

# Update on Femtosecond Laser-Assisted Cataract Surgery: A Review

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**Abstract:** The advent of femtosecond lasers has resulted in a new standard in cataract surgery, intended to overmatch the paradigm of conventional phacoemulsification. Femtosecond laser-assisted cataract surgery (FLACS) enables a higher level of reproducibility, precision, accuracy, and customization when performing several steps of cataract (or lens) surgery. Capsulotomy, corneal incisions, lens fragmentation, and arcuate incisions are the main procedures performed using FLACS. As the demand for better refractive outcomes and spectacle independence increases, the features of FLACS are highly relevant, especially when considering the implantation of premium intraocular lenses, such as toric, enhanced depth-of-focus, or multifocal lenses. The present article reviews the state of the art of femtosecond laser-assisted cataract (lens) surgery, contemplating the advantages and limitations of the two types of femtosecond laser pulses available (high and low energy) by evaluating their reported outcomes and complications.

**Keywords:** femtosecond laser, FLACS, laser-assisted surgery, cataract surgery

## Introduction

Current cataract surgery is not merely the removal of an opacified lens. It assumes intraocular lens (IOL) implantation, which characteristics (including power and design) are purposely chosen through a careful preoperative assessment.<sup>1,2</sup> This quest for better postoperative refractive results, supported by a continuous commitment to the development of biometry formulas, is unequivocal evidence of the refractive nature of cataract surgery. This refractive-driven concern clearly dilutes the old dichotomy between cataract removal and the so-called refractive lens surgery and has thrust the investment in technology regarding new techniques and IOLs, creating an unsurprisingly high status of expectation and demand from patients. Instead of a clear separation between pure cataract removal and refractive lens (or premium) surgery, and because the essence of the surgical steps is the same, the indications are better set in a continuous spectrum of patient-based needs. For example, a patient presenting with a cataract, however mature it may be, is ultimately intervened depending on the patient's informed decision, which is directly based on how autonomous he or she feels, despite the condition. The elective character of refractive lens surgery will stand on the farthest point of this spectrum, in which the autonomy of spectacles is the patient's highest desire. Expectation and deliverance, like most human activities, are turning wheels in the evolution of cataract surgery. With this regard, femtosecond laser-assisted cataract surgery (FLACS) emerged as a technique liable to offer higher standards in terms of efficacy and safety.

The proven high reproducibility and precision of femtosecond laser-assisted capsulotomy stimulated the development of femtosecond laser technology, expanding its role in substituting for the classical surgical steps of cataract surgery (as established by conventional phacoemulsification). Hence, laser-assisted lens fragmentation and corneal incisions became integrated in the FLACS scope of action, increasing the expectations of an optimization of the surgical outcomes.

Implantation of premium intraocular lenses requires no less than an optimal technique and, in this context, predictability and accuracy are of paramount relevance. This review aimed to provide an update on the role of femtosecond laser-assisted cataract (lens) surgery by visiting the technique's outcomes and related current evidence on its effectiveness and safety.

## Technology

### Femtosecond Lasers

Femtosecond laser technology derives its name from the generated pulse duration of the order of  $10^{-15}$  s.<sup>3,4</sup> Produced in the near-infrared range (1053 nm), the extremely short pulse time of this solid-state laser is liable to achieve photodisruption in target tissues, avoiding the undesired effects of previous lasers, such as thermal impact.<sup>5-7</sup> When in association with other adjustable laser parameters such as power, repetition rate, and spot size, the laser-tissue interaction can be further customized and optimized. Photodisruption is a sequential three-step process involving plasma formation, shock wave generation, and cavitation. Henceforth, femtosecond (FS) laser separates tissue by ablation and cleaving; the relative weight of each is determined mainly by the pulse energy level.<sup>7</sup> To achieve photodisruption, an energy threshold must be surpassed, depending on the nature of treated tissue and different laser features: numerical aperture (NA) and wavelength. The higher the energy pulse, the greater the ablated tissue through expanding gas bubbles; the lower the energy pulse, the lesser the ablated tissue, and separation is dependent on the cleaving occurrence (implying higher pulse frequencies and tighter spots).<sup>8</sup>

### Types of Femtosecond Laser Pulse

Presently, there are two different FS laser pulse patterns regarding energy level and frequency. On one hand, there are devices (the majority of laser systems available) that produce high-energy and low-frequency pulses on the order of  $\mu\text{J}$  and KHz, respectively. On the other hand, there is a laser platform producing low-energy high-frequency pulses in the range of nJ and MHz, respectively. The latter pulse pattern (low energy with high repetition rates) offers some advantages: high laser focusing accuracy and cutting precision, accompanied by less gas generation, which reflects on a reduced collateral damage to the surrounding tissue.<sup>8,9</sup> The mechanical thrust on adjacent tissues is, by this physical evidence, substantially bigger with high-energy pulse FS.

