



Modern laser in situ keratomileusis outcomes

Helga P. Sandoval, MD, MSCR, Eric D. Donnenfeld, MD, Thomas Kohlen, MD, PhD, FEBO, Richard L. Lindstrom, MD, Richard Potvin, OD, David M. Tremblay, MD, Kerry D. Solomon, MD

Laser in situ keratomileusis (LASIK) articles published between 2008 and 2015 that contain clinical outcomes data were reviewed and graded for quality, impression, and potential bias. All 97 relevant articles (representing 67 893 eyes) provided a positive or neutral impression of LASIK. Industry bias was not evident. The aggregate loss of 2 or more lines of corrected distance visual acuity was 0.61% (359/58 653). The overall percentage of eyes with uncorrected distance visual acuity better than 20/40 was 99.5% (59 503/59 825). The spherical equivalent refraction was within ± 1.0 diopter (D) of the target refraction in 98.6% (59 476/60 329) of eyes, with 90.9% (59 954/65 974) within ± 0.5 D. In studies reporting patient satisfaction, 1.2% (129/9726) of patients were dissatisfied with LASIK. Aggregate outcomes appear better than those reported in summaries of the safety and effectiveness of earlier laser refractive surgery systems approved by the U.S. Food and Drug Administration. Modern results support the safety, efficacy, and patient satisfaction of the procedure.

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Laser in situ keratomileusis (LASIK) is one of the most commonly performed elective procedures in the United States. To date, more than 16 million LASIK procedures

have been performed globally.¹ Laser in situ keratomileusis was introduced by Pallikaris et al.² in 1990. The excimer laser was approved by the U.S. Food and Drug Administration (FDA) in 1995, and LASIK was approved by the FDA in 1999.

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From Carolina Eyecare Physicians, LLC (Sandoval, Solomon, Tremblay), Mount Pleasant, South Carolina, Ophthalmic Consultants of Long Island (Donnenfeld), Long Island, New York, Minnesota Eye Consultants, P.A. (Lindstrom), Minneapolis, Minnesota, and Science in Vision (Potvin), Akron, New York, USA; the Department of Ophthalmology (Kohlen), Goethe University, Frankfurt, Germany.

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Corresponding author: Kerry D. Solomon, MD, Carolina Eyecare Physicians, LLC, 1101 Clarity Road, Suite 100, Mount Pleasant, South Carolina 29464, USA. E-mail: kerry.solomon@carolinaeyecare.com.

Patient selection, an important factor in LASIK success, has improved greatly over the past 2 decades. Candidacy criteria include sufficient corneal bed thickness following flap formation and corneal ablation, a healthy tear film, and the presence of a regular corneal topography.³ Results in numerous studies have shown good efficacy, safety, stability, and predictability in treating both myopia and hyperopia with or without astigmatism.^{4–7}

An analysis of early outcomes data from 1994 to 2004⁸ documented the complications associated with LASIK. Most were related to the use of early microkeratomes, excimer laser ablation profiles, and surgeon experience. An FDA panel meeting was held in 2008 in response to 140 dissatisfied LASIK patients to reevaluate the procedure. As a result of the panel, a comprehensive literature review of patient satisfaction was conducted in 2008. Results showed high patient satisfaction; approximately 95% of patients were satisfied with their visual outcome after myopic and hyperopic LASIK.¹

In October 2009, the FDA instituted the LASIK Quality of Life Collaboration Project. Two major components of this project were the first FDA-initiated clinical studies of LASIK, the Patient Reported Outcomes with LASIK (PROWL) studies.^A PROWL-1 and PROWL-2 were primarily concerned with the development and testing of a validated questionnaire to capture patient's perceptions of LASIK and the percentage of patients having difficulty after surgery. However, by necessity, the studies also included clinical outcomes data. The PROWL-1 trial was conducted by a single Naval refractive surgeon, and the PROWL-2 trial was conducted by 5 refractive surgeons in clinical practice. Industry and organized ophthalmology were not involved in the study design or the evaluation of data.

The results of the PROWL-1 and PROWL-2 trials are considered the most definitive evaluation of the efficacy of LASIK and will be highlighted and compared with studies in the peer-reviewed literature. The results of the LASIK Quality of Life Collaboration Project were presented at the American Academy of Ophthalmology in 2014 by Malvina Eydeman, MD, Director, Division of Ophthalmic and Ear, Nose and Throat Devices of the FDA.^B Questionnaire components included vision quality, symptoms of aberration (glare, halos, starbursts, ghosting), work productivity, dry-eye symptoms, depressive/anxiety symptoms, optimism, coping, expectations prior to surgery, satisfaction after surgery, and social desirability. A total of 534 patients had LASIK surgery and were followed for 6 months postoperatively.

The purpose of this review was to summarize the objective clinical outcomes of LASIK reported in the peer-reviewed literature between 2008 and 2015 and to compare these data with historical summaries of the safety and effectiveness associated with laser systems approved for use by the FDA, as well as with the results of the PROWL studies in which comparative data were available.

MATERIALS AND METHODS

A search for relevant articles related to the clinical outcomes of standard LASIK was conducted using the online search engine PubMed Central, a free full-text archive of biomedical and life-science journal literature at the U.S. National Institutes of Health's National Library of Medicine.^C The search was limited to articles published from January 2008 to August 2015. Three keywords were used to search for articles: "LASIK," "laser in situ keratomileusis," and "laser vision correction." Of interest were articles that included human clinical studies, reported primary procedures, and included visual and refractive outcomes. Articles related to retreatment, presbyopia treatment, or treatment in eyes that had previous corneal surgery (eg, radial keratometry) or any intraocular surgery (eg, cataract surgery) were not included.

