

1) Scientific results referring to the project goals and time plan

A. Project aims and primary endpoint.

Title of project: Laser treatment for glaucoma in Nigeria: A feasibility study of four different treatment modalities to provide data to design randomised controlled trials

Primary aim: Assess the feasibility of delivering different lasers for adults with primary open angle glaucoma (POAG) i.e., SLT and MLT (trabeculoplasty) or TLT with TDLC as rescue treatment in Bauchi, Nigeria to inform future RCT design.

B. Patent flow and recruitment of participants.

Outpatient flow

The first patient was recruited on 20/05/2021 but following a review and protocol amendment the recruitment restarted on 09/08/2023 following the decision to drop one arm of the study, the Transcleral Micropulse Laser Treatment (TLT) because it was unacceptably painful. The number of patients attending the eye department was poor because of economic hardship in the country. To continue recruitment we used local radio, offering free screening to members of the public, and organised outreach to create awareness and refer patients to hospital for treatment.

Recruitment

Patients were recruited at ATBUTH through walk-in presentations and referrals. However, many referred patients could not be enrolled because they were from neighbouring states specifically for laser treatment or lived more than 200 km away, which fell outside the study's inclusion criteria. The last participant was recruited on 30 April 2025, and final follow-up was completed on 30 October 2025. In total, 283 participants were recruited (Figure 1). Over 60% of eligible patients preferred to continue with medical therapy and declined participation after being informed that laser treatment was unlikely to improve vision, and they did not wish to be exposed to the perceived risks. Outright refusals were often related to concerns about pain, particularly the possibility of being randomised to TLT, which was subsequently discontinued.

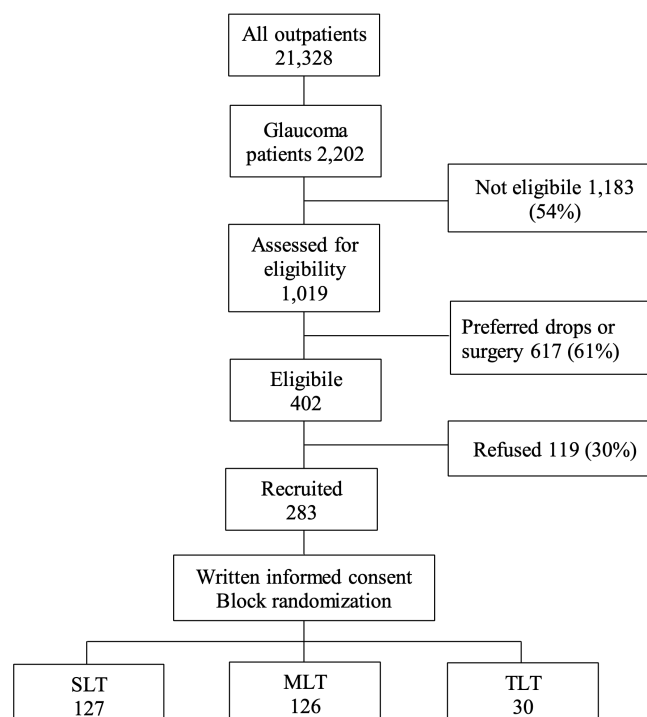


Figure 1. Flow chart of patient recruitment

C. Baseline data and follow up rates

Baseline characteristics

The majority of participants recruited had advanced glaucoma, with high baseline IOP (mean 38 mmHg, range 20-70mmHg) and high cup-to-disc ratios (mean 0.85, range 0.3-1.0). The mean age was 48 years (range 17-90 years) and more males were recruited 2:1, M: F (Table 1).

Baseline demographics and clinical features were largely comparable across laser groups, although there was some differences in age, pain at presentation, RAPD, and gonio grade in the TLT arm (Table 1). These differences could be due to the TLT group having only 30 patients compared with 127 in the SLT and 126 in the MLT arms making estimates less precise and more at risk of random variation. The smaller sample size and early withdrawal likely contributed to the apparent imbalances rather than reflecting true differences in patient randomisation.

