

Researchers report benefits of femtosecond laser flap LASIK

By Cheryl Guttman
in London

LASIK performed with the femtosecond laser (IntraLase) or mechanical microkeratomes continues to be a topic of great interest for refractive surgeons trying to identify which technique yields the best clinical results.

A series of independent investigators described the results of head-to-head studies comparing outcomes with refractive laser surgery and the femtosecond laser and various conventional microkeratomes, at the XXIV Congress of the ESCRS.

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Steve Schallhorn MD

Steve Schallhorn MD and colleagues at the Naval Medical Center, San Diego, California launched a study in 2004 to evaluate outcomes after wavefront-guided CustomVue LASIK (Visx/AMO) using three different microkeratomes – the 15 kHz femtosecond laser (IntraLase), the Amadeus (AMO), and the Hansatome (Bausch &

Lomb). The results of an updated analysis comparing the femtosecond laser group with the pooled mechanical microkeratome cohorts showed that eyes with a femtosecond laser flap had more visual symptoms on the first day after surgery, but benefited with faster visual recovery as well as better uncorrected visual acuity (UCVA) and contrast acuity outcomes at three months after surgery.

“Faster visual recovery is a prime advantage of LASIK over other laser vision correction procedures. The enhanced visual recovery achieved using the femtosecond

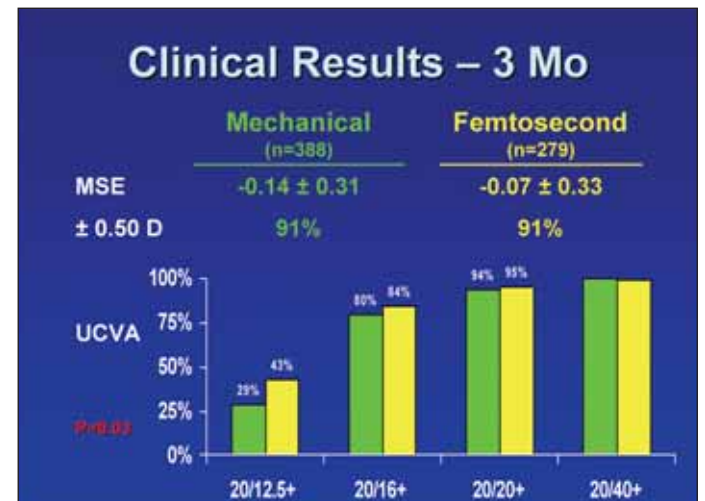
laser is even more compelling especially when coupled with improved contrast sensitivity,” commented Dr Schallhorn.

The current analysis was based on 436 eyes of 220 patients who had flaps created with a mechanical microkeratome and 298 eyes of 149 patients who had surgery with a femtosecond laser flap. Dr Schallhorn and

David J Tanzer MD performed all of the surgeries.

Patients treated with the mechanical microkeratome or the femtosecond laser were similar pre-operatively with respect to mean age (33 vs. 31 years), mean sphere (-2.71 vs. -2.51 D), mean cylinder (-0.73 vs. -0.70 D), and mean MSE (-3.07 vs. -2.86 D).

On the first day after surgery, photophobia was rated as absent or trace for 94 per cent of 249 eyes evaluated in the mechanical microkeratome group compared with only 75 per cent of 199 femtosecond laser flap eyes evaluated. In the mechanical microkeratome group, cases of more significant photophobia were mostly mild; rates of moderate or severe photophobia were each under one per cent. However, among the patients who had a femtosecond laser flap, 8.5 per cent of patients reported moderate photophobia and 2 per cent complained of severe symptoms. The difference in the outcomes between the mechanical microkeratome and femtosecond laser groups was statistically significant.



Courtesy of Steve Schallhorn MD

“It is likely that newer generations of the femtosecond laser with higher repetition rates and lower per-pulse energy will reduce, or perhaps eliminate, the differences in symptoms noted in this study,” Dr Schallhorn said.

