• Clinical Research •

Safety and efficacy of micropulse transscleral laser therapy for glaucoma: a two-year follow-up

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Abstract

● **AIM:** To evaluate the efficacy and safety of micropulse transscleral laser therapy (MP-TLT) in lowering intraocular pressure (IOP) in eyes with primary glaucoma at different stages.

● **METHODS:** In this retrospective longitudinal cohort study, data were collected from the charts of patients who undergo MP-TLT. Information regarding medication burden (including oral carbonic anhydrase inhibitor use), IOP, and visual acuity, were gathered prior to the procedure and at day 1, week 1 and at 1, 3, 6, 12, 18, and 24mo follow-up. Glaucoma severity staging was performed according to the Hodapp-Parrish-Anderson classification system based on visual field parameters assessed with standardized automated perimetry. Early glaucoma was defined as mean deviation (MD) better than -6 dB, moderate glaucoma as MD between -6 and -12 dB, and advanced glaucoma as MD worse than -12 dB.

● **RESULTS:** Totally 84 eyes of 53 patients (22 females), with a mean age of 67.14±11.39y affected by progressive primary open angle glaucoma (POAG) and primary angle-closure glaucoma (PACG) were included. Before treatment, mean best corrected visual acuity was 0.26±0.36 logMAR, mean IOP was 22.32±6.64 mm Hg and patients took a mean of 2.96±0.75 topical IOP lowering molecules; moreover, 18 patients also required acetazolamide tablets. At 1mo follow-up, a significant (P<0.001) reduction of mean IOP was detected both in POAG (-7.16±2.92 mm Hg) and PACG (-6.89±3.12 mm Hg) eyes, remaining stable during the further follow-up. A significant (P<0.01) reduction in the number of drugs taken was observed at 3-month follow-up both in POAG (-0.59±0.32) and PACG (-1.06±0.73) eyes. These effects persisted over time during the further follow-up. Furthermore, marked decreases in IOP and IOP-lowering drugs were seen in patients with early, moderate, and advanced glaucoma, and these results closely matched the findings from the entire study cohort.

● **CONCLUSION:** The results obtained suggest that MP-TLT may be an effective and safe option for managing patients with POAG and PACG at every stage of the disease.

● **KEYWORDS:** primary open angle glaucoma; primary angle-closure glaucoma; micropulse transscleral laser therapy; intraocular pressure

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INTRODUCTION

Glaucoma, a neurodegenerative disease affecting the optic nerve pathway, is responsible for progressive optic neuropathy and is recognized as the primary cause of irreversible blindness worldwide[1-2]. Primary open angle glaucoma (POAG) affects predominantly populations of African and European ancestry, whereas primary angle-closure (PACG) variants are more common in Asian populations[2-3]. In 2013, the prevalence of glaucoma was estimated to be 64.3 million with growth projected at 76.0 million in 2020 and 111.8 million in 2040[2].

Intraocular pressure (IOP) is the only proven modifiable risk factor for glaucoma progression[4]. The therapeutic approaches available nowadays, such as topical medications, laser, and surgical therapies, aim to reduce IOP by decreasing the production of aqueous humor, increasing its outflow, or by both[5].

Continuous transscleral cyclophotocoagulation (CTS-CPC) is a well-established cycloablative procedure indicated for advanced glaucoma that is refractory to medical or surgical management[6]. This approach consists of the use of a

continuous diode laser applied against the sclera to achieve photocoagulation or destruction of the underlying pigmented epithelium and vascular core of the ciliary body, thereby reducing production of aqueous humor and decreasing IOP[6]. CTS-CPC is commonly considered a nonmedical intervention for patients with advanced glaucoma and limited visual potential[6-8].

It is important to highlight that this kind of treatment is associated with significant post-treatment morbidities, including prolonged intraocular inflammation, macular oedema, hypotony, phthisis, and vision loss, probably due to the result of surplus energy transmitted by the diode-laser during therapy[9-11].

These potential adverse outcomes have therefore resulted in caution in applying this procedure in the clinical practice.

