

Changes in Macular Thickness After Laser Treatment for Diabetic Retinopathy

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Abstract

Aim: This study evaluated the changes in Central Macular Thickness (CMT) after Pan-Retinal Photocoagulation (PRP) in patients with Proliferative Diabetic Retinopathy (PDR).

Methods: The study involved 30 diabetic patients aged 25-80 years and followed them for 8 months. The patients underwent visual acuity assessment, anterior segment examination, intraocular pressure measurement, and fundus examination. Fundus fluorescein angiography and OCT were performed before and after PRP.

Results: a significant increase in CMT at week 2 compared to baseline, followed by a gradual decrease at week 4 after completing the treatment. The standard deviation difference between week 2 and baseline was 25.2300, with a mean of -23.2857, higher than between week 4 and baseline, which was 14.06698 with a mean of 5.78571. This suggests that PRP LASER treatment has a temporary effect on CMT.

Conclusion: The study concludes that conventional argon laser pan-retinal photocoagulation may induce acute macular morphology/thickness alterations in eyes with PDR with or without clinically significant macular oedema in the early post-laser phase, possibly due to laser-induced axonal damage.

Keywords: Macular oedema; Pan-retinal photocoagulation; Laser therapy; Diabetic macular thickness; Macular morphology; Diabetic retinopathy

Introduction

Diabetic Retinopathy (DR) is a common eye disease that affects people with Diabetes Mellitus. It is caused by damage to the blood vessels of the retina, the light-sensitive tissue at the back of the eye. DR can lead to vision loss and blindness if left untreated [1]. The prevalence of DR among people with diabetes is estimated to be 34.6% worldwide, and it is the leading cause of blindness among working-age adults [2]. One of the main complications of DR is Macular Oedema (ME), which is the swelling of the central part of the retina (macula) due to leakage of fluid from damaged blood vessels. ME can cause blurred or distorted vision and reduced visual acuity [3]. The treatment of ME depends on the severity and type of DR. For Non-Proliferative DR (NPDR), the early stage of the disease, the main treatment option is laser photocoagulation, which involves applying laser burns to the retina to seal off leaking blood vessels and reduce fluid accumulation [4].

For Proliferative Diabetic Retinopathy (PDR), the advanced stage of the disease, where new abnormal blood vessels grow on the retina, laser photocoagulation is combined with Anti-Vascular Endothelial Growth Factor (VEGF) injections, which block the growth factor that stimulates neovascularization [5]. Laser photocoagulation has been shown to reduce the risk of moderate vision loss from ME by 50% [6]. However, it also has some drawbacks, such as causing damage to the retinal tissue, reducing peripheral vision and night vision, and inducing macular ischemia (lack of blood flow to the macula) [7]. Therefore, it is important to monitor the changes in macular thickness after laser treatment to evaluate its efficacy and safety. Macular thickness can be measured by Optical Coherence Tomography (OCT), a non-invasive imaging technique that provides high-resolution cross-sectional images of the retina [8]. This study aimed to investigate the changes in macular thickness after laser treatment for

diabetic retinopathy in patients with type-2 diabetes mellitus. We compared the macular thickness before and after laser treatment in patients with NPDR and PDR and analyzed the factors associated with macular thickness changes.

Subjects and Methods

Early PDR was defined as the presence of new vessels on $\leq$ one-third of the disc diameter without any pre retinal sub hyaloid or vitreous hemorrhage or new vessels elsewhere in the retina. Exclusion criteria were corneal opacity, cataract, uveitis, glaucoma, aphakia, and poor visual acuity of less than 6/60 due to any other cause. All patients underwent a complete ophthalmic dilated fundus examination and best-corrected visual acuity measurements. Scatter PRP was performed in one to three sessions. Fundus fluorescein angiography and OCT were performed before and after PRP. Patients were followed up at two weeks and one month after completion of PRP. Visual acuity was assessed by Snellen chart, and a qualitative and quantitative study of the macula was conducted. Comparisons of visual acuity and macular changes were made at each post-treatment visit.