The researchers analysed data on UCVA at one month for 346 eyes in the mechanical microkeratome group and for 240 eyes in the femtosecond laser group. This revealed a significant difference favouring the femtosecond laser. Mean UCVA was 20/20 or better in 82 per cent of eyes with a conventional flap compared with 89 per cent of eyes with a femtosecond laser flap.

A greater separation of the two techniques was seen when analysing

The search for the ultimate flap

In a keynote address, John Marshall, PhD, King's College London, UK, suggested that considering the consequences of epithelial injury and flap creation on corneal wound healing responses and biomechanics, a thin flap cut below Bowman's layer using a femtosecond laser represents the “ultimate flap” for laser refractive surgery procedures.

Dr Marshall holds the original patents for excimer laser refractive surgery. Based on his premise that good science sustains attack, he has continued with research over the years to identify shortcomings of the various refractive procedures, the mechanisms underlying their limitations, and superior alternatives. Based on those investigations, Dr Marshall said induction of a wound-healing response and alterations in corneal biomechanics represent the two major outcome-limiting factors for laser vision correction procedures.

He explained that PRK simultaneously wounds the corneal epithelium and the stromal keratocytes and thereby initiates crosstalk between those two cell types that results in haze and atypical healing responses. By contrast, because LASIK damages only the keratocytes, wound healing effects and haze are minimal. However, creation of the LASIK microkeratome flap affects the biomechanical integrity of the cornea and results in long-term instability that manifests clinically with onset of refractive change beginning 2.5 to three years after surgery.

“Our follow-up of the initial cohorts of PRK-treated eyes shows that while there is a transient loss of transparency after that surface procedure, it is associated with corneal

biomechanical stability and unchanged refraction for up to 14.5 years,” Dr Marshall said.

In LASEK and epiLASIK, the cleaved epithelium remains intact. Nevertheless, stripping of the basal epithelial cells from Bowman's layer results in micro-damage that initiates a wound healing response just as in PRK, he explained.

“Collectively, these findings suggest that the ideal flap is one cut to about 80 to 90 microns in depth such that it is about 40 microns below Bowman's layer. With those characteristics it would provide the best of both worlds by avoiding epithelial damage and causing minimal interference with the stroma. As a result, it would be like LASIK with respect to absence of a wound-healing response while offering the biomechanical stability of a PRK procedure. However, only the femtosecond laser allows creation of the desired flap that is predictably thin across its entire profile,” Dr Marshall said.

Dr Marshall and colleagues, Philip Jaycock, Nathaniel Knox Cartwright, and John Tyrer have tested that hypothesis in the laboratory. In collaboration with mechanical engineers, they have developed a technique for evaluating corneal biomechanics that uses electronic speckle pattern interferometry to monitor changes in biological tissue under stress. Results from strain mapping demonstrated that the biomechanical changes following the thin flap procedure were virtually indistinguishable from those in eyes undergoing PRK.

Using a living human cornea model to investigate the effects of surgery “in vivo”, they performed wound healing studies to investigate the possibility that acoustic transients generated during the femtosecond laser procedure might still cause epithelial damage. Those experiments demonstrated absence of epithelial damage when femtosecond laser cuts were made at a level 40 microns below Bowman's layer, Dr Marshall reported.



Steve Schallhorn



Edward E Manche



Karl G Stonecipher



John Marshall

outcomes for higher acuity levels. In the femtosecond laser group 72 per cent achieved UCVA of 20/16 or better and 27 per cent were able to see 20/12.5 or better; corresponding rates for those outcomes in the mechanical microkeratome group were 51 per cent and 10 per cent, respectively. Mean MSE was -0.03 D in the mechanical keratome group and -0.08 D in the femtosecond laser group.

