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EFFICACY AND SAFETY OF 561 NM LASER PAN-RETINAL PHOTOCOAGULATION TREATMENT FOR RETINAL VASCULAR DISORDERS

Ophthalmology

Talal Al-Assil BS, Western Michigan University, Homer Stryker MD School of Medicine, Kalamazoo, Michigan, USA

Rami Madani BS, Western Michigan University, Homer Stryker MD School of Medicine, Kalamazoo, Michigan, USA

Sara Koudsi Providence College, Providence, Rhode Island, USA

Ling-Yueh Hu PhD, Department of Clinical Affairs, RusCert Technology Co., Ltd. Taipei, Taiwan.

Tarek Alasil MD, Acuity Eye Group, Los Angeles, California, USA

ABSTRACT

Objective: To evaluate the clinical efficacy and safety of the 561 nm laser wavelength in treating patients with retinal ischemia from diabetic retinopathy or retinal vein occlusion. **Study Design & Methods:** This prospective study evaluated the effects of panretinal photocoagulation (PRP) treatment using a 561 nm wavelength laser on patients with retinal ischemia secondary to diabetic retinopathy and retinal vein occlusion. The comparison was made between the patients' conditions before and after the PRP treatment. **Results:** Forty-seven eyes from 36 patients suffering from retinal vascular disorder were included in the analysis. The improvement of visual acuity after receiving PRP treatment was statistically significant and consistent with the reported outcomes using the traditional green 532 nm laser. There were no observed complications from using the 561 nm wavelength laser. **Conclusion:** The safety and efficacy of LIGHTMED LightLas 561 nm wavelength have been established for routine PRP treatment of retinal ischemia from diabetic retinopathy and retinal vein occlusion.

KEYWORDS

Retinal Vascular Disorder, Diabetic Retinopathy, Retinal Vein Occlusion, Pan-retinal photocoagulation (PRP).

INTRODUCTION

Retinal vascular disorders, such as Diabetic Retinopathy and Retinal Vein Occlusion (RVO), are common causes of vision loss in the elderly.[1,2] Diabetic Retinopathy is a critical complication of diabetes that affects blood vessels in the retina and can cause vision damage and blindness.[3] The disease is characterized by capillary non-perfusion and ischemia in the retina, which eventually leads to macular edema and retinal neovascularization with the potential for severe visual impairment. Diabetic Retinopathy is clinically divided into two types: non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).[4] After Diabetic retinopathy, RVO is the second most common type of retinal vascular disease, and it is further classified into Branch RVO (BRVO) and Central RVO (CRVO).[5] A multitude of vision-threatening complications can result from neovascularization including vitreous hemorrhage, tractional retinal detachment, and neovascular glaucoma. The presence of neovascularization is an indication for treatment with laser photocoagulation.

Pan-retinal photocoagulation (PRP) was introduced in the Diabetic Retinopathy Study (DRS) in 1976 as an effective treatment to decrease the risk of severe vision loss in patients with PDR.[6] After the revolution of anti-vascular endothelial growth factor agents, PRP has continued to provide a viable and important treatment modality in the treatment of retinal ischemia in diabetic retinopathy and retinal vein occlusion. Currently, PRP within the green range of light wavelengths (532 nm) is the first-line treatment for high-risk proliferative diabetic retinopathy.[7, 8, 9] Retinal photocoagulation reduces the risk of vision loss and helps preserve vision. Complications of this low-risk procedure include vitreous hemorrhage, crunching effects in cases of existing retinal traction, and loss of vision from accidental laser burns to the fovea. The recent modifications in the laser technology have significantly decreased these complications. Additionally, the potential reduction in vision caused by laser treatment is minimal compared to untreated retinopathy.

