THE CYCLOPHOTOCOAGULATION REVOLUTION HAS BEGUN

A summary of a webinar discussion about filling the gap in the glaucoma treatment algorithm between pharmaceuticals and invasive surgical procedures.

BY ROBERT J. NOECKER, MD, MBA, AND NATHAN RADCLIFFE, MD

There is a gap between what is safe and what is effective for treating patients with glaucoma. Topical medications are still first-line therapy in the United States. While these medications can be relatively efficacious and can be discontinued if problems arise, they require two things: patients have to acquire them, and patients have to use them on a daily basis as prescribed— sometimes for years—to control this largely asymptomatic disease. Sometimes, the treatment for this disease is worse, in terms of symptoms, than the actual disease for patients who are asked to self-treat. Patients' vision and quality of life can be affected if the medication causes hypotony. This disease requires a lot of work on the part of the surgeon as well as the patient to get the surgery to work well. **—Robert J. Noecker, MD, MBA**

A SOLUTION TO THE GAP

Nathan Radcliffe, MD: The CYCLO G6, a new glaucoma-dedicated laser system, is an 810-nanometer laser that delivers therapy in a new way—by using MicroPulse Technology (Iridex; Figure 1). The MicroPulse P3 (MP3) glaucoma probe has an excellent safety profile[1] and an efficient, straightforward treatment algorithm that works for patients and surgeons alike, with good safety and efficacy balance whether performed in the office or in the OR. Its excellent safety profile allows us to fill the gap between medications and riskier surgeries.

Figure 1. The Cyclo G6 laser console.

View the webinar on eyetube.net at **http://bit.ly/2cRdSrV**

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—Nathan Radcliffe, MD

Dr. Noecker: The MP3's on-off cycle means you do not get focal heating of the tissue. It applies the laser energy;

TABLE 1. PATIENT SCENARIOS SERVED BY THE MP3

- Patient prefers laser over incisional surgery
- Primary surgery for elderly patients
- Choroidal hemorrhage in fellow eye
- Failed tube
- Poor vision
- Severe blepharitis
- Risk of falling
- Ocular cancer
- No one to take the patient home
- Tube in other eye did not lower the pressure
- Glaucoma patient needs IOP lowering

then it gives the tissue time to cool off in between each application. The anatomy remains intact, so MP3 allows a change in function of the eye without changing the structure of the eye. All of these reasons are why it has such an excellent safety profile.

The most dreaded side effect of transsceral cyclophotocoagulation is hypotony, and this is one of the things that has held transscleral cyclophotocoagulation back as an early treatment. MicroPulse overcomes that drawback with its favorable safety profile while delivering comparable efficacy.[1] The procedure is predictable at hitting the sweet spot of where we want the patient's eye pressure to end up.

BROADENING THE POOL OF PATIENTS WHO ARE TREATABLE

Dr. Noecker: MP3 may be used in almost any part of the treatment algorithm because of the procedure's benign nature. I can use it instead of microinvasive glaucoma surgery (MIGS) or trabeculectomy, as an add-on procedure, or if there is failure with other procedures (Table 1). I can really use it in almost any part of the treatment algorithm in the appropriate patient, because the side-effect profile is immensely better than just about any other procedure that we perform. At the same time, it delivers very good efficacy that, in a lot of situations, makes the eye pressure low enough without any other treatment modality.

Dr. Radcliffe: The procedure is repeatable and titratable. It is all about balancing the safety profile with how aggressive you want to be in terms of lowering the pressure. I talk to patients about whether they would prefer one session or several sessions where we can titrate our way up. Whereas some surgeons increase the duration of laser application to increase efficacy, I will increase my power settings up to 2,250 mW or even higher in eyes with severely elevated IOPs and reduced vision. We make a decision together on the laser dose.

I have treated more than 150 patients, and over time, I have broadened the pool of patients who are treatable. MP3 has moved up in my treatment algorithm. I have also learned to tailor the therapy to my patients. The pressure reduction has been very impressive. The range that I typically see is from 30% to 80%. How do you get 80% pressure reduction? You start with someone who has an IOP of 80 mm Hg, and you get them into the normal range. I have treated patients who for a variety of reasons cannot be treated surgically.

It is impressive that despite being very aggressive with this therapy, I have not encountered a single case of cystoid macular edema or phthisis. I did have one patient who had a cataract going into laser treatment and had worsening of the cataract after the procedure. This patient also had a previous tube shunt procedure. I think it is an acceptable side effect given the amount of IOP lowering that we are getting from the therapy.

MP3 TREATMENT PARAMETERS PROVIDE VERSATILE THERAPY

Dr. Noecker: Our recommended treatment parameters have evolved over time. A good starting point, and the literature will support this (Table 2), is about 50 seconds per hemisphere, so 100 seconds total treatment. Laser power is at 2,000 mW, and the duty cycle is always set the same at 31.3%.

