ABOUT THE AUTHORS

Biana Dubinsky-Pertzov, MD, MPH

Dr. Biana Dubinsky-Pertzov is a Glaucoma Fellow at McMaster University in Ontario, Canada. She completed her ophthalmology residency at Tel-Aviv University and holds a master's in public health. Passionate about increasing public awareness of glaucoma, Dr. Dubinsky-Pertzov believes that early detection and intervention are essential for combating the disease. She advocates for broader knowledge and understanding of glaucoma among communities.

Author Affiliations: Department of Ophthalmology, Shamir Medical Center (formerly Assaf-Harofeh), Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
Department of Surgery, Division of Ophthalmology, McMaster University Faculty of Health Sciences, Hamilton, Ontario, Canada

Nir Shoham-Hazon, MD

Dr. Shoham-Hazon is a Glaucoma and Advanced anterior segment surgeon in Miramichi NB where he is the director of the Miramichi EyeNB Centre of Excellence and medical director of the Miramichi Surgical Centre of Excellence. His visions in practice are to implement equality for Ophthalmologists working in Rural Canada and raise awareness for Rural Ophthalmology focused patient care. He aims to promote medical school and residency exposure in rural communities in NB. Dr. Shoham-Hazon is affiliated with Dalhousie and Memorial universities as Assistant and Clinical Assistant Professor respectively.

Author Affiliations: Miramichi EyeNB Centre of Excellence, Miramichi, NB, Canada

doi.org/10.58931/cect.2024.3350

Standard of Care for First-line Therapy in Newly Diagnosed Glaucoma and Update on SLT from the LiGHT Trial

Biana Dubinsky-Pertzov, MD, MPH
Nir Shoham-Hazon, MD

Introduction

Glaucoma is a progressive, multifactorial disease marked by ganglion cell loss, optic nerve damage and progressive vision loss, which can result in blindness if not treated. Glaucoma accounts for 11% of registrations for blindness.[1] The disease is closely linked to increased intraocular pressure (IOP) and reducing this pressure is the sole available treatment to slow disease progression.[2] The epidemiology of glaucoma presents a significant public health challenge, with primary open-angle glaucoma (POAG) being the most common form, affecting approximately 2–3% of adults over the age of forty.[3] Many patients can be initially managed with medications; however, the treatment has significant limitations. Issues such as complications, side effects, adherence, nonresponse, reduced effectiveness over time (tachyphylaxis), and financial costs pose challenges to controlling IOP with eye drops. The global burden of glaucoma is expected to increase as the population ages, highlighting the urgency for effective management strategies. The landmark LiGHT (Laser in Glaucoma and Ocular Hypertension) trial, published in 2019, with an initial 36 months of follow-up,[4] later extended to 72 months of follow-up,[5] has conceptually influenced the management of POAG and Ocular hypertension (OHT). By demonstrating the efficacy and safety of selective laser trabeculoplasty (SLT), a “dropless” and “knifeless” alternative as a first-line treatment option, the LiGHT trial challenged the conventional treatment paradigm. The six-year results further consolidate SLT’s role as a fundamental treatment option, indicating its long-term effectiveness and durability in managing glaucoma, potentially redefining standard care protocols.

Therapeutic Options for Glaucoma: Historical Overview

The management of glaucoma has traditionally centered on the reduction of IOP to halt or slow down the progression of optic nerve damage. Therapeutic options include medications (mainly topical eye drops), laser treatments and surgical interventions. Each treatment modality aims to decrease eye pressure, either by improving aqueous humour outflow or reducing its production. Until recent years, the paradigm for treating glaucoma followed a linear and sequential approach. Initially, therapy would commence with the prescription of topical eye drops, aiming at lowering IOP to target levels. As the condition progressed or if initial treatments proved insufficient, the strategy involved the addition of other eye drops, each with a different mechanism of action, to enhance the IOP-lowering effect. If this pharmacological approach did not achieve the desired outcomes, laser trabeculoplasty (LTP) treatment was considered as the next step in the treatment paradigm. Ultimately, if both medical and laser therapies failed to control the disease adequately, traditional glaucoma surgeries were employed as the final resort. This approach was primarily guided by the principle of avoiding the potentially devastating adverse events associated with traditional filtering procedures.

IOP lowering eye drops, the primary treatment for many patients, provide a non-invasive method to manage IOP. Nonetheless, their efficacy is compromised by several challenges. Non-adherence to treatment regimens, which is reported to be as high as 50%,[6,7] significantly undermines treatment outcomes. Patients may also experience ocular

surface irritation, including symptoms such as burning, dryness, conjunctival hyperemia and a sensation of a foreign body in the eye.[8] Over time, the effectiveness of these medications can decrease, further complicating treatment efforts. Additionally, the impact on patients' quality of life[9] combined with the requirement for lifelong daily administration and the risk of potential systemic side effects, frequently results in suboptimal therapeutic success.