Table 1. Baseline characteristics of study participants

	SLT N=127	MLT N=126	TLT N=30	All N=283
Sex				
Male (n) %	84 (66.1%)	81 (64.3%)	23 (76.7%)	188 (66.4%)
Female (n) %	43 (33.9%)	45 (35.7%)	7 (23.3%)	95 (33.6%)
Mean age, years	46.6	47.9	52.4	47.8
Previous treatment n (%)				
Yes	71 (55.9%)	72 (57.1%)	22 (73.3%)	165 (58.3%)
No	56 (44.1%)	54 (42.9%)	8 (26.7%)	118 (41.7%)
Pain at presentation n (%)				
None	108 (85.0%)	112 (88.9%)	23 (76.7%)	243 (85.9%)
Mild	17 (13.4%)	14 (11.1%)	7 (23.3%)	38 (13.4%)
Moderate	2 (1.6)	0	0	2 (0.7)
RAPD n (%)				
Yes	22 (17.3%)	14 (11.1%)	10 (33.3%)	46 (16.3%)
No	105 (82.7%)	112 (88.9%)	20 (66.7%)	237 (83.7%)
VCDR n (%)				
0.3-0.7	40 (31.5)	37 (29.4)	3 (10)	80 (28.3)
0.8	10 (7.9)	18 (14.3)	2 (6.7)	30 (10.6)
0.9	32 (25.2)	28 (22.2)	13 (43.3)	73 (25.8)
1.0	45 (35.4)	43 (34.1)	12 (40)	100 (35.34)
Gonio Shaffer n (%)				
Grade 3	106 (83.5%)	107 (84.9%)	19 (63.3%)	232 (81.9%)

Grade 4	21 (16.5%)	19 (15.1%)	11 (36.7%)	51 (18.0%)
Mean CCT μm (n)	555.26 (86)	549.7 (77)	553.71 (7)	552.68 (170)
IOP Mean mmHg (n)	38 (127)	37 (126)	38 (30)	38 (283)
IOP Range n (%)				
<30mmHg	25 (19.7%)	24 (19.0%)	6 (20.0%)	55 (19.4%)
30-40mmHg	61 (48.0%)	65 (51.6%)	14 (47.0%)	140 (49.5%)
>41mmHg	41 (32.3%)	37 (29.4%)	10 (33.0%)	88 (31.1%)
Total Patients	127 (100%)	126 (100%)	30 (100%)	283 (100%)

RAPD = relevant afferent pupil defect, and sign of differences in optic nerve damage between eyes. CCT = central corneal thickness. VCDR=vertical cup:disc ratio; IOP=intraocular pressure

Follow up rates

Follow-up was excellent in the immediate post-laser period, with over 90% of patients reviewed at 1 week and nearly 80% at 1 month. Attendance declined thereafter, with only about half of patients seen at 2–4 months (55–56% at 2–3 months and 47% at 4 months). Follow-up improved again at later time points, reaching 67% at 6 months and 65% at 12 months (Table 2). Overall, this reflects strong early engagement, a mid-term drop in attendance, and a reasonable recovery in long-term follow-up, largely attributable to sustained and proactive efforts by the research team to recall patients.

Table 2. Follow up and mean intraocular pressure (IOP) at follow up, all participants.

Variable	Attended n, %		Mean IOP	Std. Dev.	Min IOP	Max IOP
Baseline	283		38	8.87	20	70
Laser day	282	99.6%	37	9.09	11	70
1 week	260	91.9%	26	9.04	9	60
1 month	223	78.8%	25	7.49	11	61
2 months	158	55.8%	25	7.49	12	55
3 months	157	55.5%	23	6.47	10	56
4 months	132	46.6%	23	6.98	6	56
6 months	190	67.1%	21	5.92	8	49
12 months	184	65.0%	22	7.05	9	50

D. Primary outcome of efficacy assessment

Success at 12 months - defined as IOP at or below target.

