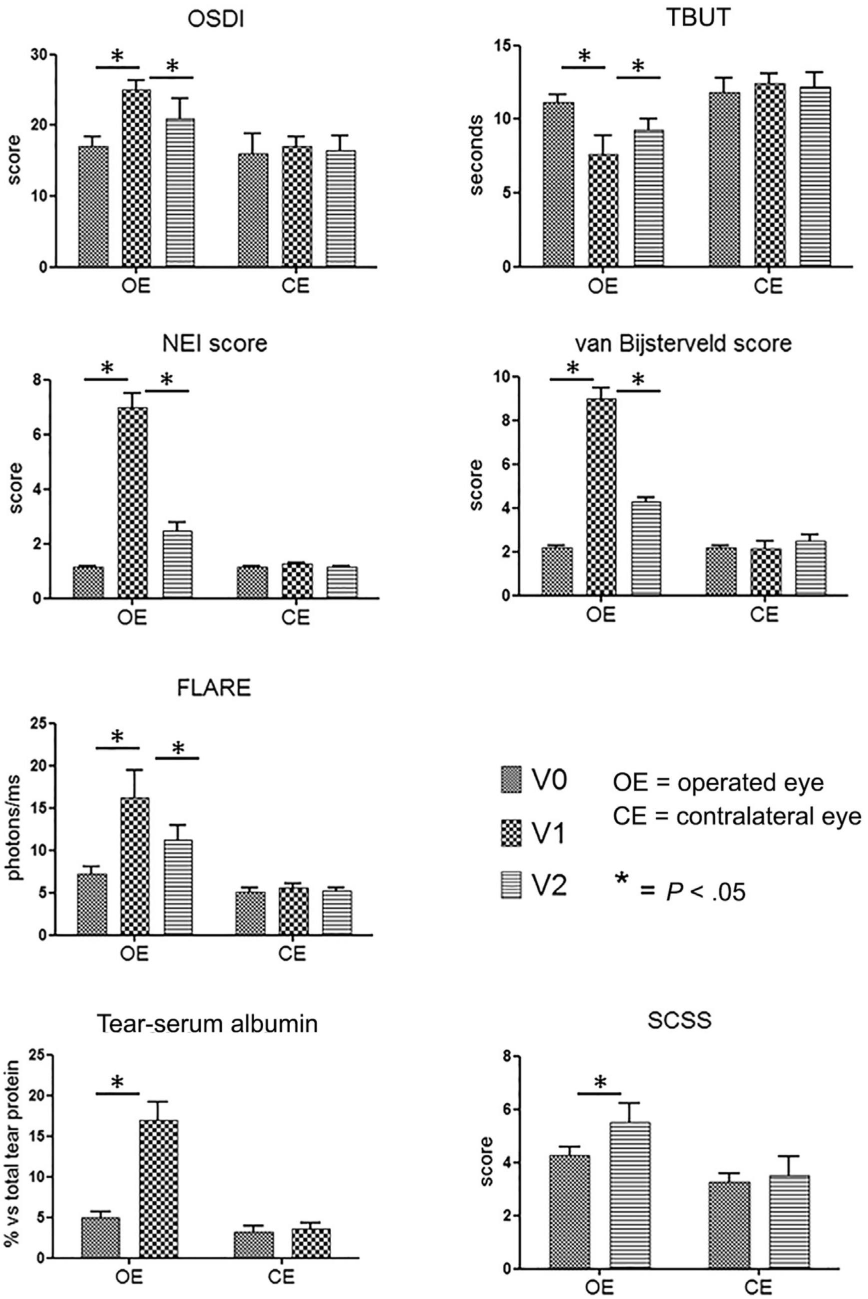

Figure 2. Values of each measurement before surgery and 7 days and 28 days after cataract surgery in the operated eye and in the contralateral eye (* = $P < .05$; CE = contralateral eye; NEI = National Eye Institute score; OE = operated eye; OSDI = Ocular Surface Disease Index; SCSS = Scraping Cytology Score System; TBUT = tear breakup time; V0 = before surgery; V1 = 7 days after surgery; V2 = 28 days after surgery).