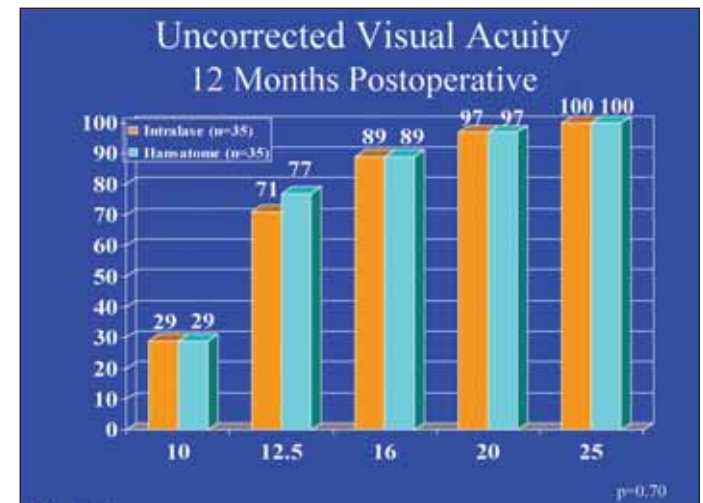
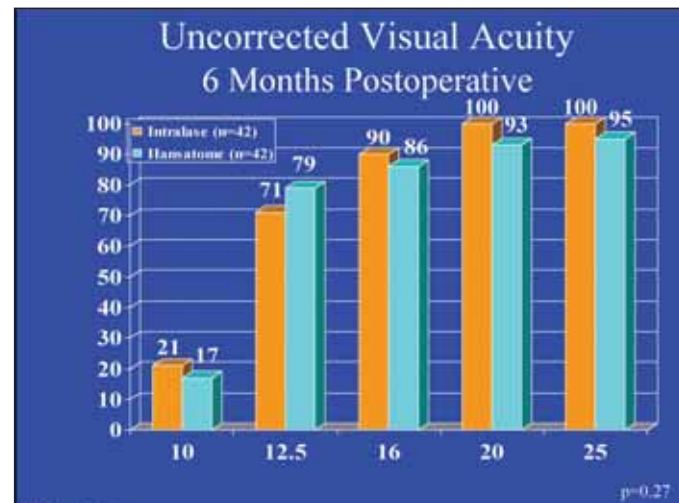
The significant difference favouring the femtosecond laser for a better visual outcome was maintained at three months. At that visit UCVA had improved in both groups so that about 95 per cent of eyes achieved UCVA of 20/20 or better regardless of the type of microkeratome used. However, 43 per cent of eyes with a femtosecond laser flap and 29 per cent of those with a mechanical microkeratome flap had UCVA of 20/12.5 or better. Mean MSE at this visit was -0.14 D in the mechanical microkeratome group and -0.07 D in the femtosecond laser group and 91 per cent of eyes were corrected to within 0.50 D of the intended refraction.

Femto appears to produce better quality flap

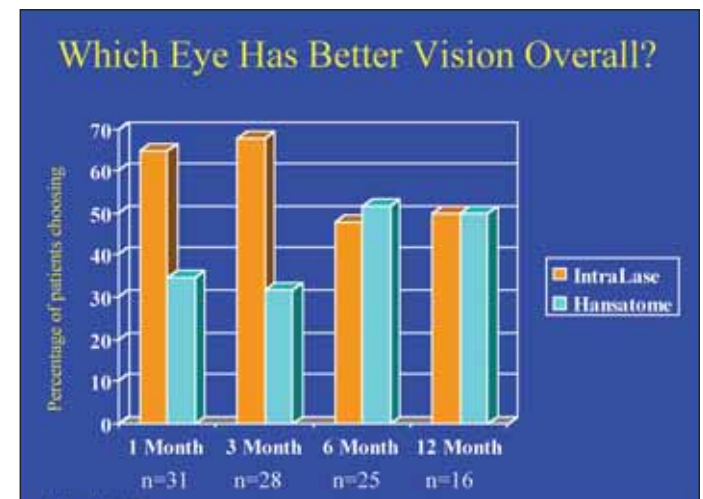
"We also did a paired analysis of 296 mechanical microkeratome eyes and 223 femtosecond laser eyes that had an MSE within the range of -0.25 to +0.50 D to determine if a simple difference in refractive outcome could explain the better UCVA of the femtosecond laser, but the significant difference between groups persisted as a result of a higher proportion of femtosecond laser eyes achieving 20/12.5 or better UCVA compared with the mechanical microkeratome group, 49 per cent vs. 35 per cent respectively. Therefore, the superior UCVA in the femtosecond group was not simply because of postop refractive differences, but is likely due to some inherently better quality of the flap," Dr Schallhorn said.

