HHS Public Access

Author manuscript

J Cataract Refract Surg. Author manuscript; available in PMC 2020 October 01.

Published in final edited form as:

J Cataract Refract Surg. 2019 October ; 45(10): 1458–1462. doi:10.1016/j.jcrs.2019.05.053.

West Indies Glaucoma Laser Study (WIGLS) 4. Crystalline Lens Changes Following Selective Laser Trabeculoplasty in Afro-Caribbeans with Open-Angle Glaucoma

Tony Realini, MD, MPH[1], **Hazel Shillingford-Ricketts, MD**[2], **Darra Burt, MD**[3], **Goundappa K. Balasubramani, PhD**[4]

[1.]West Virginia University Eye Institute, Morgantown, WV

[2.]Harlsbro Medical Center, Roseau, Dominica

[3.]Saint Lucia Blind Welfare Association, Castries, Saint Lucia

[4.]Department of Epidemiology, Epidemiology Data Center, Graduate School of Public Health, University of Pittsburgh, PA

Abstract

Purpose: To characterize changes in nuclear, cortical and posterior subcapsular lens opacities following selective laser trabeculoplasty (SLT) in Afro-Caribbean eyes with open-angle glaucoma (OAG).

Setting: Three clinical practices in Saint Lucia and Dominica

Design: Prospective stepped-wedge study

Methods: 142 phakic eyes of 72 POAG patients in the West Indies Glaucoma Laser Study underwent 360-degree SLT following medication washout. No anti-inflammatory therapy was used post-SLT. Nuclear, cortical and posterior subcapsular lens opacities were graded through dilated pupils using the Lens Opacification Classification System III (LOCS III) at baseline and 12, 24, and 36 months post-SLT, with grader masked to all prior values after baseline assessment. Changes from baseline in opacity scores were evaluated using paired t-tests.

Results: Mean (standard deviation) baseline LOCS III nuclear, cortical, and posterior subcapsular opacity scores for right/left eyes were 2.44 (1.23)/2.40 (1.16), 0.39 (1.08)/0.30 (0.85), and 0.22 (0.59)/0.15 (0.36), respectively. Aside from a small improvement in bilateral nuclear opacity scores at 12 months, no statistically or clinically significant changes in any opacity scores were seen in either eye through up to 36 months of follow-up. Three eyes (3/142, 2.1%) with pre-

Corresponding author: Tony Realini, MD, MPH, 1 Medical Center Drive, Morgantown, WV 26506, 304-598-6926, Fax 304-5986928, realinia@wvumedicine.org.

Presented in part at the World Ophthalmology Congress, June 16-19, 2018, Barcelona, Spain.

Financial Disclosure: No authors have financial relationships relevant to the content of this work.

existing lens opacities underwent cataract surgery for progressive lens changes at Months 3, 21, and 26 after SLT.

Conclusion: SLT is not associated with clinically significant changes in nuclear, cortical, or posterior subcapsular lens opacities in glaucomatous Afro-Caribbean eyes, and the rate of cataract surgery observed in WIGLS is consistent with reported rates from longitudinal natural history studies conducted in both Caribbean and non-Caribbean populations.

Introduction

Cataract and glaucoma both increase in frequency with aging and commonly coexist. Glaucoma therapies may contribute to the development and progression of cataract and the need for cataract extraction. Glaucoma surgery is well known to cause cataract development and progression. In the Advanced Glaucoma Intervention Study (AGIS), trabeculectomy increased the risk of cataract development by 78%.[1] Cataract progression was noted in 20% of eyes at 1 year in both arms of the Primary Tube versus Trabeculectomy (PTVT) Study.[2] In the Collaborative Initial Glaucoma Treatment Study (CIGTS), cataract surgery was required in 17.3% of eyes in the surgery arm compared to only 6.2% in the medication arm (p=0.0001).[3] Topical intraocular pressure (IOP)-lowering medications have also been implicated as contributory to cataract formation and extraction in the Ocular Hypertension Treatment Study,[4] the Barbados Eye Studies,[5] and the Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial.[6] Laser trabeculoplasty may also play a role in the development and progression of glaucoma. In LiGHT, 2% of eyes undergoing selective laser trabeculoplasty (SLT) underwent cataract surgery over a three-year period (compared with 4% in the medication arm),[6] which may be consistent with the natural history of nuclear cataract progression and unrelated to SLT treatment.[7] No eyes required cataract surgery during the shorter (1-year) SLT-MED study.[8] In the Early Manifest Glaucoma Trial (EMGT), nuclear opacities progressed more in the treatment group than the observation group (p=0.002), although in this study treatment considered of both topical medications and argon laser trabeculoplasty (ALT).[9]

