

Treat and Extend with PASCAL Laser

PASCAL's Endpoint Management technology reduces the injection burden for patients with DME

By Yannis M. Paulus, MD, FACS

Time and Cost Burdens of Intravitreal Injections

Diabetes is a worldwide pandemic affecting more than 387 million people globally,¹ with the number estimated to increase to 590 million people by 2035.¹ Diabetic retinopathy affects 40-45% of patients with diabetes.² The burden on health systems as well as individuals is very significant and increasing.

Frequent intravitreal injections can be difficult for patients and their families. A European study evaluated 131 retinal patients that completed a questionnaire about the impact of injection therapy on individuals with diabetic macular edema (DME) or retinal vein occlusion. Results showed that when travel time was included, each intravitreal injection appointment took an average of 4.5 hours.³

In the above-cited study, 53% of the working patients surveyed needed to take at least one day off per appointment, and 71% of all patients needed the assistance of a caregiver at the time of the injection appointment. Adding to the burden, three-quarters of patients reported anxiety about their most recent injection, and 54% reported being anxious for at least 2 days prior to the injection. The treatment regime changes the patients most desired was fewer injections and appointments, with the same visual results.

In addition, intravitreal injections can create a substantial cost burden. The wholesale cost of the approved drugs is often between \$1,000 and \$2,000, and some patients must pay out of pocket, while others may have a substantial copay.

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- **Intravitreal injections can create a substantial cost burden.**
- **The treatment regime changes the patients most desired were fewer injections and appointments, with the same visual results.**

In 2010, when intravitreal use of anti-vascular endothelial growth factor (VEGF) was predominantly for age-related macular degeneration, ophthalmologic use of anti-VEGF therapy cost approximately \$2 billion, which was about one-sixth of the Medicare Part B drug budget.⁴ In 2013, Medicare Part B expenditures for aflibercept and ranibizumab alone totaled \$2.5 billion.⁵

Endpoint Management Technology Shown to Reduce Injection Burden

During the early phase of the COVID pandemic, the burden of injection visits was especially high. People living with diabetes were especially vulnerable to COVID, as were the elderly. Many patients refused to come in for injections.

My team and I began thinking more intensely about how we could extend the time between treatments without compromising vision. I have been researching and performing laser therapy since 2005, and it remains an important part of my clinical practice. While I have had success with laser monotherapy for mild DME, I have found anti-VEGF intravitreal injections to usually be important for more severe edema. We decided to evaluate the use of adjunctive Endpoint Management® (EpM) laser technology as provided by the PASCAL Synthesis® 532 nm laser to reduce the burden of clinic visits and intravitreal injections for patients with DME.^{6,7} EpM allows clinicians to titrate the laser to subvisible, tissue-sparing levels using a proprietary energy delivery algorithm.

The PASCAL Synthesis 532 nm laser used in the study delivers a pattern of spots with each trigger.

We looked at 18 eyes from 14 patients with DME who had fairly severe macular swelling and were not happy receiving frequent injections. These patients were eager to extend the time between visits. The patients had a mean age of 62.6 years (standard deviation 17 years). 50% of eyes were receiving bevacizumab injections prior to laser treatment, 29% were receiving aflibercept, and the remaining 21% were

receiving a combination of anti-VEGF and steroid agents. Steroids have been evaluated to have no long-term effect on barely visible laser burns.⁸

**“WE FOUND A STATISTICALLY AND CLINICALLY
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All patients were treated with 30% of threshold laser with landmarks off and laser spot size of 200 μ m, pulse duration of 15 ms, and spacing of 0.25 Φ apart. Mean number of spots applied was 655.6 +/- 160.5.

We found a statistically and clinically significant reduction in the requirement for intravitreal injections after the administration of laser treatment using EpM. The mean number of intravitreal injections in the six-month period prior to laser treatment was 3.39 +/- 2.57 injections compared to 2.33 +/- 2.40 injections in the six months following laser treatment ($p=0.02$).

As we conducted the study, it was vital to be sure the reduction in number of injections was not resulting in undertreatment. We therefore monitored visual acuity and central retinal thickness on optical coherence tomography (OCT). My goal was to make sure neither of these factors was becoming worse. We found that vision did not get worse. Additionally, we observed a trend towards better vision and reduced retinal thickness, although those observations were not statistically significant, given the limited sample size.

Patient Selection

I use PASCAL's EpM technology as an adjunctive therapy for visually symptomatic patients with severe DME. These patients typically have vision of 20/30 or worse. I typically consider the treatment for patients in whom I am not able to extend the interval between monthly injections without exacerbating their DME.

Setting Expectations

Patients

It is important to set appropriate patient expectations. In patients with severe DME, I find EpM laser treatment will reduce the number of injections and visits but not eliminate the need for injections. I make sure to be clear about this. I also communicate that it will take a while to notice a change in vision. Patients receiving anti-VEGF injections are used to the rapid, significant improvement in their vision within a couple of days after the injection. I tell patients that laser delivered using

PASCAL's EpM technology is a long-term treatment, and their vision will improve slowly over the following weeks. I also let patients know that the laser treatment durability using EpM is longer than anti-VEGF. In my hands, it is often 6 to 12 months.