The energy level of an FS laser pulse at a certain wavelength depends on the focal spot size, which is inversely proportional to the numerical aperture (NA) of the focusing optics. The larger the NA, the smaller the focal spot and, ultimately, the lower the energy. There are two ways of producing an augmented NA: by increasing the lens diameter of the focusing optics or by positioning the focusing optics closer to the eye. Most of the available laser platforms, such as LenSx (Alcon Laboratories, Fort Worth, Inc.), VICTUS (Bausch & Lomb, Inc.), Catalys (Johnson & Johnson Vision Care, Inc.), and LensAR (LensAR, Inc.), have opted for the first approach, whereas Femto LDV Z8 (Ziemer Ophthalmic Systems AG) has chosen the second approach.<sup>9-11</sup> The former devices have large optics requiring relatively immobile platforms. With the latter device, the laser beam is guided through an articulated mirror arm into a handpiece that contains the focusing optics; this feature allows a reduction in pulse energy by a factor of 10 or more. Furthermore, this design enables the handpiece use under a surgical microscope, thereby rendering the whole platform more compact and portable.

### Delivery Procedure

In order to correctly apply an FS laser to the eye, an adequate, stable, and well-tolerated patient interface is of paramount importance. This device-patient engagement, described as docking, is currently achieved by means of two different methods: eye appplanation (with a curved lens) or liquid interface.<sup>12,13</sup> While the current literature shows no difference between the two methods regarding capsulotomy regularity,<sup>14</sup> there is some evidence of increased incidence of anterior capsular tears or tags with applanating interfaces due to the occurrence of corneal folds.<sup>13</sup> Among the features of non-appplanating interfaces (which use a scleral suction ring and a fluid immersion chamber) are a lower induced intraocular pressure, larger treatment area, and a more proficient compensation regarding lens tilt.<sup>13</sup>

Docking adds an additional, time-consuming step when compared to conventional phacoemulsification (CP),<sup>15</sup> and it inherently has a rate of possible complications, from mildly frequent transient conjunctival redness or hemorrhage to a very rare incomplete laser treatment due to suction loss.<sup>16-19</sup>

## Supporting Imaging Technology

Accurate and reliable imaging is necessary to perform the proposed laser-assisted surgical steps (capsulotomy, corneal incisions, and lens fragmentation). A thorough three-dimensional reconstruction of the anterior eye structures is currently provided by either optical coherence tomography (most FS platforms) or 3D confocal structured illumination combined with Scheimpflug imaging (LensAR).<sup>11,19–21</sup> In addition, most FS devices present an integrated camera system that allows a frontal view of the eye.

## Clinical Outcomes

### Surgical Steps

#### Capsulotomy

The dimensions (shape and size) of capsulotomy are determinant variables affecting the effective lens position, which in turn affects the postoperative refractive results. Inadequate sizing of the capsulotomy may result in IOL tilt, decentration, and increased posterior lens capsule opacification.<sup>22–25</sup> Furthermore, for premium IOLs (toric, enhanced-depth-of-focus, or multifocal), which have more demanding optical designs, capsulotomy centration is most relevant for achieving optimal results.<sup>26–28</sup>

Precision, predictability, and reproducibility of FS capsulotomy are the features that have been demonstrated to be superior to CP.<sup>24,28,29</sup>

The surgical step sequence differs according to the available platform. Thus, most FS devices perform capsulotomy before lens fragmentation, whereas one of them (Ziemer's) executes capsulotomy afterwards. This feature does have a clinical impact, since for white cataracts (generally, a contraindication for FS laser with most platforms), it is liable for performance with the latter device, as nucleus fragmentation equalizes the gradient pressure inside the capsular bag before capsular opening, preventing the Argentinian Flag Syndrome.<sup>30</sup>

FS platforms enable customization of the diameter and centration of the capsulotomy, adequately set via OCT (or equivalent) imaging upon docking; safety margins (from the iris) are usually adjustable, as well.