Threshold 1 was an IOP of less than 19mmHg, and threshold 2 was an IOP of less than 22mmHg. At 6 months (threshold 2 IOP) the proportions were nearly identical in all laser types (61–64%) and differences were not statistically different. (Table 3) At 12 months (threshold 2 IOP), SLT had a higher success rate (64%) than MLT (55%) and TLT (46%). However, the chi-square test ($\chi^2 = 2.804$, $p = 0.246$) showed that these differences were not statistically significant.

Table 3. Success at 6 and 12 months at IOP threshold level 2 (<22mmHg)

	SLT	MLT	TLT
Attended at 6 months (n, %)	88 (69.3%)	84 (66.7%)	18 (60%)
IOP <18-21mmHg	54 (61%)	54 (64%)	11 (61%)
IOP 22-30mmHg	29 (33%)	27 (32%)	3 (17%)
IOP 31-40mmHg	4 (5%)	3 (4%)	3 (17%)
IOP >41mmHg	1 (1%)	0	1 (6%)
Total	88 (100%)	84 (100%)	100% (18)
Statistical analysis	$(\chi^2 = 0.176, p = 0.916)$		
Attended at 12 months (n, %)	75 (59.1%)	85 (67.5%)	24 (80%)

IOP <18-21mmHg	48 (64.0%)	47 (55.3%)	11 (45.8%)
IOP 22-30mmHg	19 (25.3%)	20 (23.5%)	11 (45.8%)
IOP 31-40mmHg	6 (8.0%)	18 (21.2%)	2 (8.4%)
IOP >41mmHg	2 (2.7%)	0	0
Total	75 (100%)	85 (100%)	24 (100%)
Statistical analysis	$\chi^2 = 2.804$, p = 0.246		

Success at different thresholds by laser type

Using both thresholds and time points, no statistically significant differences were found between SLT, MLT, and TLT (Table 4). Though SLT consistently shows slightly higher success at 12 months, with TLT having the poorer results. However, the relatively small sample sizes (especially for TLT) limit statistical power. The three laser types perform equivalently at both 6 months and 12 months for both thresholds.

Table 4. Success at thresholds 1 and 2 by laser at 12 months

Threshold	Success by type of laser (%)			Chi-square
	SLT	MLT	TLT	
At 12 months				
1. <18mmHg	34.7% (26/75)	30.6% (26/85)	20.8% (5/24)	1.638. P=0.44
2. <22mmHg	64.0% (48/75)	55.3% (47/85)	45.8% (11/24)	2.804. P=0.25
At 6 months				
1. <18mmHg	28.41 (25/88)	27.38 (23/84)	33.33 (6/18)	0.258. P=0.88
2. <22mmHg	61.36 (54/88)	64.28 (54/84)	61.11 (11/18)	0.176. P=0.92

Qualified and complete success by laser treatment by threshold level

Complete success was defined as an IOP at or below the target on no IOP lowering medication. A qualified success was defined as an IOP at target on one or more medication. This was measured at two threshold levels < 19mmHg (Threshold 1) and <22 mmHg (Threshold 2). SLT and MLT showed similar and balanced proportions of complete and qualified success at both IOP thresholds, suggesting comparable efficacy. TLT demonstrated a higher proportion of qualified success at <19 mmHg, but this was based on a very small sample (n = 5). At <22 mmHg, TLT showed a distribution closer to SLT and MLT; however, the small sample size (n = 11) limits interpretation. Overall, no laser modality demonstrated a clear statistical advantage (Table 5).

It is worth noting that the overall success rate is probably significantly higher than reported. This is because we observed that many patients prescribed additional medication do not purchase or use it. Consequently, the success rate would have been higher if medication adherence had been better.