Despite the long period since the discovery of laser-based eye treatments, the use of other laser wavelengths has been an under-explored area in literature. With that said, a 2014 study in Japan has established the safety and efficacy of the yellow (577 nm) wavelength in photocoagulation and focal laser treatments. Specifically, they compared direct photocoagulation using yellow-green (561-577 nm) laser to the 810 nm micropulse laser revealing no statistical difference in efficacy between the two. However, this group showed an advantage of using the yellow laser since it was more suitable for microaneurysm coagulation and micropulse ablation due to its higher rate of absorption by melanin and oxyhemoglobin, relative to the 810 nm wavelength laser.[10]

This clinical study offers an exploratory analysis on recruited patients to assess the safety and efficacy of the 561 nm wavelength LIGHTMED laser for photocoagulation treatment, reflecting the promising potential of the yellow-green laser in PRP therapy demonstrated by previous studies.

Methods

In this prospective clinical study, we examined the effects of panretinal photocoagulation (PRP) using the FDA-approved LIGHTMED 561 nm laser system (LIGHTMED Corporation, Taiwan) on patients with retinal ischemia due to diabetic retinopathy and retinal vein occlusion (RVO). We assessed patients aged 18 and older who received PRP treatment from October 2020 to December 2021. Data were collected and analyzed from medical records documenting the effects and outcomes of the 561 nm laser PRP treatment, which was adjusted to achieve a mild grey/white retinal burn during routine clinical practice. Out of 45 patients initially screened who had undergone PRP, 42 were diagnosed with a retinal vascular disorder and had their visual acuity tested after treatment. Six participants were subsequently excluded due to non-attendance at follow-up visits. A flowchart of the study's population is summarized in Figure 1.

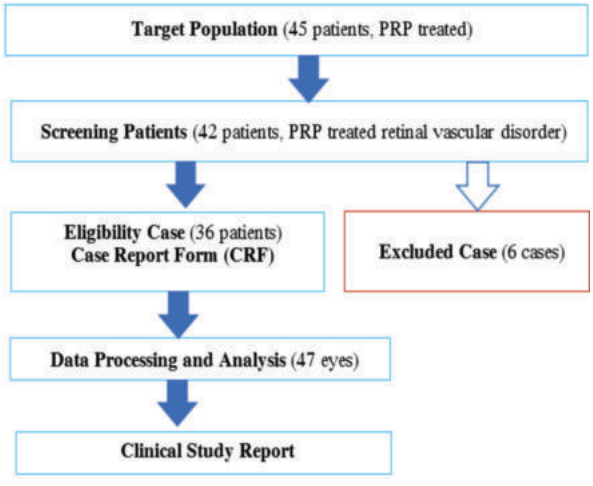

Figure 1. Study Flowchart

The trial and data gathering spanned four months, with ischemia being qualitatively evaluated through fluorescein angiography (FA), which also guided the PRP treatment. A 3x3 pattern grid was employed to enhance the efficiency of the PRP sessions. The change in visual acuity was further analyzed in three subgroups according to the severity of the retinopathy: PDR, NPDR, and RVO.

The objective endpoints were: 1) evaluation of visual acuity maintenance after PRP treatment and 2) assessment of the occurrence of PRP-related complications upon follow up visits. During patient follow-up appointments, the operating surgeon assessed for complications associated with PRP treatment. They inquired about pain post-treatment and evaluated for infection, post-laser bleeding, abnormal intraocular pressure, globe perforation, accidental laser burns to the fovea, and visual field loss.

The data of this study was analyzed via Statistical Analysis System software (SAS) according to quantitative and qualitative modalities. Quantitative variables include the number of missing values and of non-missing values, mean, standard deviation, 95% confidence interval, median, minimum, and maximum. Qualitative variables included the number of missing values and of non-missing values, frequencies, percentages, and 95% confidence intervals for each of the modalities of the variable (excluding missing data from the denominator). A minimum sample size of 40 eyes were required to demonstrate a statistically significant result of visual acuity after PRP treatment from the baseline. The primary outcome was the comparison of the visual acuity after PRP treatment with the baseline. The level of significance difference (Type I error, $\alpha = 0.05$) was obtained through a paired t-test. The $p < 0.05$ indicates a statistically significant difference between the before and after treatment. The incidence rate (%) of PRP-relevant complications after treatment represented the safety of the device in routine practice.