In recent years, innovations in CTS-CPC have been introduced, such as new devices with probes which provide better visualization of the ciliary body and a micropulse treatment mode, to apply the technique more safely[12-14].

Micropulse transscleral laser therapy (MP-TLT), a variation of CTS-CPC that delivers energy in a pulsatile manner, has emerged as an alternative to the classic cycloablative procedure in the treatment of glaucoma[9-10,12,15-17]. With this technique, the probe is able to deliver short bursts of energy (*e.g.*, 0.5ms) followed by rest time (1.1ms) to achieve a biological effect in the pars plana and pars plicata without significant damage to the surrounding tissue. Indeed, it is hypothesized that non-melanin producing tissues are spared damage during this procedure partly because they encounter less energy per burst as this dissipates in the interim between pulses. Thus, these tissues accumulate less energy per unit time and are less likely to meet the critical energy threshold required for photocoagulation[9-11]. The predominant mechanism of action (decreased aqueous humor production or increased uveoscleral outflow) of the MP-TLT has not yet been fully elucidated[12].

Several studies have shown that MP-TLT is an effective and safer alternative to traditional CTS-CPC for IOP reduction, with low risk of complications in eyes affected by refractory, advanced and complicated glaucoma[9-10,12-26].

The purpose of this study is to evaluate the effectiveness and the safety of this technique not only in eyes affected by advanced POAG and PACG but also the earlier stages of these diseases. Moreover, additional analysis will be run to detect parameters that could predict success or failure of this kind of treatment.

PARTICIPANTS AND METHODS

Ethical Approval The study protocol was reviewed and approved by the Ethics Committee of the Azienda Ospedaliera Universitaria 'Luigi Vanvitelli' (approval number 0012575/2022). All researchers adhered to the Tenets of the Declaration of Helsinki. All participants provided informed consent both for the procedures and for the further data analysis.

In this retrospective longitudinal cohort study with pre–post intervention analysis, data were collected from the charts of patients who were referred to the Glaucoma Office of the Eye Clinic of Università della Campania Luigi Vanvitelli to undergo MP-TLT. Every 6mo, each patient routinely underwent a complete eye visit at the Glaucoma Clinic including, visual acuity evaluation, IOP measurement with Goldmann applanation tonometry (Haag Streit, Koeniz, Switzerland) anterior segment scan and central corneal thickness (CCT) measurements with Pentacam HR (Oculus, Wetzlar, Germany), biomicroscopy of anterior segment, indirect ophthalmoscopy at slit lamp, gonioscopy, and visual field test with standardized automated perimetry (SAP) using a Humphrey Field Analyzer (HFAII, Carl Zeiss Meditec, Inc., Dublin, CA), standard 30-2 perimetry.

Only patients affected by unstable POAG and PACG who were routinely attending our Glaucoma Office were included in the study, and all participants had to be able to perform a reliable SAP with fixation losses <20%; false-negative error <33%; false-positive error <33% as required in other similar studies[27].

POAG was defined as the presence of an open irido-corneal angle evaluated with gonioscopy associated with the typical visual field alteration of glaucoma disease based on at least 2 reproducible SAP[27]. PACG was defined as the presence of a synechial angle-closure of at least 180 degrees, associated with a II grade angle greater than 90 degrees according to the Shaffer classification on gonioscopy, with significant glaucomatous damage to the optic nerve detected on at least 2 reproducible, consecutive SAPs performed over 2mo[28].

Instability of the disease was defined as an uncontrolled IOP, showing a 30% increase or greater when compared with the previous visit and/or values higher than 21 mm Hg, or eyes with a worsening SAP of 1.08 dB or more per year[29].

Patients who had undergone filtering, microinvasive or minimally invasive bleb glaucoma surgery were not included in the study. Patients who underwent selective laser trabeculoplasty (SLT) more than 3y earlier were included.

Each procedure was performed in theatre, in sterile conditions, and every patient received retrobulbar anesthesia through 0.8 mL of 2% lidocaine injection.