The West Indies Glaucoma Laser Study (WIGLS) was a prospective cohort study designed to evaluate the efficacy and safety of SLT in Afro-Caribbean adults with open-angle glaucoma residing in Saint Lucia and Dominica. Primary outcomes of this study have been reported; mean IOP reductions of 30% were seen at 12 months after a single SLT treatment, and 78% of eyes were medication-free.[10] The broader aim of WIGLS was to validate a laser-based treatment strategy for wide application throughout the African-derived developing world,[11] where the burden of disease and barriers to care are significant.[12] Advantages of SLT in this setting include its established efficacy and safety in people of African descent,[10,13-15] cost-effectiveness relative to medications,[11,16,17] and obviation of the need for daily adherence to medication self-dosing. The value of SLT in these resource-limited regions would be lessened, however, if the procedure led to the development and/or progression of lens opacities affective visual function, as the resources for cataract surgery are also of limited availability in these regions.

In this analysis of the WIGLS cohort, the three-year changes in nuclear, cortical, and posterior subcapsular lens opacities following SLT in eyes with open-angle glaucoma are described.

Methodology

This is an analysis of data collected in the prospective WIGLS study, which was funded by the National Eye Institute (R01 EY023620), registered on www.clinicaltrials.gov on March 2, 2015 (), and conducted in Saint Lucia and Dominica between March 9, 2015 and September 21, 2018. The study was conducted in accordance with the tenets of the Declaration of Helsinki. The protocol was reviewed and approved by all appropriate ethics committees. Subjects provided informed consent to participate.

The study methodology has been reported previously. Briefly, a convenience sample of adult subjects with open-angle glaucoma as defined by ISGEO criteria,[18] early to moderate in severity, was recruited from existing practices in St. Lucia and Dominica. The main exclusion criteria included advanced glaucoma (cup-disc ratio greater than 0.9 or automated visual field loss within the central 10 degrees in either eye), previous laser or incisional glaucoma surgery, intraocular inflammation within the past 3 months, ocular trauma or surgery within the past 6 months, or IOP outside the range of 18-32 mmHg, inclusive, after washout of all IOP-lowering medications. Qualifying subjects were randomized to immediate versus 3-month or 6-month delay before 6-week washout of topical IOP-lowering therapy followed by SLT treatment. After washout, baseline IOP was determined in two sessions 1-3 days apart, after which SLT was performed using the Lumenis Selecta II portable slit-lamp mounted laser system. Approximately 100 treatment spots were delivered to the full 360 degrees of trabecular meshwork in each eye. No prophylactic anti-inflammatory therapy was used. Post-treatment assessments occurred at 1 hour, 1 week (± 2 days), 1 month (±5 days), 3 months (±7 days), and every 3 months through January 2017 and every 4 months (±7 days) thereafter. Repeat SLT could be performed based on prespecified criteria for failure of initial SLT. The data in this report was drawn from subjects who underwent a single SLT treatment in each eye.

Nuclear, cortical and posterior subcapsular opacities were graded at baseline and Months 12, 24 and 36 (each post-baseline time point was ± 2 months of the designated visit) at the slit-lamp through dilated pupils. The slit beam was 8mm high and approximately 1mm wide. The brightest illumination setting was used. Nuclear opacities were evaluated with illumination approximately 45° off-axis to the visual axis, while posterior subcapsular opacities were evaluated with the slit beam along the visual axis (retroillumination); cortical opacities were evaluated using both on-axis and off-axis illumination. Opacities were graded using the Lens Opacities Classification System III (LOCS III). This validated system utilizes a nuclear grading scale of 0.1 (most clear) to 6.9 (most opaque) for nuclear opacities and from 0.1 (most clear) to 5.9 (most opaque) for cortical and posterior subcapsular opacities.[19] Grading was performed by a single examiner who was masked to prior readings.

