# Nanosecond laser–assisted cataract surgery: Endothelial cell study

Ivan Tanev, PhD, Vesselin Tanev, DMSc, Anastasios John Kanellopoulos, PhD

**PURPOSE:** To evaluate corneal endothelial cell density (ECD) and morphology after cataract surgery using coaxial ultrasound (US) phacoemulsification or a recently introduced coaxial nanosecond laser technique.

**SETTING:** Department of Ophthalmology, Medical University of Sofia, Sofia, Bulgaria.

**DESIGN:** Prospective cohort study.

**METHODS:** Coaxial US phacoemulsification was performed in 1 eye (US group) and coaxial nanosecond laser–assisted cataract surgery in the contralateral eye (laser group) of the same patient. Nuclear sclerosis was graded from nuclear opalescence (NO) 3, nuclear color (NC) 3 to NO4, NC4 using the Lens Opacities Classification System III. The central ECD, coefficient of variation (CoV) in cell size (objective measure of polymegethism), and percentage of hexagonal cells (an index of pleomorphism) were evaluated.

**RESULTS:** Eighty-two eyes (41 patients) had uneventful surgery. The mean ECD was 2517 cells/mm$^2$ $\pm$ 137 (SD) preoperatively and 2287 $\pm$ 155 cells/mm$^2$ at 2 years in the US group and 2521 $\pm$ 233 cells/mm$^2$ and 2420 $\pm$ 292 cells/mm$^2$, respectively, in the laser group (both $P < .001$). The mean CoV was 0.27 $\pm$ 2.4 preoperatively and 0.30 $\pm$ 2.4 at 2 years in the US group and 0.27 $\pm$ 2.8 and 0.27 $\pm$ 2.0, respectively, in the laser group (both $P < .001$). The mean percentage of hexagonal cells was 42.3% $\pm$ 3.6% preoperatively and 37.74% $\pm$ 3.54% at 2 years in the US group and 42.8% $\pm$ 3.2% and 43.00% $\pm$ 2.68%, respectively, in the laser group (both $P < .001$).

**CONCLUSION:** Nanosecond laser phacoemulsification had advantages over US phacoemulsification in terms of endothelial cell structure preservation.

**Financial Disclosures:** Dr. Kanellopoulos is consultant to Alcon Surgical, Inc., Allergan, Inc., Avedro, Inc., Keramed, Inc., Optovue, Inc., i-Optics Corp., and Carl Zeiss Meditec AG. Neither of the other authors has a financial or proprietary interest in any material or method mentioned.

*J Cataract Refract Surg 2016; 42:725–730 © 2016 ASCRS and ESCRS*

The number of cataract surgeries is continually increasing, starting from approximately 20 million surgeries in 2010 and expecting to reach 32 million procedures globally by 2020.[1] Ultrasound (US) phacoemulsification, used since the early 1970s, has been progressively refined and is now the standard reference for effective cataract surgery.

Modern cataract surgery is one of the most successful types of surgery in terms of the improvement in the patient's quality of life. The expected outcomes today include reduced surgical trauma, smaller incisions, improved intraoperative ocular stability, and the advanced performance capabilities of intraocular lenses (IOLs). Ophthalmic surgeons are in a constant search of refined techniques and instrumentation (tools, devices) to minimize surgical trauma and improve the patient's surgical outcomes.

Ultrasound energy might affect the ocular structures and has been implicated in the pathogenesis of endothelial cell loss and cystoid macular edema.[2,3] Corneal endothelial cell damage is one of the most frequent early postoperative complications of phacoemulsification. This complication can lead to corneal edema and serious visual disturbances. Postoperative corneal endothelial cell loss is related to many factors, including phacoemulsification time and energy, cataract density, corneal pathology, anterior chamber depth, axial length, ocular trauma, free radical development, mechanical


Published by Elsevier Inc.

