Femtosecond laser-assisted cataract surgery versus standard phacoemulsification cataract surgery

Case-control study from the European Registry of Quality Outcomes for Cataract and Refractive Surgery

Sonia Manning[1], MD, FRCSI (Ophth)

Peter Barry[2], FRCS, FRCOphth

Ype Henry[3], MD, FEBO

Paul Rosen[4], FRCS, FRCOphth

Ulf Stenevi[5], MD, PhD

David Young[6], PhD

Mats Lundström[7], MD, PhD

1. Department of Ophthalmology, University Hospital Waterford, Waterford, Ireland
2. Department of Ophthalmology, St. Vincent's University Hospital Group, Dublin, Ireland
3. Department of Ophthalmology, Vumc, Amsterdam, The Netherlands
4. Oxford Eye Hospital, Oxford, United Kingdom
5. Department of Ophthalmology, Sahlgren's University Hospital, Molndal, Sweden

6. Department of Mathematics and Statistics, University of Strathclyde, Glasgow, United Kingdom
7. Department of Clinical Sciences, Ophthalmology, Faculty of Medicine, Lund University, Lund, Sweden

The ESCRS FLACS Study Collaborators:

Michael Lawless, Gerard Sutton, Tim Roberts, Christopher Hodge, Erik Mertens, Werner Ingels, Pavel Stodulka, Michaela Netukova, Detlef Holland, Tim Herbst, Zoltan Z. Nagy, Tamas Filkon, Roberto Bellucci, Miriam Cargnoni, Massimo Gualdi, Luca Gualdi, Edoardo Ligabue, Leonardo Mastropasqua, Luca Vecchiarino, Giuseppe Perone, Filippo Incarbone, Rudy Nuijts, Frank van den Biggelar, José Guëll, Mar Mas, Bilgehan Sezgin Asena, Sinan Goker, Buket Ayoglu, Sheraz Daya, Crista Sunga, Marcela Espinosa-Lagana, Julian Stevens, Janet Barlett

Presented in part at the at the XXXIII Congress of the ESCRS, Barcelona, 7th September 2015

This study was funded by the European Society of Cataract and Refractive Surgeons.

FINANCIAL DISCLOSURE: No author has any financial or proprietary interest in any material, or method, mentioned.

ABSTRACT

PURPOSE: To compare the visual, refractive and adverse outcomes of femtosecond laser-assisted cataract surgery (FLACS) to conventional phacoemulsification cataract surgery (CPCS).

SETTING: Cataract surgery clinics in 9 European countries and Australia (FLACS) and in 18 European countries and Australia (CPCS).

DESIGN: Multicenter consecutive case control study from the European Registry of Quality Outcomes for Cataract and Refractive Surgery.

METHODS: Eyes undergoing FLACS were matched to eyes undergoing CPCS, for preoperative corrected distance visual acuity (CDVA), age and preoperative risk factors. The two groups were compared for intraoperative and postoperative complications, postoperative CDVA, absolute biometry prediction error (BPE), preoperative and postoperative corneal astigmatism and surgically induced astigmatism (SIA). Follow-up was 7-60 days.

RESULTS: A total of 2,814 FLACS cases were matched to 4,987 CPCS cases. The majority were female (57%) with mean age 66 years and baseline logMAR CDVA 0.32 (6/12-1). Posterior capsule complications were similar (FLACS: 0.4 %; CPCS: 0.7%). Postoperative logMAR CDVA differed by one letter (FLACS: 0.05 [6/6-3]; CPCS: 0.03 [6/6-2]). At follow-up, FLACS versus CPCS compared as follows: worse postoperative CDVA (by 5 letters or more): 1% versus 0.4%; % CDVA 0.3 (6/12) or better: 87.8% versus 90.4% ; absolute BPE: 0.43 D versus 0.40 D; % within ± 0.5D of target: 72% versus 74.3%; postoperative complications : 3.4% versus 2.3%.

CONCLUSION: FLACS does not have superior visual and refractive outcomes, but does have superior corneal astigmatic treatment outcomes, compared to CPCS. Intraoperative complications are similar and low in both groups. Postoperative complications are lower in CPCS.

INTRODUCTION

Femtosecond laser-assisted cataract surgery (FLACS) has been under the spotlight since the first publication of its use in clinical practice, in 2009. **(Nagy 2009)** Femtosecond lasers can perform the anterior capsulotomy, lens fragmentation and corneal incision construction, as well as corneal astigmatic treatment

There has been significant excitement in the peer-reviewed **(Mamalis 2013; Lindstrom 2011)** and non-peer-reviewed **(Duke Med Health News Nov 13; Duke Med Health News Jan 2012)** ophthalmic literature, regarding the potential advantages of FLACS over conventional phacoemulsification cataract surgery (CPCS).

Successful outcome in cataract surgery is measured in terms of visual outcome (visual acuity) **(Lundstrom 2012; Jaycock 2009; Hahn 2011)**, refractive outcome (biometry prediction error [BPE] of postoperative refraction) **(Lundstrom 2012; Hahn 2011)**, rate of complications (with the rate of torn posterior capsule being used as a benchmark standard against which cataract surgeons measure themselves)**(Lundstrom 2012; Johnston 2010)** and, more recently, patient-reported outcome measures (PROMs). **(McAlinden 2011; Lamoureux 2011)**

Even though several studies have shown that FLACS demonstrates better reproducibility in terms of capsulotomy diameter and centration **(Nagy 2011; Friedman 2011; Kranitz 2011; Auffarth 2013; Reddy 2013; Mastropasqua 2013)**, corneal wound construction **(Mastropasqua 2014; Grewal 2014)** and decreased ultrasound energy and time **(Takacs 2012; Conrad-Hengerer 2012 a; Abell 2013; Conrad-Hengerer 2013 c; Reddy 2013; Daya 2014)**, there is no evidence, to date, showing that visual and refractive outcomes achieved with FLACS, are superior, in a clinically meaningful way, to those achieved with CPCS. **(Kránitz 2012; Miháltz 2011; Abell 2013; Roberts 2012; Lawless 2012; Filkorn 2012)**

In addition, even though posterior capsule complication rates with FLACS are reported as similar to the lowest published rates for CPCS **(Roberts 2013)**, these findings need to be balanced against the fact that these FLACS studies excluded cases with small pupil and other difficult cases, which carry a higher risk of posterior capsule rupture.

