

Plastic Particles at the LASIK Interface

Anders Ivarsen, MD,¹ Jan Thøgersen, PhD,² Søren Rud Keiding, PhD,² Jesper Ø. Hjortdal, MD, PhD,¹ Torben Møller-Pedersen, MD, PhD¹

Purpose: To investigate the origin, composition, and persistence of the interface particles that frequently are observed after LASIK.

Design: Small case series and experimental animal study.

Methods: Four patients received LASIK using a Schwind Supratome (Schwind, Kleinostheim, Germany) and a MEL 70 G-Scan excimer laser (Asclepion, Jena, Germany) and were examined over the course of 1 year using slit-lamp and in vivo confocal microscopy. Four rabbits received a monocular microkeratome incision and were examined immediately after surgery without lifting the flap. After monthly evaluation for 4 months using in vivo confocal microscopy, 2 corneas were processed for histologic analysis and were sectioned serially. To measure the iron content, atomic absorption spectrometry was performed on 2 operated and 2 unoperated rabbit corneas. The chemical composition of the metal and plastic parts of the microkeratome blade was identified using energy dispersive x-ray fluorescence (metal part), and Raman and infrared spectroscopy (plastic part). Before and after oscillation in air, the microkeratome blade and motor-head were examined using light and fluorescence microscopy. In serial sections, interface particles were identified by fluorescence microscopy and their chemical composition was determined using Coherent Antistokes Raman Scattering microscopy.

Results: In LASIK patients, thousands of brightly reflecting particles (up to 30 μm) were observed throughout the interface. The highest particle density was detected where the microkeratome blade had first entered the cornea. Both in the center and at the flap edge, the morphologic features, distribution, and density of these particles remained unaltered throughout the 1-year observation period. In rabbit corneas, interface particles were observed immediately after the microkeratome incision, even though the flap had not been lifted. These particles were similar to those observed in humans and persisted unaltered throughout the study. The operated and unoperated rabbit corneas had comparable iron content, demonstrating that the particles were not fragments of the uncoated steel blade. Only a few particles were observed on the unused microkeratome motor head and blade, whereas numerous fluorescent particles were detected after oscillation in air, the amount of particles increasing with oscillation time. Interestingly, the only fluorescent part of the microkeratome was the plastic segment of the blade. This plastic (polyetherimide) emitted fluorescence identical to that of the observed particles, whereas all metal parts of the microkeratome blade and motor head were nonfluorescent. In serial sections, interface particles showed fluorescent properties equivalent to polyetherimide and exhibited molecular resonance at 1780 and 3100 cm^{-1} , in accordance with the Raman spectrum of polyetherimide.

Conclusions: Numerous plastic particles are generated during microkeratome oscillation and are deposited at the interface during LASIK. The particles persist unaltered for at least 1 year. *Ophthalmology* 2004;111:18–23
© 2004 by the American Academy of Ophthalmology.

After LASIK, brightly reflecting interface particles frequently are observed using slit-lamp biomicroscopy^{1–3} and are reported in almost all LASIK patients when examined using in vivo confocal microscopy.^{3–9} These interface particles may come from several sources. However, the particles generally are thought to be introduced by the micro-

keratome blade, because they have been reported to be present after incision without subsequent excimer laser treatment.⁴ Speculations on the particle source include biologic debris from the ocular surface,^{1,3} powder from surgical gloves,¹ remnants from industrial processing of the blade,⁴ and metal fragments from the steel blade.^{3,6} Still, the

Originally received: December 16, 2002.

Accepted: May 23, 2003.

Manuscript no. 220976.

¹ Department of Ophthalmology, Aarhus University Hospital, Aarhus, Denmark.

² Department of Chemistry, Aarhus University, Aarhus, Denmark.

Supported in part by The Faculty of Health Sciences at Aarhus University, The Danish Medical Research Council, The Danish Association for Prevention of Eye Diseases and Blindness, The Novo Nordisk Foundation, The Institute of Experimental Clinical Research at Aarhus University Hospital, The Synoptik Foundation, Ingeniør August Frederik Erichsens Legat, Ingrid Munkholms Legat, The Hørslev Foundation, Fonden til

Lægevidenskabens Fremme, Alice og Jørgen A. Rasmussens Memorial Grant, Jørgen Bagenkop Nielsens Myopia Foundation, The Research Foundation at Aarhus University, The Danish Eye Research Foundation, The Danish Medical Association Research Foundation, Svend H. A. Schrøders Foundation, The Toyota Foundation, Jacob Madsens Foundation, Ib Henriksens Foundation, and The Anniversary Foundation for King Christian IX and Queen Louise.

