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Technology Review

REFRACTIVE SURGERY -

(LASIK – LASER ASSISTED STROMAL IN -SITU KERATOMILEUSIS)

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1. INTRODUCTION

Patient with short-sightedness (myopia), low degrees of long sightedness (hyperopia or hypermetropia) and astigmatism can now reduce or eliminate their dependence on contact lenses and eyeglasses through refractive surgery which includes: Radial Keratotomy (RK), Laser Thermal Keratoplasty (LTK), Intrastromal Corneal Rings (ICR), Photorefractive Keratectomy (PRK), and Laser Assisted Stromal In-Situ Keratomileusis (LASIK). The objective of these procedures is to change the refractive state of the eye by changing the shape of cornea.

RK is performed to treat patients with myopia through a number of microscopic corneal incisions in a radial or spoke-like pattern. This allows the outer cornea to relax so that the central cornea flattens. The new shape of the cornea is permanently retained as it heals (Kraig, et al.2001).

LTK is performed using the non-contact Holmium:YAG laser. Ophthalmologists use the laser to symmetrically place radial sports that are outside the visual axis. This heats the cornea, resulting in stromal collagen shrinkage, thus modifying the anterior corneal curvature. LTK is used to treat patients with a hyperopic refractive error of up to +4.00 diopters who have become presbyopic and have no ocular pathology (Kraig et al., 2001).

ICR is a promising option in correcting myopic refractive errors of less than -3.00 diopters. During this procedure, the ophthalmologist places a polymethylmethacry ring in the periphery of the cornea at about two thirds of its depth to flatten the cornea, thus correcting the refractive error (Kraig et al., 2001).

PRK effectively treat patients with low to moderate myopia, myopia with astigmatism and low to moderate hyperopia without astigmatism. The corneal epithelium in the ablation zone is first removed or pushed to the side to allow a more accurate ablation of corneal tissue. Then, laser is applied to the exposed corneal stroma. PRK was the first surgical procedure developed to reshape the cornea by sculpting, using the laser. (Kraig et al., 2001)

Later, LASIK was developed using the same type of laser. The major difference between PRK and LASIK is the way the stroma, the middle layer of the cornea, is exposed before it is vaporised with the laser. In PRK, the epithelium is scraped away to expose the stromal layer underneath. In LASIK, a flap is cut in the stromal layer and the flap is folded back (*http://www.fda.gov/cdrh/LASIK).*

Laser technology and computer control software has evolved significantly since the first normally sighted eyes were treated with PRK in 1987 and by the LASIK technique since 1990. This procedure often provides immediate visual result with little or no discomfort, resulting in a high degree of patient satisfaction (*http;//www.lasik1.com/summitPresRelFinalApprov.html).*

The first refractive laser systems approved by FDA were excimer lasers for use in PRK to treat myopia, and later to treat astigmatism. Over the last several years, LASIK has become the main surgery that doctors use to treat myopia in the United States. More recently, some laser manufactures have gained FDA approval for laser systems for LASIK to treat myopia, hyperopia and astigmatism, and PRK to treat hyperopia and astigmatism. (*http://www.fda.gov/cdh/LASIK/).*

Patient selection criteria for LASIK surgery are: age of 18 years old or older; with stable refraction of at least one year duration (*http:www.lasik-benefits-usa.com/lasik-pricing/)*, myopia under 10 dioptres; hyperopia or astigmatism under 6.00 dioptres with absence of glaucoma, Queratoconus and other eye conditions (which ophthalmologist should rule out before surgery), an adequate corneal thickness, and is not recommended for pregnant women. *(http:www.clinicareinoso.com/conditns)*

2. OBJECTIVE

To assess the efficacy/effectiveness, safety and cost implication of Laser In Situ Keratomileusis (LASIK) surgery.