A six-fold better IOL centration with FSL capsulotomy compared to manual capsulorrhexis was found in some studies.<sup>26</sup> Capsulotomy can be centered on several landmarks or reference points: pupil, optical (corneal) or capsule center or custom placement (such as the lens apex or the first Purkinje reflex);<sup>31</sup> the available FS platforms share at least two of the aforementioned referential possibilities. Some authors have reported that more favorable results regarding capsule-IOL overlap with capsular bag-centered capsulotomy as opposed to pupil-centered capsulotomy;<sup>32</sup> an anterior capsule overlap of 360 degrees on the IOL anterior surface is consensually associated with a reduced incidence of posterior capsule opacification.

Regarding preoperative pupil size, normally, a diameter not inferior to 4 mm, is compatible for the FS devices available.<sup>33</sup> As to pupil size after the laser pretreatment, constriction (miosis) has been commonly reported for femtosecond laser-assisted surgery, casting this shadow on femtosecond laser-assisted cataract surgery (FLACS), in general, and presenting it as a feature of this technique in the published literature. However, the vast majority of the publications available refer to high-energy FLACS or seldom include low-energy pulse devices but without data results differentiation. In fact, recent literature on low-energy FLACS does not show evidence of miosis with this technique, demonstrating comparable results with CP, regarding pupil behavior. This may be related to the lower level of pulse energy, causing less impact on the surrounding tissue and prostaglandins release. It has also been described that applanation can decrease pupil size, by means of transient ischemia of the iris sphincter induced by applanation docking.<sup>34</sup>

Strategies have been adopted to resolve this laser-induced miosis with high-energy pulse devices. Intraoperative measures, such as intracameral viscoelastic, epinephrine (injection or perfusion), or mechanical dilation, have been used, generating a profuse literature on this particular counterback.<sup>35–37</sup>

Anterior capsule strength is related to the amount of energy applied during capsulotomy. Some studies with electron microscopy scanning have shown manual capsulorrhexis to be stronger than FSL capsulotomy, the magnitude of this difference being related to the capsulotomy edge properties; these, in turn, depend on the laser energy pulse. The higher the energy pulse, the more irregular the edges; the lower the energy pulse, the smoother the capsulotomy edges.<sup>29,38,39</sup>

Accordingly, recently published studies show a lower incidence of capsular complications (tears, tags) with low-energy pulse as compared to high-energy pulse FLACS.<sup>10,40,41</sup>

Although capsulotomy sizing can be adjusted with FS platforms, an average diameter of 5–5.25 mm is generally chosen for most cases,<sup>42,43</sup> however, this reference value may be limited by pupillary dilation and laser-specific pupil safety margins.

To summarize, in favor of FLACS, capsulotomies are more precise (in size and shape), reproducible, and better centered than manual capsulorhexis.<sup>25,44–46</sup>

However, this technique has two limitations: maintenance of pupil dilation and a considerable rate of capsule-related complications, both after laser treatment with high-energy pulse devices.

## Lens Fragmentation

Femtosecond laser allows lens nucleus fragmentation, substituting this surgical step conventionally performed by ultrasound with the CP technique. The different platforms allow fragmentation customization according to the available patterns on the laser system,<sup>47</sup> beyond ensuring anterior and posterior safety margins, as displayed upon imaging of the capsular bag;<sup>36</sup> these margins are adjustable within the program range of each FS device. Laser pre-cutting of the nucleus precludes the oxidative stress, heat, inflammation, and tissue damage associated with ultrasound as it shortens the phacoemulsification time and cumulative dissipated energy (CDE).<sup>48</sup>

Capsular block syndrome with subsequent posterior capsule rupture is an extremely rare complication that occurs when excessive pressure is generated inside the capsular bag during lens fragmentation. This phenomenon is caused by the expanding gas bubbles, a feature of the tissue ablation produced with high-energy pulse systems;<sup>49</sup> this rare occurrence is not reported with low-energy FLACS, as its lower pulse energy produces cleaving rather than ablation.

In synthesis: FLACS has proven to be advantageous over CP, as it reduces the amount of phacoemulsification energy delivered by 33–70% by softening the lens.<sup>44,45</sup> On the other hand, FS requires adequate pupillary dilation to ensure safe completion. In addition, high-energy FLACS is contraindicated in patients with white cataract.