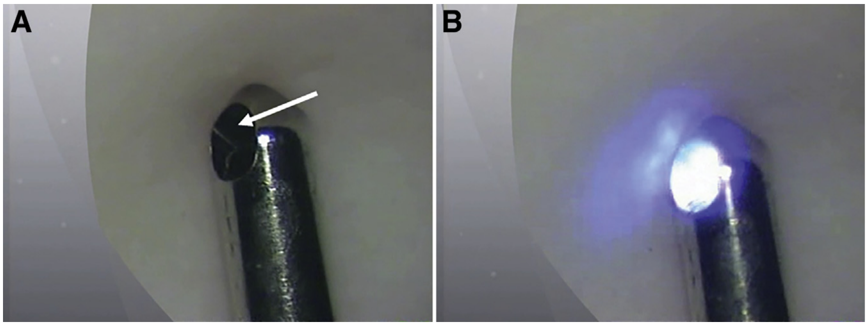


**Figure 1.** Nanosecond laser tip 20-gauge without sleeve. *A*: One millimeter aspiration opening titanium target (*white arrow*). *B*: Nanosecond laser tip at the time of plasma formation.

and heat injury, phacoemulsification technique, surgeon experience, and use of ophthalmic viscosurgical devices (OVDs).[4–10]

This study compared the corneal endothelial cell density (ECD) and corneal endothelial cell morphology in patients having bilateral cataract surgery performed using coaxial US phacoemulsification in 1 eye and coaxial nanosecond laser–assisted cataract surgery in the contralateral eye. Using a nanosecond laser for cataract removal has a relatively long history. Since the first report of phacolysis of a human cataractous lens by a neodymium:YAG (Nd:YAG) laser,[11] the technology has advanced considerably. This technology uses a pulsed Nd:YAG (1064 nm) laser that is transferred to the probe by a quartz fiber optic and is focused on a titanium target within the probe tip (Figure 1).

## PATIENTS AND METHODS

This prospective cohort study evaluated the postoperative ECD and corneal endothelial cell morphology in both eyes of the same patient over a 24-month follow-up. Ultrasound coaxial phacoemulsification was performed in 1 eye (US group), and coaxial cataract surgery assisted using a recently introduced nanosecond laser was performed in the contralateral eye (laser group). Which eye would receive which procedure was decided by random selection.

### Nanosecond Laser

In this study, an updated laser system (Cetus, ARC Laser GmbH) was used. Each pulse releases 7.5 mJ of laser energy for 5 ns. The pulsing photic energy impacts the titanium target located within the probe tip, which in turn leads to optical breakdown and plasma formation. This creates a shockwave that emanates from the tip in a cone-like fashion.[12] These shockwaves are used to disrupt the substance of the cataract. The fragmented particles of the cataract are then aspirated out of the eye through the aspiration port, the lumen of which is also contained within the laser probe. The system received the Conformité Européenne mark for clinical use in the European Union and 510K approval from the U.S. Food and Drug Administration for clinical use in the United States. The coaxial laser probe for 2.4 mm incisions (Figure 2) was used in all cases.

### Patient Assessment

Nuclear sclerosis was graded from nuclear opalescence (NO) 3, nuclear color (NC) 3 to NO4, NC4 using the Lens Opacities Classification System III.[13]

Endothelial cell density and endothelial cell size variability were determined preoperatively and 24 months after surgery in both groups. The endothelium of the central cornea was examined and imaged with a noncontact specular microscope (EM935, Haag-Streit). Endothelial structure was evaluated using the following parameters recorded from the noncontact specular microscope system: mean ECD (cell/mm$^2$), mean cell area (μm$^2$), coefficient of variation (CoV) in cell size, and the percentage of hexagonal cells. The CoV in cell size (standard deviation divided by the mean cell area) was used as an index of the extent of

