Lasers in Medical Science (2025) 40:363
https://doi.org/10.1007/s10103-025-04620-7

ORIGINAL ARTICLE

Selective laser trabeculoplasty positively impacts long-term intraocular pressure fluctuation in untreated open-angle glaucoma patients

Frederico de Miranda Cordeiro[1,2,3] · **Maria Betânia Lemos**[1,2] · **Ricardo Y. Abe**[4] · **Heloísa A. Maestrini**[5] · **Guilherme B. Guedes**[6] · **Marcelo M. Nascimento**[7] · **Tiago Santos Prata**[1,2,8,9,10]

Received: 11 March 2024 / Accepted: 20 August 2025

Abstract

We sought to investigate the influence of selective laser trabeculoplasty (SLT), as a primary treatment option, on long-term (between visits) intraocular pressure (IOP) variation parameters in eyes with ocular hypertension (OH) or open-angle glaucoma (OAG). This multicenter, real-world data based, retrospective study consecutively enrolled untreated patients that had undergone a single SLT treatment and had a minimum follow-up of 24 months post-SLT. All included patients had to have at least 3 IOP measurements before (within 90 days) the SLT procedure. Patients requiring any glaucoma medication or procedure during the follow-up were excluded. Main outcome measurements were the comparison between pre and post-SLT IOP variation parameters (mean, peak and IOP fluctuation), based on data collected from each follow-up visit. Among 835 patients that had undergone SLT between January 2011 and December 2020, 67 eyes from 67 patients (mean age, 60.5 ± 16.8 years) fulfilled all study inclusion/exclusion criteria and were included in the final analysis. After 24 months of follow-up, mean baseline IOP was significantly reduced from 19.1 ± 2.9 mmHg to 13.6 ± 2.1 following SLT (IOP change, 29%; $p < 0.001$). Regarding IOP variation parameters, mean baseline IOP peak was significantly reduced from 20.7 ± 3.5 mmHg to 15.1 ± 2.5 mmHg (IOP change, 27%; $p < 0.001$). In addition, mean baseline IOP fluctuation (based on within subject standard deviation values) was significantly reduced from 1.8 ± 0.1 mmHg to 1.2 ± 0.1 mmHg (IOP change, 33%; $p < 0.001$). Our results, derived from real world data, suggest that SLT not only effectively reduces mean IOP values, but also positively impacts (by approximately 30%) both IOP fluctuation and peak. Even though our findings provide additional support for the use of SLT on clinical practice, they certainly warrant confirmation by a prospective study.

Keywords Intraocular pressure fluctuation · Selective laser trabeculoplasty · Ocular hypertension · Open-angle glaucoma

✉ Tiago Santos Prata
tprata0807@gmail.com

1 Glaucoma Instituto, Belo Horizonte, Minas Gerais, Brazil

2 Hospital Medicina dos Olhos, Opty Group, Osasco, São Paulo, Brazil

3 AME Excelência em Visão, Congonhas, Minas Gerais, Brazil

4 Hospital Oftalmológico de Brasília, Brasília, Distrito Federal, Brazil

5 Oculare, Hospital de Olhos, Belo Horizonte, Minas Gerais, Brazil

6 Hospital de Olhos do Paraná, Curitiba, Paraná, Brazil

7 Clínica Glaukos, São José do Rio Preto, São Paulo, Brazil

8 Department of Ophthalmology, Federal University of São Paulo, São Paulo, Brazil

9 Department of Ophthalmology Mayo Clinic, Jacksonville, FL, USA

10 Glaucoma Service Department of Ophthalmology, Federal University of São Paulo, Dr Alceu de Campos Rodrigues, 229, Vila Nova Conceição, São Paulo, Brazil

Published online: 17 September 2025

Introduction

Glaucomatous optic neuropathy is a progressive and multifactorial disease characterized by retinal ganglion cell and axonal loss associated with structural damage of optic nerve head, leading to irreversible visual field loss [1]. Intraocular pressure (IOP) is the most important known risk factor for glaucoma and still the only modifiable one [1–3]. When it comes to treatment alternatives for IOP reduction, there are three main options: topical medication, laser surgery, and incisional procedures [4]. Among laser treatment options, selective laser trabeculoplasty (SLT) has been used in the past two decades as a safe and effective alternative for mean IOP lowering in patients with open angle glaucoma (OAG) and ocular hypertension (OH) [4–7].

