*Clinical and Experimental Vision and Eye Research* (2022), 5, 12–16

ORIGINAL ARTICLE

# Pupillary Abnormalities after Micropulse Transscleral Cyclophotocoagulation

Renata Prota Hussein[1], Isabella V. Wagner[1], Richard D. Ten Hulzen[1], Carolina Carvalho[2], Alyssa Stockard[1], P. Connor Lentz[1], Syril Dorairaj[1]

[1]Department of Ophthalmology, Mayo Clinic, Jacksonville, Florida, United States, [2]Department of Ophthalmology, Instituto de Olhos Ciencias Medicas de Minas Gerais, Belo Horizonte, Brazil

**Key words:**

Micropulse transscleral cyclophotocoagulation (MP-TSCPC), pupillary abnormality, intraocular pressure

**Address for correspondence:**
Isabella V. Wagner, Department of Ophthalmology, Mayo Clinic, 4500 San Pablo Rd S, Jacksonville, Florida 32224, United States. Phone: (904)-953-2377.
E-mail: wagner.isabella1@mayo.edu

Received: 02-07-2022
Accepted: 22-07-2022
doi: 10.15713/ins.clever.82

## Abstract

**Purpose:** The purpose of this study was to document pupillary abnormalities in glaucoma patients who underwent micropulse transscleral cyclophotocoagulation (MP-TSCPC).

**Patients and Methods:** This was an IRB-approved retrospective study of patients who underwent MP-TSCPC at Mayo Clinic Florida between March 2016 and August 2019. All patients were treated with a laser power of 2000 mW and duty cycle of 31.33%. Treatment time was 80 s for each 180° hemisphere, totalizing 160 s. The 3 and 9 o'clock areas were avoided due to risk of nerve and vessels damage in this region. Patients who developed pupillary abnormalities postoperatively had slit lamp photo taken to document iris color and pupil size and shape. Anterior Segment Optical Coherence Tomography was also obtained for qualitative assessment of the pupillary diameter in both light and dark conditions.

**Results:** Among the patients studied, four patients (total of five eyes) presented fixed and mildly-dilated pupils that did not react well to light or accommodation after the procedure. These patients had a mean age of 66.25 ± 8.73 years and 75% were female. Of those, 100% were myopic and had a brown iris color, and 50% were phakic. The mean pre-operative intraocular pressure (IOP) was 16.0 ± 5.87 mmHg and the mean post-operative IOP at 3 months of follow-up was 12.4 ± 3.64 mmHg. The mean pre- and post-operative number of medications was 2.4 ± 0.54 and 2.0, respectively. Out of the four patients, 75% had severe stage glaucoma. The mean pre- and post-operative LogMAR vision was 0.27 ± 0.13 and 0.25 ± 0.19, respectively.

**Conclusion:** Myopic patients with a brown iris color and phakic lens appear to be at a greater risk of developing pupillary abnormalities following MP-TSCPC. After a mean of 3 months (range: 2–4 months), all abnormalities resolved spontaneously.

## Introduction

Aqueous humor is continually produced by the ciliary body in the posterior chamber and drains into the anterior chamber of the eye. About 75% of aqueous humor drainage occurs through the trabecular meshwork (TM) with the juxtacanalicular portion of the TM being the main site of outflow resistance, and 25% is drained through the uveoscleral pathway.[1] Primary open-angle glaucoma (POAG), the most common type of glaucoma worldwide, is a chronic and progressive optic neuropathy characterized by increased resistance to aqueous humor drainage despite an open iridocorneal angle.[2] Due to this resistance, intraocular pressure (IOP) can rise and, if left untreated, lead to irreversible damage to the optic nerve and ultimately permanent visual field loss.[3] The main goal of glaucoma treatment is to lower IOP, the only modifiable variable in the disease course,[4] by either reducing aqueous humor production, increasing its drainage through TM or uveoscleral pathway, or both. At present, available treatment options include topical anti-

glaucomatous medications, incisional surgeries, laser therapies, minimally invasive glaucoma surgeries, drainage implants, and cycloablative procedures.