Paradigm Shift: The Rise of Interventional Glaucoma

In recent years, as understanding of disease progression mechanisms deepens, along with recognition of the critical need for early and effective IOP reduction and the challenges of medical treatment, the field of glaucoma has witnessed a paradigm shift toward "Interventional Glaucoma"—a concept that emphasizes early intervention (whether invasive or none) over traditional pharmacotherapy. Procedures such as minimally invasive glaucoma surgeries (MIGS) and minimally invasive bleb-based surgeries (MIBS) have revolutionized treatment by offering safer, effective alternatives to lower IOP, with fewer complications and a more favourable impact on the patient's lifestyle compared to lifelong medication use.

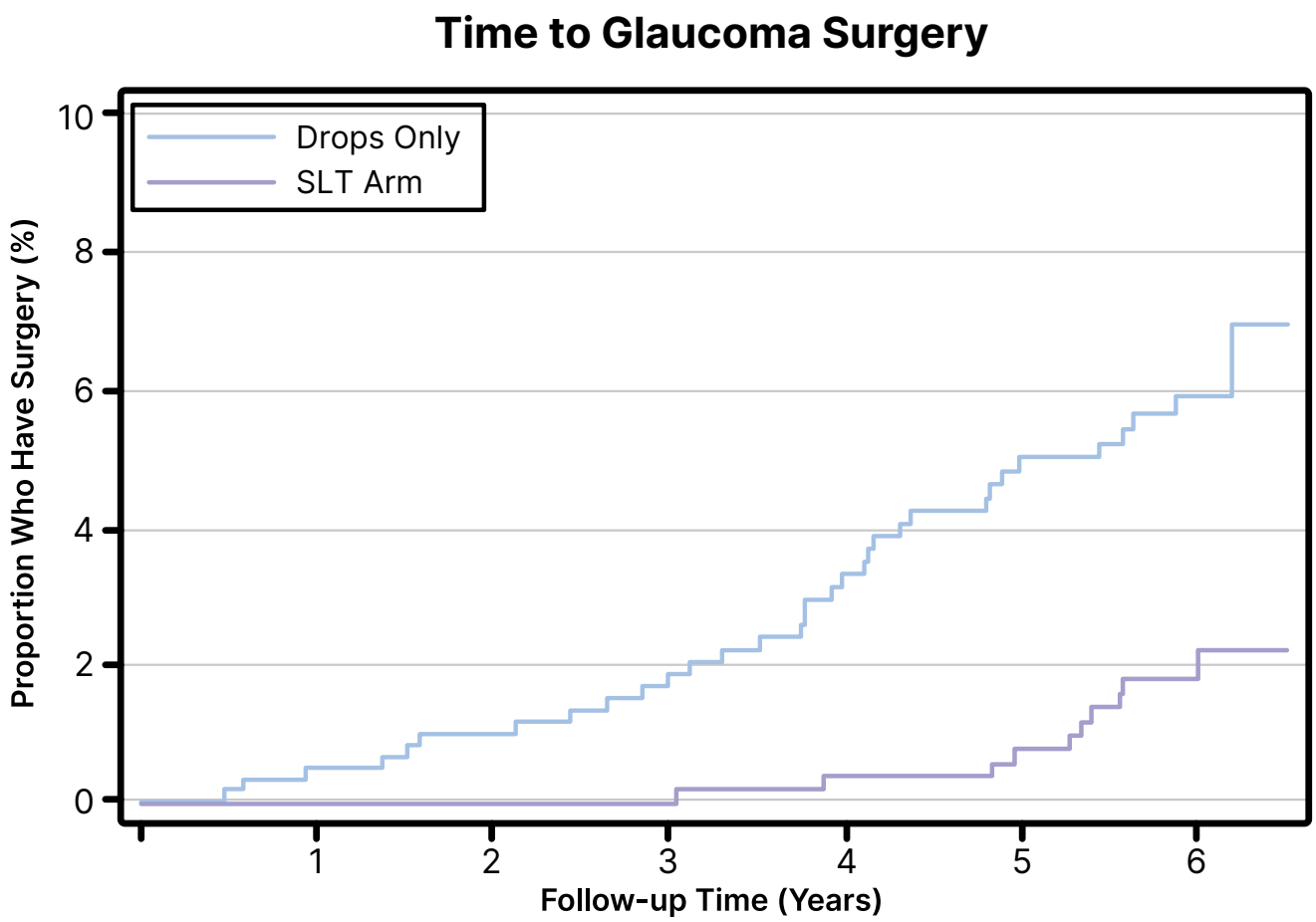
SLT, a noninvasive glaucoma intervention, has emerged as a pivotal treatment modality, particularly for patients with POAG in 1995 and was approved by the FDA in 2001.[10] SLT utilizes nanosecond low-energy light, undertaken in single-shot mode, directed at the angle to selectively target the pigmented trabecular meshwork elements. The enhanced outflow facility and reduced IOP typically manifest within 4 to 6 weeks, although the mechanism behind the improvement of outflow facility remains uncertain. Randomized controlled trials (RCTs) have demonstrated a decrease in the number of IOP medications required for IOP control in patients with POAG and OHT.[11,12] Additionally, there is increasing evidence supporting satisfactory outcomes in terms of repeatability.[13,14]