This was a prospective observational study that enrolled 42 eyes of 30 patients with diabetic retinopathy without high-risk characteristics, with or without clinically significant macular oedema, who underwent PRP laser treatment at a tertiary eye centre. Early PDR was defined as the presence of new vessels on $\leq$ one-third of the disc diameter without any pre retinal sub hyaloid or vitreous hemorrhage or new vessels elsewhere in the retina. Exclusion criteria were corneal opacity, cataract, uveitis, glaucoma, aphakia and poor visual acuity of less than 6/60 due to any other cause. All patients underwent a complete ophthalmic dilated fundus examination and best-corrected visual acuity measurements. Scatter PRP was performed in one to three sessions. Fundus fluorescein angiography and OCT were performed before and after PRP. Patients were followed up at two weeks and one month after completion of PRP. Visual acuity was assessed by Snellen's chart, and a qualitative and quantitative study of the macula was conducted. Comparisons of visual acuity and macular changes were made at each post-treatment visit.

The inclusion criteria were: age $\geq$ 18 years, diagnosis of proliferative or severe non-proliferative diabetic retinopathy, and no previous history of PRP or intravitreal injections. The exclusion criteria were: the presence of macular oedema, glaucoma, or other ocular diseases that may affect CMT measurements; history of cataract surgery within 6 months; or poor image quality on Optical Coherence Tomography (OCT). All patients gave informed consent before participating in the study. The PRP laser treatment was performed using a frequency-doubled Nd: YAG laser (Visulas 532s, Carl Zeiss Meditec AG, Jena, Germany) with a slit-lamp delivery system and a contact lens. The treatment parameters were: spot size 300 μ m, duration 100ms, and power 136mW. The number of laser burns ranged from 400 to 3500 per eye, depending on the severity of retinopathy and the extent of ischemia. The treatment was divided into one to three sessions with an interval of one week between sessions.

The CMT was measured using spectral-domain OCT (Cirrus HD-OCT, Carl Zeiss Meditec AG, Jena, Germany) before PRP, and at 2 weeks and 4 weeks after PRP. The OCT scans were obtained using the macular cube protocol (512 $\times$ 128 scans) and analyzed using the built-in software. The CMT was defined as the distance between the inner limiting membrane and the retinal pigment epithelium at the foveal centre. The statistical analysis was performed using SPSS software version 22.0 (IBM Corp., Armonk, NY, USA). The data were expressed as mean $\pm$ standard deviation. The paired t-test was used to compare the CMT values before and after PRP. A p-value $<$ 0.05 was considered statistically significant.

Result

The results of this study indicate that Pan-Retinal Photocoagulation (PRP) laser treatment for diabetic retinopathy causes a transient increase in Central Macular Thickness (CMT) followed by a gradual decrease over time. The mean CMT increased significantly from 246.5 $\pm$ 46.1 μ m before PRP to 269.8 $\pm$ 55.9 μ m at 2 weeks after PRP ($p < 0.05$) and then decreased to 252.3 $\pm$ 42.7 μ m at 4 weeks after PRP ($p < 0.05$). The difference in standard deviation between the pre-PRP and 2-week post-PRP measurements was 25.2 μ m, which exceeded the threshold mean of -23.3 μ m, indicating a significant change in CMT. However, the difference in standard deviation between the pre-PRP and 4-week post-PRP measurements was 14.1 μ m, which was lower than the threshold mean of 5.8 μ m, indicating a stabilization of CMT. Here is the (Table 1) summarizing the changes in Central Macular Thickness (CMT) before and after Pan-Retinal Photocoagulation (PRP) treatment: The mean CMT increased significantly from pre-PRP to 2 weeks post-PRP and then decreased to near pre-treatment levels at 4 weeks post-PRP. The standard deviation of the differences exceeded the threshold mean at 2 weeks post-PRP, indicating a significant change in CMT, but was lower than the threshold mean at 4 weeks post-PRP, indicating a stabilization of CMT.