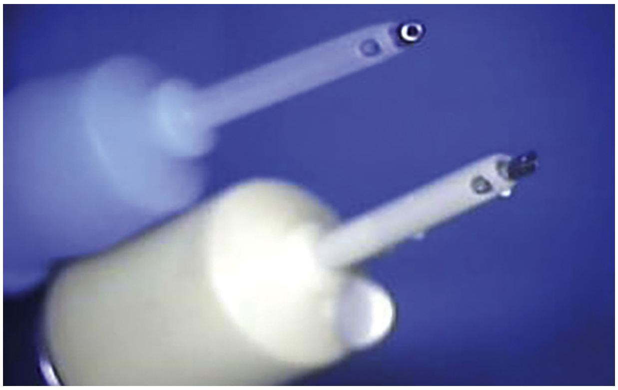

**Figure 2.** Coaxial US tip (*yellow sleeve*) and nanosecond laser tip (*blue sleeve*).

Submitted: November 24, 2015.
Final revision submitted: January 30, 2016.
Accepted: February 2, 2016.

From the Department of Ophthalmology (I. Tanev), Faculty of Medicine, Medical University, and the Eye Hospital Zrenie (V. Tanev), Sofia, Bulgaria; the LaserVision.gr Clinical & Research Eye Institute (Kanellopoulos), Athens, Greece; the New York University Medical School (Kanellopoulos), New York, New York, USA.

Corresponding author: Ivan Tanev, PhD, 22, Veliko Tarnovo Street 1504, Sofia, Bulgaria. E-mail: itanev@skycode.com.

**Table 1.** Fluidic parameters by group.

| Parameter | US Group | Laser Group |
|---|---|---|
| Bottle height (cm) | 100 | 100 |
| Power | 40% | 7.5 mJ |
| Vacuum (mm Hg) | 350 | 350 |
| Aspiration flow rate (cc/min) | 40 | 40 |

US = ultrasound

variation in the cell area (polymegathism). The percentage of hexagonal cells in the analyzed area was used as an index of variation in cell shape (pleomorphism).

The procedure for specular noncontact microscopy involved 3 successive acquisitions from the central cornea. The examiner for the analysis manually marked a minimum of 200 contiguous cells using a built-in software program.[14]

Also, the corneal transparency on the first day postoperatively was assessed with a slitlamp examination. Only transparent corneas were analyzed.

## Surgical Technique

The same surgeon (I.T.) performed all cataract procedures. The surgical protocol for both groups was based on the standard small-incision clear corneal technique (Table 1). Under topical anesthesia, 3 corneal tunnels were created (2.4 mm main incision and 2 side ports) using diamond knives (Accutome, Inc.), followed by 4-quadrant prechop of the crystalline lens. The fluidics system used (Megatron S3 VIP, Geuder AG) had flow-control aspiration and a vacuum (venturi) control machine. A peristaltic pump was used for the entire surgical procedure. After bimanual cortical cleanup and viscoexpansion of the capsular bag were complete, a hydrophobic acrylic IOL (SA60AT, Alcon Surgical, Inc.) was implanted.

## Statistical Analysis

Statistical analysis was performed using SPSS software (version 16.0, SPSS, Inc.). Both eyes of all subjects were analyzed. Variations in the corneal ECD and cell morphology in different groups were assessed using descriptive statistics, the 1-sample Kolmogorov-Smirnov test, the paired-samples $t$ test, and the Wilcoxon signed-rank test.

# RESULTS

The study comprised 82 eyes of 41 patients. All surgeries were uneventful.

On slitlamp examination, there were no significant differences in the incidence of corneal edema, the mean 1-day postoperative uncorrected distance visual acuity (UDVA), or the percentage of eyes having a UDVA of 20/40 or better between the US group and the laser group. In the patients with nuclear sclerotic cataracts of average density, the immediate postoperative vision and corneal edema were similar between eyes in the US group and eyes in the laser group.

The mean ECD was 2517 cells/mm$^2$ $\pm$ 137 (SD) preoperatively and 2287 $\pm$ 155 cells/mm$^2$ 2 years postoperatively in the US group and 2521 $\pm$ 233 cells/mm$^2$ and 2420 $\pm$ 292 cells/mm$^2$, respectively, in the laser group (Figure 3). The change was statistically significant in both groups ($P < .001$). The difference between the 2 groups was statistically significant and persisted over the 24-month follow-up.