Table 5. IOP Success with or without additional medication

	SLT	MLT	TLT	All	Chi Square
Threshold 1 (<19 mmHg)					
Qualified success	10 (38.5%)	13 (50.0%)	4 (80.0%)	27 (47.4)	
Complete success	16 (61.5%)	13 (50.0%)	1 (20.0%)	30 (52.6)	
Total	26 (100)	26 (100)	5 (100)	57 (100)	3.04. P=0.22
Threshold 2 (<22 mmHg)					
Qualified success	25 (52.1%)	24 (51.1%)	7 (63.6%)	56 (53.3)	
Complete success	23 (47.9%)	23 (48.9%)	4 (36.4%)	50 (47.6)	
Total	48 (100)	47 (100)	11 (100)	105 (100)	0.59. P=0.75

IOP reduction by 30% or more

A reduction in intraocular pressure (IOP) of at least 30% from baseline is considered a marker of treatment success in several studies.^{1,2} In this study, all laser modalities achieved an overall IOP reduction of approximately 30%. At 1 week, there were notable differences in early IOP response, with SLT (61%) and TLT (75%) outperforming MLT (34%). During the intermediate period (1–3 months), these differences were no longer apparent, as success rates converged across all lasers (approximately 50–70%). At 4 months, MLT demonstrated a significantly higher success rate (74%) compared with SLT (48%), with TLT showing an intermediate response (63%). In the longer term (6–12 months), no significant differences were observed, as success rates across all laser modalities stabilised between 67% and 81% (Table 5 and Figure 2).

Table 6. IOP reduction by 30% or more by type of laser at different time points n(%)

Follow-up period	SLT	MLT	TLT	All	Chi ²	P-value
1 week	71 (61%)	40 (34%)	21 (75%)	121 (50%)	15.8	0.00036
1 month	57 (60%)	56 (53%)	12 (52%)	124 (55%)	0.92	0.63
2 months	30 (44%)	40 (51%)	6 (54%)	76 (48%)	0.87	0.65
3 months	46 (72%)	51 (69%)	9 (64%)	108 (69%)	0.53	0.77
4 months	30 (48%)	45 (74%)	5 (63%)	97 (73%)	7.92	0.019
6 months	71 (81%)	66 (79%)	12 (71%)	149 (78%)	0.55	0.76
12 months	51 (67%)	57 (67%)	14 (61%)	122 (66%)	0.59	0.82

E. Pain, complications, loss of vision and repeat treatments

The pain scoring system used identified that 21/30 (70%) of patients treated by TLT reported moderate to severe intraoperative pain when performed without retrobulbar anaesthesia, as has been reported with other diode transscleral procedures (Table 7). SLT and MLT were well tolerated, with pain being rare and mild when present. TLT, however, was associated with a markedly higher rate of moderate/severe pain, which explains why this arm was discontinued early in the trial. The difference is statistically significant and clinically important, highlighting a clear tolerability disadvantage for TLT compared to SLT and MLT.

Table 7. Pain at the time of treatment by type of laser (n, %)

Degree of pain	SLT	MLT	TLT	All
None	108 (87.1%)	117 (92.9%)	1 (3.3%)	226 (80.7%)
Mild	16 (12.9%)	9 (7.1%)	8 (26.7%)	33 (11.8%)
Moderate/severe	0	0	21. 70.0%)	21 (7.5%)

Chi square (χ^2): 6.07. Pvalue: 0.048

Mentioning pain in the information sheet meant that some patients refused to take part in the trial. One of our criteria for feasibility was that the laser treatment can be given on the day it is recommended (i.e., same-day treatment), to increase adherence, which is not possible with retrobulbar anaesthesia which needs to be done in the operating theatre.

Complications

After treatment, transient IOP spikes (>8 mmHg) occurred in 14 (5.0%) eyes, 9 (7.1%) after SLT. Although SLT shows a slightly higher number of complications (7.1%) than MLT (2.4%) and TLT (6.7%), the differences are not statistically significant (Table 8).