Micropulse transscleral cyclophotocoagulation (MP-TSCPC) was FDA approved in 2015 as a non-invasive treatment for glaucoma patients. Since then, much clinical research has been published supporting its efficacy and high safety profile that is well tolerated by most patients. Its success can be attributed to its short pulses that allow tissues to cool during "off-cycles," protecting them from thermal damage,[5] and sparing the ciliary epithelium, unlike traditional cyclophotocoagulation.[6] However, due to low frequency of occurrences, existing studies lack data on complications derived from MP-TSCPC. Moreover, comparison between studies on MP-TSCPC is difficult due to divergences in treatment protocols, patient demographics, follow-up times, and success criteria definition.[7]

In this retrospective case series study, we examine factors associated with the development of pupillary abnormalities after MP-TSCPC in our group of patients who were followed over a 3-month period.

### Case 1

A 72-year-old phakic African American female with severe stage bilateral POAG, bilateral cataracts, and high myopia (−5.50 OD, −4.75 OS) was using Bimatoprost and Brimonidine in both eyes. Her baseline best-corrected visual acuity (BCVA) was 20/20 OD and 20/30 OS, and her baseline IOP was 9 mmHg OD and 12 mmHg OS. Her cup-to-disk ratio was 0.95 in both eyes. After discussing with the patient several different options to reduce IOP, MP-TSCPC was performed on her left eye, followed by the same procedure on her right eye. One week after the procedure on the left eye, her BCVA was 20/40 and her IOP was 9 mmHg. However, her left pupil was mildly-dilated and not responsive to light or accommodation (pupil size in dark light: 3 mm OD and 5 mm OS). After the MP-TSCPC procedure OD, she also presented at her 1-week post-operative visit with a BCVA of 20/50, an IOP of 9 mmHg, and a mildly dilated pupil in the same eye. She complained of blurry vision in both eyes after the procedures, but did not show any anterior chamber alterations, such as cell presence or flare [Figure 1]. After 3 months of treatment with topical corticosteroids OU, both pupils returned to normal size and function (i.e., reactive to light and accommodation), and the patient did not report any visual complaints.

### Case 2

A 67-year-old pseudophakic Caucasian female with severe stage bilateral POAG and myopia (−0.75 D in both eyes) had a cup-to-disk ratio of 0.8 OD and 0.95 OS. She also had a history of optic neuritis in OS. Her baseline BCVA was 20/25 OD and 20/40 OS, and her baseline IOP was 18 mmHg OU. She was using Latanoprost and Dorzolamide in both eyes. After counseling the patient regarding available treatment options, she decided to undergo MP-TSCPC OS. 1 month after the procedure, BCVA was 20/30 in OS and IOP was 16 mmHg in both eyes. Although the patient presented with a fixed and mid-dilated pupil OS, she did not complain of any visual symptoms and no anterior chamber alterations were observed [Figure 2]. After 4 months of follow-up using topical corticoids, her pupil size and function returned to normal.

### Case 3

A 74-year-old phakic Asian male presented with severe stage chronic angle closure glaucoma OS and bilateral myopia (−3.75 D OD, −5.50 D OS). The patient had a prior history of a tributary vein occlusion OS. His baseline BCVA was 20/25 OU, and baseline IOP was 11 mmHg OD and 19 mmHg OS (history of peak IOP of 51 mmHg OS). He was using Timolol Maleate, Brimonidine, and Dorzolamide OS. After discussing potential surgical options to reduce IOP, he underwent MP-TSCPC in OS. At 1 week postoperatively, BCVA was 20/30 OS, and IOP was 13 mmHg OD and 9 mmHg OS. The patient complained of blurry vision OS and a mildly dilated pupil was observed, but no anterior chamber signs of flare or cells were described [Figure 3]. Glaucoma medications were discontinued per instructions and the patient was treated with topical corticoids. The patient's pupil size and function returned to normal after 3 months.

### Case 4

A 55-year-old pseudophakic Hispanic female, with steroid-induced glaucoma and myopia bilaterally (−0.50 D OD, −0.75 D OS), was using Brimonidine, Dorzolamide, and Timolol

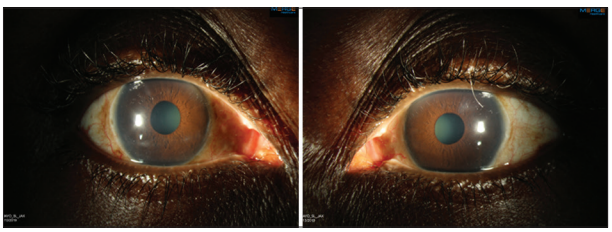

**Figure 1:** Case 1 – Both MP-TSCPC-treated eyes (OD and OS) showing a fixed and mildly-dilated pupil at 1 week after the procedure