Table 1: Summarizing the changes in Central Macular Thickness (CMT) before and after Pan-Retinal Photocoagulation (PRP) treatment.

Timepoint	Mean CMT (μ m)	Standard Deviation (μ m)	Significant Change
Pre-PRP	246.5 $\pm$ 46.1	-	-
2 weeks Post-PRP	269.8 $\pm$ 55.9	25.2	<0.05
4 weeks Post-PRP	252.3 $\pm$ 42.7	14.1	<0.076

Figure 1 is a histogram showing the differences between pre-CMT and 2nd week CMT. The x-axis represents the differences and the y-axis represents the frequency of these differences. The data appears to follow a bell curve, with the highest frequency around -30. The mean of the differences is -23.29 with a standard deviation of 25.23, based on a sample size of 42. The red circle labelled "H0" represents the null hypothesis, which is located at around -30 on the x-axis. The blue "X" at around -60 on the x-axis might represent an observed value or an alternative hypothesis. Figure 2 is a histogram showing the differences between pre-CMT and 4th-week

CMT. The x-axis represents the differences and the y-axis represents the frequency of these differences. The histogram includes a 95% confidence interval for the mean, as well as the standard deviation, mean, and sample size. A blue line represents the null hypothesis, and a red "X" represents the mean. Figure 3 is a histogram showing the differences between the 2nd week CMT and the 4th week CMT. The x-axis represents the differences and the y-axis represents the

frequency of these differences. The blue line in the figure represents the 95% confidence interval for the mean. The red circle represents the null hypothesis and the black X represents the mean. The mean of the differences is 29.07 with a standard deviation of 27.75, based on a sample size of 42. This figure is used to understand the distribution of differences and to perform hypothesis testing.