The increase was significantly and directly related to intraocular flare and tear-exudate albumin levels ($\rho = 0.582$, $P < .0001$ and $\rho = 0.564$, $P < .001$, respectively).

The surgical parameters evaluated did not correlate with temperature shifts or with ocular-surface parameters.

DISCUSSION

No information is available in the recent literature about the impact of MICS on ocular-surface temperature. A previous study[7] found that the corneal temperature increased after extracapsular cataract extraction; however, the study was of a surgical technique that is no longer used in current routine practice. Furthermore, the thermometer used in that study had a resolution of only 1°C and it was not possible to measure the temperature in different regions of the ocular surface. A more recent study that analyzed ocular-surface temperature in healthy phakic and pseudophakic patients for a time after surgery[8] found no significant differences between the 2 groups. However, data from this study do not allow one to

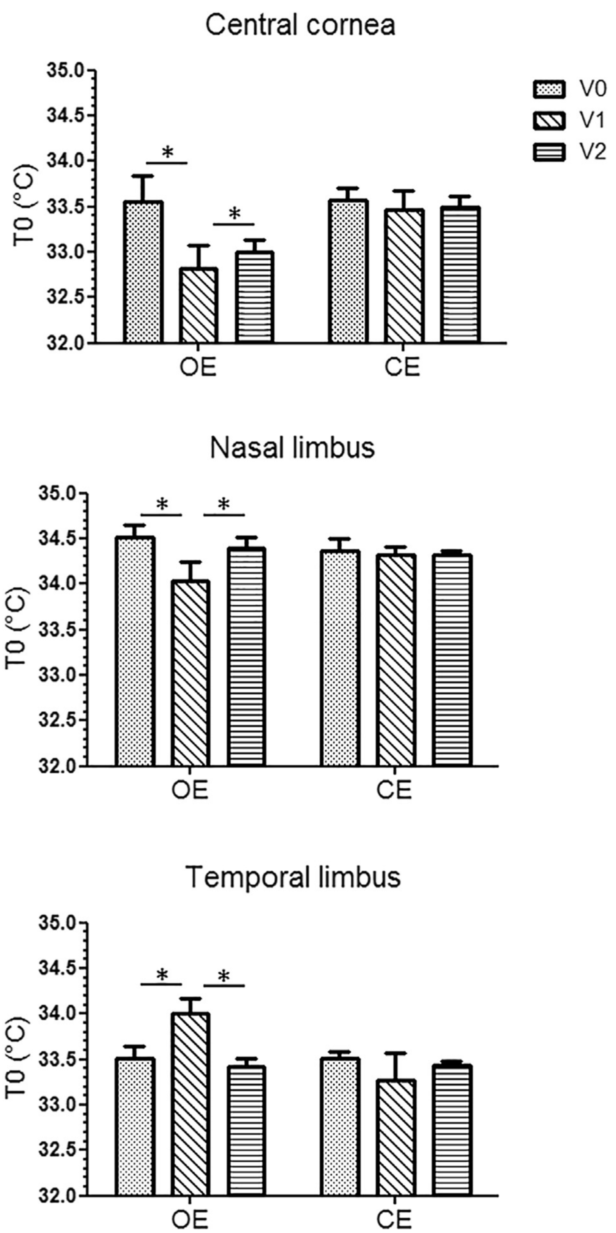

Figure 3. Changes in the temperature soon after eye opening in central corneal, nasal limbus, and temporal limbus before surgery and 7 days and 28 days after cataract surgery in the operated eye and in the contralateral eye (* = $P < .05$; CE = contralateral eye; OE = operated eye; TO = temperature soon after eye opening; V0 = before surgery; V1 = 7 days after surgery; V2 = 28 days after surgery).