Abstracts from the identified articles were reviewed to determine whether they met the above criteria. Full copies of all potentially relevant articles were then obtained for

more detailed review. Non-English articles were translated with the collaboration of the American Society of Cataract and Refractive Surgery. After article review, relevant articles were specifically identified. The references of the reviewed articles were examined to identify potential articles that might have been missed.

All relevant articles were rated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE)^D as well as the University of Michigan Practice Guidelines.^E The GRADE scoring considered study size and financial interest disclosures in evaluating the quality of the evidence. The Michigan guidelines included considerations such as whether the study was prospective or retrospective, randomized or nonrandomized. The financial interest categorization does not imply that sponsored studies are lower quality than independent research but is included to acknowledge the potential for bias in clinical outcomes. An article was rated "high" if it fulfilled both the A criteria in the University of Michigan Practice Guidelines and the definition of "high" in the GRADE system. Similarly, B and "moderate," C and "low," and D and "very low" from the University of Michigan Practice Guidelines and the GRADE rating systems, respectively, were also used to rate each article. The final grade was the lower rank from the 2 grading systems.

Additional characteristics of relevant articles were recorded. Each was subjectively reviewed for the impression they left with the reader—"positive," "neutral," or "negative"—with regard to the clinical outcomes of LASIK. Financial interest was specifically identified.

The clinical outcomes in each article were then summarized. If results from different test groups were included in an article, the groups were analyzed separately. Characteristics such as the nature of the treatment (ie, myopia, astigmatism, hyperopia), the treatment profile (eg, conventional, wavefront guided, wavefront optimized, topography guided), the laser system, and the flap creation method were recorded. Relevant preoperative and postoperative clinical outcomes were recorded when provided. Of most interest were the refractive data, the uncorrected and corrected visual acuities, and the loss or gain of lines of corrected acuity. If reported, complications and satisfaction data were also tabulated.

The aggregate data from these articles were compared with historical data from several available summaries of safety and effectiveness for various laser systems when they were approved for use by the FDA, including the Summit Apex laser system,^F the Visx Star S2 laser system,^G and the Wavelight Allegretto laser system,^H as well as with the results of the PROWL studies.

Each article was catalogued in an Access database (Microsoft Corp.) specifically designed for the purpose. Clinical data associated with each subgroup in an article were recorded in the same database. Because the raw data for all articles were not available, the analyses were limited to comparing means of means (eg, mean postoperative refractive error by group) or critical values (eg, percentage of 20/20 uncorrected visual acuity by group).

Statistical analysis of continuous variables was performed using analysis of variance (ANOVA), and categorical data were analyzed using appropriate nonparametric tests. Statistical significance was set at a *P* value of 0.05.

LITERATURE REVIEW

The PubMed search yielded 4474 potential articles, with 2189 related to the term "LASIK," 2007 related

Table 1. Study summary by impression and quality.

Impression	Study Quality				Total
	High	Moderate	Low	Very Low	
Positive	42	25	4	—	71
Neutral	6	17	3	—	26

to the term “laser in situ keratomileusis,” and 269 related to the term “laser vision correction.” The subsequent abstract review reduced the number of potentially relevant references to 213. A review of each of these identified 97 that were considered relevant.

Table 1 summarizes the relevant articles by the impression they provided and the quality of the study on which they were based. There were no peer-reviewed articles with a negative impression of LASIK; 73% (71/97) of studies had a positive impression and 27% (26/97), a neutral impression. A comparison of the ratio of high/moderate to low/very low studies by impression showed that there was no statistically significant difference in subjective impression by study quality ($P = .38$, 2-tailed Fisher exact test).

In 34% (33/97) of the articles, the authors reported a financial interest relative to the laser or procedure being tested; in 55% (53/97), the authors were independent; in 5% (5/97), neither an affiliation nor a financial interest was stated; and in 6% (6/97), there were non-company sources of funding. Comparing the ratio of positive studies to neutral studies by financial interest (affiliated or not affiliated) showed no statistically significant difference in results ($P = .49$, 1-tailed Fisher exact test).

Clinical data specific to LASIK study arms in each of the articles were tabulated. Comparative study groups using other technology (ie, implanted intraocular lenses, surface ablation) were not included. Of the 97 articles, 58 included only 1 study arm; 5 of these articles included data from several timepoints but only the latest follow-up time was included in the analysis. The

Table 2. Studies by type of refractive correction.

Preoperative Prescription	Study Arm Size				Eyes
	Total	Large	Medium	Small	
Myopia (with/without astigmatism)	128	8	44	76	66 047
Hyperopia (with/without astigmatism)	12	—	4	8	1738
Mixed astigmatism	1	—	—	1	48
Unspecified	2	—	—	2	60

remaining articles included 2 (33 studies), 3 (5 studies), and 4 (1 study) study arms. A total of 143 study arms, representing 67 893 eyes, were available for specific analysis of outcomes. Study arms varied significantly in size, from a maximum of 32 569 eyes (48% of the total) to a minimum of 10 eyes. Study arms were categorized by size for comparative purposes; large study arms had 1000 or more eyes (8 study arms); medium study arms, 100 to 999 eyes (48 study arms); and small study arms, fewer than 100 eyes (87 study arms). Table 2 summarizes the articles by the nature of the planned correction and the study arm size. Correction of myopic astigmatism accounted for 90% (128/143) of all articles and 97.3% (66 047/67 893) of all eyes. To simplify, categorization in this analysis is by article and 143 articles were identified based on the above criteria.

A large number of excimer laser systems and microkeratomes are represented in the data collected. Specific laser system data were not always available, but when the system was unspecified, it was grouped by laser manufacturer or family (eg, Allegretto). Using this categorization, 30 laser systems were identified. A similar methodology was used for the microkeratomes, including femtosecond laser systems. A total of 26 systems were identified. Table 3 contains the 7 most common excimer laser systems and the 6 most common microkeratome and femtosecond laser systems. These specific combinations represented 40%

Table 3. Most common laser/keratome combinations.