TABLE 2. SUMMARY OF MP3 DOSING IN THE LITERATURE

Clinical Studies	Laser Time	Laser Power	MicroPulse Duty Cycle
2010 & 2014 controlled, randomized studies, NUH, Singapore, Paul Chew, MD[1,2]	50s per hemisphere (100s total)	2000 mW	31.3% (0.5 ms duration, 1.1 ms interval)
AGS 2015, Drs. Radcliffe, Noecker, Ahmed, Vold, Khatana, Kammer, Parekh[3]	50 - 90s per hemisphere (100 - 180s total)	2000 – 2250 mW	31.3% (0.5 ms duration, 1.1 ms interval)
AGS 2015 abstract[4], peer-reviewed 2016[5], Wills Eye Hospital, Marlene Moster, MD	50 - 120s per hemisphere (100 - 240s total)	2000 mW	31.3% (0.5 ms duration, 1.1 ms interval)
Ongoing Prospective Pilot Study initial results, AGS 2016, Wills Eye Hospital, Marlene Moster, MD[6]	90 - 180s per hemisphere (180 - 360s total)	2000 mW	31.3% (0.5 ms duration, 1.1 ms interval)
Anatomical effects, AGS 2016, Shan Lin, MD, UCSF[7]	80s per hemisphere (160s total)	2000 mW	31.3% (0.5 ms duration, 1.1 ms interval)
Histopathological study TSCPC versus mTSCPC, AGS 2016, Robert J. Noecker, MD, Yale Univ.[8]	90s per hemisphere (180s total)	2000 mW	31.3% (0.5 ms duration, 1.1 ms interval)
1 year, 45 patient follow-up study, ARVO 2016, Robert J. Noecker, MD, Yale Univ.[9]	70 - 90s per hemisphere (140 - 180s total)	2000 mW	31.3% (0.5 ms duration, 1.1 ms interval)

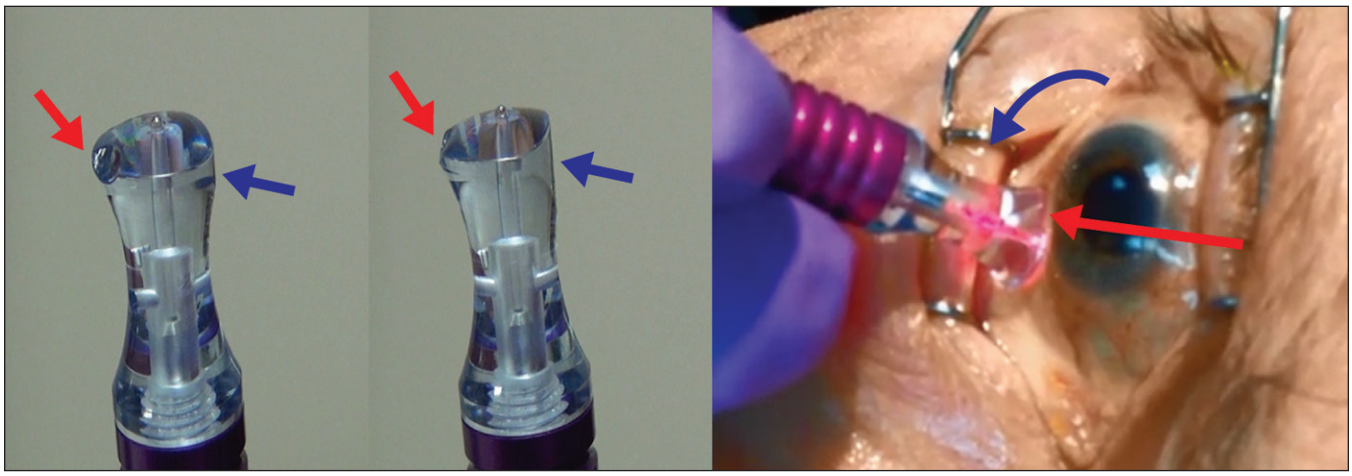

Figure 2. Proper MP3 positioning: notch toward the limbus, flat side toward the eyelid.

PREOPERATIVE PLANNING & POSTOPERATIVE REGIMEN

Dr. Noecker: It is possible to perform this extraocular procedure in an office setting, a minor procedure room, or in the OR. In terms of anesthesia, I think you need to be prepared to do a block or propofol or both. I will explain my preoperative planning. Because this procedure is all about exposure, I have forceps or a Q-tip to move the globe to treat one hemisphere and then turn it back the other way to treat the other hemisphere. I think controlling the globe to improve exposure is important. Any speculum that the surgeon prefers will work. Lastly, a lubricant may help prevent subconjunctival hemorrhages or catching the conjunctival tissue, because we are gliding this probe across the surface of the conjunctiva (Figure 2). You want to apply a light pressure to the surface with the head of the probe. If it glides easily and is always in continuous motion, then it minimizes the superficial trauma to the eye.

Postoperatively, I tend to continue glaucoma medications and adjust them based on follow-up. I add difluprednate drops (Durezol; Alcon) t.i.d. for the first week and then have them decrease to once a day for 3 weeks. I have adopted this because this is what I do with other procedures. I may be prescribing more than I need, because I have never had any rebound inflammation. I am curious to see what Dr. Radcliffe has to say; perhaps I could get away with less therapy.