The Cyclo G6 Glaucoma Laser System 810 nm diode laser (Iridex Corporation, Mountain View, CA, USA) with the MicroPulse P3 handpiece was used for all procedures. Treatment settings were 2000 mW power, 31.3% duty cycle, in micropulse mode, providing 0.5ms of "on time" and 1.1ms of "off time". Each session consisted of five probe applications lasting 20s each on both the superior and inferior

halves, for a total of 200s of treatment per eye. Treated areas comprised the superior and inferior 180 degrees of the eye with the exclusion of 3 o'clock and 9 o'clock positions. Before treatment, a solution of 2% methylcellulose was applied on the superior and inferior conjunctiva to provide protective and cupping roles. During the treatments, the MP3 probe was applied perpendicular to the scleral plane with the probe's fiber-optic tip positioned 3 mm posterior to the limbal margin. Post procedure, the following eye drops were administered: dexamethasone 1% 4 times per day for 1mo and monofloxacin 3 times per day for 1wk. Patients were advised to continue topical hypotensive therapy, whereas any oral acetazolamide treatment was suspended from the day of treatment. Routine visits after surgery occurred at 1d, 1wk, 1, 3, 6, 12, 18, and 24mo. Decisions regarding changes in topical therapy, retreatments, or undergoing surgery were made on an individual patient basis.

For patients requiring the procedure in both eyes, the second eye was treated at a distance of at least 2wk, and only when no complications were observed within this time span.

Every treatment was performed in temporal approach and by the same surgeon (Lanza M). This approach was selected for ergonomics and to maintain a perpendicular probe orientation, optimizing energy delivery and scleral apposition.

Information regarding medication burden (including oral carbonic anhydrase inhibitor use), IOP, and visual acuity, were gathered prior to the procedure and at every follow up.

Details regarding the development of complications, including pain (both intraoperative and postoperative), cystoid macular oedema, hypotony, IOP spikes, intrabulbar inflammation, and vision loss were recorded.

Regarding cystoid macular edema, every patient underwent optical coherence tomography (OCT) scan to assess eventual diagnosis and Amsler grid test was administrated to check eventual metamorphopsias.

For every patient, MP-TLT procedures were performed to meet the Canadian Target IOP Workshop specified Targets, based on disease severity stratification[30]. Eye-specific target IOP was determined in relation to IOP measurement: baseline minus 20% target IOP or below 21 mm Hg (whichever was lower) was classified as mild POAG, baseline minus 30% target IOP or below 18 mm Hg (whichever was lower) was classified as moderate POAG, and baseline minus 30% target IOP or below 21 mm Hg (whichever was lower) was classified as advanced POAG. For patients affected by PACG, the IOP target was less than 18 mm Hg or a reduction of at least 20% from baseline[29]. Moreover, the achievement of one of these parameters were considered as a success of treatment too: reduction in medical therapy and/or suspension of oral acetazolamide therapy with an IOP lower than 21 mm Hg[29].

After the treatments, the approach to IOP topical therapy reduction was the following for every study participant: with an IOP reduction of greater than 20% in both eyes after treatment compared to target values, and with patient consent, the less hypotensive drug was discontinued, the IOP was checked again at 2wk and, if the Canadian Target IOP Workshop specified Targets continued to be met, the drug was suspended until the next follow up.

Glaucoma severity staging was performed according to the Hodapp-Parrish-Anderson classification system based on visual field parameters assessed with SAP. Early glaucoma was defined as mean deviation (MD) better than -6 dB, moderate glaucoma as MD between -6 and -12 dB, and advanced glaucoma as MD worse than -12 dB. This staging system was applied to both POAG and PACG eyes at baseline to stratify the cohort by disease severity for subsequent analysis[31].

