ASCRS Presentation 2022

Title: Safety and Efficacy of Laser-Assisted Subepithelial Keratectomy (LASEK) to treat Amblyopia

Presenting Author: Semran Thamer, BS

Coauthors: Jad Ayash, MD, Matthew Riehl, MD, Isha Ingle, MD, Emil Chynn, MD

Purpose: To evaluate the safety and efficacy of laser-assisted subepithelial keratectomy (LASEK) for treating adult patients with amblyopia

Methods: A retrospective review of 53 eyes of 28 amblyopic patients who underwent LASEK using the VISX Star S4 excimer laser were included. Refractive and visual outcomes were assessed preoperatively and postoperatively at 6 months.

Results: 94.2% of all eyes gained at least 1 line of UCVA and 43.4% gained at least 1 line of CDVA. None lost any lines of UCVA or BCVA. Mean preoperative logMAR BCVA improved from 0.29 to 0.18 among amblyopic myopic eyes, 0.07 to 0.01 among fellow non-amblyopic myopic eyes, 0.26 to 0.20 among amblyopic hyperopic eyes, and 0.06 to 0.02 among fellow non-amblyopic hyperopic eyes. No eyes required retreatment and no significant complications were reported.

Conclusion: LASEK can safely and effectively treat adults with both refractive & anisometropic amblyopia, both myopes & hyperopes. Patient satisfaction was extremely high, since each patient had better UCVA & most had better BCVA. No adverse events were reported.

Safety and Efficacy of Laser-Assisted Subepithelial Keratectomy (LASEK) to treat Amblyopia

Jad Ayash, MD, Matthew Riehl, MD, Semran Thamer, BS, Isha Ingle, MD, Emil Chynn, MD, FACS, MBA

Purpose: To evaluate the effects of laser-assisted subepithelial keratectomy (LASEK) in adult patients with amblyopia.

Setting: Private Surgical practice with all procedures performed by Chief Surgeon.

Design: Retrospective cohort study.

Methods: A review of 28 patients (53 eyes) with amblyopia (best corrected distance visual acuity [BCVA] 0.1 or worse) who underwent LASEK using the Visx Star S4 excimer laser. Of the total, 11 patients were hyperopic and 17 were myopic. Patients with intended monovision were excluded as their target refraction was at or over 1 diopter of myopia. Mean patient age was 31.58 ± 10.50 years (range: 21 to 60 years). Visual outcomes were assessed by measuring uncorrected distance visual acuity (UDVA), best corrected visual acuity (BCVA) and manifest refraction in the amblyopic and fellow eyes before and after surgery.

Results: The mean preoperative logMAR UCVA improved from 1.83 to 0.21 among amblyopic myopic eyes, 1.67 to 0.01 among fellow non-amblyopic myopic eyes, 0.66 to 0.22 among amblyopic hyperopic eyes, and 0.21 to 0.02 among fellow non-amblyopic hyperopic eyes. No eyes required retreatment and no significant complications were reported.

Conclusions: Results from our study show that in adults with amblyopia, correction of refractive error with LASEK successfully improves the BCVA in the amblyopic eye. Therefore, we can conclude that LASEK is a safe and effective treatment for amblyopia in the adult population.

Introduction

Amblyopia is clinically defined as reduction of best-corrected visual acuity (BCVA) that is not solely ascribed to a structural abnormality or refractive error in the eye, rather is caused by abnormal binocular interaction during the critical period of neurosensory development [1]. Amblyopia is a result of aberrant stimulation of the brain during the critical periods of brain plasticity and visual development [2, 3]. Unilateral amblyopia is defined as ≥2-line difference in the BCVA between both eyes with a BCVA of 20/32 (0.2 logMAR) or less in the affected eye, having an amblyogenic factor that explains the weakness. Bilateral amblyopia is a deficit in BCVA of <20/40(0.3 logMAR) bilaterally for ages 48 to 72 months, or <20/50 (0.4 logMAR) bilaterally for ages <48 months, having an amblyogenic factor in both eyes that explains the weakness [6]. If not treated, amblyopia can cause low vision that persists throughout adulthood.