The primary statistical objective of this analysis was to characterize the three-year changes in lens opacities among Afro-Caribbeans with open-angle glaucoma undergoing a single

SLT treatment and to test whether the mean changes in nuclear, cortical and posterior subcapsular were significantly different from zero. Data were drawn from all phakic eyes at baseline until failure of SLT (defined as IOP above target IOP on two consecutive visits, after which repeat SLT was performed), loss to follow-up, cataract surgery, or study exit. Right and left eyes were analyzed separately. Changes from baseline at each time point were compared using paired t-tests. The sample size for WIGLS was determined by the primary statistical objective of the overall study. A power calculation for this analysis established that a sample size of 30 eyes would provide 80% power to detect a change in mean opacity score of 0.3 units assuming a standard deviation of 0.6 and alpha=0.05. Means are presented with standard deviations (SD). Analyses were performed using SAS v9.4, Cary, NC and significance was set at alpha $p < 0.05$.

Results

Overall, 72 subjects (144 eyes) participated in this study. Demographic data are given in Table 1. All were of Afro-Caribbean ethnicity, most (43/72, 59.7%) were female, and the mean (SD) age was 61.0 (11.4) years. Two eyes were pseudophakic at study entry and were excluded from this analysis.

Mean LOCS III scores for nuclear, cortical, and posterior subcapsular opacities at each time point are given in Table 2. Aside from a small improvement in nuclear opacity scores in both eyes at Month 12, no significant long-term changes in nuclear, cortical, or posterior subcapsular opacity scores were noted at any other time point in either eye.

Three eyes underwent cataract surgery during the three-year study. The first occurred 3 months after SLT. Baseline visual acuity was 20/160, at which time the nuclear/cortical/posterior subcapsular scores were 5.0/0.1/4.0. Six weeks later, visual acuity dropped to counting fingers and opacity scores were 5.0/2.0/5.0, and at 3 months post-SLT, visual acuity was hand motions with opacity scores of 5.0/5.9/5.9, indicating significant rapid progression of cortical opacity in this eye. The second occurred 21 months after SLT. Baseline visual acuity was 20/100 with opacity scores of 3.5/0.1/0.1, and by Month 21 acuity dropped to 20/640 with scores of 4/1/5, indicating development of posterior subcapsular opacity in this eye; the opacity was first noted at Month 12 (opacity score 3.5/0.1/4.0, acuity 20/200). The third occurred 26 months after SLT. Baseline acuity was 20/50 with opacity scores of 2/5/0.1, and by Month 26 acuity dropped to 20/80 with opacity scores of 2/6/0.1, indicating modest progression of cortical opacity in this eye.

Discussion

The West Indies Glaucoma Laser Study was conducted to validate the role of SLT in glaucomatous Afro-Caribbean eyes preparatory to the development of a comprehensive strategy for glaucoma management throughout the African-derived developing world.[11] Previous reports from the WIGLS data set,[10,20] along with other studies,[13-15] have demonstrated that SLT effectively and safely lowers IOP in this population.

In the current analysis, we have demonstrated that SLT is not associated with significant worsening of lens opacity in WIGLS study population. Through three years of follow-up, mean scores for nuclear, cortical, and posterior subcapsular lens opacities remained statistically unchanged in both right and left eyes of study participants. Curiously, a small and statistically significant improvement in nuclear opacity score was seen in both eyes from baseline to Month 12. Anecdotally, subjects frequently commented after SLT that their visual acuity had improved, although these unsolicited comments were not captured as data for analysis. Given no obvious biologically plausible explanation for such an occurrence, it is likely that this is a chance finding. The magnitude of the change—approximately 0.3 on a scale from 0.1 to 6.9—is an approximate 4% change in overall score and is of no practical clinical significance.