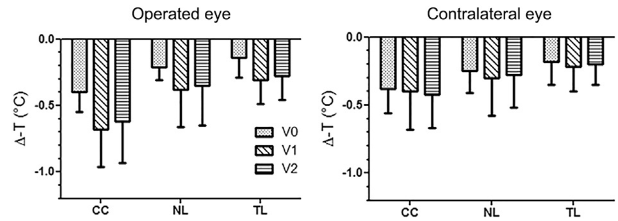

Figure 4. Change in temperature after 10 seconds of sustained eye opening minus temperature soon after eye opening in the 3 analyzed regions before surgery and 7 days and 28 days after cataract surgery in the operated eye and in the contralateral eye (CC = central cornea; Δ-T = temperature after 10 seconds of sustained eye opening minus temperature soon after eye opening; NL = nasal limbus; TL = temporal limbus).

clarify the relationship between surgery and ocular-surface temperature changes because the preoperative data of pseudophakic patients were lacking.

In the present study, we found temperature modifications in different regions of the ocular surface before and after MICS, namely the central cornea, nasal, and temporal limbus. The ocular-surface temperature decreased or increased postoperatively, depending on the region analyzed. In the central cornea, the temperature recorded immediately after eye opening significantly decreased after surgery compared with the preoperative value, and this cooling was maintained throughout the 1-month follow-up. In addition, the decrease in temperature during the 10 seconds of eye opening was higher after surgery. The same trend was also observed in the nasal limbus, although to a lesser extent. The explanation for this cooling has been hypothesized to be related to increased tear-film evaporation and instability.[2,3] When a substance changes its state, heat is transferred to or from the surroundings; similarly, as the tear film evaporates, the ocular surface cools because of the positive latent heat of vaporization as the liquid changes into gas and heat is transferred to the atmosphere.[17] This hypothesis is further strengthened in the present study by the significant correlation between the decrease in temperature during the 10 seconds of eye opening and the TBUT.

In contrast, the temperature recorded in the temporal limbus in relation to the surgical incision showed an opposite trend. In this region, the temperature significantly increased 1 week after surgery, with a complete return to presurgical values at the end of the 1-month follow-up. We hypothesized that this change could be related to postsurgical inflammation, in particular in the surgical incision area at the first postoperative visit. This heating could be related to the increased vascular and metabolic activity, as postulated in other studies.[18,19] This hypothesis was supported by the significant correlation between the temperature increase in this area and the increase in intraocular flare and tear-exudate albumin levels, which are considered indices of intraocular inflammation and ocular surface inflammation, respectively.

The development of ocular discomfort symptoms and signs is a frequent complication of uneventful cataract surgery,[20] and data in the present study agree with findings in the literature showing postoperative impairment of all clinical parameters. The main mechanisms for this event likely include reduced tear-film production and stability,[21,22] squamous metaplasia with reduced goblet cell density,[23] and damage to the corneal nerves from limbal incisions.[24] These morphologic events are accompanied by profound changes in the molecular machinery of the affected neurons, raising an apparent paradox. On the one hand, the disruption of the normal organization of corneal nerves causes spontaneous activity and abnormal responses to external stimuli, causing unpleasant sensations of itching, burning, dryness, and foreign-body sensation as a result of denervation-induced dysesthesia.[25] On the other hand, the responsiveness of damaged axons to direct mechanical, thermal, or chemical stimuli applied to the cut endings of the axons is severely impaired and the injured area shows insensitivity or a much higher threshold to natural stimuli. Cold receptors represent a separate class of corneal sensory neurons sensitive to temperature reductions of 0.1°C or less. They are transiently silenced on warming, and cooling of the corneal surface increases their firing rate.[26,27] In the present study, we found that the decrease in temperature occurring during the 10 seconds of eye opening was significantly directly related to the subjective symptoms of discomfort as measured with the OSDI score. This finding strengthens the hypothesis that the cooling occurring after cataract surgery is the trigger for the excitation of sensory nerves determining the onset of discomfort symptoms.