Statistical Analysis The population distribution of this study was evaluated by Kolmogorov Smirnoff test, differences between pre and post treatment parameters were tested with Student *t* test, correlations between the parameters evaluated was performed using the Pearson index. To eliminate paired organ intrinsic correlation bias, a linear mixed model (LMM) was used, the subject being treated as a random effect thus ensuring statistical inference validity. This approach was applied both to the overall cohort, and to glaucoma type and stage subgroups. $P<0.05$ was considered statistically significant.

RESULTS

The main characteristics of the cohort evaluated are shown in Table 1. Totally 84 eyes of 53 (22 females 31 males) patients were included, with a mean age of 67.14±11.39y (ranging from 46 to 85 years old).

The patients assuming oral acetazolamide, were taking 250 mg pills (1.44±0.45 pills, range from 1 to 2 per day). In this study, an overall significant ($P<0.001$) reduction of IOP was observed after 1mo of treatment, remaining stable during the 3, 6, 12, 18, and 24mo follow-ups, for both POAG and PACG groups (Table 2). Patients previously prescribed oral acetazolamide, suspended it from the day of treatment and no patient subsequently required it during the evaluated follow-up period (Table 2). There was a significant reduction ($P<0.05$) in the mean quantity of drugs needed to control the IOP 3mo post treatment, which remained stable until the last follow up in both groups (Table 2). MD provided by SAP also remained stable during the evaluation period in both groups (Table 2).

Moreover, the significant reduction of both IOP and IOP lowering medications was observed in the early, moderate, and advanced glaucoma eyes too, with modalities very similar to ones obtained in the overall cohort studied. On evaluation of the correlations between the reduction of mean IOP and other

Table 1 Characteristics of patients included in study

Parameters	Mean±SD (range) or *n*
Age (y)	67.14±11.39 (46–85)
Time from diagnosis (mo)	107.77±99.8 (1–480)
BCVA (logMAR)	0.26±0.36 (2–0)
Refraction (SE, D)	-0.81±2.01 (-6.37–3.25)
CCT (μm)	541.02±30.47 (400–612)
IOP (mm Hg)	22.32±6.64 (12–41)
MD (dB)	-10.28±9.16 (-32.28–1.51)
Topical drugs	2.96±0.75 (1–4)
POAG[a], eyes	58
Early	24
Moderate	16
Advanced	18
PACG[a], eyes	26
Early	11
Moderate	9
Advanced	6
Phachic	35
Pseudophachic	49
Patients assuming oral acetazolamide	18

[a]Hodapp's severity classification. BCVA: Best corrected visual acuity; SE: Spherical equivalent; CCT: Central corneal thickness; IOP: Intraocular pressure; MD: Mean deviation; POAG: Primary open angle glaucoma; PACG: Primary angle-closure glaucoma; SD: Standard deviation.

parameters (such as age, time of the disease, pre-treatment IOP value, number of drugs before treatment, CCT, pre-treatment MD values), a higher IOP before treatment proved to be the main factor connected to greater IOP reduction (Table 3). The correlation between these two parameters was present both in the POAG and the PACG groups. What is more, it was also significant (P<0.01) at every stage of the disease (Table 3). Moreover, in PACG eyes it was correlated to younger age and lower CCT, and in patients with advanced glaucoma it was also connected to younger age. The reduction in the number of drugs taken showed a significant (P<0.01) correlation with the number of drugs taken before treatment in both the POAG and the PACG group, and was also significant (P<0.01) at every stage of the disease (Table 3). Younger patients showed greater drug reduction in the PACG group and in eyes with early-stage glaucoma (Table 3).

Despite obtaining a significant reduction of both mean IOP values and mean number of drugs used, the MP-TLT procedure did not meet the success criteria adopted for this study for every patient treated during the relevant follow-up period. The success rate is reported in Figure 1, in POAG eyes it was 93% at 12mo follow up and 86% at 24mo follow up, whereas in PACG eyes, it was 88% at 12mo follow up and 81% at 24mo follow up.