So, even though there is a plethora of published reports about FLACS in the literature, there is lack of evidence regarding its superiority over CPCS. The authors believe such evidence can be delivered by a carefully constructed case-control study, using the European Registry of Quality Outcomes for Cataract and Refractive Surgery (EUREQUO), a well-established multinational cataract and refractive surgery database. EUREQUO has contributed to the formulation of evidence-based guidelines for CPCS **(Lundström 2012)** and has provided data on visual outcomes in a real-life clinical setting. **(Lundström 2013)**

The superiority of FLACS over CPCS, has not been shown. This study aims to compare the visual, refractive and adverse outcomes of a consecutive series of FLACS cases to carefully matched cases of CPCS as reported in EUREQUO.

MATERIALS AND METHODS

Ophthalmic surgeons from Europe and Australia, with known clinical experience in FLACS, were invited, to participate in the study. The laser platform was not identified in order to avoid bias. The surgeons had to have performed at least 50 cases of FLACS to account for the learning curve associated with a new procedure. The FLACS cases reported had to be consecutive and a case was included from the moment docking was attempted.

The EUREQUO web form was used as the case report form for all cases. The patients were informed about registration of their data in EUREQUO and were free to accept or refuse participation in the study, without their decision affecting their treatment. A dedicated, site-specific, registry manager, trained by the European Society of Cataract and Refractive Surgeons, ensured that reporting guidelines were met and consecutive FLACS cases were reported. Local institutional ethics committee approval was obtained for each participating clinic.

The EUREQUO web form normally used for recording CPCS preoperative, intraoperative and postoperative data underwent expansion, to allow recording of parameters specific to FLACS. **(Lundstrom 2012)** A number of FLACS-specific parameters were extracted for each FLACS case, in addition to the regular parameters related to CPCS:

Demographic data: age; gender.

Preoperative data: corrected distance visual acuity (CDVA) in logarithm of the minimum angle of resolution (logMAR) (calculated from the decimal notation in the database) [with Snellen equivalent]; target refraction [D]; keratometry (K) readings; ocular co-morbidity (glaucoma; AMD; diabetic retinopathy; amblyopia; other); surgical difficulty (previous corneal refractive surgery; white cataract; pseudoexfoliation; previous vitrectomy; corneal opacity; small pupil; other).

Intra operative data: steps of the cataract operation for which the laser platform was used (corneal incision, corneal astigmatic treatment, capsulotomy, nucleus fragmentation); type of intraocular lens (IOL) (acrylic hydrophilic; acrylic hydrophobic; hydrogel; PMMA; silicone; no IOL); additional IOL specification (accommodative; toric; multifocal; multifocal toric); surgical complications common to both procedures (torn posterior capsule; vitreous loss; iris damage; dropped nucleus; other); FLACS-specific complications (procedure abandoned and reason, conversion to CPCS or extracapsular cataract extraction, incision-related complications, capsulotomy-related complications, lens fragmentation-related complications, other laser-related complications).

Postoperative data: CDVA in logMAR (calculated from the decimal notation in the database) [with Snellen equivalent]; K-readings; postoperative refraction; postoperative complications (uveitis; corneal edema; early posterior capsule opacification; uncontrolled intraocular pressure; IOL explantation; other).

FLACS cases were recruited between December 1st 2013 and May 31st 2015. CPCS cases were recruited retrospectively from the CPCS cases reported in the EUREQUO database in 2014.

Statistical analysis

The criteria for matching CPCS cases to FLACS cases included: exact matching for preoperative logMAR CDVA in the eye to be operated on; age matched within 2 years; same number of ocular co-morbidities (see preoperative data); same number of surgical difficulty variables (see preoperative data). We aimed to match two CPCS cases for each FLACS case.

All statistical calculations were performed using IBM SPSS, version 22, IBM Ltd, Chicago, Ill. Demographic data were analyzed using descriptive statistics. CPCS cases were compared to FLACS cases for age, gender, preoperative and postoperative CDVA, intraoperative and postoperative complications, absolute biometry prediction error (BPE), preoperative and postoperative corneal astigmatism and surgically induced astigmatism (SIA) by Naeser polar value. The chi-square test was used for categorical variables and the 2-tail Student's t-test for numerical variables.

Unchanged postoperative CDVA was defined as postoperative CDVA within 0.10 logMAR of preoperative CDVA, according to *Bailey et al*. **(Bailey 1991)** (1 Snellen line of 5 letters). Accordingly, better postoperative CDVA was defined as CDVA that had increased by more than 0.10 logMAR from the preoperative value and worse postoperative CDVA was defined as CDVA that had deteriorated by more than 0.10 logMAR from the preoperative value. The percentage of CPCS and FLACS cases with better, unchanged and worse postoperative CDVA were examined as was the percentage of CPCS and FLACS cases with BPE within ± 0.5 D and within ± 1.0 D of target. Follow up period in the database ends 2 months after surgery. Multivariate analyses of relationships between the dichotomized visual outcome and the other variables were performed by logistic regression.