Three of 142 eyes, of 3 different subjects, underwent cataract surgery during the three-year study. All three eyes had some degree of lens opacity at baseline. Whether there is a causal relationship between SLT and lens opacity progression is difficult to ascertain. First, the lack of changes in mean opacity scores suggests that SLT is not associated with lens opacity progression in general. Second, the low rate of clinically significant progression leading to cataract surgery (3/142, 2.1%) suggests that this may be idiopathic rather than directly pathogenic. However, it might then be expected that fellow eyes would behave similarly, and this was not the case in these three subjects, whose fellow eye opacity scores remained essentially unchanged through 22-38 months of follow-up after SLT. Third, in only 1 of the 3 cases was there a temporal relationship between SLT and progression; one eye manifested significant progression within 6 weeks and underwent cataract extraction at 3 months post-SLT, while the other two cases first demonstrated progressive opacity scores 12 or more months post-SLT. Fourth, the nature of the opacity was not consistent among the three eyes. In one eye, cortical changes drove the need for cataract surgery; in another, posterior subcapsular changes were responsible; and in the third, only a modest change in cortical score (from 5.0 to 6.0), and the subject sought cataract extraction at Month 26 after a modest change in best-corrected visual acuity from 20/50 to 20/80.

The only long-term (>1 year), prospective, randomized trial of SLT reported to date is the LiGHT study, in which eyes were assigned to an SLT-first or medication-first treatment strategy and followed for 3 years.[21] In that study, the rate of cataract surgery was 2% in the SLT arm and 4% in the medication arm, suggesting that SLT is no more likely to promote cataract progression than standard medical therapy.[6] In fact, the rate of cataract progression and cataract surgery seen in WIGLS was entirely consistent with the known natural history of progressive lens opacification. In the Longitudinal Study of Cataract (which utilized the LOCS III schema), 3-year progression rates for pre-existing nuclear, cortical and posterior subcapsular opacities were 39%, 10%, and 49%, respectively, with an 8% rate of cataract surgery over five years.[7,22] More relevant to the WIGLS study population, the Barbados Eye Studies (using the LOCS II schema) reported the 4-year rate of progression of nuclear, cortical and posterior subcapsular opacities to be 3.6%, 12.5%, and 23%, with a 1.6% rate of cataract surgery among Afro-Caribbean subjects.[23]

WIGLS is the largest and longest study of SLT in an African-derived population reported to date. This analysis is strengthened by its prospective design, by use of a standardized system to grade lens opacities, and by masking of examiners to prior lens opacity scores. One limitation of our interpretation of study data is the possibility that the economic burden of undergoing cataract surgery may render the observed rate of cataract surgery an underrepresentation of the rate of visually significant cataract development. In fact, there are multiple programs in both countries that provide free cataract surgery, and all patients developing visually significant cataract were referred for surgery. Also, this analysis is limited to eyes undergoing a single SLT treatment, as the number of eyes with multiple SLT treatments provided inadequate power for meaningful analysis. However, no eyes underwent cataract surgery after repeat SLT— the three cases of cataract surgery in this report represent the only 3 such cases occurring during the study. Further, as visual acuity was not a planned endpoint of the study, assessment of visual acuity was not standardized across sites, did not include formal assessment of best-corrected visual acuity beyond baseline for eligibility, and is not presented herein.

In conclusion, SLT is not associated with clinically significant changes in nuclear, cortical, or posterior subcapsular lens opacities in glaucomatous Afro-Caribbean eyes, and the rate of cataract surgery observed in WIGLS is consistent with reported rates from longitudinal natural history studies conducted in both Caribbean and non-Caribbean populations.

Acknowledgments

Funding: Supported by NIH R01 EY023620 (TR)

Biography

References

1. The Advanced Glaucoma Intervention Study: 8. Risk of cataract formation after trabeculectomy. Arch Ophthalmol 2001;119:1771–9. [PubMed: 11735786]
2. Gedde SJ, Feuer WJ, Shi W, et al. Treatment Outcomes in the Primary Tube Versus Trabeculectomy Study after 1 Year of Follow-up. Ophthalmology 2018;125:650–63. [PubMed: 29477688]
3. Lichter PR, Musch DC, Gillespie BW, et al. Interim clinical outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medications or surgery. Ophthalmology 2001; 108:1943–53. [PubMed: 11713061]
4. Herman DC, Gordon MO, Beiser JA, et al. Topical ocular hypotensive medication and lens opacification: evidence from the ocular hypertension treatment study. Am J Ophthalmol 2006;142:800–10. [PubMed: 17056362]
5. Leske MC, Wu SY, Nemesure B, Hennis A. Risk factors for incident nuclear opacities. Ophthalmology 2002; 109:1303–8. [PubMed: 12093655]
6. Gazzard G The LiGHT Study: Laser in Glaucoma and Ocular Hypertension Trial. European Glaucoma Society Annual Meeting Florence, Italy2018.
7. Leske MC, Chylack LT Jr, Wu SY, et al. Incidence and progression of nuclear opacities in the Longitudinal Study of Cataract. Ophthalmology 1996;103:705–12. [PubMed: 8637678]