One possible limit of the study relates to the potential effect on ocular-surface temperature of the postoperative eyedrops being administered in the operated eye only. For ethical reasons, unnecessary drugs with potential side effects were not prescribed for the contralateral unoperated eye. However, according to the study design, eyedrops were not instilled within 2 hours before the measurements were performed to minimize a possible influence. The next step would be to analyze patients several months after surgery, when the postoperative protocol treatment is already interrupted.

In conclusion, we found that thermography could be a useful approach to noninvasively detect postsurgical inflammation and to customize postoperative antiinflammatory therapy for each patient and type of surgery. In particular, for cataract surgery, the prompt tapering and discontinuation of the combination of the topical antibiotic and steroid as soon as inflammation has resolved could help reduce the potential side effects on intraocular pressure, antibiotic resistance, and ocular-surface toxicity.

WHAT WAS KNOWN

- Ocular-surface temperature plays an important role in ocular-surface physiology, although its measure has been limited to a research setting.

WHAT THIS PAPER ADDS

- Thermography helped in noninvasively detecting the postoperative course of inflammation in cataract surgery. This finding is crucial for the prompt tapering and discontinuation of postoperative topical therapy.

REFERENCES

1. Tan L, Cai Z-Q, Lai N-S. Accuracy and sensitivity of the dynamic ocular thermography and inter-subjects ocular surface temperature (OST) in Chinese young adults. Cont Lens Anterior Eye 2009; 32:78–83
2. Kamao T, Yamaguchi M, Kawasaki S, Mizoue S, Shiraishi A, Ohashi Y. Screening for dry eye with newly developed ocular surface thermographer. Am J Ophthalmol 2011; 151:782–791
3. Versura P, Giannaccare G, Fresina M, Campos EC. Subjective discomfort symptoms are related to low corneal temperature in patients with evaporative dry eye. Cornea 2015; 34:1079–1085
4. Purslow C, Wolffsohn JS, Santodomingo-Rubido J. The effects of contact lens wear on dynamic ocular surface temperature. Cont Lens Anterior Eye 2005; 28:29–36
5. de Ortueta D, Magnago T, Triefenbach N, Arba Mosquera S, Sauer U, Brunsmann U. In vivo measurements of thermal load during ablation in high-speed laser corneal refractive surgery. J Refract Surg 2012; 28:53–58
6. Gonnermann J, Maier A-KB, Klein JP, Bertelmann E, Pleyer U, Klamann MKJ. Evaluation of ocular surface temperature in patients with pterygium. Curr Eye Res 2014; 39:359–364
7. Fujishima H, Toda I, Yagi Y, Tsubota K. Quantitative evaluation of postsurgical inflammation by infrared radiation thermometer and laser flare-cell meter. J Cataract Refract Surg 1994; 20:451–454
8. Sniegowski M, Erlanger M, Velez-Montoya R, Olson JL. Difference in ocular surface temperature by infrared thermography in phakic and pseudophakic patients. Clin Ophthalmol 2015; 9:461–466. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4358693/pdf/opth-9-461.pdf. Accessed May 5, 2016
9. Chylack LT Jr, Wolfe JK, Singer DM, Leske MC, Bullimore MA, Bailey IL, Friend J, McCarthy D, Wu S-Y; for the Longitudinal Study of Cataract Study Group. The Lens Opacities Classification System III. Arch Ophthalmol 1993; 111:831–836; erratum 1506. Available at: http://www.chylackinc.com/LOCS_III/LOCS_III_Certification_files/LOCS_III_Reprint_pdf.pdf. Accessed May 5, 2016
10. Methodologies to diagnose and monitor dry eye disease: report of the Diagnostic Methodology Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf 2007; 5:108–152. Available at: http://www.tearfilm.org/dewsreport/pdfs/Methodologies%20to%20Diagnose%20and%20Monitor%20Dry%20Eye%20Disease.pdf. Accessed May 5, 2016
11. Lemp MA. Report on the National Eye Institute/Industry Workshop on Clinical Trials in Dry Eyes. CLAO J 1995; 21:221–232
12. van Bijsterveld OP. Diagnostic tests in the sicca syndrome. Arch Ophthalmol 1969; 82:10–14