The LiGHT trial, a multicentre RCT conducted in the United Kingdom, enrolled 718 patients with POAG or OHT. The study compared SLT treatment with IOP-lowering medications, employing a stepwise strategy for adding medications or SLT as required to achieve target IOP. The results demonstrated that SLT was as effective as medications in controlling IOP. At 36 months, 78.2% of patients receiving SLT achieved their target IOP without the need for additional medication, in contrast to 64.6% in the medication group who were on a single medication. By 72 months, 69.8% of the SLT group had maintained their target IOP without requiring additional medications or surgeries. At 36 months, SLT was also found to be more cost-effective as an initial therapy compared to medications within the United Kingdom's healthcare system. Another significant outcome of this study was that while the 36-month results of the LiGHT trial indicated no measurable improvement in quality of life with SLT compared to medications, according to various quality of life surveys; yet the extended follow-up at 72 months showed improved Glaucoma Symptom Scores for the SLT group.

Nevertheless, one of the most impactful findings of this study was that at 72 months, fewer eyes in the SLT group experienced glaucoma progression (19.6% vs 26.8%), and fewer required trabeculectomy (13 eyes vs 32 eyes) (**Figure 1**). This might suggest that using SLT as a first-line treatment could not only successfully lower IOP, but also potentially alter the course of the disease. The reduced likelihood of undergoing filtration surgery and avoiding the well-known and not uncommon complications of filtration surgery is of great significance. This outcome suggests that SLT could offer a substantial benefit in reducing the progression of glaucoma, thereby decreasing the need for more invasive interventions.

The Transformative Impact of the LiGHT Trial

Smaller trials leading up to LiGHT showed similar results with SLT: It worked as well as IOP lowering drops as a first-line therapy to lower pressure with minimal side effects; still there was little movement away from drops. The Medicare billing study showed that SLT was performed in less than 5% of people with glaucoma.[15] As mentioned, the LiGHT study is the largest RCT with the longest follow-up period to date, comparing SLT as an initial treatment with IOP-lowering drops. It has already initiated a shift and is likely to continue influencing the transition from medication to laser as the first-line management approach. The study has shed clear light on previously undetermined issues. It confirmed the efficacy and safety of SLT, the potential benefits of repeated treatments and its cost-effectiveness superiority.



Number of Patients at Risk/Years	0	1	2	3	4	5	6*
Drops Arm	361	352	242	334	307	291	266
SLT Arm	355	351	345	328	304	287	270

Figure 1. Failure plot indicating time to glaucoma surgery from baseline by treatment arm (P < 0.001, log-rank test) based on intention-to-treat analysis (y-axis on a scale of 0-10%; the unit of analyses is the eye). The number at risk at 6 years includes the patients whose last visit was +/- 6 months; *adapted from Gazzard, Gus et al, 2023; doi:10.1016/j.ophtha.2022.09.009; https://creativecommons.org/licenses/by/4.0/*

Abbreviations: SLT: selective laser trabeculoplasty

Additionally, it has unveiled intriguing insights into possible disease mechanisms. The early utilization of SLT has shown significant decrease in disease progression and the need of subsequent glaucoma surgeries. This potential alteration in the course of the disease suggests that early intervention targeting the pathophysiological tissue involved could help prevent future fibrosis and stiffness in the more distal outflow system.

From a public health perspective, the results of the study would suggest laser for everybody with early-to-moderate open-angle glaucoma, and indeed, primary SLT at diagnosis is now recommended as the preferred treatment by the UK National Institute of Health and Care Excellence (NICE), and as an equivalent alternative in the European Glaucoma Society Treatment Guidelines and the American Academy of Ophthalmology Preferred Practice Patterns.