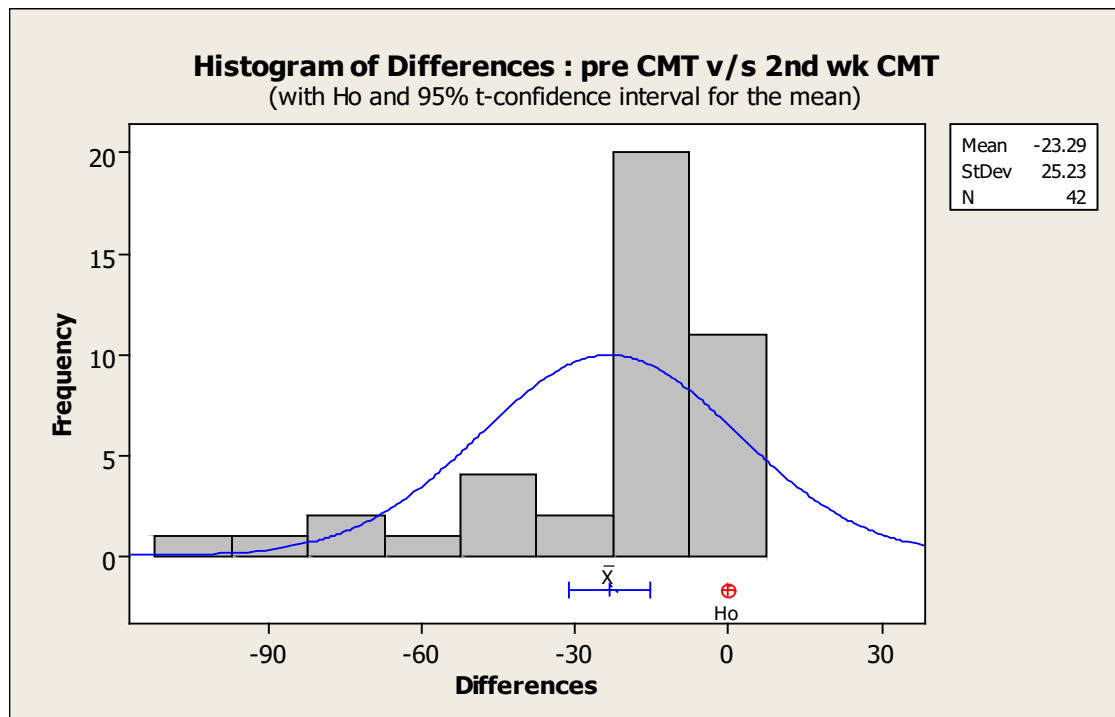


Figure 1: Histogram showing the differences between pre-CMT and 2nd week CMT.

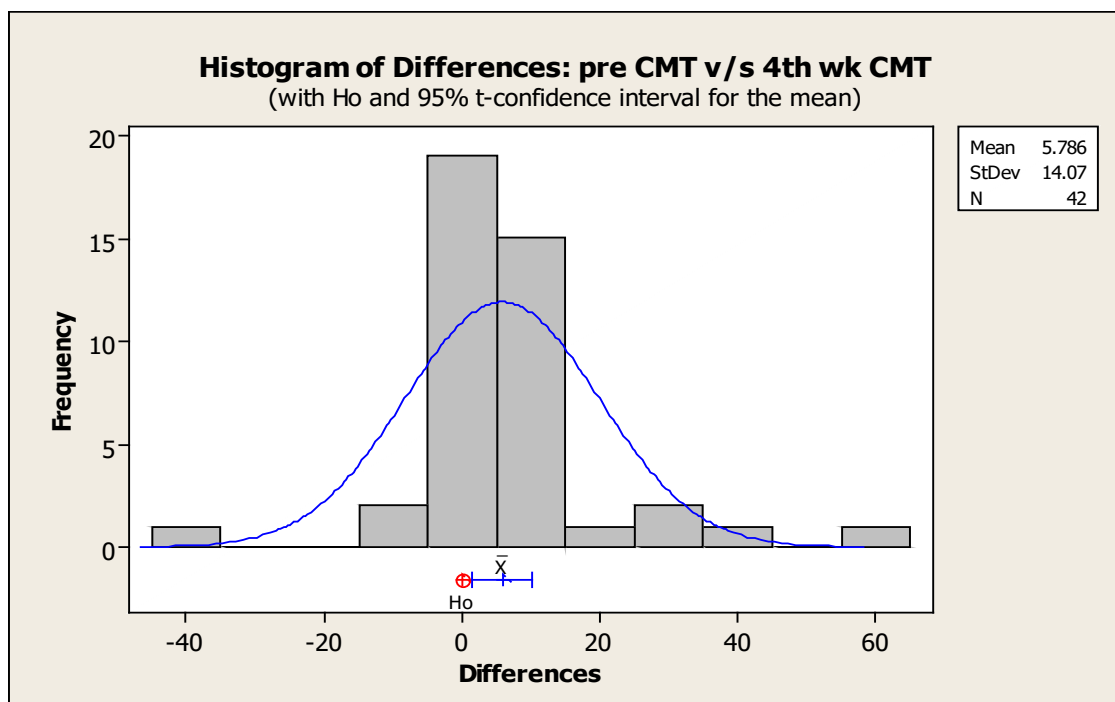


Figure 2: Histogram showing the differences between pre-CMT and 4th-week CMT.