The mean CoV was 0.27 $\pm$ 2.4 preoperatively and 0.30 $\pm$ 2.4 at 2 years in the US group and 0.27 $\pm$ 2.8 and 0.27 $\pm$ 2.0, respectively, in the laser group (Figure 4). The change was statistically significant in both groups ($P < .001$).

The mean percentage of hexagonal cells was 42.3% $\pm$ 3.6% preoperatively and 37.74% $\pm$ 3.54% 2 years postoperatively in the US group and 42.8% $\pm$ 3.2% preoperatively and 43.00% $\pm$ 2.68%, respectively, in the laser group (Figure 5). The change was statistically significant in both groups ($P < .001$).

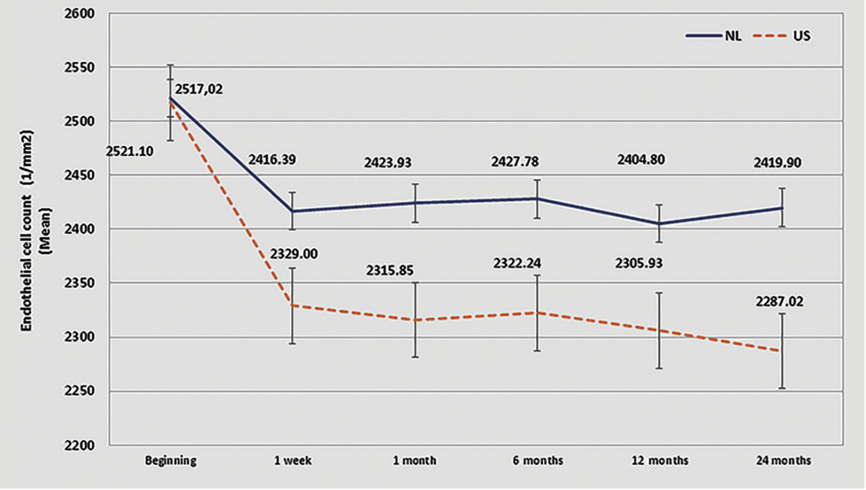


**Figure 3.** The ECD dynamics over a 24-month period ($P < .001$) (NL = nanosecond laser; US = ultrasound).

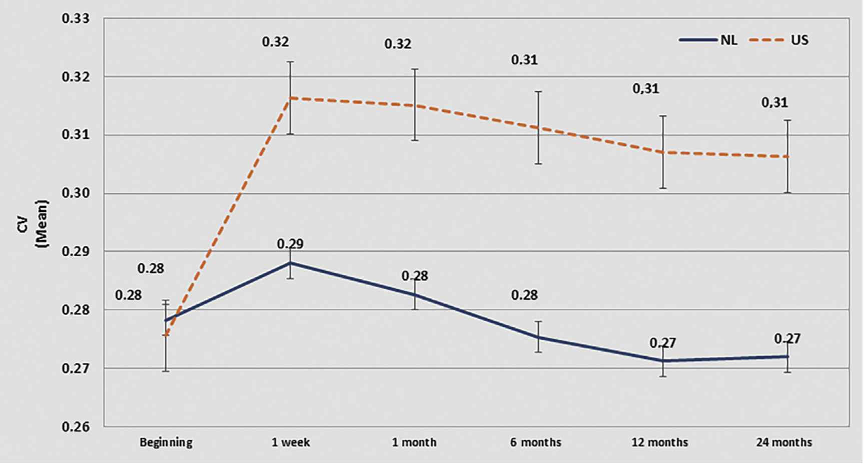


**Figure 4.** The mean CoV over a 24-month period ($P < .001$) (CV = coefficient of variation; NL = nanosecond laser; US = ultrasound).

## DISCUSSION

This contralateral-eye study compared an established emulsification technique (US energy) with another technique (nanosecond laser–assisted) using the same fluidics from the same phaco machine for cataract extraction. The 2 study groups were equally matched in mean lens density.

