Abstract

Femtosecond laser has been introduced in refractive surgery to create a thin-hinged corneal flap without using any blade. The current review was planned to analyse and compare femtosecond-assisted laser in-situ keratomileusis (LASIK), the latest refractive procedure, with conventional techniques in refractive surgery. The analysis showed that femtosecond-assisted LASIK yielded more predictable corneal flaps, lesser ocular aberrations, better uncorrected visual acuity, lesser variations in intraocular pressure (IOP) and fewer chances of developing dry eyes. Transient light sensitivity, diffuse lamellar keratitis, opaque bubble layer, corneal haze and rainbow glare are some of the demerits of femtosecond-assisted LASIK, but these can be prevented with certain precautions. The early visual rehabilitation and preservation of corneal anatomy are added benefits in the long run. Though it is expensive currently, the competition in market is expected to cut down the cost soon.

Keywords: Laser in situ keratomileusis, Femtosecond laser, FemteC, Microkeratome, Hansatome, IntraLase.

Introduction

Refractive surgery is one of the commonest “cosmetic” procedures performed worldwide to get rid of the glasses by altering the corneal curvature.1,2 With the passage of time, more and more new treatment options are becoming available in the market to meet and satisfy peoples’ needs who want to have spectacular unaided vision.3

Different procedures have been used in refractive surgery which include photorefractive keratectomy (PRK), radical keratotomy (RK), laser-assisted in situ keratomileusis (LASIK), laser thermal keratoplasty (LTK), small incision lenticule extraction (SMILE) etc.4 Refractive surgeries with laser flap makers were approved by the United States Food and Drug Administration (FDA) in 1999 and femtosecond specifically for flap creation was approved in 2001.5 Femtosecond laser-assisted LASIK (femto-LASIK) is very successful latest innovation in refractive surgery because of its better outcome, long-term stable results, and lesser complications compared to other procedures.6 Femtosecond uses ultra-short duration of the pulses (10^-15) causing significantly less damage to the collateral tissues. It can generate different effects on the tissue by varying the duration of the laser pulses and energy that is applied. Therefore, currently femtosecond LASER has been demonstrated to be the safest amongst the refractive surgical techniques.5

A large amount of literature is available about advantages and disadvantages of various refractive procedures. Studies are required to compare and contrast newer technologies with the older ones so as to allow opthalmologists and patients to select the best refractive procedure for them. The current literature review was planned with the intent to provide a detailed review and a useful comparison of femtosecond assisted LASIK with other conventional refractive surgical techniques. An ideal refractive procedure is considered to be the one that is simple, effective, minimally invasive, safe and applicable to all the patients who desire vision correction.

Since the approval of femtosecond laser for making corneal flaps in 2001, following operating devices got approval by the FDA for their use in femtosecond laser assisted refractive surgery (FLARS).7 Technolas perfect vision FEMTEC; Ziemer femto LDV; Zeiss Meditec VisuMax; and Wavelength Ultraflap.

Methods

An extensive literature search was carried out on Google Scholar, PubMed, EMBASE and the Cochrane library database for the studies published between January 1, 2011, and September 30, 2015, using the keywords: LASIK, femtosecond laser, IntraLase, FemteC, Moria, microkeratome and Hansatome. The literature search yielded 513 articles out of which 30 were included in this study. The articles were filtered on the basis of selection criteria (Table).

Two researchers carried out the literature review independently, strictly following the inclusion and exclusion criteria. A proforma was filled, noting the first author of the study, year of publication, and the type of study. Only those

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Femto-LASIK: The recent innovation in laser assisted refractive surgery

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articles that were published in open access journals and were available in full text form were included. Besides, the references of the selected articles were also utilised as a resource to access further information.