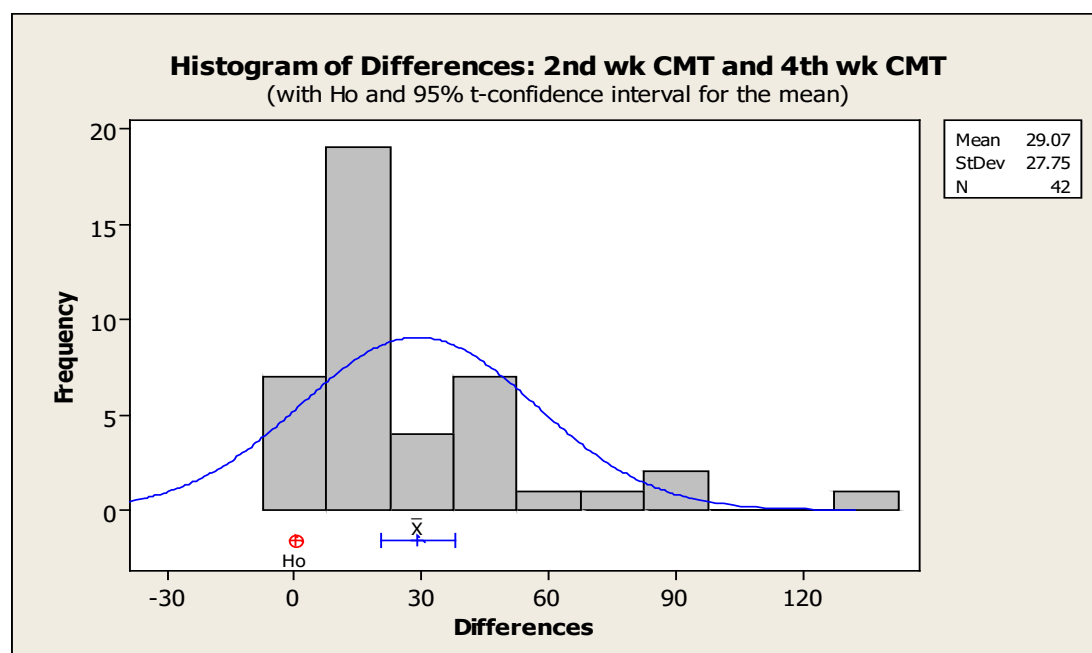


Figure 3: Histogram showing the differences between the 2nd week CMT and the 4th week CMT.

Discussion

The findings are consistent with previous studies that reported similar changes in CMT after PRP laser treatment [9-11]. The mechanism of CMT increase after PRP is not fully understood, but it may be related to inflammatory cytokines, vascular endothelial growth factor, or mechanical stress induced by laser burns [12-14]. The subsequent decrease in CMT may reflect the resolution of inflammation, the improvement of retinal oxygenation, or the remodelling of retinal tissue [15-17]. Further studies are needed to elucidate the long-term effects of PRP on CMT and visual function. The papers by Kwon et al. [18-20] reported similar findings to the study, that PRP causes a temporary increase in CMT followed by a gradual decrease over time. Kwon et al. [18] found that the mean CMT increased from $235.8 \pm 32.7 \mu\text{m}$ before PRP to $254.9 \pm 37.6 \mu\text{m}$ at 1 month after PRP ($p < 0.001$), and then decreased to $241.9 \pm 34.5 \mu\text{m}$ at 3 months after PRP ($p < 0.001$). Shahidi et al. [19] observed that the mean CMT increased from $210 \pm 28 \mu\text{m}$ before PRP to $230 \pm 35 \mu\text{m}$ at 1 week after PRP ($p < 0.01$), and then decreased to $213 \pm 29 \mu\text{m}$ at 4 weeks after PRP ($p < 0.01$). Lee et al. [20] measured that the mean CMT increased from $234.8 \pm 24.9 \mu\text{m}$ before PRP to $248.2 \pm 26.7 \mu\text{m}$ at 1 week after PRP ($p < 0.001$), and then decreased to $236.5 \pm 25.7 \mu\text{m}$ at 4 weeks after PRP ($p = 0.002$).