Refractive surprise was defined as a BPE outside ± 2 D of target. Corneal astigmatism [mean K] was defined as [mean K_{steep}] - [mean K_{flat}], both before and after surgery. Clinically significant residual postoperative corneal astigmatism was defined as corneal astigmatism ≥ 1.5 D. Multivariate analyses of relationships between postoperative corneal astigmatism and other variables were performed by logistic regression. Multivariate analyses of relationships between SIA and other variables were performed by linear regression. In all analyses, a p-value of 0.05 or less was considered significant.

RESULTS

Surgeons from 10 countries (Australia; Belgium; Czech Republic; Germany; Hungary; Italy; the Netherlands; Spain; Turkey; United Kingdom) contributed data from FLACS cases, between December 2013 and May 2015. Surgeons from 19 countries (Australia; Austria; Belgium; Czech Republic; Denmark; Germany; Greece; Hungary; Iceland; Ireland; Italy; Lithuania; the Netherlands; Norway; Slovak Republic; Spain; Switzerland; Turkey, United Kingdom) contributed data from CPCS cases, between January and December 2014. The number of FLACS cases and matched CPCS controls are given in Figure 1. The achieved 1:1.8 case-control ratio did not reach the intended 1:2 case-control ratio. The preoperative characteristics of the two groups are given in Table 1.

In the 2,814 FLACS cases with matched CPCS controls, a femtosecond laser was used to carry out the corneal incisions in 34.7% of cases, the capsulotomy in 99.4% of cases and the nucleus fragmentation in 94.7% of cases. In addition, 4.5% of FLACS cases had corneal astigmatism treated by the femtosecond laser at the time of cataract surgery.

Intra operative complications of FLACS and CPCS are given in Table 2. FLACS-specific complications are given in Table 3. Data on type of IOL implanted are given in Table 4.

Postoperative outcomes, including visual outcomes, refractive outcomes and postoperative complications, are given in Table 5, for all FLACS cases compared to all CPCS cases. Due to the high rate of use of multifocal IOLs in the FLACS group (see Table 4), we compared postoperative outcomes between FLACS cases and CPCS cases, including only cases where monofocal IOLs were used.

Multivariate logistic regression analysis results for the association between worse postoperative CDVA after FLACS or CPCS and significant preoperative, intraoperative and postoperative variables, are reported in Table 6A for monofocal IOLs only and in table 6B for all cases. Multivariate logistic regression analysis results for the association between refractive outcome of FLACS or CPCS and significant preoperative and intraoperative variables are reported in Table 7. Multivariate logistic regression analysis results for the association between postoperative corneal astigmatism after FLACS or CPCS and significant preoperative and intraoperative variables are reported in Table 8.

In a multivariate linear regression analysis for the association between postoperative SIA (reported by the Naeser polar value) after FLACS or CPCS and significant preoperative and intraoperative variables, a higher Naeser polar value was predicted (standardized beta coefficient [CI]) by poorer preoperative logMAR CDVA (0.69 [0.114 – 0.224]), previous astigmatic treatment (0.71 [0.207 – 0.406]), any ocular co-morbidity (0.52 [0.068 – 0.169]), CPCS (0.061 [0.069 – 0.155]), previous corneal refractive surgery (0.58 [0.262 – 0.587]) and female gender (0.028 [0.11 – 0.091]).

DISCUSSION

The intention of this study was to compare FLACS to CPCS, in terms of visual outcome, refractive outcome and complications, by means of a case-control study using data from EUREQUO.

The intended 1:2 case-control ratio was not achieved despite the large number of CPCS cases submitted to EUREQUO during the study period (over 295,000 cases), because there were not enough CPCS controls in the database with matching preoperative CDVA and matching (young) age. The trend for FLACS patients to have better preoperative CDVA has been reported before **(Ewe 2015)** and may indicate surgeon or patient preference for FLACS, or possibly, socioeconomic influences on the selected mode of surgery. The trend for younger age in FLACS, compared to CPCS patients, which was overcome with meticulous matching, has not been reported in previous comparative studies. **(Abell 2013; Abell 2014; Mayer 2014b; Ewe 2015).** However, age may be a confounding factor for other characteristics in the FLACS group, such as previous corneal refractive surgery and preference for non-monofocal IOLs.

There was a difference in the type of detailed? ocular co-morbidities and surgical difficulty variables between the two groups. There were more patients with diabetic retinopathy in the CPCS than the FLACS group and more patients with amblyopia in the FLACS than the CPCS group. Other studies comparing FLACS to CPCS either excluded patients with coexistent ocular disease **(Conrad-Hengerer 2015)** or did not report preoperative ocular co-morbidities. **(Ewe 2015).** In one study where patients with ocular co-morbidities, other than corneal were included, the preoperative and postoperative CDVA did not differ in the two groups. **(Abell 2013)**. The difference in diabetic retinopathy rates in this study may indicate surgeon preference for eyes with less disease for the newer surgical technique, while the difference in amblyopia rates may indicate surgeon preference for eyes with a wider visual safety margin for the newer surgical technique. The FLACS group had a much higher rate of previous corneal refractive surgery and pseudoexfoliation, while the CPCS group had a much higher rate of white cataracts, small pupils and other surgical difficulty variables (such as deep-set eyes, patients with kyphosis or other inability to position for surgery etc).