8. Katz LJ, Steinmann WC, Kabir A, Molineaux J, Wizov SS, Marcellino G. Selective laser trabeculoplasty versus medical therapy as initial treatment of glaucoma: a prospective, randomized trial. J Glaucoma 2012;21:460–8. [PubMed: 21543992]
9. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol 2002;120:1268–79. [PubMed: 12365904]
10. Realini T, Shillingford-Ricketts H, Burt D, Balasubramani GK. West Indies Glaucoma Laser Study (WIGLS): 1. 12-Month Efficacy of Selective Laser Trabeculoplasty in Afro-Caribbeans With Glaucoma. Am J Ophthalmol 2017;184:28–33. [PubMed: 28962966]
11. Realini T, Olawoye O, Kizor-Akaraiwe N, Manji S, Sit A. The Rationale for Selective Laser Trabeculoplasty in Africa Asia-Pacific journal of ophthalmology 2018.
12. Kyari F, Adekoya B, Abdull MM, Mohammed AS, Garba F. The Current Status of Glaucoma and Glaucoma Care in Sub-Saharan Africa. Asia-Pacific journal of ophthalmology 2018;7:375–86. [PubMed: 30574693]
13. Realini T. Selective laser trabeculoplasty for the management of open-angle glaucoma in St. Lucia. JAMA Ophthalmol 2013;131:321–7. [PubMed: 23348420]
14. Goosen E, Coleman K, Visser L, Sponsel WE. Racial Differences in Selective Laser Trabeculoplasty Efficacy. Journal of current glaucoma practice 2017;11:22–7. [PubMed: 28138214]
15. Seck SM, Agboton G, Dieng M, et al. [Selective laser trabeculoplasty (SLT): our experience in African blacks]. J Fr Ophtalmol 2015;38:238–46. [PubMed: 25748106]
16. Wittenborn JS, Rein DB. Cost-effectiveness of glaucoma interventions in Barbados and Ghana. Optom Vis Sci 2011;88:155–63. [PubMed: 21076360]
17. Stein JD, Kim DD, Peck WW, Giannetti SM, Hutton DW. Cost-effectiveness of medications compared with laser trabeculoplasty in patients with newly diagnosed open-angle glaucoma. Arch Ophthalmol 2012;130:497–505. [PubMed: 22332202]
18. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol 2002;86:238–42. [PubMed: 11815354]
19. Chylack LT Jr, Wolfe JK, Singer DM, et al. The Lens Opacities Classification System III. The Longitudinal Study of Cataract Study Group. Arch Ophthalmol 1993;111:831–6. [PubMed: 8512486]
20. Realini T, Shillingford-Ricketts H, Burt D, Balasubramani GK. West Indies Glaucoma Laser Study (WIGLS)-2: Predictors of Selective Laser Trabeculoplasty Efficacy in Afro-Caribbeans With Glaucoma. J Glaucoma 2018;27:845–8. [PubMed: 29965865]
21. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Laser in Glaucoma and Ocular Hypertension (LiGHT) trial. A multicentre, randomised controlled trial: design and methodology. Br J Ophthalmol 2018;102:593–8. [PubMed: 28903966]
22. Leske MC, Chylack LT Jr, He Q, et al. Incidence and progression of cortical and posterior subcapsular opacities: the Longitudinal Study of Cataract. The LSC Group. Ophthalmology 1997;104:1987–93. [PubMed: 9400756]
23. Leske MC, Wu SY, Nemesure B, Li X, Hennis A, Connell AM. Incidence and progression of lens opacities in the Barbados Eye Studies. Ophthalmology 2000;107:1267–73. [PubMed: 10889096]