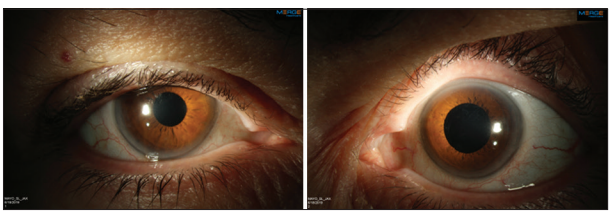

**Figure 2:** Case 2 – Untreated right eye (normal pupil). MP-TSCPC-treated left eye 2 weeks after surgery. Left pupil is fixed and mildly dilated

OU. Her baseline BCVA was 20/30 OU, and her baseline IOP was 24 mmHg OD and 26 mmHg OS. She underwent Selective Laser Trabeculoplasty OD 1 month prior with no adequate IOP-lowering effect. Options to manage persistently high IOP in both eyes were discussed with the patient, who underwent MP-TSCPC OD. One week after the procedure, BCVA was 20/50 OD, and IOP was 14 mmHg OD and 18 mmHg OS. She complained of blurry vision and redness OD, and a mildly dilated pupil was present; however, no anterior chamber alterations were noticed [Figure 4]. She was treated with topical corticoids and pupil size and function returned to normal after 3 months.

## Discussion

Conventional transscleral cyclophotocoagulation has been used for years as a non-invasive treatment for patients with poor visual potential or who are not good surgical candidates. Despite reductions in IOP, it has been associated with a few known complications such as hypotony, phthisis bulbi, and vision loss. The severity of these complications is secondary to the collateral damage to surrounding tissues, including the non-pigmented epithelium, ciliary body stroma, and ciliary muscles.[8] By delivering energy in an intermittent fashion, MP-TSCPC is believed to spare these structures from significant damage by gradually building up a photocoagulative state mainly in the pigmented epithelium.[9]

Post-operative reversible fixed mydriasis is an uncommon adverse event after MP-TSCPC. To the best of our knowledge, such cases have not been previously fully discussed. Al Habash *et al.* analyzed MP-TSCPC outcomes in different types of glaucoma and demonstrated, as one of the complications from the procedure, a low and transient rate of eyes with tonic pupil (dilated with loss of accommodation) in 5.6% of the patients that resolved 1 month postoperatively.[10] The mechanism of this condition has not been fully determined and is probably multifactorial. Existing theories for pupil changes after MP are probe position/angulation, cyclotorsion, anatomy, and anterior segment ischemia (ASI).

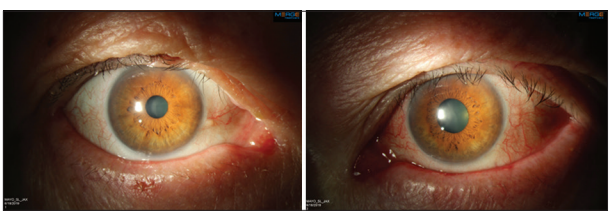

**Figure 3:** Case 3 – Untreated right eye (normal pupil), MP-TSCPC-treated left eye with fixed and mildly-dilated pupil

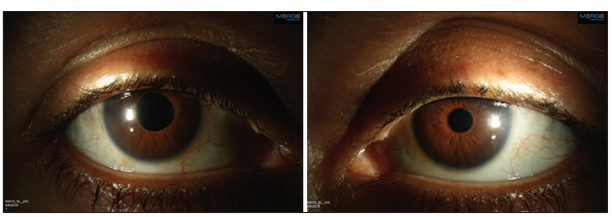

**Figure 4:** Case 4 – MP-TSCPC-treated right eye (fixed and mildly-dilated pupil) and untreated left eye (normal pupil)

### Probe position/angulation

Individual variations regarding ciliary process position (between 1.5 and 2.0 mm in different meridian) can affect the region, where laser is delivered. For example, myopic eyes have a larger axial length, and therefore, the ciliary process position may be more posterior than in normal eyes.[11] In these cases, the probe angulation may be too anterior, displacing energy to the peripheral iris and directly damaging it. Surgical technique regarding body position and handedness when holding the laser probe can also affect the results. Anatomic variation may require further exploration (e.g., through transillumination analysis) to help the surgeon identify the anatomic landmarks and correctly place the probe over the target tissue before applying the laser.