RESULTS

Overall, 47 eyes from 36 patients were analyzed upon follow up within 12 months after the treatment to determine the two efficacy endpoints with an average follow-up interval of 3.4 months per eye. The mean age of our subjects was 64 ±13 years. Our patients were evenly represented gender-wise (18 male, 18 female). Diagnostically, and per the severity of the retinopathy, the most common condition eligible for PRP was PDR. There were 27 (out of 46) eyes (57%) diagnosed with PDR; and 12 eyes (26%) with NPDR (1 moderate and 11 severe cases); and 8 (17%) RVO cases. In addition to PRP treatment, 36 eyes (77%) received intravitreal injections to inhibit retinal vascular proliferation including Aflibercept (n=2) and Bevacizumab (n=33), and one eye received Dexamethasone implant & Bevacizumab, while 11 eyes (23%) did not receive injections. A summary of patients' demographics and clinical characteristics are summarized in Table 1.

Table 1. Patient Demographics and Clinical Characteristics at Baseline	
Subjects N=36	
Age(year) Mean (SD)	64.06 (±13.44)
Gender	
Male N (%)	18 (50.00%)
Female N (%)	18 (50.00%)
	Eyes n=47
Diagnosis	
PDR n (%)	27 (57.45%)
NPDR n (%)	12 (25.53%)
NPDR (moderate) n (%)	1 (2.13 %)
NPDR (severe) n (%)	11 (23.40 %)
RVO n (%)	8 (17.02%)
History of medication (intravitreal injection) [before or after PRP treatment]	
No n (%)	11(23.40%)
Yes n (%)	36 (76.60%)
IVE (Eylea®) n (%)	2 (4.26%)
IVA (Avastin®) n (%)	33 (70.21%)
IVO (Ozurdex®) & IVA (Avastin®) n (%)	1 (2.13%)

The 561 nm laser treatment settings were spot size of 150-200 microns, duration of 20-30 milliseconds, power of 200-340 mW and number of spots 800-1200 spots. The direct clinical effectiveness metric for retinopathy treated with PRP is the maintenance of visual acuity. This study presents visual acuity values as decimal visual acuity (VAdec). The visual acuity (VA) values were converted to log MAR for statistical analysis. The findings are presented in Table 2, which details the changes in visual acuity (VAdec), and in Table 2-1 of the Supplemental Section, which provides the Logarithm of the Minimum Angle of Resolution (Log MAR) visual acuity outcomes.

Table 2. Change in Visual Acuity After PRP Treatment Relative to Baseline				
VAdec	Pretreatment (baseline)	Follow up	Change from baseline	P value &
Eyes (n)	47	47	47	<0.0001*
Mean (SD)	0.39 (0.25)	0.49 (0.27)	0.10 (0.15)	
Range (Min, Max)	(0.01, 0.79)	(0.01, 1.00)	(-0.21, 0.53)	
Median	0.40	0.63	0.09	
95% C.I.	(0.32, 0.47)	(0.41, 0.57)	(0.05, 0.14)	
&: Paired t-test is used in continuous variables *: Statistically significant				

The mean VAdec before treatment was 0.39 (±0.25), and the mean VAdec after treatment was 0.49 (±0.27). The change in mean VAdec following laser treatment, 0.10, was statistically significant (P <0.0001).

Our sample size is estimated at the 5% significance level with 80% power. The mean VAdec before treatment was 0.39 (±0.25), and the mean VAdec after treatment was 0.49 (±0.27). The change in mean VAdec following laser treatment, 0.10, was statistically significant (P <0.0001). The Box Plot for the visual acuity before and after PRP treatment is demonstrated in Figure 2. The subgroup analysis is listed in Table 3 (VAdec). VA LogMAR results can also be found in Table 3-1 in the Supplemental Section.