What Was Known

- SLT effectively lowers IOP in people of African descent
- The effects of SLT on lens opacity progression have not been characterized in this population

What This Paper Adds

- SLT is not associated with progression of nuclear, cortical, or posterior subcapsular lens opacities in Afro-Caribbeans with OAG, and the rate of cataract surgery in this study cohort was consistent with the known natural history of lens changes in this population
- SLT can be deployed in low-resource setting populated by people of African descent without concern for causing visually significant cataracts

Synopsis

Selective laser trabeculoplasty therapy is not associated with progressive nuclear, cortical, or posterior subcapsular lens opacities through 3 years of follow-up in Afro-Caribbean eyes with open-angle glaucoma.

Table 1.

Demographic and glaucoma status data of subjects participating in the West Indies Glaucoma Laser Study.

Characteristic	Value	
Gender, n (%)		
Male	29 (40.3%)	
Female	43 (59.7%)	
Age, yr	61.0 (11.4)	
Ethnicity, n (%)	72 (100) African descent	
Number of glaucoma medications, n (%)		
0	5 (6.9)	
1	45 (62.5)	
2	18 (25)	
3	4 (5.6)	
Glaucoma medication classes, n (%)		
Beta-blockers	42 (58.3)	
Prostaglandins	35 (48.6)	
Carbonic anhydrase inhibitors	8 (6.9)	
Adrenergic agonists	8 (6.9)	
	Right eye Mean (SD)	Left eye Mean (SD)
Intraocular pressure, mm Hg	21.0 (3.3)	20.9 (3.0)
Central corneal thickness, microns	537.4 (35.6)	543.3 (37.9)
Vertical cup-disc ratio	0.7 (0.1)	0.7 (0.1)
Visual field mean deviation, dB	−4.6 (5.2)	−3.9 (3.8)
Laser parameters, mean (SD)		
Total energy (mJ)	86.0 (21.2)	87.7 (20.6)
Number of treatment spots	102.3 (2.5)	101.7 (1.7)

Table 2.

Lens opacity scores at each time point and changes from baseline.

			Baseline	Month 12	Month 24	Month 36
Right Eyes		N	70	58	36	29
	Nuclear	Mean (SD)	2.44 (1.23)	2.1 (1.26)	2.03 (1.22)	1.97(1.31)
		Mean (SD) change from baseline	---	**−0.29 (0.68)**	−0.19 (0.60)	−0.2(0.68)
		p-value	---	**0.0022**	0.0707	0.1252
	Cortical	Mean (SD)	0.39 (1.08)	0.33 (0.96)	0.37 (1.14)	0.13(0.17)
		Mean (SD) change from baseline	---	−0.12 (0.78)	−0.06 (0.66)	−0.07(0.57)
		p-value	---	0.2416	0.6195	0.5197
	Posterior Subcapsular	Mean (SD)	0.22 (0.59)	0.20 (0.57)	0.04 (0.05)	0.10(0)
		Mean (SD) change from baseline	---	0.02 (0.71)	−0.17 (0.51)	−0.13(0.56)
		p-value	---	0.8398	0.0592	0.2165
Left Eyes		N	72	61	40	34
	Nuclear	Mean (SD)	2.4 (1.16)	2.07 (1.23)	2.09 (1.15)	2.04(1.27)
		Mean (SD) change from baseline	---	**−0.27 (0.69)**	−0.15 (0.63)	−0.1(0.59)
		p-value	---	**0.0033**	0.1522	0.3275
	Cortical	Mean (SD)	0.3 (0.85)	0.39 (0.98)	0.36 (0.96)	0.3(0.86)
		Mean (SD) change from baseline	---	0.05 (0.65)	0.07 (0.45)	0.08(0.27)
		p-value	---	0.5815	0.3717	0.0835
	Posterior Subcapsular	Mean (SD)	0.15 (0.36)	0.19 (0.45)	0.04 (0.05)	0.16(0.33)
		Mean (SD) change from baseline	---	0.05 (0.59)	−0.14 (0.47)	−0.03(0.17)
		p-value	---	0.5479	0.0753	0.3246