Correspondence to Torben Møller-Pedersen, MD, PhD, Department of Ophthalmology, Aarhus University Hospital, Nørrebrogade 44, DK-8000 Aarhus C, Denmark. E-mail: tmp@akphd.au.dk.

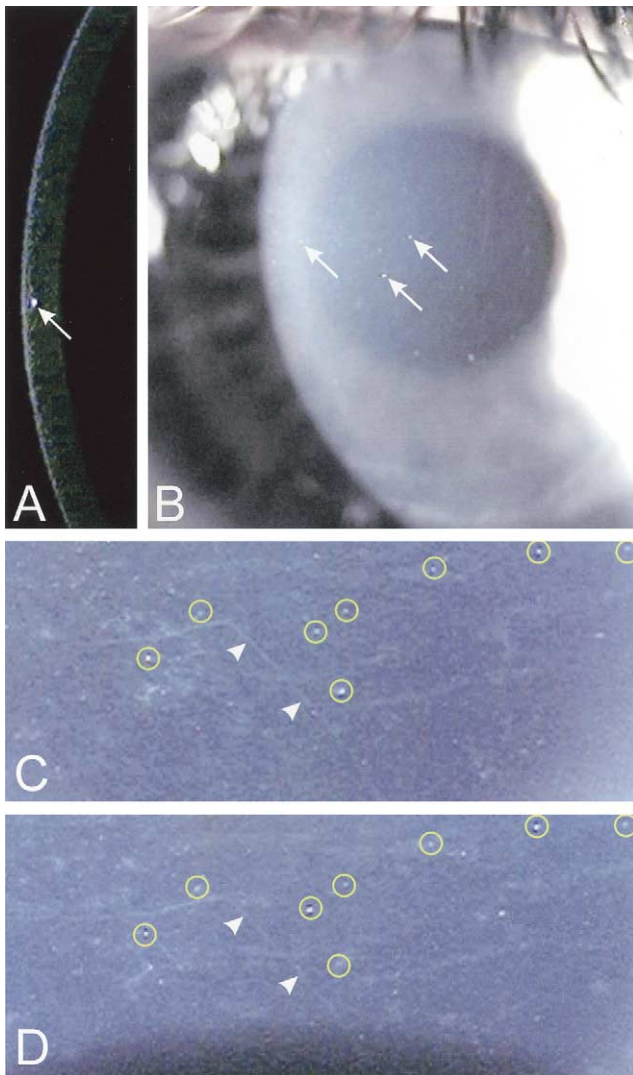


Figure 1. A, B, Slit-lamp biomicroscopy of a patient 3 months after myopic LASIK showing multiple, brightly reflecting particles (arrows) at the interface. High-resolution biomicroscopy of the patient at 3 months (C) and 12 months (D) demonstrating an unaltered particle distribution (yellow circles). Note the small nerve branch (arrowheads) that acts as a biologic landmark.

exact composition and origin remain to be established. The clinical consequences of interface particles are largely unknown. However, such particles are likely to interfere with the excimer laser photoablation and may have visual consequences because of unwanted light scattering. Furthermore, they may give rise to toxic or allergic reactions and may play a role in the development of diffuse lamellar keratitis.⁴ Obviously, deposition of interface particles should be avoided. The aim of the present study was to establish the origin, composition, and persistence of interface particles after LASIK.