Low contrast acuity (LCA) testing was performed under photopic (five per cent) and mesopic (25 per cent) conditions. For both studies, a significantly higher proportion of eyes in the mechanical microkeratome group compared with the femtosecond laser group lost two or more lines. For photopic LCA, the loss rate was nearly twofold higher in the mechanical microkeratome group compared with the femtosecond laser group, 5.5 per cent vs. 2.9 per cent, and there was a threefold higher rate of loss of two or more lines in mesopic LCA testing, 3.1 per cent vs. 1.1 per cent.

At Stanford University School of Medicine, Stanford, CA, Edward E Manche MD, conducted a prospective trial that randomised 100 eyes of 50 subjects to CustomVue LASIK (Visx/AMO) with a 110 micron femtosecond laser flap in one eye



	IntraLase	Hansatome
1M Sphere	-0.23 ± 0.30	-0.24 ± 0.28
1M Cylinder	0.16 ± 0.22	0.24 ± 0.25
1M SEQ	-0.15 ± 0.30	-0.12 ± 0.29
3M Sphere	-0.29 ± 0.30	-0.30 ± 0.32
3M Cylinder	0.18 ± 0.25	0.29 ± 0.25
3M SEQ	-0.20 ± 0.29	-0.16 ± 0.34
6M Sphere	-0.36 ± 0.24	-0.30 ± 0.26
6M Cylinder	0.20 ± 0.23	0.24 ± 0.29
6M SEQ	-0.26 ± 0.25	-0.18 ± 0.30
12M Sphere	-0.42 ± 0.26	-0.31 ± 0.31
12M Cylinder	0.22 ± 0.21	0.21 ± 0.25
12M SEQ	-0.32 ± 0.25	-0.22 ± 0.32



and a 160 micron flap created with the Hansatome microkeratome in the fellow eye. The two groups were nearly identically matched with respect to mean refraction (SE

(through three to six months) as well as a strong patient preference for the femtosecond laser-treated eyes. However, those differences disappeared as follow-up

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Edward E Manche MD

-3.76 D, cylinder +0.45 D) and wavefront data (higher order RMS 0.34 microns). Some 43 patients were seen at six months and 35 patients had reached the one-year visit. The results over time showed that there were statistically and clinically significant differences favouring the femtosecond laser eye in a number of vision outcomes in the early postoperative period

continued, and by one year, all clinical outcomes were identical in both groups. "The advantages observed in the femtosecond laser eyes are most likely a result of the uniform architecture of the femtosecond laser flap that resulted in less induced cylinder and higher order aberrations. The reason why the differences disappear by one year is likely related to

remodelling of the corneal epithelium," Dr Manche said. The Fourier software upgrade was used for the ablations beginning with the ninth patient in the series. For procedures done prior to that, a nomogram adjustment was used only in the mechanical microkeratome eyes as an offset for undercorrection. Flap analysis showed the femtosecond laser created flaps of more accurate and more reproducible thickness (mean ± SD 119.1 ± 18.1 microns) compared with the mechanical microkeratome (137.3 ± 21.2 microns). "In contrast to mechanical microkeratomes, flap dimensions achieved using the femtosecond laser are independent of pre-operative parameters such as keratometry and corneal thickness," noted Dr Manche. Uncorrected visual acuity was excellent in both groups beginning at day one, but there was a trend favouring the IntraLASIK eyes for better vision at one month when 86 per cent of eyes in that group achieved 20/12.5

or better UCVA compared with 74 per cent of those having a mechanical microkeratome flap. In addition, twice as many IntraLASIK eyes compared to Hansatome eyes had postoperative UCVA superior to their pre-operative BCVA at one month, 33 per cent vs. 16 per cent, respectively.