Laser Group	Total Articles (Eyes)	Moria Evo3 One Use-Plus	Ziemer LDV				Ziemer LDV		
			Intralase	Moria M2	Visumax	Crystal Line	Multiple	Other	
Visx Star S4	31 (38 199)	2 (33 569)	—	10 (2037)	4 (1154)	—	—	3 (399)	12 (1040)
Tecnolas 217z	27 (1873)	—	—	—	—	—	—	3 (389)	24 (1484)
Allegretto Eye-Q 400	20 (6222)	—	—	8 (2797)	—	2 (426)	1 (887)	3 (1699)	6 (405)
Schwind Amaris	14 (13 082)	—	7 (11 230)	3 (133)	1 (31)	—	1 (1280)	1 (358)	1 (50)
Schwind Esiris	8 (525)	—	—	1 (72)	1 (72)	—	—	—	6 (381)
Mel 80	6 (1557)	—	—	—	—	5 (1453)	—	—	1 (104)
Nidek CXIII	5 (731)	—	—	—	1 (74)	—	—	—	4 (657)
Other (eg, unspecified)	31 (5712)	—	1 (0)	—	8 (0)	2 (282)	—	2 (82)	18 (4642)
Total	—	2 (33 769)	8 (11 230)	22 (5059)	15 (1331)	9 (2161)	2 (2653)	12 (2927)	72 (8763)

Table 4. Articles and number of eyes by ablation profile.

Treatment Category	Treatment Type	Number of Articles	Eyes
Conventional	Conventional	26	2492
Advanced	Wavefront guided	49	39880
	Wavefront optimized	20	4512
	Topography guided	5	2959
Other	Other	34	15308
	Not specified	9	2742
Total	—	143	67893

(57/143) of the articles and 85% (58 099/67 893) of the eyes in the data set.

The laser systems were used to create a variety of profiles in the eye. The profiles were categorized as “conventional” for standard treatment; “advanced treatment profile” for treatments that involved wavefront-guided, wavefront-optimized, or topography-guided treatments; and “other” when the treatment was neither conventional nor advanced or the ablation profile was not specifically identified. Table 4 summarizes the articles by ablation profile.

Loss or Gain of Corrected Distance Visual Acuity

The loss or gain of corrected distance visual acuity (CDVA) was reported in 64% of the articles (92/143), comprising 86.4% of all eyes (58 653/67 893). In most eyes, there was no measured change in CDVA. In aggregate, more than twice as many eyes gained 2 or more lines of CDVA (1.45%, 853/58 653) as lost 2 or more lines (0.61%, 359/58 653). In the PROWL-1

study, 1/450 eyes (0.2%) lost 2 lines of visual acuity and had a CDVA of 20/25. In the PROWL-2 study, 0/540 eyes lost 2 lines of CDVA.

From the point of view of safety, the percentage of eyes that lost 2 or more lines of CDVA, a required measure in any submission for FDA approval, was significant. Figure 1 shows the aggregate percentage of eyes that lost 2 or more lines of CDVA by treatment type (conventional, advanced, and other) in the peer-reviewed literature, along with the reported losses from the summaries of safety and effectiveness data of several approved laser systems. In the peer-reviewed literature, there was a statistically significant difference in the reported losses of 2 or more lines of CDVA by treatment type ($P < .01$, ANOVA). The percentage of eyes with a loss of 2 or more lines was statistically significantly lower in the advanced group than in the conventional group (0.6% versus 0.94%; $P < .03$, Tukey honest significant difference test). The results appear consistent with the results in the PROWL studies, in which a rate of 0.44% (1/225) was reported in PROWL-1 and a rate of 0% (0/540) was reported in PROWL-2.^A

Although several studies accounted for most eyes in the peer-reviewed literature, the loss of 2 or more lines of CDVA was uniformly low in all studies. Figure 2 shows the distribution of the percentages of eyes in each study that lost 2 or more lines of CDVA categorized by treatment type. More than half of all articles and 82% (42/51) of the advanced treatment articles reported no loss of 2 or more lines of CDVA. Also shown is the nominal indicator of safety used by the FDA, a

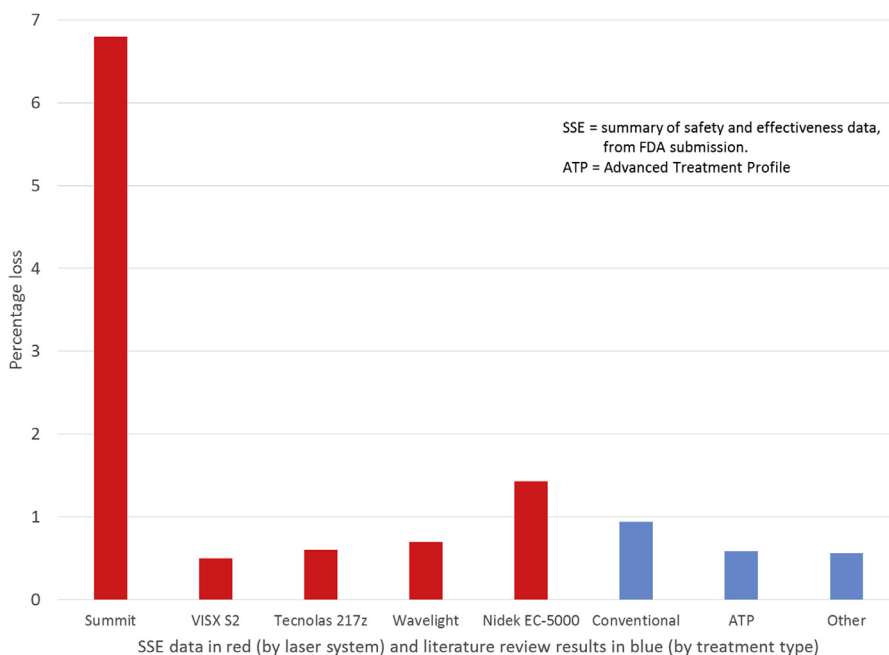


Figure 1. Percentage loss of 2 or more lines of CDVA (FDA = U.S. Food and Drug Administration).