SLT is a minimally invasive laser treatment by selectively targeting pigmented trabecular meshwork (TM) cells with a 532-nm Q-switched Nd: YAG laser. The mechanism is to induce biological responses such as extracellular matrix remodeling, increase cellular activity in the TM, enhancing aqueous humor outflow and reducing IOP [7, 8]. The LiGHT trial study [6] demonstrated that SLT is effective in maintaining target IOP, reporting 70% of eyes being drop free after 6 years follow-up, slowing glaucoma progression and delaying the need for glaucoma surgery, with a favorable safety profile and potential for repeat the treatment. Among its advantages, SLT is minimally invasive, has a favorable safety profile with minimal and transient side effects, and does not depend on patient adherence to medical regimens [6]. However, variability in individual response, with some patients showing suboptimal or no IOP reduction should be considered.

Regarding the relationship between the different IOP parameters and glaucoma prognosis, many studies have indicated that not only mean IOP values, but also IOP peak and fluctuation could be significantly correlated with disease progression [10–13]. Nonetheless, while the mean IOP reduction with SLT is well established, data on its impact on peak and fluctuation remain limited. For instance, Collaer and coleagues [11] have shown that patients with progressive glaucoma, despite seemingly well controlled IOP during office visits, presented greater short-term (diurnal) IOP fluctuation than those with stable disease. Caprioli and Coleman [9] documented a significant correlation between long-term IOP fluctuation and visual field (VF) progression in the Advanced Glaucoma Intervention Study cohort. When it comes to the role of IOP peak, a retrospective analysis of the Glaucoma Progression Study revealed that long-term IOP peak, among other risk factors, was a better predictor of disease progression than long-term mean IOP [14].

Even though SLT effectiveness on mean IOP reduction has been extensively demonstrated by many studies [4, 6, 16–19], there are scant data when it comes to its effects on IOP fluctuation, especially on long-term (between visits) variation. Therefore, we sought to investigate the influence of SLT, as a primary treatment option, on long-term IOP variation parameters (peak and fluctuation) in eyes with untreated OAG.

Methods

This was a multicenter, real-world data based, retrospective study (chart review). We recruited participants from the Glaucoma Clinic at the Hospital Oftalmológico de Brasília, Hospital Medicina dos Olhos in Osasco, Glaukos Clinic in São José do Rio Preto, Oculare Clinic in Belo Horizonte, and Hospital de Olhos do Paraná in Curitiba. The study protocol was revised and approved by the Institutional Review Board from the Hospital Oftalmológico de Brasília. All study methods complied with the Declaration of Helsinki guidelines for human subject research and informed consent from each patient was not required due to the retrospective nature of the study, and need for informed consent was waived by the Institutional Review Board. The clinical trial number is not applicable for this study.

Participants

We enrolled consecutive untreated patients with OAG or OH that had undergone a single and primary SLT treatment between January 2011 and December 2020 [17]. All patients were required to be older than 18 years of age and had a minimum follow-up of 24 months post-SLT. Patients with OH needed to have all baseline untreated IOP values greater than 21 mmHg. In addition, in order to be included, each patient had to have at least 3 IOP measurements before (within 90 days) the SLT procedure. Post-SLT measurements were collected from the following visits: 7 days and 1,3,6,12 and 24 months. Patients requiring any glaucoma medication or procedure during the follow-up were excluded from the analysis. Other exclusion criteria were: previous laser or incisional glaucoma surgery, use of topical or oral steroids, ocular trauma and any ocular comorbidity.

Data collection

During follow-up, subjects underwent comprehensive ophthalmologic examinations including visual acuity, slit-lamp biomicroscopy, IOP measurement (Goldmann tonometer), gonioscopy, dilated fundoscopic examination, and optic disc photography. All patients underwent standard automated perimetry (SAP) using the 24−2 Swedish interactive threshold algorithm (Carl Zeiss Meditec, Inc, Dublin, CA).