Amblyopia is the leading cause of unilateral low vision, affecting 1-5% of the world population [2, 7]. The high prevalence leads to widespread disability, with significant financial efforts directed towards its prevention and treatment. In addition to the economic impact, individuals with amblyopia often have reduced quality of life, including limited career options, minimized social interaction, and anxiety towards losing vision in the contralateral eye [2].

Amblyopia may be classified according to its main etiological factor: strabismic, deprivational, refractive (anisometropic or ametropic), or a mix of more than one. Strabismus is the misalignment of both eyes which results in different images on the fovea, leading to unilateral amblyopia [8]. Anisometropia, defined as the difference in refractive error between both eyes of ≥1.50 D difference in hypermetropia, ≥3.00 D difference in myopia, or ≥1.50 D difference in astigmatism in any meridian leading to one foveal image being more blurred than the other leading to unilateral amblyopia. Ametropia is described as hypermetropia ≥4.00 D, myopia ≥ 6.00 D, or astigmatism ≥ 2.50 D that can induce either unilateral or bilateral amblyopia. Deprivational amblyopia is usually due to evidence of past or present obstruction of the visual axes including cataract or ptosis among other causes [6, 8].

The conventional treatment options of amblyopia in children include refractive correction, patching, or penalization using pharmacological agents [1, 9]. Refractive correction alone improves visual acuity and resolves amblyopia in at least one third of 3 to 7-year-olds with anisometric amblyopia. It is important to note the cases which resolve usually have moderate (0.3 to 0.7 logMAR) amblyopia, nevertheless treating the more advanced levels of amblyopia with glasses decreases the burden of the subsequent therapy [9]. When refractive correction alone does not restore normal vision in the amblyopic eye, patching the contralateral eye is necessary. Covering the fellow eye reduces neural stimulation of areas devoted to input from the normal eye, as depicted in experimental animal studies [10]. Consequently, this will increase reliance on visual input, and firing of neural pathways of the amblyopic eye. Over time neuronal plasticity will rearrange the cortical ocular dominance columns if early enough, or lead to less functional suppression. Compliance with patching is usually suboptimal for many reasons like child's compliance, skin irritation due to the patch and relying on the vision of the normal eye commonly outweigh the enthusiasm of the patients and their parents to protect themselves from the consequences of not treating amblyopia [11]. Penalization of the unaffected eye with 1% atropine solution causes cycloplegia, preventing it from focusing. This method is used as a substitute or in addition to patching for treatment of mild to moderate amblyopia, if the healthy eye is hyperopic. However, penalization has been associated with photosensitivity [12] and systemic adverse effects of atropine: dry mouth, tachycardia, and delirium [13].

Initially the resolution of amblyopia was noted to be limited to the age in which treatment began, due to the "critical period" of brain plasticity. Optimal efficacy of patching was reported before 3 years and the efficiency was decreased until negligible by 12 years of age [14]. However, recent studies have reported plasticity in the visual cortex in adult amblyopic patients past the critical period [15]. Transient enhancement of contrast sensitivity in the amblyopic visual cortex, and improvement in letter recognition tasks with repetitive transcranial magnetic stimulation (rTMS) have been noted in adults [16, 17]. Moreover, it has been observed that the window of plasticity may be reopened beyond the critical period with a short decrease of the gamma-aminobutyric acid-ergic (GABAergic) inhibition in rats [18]. Multiple intrinsic and extrinsic means of enhancing plasticity to increase efficacy in treating amblyopia post critical period have been investigated. Intrinsic methods include perceptual learning with demanding visual tasks to stimulate the manipulation of endogenous neurotransmitters in the brain. On the other hand, extrinsic augmentation uses external approaches, which include levodopa, to modulate the internal neurotransmitters to improve neuronal plasticity. However, it is worth pointing out that clinical studies have shown that there is no statistical significance in visual acuity improvement between those given levodopa and those on placebo. Development of the visual system continues throughout adolescence, during a time known as the critical period. Proper development relies on 3 fundamental conditions: adequate stimuli reaching retinal photoreceptors of each eye, ocular parallelism, and integrity of visual pathways [19]. Lastly, animal studies promote valproate's use as a histone deacetylase inhibitor to modify gene expression, reversing the "brakes" on neural plasticity [19]. Fortunately, this implies that the adult visual system may still have capacity for functional recovery.