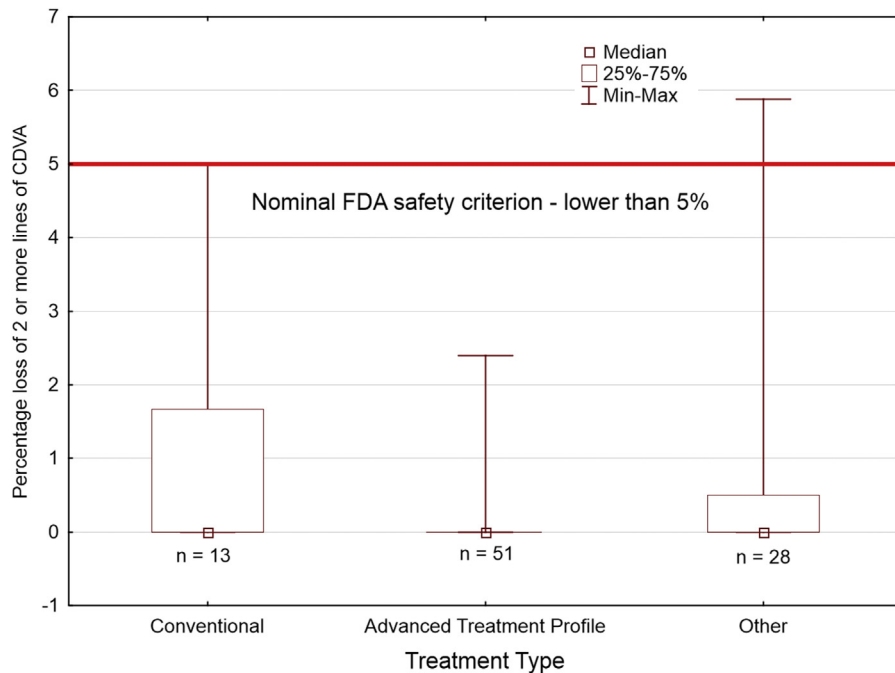


Figure 2. Percentage loss of 2 or more lines of CDVA by article (n = 92) and treatment type (CDVA = corrected distance visual acuity; FDA = U.S. Food and Drug Administration).

level lower than 5% loss of 2 or more lines of CDVA. Only 2 study groups had a level higher than this. The first included patients treated for 5.0 D or more of hyperopia, and the second included patients treated for 1.0 D to 4.25 D of astigmatism.

The percentage of eyes with a loss of 2 or more lines of CDVA was statistically significantly higher in eyes treated for hyperopia than in those treated for myopia (2.13% versus 0.95%; $P < .01$, chi-square test). There was no statistically significant difference by study size.

Uncorrected Distance Visual Acuity

The final uncorrected distance visual acuity (UDVA) is a measure of the effectiveness of LASIK surgery. Of most interest are the rates of 20/20 and 20/40 Snellen acuity. In 68% (98/143) of the groups, comprising 90% (61 331/67 893) of eyes, the percentage of eyes with a UDVA of 20/20 or better was reported and in 65% (93/143) of studies, comprising 88% (59 833/67 901) of eyes, the percentage of eyes with a UDVA of 20/40 or better was reported. Figure 3 shows the rates

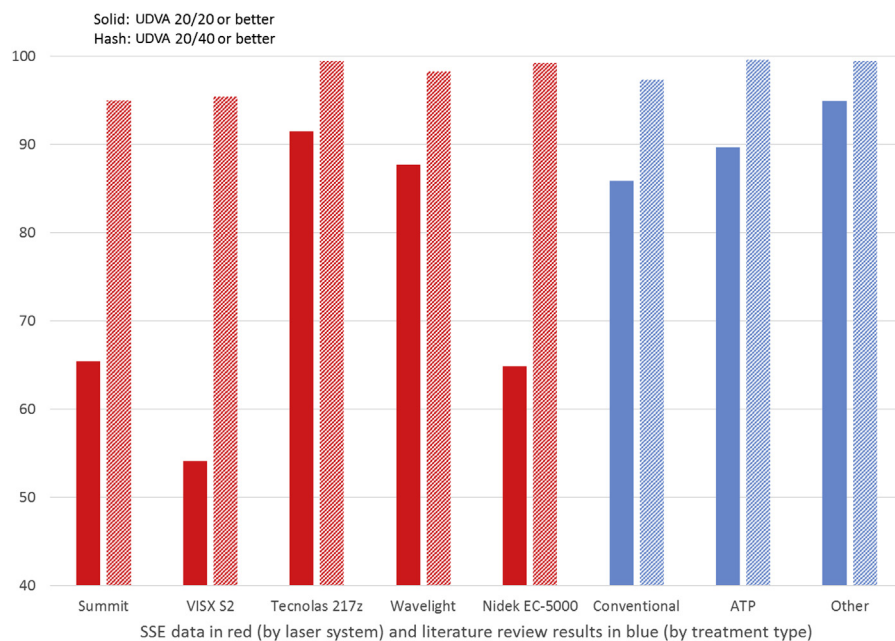


Figure 3. Percentage of eyes with 20/20 and 20/40 UDVA by treatment type (ATP = Advanced Treatment Profile; SSE = summary of safety and effectiveness data, from U.S. Food and Drug Administration data; UDVA = uncorrected distance visual acuity).