Table 1 Baseline characteristics of study patients

Variables*	
Age (years)	60.5±16.8
Gender (Female/Male)	56.7%/43.3%
Central corneal thickness (µm)	528.9±35.2
Visual field mean deviation (dB)	−2.2±2.3
Etiology	
Ocular hypertension	36%
Open-angle glaucoma	64%
Degree of angle pigmentation	
+/++++	15%
++/++++	30%
+++/++++	29%
++++/++++	26%

*Data are given as mean ± standard deviation and percentages

Table 2 Intraocular pressure parameters before and after SLT

IOP parameters*	Pre-SLT	Post-SLT	Mean Change
Mean (mmHg)	19.1 ± 2.9	13.6 ± 2.1	29% ($p<0.001$)
Peak (mmHg)	20.7 ± 3.5	15.1 ± 2.5	27% ($p<0.001$)
Fluctuation (mmHg)**	1.8 ± 0.1	1.2 ± 0.1	33% ($p<0.001$)

IOP intraocular pressure

*Data are given as mean ± standard deviation

**Based on within subject standard deviation values

SLT procedure

All SLT procedures were performed by experienced glaucoma specialists using standardized parameters with the LIGHTLas SLT Deux-V, SLT/YAG combinantion system) Lightlas SeLecTor Deux, Lightmed, San Clemente, CA, USA). Approximately 100 non-overlapping shots (25 per quadrant) were applied over 360 degrees, except in cases of pigmentary glaucoma, in which only 180 degrees were treated. Laser energy varied from 0·4 to 1·3 mJ according to clinician discretion based on angle pigmentation and bubble formation. Following SLT, all patients received topical anti-inflammatory treatment [16, 17].

Outcome measures

Primary outcome measures were changes in IOP peak and fluctuation, comparing pre and post-SLT values. Long-term IOP peak was defined as the maximum IOP measurement along the 24 months of follow-up. Long-term IOP fluctuation was defined as the within subject standard deviation of each patient's mean IOP during the follow-up. The within subject standard deviation was used as a variation metric, instead of the IOP range, as it is less affected by outlier measurements [19]. Changes in mean IOP after SLT treatment were also investigated as a secondary outcome. Whenever both eyes were eligible, only one randomly selected eye was included in the analysis.

Statistical analysis and sample size calculation

The ocular parameter chosen for sample size calculation was IOP peak delta (comparison between pre and post-SLT values). Considering an estimated mean baseline IOP peak of 20 mmHg (standard deviation of 5 mmHg), and an expected pressure reduction of 20% following SLT, it would be required 50 patients (1 eye per patient; for an α-error of 0.05) to reach a statistical power of 80%.

Descriptive analysis was used to present demographic and clinical data. D'Agostino-Pearson test was performed to determine whether the data had a normal distribution. As normally distributed, data were presented as mean and standard deviation. Paired t test was used to compare pre and post-SLT IOP parameters (continuous data). Computerized statistical analysis was performed using the MedCalc software (MedCalc Inc., Mariakerke, Belgium) and statistical significance was set at $P<0.05$.

Results

A total of 835 eyes from 835 patients underwent SLT procedure between the years of 2011 and 2020. From this initial patients' list, 67 eyes from 67 patients fulfilled all study inclusion/exclusion criteria and were included in the final analysis. The study population was predominantly female (56.7%) and white (75%), with a mean age of 60 years old. Most patients (64%) had OAG, and the mean visual field mean deviation indicated mild to moderate disease severity. The majority of eyes (91%) underwent 360-degree SLT treatment. Baseline characteristics of study patients are provided in Tab. 1.

Following SLT, there was a significant and sustained reduction in IOP over the follow-up. Mean IOP decreased by 29% ($p<0.001$) after SLT treatment, significantly reduced from 19 mmHg to 13 mmHg. Additionally, other IOP parameters, such as IOP peak and IOP fluctuation, showed significant improvement, decreasing by 27% and 33%, respectively (both $p<0.001$; Tab. 2). These findings suggest that SLT not only lowers mean IOP but also contributes to stabilizing IOP peak and fluctuation, which are relevant for glaucoma progression risk.

All data supporting the results and analysis of this study are available upon request.