Case Reports

Four patients received myopic LASIK (9-mm diameter flap; 6-mm diameter photoablation) using a Supratome microkeratome

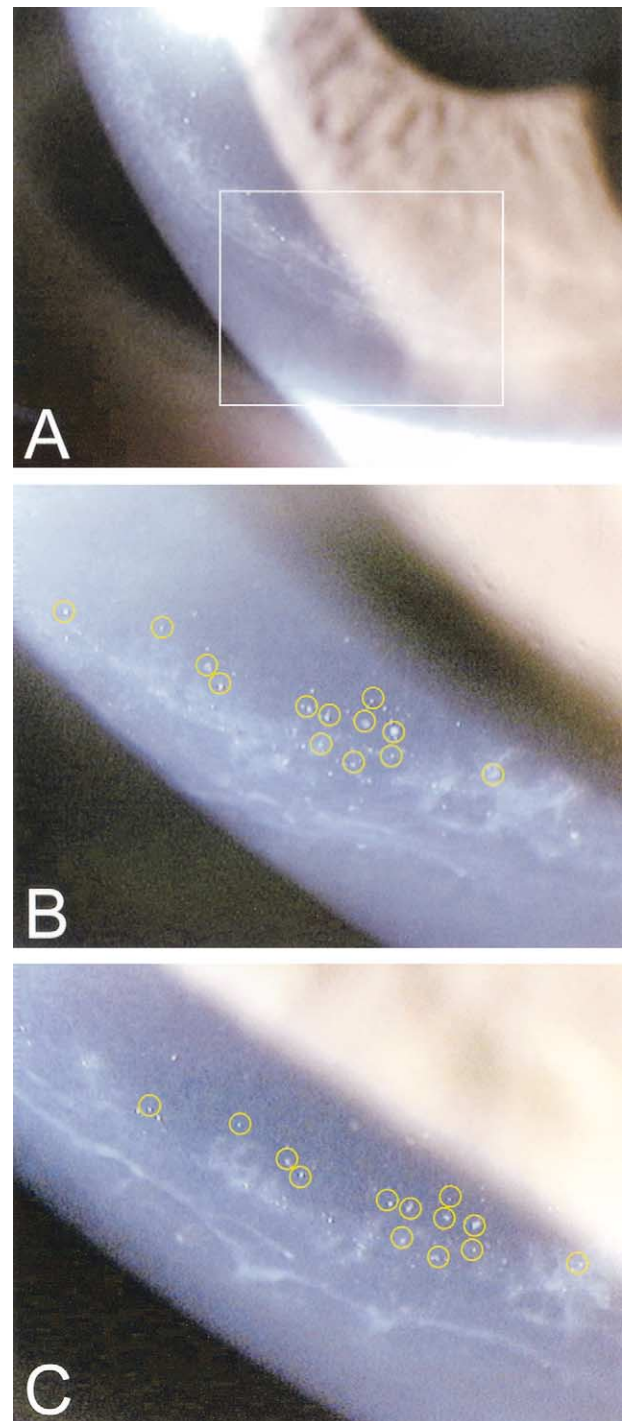


Figure 2. Slit-lamp biomicroscopy of the flap edge in a LASIK patient 3 (A, B) and 12 (C) months after surgery. The box in A outlines the position of B and C where the particles remain at the same positions over time (yellow circles). Note the remodeling of the flap edge.

(Schwind, Kleinostheim, Germany) and a MEL 70 G-Scan excimer laser (Asclepion, Jena, Germany). The patients underwent surgery using 2 separate but identical microkeratome units (2 patients each unit). All treatments were performed using disposable Supratome blades (no. 19407) provided by Schwind. The LASIK interface was evaluated at varying time points over the