### Cyclotorsion

There is no current consensus on cyclotorsion due to positional changes from upright to supine position. However, Zhao *et al.* explored this correlation and indicated that the total cyclotorsion rate when changing from sitting to supine position was 88.24%, ranging from −14° to +12° and the predominance of excyclotorsion in OD and incyclotorsion in OS.[12] This can explain thermal damage to ciliary nerves and vessels when, due to cyclotorsion, these structures are actually near to or outside the spared 15° deviation from the perceived horizontal meridian commonly used for MP-TSCPC. Therefore, it would be wise to allow for potential cyclotorsion and create an additional 15° "buffer zone" to prevent injury to the long posterior ciliary arteries (LPCA), long posterior ciliary nerves (LPCN), and parasympathetic fibers innervating the ciliary muscles and constrictor pupillae. This would mean the surgeon should only treat from 10 to 2 o'clock superiorly and from 4 to 8 o'clock inferiorly, and spare the 2 to 4 o'clock and 8 to 10 o'clock zones.

### Anatomy

LPCA and LPCN run radially in the horizontal meridian, to supply the medial and lateral segments of the ciliary body and iris. Hayreh *et al.* demonstrated for the first time that the *in vivo* vascular pattern of the posterior ciliary arteries and their branches is strictly segmental, with no anastomosis between the adjacent segments. Thus, the presence of watershed areas between these segments may explain the greater susceptibility to ischemic disorders.[13]

Denervation of the constrictor pupillae muscle after thermal injury to radial fibers of the parasympathetic nerves results in an unopposed action of the sympathetic portion of

the muscle, leading to pupil dilation. Similarly, thermal injury to the parasympathetic nerves may alter ciliary muscle tone and contribute to blurred vision due to temporary loss of accommodation. A gradual process of injury recovery and/or nerve regeneration may explain the slow restitution of the pupillary function with time. It remains unclear in this case series whether the reported blurred vision was a result of aberrations due to an enlarged pupillary aperture alone, or whether there was concomitant loss of accommodation (due to injury to parasympathetic innervation of ciliary musculature along with parasympathetic innervation of constrictor pupillae).

It is worth noting that all four patients were myopic. Due to the thinner sclera in myopic eyes, greater permeability allows facilitated laser penetration,[14] thus leading to greater thermal damage and possible side effects to structures (such as the LPCA, LPCN, and their associated parasympathetic fibers) travelling in the plane between sclera and choroid.

Different from what was initially suggested, it has been proposed that MP-TSCPC decreases IOP by combining two mechanisms. The first mechanism is probably the thermal destruction of the ciliary body, and the second mechanism is the improvement in aqueous humor outflow.[7] Johnstone *et al.* presented a theory called "pilocarpine-like effect," in which transscleral laser induces contraction and consequent shortening of the ciliary muscle, causing posterior and inward movement of scleral spur and TM movement. This would lead to aqueous outflow pathway modification and reorganization, thus improving aqueous humor outflow and reducing IOP.[15] We consider the hypothesis of this anatomic modification as being responsible for the creation of a congestion or injury to the parasympathetic fibers travelling in the space between sclera and choroid, leading to injury of these structures.

### ASI

The majority of cases of ASI present after strabismus surgery (if more than two recti muscles are detached at the same procedure due to anterior ciliary artery transection or injury) and after retinal detachment surgery (possible venous congestion following scleral buckle procedures). However, ASI may also occur spontaneously in highly myopic patients. The common symptoms of ASI are pain, photophobia, and blurred vision initially and can progress to conjunctival edema, flare and cells, pupillary distortion and dilation, and iris atrophy.[16]

In 1989, Olver *et al.* graded the degree of acute ASI after strabismus surgery based on clinical and fluorescein iris angiographic signs.[17] The anterior segment was examined for functional signs of ischemia, such as the presence of uveitis, keratitis, and irregular pupil reaction in the segment corresponding to angiographic delay. We hypothesize that MP-TSCPC could cause lesser grades of ASI, and therefore, "recovery" of pupillary function would be possible over time.[17]

It is yet to be clarified why this phenomenon has been observed in only a small number of patients who underwent MP-TSCPC. Further studies regarding MP-TPCPC side effects are still needed.