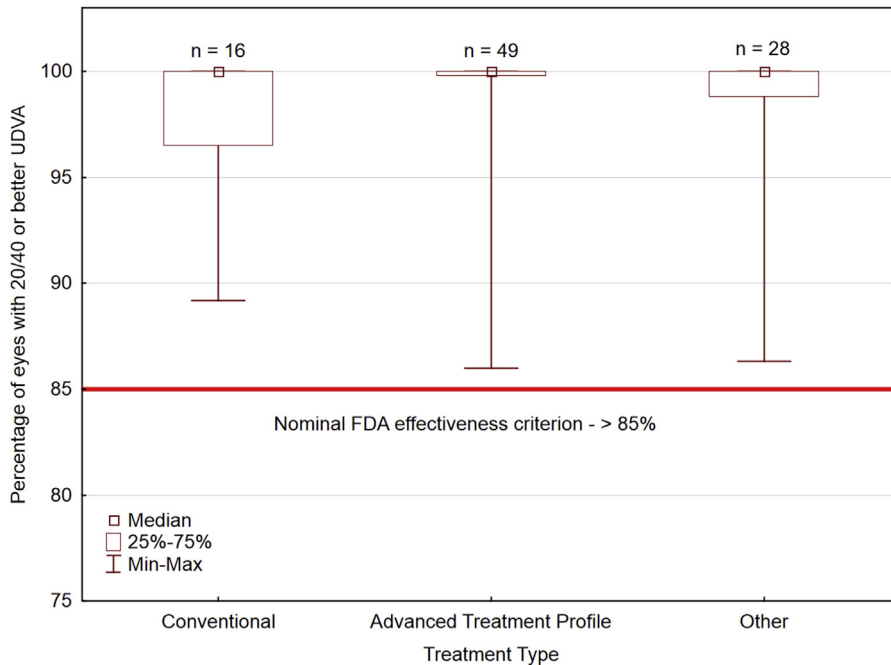


Figure 4. Percentage of eyes with 20/40 or better UDVA by article ($n = 93$) and treatment type (FDA = U.S. Food and Drug Administration; UDVA = uncorrected distance visual acuity).

of 20/20 and 20/40 by treatment type along with historical summaries of safety and effectiveness data. In the peer-reviewed literature, there were no statistically significant differences in the percentage of eyes with 20/20 or better and 20/40 or better between treatment types or by refractive error corrected. In aggregate across all articles, the weighted percentage of eyes with a UDVA of 20/20 or better was 90.8% (55 689/61 331) and the percentage with a UDVA 20/40 or better was 99.5% (59 503/59 833). A UDVA of 20/20 or better was reported in 97% of right eyes, 98% of left eyes, and 99% of both eyes in the PROWL-1 study and in 91% of right eyes, 92% of left eyes, and 96% of both eyes in the PROWL-2 study, consistent with the results in this review.^A Of note is that no patient in either PROWL study had refractive enhancements and the results were at 3 months, prior to the normal resolution of dry eye following LASIK.

Figure 4 shows the distribution of the percentages of eyes with a UDVA of 20/40 or better by treatment type in the 93 articles with data. The nominal effectiveness rate for FDA reporting, 85%, is also shown. The percentage of eyes with a UDVA of 20/40 or better was 99% or higher in 70 of the 93 articles with available data, representing 95.5% of all eyes for which these data were reported. In 68% (63/93) of articles, all eyes had a UDVA of 20/40 or better. No article reported a value lower than the nominal FDA effectiveness value of 85%.

The mean UDVA logMAR was tabulated in 67 articles, comprising 30% of eyes (20 273 of 67 893). Applying a weighted mean based on the number of eyes in each of these articles, the mean UDVA was

$-0.10 \log\text{MAR} \pm 0.10$ (SD), with an estimated 77% of eyes (15 619 of 20 273) having a postoperative UDVA of 20/20 or better (0.0 logMAR). The postoperative UDVA was statistically significantly better ($P < .01$, ANOVA) in the articles reporting advanced treatment results ($-0.04 \log\text{MAR}$) than in the articles reporting conventional treatment results ($+0.05 \log\text{MAR}$); the difference was almost 1 line of acuity. In the advanced treatment group, there was no difference between wavefront-guided, wavefront-optimized, or topography-guided treatments ($P > .15$, ANOVA). There was no statistically significant difference by group size ($P > .05$, ANOVA) or preoperative refractive status ($P > .05$, ANOVA) between the advanced treatment results and the conventional treatment results.

Residual Refractive Error

Another measure of LASIK effectiveness is the residual refractive error after surgery, with the most often reported aggregate data being the percentage of eyes within ± 0.5 D of the target refraction. The residual refractive error was reported in 84% (120 of 143) of study groups, comprising 97.2% (65 974 of 67 893) of all eyes. The percentage of eyes within ± 1.0 D of the target refraction was also reported in 78% (111 of 143) of study groups, comprising 88% (60 329 of 67 893) of eyes. Summary data for the study groups and the comparative summaries of safety and effectiveness data are shown in Figure 5. All aggregate data from the literature review were better than the corresponding summaries of safety and effectiveness data. Including all articles in which data were