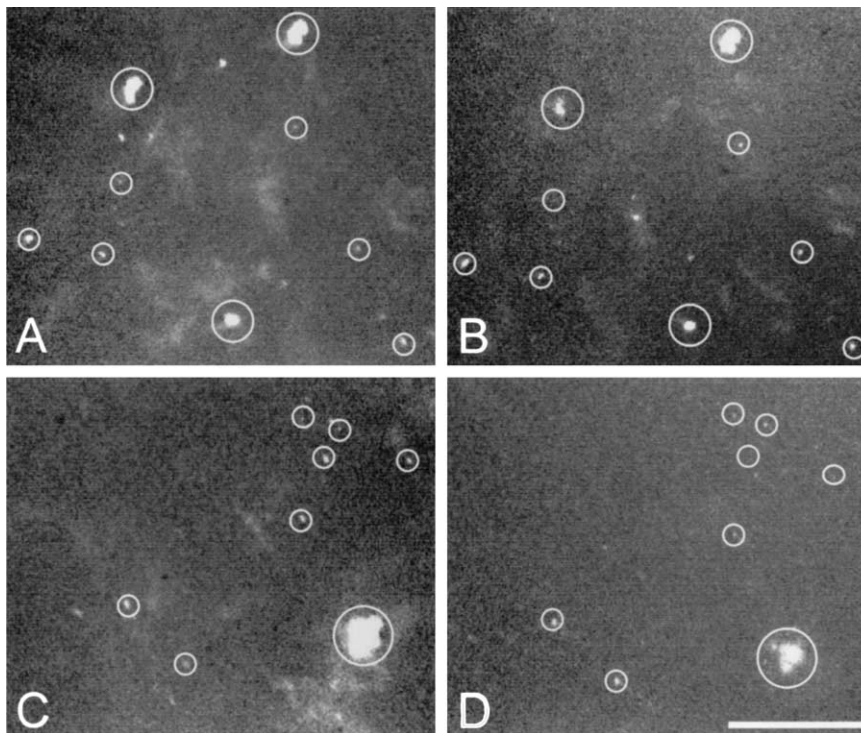


Figure 3. In vivo confocal microscopy of 2 LASIK patients demonstrating numerous brightly reflecting interface particles with unaltered localizations (circles) at 3 months (A) and 6 months (B), and at 1 month (C) and 12 months (D), respectively. Note that the background reflectivity decreases over time as a result of wound repair. The slight variation in particle morphologic features is related to sampling differences. Bar = 100 μm .

course of 1 year using slit-lamp and in vivo confocal microscopy (Tandem Scanning Corporation, Reston, VA).^{10,11} At all examinations, slit-lamp biomicroscopy demonstrated numerous brightly reflecting particles scattered throughout the interface (Fig 1A, B, arrows). These particles remained at the same positions during the 1-year observation period (compare Fig 1C, 1D, circles). At the flap edge, persisting interface particles also were observed (Fig 2). Interestingly, the particle density varied topographically along the edge and was highest where the microkeratome blade had first entered the cornea. This variation may be related to particles being generated and deposited on the blade during microkeratome testing immediately before surgery. Using in vivo confocal microscopy, reflecting interface particles were similarly demonstrated with no changes in morphologic features, distribution, or density up to 1 year after surgery (compare Fig 3A with 3B, and Fig 3C with 3D; circles). In the flap center, the particle density seemed uniform, with approximately 5 to 10 per field of view ($450 \times 340 \mu\text{m}$), giving a total of 2100 to 4200 particles beneath a 9-mm diameter LASIK flap. Most of the particles were less than 5 μm in diameter; however, a few were up to 30 μm (Fig 3).

Materials and Methods

In 4 New Zealand White rabbits (weight, 4.5–5.5 kg), a monocular, 9-mm diameter, hinged corneal flap was cut using a microkeratome (Supratome). Surgery was preceded by anesthesia as previously reported,^{10,11} and the study was approved by the Danish Animal Experiments Inspectorate. To avoid environmental contamination of the interface, the flap was not lifted and the animals were examined immediately after surgery, using in vivo confocal microscopy. Two rabbits were evaluated monthly using confocal

microscopy and were killed after 4 months by injecting sodium pentobarbital 150 mg/kg. The corneas (central 10-mm diameter) were excised, embedded in Tissue-Tek (Sakura, Tokyo, Japan), and snap-frozen in liquid nitrogen. Serial cryostat cross-sections (thickness approximately 5 μm) were cut, air dried, fixed in acetone for 10 minutes, and evaluated using fluorescence microscopy. The remaining 2 rabbits were killed immediately after surgery and the corneas were excised using a diamond knife and plastic forceps, followed by freeze-drying of the tissue. The iron contents of these 2 corneas and the 2 unoperated, contralateral corneas were measured using graphite furnace atomic absorption spectrometry (courtesy of the Danish Technological Institute, Aarhus, Denmark). The mineral composition of the metal part of the microkeratome blade was determined using energy dispersive x-ray fluorescence spectroscopy, whereas the plastic part was analyzed using infrared and Raman spectroscopy (courtesy of the Danish Technological Institute, Taastrup, Denmark). Light and fluorescence microscopy were used to examine the microkeratome blade and motor head before and after oscillation in air for 2 full passes (simulating 1 test pass and 1 cut), as well as for multiple passes. Both microkeratome units were examined. In the serial sections, interface particles were detected by fluorescence microscopy, and their chemical composition was identified using Raman spectroscopy and Coherent Antistokes Raman Scattering microscopy.¹²

Results

Immediately after the microkeratome incision, in vivo confocal microscopy of rabbit corneas revealed numerous particles (up to 30 μm) at the interface, even though the flap had not been lifted.