The higher rate of previous corneal refractive surgery in the FLACS group is, clinically, very significant. A recent study showed that CPCS patients with previous corneal refractive surgery are younger and at much higher risk of worse postoperative CDVA than patients without previous corneal refractive surgery, especially when they have good preoperative CDVA. **(Manning 2015)** Studies comparing FLACS to CPCS to date, either excluded patients with previous corneal refractive surgery **(Abell 2013)** or did not report on that preoperative characteristic. **(Ewe 2015)** It is possible that FLACS surgeons also perform corneal refractive surgery, so they have an over representation of patients with previous corneal refractive surgery, who subsequently undergo cataract surgery.

There were more white cataracts in the CPCS than in the FLACS group. This is likely because laser is unable to penetrate through opaque lens material, so that the laser cannot perform the step of lens fragmentation. Also, even though anterior capsulotomy in white cataracts is technically feasible with FLACS, the rate of capsule related complications such as radial tears, capsular tags and incomplete capsulotomy buttons, is still high in such cases. **(Conrad-Hengerer 2014)**

The rate of pseudoexfoliation was higher in the FLACS compared to the CPCS group. However, the two groups were not matched for race. In addition, there can be up to 50% clinical under-diagnosis of pseudoexfoliation, according to a histopathologic study of 40 eyes with late in-the-bag subluxation or dislocation. (Liu 2015)

In contrast, the rate of small pupils was higher in the CPCS compared to the FLACS group. This is because laser capsulotomy requires direct line of site to the capsule and a safety zone of 1000 µm between iris and capsule to avoid inadvertent laser damage to the iris and subsequent intraoperative pupil miosis. Techniques to assist FLACS in eyes with a small pupil have been described. **(Conrad-Hengerer 2013)** However, in such cases, it is recommended that both the FLACS treatment and the manual part of the cataract operation be performed in the same sterile room, without moving the patient, to reduce the risk of infection. This may limit the use of FLACS in eyes with small pupils to surgeons with access to that particular operating theatre arrangement. The particular operating theatre organization of each participating FLACS clinic in this study is not known. However, there were no cases of postoperative endophthalmitis in either study group.

Other surgical difficulty variables, not specified in the EUREQUO database, but grouped under the term “other”, were higher in the CPCS than in the FLACS group. The reason could be that FLACS surgeons avoid these cases as they affect the ability to obtain successful docking, such as narrow palpebral fissure, deep set orbit, severe blepharospasm, pterygia and conjunctival chalasis, or variables that affect the ability to position the patient underneath the laser, such as cervical kyphosis and inability of the patient to stay still.

The laser was used for the capsulotomy in over 99% of FLACS cases, for nucleus fragmentation in 95% of cases, for corneal incisions in 35% of cases and for astigmatic incisions in 5% of cases. This breakdown is different from the results of the most recent ESCRS and ASCRS members’ survey, where astigmatic incisions were used in over 70% of cases. **(Duffey 2015)** It may also reflect the steps of

CPCS which surgeons find more challenging **(Travella 2011)**, or the steps during which cataract surgeons are more likely to encounter posterior capsule rupture (nuclear dismantling, and cortical aspiration) and which they would, therefore, like to be automated.

Overall, the rate of complications was higher in FLACS than in CPCS cases. However, there are a number of FLACS-specific minor complications, such as imperforate corneal incisions, capsular tags and bridges and incomplete laser capsulotomies, which cannot occur during CPCS cataract surgery. This explains the higher overall rate of complications with FLACS. For this reason, during the analysis we also excluded FLACS-specific complications and we compared the rate of torn posterior capsule, with or without vitreous loss, with or without dropped nucleus (complications which are likely to affect the visual and refractive outcome) in the two groups. The rates of these complications were low and similar in both groups. Also they were similar to other large series of CPCS **(Lundstrom 2012, Sparrow 2011)** and FLACS **(Roberts 2013, Chee 2015)** cases.

The rate of FLACS-specific complications was 2%. This included complications that are unlikely to affect the final visual and refractive outcomes of the surgery (imperforate corneal incisions, capsular tags and bridges and incomplete capsulotomies), but are more likely to lengthen the surgery a little, because they require the surgeon to manually complete those steps not fully completed by the laser. The concern that FLACS is more time-consuming than CPCS and may affect patient flow and volumes has been previously expressed. **(Feldman 2015, Hatch 2013, Donaldson 2013, Lubahn 2014)**

The rate of use of non-monofocal IOLs was much higher in the FLACS than in the CPCS group. The choice of IOL to be implanted was at the discretion of the surgeon, in consultation with the patient, according to the routines of each participating clinic. High rates of non-monofocal IOL implantation in FLACS have been reported before **(Ewe 2015)**, while some studies have found similar, albeit high rates of non-monofocal IOL use in both FLACS and CPCS cases. **(Chee 2015)** This may suggest that FLACS patients have different preconceptions, demands and expectations from their cataract surgery than CPCS patients and may be being treated in a different healthcare system.

Improvement in CDVA was defined as a gain of more than 0.1 logMAR (one line or 5 letters on the chart) and deterioration as loss of more than 0.1 logMAR. These definitions were used in order to ensure that clinically meaningful changes in CDVA were captured. A meta-analysis of 9 randomized controlled trials comparing FLACS to CPCS found that CDVA was better in the FLACS group, but only by one logMAR letter. **(Chen 2015)** Similarly, a non-randomized cohort study of 1105 FLACS eyes with 410 matched historical controls, found that UDVA was better in the FLACS group, but by less than one logMAR letter. **(Chee 2015)** These differences are not clinically meaningful. Indeed, in this study, there was significant and clinically meaningful improvement in postoperative CDVA of 2 ½ to 3 lines, following surgery by either method. The improvement was similar in both groups, with the FLACS group gaining, on average, one logMAR letter more than the CPCS group. There was a difference in the proportion of patients with better, unchanged or worse postoperative CDVA, with the CPCS group performing better in these categories.