In patients through 1 year of follow-up, I find very similar IOP reduction to what is in the literature (Table 3). My patient population tends to start with lower overall pressures, on average, about mid-20s. Most of my patients have an IOP of 15 mm Hg after treatment. The ability to get into the midteens is great. With some patients, I can get a lower IOP, but midteens is good enough in a lot of glaucoma patients.

Dr. Radcliffe: The postoperative inflammation is totally different from other procedures. After most procedures, I have to examine the patient before I can decide if I can withdraw the steroid therapy, but with the MP3 procedure I prescribe prednisolone q.i.d. for only 1 week. I have not had problems controlling inflammation like I might, for example, with transscleral cyclophotocoagulation or other surgeries. The patient's downtime is significantly low, so this therapy is great for patients who are working, traveling, have difficulty making postoperative visits, or who are at increased risk of falling.

TABLE 3. MP3 1-YEAR FOLLOW-UP, ARVO 2016

N = 46
Mean preoperative IOP: 26.2 mm Hg
Mean 12-mos postoperative IOP: 15.4 mm Hg
41% IOP reduction

My standard regimen is a subconjunctival steroid injection such as dexamethasone (Ozurdex; Allergan) or methylprednisolone (Solu-Medrol; Pharmacia and Upjohn) on the day of the laser and prednisolone acetate (Pred Forte; Allergan) q.i.d. for a week. I generally have them stop on their own at week 1, and I see them at 2 weeks. In some of these extreme cases, when the pressure is in the 70s or the patient is monocular, I may see him or her sooner, but I think you do not get the full response until 1 to 2 weeks. Patients have done very well with that abrupt taper, the same taper I use for selective laser trabeculoplasty or iridotomy. In heavily pigmented eyes, I think the laser is absorbed a little bit better; that is where you might get a little rebound iritis, but it is not a very frequent occurrence.

We do not expect the full pressure reduction on postoperative day 1, although you may get it. As a safety check, you want to see how much inflammation there is and adjust your anti-inflammatory treatment accordingly. Typically, the eye is reasonably "quiet." At week 1 to 2 is when the pressure begins to decrease, which does not continue much beyond week 2.

A SAMPLING OF THE LITERATURE

Clinical Study 1

The study[2] by Paul Chew, MD, was the first to give us insight into the efficacy and safety of MicroPulse use in a transscleral cyclophotocoagulation treatment. The study's 38 patients had a very high baseline IOP: 39.3 mm Hg. Patients had about a 25% IOP reduction by day 1 of treatment and 33% IOP reduction by 18 months. There was a medication reduction along with that, from a mean of 2.1 medications to 1.3 medications.

Clinical Study 2

In the United States, we pooled our data together with those of Iqbal Ahmed, MD; Jeffrey Kammer, MD; Anup Khatana, MD; Parag Parekh, MD; and Steve Vold, MD, to look at our initial US experience using the MP3.[3] We started with a baseline IOP of about 26 mm Hg, and by the third month, the IOP was down on average to 17 mm Hg, which is a 30% IOP reduction. We were also able to reduce the number of medications from 3.3 to 2.4. In many cases, that meant getting patients off of Diamox (acetazolamide; Wyeth Pharmaceuticals), which counted as one medication, but for patients it can be a really dramatic improvement in their quality of life.

Clinical Study 3

At the same time in the United States, a group from Wills Eye Hospital, with Marlene Moster, MD, looked at their data, which began with a very high IOP of 38 mm Hg and went down to 23 mm Hg at the final follow-up.[4] That was almost a 40% IOP reduction. Again, there was a medication reduction, from 2.5 medications to about 1.8. This was a pilot case series with 19 consecutive patients and about 50 days of follow-up on average. I think when you see data like this, and you see high baseline pressures, you know you are talking about tough-to-treat patients, patients in whom certain medications and probably other interventions have failed, including laser trabeculoplasty as well.

Clinical Study 4

This study compared MicroPulse with standard transscleral cyclophotocoagulation head to head in the same population.[1] The starting eye pressures in the treatment population were very similar, starting in the mid-30s. Mean IOP reduction between the two treatment arms was very similar in the two groups, about a 45% reduction; however, when we look at the incidence of prolonged hypotony, we see that there were no cases of hypotony in the MicroPulse group versus five of the cases, or over 20% of the patients, in the transscleral group.

—presented by Dr. Noecker and Dr. Radcliffe

You may see a single-digit pressure on week 1 or 2 that will eventually rise into the low teens. At month 1, you will see both resolution of any inflammation and the majority of the pressure reduction realized. I do not re-treat at month 1; I wait for month 2.

CONCLUSION

Dr. Radcliffe: We are in an era of personalized glaucoma therapy. The MP3 is able to deliver a therapy that meets a variety of patients' needs, including different stages of glaucoma, different levels of IOP, and different risk scenarios. Its safety profile creates a versatile treatment regimen. ■

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