## Corneal Incisions

Femtosecond laser technology enables customized, precise and predictable sizing (width, length, and depth), shaping and location of full-thickness corneal incisions.<sup>50</sup> Corneal incisions constructed with FS have been proven stable, repeatable and safe as compared with CP in numerous studies.<sup>51–53</sup> Namely, it has been found that there is less wound gape and decreased wound edema with laser-created incisions than with manual incisions.<sup>54</sup>

The main corneal incision and paracentesis are accomplished using FS platform customizable settings, generally upon imaging of the eye. Laser allows the construction of a more complex wound shape (such as biplanar or triplanar), with higher consistency regarding reproducibility when compared to CP. Likewise, the incidence of Descemet's membrane detachment, endothelial misalignment, and posterior wound contraction is low in FLACS.<sup>53,54</sup>

However, as a counter back of FS, peripheral vascularization of the cornea prevents completion of the laser cut (forcing manual aid) because of the suction-driven blanching of the limbic vasculature; therefore, less vascularized areas should be looked for (if possible) when adjusting the laser cut parameters upon imaging.<sup>55</sup>

Therefore, in favor of FLACS, incisions are less prone to wound gape and leakage;<sup>45</sup> also, surgically induced astigmatism is more predictable. The limitations include the location and completion of the FSL wounds in some cases.

## Arcuate Keratotomy

Corneal partial-thickness incisions are included in the armamentarium of corneal astigmatism surgical correction. Classically performed in a manual (blade) manner, keratotomy with FS technology shows higher predictability and repeatability, adding the possibility of completely intrastromal incisions beyond the standard anterior penetration.<sup>56</sup> These designated arcuate incisions (AIs) can be performed by the FS laser at the surgeon's predetermined depth, length, location and treatment axis; additionally, anterior penetrating AIs can be opened up manually intraoperatively or post-operatively to enhance the effect.<sup>57,58</sup> Femtosecond laser-assisted arcuate keratotomy (FSAK) is associated to less irritation, epithelial ingrowth or loss of corneal sensation, beyond diminishing the risk of infection for patients;<sup>59</sup> thus, it can be safely used in patients with ocular surface disease or after keratoplasty. Nevertheless, it is believed that

intraström AIIs may have a reduced astigmatic effect when compared to anterior-penetrating AIIs because the former does not involve Bowman's membrane.

Intraström incisions are also used for non-refractive marking of the implantation axis of toric IOLs.<sup>60</sup>

Several studies point out to comparable results between FS laser-assisted corneal incision and toric IOLs implantation for correcting mild (<1.25 D), central, and with-the-rule astigmatism in terms of safety, efficacy and stability.<sup>61–64</sup>

However, most available studies show some superiority of toric IOLs implantation over FSAK in moderate-to-high (>1.25 D), against-the-rule, or limbus-to-limbus astigmatism correction.<sup>64–66</sup>

Literature on nomograms for femtosecond laser-created AIIs is scarce. Wortz & Gupta developed a nomogram for correction of low levels of astigmatism.<sup>67,68</sup> Baharozian et al's FSL anterior penetrating AI nomogram was designed for patients with <1.25 D of astigmatism, which is a modification of Donnenfeld's manual LRI nomogram; it accounts for the influence of posterior corneal astigmatism relative to the type of astigmatism being treated and uses a 9.0 mm optical zone.<sup>69</sup>

Hence, FLACS has notable advantages over CP. First, the treatment of astigmatism is much more accurate with FSAK than with manual keratotomy, given the ability to control depth and location.<sup>45</sup> Secondly, the ability to perform intraström incisions is unique to FSL. Finally, postoperative tuning of the astigmatic correction is feasible with the opening of laser-assisted incisions (at the slit lamp).

Nevertheless, FLACS' range of correction is limited to low levels of corneal astigmatism, and improved FSAK-specific nomograms are yet to be developed.

## Refractive and Visual Outcomes

It has been reported in several studies that no statistically significant differences between FLACS and CP were found regarding corrected, uncorrected distance vision acuities, and refractive outcomes in the long term.<sup>70–74</sup> Meanwhile, some systematic reviews and meta-analyses<sup>40</sup> have shown better medium-term uncorrected and corrected visual acuities with FLACS than with CP; however, this finding, although statistically significant, does not translate into a clinically significant difference (inferior to 0.05 logMAR).