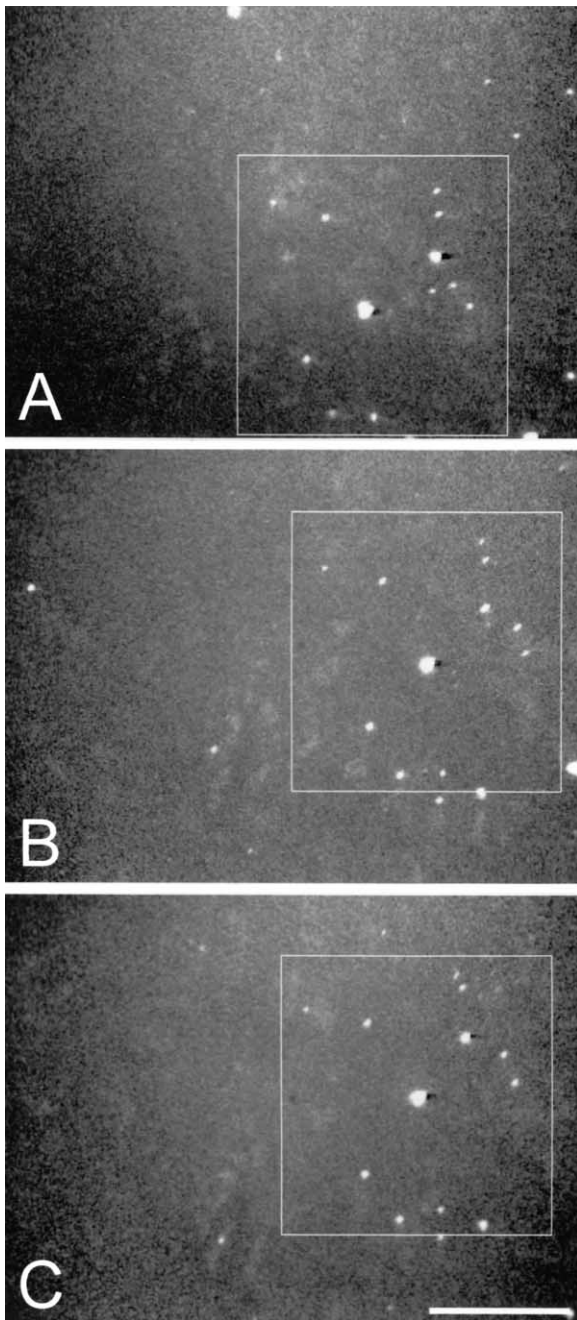


Figure 4. In vivo confocal microscopy of a rabbit cornea 1 month (A), 2 months (B), and 4 months (C) after microkeratome incision. No major changes in particle morphologic features, distribution, or density are observed over time (box delimits the same area in all images). Bar = 100 μm .

The morphologic features, distribution, and density of these particles remained unchanged throughout the 4-month observation period (Fig 4) and were similar to those observed in patients in the year after undergoing LASIK (Fig 3).

Using energy dispersive x-ray fluorescence spectroscopy, the microkeratome metal blade was found to consist of chromium-alloyed steel containing more than 85% iron, 13% chromium, and less than 2% of other elements (copper, nickel, manganese, and silicon). Atomic absorption spectrometry of 2 operated rabbit

corneas (total dry weight, 30.6 mg) showed an iron content of 10.1 μg per gram of tissue. This iron content was less than the 14.3 μg per gram detected in 2 unoperated corneas (total dry weight, 20.3 mg). Assuming that operated corneas contain an average of 8 spherical particles (with an average diameter of 3 μm) per field of view ($450 \times 340 \mu\text{m}$), the iron content attributable to metal particles in 1 cornea (9-mm diameter flap; 12.5 mg dry-weight) would be approximately 25 μg iron per gram of tissue. Thus, LASIK interface particles do not seem to be of metal origin.