Stratified analysis by disease severity revealed that MP-TLT demonstrated efficacy across all glaucoma stages (Table 2). Analysis according to the Hodapp-Parrish-Anderson classification[31] showed that mild, moderate, and advanced glaucoma eyes all achieved significant IOP reductions. Success rates were comparable across severity stages, suggesting that MP-TLT may be effective not only in advanced glaucoma but also in earlier disease stages

On follow-up, no complications were detected in any of the eyes treated, and no visual acuity reduction was noted in the patients treated.

DISCUSSION

Until recent years, physicians limited the application of the CPC procedure to treating refractory glaucoma, as an alternative to cryoablation of the ciliary body. Although safer than cryoablation, continuous-wave CPC has been constrained by adverse events, including pain, hypotony, phthisis bulbi, and cystoid macular edema[12-14,17-25].

Over the last few years, a new generation of devices and probes has been released providing glaucoma specialists with a wider range of options in the management of both refractory eyes and those unresponsive to first line therapies. Early reports of micropulsed treatments, however, showed contradictory results, so the procedure was regarded as providing unpredictable results[12-14,17-25].

IOP reduction following MP-TLT may be explained through the damage of the pigmented epithelium of the ciliary body, which is the tissue targeted in this treatment thus, leading to a decrease in aqueous production. Another type of mechanism has also been hypothesized: an increase in the trabecular and uveoscleral outflow due to the inflammation caused by energy delivery through these tissues[12,18].

Whilst the most of studies published on MP-TLT have reported on the treatment of eyes with very advanced, secondary or congenital stages of glaucoma, the newly improved safety profile of MP-TLT has now allowed the therapeutic spectrum to be broadened, granting physicians a new approach to the management of earlier stage glaucoma in earlier stages than those typically treated with CTS-CPC[18].

Some recent papers suggest that MP-TLT should be taken into consideration earlier in the management of glaucoma and might possibly be offered as an alternative to incisional glaucoma surgeries where patients are at high risk for incisional procedures, or for patients with failed surgeries[21-22]. In fact, it is for precisely this reason that for this study our patient selection criteria for treatment were different: treatment was proposed to those patients with glaucoma that showed progression of the disease or an uncontrolled IOP even if they were at mild stages of the disease. In this study, eyes which had undergone previous SLT, 3y before or more, were included

Table 2 IOP, topical drugs, and MD before treatments and at every follow-up in overall cohort, POAG, and PACG eyes mean±SD (range)