13. Versura P, Profazio V, Fresina M, Campos EC. A novel scraping cytology score system (SCSS) grades inflammation in dry eye patients. Curr Eye Res 2009; 34:340–346
14. Versura P, Bavelloni A, Grillini M, Fresina M, Campos EC. Diagnostic performance of a tear protein panel in early dry eye. Mol Vis 2013; 19:1247–1257. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3675053/pdf/mv-v19-1247.pdf. Accessed May 5, 2016
15. Sawa M, Tsurimaki Y, Tsuru T, Shimizu H. New quantitative method to determine protein concentration and cell number in aqueous in vivo. Jpn J Ophthalmol 1988; 32:132–142
16. Mori A, Oguchi Y, Okusawa Y, Ono M, Fujishima H, Tsubota K. Use of high-speed, high-resolution thermography to evaluate tear film layer. Am J Ophthalmol 1997; 124:729–735
17. Craig JP, Singh I, Tomlinson A, Morgan PB, Efron N. The role of physiology in ocular surface temperature. Eye 2000; 14:635–641. Available at: http://www.nature.com/eye/journal/v14/n4/pdf/eye2000156a.pdf. Accessed May 5, 2016
18. Shih S-R, Li H-Y, Hsiao Y-L, Chang T-C. The application of temperature measurement of the eyes by digital infrared thermal imaging as a prognostic factor of methylprednisolone pulse therapy for Graves' ophthalmopathy. Acta Ophthalmol 2010; 88:e154–e159. Available at: http://onlinelibrary.wiley.com/doi/10.1111/j.1755-3768.2010.01941.x/pdf. Accessed May 5, 2016
19. Klamann MKJ, Maier A-KB, Gonnermann J, Klein JP, Bertelmann E, Pleyer U. Ocular surface temperature gradient is increased in eyes with bacterial corneal ulcers. Ophthalmic Res 2013; 49:52–56
20. Movahedan A, Djalilian AR. Cataract surgery in the face of ocular surface disease. Curr Opin Ophthalmol 2012; 23:68–72
21. Ram J, Gupta A, Brar GS, Kaushik S, Gupta A. Outcomes of phacoemulsification in patients with dry eye. J Cataract Refract Surg 2002; 28:1386–1389
22. Khanal S, Tomlinson A, Esakowitz L, Bhatt P, Jones D, Nabili S, Mukerji S. Changes in corneal sensitivity and tear physiology after phacoemulsification. Ophthalmic Physiol Opt 2008; 28:127–134
23. Li X-M, Hu L, Hu J, Wang W. Investigation of dry eye disease and analysis of the pathogenic factors in patients after cataract surgery. Cornea 2007; 26(suppl 1):S16–S20
24. Kohlhaas M. Corneal sensation after cataract and refractive surgery. J Cataract Refract Surg 1998; 24:1399–1409
25. Belmonte C. Eye dryness sensations after refractive surgery: impaired tear secretion or "phantom" cornea? J Refract Surg 2007; 23:598–602
26. Gallar J, Pozo MA, Tuckett RP, Belmonte C. Response of sensory units with unmyelinated fibres to mechanical, thermal and chemical stimulation of the cat's cornea. J Physiol 1993; 468:609–622. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1143846/pdf/jphysiol00371-0601.pdf. Accessed May 5, 2016
27. Carr RW, Pianova S, Fernandez J, Fallon JB, Belmonte C, Brock JA. Effects of heating and cooling on nerve terminal impulses recorded from cold-sensitive receptors in the guinea-pig cornea. J Gen Physiol 2003; 121:427–439. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2217380/pdf/200308814.pdf. Accessed May 5, 2016

First author:
Giuseppe Giannaccare, MD

Ophthalmology Unit, Department of Experimental, Diagnostic and Specialty Medicine, Alma Mater Studiorum University of Bologna and Saint Orsola-Malpighi Teaching Hospital, Bologna, Italy