I tell patients about the procedure itself, so that there will not be surprises. I let them know they will not feel any pain. They will only feel the contact lens and some contact lens gel running down their cheek. I also explain that things will seem dark for a while right after the procedure and they may see colors as the vision returns thereafter.

To manage patient expectations, I tell them that laser treatment using EpM technology will reduce the number injections and visits, not eliminate the need for injections.

Physicians

Physicians can expect the outcomes described above. I would add that the use of EpM in treatment is very easy to learn, and patients report that it is comfortable. They are very pleased with the treatment and outcomes.

PASCAL's laser treatment using EpM is a rapid procedure and therefore fits readily in the busy modern retinal clinic workflow. The procedure does not take me longer than a return visit and can be scheduled into any short return appointment slot.

Treatment Settings

I use the following EpM settings:

- 30% of threshold laser
- Mean threshold power of ~140 mW*
- Landmarks off
- Laser spot size of 200 μ m
- Pulse duration of 15 ms
- Spacing of 0.25 Φ apart
- Mean number of spots has been about 655*

**Power level and number of spots may change depending on patient.*

I titrate the power, typically beginning at about 100 mW, depending on patient pigmentation and a number of other factors. I increase power, in the periphery of the eye, until I detect a barely visible burn. This is usually in the 130 mW to 150 mW range. Treatment using EpM is then performed with a fraction of this power (30%).

I typically use a circular pattern excluding the 2 nasal wedges to avoid the maculopapular bundle. I then add supplemental 4x4 squares to cover the area from arcade to arcade outside this ring temporally.

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Treatment Pearls

Use shorter pulse duration, so that you can more rapidly treat the whole macula. Since reducing pulse duration necessitates increasing laser power, I recommend between 10 ms and 20 ms as a compromise between speed and safety.

During treatment, keep track of the areas you have treated. You will not see visible changes to the retina, so it is important to develop a treatment protocol that covers the full area of the macula and apply the protocol consistently.

Repeat treatment as necessary. The laser treatment is sub-visible on the retina, so it is safe to repeat treatment. When appropriate, I retreat after 6 to 12 months.

Benefits and Versatility of the PASCAL System

Rapid Treatment

PASCAL's pattern treatment is fast. A randomized clinical trial comparing PASCAL's pattern treatment using single-session panretinal photocoagulation (PRP) with PASCAL single-spot multiple-session PRP found mean treatment time for the pattern PRP was 5.04 minutes versus 59.3 minutes for the single-spot PRP.⁹

No Patient Pain with Treatment

The patient only feels the macular contact lens and the contact lens gel that can run down the cheek. If it were not for the beep of the laser, the patient would not know when they were being treated.

No Requirement for Fluorescein Angiography

When treating with a conventional focal laser, fluorescein dye is administered intravenously. The patient must then wait about 10-15 minutes before images are completed, and occasionally patients will have nausea and vomiting in reaction to the dye. Angiography is not necessary for PASCAL EpM treatment, making it faster and more pleasant for the patient. Treatment also becomes more streamlined for the physician because there is no need to consult images during the procedure.

No Risk of Infection

The laser procedure is minimally invasive and the treatment does not carry the risk of infection. It is rare for eye infections (endophthalmitis) to occur as a result of intravitreal injections (1:3000),¹⁰ but when they do occur, they can be very serious and lead to permanent blindness.

Reduction of Injection Requirements, so the Interval Between Clinic Visits Can be Increased

PASCAL's EpM technology is associated with a clinically and statistically significant reduction in the number of intravitreal injections required in the six-month period immediately following treatment. Longer intervals between injections reduces the burden on both patients and clinics.

Case Study

A 61-year-old Caucasian female presented with proliferative diabetic retinopathy and diabetic macular edema in both eyes and had constant blurry vision in the right eye. She was receiving monthly bevacizumab injections in her right eye.

Her vision OD, despite the injections, was 20/70 with pinhole improvement to 20/40 OD. Her intraocular pressure was 12 mm Hg OD and 14 mm Hg OS, and the central macular thickness in the symptomatic right eye was 347 μ m.

This was the summer of 2020 and the patient refused to come into my office monthly, because she viewed it as a very high risk situation because of COVID. She also considered the copays for aflibercept or ranibizumab prohibitive. When we discussed other options, she was very concerned about steroids, because a family member had gone blind from glaucoma, and she was a glaucoma suspect. She chose to proceed with PASCAL's laser treatment using EpM for the right eye.

Following the laser treatment, she went from needing six intravitreal injections in the six months before her laser treatment using EpM to only needing two intravitreal injections in the six months after treatment. Her central macular thickness decreased from 347 μ m to 279 μ m. Vision in her right eye improved from 20/70 to 20/30, and she was very pleased with the results and thankful.

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