Table 8. Complications after treatment, by type of laser

At treatment	SLT	MLT	TLT	All	Chi² Stat
No complication	118 (92.9%)	123 (97.6%)	28 (93.3%)	269 (95.1%)	
Spike in IOP	8 (6.3%)	2 (1.6%)	2 (6.7%)	12 (4.2%)	
Severe uveitis	1 (0.8%)	1 (0.8%)	0	2 (0.7%)	
Total	127 (100)	126 (100)	30 (100)	283 (100)	3.19. P=0.2
At 1 month					
No complication	93 (93.9%)	96 (93.3%)	19 (95.0%)	208 (93.3%)	
Spike in IOP	6 (6.1%)	8 (7.7%)	1 (5.0%)	15 (6.7%)	
Total	99 (100)	104 (100)	20 (100)	223 (100)	0.33. P=0.85

Immediately after treatment, four eyes (two patients) developed transient moderate corneal erosions, which was attributed to the coupling fluid (KY jelly) which was probably adulterated or not of medical grade. Inflammatory episodes stopped once the suspected tube of coupling gel was changed. Both patients were managed successfully with complete reepithelialisation of the cornea and complete resolution of symptoms in 1-2 days.

At one month after treatment, 14 patients had complication which were all spike in IOP. They were managed with medication or TDLC on a case by case basis.

Loss of vision

Significant loss of visual acuity (defined as at least 2 lines) in treated eyes was noted in 17 eyes at 12 months, most of which was attributed to glaucoma progression (Table 9). The distribution of causes of loss of vision is broadly similar in all treatment groups. While MLT shows slightly more cataract progression and TLT has proportionally more corneal oedema, these differences are not statistically significant though the cataract progression in MLT may still be clinically relevant

Table 9. Loss of at least 2 lines of VA at 12 months by laser

Cause of loss vision	SLT	MLT	TLT	All	Chi Square
None	69 (92.0%)	77 (90.6%)	21 (87.5%)	167 (90.8%)	
Corneal oedema	0	1 (1.2%)	1 (4.2%)	2 (1.1%)	
Cataract progression	0	2 (2.4%)	0	2 (1.1%)	
Glaucoma progression	6 (8.0%)	5 (5.9%)	2 (8.3%)	13 (7.1%)	

Total	75 (100)	85 (100)	24 (100)	184 (100)	3.62. P=0.73
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Repeat Failure and repeat treatment

At three months post treatment most eyes achieved target IOPs across all treatment groups. Also, 64 (41%) patients were offered repeat treatment, but only 15 (23%) accepted. Outright treatment failure with IOP ≥ 30 mmHg requiring escalation to TDCL occurred in 10 patients (6.4%) of patients. This was observed in the trabeculoplasty groups but not in the TLT group likely due to the small sample size. Three (30%) out of the 10 offered TDCL received it. Overall, there was no statistically significant difference between the different laser groups.

Retreatment with laser was uncommon as many patients preferred to return to or continue medical therapy rather than a repeat laser once first treatment failed. This preference is being documented and will help to inform the design on a RCT.

Table 10. Response to treatment at 3 months

IOP Category	SLT	MLT	TLT	ALL	Chi Square
<22mmHg	33 (48.5%)	42 (56.8%)	8 (53.3%)	83 (52.9%)	
22–29mmHg Repeat treatment recommended	30 (44.1%)	27 (36.5%)	7 (46.7%)	64 (40.8%)	
≥ 30 mmHg TDCL recommended	5 (7.4%)	5 (6.8%)	0 (0.00%)	10 (6.4%)	
Total	68 (100%)	74 (100%)	15. 100%)	157 (100%)	2.18 P=0.703

F. Patient Experience Outcome Measure (POEM)

An existing 6-question Patient Experience Outcome Measure (POEM) was pilot tested in this setting and administered at one week and at the 12 months follow up. The questionnaire had six items with three items “negative” meaning high score = better. These are: Are you frightened of going blind? Does glaucoma interfere with daily life? Do you think your glaucoma is getting worse? And three were “positive” items meaning higher score = worse. These are: Is your treatment acceptable? Do you feel safe under the care of your glaucoma team?, Do you understand your diagnosis and treatment plan? For analysis all items were reverse scored so that higher scores = better outcomes. The following was used for interpretation. Poor glaucoma experience/outcome 6-14, moderate 15-22 and good experience/outcome 23-30 (Table 10).