**Mode of Action of Femtosecond Laser**
The femtosecond laser has pulse duration of $10^{-15}$ and works on the principle of photodisruption that generates high-intensity electrical field by highly focussed and strong pulses. This field causes breakdown of optical tissues. In this process plasma state consisting of free electrons and ions is generated that displaces the surrounding material by expanding at supersonic velocity. This initial displacement spreads through the tissue as shockwave despite slowing of the plasma expansion. As a cavitation gas bubble is formed by the vapourised tissue in the focal volume of laser beam, the temperature of rapidly expanding plasma quickly decreases. The cavitation bubble, which consists of carbon dioxide (CO$_2$), nitrogen (N$_2$) and water (H$_2$O), diffuses out of the tissue by normal mechanisms. The ablation is non-thermal due to extremely short interaction time. It uses an infrared (1053nm) scanning pulse focussed to 3 microns with an accuracy of 1 micron to cut a spiral pattern in the corneal stroma, creating precise lamellar flaps for LASIK.$^8$

**Steps in Femtosecond Assisted Lasik**
The main steps in this procedure include:

**Topical Anaesthesia:** It is applied using proparacaine, a local anaesthetic. These drops are used to decrease the discomfort and pain which the patient might face during the procedure. These drops are repeated every 2 minutes during the operation to maintain a pain-free surgical field.

**Docking:** The patient lies supine on the table and the docking system flattens the corneal surface artificially by applying equal pressure over the corneal surface. The head is secured and slightly tilted with the eye to be operated higher than the other eye. This clears the nose from the operating field.$^2$ Since this essential step is difficult to be performed in certain skeletal abnormalities like kyphoscoliosis, the procedure becomes contraindicated in all such conditions. Femtosecond laser consists of both hard and soft docking platforms. The hard docking platform is preferred in refractive surgery unlike cataract surgery. In docking we place suction ring on the eye that is separate from the patient interface (Figure-1). The eye is then docked using contact (applanating) system. Contact systems tend to have a smaller diameter and may fit a smaller orbit better. An applanating glass contact lens is used to stabilise the globe and to flatten the cornea. It is important to achieve complete applanation of the cornea to avoid an incomplete flap or other flap related complications. Visumax and Femtec use curved docking systems.$^9$

**Corneal Incision and Flap Creation:** The cornea is incised by femtosecond laser which creates an expanding bubble layer of CO$_2$ and water. The laser is directed at a certain corneal thickness in a spiral and raster pattern to achieve planar corneal flap. This focussed corneal thickness is 1mm which expands to 2-3mm after the photo-disruptive procedure that separates the corneal layers. During entire procedure, suction is applied that is removed after the flap is created (Figure-1). Then, with the help of spatula, the flap is lifted to allow the excimer laser to perform photoablation.

**Excimer Laser:** It removes tissues from the anterior corneal surface by photoablative decomposition, altering the refractive state of the eye. This process involves ultraviolet (UV) energy disrupting the chemical bonds in cornea without damaging the surrounding tissue thermodynamically. This enables light, refracting from modified corneal surface, to focus on retina reducing the dependence on spectacles and lenses. After laser is applied, the surgeon irrigates the stromal bed with...
Advantages of Femto-Lasik

1. Better Flap Thickness Predictability

Creation of highly predictable, reproducible, and stable corneal flaps within a narrow range of intended flap thickness and diameter is considered to be the hallmark of femtosecond laser. Conventional microkeratome used to make flaps that were thinner in the centre compared to periphery which could lead to buttonhole perforations. This flap-related complication has been drastically overcome by femtosecond laser that creates corneal flaps with uniform thickness i.e. same in the centre as well as in the periphery. Many studies have confirmed these findings so far.

Salomao et al. found the flaps to be within desired thickness with a standard deviation of 25µm with the Hansatome microkeratome (Bausch & Lomb) and within 14.5µm with the IntraLase femtosecond laser.12 Similarly, Issa et al. also proved that femtosecond laser yielded precise flap dimensions with a narrow standard deviation and a high level of safety.11

Zhang et al. showed that femtosecond treatment yielded satisfactory clinical outcomes with accurate and predictable flap thickness for patients with low and moderate refractive error. They created, using IntraLase FS60 femtosecond laser, 100-µm, 110-µm, and 120-µm corneal flaps for patients with middle and low refractive error. All the three groups achieved satisfactory postoperative outcomes. The standard deviation noted was ±4.3µm (target 100µm), ±3.6µm (target 110µm), and ±2.9µm (target 120µm).12