3. METHODOLOGY

A literature search was carried using search engines such as Pubmed MEDLINE, MEDLINE, OVID, Google and PROQUEST. In addition, an electronic search using HUKM library was also carried out. The following databases were also used: HEBW, ASERNIPS, EUROSCAN, BCBS, INAHTA, AHRQ, NCCHTA and AHFMR. The following keywords were used: *lasik, lasik eye surgery, laser eye surgery, excimer laser, safety, effectiveness, cost and refractive surgery* either singly or combinations.

4. TECHNICAL FEATURES

LASIK stands for Laser Assisted In Situ Keratomileusis and is a procedure that permanently changes the shape of the cornea, the clear covering of the front of the eye, using an excimer laser. (http://www.fda.gov/cdrh/lasik/**).** Excimer laser actually cleaves individual molecular bonds to remove tissue with no damage to surrounding tissue. A knife called a microkeratome is used to cut a flap in the cornea (figure 1). A hinge is left at one end of this flap. The flap is folded back revealing the stroma, the middle section of the cornea.

Pulses from a computer-controlled laser vaporise a portion of the stroma and the flap is then replaced. Once the laser treatment is completed the surface flap is repositioned. The corneal flap is stabilised without sutures by the relative corneal dehydration created by the endothelial pump. The stability of the corneal flap and adherence to the corneal stroma is checked following surgery, and patients are usually sent home with topical antibiotic and topical NSAID (non-steroidal anti inflammatory drug) eye drops. In addition, the patient is instructed to use an eye shield overnight, and follow-up is typically scheduled on post-operative day 1, again at one week, and checked again at one , three and six months.

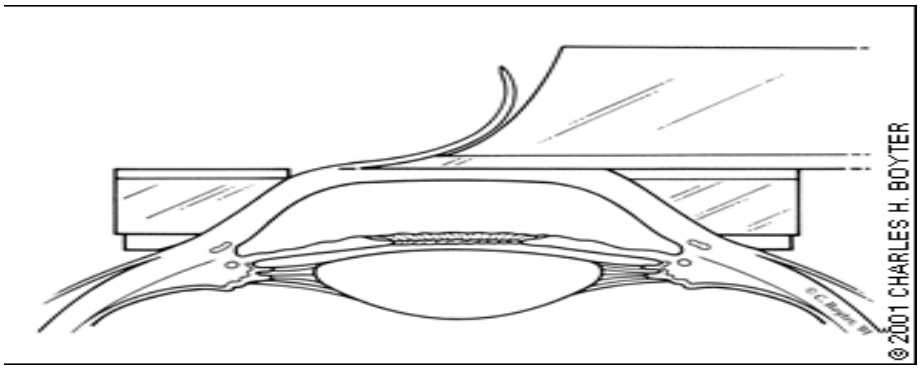

FIGURE 1 *Laser-assisted in situ keratomileusis (LASIK) microkeratome. The microkeratome is used to shave a thin layer of the cornea, creating a hinged "flap." A predetermined amount of cornea is removed*

5. RESULTS AND DISCUSSION

5.1 Safety

A systematic review indicated that it is difficult to compare complications between studies due to the different ways in which complications are defined. It was, however, reported that approximately 4% of primary procedures resulted in complications involving the flap intra-operatively. These include free, incomplete, or buttonholed flaps. Post-operatively, they include striae /folds or slipped flaps. The rate of lamellar keratitis ranged from 0% to 5% of cases and epithelial ingrowths occurred in 0.2%-2.2% of cases. Other common side-effects include a decrease in contrast sensitivity, light halos and glare. (*http://www.nice.org.uk/page*).

In a study by Sun et al. (2005), it was indicated that the LASIK is a safe and effective method for the treatment of myopia. This is based on the evaluation of 5081 patients (10,052 eyes) diagnosed with myopia at The Third Hospital of Handan, China.