Parameters	Before treatment	Follow-ups					
		1mo	3mo	6mo	12mo	18mo	24mo
Overall cohort							
IOP (mm Hg)	22.32±6.64 (12–41)	14.94±3.05[a] (10–22)	14.51±2.59[a] (10–20)	14.78±2.27[a] (10–22)	14.32±2.13[a] (10–20)	13.88±2.14[a] (10–18)	14.05±2.12[a] (10–18)
Medications	2.96±0.75 (1–4)	2.67±0.61 (1–4)	2.39±0.66[a] (1–4)	2.09±0.73[a] (1–4)	2.56±0.79[a] (1–3)	2.53±0.66[a] (1–3)	2.38±0.61[a] (1–3)
MD (dB)	-10.28±9.16 (-32.28–1.51)	-	-	-10.53±9.39 (-33.24–1.25)	-11.72±0.95 (-32.14–0.71)	-11.45±9.77 (-32.14–1.29)	-10.96±9.37 (-31.87–1.58)
PAOA	18	None	None	None	None	None	None
POAG							
IOP (mm Hg)	22.08±6.78 (12–41)	14.92±2.92[a] (10–22)	14.51±2.42[a] (10–20)	14.84±2.35[a] (10–21)	14.13±2.20[a] (10–19)	13.8±2.21[a] (10–18)	13.95±2.11[a] (10–18)
Medications	2.92±0.84 (1–4)	2.68±0.63 (1–4)	2.33±0.71[a] (1–4)	2.08±0.74[a] (1–4)	2.04±0.71[a] (1–3)	2.01±0.64[a] (1–3)	2.05±0.61[a] (1–3)
MD (dB)	-11.01±9.4 (-32.28–1.51)			-11.43 ±9.38 (-33.24–1.25)	-12.16±9.67 (-32.14–0.71)	-11.89±9.71 (32.14–1.29)	-11.45±9.06 (-31.87–1.58)
PAOA	10	None	None	None	None	None	None
PACG							
IOP (mm Hg)	21.22±6.8 (12–34)	14.33±3.12[a] (10–20)	13.78±2.92[a] (10–19)	14.06±1.77[a] (12–18)	14.47±1.82[a] (12–17)	14.67±1.73[a] (12–17)	13.77±1.01[a] (12–16)
Medications	3.17±0.38 (3–4)	2.72±0.46 (2–3)	2.11±0.73[a] (1–3)	2.26±0.82[a] (1–3)	2.34±0.92[a] (1–3)	1.89±0.76[a] (1–3)	1.92±0.84[a] (1–3)
MD (dB)	-8.62±7.73 (-30.44– -2.64)	-	-	-8.62±8.29 (-30.62– -2.15)	-9.12±7.69 (-29.36– -3.11)	-10.07±10.23 (-26.32– -3.27)	-10.11±7.89 (-30.91– -3.12)
PAOA	8	None	None	None	None	None	None
Early glaucoma							
IOP (mm Hg)	22.88±6.01 (12–36)	15.22±2.79[a] (10–20)	14.56±2.36[a] (10–18)	14.89±2.18[a] (12–18)	14.53±2.08[a] (12–19)	13.92±2.24[a] (11–18)	13.78±2.11[a] (11–17)
Medications	3.08±0.7 (1–4)	2.63±0.62 (1–4)	2.44±0.63 (1–3)	2.08±0.71[a] (1–3)	1.89±0.68[a] (0–3)	1.78±0.68[a] (0–3)	1.74±0.69[a] (0–3)
MD (dB)	-3.62±1.35 (-5.68–1.51)	-	-	-3.79±1.51 (-5.94–1.25)	-3.63±1.74 (-6.24–1.32)	-3.94±1.67 (-6.57–1.29)	-3.24±2.17 (-6.72–1.58)
PAOA	None	None	None	None	None	None	None
Moderate glaucoma							
IOP (mm Hg)	21.21±7.74 (12–41)	14.74±3.6[a] (10–22)	14.79±3.78[a] (10–20)	14.63±2.71[a] (10–18)	14.32±2.64[a] (10–18)	13.92±2.38[a] (10–19)	14.52±2.45[a] (11–18)
Medications	3.02±0.82 (1–4)	2.26±0.56[a] (1–3)	2.32±0.67[a] (1–3)	2.26±0.66[a] (1–3)	2.11±0.74[a] (1–3)	2.14±0.53[a] (1–3)	2.25±0.46[a] (1–3)
MD (dB)	-8.01±1.64 (-11.64– -6.18)	-	-	-7.96±1.73 (-11.24– -6.26)	-8.19±1.87 (-12.35– -5.96)	-8.33±1.99 (-12.53– -6.12)	-7.82±1.18 (-12.47– -6.24)
PAOA	5	None	None	None	None	None	None
Advanced glaucoma							
IOP (mm Hg)	22.25±6.89 (12–35)	14.63±3.09[a] (10–22)	14.17±2.32[a] (10–18)	14.72±2.12[a] (10–18)	14.08±1.73[a] (11–17)	13.84±1.94[a] (10–16)	13.88±1.96[a] (10–16)
Medications	2.88±0.79 (1–4)	2.38±0.58 (1–3)	2.38±0.71 (1–3)	1.96±0.81[a] (1–3)	1.87±0.69[a] (1–3)	1.94±0.68[a] (1–3)	2.06±0.64[a] (1–3)
MD (dB)	-23.47±5.71 (-32.28– -12.23)	-	-	-23.73±5.65 (-33.24– -12.01)	-23.39±5.32 (-31.33– -11.67)	-23.61±5.69 (-32.14– -11.76)	-22.79±6.81 (-31.87– -11.58)
PAOA	13	None	None	None	None	None	None

[a]*P*<0.05 compared pre-treatment values. IOP: Intraocular pressure; MD: Mean deviation; POAG: Primary open angle glaucoma; PACG: Primary angle-closure glaucoma; PAOA: Number of patients prescribed oral acetazolamide; SD: Standard deviation.

whereas those that had previously undergone any kind of glaucoma surgery were not. The aim of this was to provide a more homogeneous cohort for evaluation, to understand the safety and efficacy of this procedure, not only in eyes with refractory or last stage glaucoma.