Multivariate regression analysis revealed that worse postoperative CDVA was associated with better preoperative CDVA, ocular co-morbidity, FLACS, posterior capsule opacification (PCO), uveitis and other postoperative complications. Given the fact that the two groups were exactly matched for preoperative CDVA, a possible reason why the FLACS group had more cases with worse postoperative CDVA than the CPCS group is the higher rate of postoperative complications.

Postoperative complications including corneal oedema, early PCO reducing visual acuity, uveitis requiring treatment and uncontrolled intraocular pressure, were higher in the FLACS than the CPCS group. A study of 1105 FLACS eyes with 6 weeks follow-up, found similar rates of corneal oedema, and higher rates of posterior capsule opacification and raised intraocular pressure, than our study. **(Chee 2015)** Even though this study **(Chee 2015)** contained matched historical CPCS cases, a comparison of postoperative complications between groups was not done. The meta-analysis of nine randomized controlled trials, including 989 eyes (512 FLACS and 477 CPCS) found no difference in postoperative endothelial cell counts and central corneal thickness past the first day of follow-up and no difference in the rate of macular oedema and elevated intraocular pressure. **(Chen 2015)** Both intraocular surgery and the delivery of laser energy to intraocular tissues are pro-inflammatory, through disruption of the blood-aqueous barrier. Our data suggest that FLACS may be a little more pro-inflammatory than CPCS, leading to higher rates of corneal oedema, early PCO reducing visual acuity, uveitis requiring treatment and uncontrolled intraocular pressure. One prospective comparative study found that prostaglandin levels in the aqueous of patients increased following FLACS compared to CPCS. **(Schultz 2013)** However, in a prospective intra individual study of 204, the levels of postoperative laser flare photometry as a measure of postoperative intraocular inflammation were higher 2 hours following the procedure, in the CPCS than in the FLACS group. **(Conrad-Hengerer 2014b)** The rates of postoperative complications in the CPCS group were low, compared to a previous EUREQUO-based study. **(Lundstrom 2012)**

Absolute BPE (also called mean absolute error) was 0.43D in the FLACS group and 0.40D in the CPCS group, with the difference being statistically but not clinically significant. The percent of eyes within ± 0.5 D and within ± 1.0 D of target was higher in the CPCS than the FLACS group (74% versus 72% and 94% versus 92%, respectively). Multivariate regression analysis revealed that younger age, poor preoperative CDVA, previous corneal refractive surgery, ocular co-morbidity and FLACS was related to BPE outside ± 1D of target. The refractive outcomes of other studies comparing FLACS to CPCS are variable. A prospective multicenter comparative cohort study of 1876 eyes (988 FLACS versus 888 CPCS) with 6 moths follow-up found that CPCS had better refractive results than FLACS (absolute BPE of 0.35 D versus 0.41D and 83% within ± 0.5 D versus 72%). **(Ewe 2015)** A nonrandomized cohort study of 1105 FLACS eyes with 420 matched, historical controls with 6 weeks follow-up, found no difference in the absolute BPE between the two groups (0.33 D versus 0.30 D). **(Chee 2015)** A prospective randomized intra individual cohort study of 200 eyes with 6 months follow-up found that in the FLACS group 92% and 100% of eyes were within ± 0.5 D and ± 1.0 D of target, respectively, the highest reported rates in the peer-reviewed literature to-date. **(Conrad-Hengerer 2015)** Overall, the published refractive results for FLACS are very good and within the accepted benchmark standards for CPCS. **(Lundstrom 2012)** In our study, the superior refractive results in the CPCS group could be explained by smaller proportion of eyes with previous corneal refractive surgery.

Corneal astigmatism was considered clinically meaningful if the mean K was ≥ 0.25 D, because this is the smallest amount that can be corrected by glasses or contact lenses. Cases that received FLACS corneal astigmatic treatment, were analyzed separately from FLACS cases that did not. When compared to CPCS cases, FLACS cases without corneal astigmatic treatment had similar preoperative astigmatism to CPCS cases (0.93 D versus 0.97 D). In contrast, FLACS cases that received corneal astigmatic treatment had much higher preoperative astigmatism (1.30 D). CPCS cases with high preoperative astigmatic treatment were not analyzed separately. Postoperative corneal astigmatism was statistically lower, but clinically similar in both FLACS and CPCS groups (0.89 D versus 0.95 D). In addition, corneal astigmatism did not change significantly following cataract surgery in either group, except in the FLACS subgroup that received corneal astigmatic treatment (1.30 D preoperatively and 0.87 D postoperatively). This represented 4.5% of all FLACS cases. Our results are very similar to a previous retrospective interventional case series of 54 eyes that underwent FLACS including corneal astigmatic treatment. **(Chan 2015)** In our study almost double the number of CPCS, compared to FLACS eyes had residual postoperative cylinder of 1.5 D or higher (18.4% versus 9.2%). Surgically induced astigmatism in the two groups was measured by the Naeser polar value at the surgical meridian, which indicates the power of the efficacy of the surgical procedure. **(Naeser 1997)** The Naeser polar value was smaller in the FLACS groups by 0.06 D. This difference increased to 0.1 D, when all cases that received a toric IOL, FLACS corneal astigmatic treatment or previous corneal refractive surgery were excluded.