The report from the Royal College of Ophthalmologists stated that there is a risk (between 2.7 % and 4.8 %) of loss of two or more lines of best corrected visual acuity (BCVA) after LASIK. Other complications of LASIK include instability of the cornea, corneal haze due to cutting of the cornea, there is less healing and greatly reduced incidence of haze, problem specifically related to the LASIK surgical procedure due to the creation of the hinged corneal flap, dry eye because the surface nerves have been cut (this nerve take 6 months to re-grow). *(www.rcophth.ac.uk).*

There is limited evidence on long-term complications that may arise as a result of the cornea being weakened, which is the main safety concern, which may lead to keratecsia. Other potential complications include the reduction in best corrected visual acuity, dry eye reaction, and difficulty with night vision, problem with the flap, retinal haemorrhage or retina artery occlusion. Infection and loss of the eye are very rare but are potential complications. (*http://www.nice.org.uk/page*).

In a study done by Iskander et al. (2000), it was found that the rate of postoperative complications after LASIK is between 1.8 % and 2.6 %.The safety of LASIK as measured by best corrected visual acuity (BCVA) was investigated and the findings was that between 1.6 % and 4.7 % of patients lost two or more lines of BCVA, where as 0.7 % to 7 % gained two or more lines of BCVA.

A review by Bower et al. (2001), found that LASIK is efficacious, predictable and safe with additional advantages of rapid vision recovery and minimal pain. A study by Sugar et al. (2002) indicated that LASIK is safe in terms of minimal loss of visual for correcting myopia and minimal loss of visual acuity. Serious adverse complications leading to significant permanent visual loss such as infections and corneal ectasia probably occur rarely in LASIK procedures. However, side effects such as dry eyes, night time starbursts, and reduced contrast sensitivity occur frequently.

5.2 Effectiveness

A Health Technology Assessment by the National Institute for Clinical Excellence (NICE) 2004 revealed that the evidence on laser in situ keratomileusis for the treatment of refractive errors suggested that it is efficacious in selected patients with mild or moderate myopia. However, evidence is weaker for its efficacy in patients with severe myopia and hyperopia.

LASIK was shown to be effective and predictable in terms of obtaining very good to excellent uncorrected visual acuity (UCVA). For moderate to high myopia (>6.0 D), the results were more variable, given the wide range of pre-operative myopia. The results were similar for treated eyes with mild to moderate degrees of astigmatism (< 2.0 D). However, it was found that it is difficult to extrapolate results from previous studies and comparing it with current practices with the most recent generation lasers. Besides that, it is also difficult to compare studies because of the variations in the range of pre-operative myopia, follow-up periods, lasers, nomograms, microkeratomes, techniques, the time frame of studies, and the investigators experience (Sugar et al., 2002).

A meta-analysis which included five randomised controlled trials (RCT) indicated that the LASIK and PRK are similarly effective for the correction of myopia from 1.5 to 15.0 D after 6 months follow up (Yang et al., 2003).

A randomised controlled trial compared two procedures, photorefractive keratectomy versus LASIK for low to moderate myopia. The findings for UCVA were 62.2% for LASIK and PRK 77.8 % (Lee et al., 2001).

Specialist Advisors did not highlight any specific concerns regarding efficacy of the procedure, providing that the degree of refractive error is within the accepted criteria *(http://www.nice.org.uk)*

5.3 Cost

There were three independent meta-analyses implemented at the Clinical Epidemiology and Health Economy Unit, Dresden University of Technology, Germany, which estimated the refractive gain (dpt) due to conventional LASIK procedures. These studies indicated that the total direct costs from the patients' perspective were estimated at 2426 Euro per eye. This associated with a refractive meta benefit of 5.93 dpt (95% meta confidence interval 5.32 - 6.54 dpt) and a meta predictability of 67% (43% - 91%). In terms of incremental costs, the unilateral LASIK implied a patient investion of 409 Euro (sensitivity range 351 - 473 Euro) per gained refractive unit or 36 Euro (27 - 56 Euro) per gained percentage point in predictability. When LASIK-associated complication patterns were considered, the total direct costs amounted up to 3075 Euro, resulting in incremental costs of 519 Euro / dpt (sensitivity range 445 - 600 Euro / dpt) or 46 Euro / % (34 - 72 Euro / %) (Lamparter, et al, 2005).