Vryghem et al. also showed predictable flap dimensions and refractive results after femto-LASIK.13 Similarly, in another study, Solomao et al. observed little variability in flap diameter in corneas with a high mean curvature compared with those with a low mean curvature using femtosecond. Since tissue saving is more with femto-LASIK group, their results concluded that femto-LASIK is especially beneficial for patients with relatively thinner corneas. They further added that refractive surgeons can also select the position and diameter of the hinge of the corneal flaps with femtosecond laser — a characteristic rarely achieved with conventional microkeratome flaps.14

2. Better Uncorrected Visual Acuity

Kanellopoulos et al. looked at 109 consecutive patients that underwent myopic LASIK using the FS200 femtosecond and EX500 excimer laser at 1, 3, 6 and 12 months. They found that 94.7% of eyes had postoperative unaided visual acuity better than 1.0 (decimal) at month 3, and maintained this till 12th month.15 Similarly, Gil-Cazorla et al. performed a retrospective, non-randomised, interventional, comparative case series that looked at 72 eyes that had hyperopic LASIK using the 60 kHz IntraLase femtosecond laser, and 72 eyes that underwent hyperopic LASIK using the Moria M2 microkeratome. They found out that the femto-LASIK group had statistically significantly lower mean residual sphere and better uncorrected visual acuity compared to microkeratome group.16

Raoof et al. demonstrated that femto-LASIK was more successful in correcting astigmatism compared to Hansatome microkeratome. The superiority was in terms of better visual acuity in the early postoperative period (upto 3 months) and less residual postoperative astigmatism. In addition, the procedure was safe and more precise than all the other procedures currently used to correct astigmatism. This again was attributed to the higher precision and better quality of femtosecond laser as a blade in modifying the cornea than microkeratome.17

A study looked at topographically-guided hyperopic femto-LASIK using the IntraLase FS60 and Wavelight FS200 with the Wavelight 400Hz excimer laser in 208 eyes over a follow-up period of 24 months. The results showed that the flaps were safe and very effective for correction of hyperopia and/or hyperopic astigmatism. The results showed stability and improvement of both uncorrected and corrected distance visual acuity.18

3. Lesser Variation in the IOP During Surgery

It has been shown that IOP varies during different phases of LASIK flap creation, especially during docking of the instrument at the start of surgery. Chaurasia et al. studied fluctuations in IOP during femto-LASIK and compared them with those in microkeratome LASIK. They observed that fluctuations in IOP were significantly lower in femto-LASIK group than in the microkeratome group during globe suction (81.78 ± 10.55 vs. 122.51 ± 16.95 mm Hg), cutting (62.25 ± 3.28 vs. 141.02 ± 20.46 mm Hg), and suction (41.40 ± 2.99 vs. 89.30 ± 12.15)19 respectively.

Zhang et al. showed that the suction of femtosecond laser and mechanical microkeratome led to the increase in macular central fovea thickness and the decrease in retinal nerve fiber layer (RNFL) thickness values at an early...
stage after LASIK. The effect of suction on macular and the RNFL thicknesses in Ziemer Femtosecond group was smaller than that in Moria Microtome group.20,21

4. Lesser Likelihood of Ocular Aberrations
The eye forms a sharp image to distinctly see an object. This is achieved by the optical system of the eye that focuses all the different light rays coming from the object on a single point on retina. If the refractive medium is rough (e.g. cornea after any refractive surgery), the light rays undergo diffuse refraction leading to distortion of the image quality. Several different types of such distortions are identified as lower order and higher order aberrations.

Mahmoud et al. showed in a study that refractive surgery, which manipulates the corneal curvature, tends to cause ocular aberrations. They compared the different techniques of refractive surgery for postoperative aberrations and visual acuity. The higher order aberrations after femto-LASIK and conventional LASIK surgery were observed in the subjects for 3 months postoperatively. Spherical aberrations were the commonest aberrations observed. They concluded that spherical aberrations were significantly low in femto-LASIK treated eyes than in microkeratome LASIK (p < 0.001).22,23