Table 10. POEM results at 1 week and at 12 months

At one week	Total score	Score %	Interpretation
6–14	0	0	Poor glaucoma experience/outcome
15–22	60	21.2	Moderate
23–30	203	71.7	Good
Did not attend at 1 week	19	7.1	

Total	282	100	
	Average interitem covariance 0.1921, Cronbach's alpha 0.615		
At 12 months			
6–14	0	0	Poor glaucoma experience/outcome
15–22	33	18	Moderate
23–30	147	82	Good
Total	180	100	
	Average interitem covariance 0.349, Cronbach's alpha 0.738		

Glaucoma patients reported better experiences at one year than at one week, with none in the poor category, fewer in the moderate category and more in the good category. The POEM scale also demonstrates stronger reliability over time (Cronbach's alpha increased from 0.615 to 0.738), making it a more robust measure for long-term patient-reported outcomes than for immediate post-treatment assessment, at least in this pilot study.

Combined POEM and 30% reduction in IOP

Patient-reported “good” outcomes improved from 77% at 1 week to 82% at 1 year. SLT and MLT had sustained IOP reduction at 1 year which aligns closely with the improved POEM outcomes, showing that maintenance of normal IOP drives patient satisfaction (Figure 3). Despite the strongest early IOP reduction with TLT, the decline by 1 year means patient-reported outcomes did not surpass or were lower than with SLT and MLT. Overall the combined results suggest that patients value longterm stability in IOP reduction more than dramatic early control of IOP.

G. Adverse events

1. No widespread unexpected safety signals for SLT/MLT cohorts were reported apart from the issue with coupling gel mentioned above.
2. TDLC (Stage 2 rescue) requires retrobulbar block and was carried out in theatre when/where indicated. At 2 months 49 patients (49/158 =31%) were offered TDLC but only 8 (16%) accepted the treatment
3. Two eyes of 2 patients (0.7%) after repeat SLT developed angle closure that was successfully managed (mannitol, urgent laser peripheral iridotomy) with pressure stabilization.
4. SAE reporting pathways and local safety committee processes were used.

H. Feasibility outcomes

Operational costs (equipment maintenance, transport reimbursements).

Equipment maintenance was a major reason for seeking an extension during the first phase of the project. One of the laser machines (SLT) broke down, and because there was no accredited service representative in Nigeria, the equipment had to be shipped to the UK for repair and recalibration. This resulted in significant costs and substantial delays. I have learnt that the company now has an in-country service representative. This is a welcome development that will facilitate routine maintenance and help prevent similar project delays in the future.

Reimbursement of transport costs was a key factor in achieving the follow-up rates observed. In this setting, the cost of transport is a major barrier to follow-up, particularly for patients from rural areas who must travel long distances on poor roads. This challenge is compounded by the fact that

glaucoma treatment often does not result in noticeable improvement in vision, reducing patients' perceived benefit of returning to the hospital.

Design and major amendments

1. One of the lasers was withdrawn (TLT) as it caused unacceptably high levels of pain (Version 8.2, 01 Aug 2024).
2. The sample size was reduced from 480 to 280 and the end date of the study was extended to 31 October 2025. The reduced target was chosen to balance operational feasibility with sufficient precision to answer feasibility questions (the amendment states with 80% power to estimate proportions with $\pm 20\%$ precision at 1 year given expected retention).

Protocol actions completed after Amendment

Updated sample-size appendix and analysis plan; outreach and transport-support logistics; updated consent/POEM materials updated and translated to Hausa and staff retrained; monthly monitoring procedures implemented.

Feasibility of online randomisation and data capture

Sealedenvelope online randomisation was easy to use, and led to balanced allocation of participants. As there was adequate internet connectivity the coin-flip alternative did not have to be used. Epidata was used to collect patient information with paper backup.

Operational findings relevant to RCT design

Data systems

- online randomisation functioned effectively and network connectivity was always available.
- Paper backup and double data entry provided resilience.
- Documentation of the proportion of cases randomised via Sealedenvelope versus coin flip was captured for future costing and feasibility assessment and it was 100% Sealedenvelope versus zero coin flip. Sealedenvelope was cost effective and easy to use while being highly accurate, reliable and easily verifiable.