On the unused microkeratome motor head and blade, only a few particles were observed using light or fluorescence microscopy. However, after oscillation in air for 2 full passes (simulating 1 test pass and 1 cut), numerous fluorescent particles were scattered over the microkeratome blade (Fig 5A, B), the number increasing with further oscillation. Interestingly, the only fluorescent part of the microkeratome blade and motor head was the plastic segment of the blade that showed the same fluorescent properties as the particles (Fig 5C, compare with Fig 5B). Using infrared spectroscopy, the plastic was shown to be polyetherimide. In histologic serial sections, interface particles could be identified and were observed to emit fluorescence identical to that of the plastic section on the microkeratome blade (Fig 5D, E, compare with Fig 5C). Using Coherent Antistokes Raman Scattering microscopy, these particles exhibited molecular resonance at 1780 and 3100 cm^{-1} (Fig 5F) and no resonance at 2400 cm^{-1} , in accordance with the Raman spectrum of polyetherimide.

Discussion

The present study demonstrates that plastic fragments are a major source of interface particles after LASIK. Numerous small plastic fragments (up to 30 μm) are generated by the oscillating microkeratome and introduced into the interface during surgery. The underlying mechanism may be related to: (1) mechanical interaction between the eccentric metal pin on the motor (Fig 6A, arrow) and the plastic groove on the microkeratome blade (Fig 6B, arrow); and (2) friction between this plastic and the blade housing of the motor head (Fig 6C, arrow). Thus, friction between the plastic and metal parts during high-speed oscillation (approximately 10,000 rpm) seems to generate plastic fragments that are scattered on the microkeratome. It should be noted that 2 separate but identical Supratome units were examined and yielded similar results. A comparable microkeratome design is currently used by other manufacturers, and reflective interface particles have been observed using other microkeratomes.⁶⁻⁸ Thus, it is likely that several types of microkeratomes may shed polymers (polyetherimide, Teflon [DuPont, Wilmington, DE], etc.) below the flap during LASIK.

The short-term and long-term clinical consequences of plastic particles at the interface are largely unknown. However, particles in the stromal bed can interfere with the excimer laser beam during photoablation, giving rise to irregularities in the tissue ablation profile. Interface particles also may disturb corneal wound healing, may cause toxic or allergic reactions, or may induce diffuse lamellar keratitis.⁴ Furthermore, interface particles may have direct visual consequences as a result of unwanted light scattering. Because plastic is not readily degraded in a biologic system, the fragments are likely to stay at the LASIK interface. Indeed, the present study demonstrates that the particles have the