There are limitations to this study. It is registry based, not a randomized controlled trial. FLACS is in its infancy whilst CPCS is tried and tested. There was no standardization of visual acuity testing, nor was there independent validation of entered data. The allocation to femto was at the discretion of the surgeon. We did not measure circularity or centration of the rhexis, effective lens position, or record the femto platform used, phacoemulsification energy used, endothelial cell counts. Although these parameters are relevant, but because there were no comparators in the EUREQUO database for matching, we could not include them in this study.

In conclusion, in a case-control study in the real-life clinical setting, both FLACS and CPCS have excellent visual outcomes and low complications. This study dispels the claims that FLACS is a major advance and superior to the non-laser method. FLACS has superior astigmatic outcomes, whilst CPCS has slightly better visual outcomes. Intraoperative complications are similar and low in both groups. Postoperative complications are higher in the FLACS group and specifically the FLACS patients had a higher incidence of postoperative visual acuity worse than that prevailing preoperatively, due specifically to corneal edema, early PCO and uveitis requiring treatment. Future sophistication of FLACS may eliminate these differences.

ACKNOWLEDGEMENTS

The authors are indebted to the pioneering participating surgeons for their enthusiasm and support of this early study. We also acknowledge all surgeons reporting to the EUREQUO database.

REFERENCES

Nagy 2009
Initial clinical evaluation of an intraocular femtosecond laser in cataract surgery.
Nagy Z, Takacs A, Filkorn T, Sarayba M.
J Refract Surg. 2009 Dec;25(12):1053-60

Mamalis 2011
Femtosecond laser: the future of cataract surgery?
Mamalis N.
J Cataract Refract Surg. 2011 Jul;37(7):1177-8

Lindstrom 2011
The Future of Laser-assisted Refractive Cataract Surgery
Lindstrom R. M.
J Refract Surg. 2011 Aug;27(8): 552-553

Vann 2012
Game-changer for cataract surgery. Femtosecond lasers enable more efficient, faster and safer cataract surgery and are expected to be the standard of care within about 5 years.
Vann R. R.
Duke Med Health News. 2012 Jan;18(1):1-2

[No authors listed 2013]
New laser method could revolutionize cataract surgery. The femtosecond laser will enable safer, more precise surgery.
Duke Med Health News. 2013 Nov;19(11):3-4

Lundström 2012
Lundström M, Barry P, Henry Y, Rosen P, Stenevi U.
Evidence-based guidelines for cataract surgery: guidelines based on data in the European Registry of Quality Outcomes for Cataract and Refractive Surgery database.
J Cataract Refract Surg. 2012 Jun;38(6):1086-93

Jaycock 2009
Jaycock P, Johnston RL, Taylor H, Adams M, Tole DM, Galloway P, Canning C, Sparrow JM; UK EPR user group.
The Cataract National Dataset electronic multi-centre audit of 55,567 operations: updating benchmark standards of care in the United Kingdom and internationally.
Eye (Lond). 2009 Jan;23(1):38-49

Hahn 2011
Hahn U, Krummenauer F, Kölbl B, Neuhann T, Schayan-Araghi K, Schmickler S, von Wolff K, Weindler J, Will T, Neuhann I.
Determination of valid benchmarks for outcome indicators in cataract surgery: a multicenter, prospective cohort trial.

Ophthalmology. 2011 Nov;118(11):2105-12. doi: 10.1016/j.ophtha.2011.05.011. Epub 2011 Aug 19

Johnston 2010
Johnston RL, Taylor H, Smith R, Sparrow JM.
The Cataract National Dataset electronic multi-centre audit of 55,567 operations: variation in posterior capsule rupture rates between surgeons.
Eye (Lond). 2010 May;24(5):888-93

McAlinden 2011
McAlinden C, Gothwal VK, Khadka J, Wright TA, Lamoureux EL, Pesudovs K.
A head-to-head comparison of 16 cataract surgery outcome questionnaires.
Ophthalmology. 2011 Dec;118(12):2374-81

Lamoureux 2011
Lamoureux EL, Fenwick E, Pesudoversus K, Tan D.
The impact of cataract surgery on quality of life.
Curr Opin Ophthalmol. 2011 Jan;22(1):19-27

Nagy 2011
Comparison of intraocular lens decentration parameters after femtosecond and manual capsulotomies.
J Refract Surg. 2011 Aug;27(8):564-9

Friedman 2011
Femtosecond laser capsulotomy.
Friedman NJ, Palanker DV, Schuele G, Andersen D, Marcellino G, Seibel BS, Batlle J, Feliz R, Talamo JH, Blumenkranz MS, Culbertson WW.
J Cataract Refract Surg. 2011 Jul;37(7):1189-98
Erratum in: J Cataract Refract Surg. 2011 Sep;37(9):1742

Kranitz 2011
Femtosecond laser capsulotomy and manual continuous curvilinear capsulorrhexis parameters and their effects on intraocular lens centration.
Kránitz K, Takacs A, Mihály K, Kovács I, Knorz MC, Nagy ZZ.
J Refract Surg. 2011 Aug;27(8):558-63

Auffarth 2013
Comparison of the maximum applicable stretch force after femtosecond laser-assisted and manual anterior capsulotomy.
Auffarth GU, Reddy KP, Ritter R, Holzer MP, Rabsilber TM.
J Cataract Refract Surg. 2013 Jan;39(1):105-9

Reddy 2013
Effectiveness and safety of femtosecond laser-assisted lens fragmentation and anterior capsulotomy versus the manual technique in cataract surgery.
Reddy KP, Kandulla J, Auffarth GU.
J Cataract Refract Surg. 2013 Sep;39(9):1297-306

Mastropasqua 2013

Scanning electron microscopy evaluation of capsulorhexis in femtosecond laser-assisted cataract surgery.
Mastropasqua L,Toto L,Calienno R,Mattei PA,Mastropasqua A,Vecchiarino L,DiIorio D.
J Cataract Refract Surg. 2013 Oct;39(10):1581-6

Mastropasqua 2014
Femtosecond laser versus manual clear corneal incision in cataract surgery.
J Refract Surg. 2014 Jan;30(1):27-33.
Mastropasqua L, Toto L, Mastropasqua A, Vecchiarino L, Mastropasqua R, Pedrotti E, Di Nicola M.