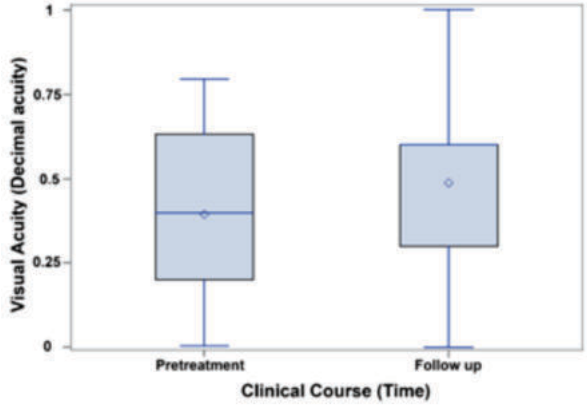

Figure 2. Box Plot for the Visual Acuity After PRP Treatment.

The box plot showing the mean value (diamond symbol ¯) and 25th–75th percentile range of visual acuity levels.

Table 3. Analysis for visual acuity values after PRP treatment in PDR, NPDR and RVO group				
VAdec	Pretreatment (baseline)	Follow up	Change from baseline	P value &
PDR				
Eyes (n)	27	27	27	<0.0001*
Mean (SD)	0.38 (0.22)	0.50(0.23)	0.12(0.17)	
Range (Min,Max)	(0.01,0.79)	(0.01,0.79)	(-0.21,0.53)	
Median	0.40	0.63	0.13	
95% C.I.	(0.29,0.47)	(0.41,0.59)	(0.06,0.19)	
NPDR				
Eyes (n)	12	12	12	0.043*
Mean (SD)	0.53(0.22)	0.62(0.29)	0.09(0.14)	
Range (Min,Max)	(0.01,0.79)	(0.05,1.00)	(-0.11,0.37)	
Median	0.57	0.63	0.11	
95% C.I.	(0.39,0.67)	(0.43,0.80)	(0.00,0.17)	
RVO				
Eyes (n)	8	8	8	<0.0001*
Mean (SD)	0.25(0.28)	0.27(0.28)	0.03(0.12)	
Range (Min,Max)	(0.01,0.79)	(0.01,0.63)	(-0.16,0.25)	
Median	0.15	0.18	0.00	

95% C.I.	(0.01,0.48)	(0.04,0.51)	(-0.07,0.13)	
&: Paired t-test is used in continuous variables *: Statistically significant				

In our study population, there were no reported complications related to the laser including pain, infection, abnormal intraocular pressure, perforation, accidental laser burns of the fovea, or subjective complaint of visual field loss. However, there was one patient who developed recurrent vitreous hemorrhage 6 weeks after PRP treatment.

DISCUSSION

While PRP is currently the first-line treatment for PDR, data has been reported about PRP outcomes in patients with NPDR. One study found that PRP reduces the risk of severe vision loss in PDR patients by 54%, while this risk is reduced by 12.5% in NPDR patients.[11]

Further, a study by Sabaner et al. supports that the foveal avascular zone, whose enlargement is a marker of poor prognosis in diabetics, significantly decreases in NPDR patients following PRP treatment. [12] Additional studies have also demonstrated that PRP treatment administered at the severe NPDR stage can provide promising outcomes, including preventing progression to PDR. [13, 14] On the other hand, no direct treatment has been observed for RVO; rather, treatment focuses on preventing sequalae such as macular edema and neovascularization, for which PRP with green laser has been deemed effective. [15, 16] With the risk of PRP being minor, we have additionally demonstrated that PRP is effective and safe in patients with severe NPDR and RVO.

In our study, using the 561 nm laser for PRP treatment improved the VAdec of 47 eyes by a mean of 0.10 (P<0.0001) without reported complications. While our study did not control for a group treated with the standard 532 nm green laser, our outcome matches the expected outcome of using the green laser in both common practice and literature as was the case in Talwar's study where VAdec improved by a mean of 0.10 as well. [17] Therefore, the evaluation of visual acuity after PRP treatment, demonstrated in Table 2, Table 2-1, and Figure 2 indicate that patients with diabetic retinopathy receiving 561 nm PRP treatment can effectively maintain their vision proving the 561 nm laser treatment to be effective across all three subgroups of retinal vascular disease (PDR, NPDR, and RVO). More significantly, we observed no adverse effects or harm of utilizing the 561 nm laser.