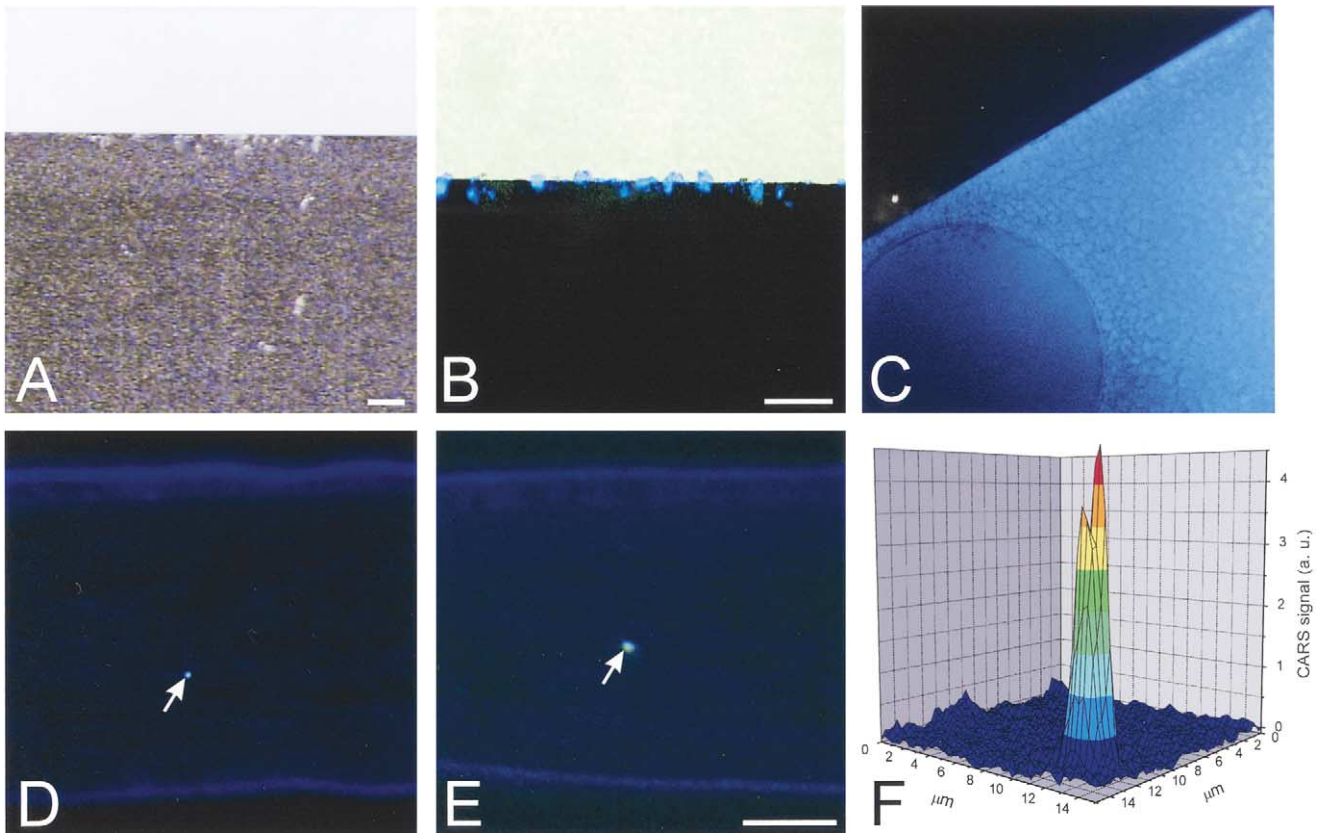


Figure 5. After oscillation in air, numerous particles are detected on the microkeratome blade using light (A) and fluorescence (B) microscopy. The only fluorescent part of the microkeratome blade and motor head is the plastic segment of the blade (C). This plastic emits fluorescence identical to that of the particles. Fluorescence microscopy of bright interface particles (D, E, arrows) in 2 rabbit corneas 4 months after the microkeratome incision. The particles show fluorescent properties similar to the plastic part of the microkeratome blade. Using Coherent Antistokes Raman Scattering microscopy (F) tuned to the prominent molecular resonance of polyetherimide at 3100 cm^{-1} , a strong signal is demonstrated from the interface particle (diameter approximately $3\ \mu\text{m}$) as compared with the surrounding cornea. Bars = $100\ \mu\text{m}$.

same morphologic features, distribution, and density during the first year after surgery. This observation is in accordance with a previous study that reported a constant density of interface particles for the first year after LASIK.⁷ Thus, any direct impact of the plastic fragments is not likely to disappear over time.

In summary, the current study demonstrates that thousands of small plastic fragments (up to $30\ \mu\text{m}$) are generated by the metal and plastic interaction inside the oscillating microkeratome. Such plastic particles are introduced into the LASIK interface, where they persist and may have direct consequences for the clinical and visual outcome.