At six months, more IntraLase than Hansatome eyes had achieved UCVA of 20/16 or better, 79 per cent vs. 71 per cent. The proportion of eyes with a gain in postoperative UCVA compared with pre-op BCVA was still twice as high in the IntraLASIK vs. Hansatome group, 26 per cent vs. 14 per cent. At one year, UCVA outcomes were similar in the two groups.

At follow-up from one month to 12 months, postop BCVA was improved from pre-operative levels in between 41 per cent and 50 per cent of IntraLASIK eyes versus in only 28 per cent to 39 per cent of Hansatome eyes. The biggest difference between the groups was seen at one month when there was a 0.41 average line gain in the IntraLase eyes and a 0.17 line gain in the Hansatome eyes. The average gain at one year remained the same in the IntraLase eyes and had increased slightly to 0.26 lines in the Hansatome eyes.

Patients underwent contrast acuity testing under photopic and mesopic conditions. In both studies, there was an early average improvement in the IntraLase eyes and a slight loss in the Hansatome eyes. However, at 12 months, both groups of eyes had a slight average gain.

"In photopic testing, the IntraLase eyes gained 1.5 letters by three months and two letters by six months, while at 12 months, both groups had a half letter gain. Other studies have also reported a similar pattern where the mechanical microkeratome group catches up over time. Perhaps that reflects a wound healing effect," Dr Manche said.

Predictability was excellent in both groups and refractive stability was similar as well. However, residual cylinder was significantly less in the IntraLase eyes through six months, and the difference was statistically significant through three months.

"Other investigators have also noted an advantage of the IntraLase procedure for reducing postoperative cylinder," Dr Manche said.

At 12 months, total higher order aberrations had increased slightly in both groups (≤ 0.07 microns) with both showing slight increases in coma and spherical aberration and a decrease in trefoil. There were no statistically significant differences between groups in any of those measures.

Patients were also asked at each visit if they preferred the vision in either eye. The number of patients who noticed an inter-eye difference decreased over time, as did an initial preference for the IntraLase eye.



Reducing retreatments

Karl G Stonecipher MD, a private practitioner in Greensboro, NC, also reported results favouring the femtosecond laser flap. His primary analysis considered enhancement rates for two groups of eyes undergoing wavefront-optimised LASIK with the Allegretto Wave excimer laser (Wavelight). Among 13,721 procedures he performed with a mechanical microkeratome, he had 572 enhancements (4.17 per cent). There were 91 (1.73 per cent) enhancements among 5,258 eyes having a femtosecond laser flap, representing an almost 60 per cent reduction in the re-operation rate.

"The femtosecond laser results in a better fit when it is replaced. As we and several others have demonstrated, that feature translates into significantly better outcomes in terms of both induced higher order aberrations and astigmatism compared with procedures performed with a mechanical microkeratome"