Laser refractive surgeries for correction of amblyopia is engrossing and evolving. Laser therapies are well tolerated, have low complication rates and have validated BCVA gains [20]. Regression is a common concern across with preoperative refractory errors, and mostly happens during the first year following surgery with smaller shifts in next 2-3 years. Anticipating these shifts, overcorrection by 1-2D may be a pragmatic approach. Anecdotal reports suggest application of antimetabolite mitomycin-c (MMC) has to reduce regression in both myopic and hypermetropic treatment [21]. Therefore, refractive surgery is a feasible option for children with refractive amblyopia who are non-compliant with spectacle wear or non-responsive to traditional treatment. In children with neurobehavioral disorders, correction of ametropia with PRK (Photorefractive keratectomy) and Phakic IOL have demonstrated significant improvement in vision and outcomes in global functioning. These strategies need further affirmation with randomized control studies. Currently PEDIG (pediatric eye disease investigation group) is planning Amblyopia Treatment study 19, intended to compare PRK versus non-surgical treatment of anisometric amblyopia in children who have failed conventional treatment [22]. Results from this trial may provide further evidence in support of refractive surgery in the management of amblyopia. As most of the research pertaining to these topic is limited to pediatric population, our study is to evaluate the effects of laser refractive surgery in adult patients with amblyopia due to strabismus, refractive error, or both. Our study will be the first study to prove the efficacy of laser assisted Subepithelial Keratectomy (LASEK) in this patient population.

Methods

A retrospective review of eyes of patients with a history of amblyopia were included in this study. All eyes underwent LASEK to correct refractive error by the same surgeon at a single-site high volume refractive surgery center.

Preoperative and postoperative uncorrected visual acuity and best-corrected visual acuity, manifest refraction, and length of follow-up were factors in the study. Inclusion criteria for the study were the same as routine criteria for considering any refractive corneal procedures: age 20 years or more; refractive stability for at least 2 years; corneal thickness of at least 400 μm, normal corneal topography. BCVA 20/30 (0.2 logMAR) or worse, or documented deficit on binocular function.

Exclusion criteria for this study were patients who failed to complete a minimum of 6 months follow-up, those who were corrected with intended monovision, as the target refraction was not optimized for distance acuity, and those who underwent an enhancement procedure. Patients with abnormal corneal topography and/or irregular astigmatism and previous intraocular or corneal surgery were also excluded.

Preoperative examination included uncorrected visual acuity (UCVA), best spectacle-corrected visual acuity (BCVA), manifest refraction, slit-lamp microscopy, intraocular pressure measurement (IOP), cycloplegic refraction, and fundus examination. Preoperative evaluation included measurement of the corneal thickness using the Orbscan corneal topography system and the Wavescan wavefront aberrometer for customvue treatment. All patients were followed for a minimum of six months after undergoing LASEK.

All patients were treated on the VISX Star S4 IR platform. For the LASEK procedure we used a 35% isopropyl alcohol solution to promote the separation between epithelium and stroma; stromal hydration changes with the variation of the time of exposure to alcohol [23]. This alcohol may cause necrosis of the anterior keratocytes, especially when used at high concentration and for a longer time [24]. During surgery, MMC 0.01% was applied for 10 sec intraoperatively to prevent scarring. A bandage contact lens (BCL) was placed to protect the eye while the epithelial layer grows back.

UCVA, manifest refraction, and slit lamp exams were obtained at 1 week, 1 month, 2 months, and 6 months post-op. At the initial 1 week post op the eyes were examined and BCL removed provided there was no persistent epithelial defect.

In order to prevent corneal scarring, patients followed a strict regimen of medications: Oral Steroid Methylprednisolone 4 mg dose pack starting from day 1 and were tapered to off by day 6. Additionally, patients took Doxycycline 100 mg twice a day for two months.

Along with oral medications, patients were given topical steroid Prednisolone acetate 1% suspension. In the initial month after surgery they used the drops 4 times a day but were then tapered off to three times a day for month 2, twice a day for month 3, once daily for month 4, every other day for month 5 and then discontinued. Vitamin C 1000 mg daily, topical lubricating night ointment, and UV protection was instructed for up to 6 months post op. Preservative free tears were recommended hourly the initial month post op but then decreased to as needed.