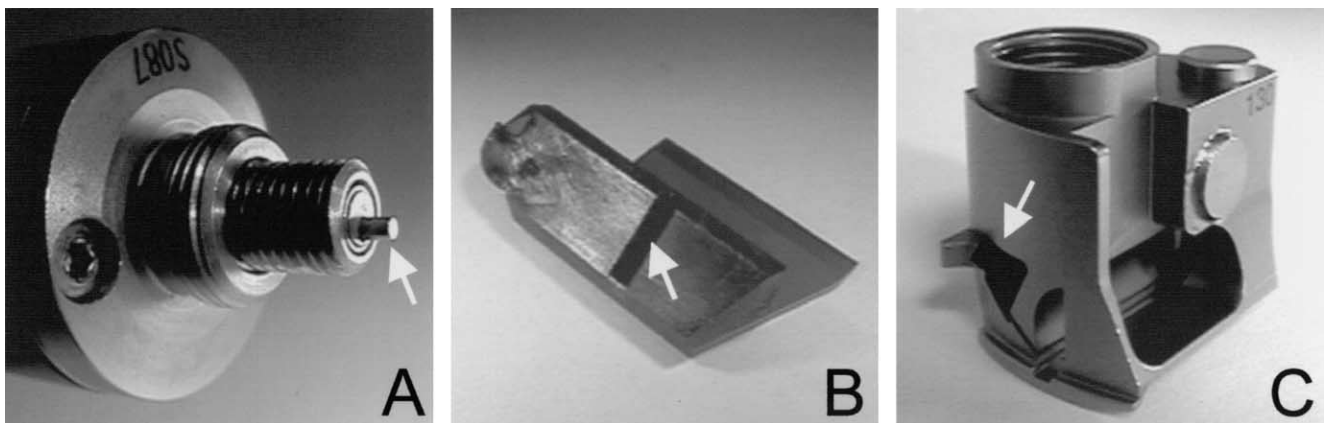


Figure 6. On the microkeratome motor (A), an eccentric metal pin (arrow) interacts with a groove (B, arrow) on the plastic part of the blade to generate oscillation. In the motor head (C), the blade housing (arrow) keeps the blade at a constant angle during oscillation.

Development of new microkeratomes should be encouraged.

Acknowledgments. The authors thank Lone Knudsen and H. C. Wulf, Bispebjerg Hospital, Copenhagen, Denmark, for assistance with Raman spectroscopy measurements.

References

1. Alió JL, Pérez-Santonja JJ, Tervo T, et al. Postoperative inflammation, microbial complications, and wound healing following laser in situ keratomileusis. *J Refract Surg* 2000;16:523–38.
2. Suarez C, Cardenas JJ. Intraoperative complications of LASIK. In: Burrato L, Brint SF, eds. *LASIK: Principles and Techniques*. Thorofare, NJ: Slack; 1998:371–81.
3. Vesaluoma M, Pérez-Santonja J, Petroll WM, et al. Corneal stromal changes induced by myopic LASIK. *Invest Ophthalmol Vis Sci* 2000;41:369–76.
4. Kaufman SC, Maitchouk DY, Chiou AG, Beuerman RW. Interface inflammation after laser in situ keratomileusis: Sands of the Sahara syndrome. *J Cataract Refract Surg* 1998;24:1589–93.
5. Slowik C, Somodi S, Richter A, Guthoff R. Assessment of corneal alterations following laser in situ keratomileusis by confocal slit scanning microscopy. *Ger J Ophthalmol* 1996;5:526–31.
6. Pisella PJ, Auzeir O, Bokobza Y, et al. Evaluation of corneal stromal changes in vivo after laser in situ keratomileusis with confocal microscopy. *Ophthalmology* 2001;108:1744–50.
7. Mitooka K, Ramirez M, Maguire LJ, et al. Keratocyte density of central human cornea after laser in situ keratomileusis. *Am J Ophthalmol* 2002;133:307–14.
8. Bühren J, Baumeister M, Kohnen T. Diffuse lamellar keratitis after laser in situ keratomileusis imaged by confocal microscopy. *Ophthalmology* 2001;108:1075–81.
9. Gokmen F, Jester JV, Petroll WM, et al. In vivo confocal microscopy through-focusing to measure corneal flap thickness after laser in situ keratomileusis. *J Cataract Refract Surg* 2002;28:962–70.
10. Ivarsen A, Stultiens BA, Møller-Pedersen T. Validation of confocal microscopy through focusing for corneal sublayer pachymetry. *Cornea* 2002;21:700–4.
11. Ivarsen A, Laurberg T, Møller-Pedersen T. Characterization of corneal fibrotic wound repair at the LASIK flap margin. *Br J Ophthalmol* 2003;87:1272–8.
12. Volkmer A, Chen JX, Xie XS. Vibrational imaging with high sensitivity via epidetected coherent anti-stokes Raman scattering microscopy. *Phys Rev Lett* 2001;87(2):023901.