Discussion

Although mean IOP remains the most clinically useful IOP parameter, many studies have shown that both IOP fluctuation and peak could be related to the disease stability overtime [9, 21–23]. The LiGHT Trial [6] demonstrated that SLT had a greater positive impact on functional progression over the six-years of follow-up compared to conventional clinical treatment, highlighting not only its effectiveness in lowering mean IOP but also its potential for providing more stable IOP control in the long term, indicating good predictability and stability of the treatment effect. This contrasts with pharmacological therapies, where adherence issues, variable pharmacokinetics and side effects can contribute to fluctuating IOP levels and long-term stability.

In this context, a broader approach to IOP control has been advocated, emphasizing not only IOP reduction, but also the modulation of IOP fluctuation overtime. It has been suggested that physicians should consider IOP modulation as part of a comprehensive management strategy, rather than focusing exclusively on reducing mean IOP [20]. Our study, which evaluated almost 70 patients over a 2-years period following primary SLT, found that SLT not only effectively reduced mean IOP values, but also positively impacted both IOP fluctuation and peak. These findings provide valuable insights into the variability of IOP between visits in eyes treated with SLT and offer additional support for its use in clinical practice.

Despite the promising results, there are scant data in the literature regarding SLT's influence on long-term IOP variation parameters. Moreover, previous studies have primarily investigated the effect of SLT on short-term (diurnal) IOP control [23, 24, 25]. For example, Tojo et al. [23] monitored 24-hour IOP fluctuations using a contact lens sensor in patients with normal-tension glaucoma (NTG) treated with SLT, observing significant reduction in nocturnal IOP fluctuations, underscoring the potential of SLT in controlling IOP during non-office hours. Similarly, Kiddee and Atthavuttisilp [24] compared SLT and travoprost treatment, both effectively lowering nocturnal IOP. In a different study, Nagar and colleagues [25] reported that half of SLT-treated patients experienced a 50% reduction in diurnal IOP fluctuation. Moreover, a study evaluating 180º and 360º SLT treatments showed that 360º SLT had a more pronounced effect in maintaining IOP fluctuation between-visits ≤ 2 mmHg over 24 months [21]. These studies collectively support the hypothesis that SLT has a significant role in modulating IOP variation, beyond its effect on mean IOP, including both short- and long-term evaluations.

At this point, it is important to discuss the clinical implications of our findings. Previous studies have demonstrated that both IOP fluctuation and peak can be related to glaucoma progression and stability overtime [9, 21–23]. Clinically, our results suggest that in untreated OAG eyes, undergoing a single SLT session as a primary treatment, IOP peak and fluctuation values are significantly reduced over at least 24 months of follow-up. Unlike traditional pharmacological treatments, where IOP control is often influenced by medication half-life, side effects, and patient adherence, SLT offers a more predictable and stable IOP profile. This stability may be due to SLT's biological mechanism of action, which induces remodeling of the TM and improves aqueous outflow, independent of patient compliance. Consequently, SLT could be an effective option for IOP modulation in these patients, potentially improving disease prognosis and reducing the need for further incisional surgeries [6]. This is particularly relevant in cases where non-invasive management options are preferable, such as mild and moderate glaucoma patients.

Regarding the long-term effectiveness of SLT, while many studies demonstrate sustained IOP lowering effects up to 2–3 years, some evidence suggests a gradual decline in efficacy beyond this period, with retreatment often required to maintain the target IOP. However, repeat SLT treatments have been shown to be safe and can restore IOP control in many cases [6, 17, 18]. Therefore, SLT represents a valuable tool in the long-term management of glaucoma, especially when considering its safety profile and potential to reduce medication side effects.

Our study has some specific characteristics and limitations that should be considered when interpreting the results. First, the follow-up period of 24 months, although sufficient to assess short- to mid-term effects, may limit conclusions regarding long-term disease progression and sustained SLT efficacy. Furthermore, as this was a retrospective study, there was no standardization in measurements and data collection period to better characterize the IOP fluctuation over time. Second, retinography, automated perimetry and optical coherence tomography data were not analyzed to assess structural or functional progression during follow-up. Third, as we included only patients with OAG or OH who were not on hypotensive medications, our results may not be generalizable to patients under pharmacological treatment. It is important to emphasize the absence of a control group using topical hypotensive medications. This precludes direct comparison of the long-term stability and effectiveness between SLT and medical therapy, which should be addressed in future prospective studies. Fourth, IOP fluctuation may have a more pronounced effect in advanced glaucoma patients, who were not the majority in our study population. Finally, our IOP variation results were derived from regular office-hour visits, and therefore, these findings should not be directly compared with measurements of diurnal or 24-hour IOP fluctuation assessments.