5. Lesser Rate of Dry Eyes
Several studies are performed to assess the effect of femtosecond laser use on the incidence of dry eyes after LASIK. Dry eyes in femto-LASIK operated eyes were independent of flap thickness. However, the microkeratoremeasured operated eyes showed significantly higher incidence of dry eyes than femto-LASIK operated eyes (p < 0.001).24 Mirishova et al. reported incidence of dry eyes to be 47% in patients undergoing photorefractive keratectomy (PRK) compared to femto-LASIK in which it was 37.8%.25

A research was done by Petznick et al. to evaluate various parameters of tear film stability and dry eyes after LASIK using two different femtosecond lasers i.e. VisuMax (Carl Zeiss Meditec) and IntraLase (Abbott Medical Optics). The results showed no statistical differences in any clinical outcome measure between the two femtosecond lasers (p> 0.05), but VisuMax offered faster recovery of corneal sensitivity and tearfilm break-up time.26

6. Early Visual Rehabilitation and Stability
The visual rehabilitation is very rapid after femto-LASIK. In contrast, surface ablation using PRK takes 3 to 6 days to offer reasonable visual function. PRK may take up to 2 weeks to reach the vision level of post-LASIK day 1. PRK is associated with risk of infection up to 3 to 5 days (i.e. until the epithelium completely heals).27

7. Epithelial Remodelling and Preservation of Corneal Anatomy
Epithelial remodelling after kerato-refractive treatment has been recognised for a considerable time. Although there are no published studies to date that directly compare epithelial remodelling following femto-LASIK with microkeratome-LASIK, the plausible explanations for epithelial remodelling, such as the rate of stromal curvature change28 and the change in biomechanical stability especially in large corrections,29 should have a much smaller impact in femto-LASIK compared to microkeratome-LASIK. The Bowman’s membrane and the epithelium are preserved in femto-LASIK unlike PRK. As a result, the incidence of light sensitivity in femto-LASIK is decreased considerably due to early healing in contrast to PRK which might take around two weeks to heal.25

Disadvantages of Femto-Lasik Compared to Traditional Procedures
1. Corneal Haze
Corneal haze is a dilemma which can affect the clarity of vision causing considerable distress to the patient. It is more likely to be seen with femto-LASIK refractive surgery compared to conventional microkeratome LASIK. It was noted by Patel et al. when they examined the eyes of 21 patients operated with different techniques. Each eye of the patient underwent a different procedure keeping the variables of age, gender and other possible confounders. Postoperatively the patients were examined for different parameters at set time intervals. These parameters included refractive errors, high contrast visual acuity, contrast sensitivity, corneal back scatter and intraocular forward light scatter. Among these parameters only corneal backscatter’s incidence was 6% higher in femto-LASIK group compared to conventional microkeratome operated group. However, this difference was only significant in the early postoperative period. In the long run and subsequent follow-ups this difference was not found to be significant.30

2. Transient Light Sensitivity
Transient light sensitivity, also known as good acuity plus photosensitivity (GAPP), occurs days to weeks (usually 2-6 weeks) following femto-LASIK. The patients present with complaints of acute onset of photophobia without any change in visual acuity on examination. The likely pathogenesis is opaque bubble layer formation or inflammatory response of ancillary tissues to the gas used during corneal applanation which escapes into deep stromal tissues. Besides, biochemical changes in
keratinocytes due to near infrared laser energy and inflammatory cytokines released by the gas bubble during healing of flap lead to photosensitivity. The treatment includes use of anti-inflammatory eye drops like prednisolone acetate drops with resolution of symptoms occurring within one week. Use of cyclosporine ophthalmic solution 0.05% is also recommended. Moreover, it has been found that decreasing the side-cut and raster energy settings to 33%, and 24% respectively, results in significant reduction in light sensitivity.31

3. Diffuse Lamellar Keratitis (DLK)
Netto et al. conducted a research on 801 eyes of 419 patients out of which 99 eyes of 70 patients developed diffuse lamellar keratitis (DLK) (Figure-2). The overall incidence of DLK was 12.4%. No significant differences in age or gender were found. Preoperative characteristics, including corneal thickness, IOP, presence of allergy or meibomian gland dysfunction, and Schirmer test results, were not significantly different between those who developed DLK and those who did not. An increased incidence of DLK was associated with several femtosecond treatment parameters, including larger flap diameter (p=0.0171), increased levels of raster energy (p=0.0033), and increased side-cut energy (p=0.0037) used for flap creation. There was no difference in the incidence of DLK with variations in flap thickness. There were no significant associations between the incidence of DLK and preoperative refractive error, treated refraction, ablation depth, or other treatment parameters.32 However, another study comparing the complications between microkeratome and femto-LASIK showed significantly more cases of DLK in femto-LASIK group postoperatively.33 Since the studies show contradictory results, this area still needs more research to reach a final conclusion.