Results

Data for myopes and hyperopes were segregated, then averages were obtained for spherical power, cylindrical power, UCVA, and BCVA for both groups pre- and post-operatively for each of the amblyopic and fellow eyes. Subjective measurements were obtained via survey to assess improvement in quality of life. Additionally, subjects were asked if they were happy with their choice to undergo laser vision correction and whether they would suggest it as an option to a family member or friend.

Paired t-tests were performed comparing the patients' UCVA post-op to their UCVA pre-op, to show there is a significant visual benefit to the patient (name table and reference it here). Patients' BCVA post-op was also compared to their BCVA pre-op, to conclude that there is plasticity in the adult brain (name table and reference it here). Finally, UCVA post-op was compared to BCVA pre-op, to show that not only are subjects decreasing their dependence on spectacles, but at the same time they are having better vision (name table and reference it here).

Table 1: Summary Refractive Measures for Amblyopic Eyes with Myopia

Mean Preop Sph (D)	Mean Preop Cyl (D)	Mean Postop Sph (D)	Mean Postop Cyl (D)	Preop UCVA (logMAR)	Postop UCVA (logMAR)	Preop CDVA (logMAR)	Postop CDVA (logMAR)
-8.4 ± 3.8	-1.7 ± 0.9	0.24 ± 1.2	-0.73 ± 0.22	1.8 ± 0.67	0.21 ± 0.18	0.29 ± 0.15	0.18 ± 0.17

Table 2: Summary Refractive Measures for Fellow non-amblyopic Eyes with Myopia

Mean Preop Sph (D)	Mean Preop Cyl (D)	Mean Postop Sph (D)	Mean Postop Cyl (D)	Preop UCVA (logMAR)	Postop UCVA (logMAR)	Preop CDVA (logMAR)	Postop CDVA (logMAR)
-6.8 ± 3.5	-1.5 ± 1.0	0.37 ± 0.48	-0.49 ± 0.45	1.7 ± 0.68	0.01 ± 0.07	0.07 ± 0.08	0.01 ± 0.07

Table 3: Summary Refractive Measures for Amblyopic Eyes with Hyperopia

Mean Preop Sph (D)	Mean Preop Cyl (D)	Mean Postop Sph (D)	Mean Postop Cyl (D)	Preop UCVA (logMAR)	Postop UCVA (logMAR)	Preop CDVA (logMAR)	Postop CDVA (logMAR)
5.0 ± 1.7	-1.8 ± 1.8	0.74 ± 0.39	-0.90 ± 0.43	0.66 ± 0.33	0.22 ± 0.12	0.26 ± 0.15	0.20 ± 0.14

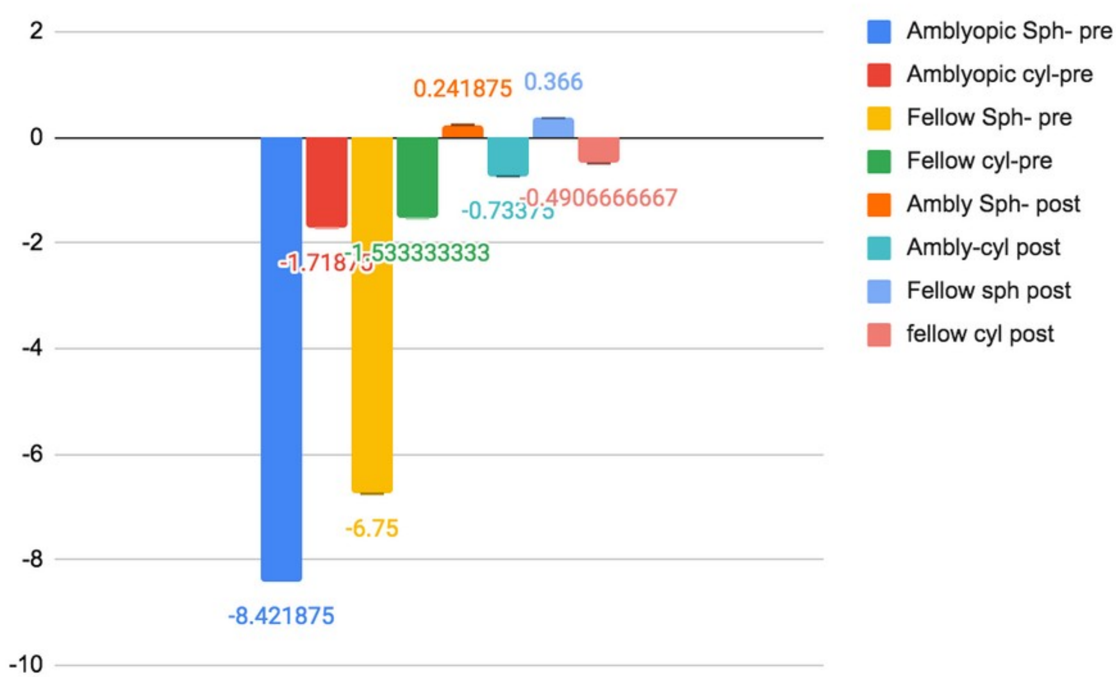
Table 4: Summary Refractive Measures for Fellow non-amblyopic Eyes with Hyperopia