Notwithstanding the robust evidence regarding the efficacy, safety and cost-effectiveness of SLT, little is known about its impact on long-term IOP variation (between visits). Our results, based on real-world data, suggest that SLT, when used as a primary treatment modality, not only effectively reduces mean IOP values but also has a positive effect on both IOP fluctuation and peak, with an estimated improvement of approximately 30%. While these findings provide additional support for the integration of SLT into clinical practice, they warrant further validation through prospective, controlled studies with longer follow-up periods and medically control group. Additionally, longitudinal data evaluating how changes in IOP variation parameters influence anatomical and functional stability in glaucomatous eyes are essential to fully understand the long-term benefits of SLT.

Author contribution All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by all authors. The first draft of the manuscript was written by Frederico de Miranda Cordeiro, Ricardo Y Abe and Tiago Santos Prata and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding The authors did not receive support from any organization for the submitted work.

Declarations

Informed consent Informed consent from each patient was not required due to the retrospective nature of the study, and need for informed consent was waived by the Institutional Review Board.

Competing interest The authors have no competing interests to declare that are relevant to the content of this article.

References

1. Weinreb RN, Khaw PT (2004) Primary open-angle glaucoma. Lancet 363(9422):1711–1720. https://doi.org/10.1016/S0140-6736(04)16257-0
2. Collaborative Normal-Tension Glaucoma Study Group (1998) Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. Am J Ophthalmol 126(4):487–497. https://doi.org/10.1016/S0002-9394(98)00223-2
3. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M (2002) Early manifest glaucoma trial group. Reduction of intraocular pressure and glaucoma progression: results from the early manifest glaucoma trial. Arch Ophthalmol 120(10):1268–1279. https://doi.org/10.1001/archopht.120.10.1268
4. Freitas AL, Ushida M, Almeida I et al (2016) Selective laser trabeculoplasty as an initial treatment option for open-angle glaucoma. Arq Bras Oftalmol 79(6):417–421. https://doi.org/10.5935/0004
5. Latina MA, Tumbocon JA (2002) Selective laser trabeculoplasty: a new treatment option for open angle glaucoma. Curr Opin Ophthalmol 13(2):94–96. https://doi.org/10.1097/00055735-200204000-00007
6. Gazzard G, Konstantakopoulou E, Garway-Heath D, Adeleke M, Vickerstaff V, Ambler G, Hunter R, Bunce C, Nathwani N, Barton K, LiGHT Trial Study Group (2023) 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 130(2):139–151. https://doi.org/10.1016/j.ophtha.2022.09.009
7. Gulati V, Fan S, Gardner BJ, Havens SJ, Schaaf MT, Neely DG, Toris CB (2017) Mechanism of action of selective laser trabeculoplasty and predictors of responde. Invest Ophthalmol Vis Sci 58:1462–1468. https://doi.org/10.1167/iovs.16-20710
8. Chen YF, Zeng W (2024) Mechanism of selective laser trabeculoplasty: a systemic review. Int J Ophthalmol 17(5):963–968. https://doi.org/10.18240/ijo.2024.05.22
9. Caprioli J, Coleman AL (2008) Intraocular pressure fluctuation a risk factor for visual field progression at low intraocular pressures in the advanced glaucoma intervention study. Ophthalmology 115(7):1123–1129e3. https://doi.org/10.1016/j.ophtha.2007.10.031
10. Caprioli J (2007) Intraocular pressure fluctuation: an independent risk factor for glaucoma? Arch Ophthalmol 125(8):1124–1125. https://doi.org/10.1001/archopht.125.8.1124