6. CONCLUSION

The LASIK procedure, in terms of safety, causes little pain, provides quick recovery of vision. LASIK has also been found to be safe and effective in treating both eyes on the same day. Among many different studies, the refractive outcomes of PRK and LASIK vary greatly for patients with mild myopia (0 to -3.00 dioptres), moderate myopia (-3.25 to -6.00 dioptres), high myopia (> -6.00 dioptres) with or without astigmatism , low hyperopia (0 to 3.00 diopters), and moderate hyperopia (+3.00 - +6.00 diopters) with and without astigmatism.

7. RECOMMENDATION

The NICE Guidelines found that clinicians should have adequate training before performing the technique. The Royal College of Ophthalmologists has produced standards for laser refractive surgery
(http://www.rcophth.ac.uk/about/aboutcollegedocs/RefractiveSurgeryStandardsMay2004.pdf).

8. REFERENCES

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DA panel recommends approval of summit laser for widest ranges of myopia and astigmatism with LASIK (July 1999), http://www/lasik1.com/SummitPressReFinalApprov.html)

Iskander NG, Peters NT, Penno EA, Gimbel HV (2000). Postoperative complications in laser insitu keratomileusis. *Ophthalmology*. 11(4):273-279.

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Sun L, Liu G, Ren Y, Li J, Hao J, Liu X, Zhang Y (2005). Efficacy and safety of LASIK in 10,052 eyes of 5081 myopic Chinese patients. *J Refract Surg*. Sep-Oct;(5 Suppl):S633-635.

Sugar A, Rapuano CJ, Culbertson WW, Huang D, Varley GA, Agapitos PJ, de Luise VP, Koch DD (2002). Laser In Situ Keratomileusis for myopia and astigmatism safety and efficacy: a report by the American Academy of Ophtalmology. *Ophtalmology*. 109(1):175-187.

Yang XJ, Yan HT, Nakahori Y (2003). Evaluation of the effectiveness of laser insitu keratomilleusis and photorefractive keratectomy for myopia: meta – analysis. *J Med Invest Aug*. 50(3-4):180-186

EVIDENCE TABLE

Title : REFRACTIVE SURGERY – LASIK
Aspect : SAFETY

No	Author,Title,Journal,Year	Study Design,Sample Size, Follow Up	Outcomes And Characteristic	Grade/Level Of Evidence	Comments
1	Sun L, Liu G ,et al Efficacy and safety of LASIK in 10,052 eyes of 5081 myopic Chinese patients. J Refract Surg. 2005 Sep-Oct;21	Clinical trial 5081 patients (10,052 eyes) diagnosed with myopia. 1-month follow-up	Uncorrected visual acuity at 1-month follow-up of 9555 (95.1%) eyes reached or exceeded the preoperative BSCVA. Hemorrhage of corneal limbus during surgery occurred in 1060 (10.5%) eyes, Sands of Sahara syndrome occurred in 232 (2.3%) eyes, interface infection responsive to treatment occurred in 4 (0.04%) eyes, and epithelial ingrowth occurred in 1 (0.01%) eye BSCVA-(best spectacle-corrected visual acuity)	Abstract	It safe for the treatment of myopia

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Title : REFRACTIVE SURGERY – LASIK
Aspect : SAFETY

No	Author,Title,Journal,Year	Study Design,Sample Size, Follow Up	Outcomes And Characteristic	Grade/Level Of Evidence	Comments
2	Bower KS, Weichel ED Overview of refractive surgery. Am Fam Physician. 2001 Oct 1;64(7):1183-90.	Review	Since the approval of the excimer laser in 1995, the popularity of RK has declined because of the superior outcomes from PRK and LASIK. LASIK is also efficacious, predictable and safe, with the additional advantages of rapid vision recovery and minimal pain. Noncontact Holium: YAG LTK provides satisfactory correction in patients with low hyperopia.	9 poor	