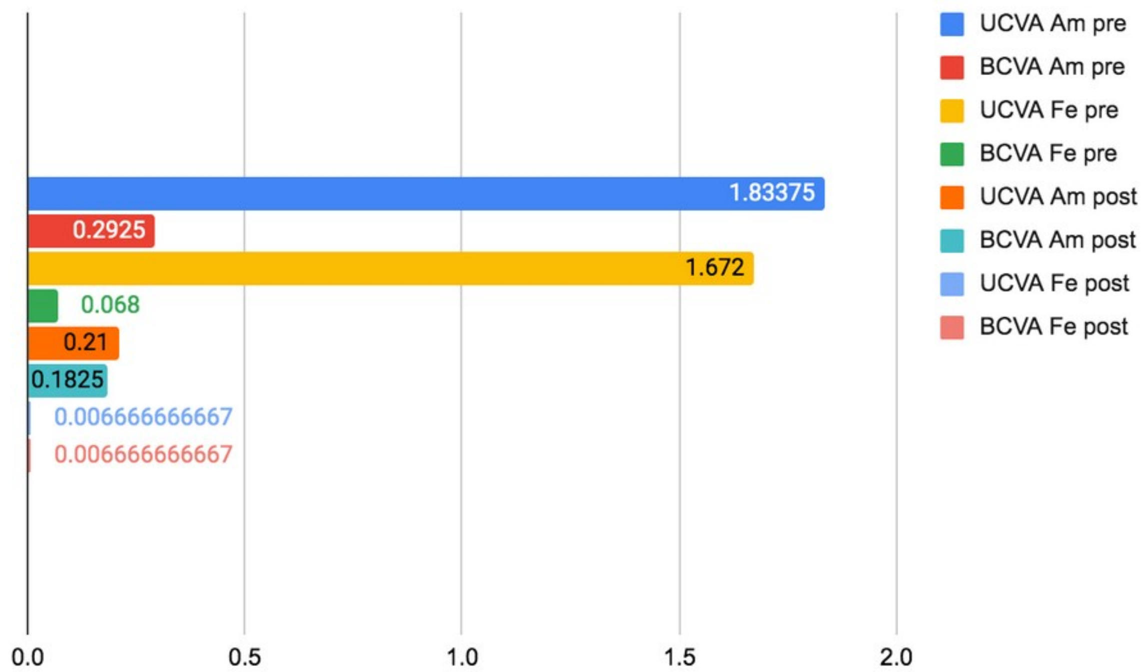
Mean Preop Sph (D)	Mean Preop Cyl (D)	Mean Postop Sph (D)	Mean Postop Cyl (D)	Preop UCVA (logMAR)	Postop UCVA (logMAR)	Preop CDVA (logMAR)	Postop CDVA (logMAR)
3.0 ± 1.7	-1.0 ± 0.9	0.58 ± 0.57	-0.56 ± 0.21	0.21 ± 0.22	0.02 ± 0.08	0.06 ± 0.08	0.02 ± 0.08