The 2 groups had similar corneal transparency and visual rehabilitation results. Also, the findings with the nanosecond laser–assisted technique as well as with US phacoemulsification were comparable with those reported in the literature.[15–21]

Cataract surgery can lead to a reduction in ECD, a proportional increase in the mean cell size, and a disruption of the normal hexagonal pattern.[22,23] Although modern US phacoemulsification has minimized endothelial damage, all surgical procedures that involve entry into the anterior segment will inevitably damage a proportion of the endothelial cells as a result of intraoperative corneal manipulations.[23,24]

Analysis of cell shape and pattern is a more sensitive indicator of endothelial damage than ECD.[25] The intercellular space becomes larger during the healing period. After surgical trauma, the undamaged endothelial cells undergo morphologic changes to fill the cell-free areas and restore normal function. Once endothelial repair is complete, the intercellular space is reduced to its previous size and the endothelial layer is restored.[26]

Regarding normalization of the morphometric indices in our study, there was a significant difference between the 2 groups. The US group showed such a tendency toward normalization up to 8 months after surgery. In contrast, stabilization of the endothelial monolayer occurred by 1 month in the nanosecond laser group.

Schultz et al.,[27] Galin et al.,[28] and Kraff et al.[29] also found stabilization of the corneal endothelium 3 months after cataract surgery based on the normalization of the postoperative morphologic status. However, it is not clear exactly how long it takes the

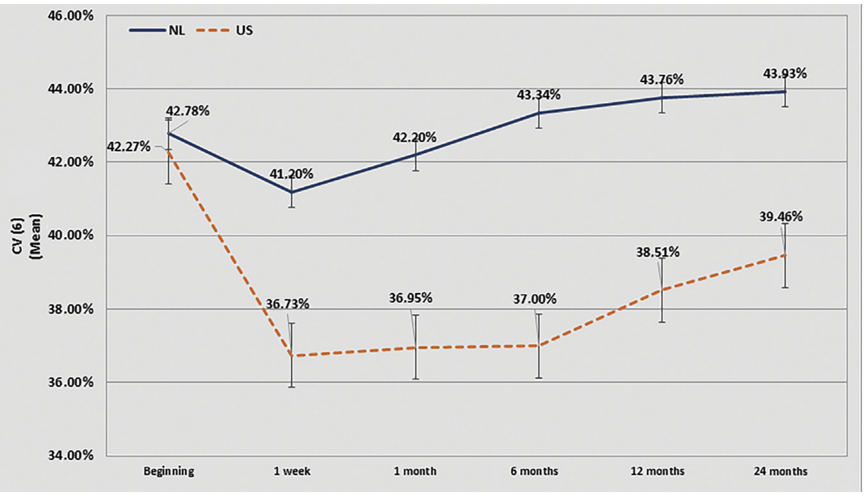


**Figure 5.** The mean CoV of hexagonal cells over a 24-month period ($P < .001$) (CV = coefficient of variation; NL = nanosecond laser; US = ultrasound).

endothelial cell count to stabilize after US cataract surgery. Liesegang et al.[30] and Bourne et al.[31] reported continued endothelial cell loss several years after IOL implantation. It is also possible that the time to apparent return to normalcy of the cornea after cataract surgery might be approximately 3 months, as evidenced by epithelial thickness normalization.[32] There is also evidence of continuing cell loss despite an apparent normalization of the endothelial morphologic characteristics after cataract surgery.[33]

In conclusion, nanosecond laser cataract surgery appears to be an alternative to small-incision US phacoemulsification. It is minimally invasive, and the recovery period for the endothelium is shorter. In this study, nanosecond laser cataract surgery was an effective procedure for NO3, NC3 to NO4, NC4 of nuclear sclerosis. For higher grades of nuclear sclerosis, further improvements in technical-related and surgical-related parameters are required. Further studies are necessary to evaluate the safety and efficacy of this technique for cataract removal.

### WHAT WAS KNOWN

- An updated version of a nanosecond laser, formerly known as the photolysis device, changes the endothelium after cataract surgery.