11. Asrani S, Zeimer R, Wilensky J, Gieser D, Vitale S, Lindenmuth K (2000) Large diurnal fluctuations in intraocular pressure are an independent risk factor in patients with glaucoma. J Glaucoma 9(2):134–142. https://doi.org/10.1097/00061198-200004000-00002
12. Scoralick ALB, Gracitelli CP, Dias DT, Almeida I, Ushida M, Dorairaj S, Kanadani FN, Paranhos A Jr, Prata TS (2019) Peak, fluctuation, or mean?? A correlation analysis of long-term intraocular pressure variation parameters in patients with stable glaucoma. J Curr Glaucoma Pract 13(1):28–31. https://doi.org/10.5005/jp-journals-10078-1240
13. Collaer N, Zeyen T, Caprioli J (2005) Sequential office pressure measurements in the management of glaucoma. J Glaucoma 14(3):196–200. https://doi.org/10.1097/01.ijg.0000159125.34241.79
14. De Moraes CG, Juthani VJ, Liebmann JM, Teng CC, Tello C, Susanna R Jr, Ritch R (2011) Risk factors for visual field progression in treated glaucoma. Arch Ophthalmol 129(5):562–568. https://doi.org/10.1001/archophthalmol.2011.72
15. Almeida ED Jr, Pinto LM, Fernandes RA, Prata TS (2011) Pattern of intraocular pressure reduction following laser trabeculoplasty in open-angle glaucoma patients: comparison between selective and nonselective treatment. Clin Ophthalmol 5:933–936. https://doi.org/10.2147/OPTH.S21759
16. Chun M, Gracitelli CP, Lopes FS, Biteli LG, Ushida M, Prata TS (2016) Selective laser trabeculoplasty for early glaucoma: analysis of success predictors and adjusted laser outcomes based on the untreated fellow eye. BMC Ophthalmol 16(1):206. https://doi.org/10.1186/s12886-016-0385-z
17. Abe RY, Maestrini HA, Guedes GB, Nascimento MM, Iguma CI, de Miranda Santos HD, Nasr MG, Lucena-Junior RP, Prata TS (2022) Real-world data from selective laser trabeculoplasty in Brazil. Sci Rep 4(1):1923. https://doi.org/10.1038/s41598-022-05699-6
18. Realini T (2008) Selective laser trabeculoplasty: a review. J Glaucoma 17(6):497–502. https://doi.org/10.1097/IJG.0b013e31817d2386
19. Moore Ds, McCabe GP, Craig BA (2016) Introduction to the practice of statistics. W.H. Freeman, United States of America
20. Kim JH, Caprioli J (2018) Intraocular pressure fluctuation: is it important?? J Ophthalmic Vis Res 13(2):170–174. https://doi.org/10.4103/jovr.jovr_35_18
21. Prasad N, Murthy S, Dagianis JJ, Latina MA (2009) A comparison of the intervisit intraocular pressure fluctuation after 180 and 360 degrees of selective laser trabeculoplasty (SLT) as a primary therapy in primary open angle glaucoma and ocular hypertension. J Glaucoma 18(2):157–160. https://doi.org/10.1097/IJG.0b013e3181752c97

22. Nouri-Mahdavi K, Hoffman D, Coleman AL, Liu G, Li G, Gaasterland D, Caprioli J, Advanced Glaucoma Intervention Study (2004) Predictive factors for glaucomatous visual field progression in the advanced glaucoma intervention study. Ophthalmology 111(9):1627–1635. https://doi.org/10.1016/j.ophtha.2004.02.017
23. Tojo N, Oka M, Miyakoshi A, Ozaki H, Hayashi A (2014) Comparison of fluctuations of intraocular pressure before and after selective laser trabeculoplasty in normal-tension glaucoma patients. J Glaucoma 23(8):e138–e143. https://doi.org/10.1097/IJG.0000000000000026
24. Kiddee W, Atthavuttisilp S (2017) The effects of selective laser trabeculoplasty and Travoprost on circadian intraocular pressure fluctuations: a randomized clinical trial. Medicine 96(6):e6047. https://doi.org/10.1097/MD.0000000000006047
25. Nagar M, Luhishi E, Shah N (2009) Intraocular pressure control and fluctuation: the effect of treatment with selective laser trabeculoplasty. Br J Ophthalmol 93(4):497–501. https://doi.org/10.1136/bjo.2008.148510

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.