Amblyopic Sph- pre	Amblyopic cyl-pre	Fellow Sph- pre	Fellow cyl-pre	Ambly Sph- post	Ambly-cyl post	Fellow sph post	fellow cyl post	UCVA Am pre	BCVA Am pre
-8.421875	-1.71875	-6.75	-1.533333333	0.241875	-0.73375	0.366	-0.4906666667	1.83375	0.2925
3.792227523	0.9031195934	3.453776401	1.038829469	1.226671479	0.2182620749	0.4826977759	0.4517342244	0.6727741077	0.155241747

UCVA Fe	BCVA Fe	UCVA	BCVA Am	UCVA Fe	BCVA Fe	Lines imp	Line imp	Line imp	Line imp Fe

pre	pre	Am post	post	post	post	Am UC	Am BC	Fellow UC	BC
1.672	0.068	0.21	0.1825	0.006666666667	0.006666666667	1.62375	0.11	1.665333333	0.06133333333
0.6849734093	0.0802852059	0.182428068	0.1695287586	0.07037315505	0.07037315505	0.7266808103	0.1222020185	0.6650656967	0.06822930525





Myopic AM UCVA	Mean diff	1.622352941
	STDdev	0.7036292473
	SEM	0.1706551593
	T-value	9.506615258
(t* x SEM)	0.3617889377	
CI 95%	1.984141879	1.260564003

Myopic AM BCVA	mean diff	0.1082352941	
	STDdev	0.1185451019	
	SEM	0.02875141038	
	T-value	3.764521208	

	(t* x SEM)	0.06095299	
	CI 95%	0.1691882841	0.04728230412

BCpre vs. UCpost	mean diff	0.04705882353	
AM	STDdev	0.1737730095	
myopic	SEM	0.04214614547	
	T-value	1.116562927	
	(t* x SEM)	0.08934982839	
	CI 95%	0.1364086519	-0.04229100486

Hyperopic AM	UC	
	Mean diff	0.4345454545
	STDdev	0.3451481895
	SEM	0.1040660947
	T-value	4.175667933
(t* x SEM)	0.2353975062	
CI 95%	0.6699429608	0.1991479483

Hyper AM	BC	
	Mean diff	0.05636363636
	STDdev	0.1323081802
	SEM	0.03989241731

	T-value	1.412890974
(t* x SEM)	0.09023664795	
CI 95%	0.1466002843	-0.03387301159

Hyper AM	BCpre vs. UCpost	
	Mean diff	0.03272727273
	STDdev	0.108544084
	SEM	0.03272727273
	T-value	1
(t* x SEM)	0.07402909091	
CI 95%	0.1067563636	-0.04130181818

Discussion

The American Academy of Ophthalmology Preferred Practice Patterns guidelines for amblyopia treatment discussed new therapeutic approaches, which include refractive surgery, acupuncture, and vision therapy [13]. Patients with severe anisometropia corrected by spectacles results in aniseikonia, a difference in the perceived sizes of images. A human can withstand approximately 5-6% aniseikonia, occurring with 2-3 diopters of anisometropia, beyond which the disproportion is intolerable [25]. This is a distinctive gain of treating anisometropic amblyopia with refractive surgery [23]. Currently, the use of keratorefractive surgery for children is an off-label use of an FDA-approved device, thus their use as a modality of treatment for anisometropic amblyopia remains controversial [24]. Maintaining emmetropia is challenging in a population with growing eyes, leading to constant changes in refractive error. Nonetheless, the literature has reported that PRK can be safely performed on children leading to improved BCVA and stereopsis, with insignificant persistent corneal haze [24]. This has shown promising results that refractive surgeries will have a role in those who failed the traditional treatment.

The concept of restoring plasticity can be utilized in discovering various ways to stimulate the visual cortex to treat adult amblyopic patients. One of the approaches was to enhance BCVA and improving the image quality which results in refractive “amblyopic therapy”. Refining BCVA significantly in adult amblyopes could be achieved by refractive surgery [27]. Laser-assisted subepithelial keratomileusis (LASEK) is an advancement in laser surgery which combines components of laser in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK) to decrease long term complications that include erosions, scars, corneal haziness, infections up to 5 years post-surgery [28]. Laser in situ keratomileusis (LASIK) was associated with the most major postoperative complications when comparing LASIK to LASEK and PRK [29]. Additionally, LASEK is an option to those with thin corneas who are not eligible for LASIK surgery. This advantage is attributed to the fact that it is a non-cutting procedure. LASEK is performed by adding alcohol solution to the epithelium to loosen it and push it away from the treatment zone only. It is important to note that studies have shown an epithelial recovery period post operatively of 4-7days in the majority of patients. Moreover, there is a risk of overcorrection hypothesized due to the wound healing response leading to myopic regression with LASEK [28]. Nevertheless, LASEK remains a promising therapeutic method which possesses potential superiority to treat adult amblyopia hypothesized in our study.