## Conclusion

Myopic patients with a brown iris color undergoing MP-TSCPC appear to be at a high risk of developing post-operative pupillary abnormalities. All four patients (five eyes) showed complete resolution of pupil size and function after 3 months of corticosteroid treatment.

## Financial Disclosure

All authors do not have any conflicting commercial associations.

## References

1. Goel M, Picciani RG, Lee RK, Bhattacharya SK. Aqueous humor dynamics: A review. Open Ophthalmol J 2010;4:52-9.
2. Grzybowski A, Och M, Kanclerz P, Leffler C, De Moraes CG. Primary open angle glaucoma and vascular risk factors: A review of population based studies from 1990 to 2019. J Clin Med 2020;9:761.
3. Bartelt-Hofer J, Ben-Debba L, Flessa S. Systematic review of economic evaluations in primary open-angle glaucoma: Decision analytic modeling insights. Pharmacoecon Open 2019;4:5-12.
4. Artero-Castro A, Rodriguez-Jimenez FJ, Jendelova P, VanderWall KB, Meyer JS, Erceg S. Glaucoma as a neurodegenerative disease caused by intrinsic vulnerability factors. Prog Neurobiol 2020;193:101817.
5. Emanuel ME, Grover DS, Fellman RL, Godfrey DG, Smith O, Butler MR, *et al.* Micropulse cyclophotocoagulation: Initial results in refractory glaucoma. J Glaucoma 2017;26:726-9.
6. Gavris MM, Olteanu I, Kantor E, Mateescu R, Belicioiu R. IRIDEX MICROPulse P3: Innovative cyclophotocoagulation. Rom J Ophthalmol 2017;61:107-11.
7. Sanchez FG, Peirano-Bonomi JC, Grippo TM. Transscleral cyclophotocoagulation: A hypothesis for the ideal parameters. Med Hypothesis Discov Innov Ophthalmol 2018;7:94-100.
8. Wong KY, Aquino CM, Macasaet AM, Suwandono ME, Chew PT, Koh VT. 5MP3 Plus: A modified micropulse transscleral cyclophototherapy technique for the treatment of refractory glaucoma. J Glaucoma 2020;29:264-70.
9. Aquino MC, Barton K, Tan AM, Sng C, Li X, Loon SC, *et al.* Micropulse versus continuous wave transscleral diode cyclophotocoagulation in refractory glaucoma: A randomized exploratory study. Clin Exp Ophthalmol 2015;43:40-6.
10. Al Habash A, Alahmad AS. Outcome of micropulse® transscleral photocoagulation in different types of glaucoma. Clin Ophthalmol 2019;13:2353-60.
11. Vieira GM, Vieira FJ, Ritch R. Urretz-Zavalia syndrome after diode laser transscleral cyclophotocoagulation. J Glaucoma 2017;26:678-82.
12. Zhao F, Li L, Zhou W, Shi D, Fan Y, Ma L. Correlative factors' analysis of postural-related ocular cyclotorsion with image-guided system. Jpn J Ophthalmol 2018;62:237-42.

13. Hayreh SS. Posterior ciliary artery circulation in helath and disease. The weisenfeld lecture. Invest Ophthalmol Vis Sci 2004;45:749-57.
14. Olsen TW, Edelhauser HF, Lim JI, Geroski DH. Human scleral permeability. Effects of age, cryotherapy, transscleral diode laser, and surgical thinning. Invest Ophthalmol Vis Sci 1995;36:1893-903.
15. Johnstone MJ, Padilla S, Wen K, Wang R. Transcleral Laser Induces Aqueous Outflow Pathway Motion and Reorganization. Paper Presented at: 2017 American Glaucoma Society Meeting. Coronado, CA; 2017.
16. Lee JP, Olver JM. Anterior segment ischemia. Eye 1990;4:1-6.
17. Olver JM, Lee JP. The effects of strabismus surgery on anterior segment circulation. Eye (Lond) 1989;3:318-26.

**How to cite this article:** Hussein RP, Wagner IV, Ten Hulzen RD, Carvalho C, Stockard A, Lentz PC, Dorairaj S. Pupillary Abnormalities after Micropulse Transscleral Cyclophotocoagulation. Cli Exp Vis Eye Res J 2022;5(1):12-16.