While the 561 nm laser's properties cannot be argued to be clinically superior to the traditional green laser in PRP treatment, Figure 3 demonstrates several advantages to using the 561 nm laser upon treating the macula. First, the 561 nm laser is less absorbed by the melanin present in the choroid and retinal pigment epithelium, thus providing some protection to the choroid and outer retina. Additionally, the 561 nm wavelength, unlike the green laser, is not absorbed by the Xanthophyll, the protective pigment within the macula. Third, and as mentioned by Inagaki's group, yellow laser is absorbed to a greater extent by oxyhemoglobin, rendering it more effective in treating microaneurysms, the leakage of which can worsen macular edema. [10,18,19]

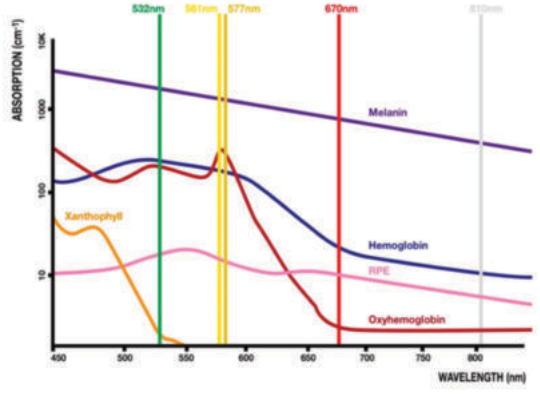

Figure 3. Tissue Absorption of Sifferent Light Wavelengths (nm)

Despite the relatively small sample size of 47 eyes in our study, we believe that providing further data on the outcomes and safety of utilizing the 561 nm laser for PRP, when treating retinal ischemia, is of value given its limited presence in the literature.

In conclusion, the safety and efficacy of LIGHTMED LightLas 561 nm in the treatment of retinal vascular disorders were demonstrated. The 561 nm PRP laser treatment offers the benefit of vision maintenance, and at times improvement, in patients with retinal vascular ischemia as it preserves visual acuity and decreases the risk of vision loss. The safety profile of the 561 nm wavelength, similar to the 577 nm wavelength, can be attributed to the lower absorption by melanin (concentrated in the RPE and the choroid), lack of absorption by the Xanthophyll (protective pigment within the macula), and peak absorption by oxyhemoglobin (present in the leaking microaneurysms). [18, 19] This demonstration of the safety and performance of the 561 nm provides real-world evidence supporting its use in routine clinical practice to treat retinal ischemia. Future randomized studies with larger sample size, longer follow-up, and direct comparison of the outcomes of green (532 nm) and 577 nm as well as 561 nm lasers are warranted.

Conflict of Interest & Financial Statement

This study was sponsored by Meditek Laser Research Inc. (locally) and LIGHTMED Corporation (internationally), which provided funding and the 561-nm laser equipment used in our PRP studies. The company was not involved in study design, data analysis, or any aspect of preparing this manuscript. The authors declare that while financial support was received from LIGHTMED, it did not influence the outcome of this research. There are no other potential conflicts of interest relevant to this article.

Supplemental Section

Table 2-1. Change in visual acuity after PRP treatment when compared with baseline				
VA (logMAR)	Pretreatment (baseline)	Follow up	Change from baseline	P value &
Eyes (n)	47	47	47	0.0005*
Mean (SD)	0.64(0.64)	0.49(0.58)	-0.14(0.27)	
Range (Min, Max)	(0.10,2.30)	(0.00,2.30)	(-1.20,0.24)	
Median	0.40	0.20	-0.10	
95% C.I.	(0.45,0.82)	(0.32,0.66)	(-0.22, -0.07)	
&: Paired t-test is used in continuous variables *: Statistics significant				

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