Visual acuity can be affected in the long term by capsular bag-IOL interactions, such as tilt, decentration, or posterior capsule opacification. These events have been reported to occur less frequently after FLACS.<sup>75,76</sup> Long-term IOL positioning relates to several factors, with capsular bag shrinkage standing out as a major factor for tilt and decentration; this phenomenon is more prominent in CP.<sup>77</sup>

IOL positioning affects the effective lens position (which is essential for IOL power calculations), ergo, the refractive results. Furthermore, such positioning impacts decisively on the performance of premium IOLs such as toric, EDOF, and multifocal lenses. Kranitz et al identified significantly higher levels of IOL decentration and worse CDVA in the CP group.<sup>26</sup> In addition, Reddy et al registered a higher IOL decentration with CP when compared to FLACS.<sup>78</sup>

Regarding posterior capsule opacification, most studies show a higher incidence with FLACS,<sup>19,79</sup> probably related to adjacent laser treatment, which may induce mesenchymal transformation of lens epithelial cells (LEC). This impact is assumed to override the expected benefits of a laser driven LEC apoptosis close to the capsulotomy edge; again, laser pulse energy and duration are relevant features regarding this impact.<sup>80–82</sup> Subgroup analysis of PCO with different pulse energy (high vs low) FLACS is almost inexistent.

However, Nd: YAG capsulotomy rates in FLACS are reportedly lower than those in CP. This may be accounted for by a lower PCO grade and, consequently, a minor impact on visual acuity; such grading is lacking in most published literature.

Another measure of refractive predictability is mean absolute error (MAE). Depending on the number and study design of the included trials, review and meta-analysis reports are not clear regarding the superiority of FLACS over CP in terms of postoperative SE. Hence, large reviews based on randomized control trials (RCTs) point to a higher predictability of FLACS in the short term but not in the long term,<sup>83</sup> whereas reviews based on a small number of RCTs<sup>78</sup> report an advantage in favor of FLACS MAE at 12 months follow-up. Other systematic reviews, including both prospective and retrospective trials, found a clinically important difference in MAE only in the mid-term (1 month to 3 months follow-up).<sup>40</sup>

Surgical induced astigmatism (SIA) is caused by the wound healing process after corneal incision.<sup>84</sup> This form of astigmatism is caused by the processes at the place where the corneal incision took place, and it is most relevant to toric



IOLs implantation. Differences between FLACS and CP regarding SIA only seem to be clinically significant at the predictability level (achieved vs attempted), without statistically significant differences with respect to the overall magnitude of the SIA.<sup>40,55</sup>

## Other Surgical Outcomes

Commonly assessed surgical endpoints are effective phacoemulsification time (EPT), cumulative dissipated energy (CDE), and circularity of capsulotomy. EPT represents the value of the phacoemulsification time length at 100% power in continuous mode,<sup>40</sup> whereas CDE is the EPT in seconds divided by 6000 or the EPT in minutes divided by 100. There is sufficient evidence that FLACS is superior to CP in every and each of the aforementioned parameters.<sup>24,43,54,83,85–90</sup> A more precise and reproducible capsulotomy circularity is registered with FLACS, which allows for better lens centration and a lower risk of lens mispositioning,<sup>91,92</sup> this, in turn, is liable to translate into better optical performance.<sup>93</sup>

## Patient Reported Outcomes

Literature on patient-reported outcomes (PROs) is very scarce. The heterogeneity of the methodology is employed to assess patient satisfaction and other subjective parameters, the difficult global assessment of differences between FLACS and CP.<sup>94</sup> Patient-reported outcome measures (PROMs) vary greatly among several studies. Given the increasing number of refractive cataract or lens surgeries and their inherent elective nature, patient-reported outcomes are paramount when choosing an adequate premium IOL. Thus, more comprehensive and standardized PROMs are required for a rigorous analysis.

## Complications

Complications associated with FLACS can be either intraoperative or postoperative. Intraoperative complications usually include suction loss, subconjunctival hemorrhage, and capsule- or pupil-related complications.<sup>18,46</sup>

Suction loss is a consequence of deficient docking driven by interface defects, patient movement, anatomical particularities, or conjunctival chemosis. Among the anatomic conditions, conjunctivochalasis, pinguecula, pterygia, or bleb filtration surgery are the most frequent. Some FS platforms have suction rings with different diameters to improve the fitting of the docking piece. In the event of suction loss, laser treatment is to be immediately suspended to avoid mistreatment.