4. Rainbow glare
Rainbow glares (Figure-3) are caused by femtosecond laser spots which cause constructive interference due to plasma disruption leading to splitting of light into its constituent colours with blue being closest to point light source and red colour being farthest. So defect lies in the poor laser alignment during raster type pattern of corneal flap formation. But if the laser spots are made in a random array rather than in a regular pattern, this phenomenon usually disappears. Patients who undergo this treatment develop around 4 to 12 bands usually with 6 being the commonest. With study it has been found that there’s no relationship of developing rainbow glare with age, gender and refractive error but a positive association has been found with laser energy used particularly seen with 1.0 microJ or 1.1 microJ.34 Another study has reported the corneal flap interface to be the source of rainbow glare postoperatively.35

5. Opaque Bubble Layer (OBL)
Gas bubbles which are created infrequently appear in the anterior chamber after application of the femtosecond laser. These bubbles are probably associated with formation of pocket and expansion through posterior corneal or stromal layers into the anterior chamber. Though these bubbles are benign, they may interfere with the eye tracker of the excimer laser if they are multiple or large.15

In a retrospective cohort study, 198 eyes of 102 consecutive patients who underwent LASIK flap creation performed with the Alcon WaveLight FS200 laser (Alcon Laboratories, Inc., Fort Worth, TX) were analysed. Preoperative manifest refraction, corneal keratometry, central corneal thickness, white-to-white corneal

Figure-2: Diffuse lamellar keratitis.

Figure-3: Image of a point like light source after rainbow glare.
diameter, corneal hysteresis, corneal resistance factor, and programmed flap parameters were collected. Digital images automatically recorded after creation of flap were analysed to measure OBL areas (Figure-4). Correlation tests were performed between preoperative corneal parameters and OBL areas. It was seen that the incidence rate of OBL was 48% (103 eyes). The mean OBL area as a percentage of the corneal flap area in the OBL group was 4.25±7.16% (range: 0 - 32.9%). The central corneal thickness, corneal resistance factor, and corneal hysteresis were significantly positively correlated with the OBL area (p = 0.001, 0.028 and < 0.0001 respectively).36

6. Cost Related Issues
There is considerable installation cost of femtosecond and excimer laser equipment. Since both of these two separate independent laser units are involved in femto-LASIK, the ultimate cost of the procedure is bound to be more than the traditional microkeratome LASIK. The expensive procedure also demands high level of professional surgical skills to deliver excellent results to heavily paying patients. To reach break even point for initial investment in the setup and to acquire excellent surgical skills in the procedure, a large number of patients is ideally required, which is not the case with every ophthalmologist. According to a study conducted by Corcoran et al., less than 7% of American ophthalmologists met the aforementioned requirements — heavy initial investment, excellent skill and results, and high patient turnover — to successfully run an independent femto-LASIK facility.37

Lastly, femto-LASIK costs around $1250-$2500 in Pakistan currently, and has been selected as procedure for their refractive surgery by a large number of patients.38

Conclusion
Femtosecond laser creates corneal flaps that have greater safety and thickness predictability. The flaps cut are planar and uniformly thick compared to meniscus-shaped flaps in mechanical microkeratome. In addition, the flap adherence is stronger and less influenced by trauma; it shows better contrast sensitivity, less incidence of dry eyes and lesser rate of epithelial ingrowth. Moreover, femtosecond reduces the likelihood of short flaps, epithelial abrasions, button-hole perforations, and blade marks. Though it is associated with more chances of developing corneal haze, photosensitivity, diffuse keratitis, rainbow glare etc., given the exceptional results it is proposed that the femto-LASIK will give a tough time to its rivals. The coming years of research will show how far the femto-LASIK will go in refractive surgery.

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References