Adult patients with amblyopia have traditionally been told they are not candidates for laser vision correction (LVC). When treated early with spectacles or penalization, those with anisometropic or ametropic amblyopia have seen high success rates. Correction with spectacles alone cannot usually completely resolve the problem in a majority of cases in children. When that fails, patching or atropine penalization can help equalize vision leading to improved visual acuity in the amblyopic eye. However, in pediatric patients maintaining symmetry it can be a challenge due to visual development that leads to constant changes in refractive error.

Another challenge in pediatric patients is compliance, whether to spectacles, patching, or eye drops. Those that fail early treatment are often told there is nothing that can be done to improve the BCVA in the amblyopic eye by the time they reach adulthood. Studies have compared outcomes of surgical intervention in pediatric patients [24], including those who had LVC. Modern advances in Wavefront-guided laser treatments, combined with the enhanced safety of advanced surface ablation (ASA) over cutting procedures that result in a corneal flap, have enabled adult amblyopic patients to be candidates for refractive surgery. Treatment of higher-order aberrations with a non-cutting procedure reduces complications such as night glare, halos, and dry eyes, while also offering a prescription more precise than glasses or contacts alone. As a result, patients undergoing an ASA procedure have the best chance to improve their BCVA, in addition to the obvious improvement of UCVA and decreased dependency on corrective lenses. As evident with this patient population, LASEK offers an opportunity for adults with amblyopia to improve their quality of life, not only by improving their visual acuity, but also by decreasing their dependence on corrective lenses.

Conclusion

Our study looked at 28 adult amblyopic patients. Objective measurements showed that in this patient population LASEK can successfully improve the BCVA in the amblyopic eye; these results are supported by subjective measures of the treatment outcome that demonstrate improvement in the quality of life amongst patients postoperatively. Treatment of amblyopia with this non-cutting procedure offers multiple advantages over other forms of treatment: it reduces complications such as night glare, halos and dry eyes, offers a prescription that is more precise than glasses or contacts alone, reduces dependence on corrective lenses and contacts. Therefore, we propose that LASEK is a safe and effective treatment for adults with amblyopia.

References

1. American Academy of Ophthalmology Pediatric Ophthalmology/Strabismus Panel **Preferred Practice Pattern Guidelines: Amblyopia** (2017)

2. Agnes M.F. Wong, New concepts concerning the neural mechanisms of amblyopia and their clinical implications, Canadian Journal of Ophthalmology,Volume 47, Issue 5, (2012), Pages 399-409,

3. Wiesel, T. Postnatal development of the visual cortex and the influence of environment. *Nature* **299,**(1982), 583–591

4. T.N. Wiesel, D.H. Hubel **Effects of visual deprivation on morphology and physiology of cells in the cats lateral geniculate body** J Neurophysiol, 26 (1963), pp. 978-993

5. L.J. Garey, C. Blakemore **Monocular deprivation: morphological effects on different classes of neurons in the lateral geniculate nucleus** Science, 195 (1977), pp. 414-416

6. Varma, Rohit & Deneen, Jennifer & Cotter, Susan & Paz, Sylvia & Azen, Stanley & Tarczy-Hornoch, Kristina & Zhao, Peng. (2006). The Multi-Ethnic Pediatric Eye Disease Study: Design and Methods. Ophthalmic epidemiology. 13. 253-62.

7. Braverman, Rebecca S. (2015). Introduction to Amblyopia, American Academy of Ophthalmology

8. Jonathan M Holmes, Michael P Clarke, Amblyopia, The Lancet, Volume 367, Issue 9519, 2006, Pages 1343-1351,

9. Susan A. Cotter, Treatment of Anisometropic Amblyopia in Children with Refractive Correction, Ophthalmology, Volume 113, Issue 6, 2006, Pages 895-903

10. Hubel DH, Wiesel TN. Receptive fields and functional architecture of monkey striate cortex. J Physiol 1968;195(1):215-43.