Subconjunctival hemorrhage is caused by the vacuum applied, total treatment time, and specific docking interface; this complication is more frequent with applanation docking than with liquid-interface.<sup>10</sup>

Posterior capsule rupture (PCR) has been reported to be less frequent with FLACS than with CP.<sup>40,75</sup> Regarding anterior capsule complications (tears or tags), the reported evidence of a higher incidence with FLACS is two-fold: first, it is described to be variable, ranging from 0.1% to as high as 4%,<sup>17,95</sup> and second, this complication is mostly related to high-energy pulse FS platforms.<sup>18,28,40,95</sup> These findings can be explained by the microscopically different capsulotomy edges, as produced by the different laser settings. Commonly, high-energy FLACS produces less smooth and notched capsulotomy edges than low-energy pulse FS;<sup>9,96</sup> this microscopic difference may account for the very low incidence of anterior capsule complications in low-energy FLACS, comparable to CP.<sup>10,41,97</sup>

Either way, the overall implications of all capsule-related complications (such as the need for vitreoretinal or affecting visual outcomes) seem to be not statistically significant in a global comparison between FLACS and CP.<sup>40,79,98</sup> Nevertheless, the impact of such events should not be underestimated in the context of premium IOL implantation, as it irrevocably compromises surgical success, as capsular integrity and further optimal centration are paramount in the final result. Unfortunately, literature comparing low-energy FLACS and CP that contemplates this niche or subgroup of refractive cataract surgery is scarce, although not absent.<sup>41,99</sup>

Pupil constriction is a commonly reported feature of FLACS,<sup>18,34,96</sup> and is associated with prostaglandin release during laser treatment of the anterior capsule.<sup>47,71,100,101</sup> Pupil miosis is a severe and undesirable event as it affects the feasibility of cataract surgery. The consensual use of pre-operative non-steroid anti-inflammatory drugs (NSAIDs) in cataract surgery is among the strategies for preventing the loss of dilation with FLACS. However, pre-operative NSAIDs administration is normally insufficient to avoid the laser-induced miosis associated with FLACS. Therefore, a multitude

of actions, either single or in combination, have arisen to address this issue.<sup>42,102</sup> It is also recommended to observe specific laser-related conditions, such as the distance from the intended capsulotomy edge and pupillary margin ( $>1$  mm recommended) and duration of laser treatment.<sup>103,104</sup>

However, most published literature reports this complication without differentiating between types of FS pulses, ie, high or low energy (or even excluding the latter type). Recent publications show evidence of the absence of laser-induced miosis with low-energy FLACS.<sup>10,99,105</sup> Moreover, in the few systematic reviews and meta-analyses that include low-energy FLACS and subgroup analysis, the reported incidence of laser-induced pupil miosis is virtually null and comparable to CP;<sup>9,106</sup> on the contrary, high-pulse energy FLACS is associated with pupil constriction almost universally.<sup>40,74,94,96</sup> The impact of such evidence should not be ignored and is still to be integrated in the common knowledge of femtosecond laser-assisted cataract surgery.

With regard to postoperative complications, endothelial and retinal status have been the subject of several studies. Although recently published literature based on well-powered randomized controlled trials (RCTs) do not present evidence of a statistically significant difference between the techniques in normal eyes,<sup>107–111</sup> endothelial cell loss (ECL) has been reported to be lower in FLACS than in CP in several reviews and meta-analyses.<sup>40,78,83,85,112</sup> Laser-assisted lens fragmentation reduces phacoemulsification time with less volume irrigation and EPT, especially in harder cataracts;<sup>85,109</sup> this, in turn, translates into less ECL. Moreover, some studies have enhanced the evidence of this protective effect in corneal dystrophies (such as Fuchs') through the above cited mechanisms.<sup>113–115</sup>

Regarding the incidence of cystoid macular edema (CME), most systematic reviews and meta-analyses showed no significant differences between FLACS and CP.<sup>83,85,112</sup> Similarly, measurement of most retinal parameters (total macular volume, foveal thickness, and outer macular ring) showed comparable results in both techniques,<sup>116–118</sup> although a short term, postoperative lower central macular volume with FLACS was reported in some studies involving patients with age-related macular degeneration (AMD).<sup>119</sup> Hence, FLACS may be advantageous in patients with macular vulnerability;<sup>40</sup> this indication being further supported by evidence of the higher impact of ultrasound energy on the inflammatory response of the posterior segment compared with FLACS.<sup>52,117,120</sup>

A considerable learning curve is in demand for FLACS, with an estimate minimum of 100–200 cases, depending on the surgeons' experience; above these numbers, a significant decrease in intraoperative complications is registered in most studies.<sup>16,17,36,121,122</sup>

## Indications and Contraindications

### Indications

FLACS has been advocated for refractive cataract or lens surgery with premium IOL implantation because of its ability to produce a highly precise, reproducible, and customizable capsulotomy (regarding width and centration), surpassing CP standards. This is paramount for achieving an optimized IOL centration, essential to a premium IOL's performance. Furthermore, low-to-moderate amounts of astigmatism can be addressed by FS arcuate keratotomy (FSAK).