EVIDENCE TABLE

Title : REFRACTIVE SURGERY – LASIK
Aspect : SAFETY

No	Author,Title,Journal,Year	Study Design,Sample Size, Follow Up	Outcomes And Characteristic	Grade/Level Of Evidence	Comments
3	Sugar A, Rapuano CJ et al Laser in situ keratomileusis for myopia and astigmatism: safety and efficacy: a report by the American Academy of Ophthalmology. Ophthalmology. 2002 Jan;109(1):175-87.	RCT 1968 to 2000 retrieved 486 citations and an update, 2001 yielded an additional 243 articles. The panel members reviewed 160 of these articles and selected 47 for the panel methodologist to review and rate according to the strength of evidence	. It is difficult to extrapolate results from these studies that are comparable to current practices with the most recent generation lasers because of the rapid evolution of LASIK technology and techniques. It is also difficult to compare studies because of variations in the range of preoperative myopia, follow-up periods, lasers, nomograms, microkeratomes and techniques, the time frame of the study, and the investigators' experience. Serious adverse complications leading to significant permanent visual loss such as infections and corneal ectasia probably occur rarely in LASIK procedures; however, side effects such as dry eyes, night time starbursts, and reduced contrast sensitivity occur relatively frequently	Abstract	The assessment describes randomized controlled trials published 1997.

EVIDENCE TABLE

Title : REFRACTIVE SURGERY – LASIK
Aspect : SAFETY

No	Author,Title,Journal,Year	Study Design,Sample Size, Follow Up	Outcomes And Characteristic	Grade/Level Of Evidence	Comments
4	Iskander NG, Peters NT, Penno EA, Gimbel HV. Postoperative complications in laser in situ keratomileusis. Curr Opin Ophthalmol. 2000 Aug;11(4):273-9	Review Review the most commonly encountered early and late postoperative complications after LASIK and the most current methods in prevention and treatment.	Postoperative complications after LASIK is between 1.8% and 2.6%. The safety of LASIK as measured by best corrected visual acuity (BCVA) also has been investigated . Between 1.6% and 4.7% of patients lost two or more lines of BCVA, whereas 0.7% to 7% gained two or more lines of BCVA.	9/poor	The most common postoperative complications after LASIK, with emphasis on management and prevention. These complications can be divided into those presenting within the first few days after surgery (early) and those presenting weeks to months after surgery (late).

EVIDENCE TABLE

Title : REFRACTIVE SURGERY – LASIK
Aspect : EFFECTIVENESS

No	Author,Title,Journal,Year	Study Design,Sample Size, Follow Up	Outcomes And Characteristic	Grade/Level Of Evidence	Comments
1	Sugar A, Rapuano CJ et al Laser in situ keratomileusis for myopia and astigmatism: safety and efficacy: a report by the American Academy of Ophthalmology. Ophthalmology. 2002 Jan;109(1):175-87.	Clinical Trial 1968 to 2000 retrieved 486 citations and an update, 2001 yielded an additional 243 articles. The panel members reviewed 160 of these articles and selected 47 for the panel methodologist to review and rate according to the strength of evidence	. For low to moderate myopia, results from studies in the literature have shown that LASIK is effective and predictable in terms of obtaining very good to excellent uncorrected visual acuity(UCVA) and that it is safe in terms of minimal loss of visual acuity. For moderate to high myopia (>6.0 D), the results are more variable, given the wide range of preoperative myopia. The results are similar for treated eyes with mild to moderate degrees of astigmatism (<2.0 D) similar for treated eyes with mild to moderate degrees of astigmatism (<2.0 D) It is difficult to extrapolate results from these studies that are comparable to current practices with the most recent generation lasers because of the rapid evolution of LASIK technology	Abstract	The assessment describes randomized controlled trials published 1997.

			and techniques. It is also difficult to compare studies because of variations in the range of preoperative myopia, follow-up periods, lasers, nomograms, microkeratomes and techniques, the time frame of the study, and the investigators' experience.		