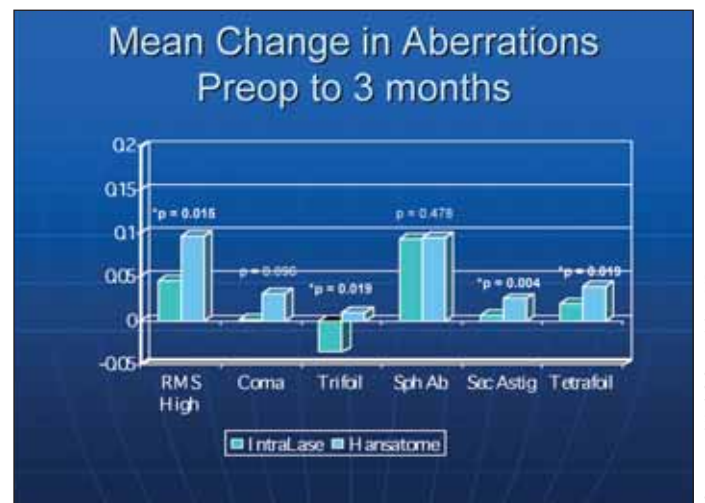
"It was clear from another analysis I did of enhancement rates using data from 92 surgeons that better lasers have made us better surgeons, and I suspected based on reports from other refractive surgeons and the characteristics of the femtosecond laser flap, that IntraLASIK had an advantage for achieving better outcomes to reduce enhancement rates compared with a mechanical microkeratome. However, it was important to investigate that hypothesis using the cleanest dataset possible, and that is described by this series of cases performed by a single surgeon using the same laser and the same ablation technique with the flap creation device being the only variable," explained Dr Stonecipher.

A second analysis considered one-year results from the first FDA trial of the Allegretto Wave laser using the wavefront-optimised ablation profile and the second FDA trial comparing the wavefront-optimised and wavefront-guided techniques. In the first study, all surgeries were performed with a mechanical microkeratome whereas in the second study all of the surgeons used the femtosecond laser keratome. Including only patients who had wavefront-optimised LASIK, the enhancement rate was 3.8 per cent among 585 eyes in the first FDA trial using the mechanical keratome, whereas none of 332 patients who had an IntraLASIK procedure had been enhanced by one year.

Karl G Stonecipher MD

Dr Stonecipher cited differences in bed smoothness and flap architecture as the factors accounting for better outcomes in the IntraLASIK groups. Whereas the femtosecond laser has always performed well in creating flaps of reproducible thickness, thickness variability of mechanical microkeratome flaps has been reduced with improvements in that technology. However, the femtosecond laser still uniquely creates a planar flap that is uniformly thick across, whereas the mechanical microkeratome flaps are meniscus-shaped and exhibit marked regional variability in thickness.

"The femtosecond laser flap results in a better fit when it is replaced. As we and several others have demonstrated, that feature translates into significantly better



outcomes in terms of both induced higher order aberrations and astigmatism compared with procedures performed with a mechanical microkeratome. Ultimately, those benefits can be measured by lower enhancement rates," Dr Stonecipher said.

Dr Stonecipher also analysed his personal data to see if advances in femtosecond laser technology have resulted in improved outcomes. Considering eyes operated on with the 10, 15, or 30 kHz femtosecond lasers that had at least one year of follow-up, the enhancement rate for all eyes combined was 1.78 per cent. The enhancement rate was reduced by about 30 per cent, to 1.2 per cent, for the subgroup that had flap creation with the 30 kHz femtosecond laser.

Noting that the total group includes both wavefront-optimised procedures with the Allegretto Wave laser and wavefront-guided CustomVue LASIK, Dr Stonecipher also analysed outcomes for the CustomVue group alone and showed the enhancement rate was similar to the entire group at 1.8 per cent.

"These results tell me that it is all about speed. Ask a bull rider what eight seconds feels like and he'll tell you it's a long time. Flap creation took over 60 seconds using the original 10 kHz femtosecond laser, was reduced to under 30 seconds with the 30 kHz device, and with the fourth generation 60 kHz laser, the procedure is done in about 16 seconds. I believe that as the procedural time is reduced, so is the energy applied to the bed, which could translate into reduced postoperative inflammation with improved healing and therefore fewer enhancements," Dr Stonecipher said.

Dr Stonecipher is currently using the 60 kHz laser. He did not include that data in his analyses because one-year follow-up for those procedures is not yet available.

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