Hard or dense cataracts can be an indication for FLACS, as laser fragmentation of the lens nucleus reduces the total phacoemulsification time, EPT, and CDE, lowering the risk of corneal endothelial loss.<sup>123</sup>

FLACS may be indicated in complex cases with challenging capsulotomies, such as traumatic subluxated cataracts or zonular instability, intumescent cataracts, and pseudoexfoliation syndrome, by reducing the stress on the zonular fibers and posterior capsule, consequently lowering the rate of postoperative complications. Cataract grade can help determining the choice of FLACS over CP, as the lower EPT or CDE associated with FLACS can be beneficial in hard cataracts, translated into a faster visual recovery,<sup>124,125</sup> in the same manner, eyes with particular conditions, such as shallow anterior chambers, can benefit from such approach.<sup>126</sup>

The reported lower impact of FLACS on endothelial cell count compared to CP may indicate that the former technique in cases of Fuchs' dystrophy and other types of endothelial degeneration.<sup>127</sup>

FSL can also be used to enlarge the anterior capsulotomy to the desired size in cases of capsular contraction syndrome.<sup>128</sup>

Likewise, regarding pupil status, recent literature shows strong evidence that pupil constriction after FS laser delivery, classically attributed to FLACS in general, is not a feature of low-energy pulse FLACS. This difference should not be taken lightly, as it has a relevant impact on the performance of the several surgical step onwards.

## Contraindications

Patients with several conditions may not be ideal candidates for FLACS treatment. Anatomical characteristics affecting docking feasibility, such as deep-set eye globe, narrow palpebral fissure, prominent nose, or brow or inability to lay supine, present as contraindications for FLACS.<sup>35,129</sup> In addition, any condition affecting OCT (or equivalent) imaging of the anterior segment, namely, previous corneal additive (eg, ring or inlay implants) surgery, severe corneal opacity, or edema, are the main contraindications for FLACS.<sup>45,129</sup>

Other conditions can pose an increased challenge to FS laser-assisted cataract surgery and can be considered relative contraindications. Among them are poor pupillary dilation (<6 mm diameter), corneal surgeries (such as keratoplasty), glaucoma surgery, white cataracts, mild corneal scarring, and edema.

Poor preoperative pupillary dilation has been addressed using multiple approaches, including several preoperative administration schemes, contemplating topical medications such as phenylephrine, cyclopentolate, atropine, and/or nonsteroidal anti-inflammatory drugs (NSAIDs),<sup>130,131</sup> intracameral epinephrine or phenylephrine, viscomydriasis with viscoelastic, or placement of iris expansion devices. It should be stressed that deficient pupil dilation poses a different challenge, depending on the pulse energy level of the FLACS platform. As has been extensively described, laser-induced miosis with high-energy FLACS adds extra difficulty to a narrow preoperative pupil. This fact gave birth to a vast body of literature covering multiple strategies to address pupil constriction with high-energy FS platforms.<sup>70,73,132,133</sup> In contrast, low-energy pulse FLACS is reportedly not associated with pupil narrowing and therefore poses no additional dilation strategies compared with conventional phacoemulsification.<sup>134</sup>

Lens fragmentation is not advised in white cataracts due to the low feasibility of adequate imaging of opaque tissue.<sup>45,135</sup> Laser energy absorption is also affected by variations in water content, as is the case of white or brunescant cataracts. For FS platforms performing lens fragmentation after the capsulotomy step, intumescent cataracts pose an additional risk of posterior capsule rupture, caused by a posterior capsule depth change after capsulotomy decompression.<sup>136</sup> This feature is not shared by other FS platforms that perform a different step sequence, accomplishing capsulotomy after lens fragmentation.<sup>9,99</sup>