This selection was made possible because the new device and new probe now available on the market, and utilized in this study, have been shown to allow safer treatments, and to reduce the incidence of the most common complications of this procedure[12-14,18].

The device used in every treatment, was set to provide 2000 mW of power with a 31.3% duty cycle, in micropulse mode, providing 0.5ms of "on time" and 1.1ms of "off time" to allow target tissue to cool down gradually thus, avoiding a cyclodestructive threshold. It has also been demonstrated histologically that the "cooling" period also avoids collateral tissue damage[20].

The reductions of both IOP and IOP lowering drugs observed in this study are similar to ones reported by recently published papers on the same topic[17-19,22-25]. However, when compared

Table 3 Correlations of IOP and medications change with clinical parameters in different glaucoma subtypes and severity stages

Correlation coefficients (*P*)

Parameters	Age	Duration of disease	Before treatment			
			IOP	CCT	Medications	MD
POAG						
ΔIOP	-0.266 (*P*=0.057)	0.183 (*P*=0.195)	-0.959 (*P*<0.001)	0.044 (*P*=0.759)	0.077 (*P*=0.590)	0.116 (*P*=0.414)
ΔMedications	-0.170 (*P*=0.229)	-0.223 (*P*=0.111)	0.138 (*P*=0.329)	-0.212 (*P*=0.131)	-0.743 (*P*<0.001)	0.016 (*P*=0.908)
PACG						
ΔIOP	0.521 (*P*=0.027)	-0.058 (*P*=0.818)	-0.965 (*P*<0.001)	-0.501 (*P*=0.034)	0.368 (*P*=0.133)	-0.190 (*P*=0.449)
ΔMedications	-0.559 (*P*=0.016)	0.160 (*P*=0.526)	0.608 (*P*=0.007)	0.231 (*P*=0.356)	-0.610 (*P*=0.007)	0.143 (*P*=0.570)
Early glaucoma						
ΔIOP	0.160 (*P*=0.317)	0.238 (*P*=0.134)	-0.955 (*P*<0.001)	-0.219 (*P*=0.169)	0.093 (*P*=0.564)	0.145 (*P*=0.366)
ΔMedications	-0.505 (*P*<0.001)	0.029 (*P*=0.859)	0.281 (*P*=0.075)	0.117 (*P*=0.468)	-0.689 (*P*<0.001)	-0.130 (*P*=0.416)
Moderate glaucoma						
ΔIOP	-0.148 (*P*=0.558)	0.142 (*P*=0.573)	-0.955 (*P*<0.001)	0.021 (*P*=0.936)	0.303 (*P*=0.221)	-0.116 (*P*=0.646)
ΔMedications	-0.263 (*P*=0.292)	-0.021 (*P*=0.933)	0.466 (*P*=0.051)	-0.346 (*P*=0.159)	-0.825 (*P*<0.001)	0.036 (*P*=0.887)
Advanced glaucoma						
ΔIOP	-0.455 (*P*=0.025)	0.069 (*P*=0.748)	-0.973 (*P*<0.001)	0.098 (*P*=0.650)	0.099 (*P*=0.646)	0.370 (*P*=0.075)
ΔMedications	-0.127 (*P*=0.556)	-0.354 (*P*=0.090)	0.128 (*P*=0.550)	-0.026 (*P*=0.903)	-0.678 (*P*<0.001)	-0.209 (*P*=0.326)

IOP: Intraocular pressure; MD: Mean deviation; POAG: Primary open angle glaucoma; PACG: Primary angle-closure glaucoma; CCT: Central corneal thickness.