### WHAT THIS PAPER ADDS

- Nanosecond laser phacoemulsification preserved the endothelial cell structure better than US phacoemulsification.

## REFERENCES


1. World Health Organization. Vision 2020. The Right to Sight. Global Initiative for the Elimination of Avoidable Blindness; Action Plan 2006–2011. Geneva, Switzerland, WHO, 2007; Available at: http://www.who.int/blindness/Vision2020_report.pdf. Accessed March 12, 2016
2. Dick HB, Kohnen T, Jacobi FK, Jacobi KW. Long-term endothelial cell loss following phacoemulsification through a temporal clear corneal incision. J Cataract Refract Surg 1996; 22:63–71
3. Ecsedy M, Miháltz K, Kovács I, Takács Á, Filkorn T, Nagy ZZ. Effect of femtosecond laser cataract surgery on the macula. J Refract Surg 2011; 27:717–722
4. Baradaran-Rafii A, Rahmati-Kamel M, Eslani M, Kiavash V, Karimian F. Effect of hydrodynamic parameters on corneal endothelial cell loss after phacoemulsification. J Cataract Refract Surg 2009; 35:732–737
5. Takahashi H. Free radical development in phacoemulsification cataract surgery. J Nippon Med Sch 2005; 72:4–12. Available at: https://www.jstage.jst.go.jp/article/jnms/72/1/72_1_4/_pdf. Accessed March 12, 2016
6. Yeniad B, Corum I, Ozgun C. The effects of blunt trauma and cataract surgery on corneal endothelial cell density. Middle East Afr J Ophthalmol 2010; 17:354–358. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2991455/. Accessed March 12, 2016
7. Richard J, Hoffart L, Chavane F, Ridings B, Conrath J. Corneal endothelial cell loss after cataract extraction by using ultrasound phacoemulsification versus a fluid-based system. Cornea 2008; 27:17–21
8. Storr-Paulsen A, Nørregaard JC, Farik G, Tårnhøj J. The influence of viscoelastic substances on the corneal endothelial cell population during cataract surgery: a prospective study of cohesive and dispersive viscoelastics. Acta Ophthalmol Scand 2007; 85:183–187. Available at: http://www3.interscience.wiley.com/cgi-bin/fulltext/118515552/PDFSTART. Accessed March 12, 2016
9. Hayashi K, Manabe SI, Yoshimura K, Kondo H. Corneal endothelial damage after cataract surgery in eyes with pseudoexfoliation syndrome. J Cataract Refract Surg 2013; 39:881–887
10. Lundberg B, Jonsson M, Behndig A. Postoperative corneal swelling correlates strongly to corneal endothelial cell loss after phacoemulsification cataract surgery. Am J Ophthalmol 2005; 139:1035–1041
11. Dodick JM. Laser phacolysis of the human cataractous lens. Dev Ophthalmol 1991; 22:58–64
12. Dodick JM, Christiansen J. Experimental studies on the development and propagation of shock waves created by the interaction of short Nd:YAG laser pulses with a titanium target; possible implications for Nd:YAG laser phacolysis of the cataractous human lens. J Cataract Refract Surg 1991; 17:794–797
13. 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. Available at: http://www.chylackinc.com/LOCS_III/LOCS_III_Certification_files/LOCS_III_Reprint_pdf.pdf. Accessed March 12, 2016
14. McCarey BE, Edelhauser HF, Lynn MJ. Review of corneal endothelial specular microscopy for FDA clinical trials of refractive procedures, surgical devices, and new intraocular drugs and solutions. Cornea 2008; 27:1–16. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3062434/pdf/nihms239342.pdf. Accessed March 12, 2016
15. Alzner E, Dodick JM, Thyzel R, Grabner G. Experimentelle Laser-Phakolyse mit dem ARC-Puls-Nd-YAG-Laser [Experimental laser phacolysis using the ARC-Puls-Nd-YAG laser]. Spektrum Augenheilkd 1988; 12:24–27
16. Huetz WW, Eckhardt HB. Photolysis using the Dodick-ARC laser system for cataract surgery. J Cataract Refract Surg 2001; 27:208–212
17. Sameja D, Krueger RR. Femtosecond laser: applications in cataract surgery. In: Boyd S, Boyd BF, eds, New Trends in Ophthalmology; Medical and Surgical Management. Panama, Republic of Panama, Jaypee-Highlights Medical Publishers, 2013; 159–165
18. Kanellopoulos AJ, Dodick JM, Brauweiler P, Alzner E. Dodick photolysis for cataract surgery; early experience with the Q-switched neodymium:YAG laser in 100 consecutive patients. Ophthalmology 1999; 106:2197–2202
19. Kanellopoulos JA, and the Photolysis Investigative Group. Laser cataract surgery; a prospective clinical evaluation of 1000 consecutive laser cataract procedures using the Dodick photolysis Nd:YAG system. Ophthalmology 2001; 108:649–654; discussion by RJ Mackool, 654–655
20. Kanellopoulos AJ. All-laser bladeless cataract surgery, combining femtosecond and nanosecond lasers: a novel surgical technique. Clin Ophthalmol 2013; 7:1791–1795. Available