Although the completeness of capsulotomy and fragmentation may be jeopardized in the presence of corneal opacities (scar or edema), there are isolated case reports of successful FLACS;<sup>137</sup> undoubtedly, the magnitude of such opacities is a relevant parameter in this context. Distortions in normal anatomy, either natural (pterygium or pinguecula) or iatrogenic (filtering blebs or tubes, as in glaucoma surgery), present themselves as challenging cases but should not constitute absolute contraindications, rather demanding additional care; with this regard, success has been reported in such cases.<sup>138</sup>

Another concern is the impact of docking on intraocular pressure, due to suction and type of docking; applanating systems are associated with higher pressure upon docking than liquid interfaces.<sup>13,33</sup> So far, however, there is no evidence of disease progression with well-controlled glaucoma or other optic neuropathies, for such matter.<sup>83,112</sup>

## Cost-Effectiveness

Although performing major steps in cataract or lens surgery has high standards of efficacy and safety, FLACS currently presents itself as a more expensive technology than CP. The weight of the platform acquisition costs plus the consumables attached to it render FLACS a less cost-effective procedure than CP.<sup>77,139–141</sup> Another point is the fact that an FS laser platform cannot substitute for CP altogether. To accomplish the full steps of cataract or lens removal, a phacoemulsification/aspiration device is required; that is, aspiration of the lens material and further polishing of the capsular bag. Some attempts have been made to reduce the need for phacoemulsification machines in the context of low-grade cataract or refractive lens surgery;<sup>122</sup> such endeavor is understandable, taken that FLACS may be beneficial in such cases by enabling higher precision and customization for capsulotomy and its impact on premium IOL positioning.



## Conclusions

Current evidence of the low rate of anterior capsule complications and near absence of laser-induced miosis with low-energy FLCAS (comparable to CP) is relevant to the field of knowledge regarding this technology. This evidence obviates the historically associated counter backs of FLACS, with reports traditionally disregarding the clinical impact of different pulse energy levels of femtosecond lasers.

With this updated view, FLACS has proven to be non-inferior to CP in terms of the rates of complications and adverse events. Furthermore, there is evidence that FLACS can be safer than CP in more demanding cases such as corneal dystrophies, lens subluxation, zonular instability (eg, pseudoexfoliation or Marfan syndrome), harder cataracts, or macular vulnerability. Regarding visual outcomes, some evidence has been collected on the mid-term advantages of FLACS over CP. This evidence may expand further in the universe of toric or presbyopia lens surgery, since higher levels of precision and customization are paramount for the efficacy of such procedures. However, there are limitations regarding the evaluation of FLACS in the context of premium IOLs implantation, with the vast majority of published studies not presenting subgroup analyses of the type of IOL implanted.

Time duration related to FLACS is another concern when compared to CP. Most FS platforms require patient mobilization from the laser device to the surgical bed or the operating room. This translation is time-consuming and lengthens the overall duration of surgery. However, one platform is portable, thus obviating this counterback and enabling comparable surgical time durations between FLACS and CP.

Regarding cost-effectiveness, it is evident that FLACS cannot currently compete with CP, the main difference being the high cost of the laser equipment and consumables. Therefore, CP keeps the crown of the standard technique of cataract surgery, limiting the use of FLACS as an option, mainly for the above indications; this choice has inherent additional expenses, usually charged to the patient. However, taking the attractive grounds of attractive laser-based techniques, this high-cost scenery is liable to change, subject to the old laws of offer and demand; for this matter, further developments on delivery outcomes are on the wait.

The behavioral differences between different low- and high-energy FS pulses are currently being unveiled, although they are seldom published. Increased knowledge of the spectrum of differences in FS technologies allows for better judgment and appraisal of surgical planning.

In summary, FLACS has evolved technically since its dawn, namely with the development of different types of pulse energy levels and broader surgical step coverage and refinement. Among the benefits of FLACS, there is gathered evidence of some advantage over CP regarding visual outcomes on the mid-term. Customization of capsulotomy can be an advantageous feature of FLACS over CP, notably in the universe of premium IOLs. The rate of complications and adverse events is similar to CP when taken into consideration the behavioral difference between the FS pulse patterns. FLACS can also be a first option in eyes with comorbidities. To these improvements, portability (for at least one FS platform) should be added as a favorable feature.

Like other surgical techniques in its youth, the indications have been simultaneously widened and fine-tuned; this enlargement of the spectrum of indications may impact on the use of FLACS and, by the law of offer and demand, reflect favorably on its costs. Further improvements in this technique should be expected, along with larger studies approaching the different laser systems.

## Disclosure

The authors report no conflicts of interest in this work.

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