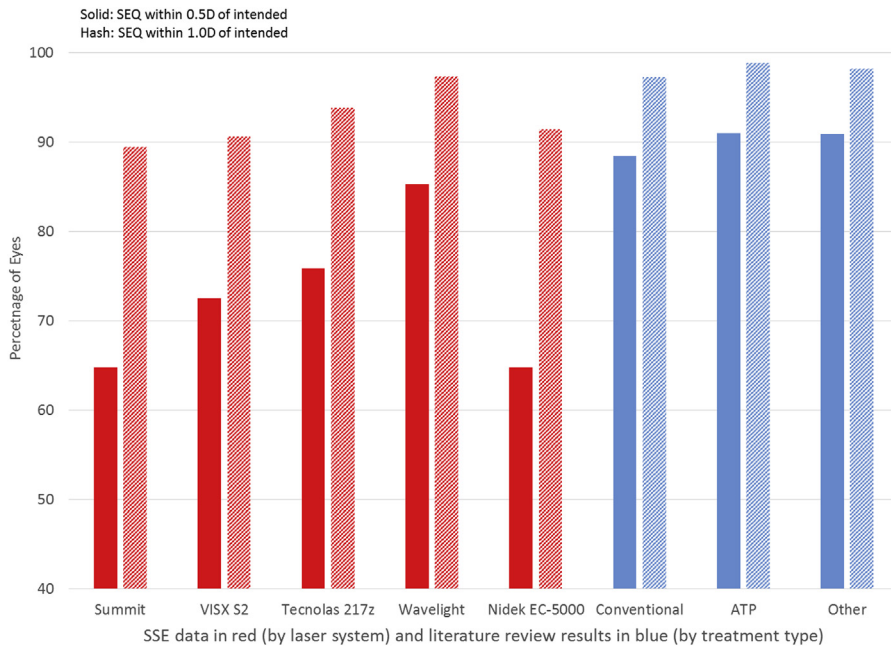


Figure 5. Percentage of eyes within ± 0.5 D and ± 1.0 D of the target SE refraction (ATP = Advanced Treatment Profile; SEQ = spherical equivalent; SSE = summary of safety and effectiveness data, from the U.S. Food and Drug Administration).

reported, the percentage of eyes within ± 0.5 D was 90.9% (59 954 of 65 974) and the percentage within ± 1.0 D was 98.6% (59 476 of 60 329).

To ensure that the few large studies do not account for the high performance relative to the summaries of safety and effectiveness data, the distribution of the percentage of eyes within ± 1.0 D of the target refraction for all studies is shown in Figure 6. The nominal FDA effectiveness standard for this measure is 75%. In all articles, the percentage of eyes within ± 1.0 D of the target refraction was greater than 80%; in

more than half the articles (59 of 111), comprising 80.7% of eyes with available data (48 684 of 60 329), the percentage was greater than 99%.

The mean postoperative spherical equivalent (SE) refraction was reported in 114 articles. In 77% (88 of 114) of them, comprising 95% of eyes with data reported (61 861 of 65 278), the mean SE was within ± 0.25 D of the intended target. In only 2 articles (including only 113 of 65 278 eyes) was the mean SE greater than ± 0.50 D; 1 of these included myopic patients with a preoperative SE between -6.00 D and

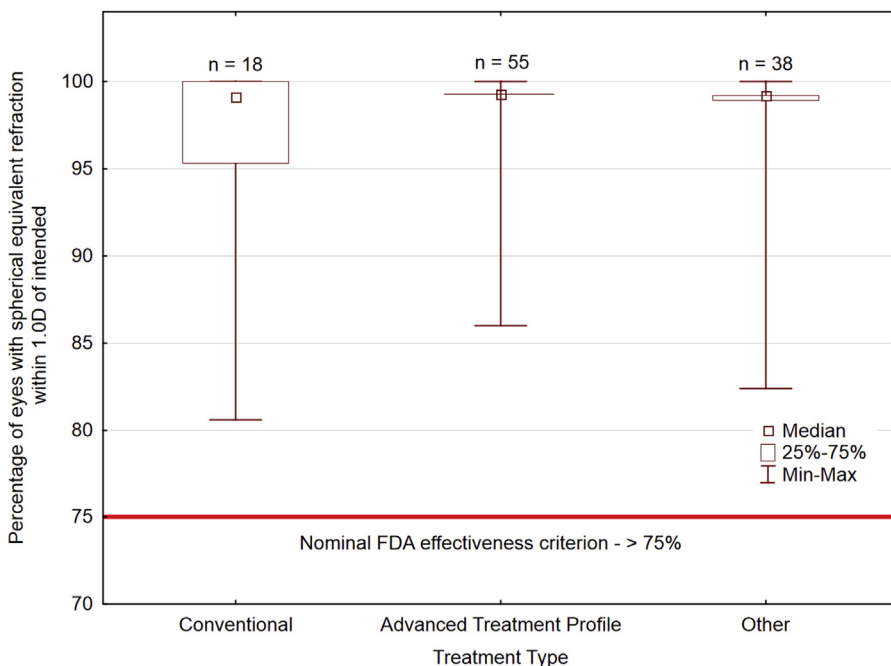


Figure 6. Percentage of eyes within ± 1.0 D of the target refraction by article (n = 111) and treatment type (FDA = U.S. Food and Drug Administration).

–10.00 D, and the other included hyperopic patients. The postoperative SE was statistically significantly different between the hyperopic group and the myopic group ($P < .01$, ANOVA), with a likelihood of slight residual hyperopia in hyperopic eyes and slight residual myopia in myopic eyes. The difference in these mean values was less than 0.25 D. There was no statistically significant difference by treatment type or study size ($P > .05$ in both cases, ANOVA).

Subjective Patient Impressions

This review includes articles that reported clinical outcomes data. Few of the articles included patient satisfaction or other subjective impression data. In addition, there was no standard reporting methodology, so only qualitative comments can be made based on the available data.

Only 5% of articles (7 of 143) included specific data on patient satisfaction after surgery, but these included 14.3% of all eyes (9726 of 67 893). Just under half the respondents (46.4%) reported being “very satisfied” after surgery; 1.2% of patients reported being dissatisfied. This is consistent with the Summit Apex summaries of safety and effectiveness in which 50.1% of patients reported a satisfaction score of 5 of 5 at 12 months postoperatively. No comparative patient satisfaction data were available from the summaries of safety and effectiveness data for the other approved laser systems included in this review. One other article included in the review included more than 10 108 eyes and reported that 93.4% of patients thought their vision was the same or better after LASIK relative to their preoperative vision using spectacles or contact lenses. This appears consistent with the PROWL-1 and PROWL-2 study data in which 98% and 96% of patients, respectively, reported satisfaction with their vision.