at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3775700/pdf/opth-7-1791.pdf. Accessed March 12, 2016
21. Hashemi H, Khanlari M. Photolysis using the Dodick-ARC laser system for cataract surgery. Iran J Opthalmol 2004; 16:1–8
22. Pirazzoli B, D'Eliseo D, Ziosi M, Acciarri R. Effects of phacoemulcification time on the corneal endothelium using phacofracture and phaco chop techniques. J Cataract Refract Surg 1996; 22:967–969
23. Hayashi K, Hayashi H, Nakao F, Hayashi F. Risk factors for corneal endothelial injury during phacoemulsification. J Cataract Refract Surg 1996; 22:1079–1084
24. DeBry P, Olson RJ, Crandall AS. Comparison of energy required for phaco-chop and divide and conquer phacoemulsification. J Cataract Refract Surg 1998; 24:689–692
25. Mishima S. Clinical investigations on the corneal endothelium; the XXXVIII Edward Jackson Memorial Lecture. Am J Ophthalmol 1982; 93:1–29
26. Goebbels M, Spitznas M. Endothelial barrier function after phacoemulsification: a comparison between diabetic and non-diabetic patients. Graefes Arch Clin Exp Ophthalmol 1991; 229:254–257
27. Schultz RO, Glasser DB, Matsuda M, Yee RW, Edelhauser HF. Response of the corneal endothelium to cataract surgery. Arch Ophthalmol 1986; 104:1164–1169
28. Galin MA, Lin LL, Fetherolf E, Obstbaum SA, Sugar A. Time analysis of corneal endothelial cell density after cataract extraction. Am J Ophthalmol 1979; 88:93–96
29. Kraff MC, Sanders DR, Lieberman HL. Specular microscopy in cataract and intraocular lens patients; a report of 564 patients. Arch Ophthalmol 1980; 98:1782–1784
30. Liesegang TJ, Bourne WM, Ilstrup DM. Short- and long-term endothelial cell loss associated with cataract extraction and intraocular lens implantation. Am J Ophthalmol 1984; 97:32–39
31. Bourne WM, Nelson LR, Hodge DO. Continued endothelial cell loss ten years after lens implantation. Ophthalmology 1994; 101:1014–1022; discussion by A Sugar, 1022–1023
32. Kanellopoulos AJ, Asimellis G. Corneal epithelial remodeling following cataract surgery: three-dimensional investigation with anterior-segment optical coherence tomography. J Refract Surg 2014; 30:348–353
33. Bates AK, Cheng H. Bullous keratopathy: a study of endothelial cell morphology in patients undergoing cataract surgery. Br J Ophthalmol 1988; 72:409–412. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1041471/pdf/brjopthal00610-0010.pdf. Accessed March 12, 2016

First author:
Ivan Tanev, PhD

*Department of Ophthalmology, Faculty of Medicine, Medical University, Sofia, Bulgaria*