11. Gregson, R. Why are we so bad at treating amblyopia?. *Eye* **16,** 461–462 (2002)

12. Osborne, D.C., Greenhalgh, K.M., Evans, M.J.E. *et al.* Atropine Penalization Versus Occlusion Therapies for Unilateral Amblyopia after the Critical Period of Visual Development: A Systematic Review. *Ophthalmol Ther* **7,** 323–332 (2018)

13. DeSantis, Diana, Pediatric Clinics of North America, 2014-06-01, Volume 61, Issue 3, Pages 505-518

14. Marc Epelbaum, Chantal Milleret, Pierre Buisseret, Jean Louis Duffer, The Sensitive Period for Strabismic Amblyopia in Humans, Ophthalmology, Volume 100, Issue 3, 1993, Pages 323-327

15. Levi DM. Visual processing in amblyopia: human studies. Strabismus. 2006 Mar;14(1):11-9.

16. Benjamin Thompson, Behzad Mansouri, Lisa Koski, Robert F. Hess, Brain Plasticity in the Adult: Modulation of Function in Amblyopia with rTMS, Current Biology, Volume 18, Issue 14, 2008, Pages 1067-1071

17. Improving vision in adult amblyopia by perceptual learning Uri Polat, Tova Ma-Naim, Michael Belkin, Dov Sagi Proceedings of the National Academy of Sciences Apr 2004, 101 (17)

18. Harauzov A, Spolidoro M, DiCristo G, De Pasquale R, Cancedda L, Pizzorusso T, et al. Reducing intracortical inhibition in the adult visual cortex promotes ocular dominance plasticity. *J Neurosci*. 2010;30(1):361-371

19. M Benetti Zagui, Roberta, **Amblyopia: Types, Diagnosis, Treatment, and New Perspectives, American Academy of Ophthalmology (2019)**

20. Paysse EA, Coats DK, Hussein MA, et al. . Long-term outcomes of photorefractive keratectomy for anisometropic amblyopia in children. *Ophthalmology* 2006;113:169–76. 10.1016/j.ophtha.2005.06.010

21. Dai S, Ghasia F, Hoekel J, et al. . Refractive regression after pediatric excimer laser surgery with and without use of mitomycin. *JAAPOS* 2011;15:e3 10.1016/j.jaapos.2011.01.013

22. New advances in amblyopia therapy II: refractive therapies Courtney L Kraus and Susan M Culican

23. Kraus CL, Culican SM New advances in amblyopia therapy II: **refractive therapies** *British Journal of Ophthalmology* 2018;**102:**1611-1614.

24. Evelyn A. Paysse, David K. Coats, Mohamed A.W. Hussein, M. Bowes Hamill, Douglas D. Koch, Long-term Outcomes of Photorefractive Keratectomy for Anisometropic Amblyopia in Children, Ophthalmology, Volume 113, Issue 2, 2006, Pages 169-176,

25. E.C. Campos, J.M. Enoch**Amount of aniseikonia compatible with fine binocular vision: some old and new concepts** J Pediatr Ophthalmol Strabismus, 17 (1980), pp. 44-47

26. Epstein D, Renard GJ, Jackson WB, et al. Photorefractive

keratectomy for low myopia. In: Serdarevic ON, editor.

Refractive surgery: current techniques and management.

New York: Igaku-Shoin, 1997:49.

27. Jasrajbir S. Baath, Michael D. O'Connor, WB Jackson; Can Refractive Surgery Treat Amblyopia In Adults?. *Invest. Ophthalmol. Vis. Sci.*

2011;52(14):5780.

28. Suphi Taneri, James D. Zieske, Dimitri T. Azar, Evolution, techniques, clinical outcomes, and pathophysiology of LASEK: review of the literature, Survey of Ophthalmology, Volume 49, Issue 6, 2004, Pages 576-602,

29. Faisal Ghadhfan, Ali Al-Rajhi, Michael D. Wagoner, Laser in situ keratomileusis versus surface ablation: Visual outcomes and complications, Journal of Cataract & Refractive Surgery, Volume 33, Issue 12, 2007, Pages 2041-2048