Dry-eye data were reported in only 12 of 143 articles, and reporting was not sufficiently uniform to allow aggregation. The largest study (32 569 eyes, 48% of the total) reported a postoperative dry-eye rate of 0.18%. The highest percentage of dry eye noted, based solely on a question related to the use of artificial tears, was 41% in a set of 207 eyes at 3 months postoperatively. However, no preoperative data were collected in that study and only 12% of the patients reported using artificial tears 2 or more times per day. Other articles reported a mean dry-eye score, but this did not allow determination of frequency in the patient population. No comparative preoperative data were available. In the PROWL-1 trial, dry eye was assessed preoperatively and at 3 months; no corneal staining was 90.9% preoperatively and 87.3% postoperatively. In the PROWL-2 trial, no corneal staining was 78.7%

preoperatively and 83.5% postoperatively. Oxford grade 2 or greater staining was 1.4% preoperatively and 2.0% postoperatively in PROWL-1 and 1.8% and 2.6%, respectively, in PROWL-2.

Similarly, night vision, glare, and halos were recorded in very few articles and were often combined. The lowest reported rate was 0.06% in the largest study (32 569 eyes), and the highest rate was 3.5% in the second largest study (10 235 eyes). The weighted mean based on these 2 studies was 0.89%. These results are comparable to the 1.0% or lower rates of visual symptoms reported in the 2 PROWL trials.^A In the PROWL trials, ghosting, glare, halos, and starburst symptoms were compared preoperatively (with glasses or contact lenses) with uncorrected symptoms at 3 months. The prevalence of all 4 symptoms was less than preoperatively in both trials. The prevalence of bothersome visual symptoms was evaluated preoperatively with glasses or contact lenses and compared with symptoms postoperatively without correction. Bothersome ghosting, glare, halos, and starburst following LASIK were less in every category in both trials. The reduction in bothersome symptoms was significant in many categories. The number of patients who had difficulty with or inability to perform usual activities because of visual symptoms was evaluated preoperatively and at 3 months. In all 8 groups, the decrease in symptoms was as follows: In PROWL 1, ghosting 0.8% preoperatively, 0% postoperatively; glare 2.8% preoperatively, 0.5% postoperatively; halos 2.8% preoperatively, 0% postoperatively; starburst 2.8% preoperatively, 0% postoperatively. In PROWL-2, ghosting 1.0% preoperatively, 0% postoperatively; glare 0.3% preoperatively, 0% postoperatively; halos 1.7% preoperatively, 0.4% postoperatively; starburst 2.4% preoperatively, 0.4% postoperatively.

DISCUSSION

Two general findings related to the comprehensive literature review we conducted are important to the overall context of the results. First, there were no peer-reviewed articles with a negative impression of LASIK. Second, there was no apparent industry bias; ie, there was no evidence that financial interests affected the impression of LASIK in the articles reviewed. The most definitive study (PROWL) was performed by the FDA with no industry or physician oversight; although it remains unpublished, the study's detailed findings are available and were used for comparison purposes.

Over time, technological advancements have generally improved LASIK outcomes. Summaries of the safety and effectiveness FDA data from 1998 to 2004 for 12 FDA-approved laser devices were analyzed.⁸ The results showed that in a subset of nearsighted

patients, the percentage of patients with improved UDVA and decreased residual refractive error improved, probably due to laser technological advancements. A large study of 19753 myopic and mostly Chinese patients (37932 eyes) conducted by Yuen et al.⁹ between February 1998 and December 2007 found a general improvement in surgical outcomes over the years: an increase in the percentage of eyes with a UDVA of 20/40 or better and 20/20 or better, a reduction in the percentage of eyes with a loss of 1 and 2 lines of CDVA, and an increase in the percentage of eyes within ± 1.0 D of the target refraction. Our analysis of the peer-reviewed literature appears to corroborate this continuous improvement in LASIK outcomes. With rare exceptions, which appear to be a function of the more extreme patient populations in some articles, the results reported in the recent literature are consistently as good as or better than the data submitted for approval of various laser systems in the U.S. This is even though the summaries of safety and effectiveness data reported for the various laser systems related to the correction of myopic astigmatism only, whereas the analysis in this review included all eyes for which data were available, including hyperopia and/or hyperopic astigmatism, and even though the enrollment criteria are often more relaxed in post-market research studies than in studies designed to submit to the FDA.

In studies in which CDVA was reported, there was generally no change in CDVA; twice as many eyes gained 2 or more lines of vision as lost 2 or more lines. The percentage of eyes that lost 2 or more lines of CDVA was lower in the advanced treatment group than in the conventional treatment group. Both percentages were significantly lower than original data reported 20 years ago for the Summit Apex laser. (The Summit Apex laser, which had the highest reported loss of corrected vision in all summaries of safety and effectiveness data, is no longer available; it was retired in favor of faster, more precise excimer laser systems.)

The benchmark of limiting CDVA loss of 2 or more lines to 5% or less was met in all but 2 studies; both had extreme treatment ranges (high hyperopia in 1 case, high astigmatism in the other). The percentage of eyes with a loss of 2 or more lines was statistically significantly higher ($P < .01$) in hyperopia than in myopia (2.13% versus 0.95%), but both percentages were well below 5%.

In none of the study groups in which UDVA was reported was the percentage of eyes with 20/40 or better UDVA below the nominal standard of 85%. The weighted mean UDVA was significantly better than outcomes reported by Bailey and Zadnik⁸ for a range of early laser systems: 62.5% of 6250 eyes achieved a UDVA of 20/20 or better. The aggregate results are

also better than the 2007 results reported by Yuen et al.,⁹ in which 72.8% of 37932 eyes had a UDVA of 20/20 or better. The mean UDVA of -0.10 logMAR is also better than the mean UDVA of 0.07 reported in 2007 by Yuen et al.⁹ The percentages of eyes with a UDVA of 20/20 or better and 20/40 or better were higher than the percentages reported in the original FDA summaries of safety and effectiveness data.