Nonetheless, like everything in life, the implementation of new guidelines is not without its challenges and barriers, requiring time, effort and perseverance to overcome these. One significant challenge is overcoming clinical inertia and tradition, as many ophthalmologists are accustomed to initiating treatment with topical medications, a practice deeply rooted in decades of clinical experience. Additionally, not all ophthalmologists may be trained or have experience in performing SLT, limiting their ability to offer this treatment option, especially in areas where access to training or laser equipment is scarce. Patient's acceptance and perception also play a crucial role; many might prefer starting with what they perceive as less invasive options like eye drops, necessitating thorough patient education about the benefits of SLT. Access to the necessary laser equipment can be a barrier, particularly in under-resourced or rural areas. Furthermore, the initial cost of SLT, compared to that of topical medications, and potential reimbursement issues could make it financially unfeasible for some patients. Last, there is a lack of awareness among healthcare providers and patients about the latest evidence supporting SLT as a first-line treatment option. To address many of the challenges outlined previously, a key solution lies in education. This education is targeted not only at glaucoma specialists but also at primary care physicians, general ophthalmology specialists, optometrists, and patients themselves. For instance, NICE has recognized these barriers and has put forth initiatives to support healthcare professionals. These initiatives include providing comprehensive training on the suitability and safety of SLT, along with its benefits and risks, and enhancing the skills needed to effectively discuss these factors with patients.

Conclusion

By addressing the drawbacks of traditional treatments and presenting a viable, less invasive alternative, the LiGHT trial has set a precedent in the glaucoma treatment landscape, advocating for a shift toward more patient-friendly and efficacious management strategies. This long-term data provided a stronger case for the adoption of SLT as a preferable first-line treatment in glaucoma management, underscoring its benefits not just in controlling IOP but also in enhancing patients' overall well-being by changing the course of their disease.

Correspondence

Biana Dubinsky-Pertzov, MD, MPH
Email: bianad@gmail.com

Financial Disclosures

NS-H: Consulting Honoraria: Bayer, Biogen, Nova Eye Medical, Roche,
Speaker Honoraria: AbbVie, Bayer, B&L, Hexiris pharma (co-founder), Lightmed, Roche,
BD-P: None declared.

The authors wish to acknowledge the contribution of Medhaj Garg, New Brunswick Community College, Practical Nursing Department, Miramichi Campus, Miramichi, NB for his help in the research for this manuscript.

References

1. Liu WJ, Taylor LJ, MacLaren RE, et al. Clinical research on the leading causes of severe sight impairment in the UK general and working populations. Clin Ophthalmol. 2023;17:2729-35.
2. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002 Jun;120(6):701-13; discussion 829-830.
3. Varma R, Lee PP, Goldberg I, et al. An assessment of the health and economic burdens of glaucoma. Am J Ophthalmol. 2011 Oct;152(4):515-22.
4. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. Lancet. 2019 Apr 13;393(10180):1505-16.
5. Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial: Six-year results of primary selective laser trabeculoplasty versus eye drops for the treatment of glaucoma and ocular hypertension. Ophthalmology. 2023 Feb 1;130(2):139-51.
6. Sheer R, Bunniran S, Uribe C, et al. Predictors of nonadherence to topical intraocular pressure reduction medications among Medicare members: a claims-based retrospective cohort study. J Manag Care Spec Pharm. 2016 Jul;22(7):10.18553/jmcp.2016.22.7.808.
7. Reardon G, Kotak S, Schwartz GF. Objective assessment of compliance and persistence among patients treated for glaucoma and ocular hypertension: a systematic review. Patient Prefer Adherence. 2011;5:441-63.
8. Roughead EE, Kalisch LM, Pratt NL, et al. Managing glaucoma in those with co-morbidity: not as easy as it seems. Ophthalmic Epidemiol. 2012 Apr;19(2):74-82.
9. Kaur D, Gupta A, Singh G. Perspectives on quality of life in glaucoma. J Curr Glaucoma Pract. 2012;6(1):9-12.
10. Latina MA, Park C. Selective targeting of trabecular meshwork cells: in vitro studies of pulsed and CW laser interactions. Exp Eye Res. 1995 Apr;60(4):359-71.
11. Lee JW, Chan CW, Wong MO, et al. A randomized control trial to evaluate the effect of adjuvant selective laser trabeculoplasty versus medication alone in primary open-angle glaucoma: preliminary results. Clin Ophthalmol. 2014 Sep 25;8:1987-92.
12. De Keyser M, De Belder M, De Belder J, et al. Selective laser trabeculoplasty as replacement therapy in medically controlled glaucoma patients. Acta Ophthalmol. 2018 Aug;96(5):e577-81.
13. Hong BK, Winer JC, Martone JF, et al. Repeat Selective Laser Trabeculoplasty. J. Glaucoma. 2009 Mar;18(3):180.
14. Garg A, Vickerstaff V, Nathwani N, et al. Efficacy of repeat selective laser trabeculoplasty in medication-naïve open-angle glaucoma and ocular hypertension during the LiGHT Trial. Ophthalmology. 2020 Apr;127(4):467-76.
15. Friedman DS, Nordstrom B, Mozaffari E, et al. Variations in treatment among adult-onset open-angle glaucoma patients. Ophthalmology. 2005 Sep;112(9):1494-9.