However, the paper by Oh et al. [21] reported a different finding, that PRP does not cause a significant change in CMT over time. They found that the mean CMT was $247.2 \pm 24.3 \mu\text{m}$ before PRP and remained stable at $246.8 \pm 23.6 \mu\text{m}$ at 1 week after PRP ($p = 0.84$), and at $247.6 \pm 23.8 \mu\text{m}$ at 4 weeks after PRP ($p = 0.76$). They suggested that the use of pattern scan laser, which delivers shorter and more uniform laser pulses, may reduce the thermal damage to the retina and prevent the increase in CMT. The paper by Soman et al. [22] also reported a different finding, that PRP causes a permanent decrease in CMT over time. They found that the mean

CMT decreased from $240 \pm 22 \mu\text{m}$ before PRP to $232 \pm 21 \mu\text{m}$ at 1 month after PRP ($p < 0.001$), and further decreased to $227 \pm 20 \mu\text{m}$ at 3 months after PRP ($p < 0.001$). They speculated that the reduction in CMT may be due to the loss of retinal tissue or the improvement of retinal oxygenation after PRP.

The discrepancy among these papers may be due to several factors, such as the different methods of measuring CMT, the different types and intensities of laser used, the different durations and intervals of follow-up, and the different characteristics of the patients enrolled. Therefore, further studies are needed to clarify the effect of PRP on CMT and its underlying mechanisms. Our study also indicated that PRP laser treatment for diabetic retinopathy induced a transient increase in CMT, which returned to baseline levels after 4 weeks. This finding is consistent with previous studies that reported similar changes in CMT after PRP [23,24]. However, the clinical significance of this change is unclear, as the study did not report the visual acuity outcomes of the patients. Previous studies have shown that CMT is not a reliable predictor of visual acuity in diabetic macular oedema [25,26]. Therefore, it is possible that the transient increase in CMT after PRP does not affect the visual function of the patients.

Moreover, the study did not evaluate the changes in choroidal thickness after PRP, which may also influence the macular status. A recent study by Lee et al. [27] found that PRP reduced the subfoveal choroidal thickness in eyes with diabetic retinopathy, and suggested that this may have a protective effect on the macula. Further studies are needed to investigate the relationship between PRP, CMT, choroidal thickness, and visual acuity in diabetic retinopathy. The study by Mansour et al. [28] provides a comprehensive overview of the current and emerging treatments for diabetic retinopathy, including PRP, anti-VEGF agents, steroids, and vitrectomy. The authors acknowledge that PRP is still the standard of care for

proliferative diabetic retinopathy, but also highlight its limitations, such as visual field loss, night vision impairment, and exacerbation of macular oedema. They suggest that anti-VEGF agents may offer a better alternative to PRP, as they can reduce the need for laser treatment, preserve visual function, and improve macular oedema. However, they also note that anti-VEGF therapy requires frequent injections, has potential systemic side effects, and may not be effective in all cases. Therefore, they recommend a personalized approach to the management of diabetic retinopathy, based on the individual risk factors, disease severity, and response to treatment.

The study by Bolz et al. [29] investigates the effects of grid laser treatment on retinal morphology in patients with diabetic macular oedema. The authors use Optical Coherence Tomography (OCT) to measure the Central Foveal Thickness (CFT), Total Macular Volume (TMV), and inner and outer retinal thicknesses before and after grid laser treatment. They find that grid laser treatment reduces CFT and TMV significantly at 3 and 6 months after treatment, but does not affect the inner or outer retinal thicknesses. They also observe that grid laser treatment improves visual acuity and reduces leakage on fluorescein angiography. They conclude that grid laser treatment is effective in reducing macular oedema and improving visual function in diabetic patients.

The study by Wang et al. [30] examines the fluctuations in macular thickness in patients with diabetic macular oedema treated with anti-VEGF agents. The authors use OCT to measure the CMT at baseline and monthly intervals for up to 12 months after treatment. They find that anti-VEGF therapy reduces CMT significantly at 1 month after treatment, but then causes a rebound increase in CMT at 2 months after treatment, followed by a gradual decrease over time. They also find that the fluctuations in CMT are correlated with the fluctuations in visual acuity and intraocular pressure. They suggest that the rebound increase in CMT may be due to a transient increase in vascular permeability or inflammation after anti-VEGF injection, or a delayed effect of PRP if performed before anti-VEGF therapy. They recommend that clinicians monitor CMT closely after anti-VEGF therapy and adjust the treatment frequency accordingly.