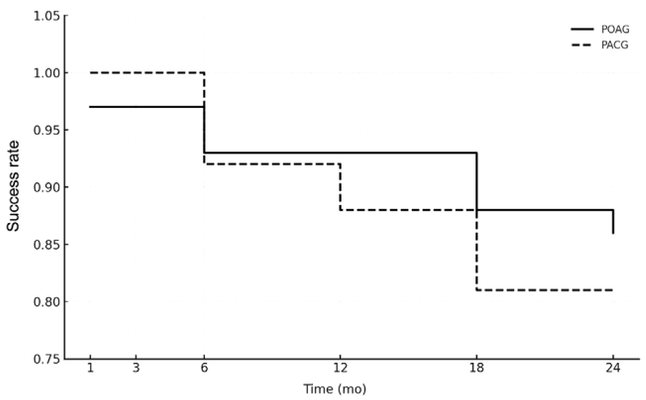

Figure 1 Keplan-Maier curve of the success rate in primary open angle glaucoma (POAG) eyes and in primary angle-closure glaucoma (PACG) eyes at each follow up.

to other published studies, this one has some distinctions: MP-TLT was performed on primary glaucoma eyes only, congenital and secondary glaucoma eyes being excluded towards the objective of evaluating a more homogeneous cohort, and avoid any bias relating to the pathogenesis of the disease. Thus, we were able to run a deeper statistical analysis relating to the factors connected with the success/unsuccess of the treatment and interesting information in this regard is provided. Furthermore, data regarding visual field defect variations are provided, a parameter which is very rarely reported in publications focusing on this procedure. Moreover, an evaluation of different stages of glaucoma has been reported, allowing to obtain data also the early and moderate glaucoma eyes treated with this technique. According to the results, this treatment would be more suitable in eyes with higher IOP and where the patient takes more IOP lowering drugs. What is more, younger patients seem to achieve better results. It is important to highlight that this is the first study to evaluate the treatment focusing on eyes affected by earlier stage, rather than later stage, glaucoma, and most previous studies observed their population for less than the 2y reported here. It is important to highlight that in this study the high level of IOP reduction observed, associated with no complications, could also be due to the patient selection process. In fact, eyes at a late stage of the disease, which have already undergone multiple procedures and/or surgeries, might well be more sensitive to the inflammation caused by the treatment. Another reason might be the surgical approach selected in this study: the temporal approach selected for this study allows the surgeon to perform the procedure in a more ergonomic position, relying on the help of the second hand to move the eye-globe thus, gaining the space required to apply the probe correctly and for the full length of time required.

Limitations of this study include the design: as a retrospective study, additional comparisons and/or analysis were not permitted such as a comparison with a control group, the cohort evaluated is not large and a two-year follow-up is not adequate to reliably evaluate variations in the visual field. Moreover, additional data such as the retinal fiber nerve layer and the ganglion cell complex thickness were not collected because of the retrospective design.

We are seeing increasing interest in performing MP-TLT in the glaucoma community, most likely due to the number of papers

recently published that testify to the increased reliability and efficaciousness of the procedure[12-13,17-19,22-25]. Nevertheless, most of the studies published have included a highly inhomogeneous cohort, generally with final stage or refractory glaucoma eyes[12-13,17-19,22-25].

This study evaluated MP-TLT in primary glaucoma, extending evidence beyond end-stage disease. According to the data observed, despite requiring further confirmation through additional studies of larger populations and with longer follow-ups, MP-TLT treatment successfully provides safe and effective IOP reduction and drug reduction both in POAG and in PACG eyes, and at every stage of the disease. Moreover, it seems to help in stabilizing the visual field defects over a two-year span in POAG and in PACG eyes, at every stage of the disease. With confirmation through further studies, MP-TLT is likely to become an increasingly valuable tool for glaucoma specialists in the management, delay or prevention of disease progression in POAG and PACG eyes.

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