Dry eye following LASIK is due to a reduction in corneal innervation. Multiple studies have shown that corneal sensation returns to normal in almost all cases at 6 months postoperatively. Bower et al.¹⁰ conducted a long-term prospective follow-up of dry eye following LASIK and photorefractive keratectomy (PRK); they evaluated patients preoperatively and 1 year following surgery. The study reported an incidence of dry eye of 5% following PRK and 0.8% following LASIK. Preoperative dry eye was predictive of postoperative dry eye. For this reason, it is important to evaluate and treat patients preoperatively to improve the ocular surface and reduce postoperative symptoms.

The percentage of eyes within ± 1.0 D of the target refraction found in this review was significantly higher than the percentage reported by Yeun et al.⁹ in a large sample. The percentage of eyes within ± 0.5 D of the target refraction in the aggregate data reported is also significantly higher than the 71.6% reported by Bailey and Zadnik.⁸ Only 2 articles (113 eyes) in the current aggregate data reported a mean SE refraction greater than ± 0.50 D of the target refraction. Again, more extreme corrections were a factor: hyperopia in 1 case, high myopia in the other. There was a trend toward mild residual hyperopia in hyperopic eyes and mild residual myopia in myopic eyes.

Although only limited patient satisfaction data were available, results showed very high satisfaction rates, particularly compared with rates of other cosmetic surgery procedures¹¹⁻¹⁴; 98.7% of all patients were satisfied or very satisfied after their LASIK surgery. This aggregate result is consistent with other recent study data in which patient satisfaction higher than 95% has been reported for patients having myopic or hyperopic LASIK; the high satisfaction was attributed to a low postoperative refraction.^{1,15} Results from 2 other articles are worth reporting. The first, by Pasquali et al.,¹⁶ involved a survey of physicians who had a refractive surgery procedure. The overall satisfaction rate in this demanding group was 95.3%. A recent study by Kezirian et al.¹⁷ included satisfaction data for ophthalmologists who perform refractive surgery and who had the procedure themselves; 97% of respondents (65 of 67) to a survey question indicated they felt they were better off having had the surgery.

The satisfaction rates reported are similar to the 98.7% reported in the PROWL-1 trial and higher

than the 96.2% reported in the PROWL-2 trial. In the PROWL trials, patient satisfaction was also evaluated preoperatively with glasses or contact lenses; in PROWL-1, it increased from 25.3% preoperatively to 98.7% postoperatively and in PROWL-2, from 44.3% to 96.2%, respectively. The PROWL studies showed a marked improvement in visual symptoms of ghosting, glare, halo, and starburst after LASIK. These findings suggest that for most patients with visual symptoms, LASIK improves quality of vision. The PROWL trials noted that although many patients with preoperative symptoms showed resolution of these symptoms after surgery, a minority of patients who were asymptomatic preoperatively developed new symptoms after LASIK. Most of the new symptoms were mild and not visually significant. The PROWL trials showed that dissatisfaction is associated with symptoms such as glare, halos, starbursts, and ghosting. The results of the PROWL trials were reported after only 3 months, so it may be that more time was needed for visual symptoms or conditions such as dry eye to resolve.^A In addition, in the PROWL trials, postoperative evaluation was performed without correction of residual refractive error with glasses or additional laser treatment. Correction of residual refractive error would reduce visual symptoms and, therefore, might further increase overall satisfaction. In the future, it may be possible to eliminate the majority of postoperative symptoms with improved technology.

Two general comments can be made based on the overall results in this review. First, the clinical results of correcting myopia appear slightly better than those of correcting hyperopia. Despite this difference, patients treated with hyperopic LASIK have reported satisfaction rates as high as 96.3%.¹ Second, advanced treatment seems to provide slightly better outcomes than those achieved with conventional treatment. In the review, the UDVA achieved in the advanced treatment group was almost 1 line better than that achieved in the conventional group, although the conventional group mean was within half a line of 20/20.

There are limitations to any review such as the one we report. There is no way to resolve likely differences in test conditions (eg, illumination, chart reflectance), enrollment criteria, or length of follow-up. Even the range of refractive error corrected varies considerably across the reviewed studies. Aggregating data can be confounded by limitations in the clinical outcomes reported; not all studies reported all data of interest. On balance, however, the ability to aggregate results from a broad range of laser systems and generate summary statistics makes this effort worthwhile.

Another important limitation of the current review is the lack of comprehensive subjective data related to visual outcomes such as glare, halos, or night-driving

complaints. These are often the subject of separate studies. Although the lack of data in the current data set is regrettable, a more serious concern might be that studies analyzing subjective complaints do not appear to include objective data, as they were not identified in our search. If that is the case, symptoms such as glare and halos or night-vision difficulty may be over-reported as they may be a function of uncorrected refractive error rather than a symptom of the surgery. Without objective and subjective data, this possible correlation cannot be adequately investigated.

In summary, the aggregate data from a large number of recent articles demonstrate that the overall clinical outcomes of modern LASIK surgery are significantly better than when the technology was first introduced. Improved diagnostic and laser technology and patient selection, better refinement of nomograms, more sophisticated ablation patterns, and the introduction of new technology such as the femtosecond laser for flap creation are likely to have played a role. Investigating the specific impacts of these factors was not possible in the current analysis due to the wide variety of lasers and microkeratomes included. It is realistic to expect that with continued technological advancements, LASIK surgical outcomes and safety will continue to improve.

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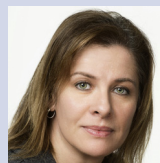
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First author:

Helga P. Sandoval, MD, MSCR

Carolina Eyecare Physicians, LLC,
Mount Pleasant, South Carolina, USA