Grewal 2014
Comparison of morphologic features of clear corneal incisions created with a femtosecond laser or a keratome.
J Cataract Refract Surg. 2014 Apr;40(4):521-30. doi: 10.1016/j.jcrs.2013.11.028. Epub 2014 Feb 22.
Grewal DS, Basti S.

Takacs 2012
Central corneal volume and endothelial cell count following femtosecond laser-assisted refractive cataract surgery compared to conventional CPCSemulsification.
Takács AI, Kovács I, Miháltz K, Filkorn T, Knorz MC, Nagy ZZ.
J Refract Surg. 2012 Jun;28(6):387-91

Conrad-Hengerer 2012 a
Effect of femtosecond laser fragmentation on effective CPCSemulsification time in cataract surgery.
Conrad-Hengerer I, Hengerer FH, Schultz T, Dick HB.
J Refract Surg. 2012 Dec;28(12):879-83

Conrad-Hengerer 2013 c
Corneal endothelial cell loss and corneal thickness in conventional compared with femtosecond laser-assisted cataract surgery: three-month follow-up.
Conrad-Hengerer I, Al Juburi M, Schultz T, Hengerer FH, Dick HB.
J Cataract Refract Surg. 2013 Sep;39(9):1307-13

Mayer 2014
Impact of crystalline lens opacification on effective CPCSemulsification time in femtosecond laser-assisted cataract surgery.
Mayer WJ, Klaproth OK, Hengerer FH, Kohnen T.
Am J Ophthalmol. 2014 Feb;157(2):426-432.e1
Erratum in: Am J Ophthalmol. 2014 Apr;157(4):920

Daya 2014
Translenticular hydrodissection, lens fragmentation, and influence on ultrasound power in femtosecond laser-assisted cataract surgery and refractive lens exchange.
Daya SM, Nanavaty MA, Espinosa-Lagana MM.
J Cataract Refract Surg. 2014 Jan;40(1):37-43

Kránitz 2012
Intraocular lens tilt and decentration measured by Scheimpflug camera following manual or femtosecond laser-created continuous circular capsulotomy.
Kránitz K, Mihåltz K, Sándor GL, Takacs A, Knorz MC, Nagy ZZ.
J Refract Surg. 2012 Apr;28(4):259-63

Mihåltz 2011
Internal aberrations and optical quality after femtosecond laser anterior capsulotomy in cataract surgery.
Mihåltz K, Knorz MC, Alió JL, Takács AI, Kránitz K, Kovács I, Nagy ZZ.
J Refract Surg. 2011 Oct;27(10):711-6

Abell 2013
Toward zero effective CPCSemulsification time using femtosecond laser pretreatment.
Abell RG, Kerr NM, Vote BJ.
Ophthalmology. 2013 May;120(5):942-8

Roberts 2012
Femtosecond laser cataract surgery: technology and clinical practice.
Roberts TV, Lawless M, Chan CC, Jacobs M, Ng D, Bali SJ, Hodge C, Sutton G.
Clin Experiment Ophthalmol. 2013 Mar;41(2):180-6

Lawless 2012
Outcomes of femtosecond laser cataract surgery with a diffractive multifocal intraocular lens.
Lawless M, Bali SJ, Hodge C, Roberts TV, Chan C, Sutton G.
J Refract Surg. 2012 Dec;28(12):859-64

Filkorn 2012
Comparison of IOL power calculation and refractive outcome after laser refractive cataract surgery with a femtosecond laser versus conventional CPCSemulsification.
Filkorn T, Kovács I, Takács A, Horváth E, Knorz MC, Nagy ZZ.
J Refract Surg. 2012 Aug;28(8):540-4

Lundström 2013
Visual outcome of cataract surgery; study from the European Registry of Quality Outcomes for Cataract and Refractive Surgery.
Lundström M, Barry P, Henry Y, Rosen P, Stenevi U.
J Cataract Refract Surg. 2013 May;39(5):673-9

Roberts 2013
Surgical outcomes and safety of femtosecond laser cataract surgery: a prospective study of 1500 consecutive cases.
Roberts TV, Lawless M, Bali SJ, Hodge C, Sutton G.
Ophthalmology. 2013 Feb;120(2):227-33

Bailey 1991
Clinical grading and the effects of scaling.
Bailey IL, Bullimore MA, Raasch TW, Taylor HR.

Invest Ophthalmol Vis Sci. 1991 Feb;32(2):422-32.

Ewe 2015
A Comparative Cohort Study of Visual Outcomes in Femtosecond Laser-Assisted versus CPCSemulsification Cataract Surgery.
Ewe SY, Abell RG, Oakley CL, Lim CH, Allen PL, McPherson ZE, Rao A, Davies PE, Vote BJ.
Ophthalmology. 2015 Oct 31. pii: S0161-6420(15)01095-7. doi: 10.1016/j.ophtha.2015.09.026. [Epub ahead of print]

Conrad-Hengerer 2015
Comparison of visual recovery and refractive stability between femtosecond laser-assisted cataract surgery and standard CPCSemulsification: six-month follow-up.
Conrad-Hengerer I, Al Sheikh M, Hengerer FH, Schultz T, Dick HB.
J Cataract Refract Surg. 2015 Jul;41(7):1356-64.