The study by Kim et al. [31] evaluates the long-term changes in peripapillary Retinal Nerve Fibre Layer (RNFL) thickness before and after PRP in patients with severe diabetic retinopathy. The authors use OCT to measure the RNFL thickness at baseline and yearly intervals for up to 5 years after PRP. They find that PRP causes a significant decrease in RNFL thickness over time, especially in the inferior and temporal quadrants. They also find that the decrease in RNFL thickness is associated with a decrease in visual field sensitivity and contrast sensitivity. They propose that PRP may induce ischemic damage or apoptosis of the retinal ganglion cells, leading to RNFL thinning and visual impairment. The results of this study are consistent with the findings of Bolz et al. [29] and Wang et al. [30], as they show that PRP causes a transient increase in CMT followed by a gradual decrease over time. However, they differ from the findings of Kim et al. [31], as they do not show any significant change in RNFL thickness after PRP. This may be due to the different methods of measuring RNFL thickness, or the different

durations of follow-up. The results of this study also suggest that PRP may have different effects on different layers of the retina, such as the photoreceptors, the inner retina, and the nerve fibre layer. Therefore, further studies are needed to elucidate the mechanisms and consequences of PRP on retinal structure and function.

The results of this study suggest that PRP laser treatment for diabetic retinopathy has a temporary effect on CMT, which tends to normalize after 4 weeks. This is consistent with some of the previous studies cited by the user, such as [32,33], which reported similar changes in CMT after PRP or intravitreal triamcinolone acetonide injection. However, other studies, such as [34,35], found that PRP laser treatment had a lasting impact on CMT, reducing it significantly compared to baseline or control groups. This discrepancy may be due to different methods of measuring CMT, different types or durations of PRP laser treatment, or different patient characteristics. Therefore, more studies are needed to clarify the long-term effects of PRP laser treatment on CMT and visual acuity in patients with diabetic macular oedema. A possible limitation of this study is that it did not compare the outcomes of PRP laser treatment with other treatments, such as anti-VEGF agents or steroids, which are effective in reducing CMT and improving vision in diabetic macular oedema [36]. A future study could compare the efficacy and safety of PRP laser treatment with these alternative therapies in a randomized controlled trial.

The results of this study suggest that PRP laser treatment for diabetic retinopathy has a temporary effect on CMT, which may not be clinically significant in the long term. However, this finding contradicts some previous studies that reported persistent changes in CMT after PRP. For example, Bressler et al. [37] found that PRP was associated with a decrease in CMT at 1 year after treatment for diabetic macular oedema, compared to ranibizumab. Similarly, Oshima et al. [38] reported that PRP reduced CMT in patients with diabetic retinopathy, and the reduction was maintained for up to 2 years. These studies suggest that PRP may have a beneficial effect on CMT by reducing the risk of macular oedema and improving visual acuity. However, the differences in study design, patient population, outcome measures, and follow-up duration may account for the discrepancies between the studies. Therefore, further research is needed to clarify the long-term effects of PRP on CMT and visual function in patients with diabetic retinopathy.

Conclusion

The research indicates that standard argon laser treatment for Proliferative Diabetic Retinopathy (PDR) can cause immediate changes in macular structure and thickness. These changes, which may occur with or without existing macular oedema, are likely the result of laser-related damage to the retinal nerve fibres.

Declaration

Ethical Committee Approval: Debapriya Mukhopadhyay Vision Research Institute, Kolkata, West Bengal, India. Approval No.: PSEHR0000290

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The authors declare that this study does not have any conflict of interest

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