EVIDENCE TABLE

Title : REFRACTIVE SURGERY – LASIK
Aspect : EFFECTIVENESS

No	Author,Title,Journal,Year	Study Design,Sample Size, Follow Up	Outcomes And Characteristic	Grade/Level Of Evidence	Comments
2	Yang XJ,Yan HT et al Evaluation of the effectiveness of laser insitu keratomileusis and photorefractive keratectomy for myopia :meta-analysis. J Med Invest 2003 Aug	Meta analysis including 5 RCT 6 month follow up	LASIK and PRK similarly effective for correction of myopia from – 1.5 to – 15.0 D in a greater than 6 month follow up.	Abstract	

EVIDENCE TABLE

Title : REFRACTIVE SURGERY – LASIK
Aspect : EFFECTIVENESS

No	Author,Title,Journal, Year	Study Design,Sample Size, Follow Up	Outcomes And Characteristic	Grade/Level Of Evidence	Comments
3	Lee JB,Kim JS,et al Comparison of two procedures : photorefractive keratectomy versus laser insutu keratomileusis for low to moderate myopia. Jpn J Ophthalmol 2001 Sept - Oct	Clinical Trial LASIK = 45 eyes RK = 45 eyes	UCVA 20/20 or better : LASIK = 62.2 % PRK = 77.8 %	Abstract	

EVIDENCE TABLE

Title : REFRACTIVE SURGERY – LASIK

Aspect : COST

No	Author,Title,Journal,Year	Study Design,Sample Size, Follow Up	Outcomes And Characteristic	Grade/Level Of Evidence	Comments
1	Lamparter J, Dick HB,et al Clinical benefit, complication patterns and cost effectiveness of laser in situ keratomileusis (LASIK) in moderate myopia: results of independent meta analyses on clinical outcome and postoperative complication profiles. Eur J Med Res. 2005 Sep 12;10(9):402-9	Meta analysis Three independent meta analyses were implemented to estimate the refractive gain (dpt) due to conventional LASIK procedures as well as the predictability of the latter (%) (fraction of eyes achieving a postoperative refraction with maximum deviation of +/- 0.5 dpt from the target refraction). Study reports of 1995 - 2004 (English or German language) were screened for appropriate key words. Meta effects in refractive gain and predictability were estimated by means and standard deviations of reported effect measures. Cost data were estimated by German DRG rates and individual clinical pathway calculations; cost effectiveness was then computed in terms of the incremental cost effectiveness ratio (ICER) for both clinical benefit endpoints. A sensitivity analysis comprised cost variations of +/- 10 % and utility variations alongside the meta effects' 95% confidence intervals.	Total direct costs from the patients' perspective were estimated at 2426 Euro per eye, associated with a refractive meta benefit of 5.93 dpt (95% meta confidence interval 5.32 - 6.54 dpt) and a meta predictability of 67% (43% - 91%). In terms of incremental costs, the unilateral LASIK implied a patient investion of 409 Euro (sensitivity range 351 - 473 Euro) per gained refractive unit or 36 Euro (27 - 56 Euro) per gained percentage point in predictability. When LASIK associated complication patterns were considered, the total direct costs amounted up to 3075 Euro, resulting in incremental costs of 519 Euro / dpt (sensitivity range 445 - 600 Euro / dpt) or 46 Euro / % (34 - 72 Euro / %). Most frequently reported LASIK complications were "central islands / over- / undercorrection / regression" (meta incidence estimate 24%) and "haze" (15%), which were identified by means of an independent meta analysis.	Abstract	Bearing incremental costs of 519 Euro per gained refractive unit in mind, the conventional LASIK procedures showed an encouraging cost effectiveness range; the latter estimate may serve as a rationale for future allocation discussions in ophthalmology.