Manning 2015
Cataract surgery outcomes in corneal refractive surgery eyes
Study from the European Registry of Quality Outcomes for Cataract and Refractive Surgery
Manning S, Barry P, Henry Y, Rosen P, Stenevi U, Lundström M.
J Cataract Refract Surg. 2015 Nov;41(11): 2358–2365

Conrad-Hengerer 2014
Femtosecond laser-assisted cataract surgery in intumescent white cataracts.
Conrad-Hengerer I, Hengerer FH, Joachim SC, Schultz T, Dick HB.
J Cataract Refract Surg. 2014 Jan;40(1):44-50

Liu 2015
Pathologic evidence of pseudoexfoliation in cases of in-the-bag intraocular lens subluxation or dislocation.
Liu E, Cole S, Werner L, Hengerer F, Mamalis N, Kohnen T
J Cataract Refract Surg. 2015 May;41(5):929-35

Conrad-Hengerer 2013
Femtosecond laser-assisted cataract surgery in eyes with a small pupil.
Conrad-Hengerer I, Hengerer FH, Schultz T, Dick HB.
J Cataract Refract Surg. 2013 Sep;39(9):1314-20. doi: 10.1016/j.jcrs.2013.05.034.

Travella 2011
Characterizing the learning curve in CPCSemulsification.
Taravella MJ, Davidson R, Erlanger M, Guiton G, Gregory D.
J Cataract Refract Surg. 2011 Jun;37(6):1069-75.

Sparrow 2011
The cataract national data set electronic multi-centre audit of 55,567 operations: case-mix adjusted surgeon's outcomes for posterior capsule rupture.
Sparrow JM, Taylor H, Qureshi K, Smith R, Johnston RL; UK EPR user group.
Eye (Lond). 2011 Aug;25(8):1010-5.

Feldman 2015
Femtosecond laser will not be a standard method for cataract extraction ten years from now.
Feldman BH.
Surv Ophthalmol. 2015 Jul-Aug;60(4):360-5. doi: 10.1016/j.survophthal.2015.02.002. Epub 2015 Feb 17.

Hatch 2014
Laser-assisted cataract surgery: benefits and barriers.
Hatch KM, Talamo JH.
Curr Opin Ophthalmol. 2014 Jan;25(1):54-61.

Donaldson 2013
Femtosecond laser-assisted cataract surgery.
Donaldson KE, Braga-Mele R, Cabot F, Davidson R, Dhaliwal DK, Hamilton R, Jackson M, Patterson L, Stonecipher K, Yoo SH; ASCRS Refractive Cataract Surgery Subcommittee.
J Cataract Refract Surg. 2013 Nov;39(11):1753-63.

Lubahn 2014
Operating times of experienced cataract surgeons beginning femtosecond laser-assisted cataract surgery.
Lubahn JG, Donaldson KE1, Culbertson WW1, Yoo SH2.
J Cataract Refract Surg. 2014 Nov;40(11):1773-6.

Abell 2015
Femtosecond laser-assisted cataract surgery versus standard CPCSemulsification cataract surgery: outcomes and safety in more than 4000 cases at a single center.
Abell RG, Darian-Smith E, Kan JB, Allen PL, Ewe SY, Vote BJ.
J Cataract Refract Surg. 2015 Jan;41(1):47-52.

Conrad-Hengerer 2014b
Femtosecond laser-induced macular changes and anterior segment inflammation in cataract surgery.
Conrad-Hengerer I, Hengerer FH, Al Juburi M, Schultz T, Dick HB.
J Refract Surg. 2014 Apr;30(4):222-6. doi: 10.3928/1081597X-20140321-01.

Chen 2015
Efficacy and safety of femtosecond laser-assisted cataract surgery versus conventional CPCSemulsification for cataract: a meta-analysis of randomized controlled trials.
Chen X, Xiao W, Ye S, Chen W, Liu Y.
Sci Rep. 2015 Aug 13;5:13123.

Schultz 2013
Changes in prostaglandin levels in patients undergoing femtosecond laser-assisted cataract surgery.
Schultz T, Joachim SC, Kuehn M, Dick HB.
J Refract Surg. 2013 Nov;29(11):742-7.

Chan 2015
Vector Analysis of Corneal Astigmatism After Combined Femtosecond-Assisted CPCSemulsification and Arcuate Keratotomy.
Chan TC, Cheng GP, Wang Z, Tham CC, Woo VC, Jhanji V.
Am J Ophthalmol. 2015 Aug;160(2):250-255.e2. doi: 10.1016/j.ajo.2015.05.004. Epub 2015 May 14.

Naeser 1997
Correlation between polar values and vector analysis.
Naeser K, Behrens JK.
J Cataract Refract Surg. 1997 Jan-Feb;23(1):76-81.

OTHER CITED MATERIAL

Duffey 2015
Duffy RJ, “U.S. Trends in refractive surgery: 2015 ISRS survey”, presented at the AAO Refractive Subspecialty Day, Las Vegas, Nevada, USA, November 2015

Figure legends

Figure 1: Number of FLACS cases and matched CPCS controls. Number of cases excluded from the matching process and reasons for the exclusion are also given. FLACS: femtosecond laser-assisted cataract surgery; CPCS: conventional phacoemulsification cataract surgery; EUREQUO: European Registry of Quality Outcomes for Cataract and Refractive Surgery; K: keratometry; CDVA: corrected-distance visual acuity