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ORIGINAL ARTICLE

Randomized Controlled Trial

Efficacy comparison of multipoint and single point scanning panretinal laser photocoagulation in non-proliferative diabetic retinopathy treatment

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Abstract

BACKGROUND

Non-proliferative diabetic retinopathy (NPDR) poses a significant challenge in diabetes management due to its microvascular changes in the retina. Laser photocoagulation, a conventional therapy, aims to mitigate the risk of progressing to proliferative diabetic retinopathy (PDR).

AIM

To compare the efficacy and safety of multi-spot *vs* single-spot scanning panretinal laser photocoagulation in NPDR patients.

METHODS

Forty-nine NPDR patients (86 eyes) treated between September 2020 and July 2022 were included. They were randomly allocated into single-spot (n = 23, 40 eyes) and multi-spot (n = 26, 46 eyes) groups. Treatment outcomes, including best-corrected visual acuity (BCVA), central macular thickness (CMT), and mean threshold sensitivity, were assessed at predetermined intervals over 12 months. Adverse reactions were also recorded.

RESULTS
Energy levels did not significantly differ between groups ($P > 0.05$), but the multi-spot group exhibited lower energy density ($P < 0.05$). BCVA and CMT improvements were noted in the multi-spot group at one-month post-treatment ($P < 0.05$). Adverse reaction incidence was similar between groups ($P > 0.05$).

CONCLUSION
While energy intensity and safety were comparable between modalities, multi-spot scanning demonstrated lower energy density and showed superior short-term improvements in BCVA and CMT for NPDR patients, with reduced laser-induced damage.

Key Words: Panretinal laser photocoagulation; Non-proliferative diabetic retinopathy; Efficacy comparison; Multipoint; Single point; Treatment assessment

Core Tip: This study compares the therapeutic effectiveness of multipoint and single-point scanning panretinal laser photocoagulation in non-proliferative diabetic retinopathy (NPDR) patients. The results showed that both treatment modalities had similar energy intensity and safety profiles, but the multipoint scanning mode had a lower energy density. In the short term, the multipoint scanning mode demonstrated better improvement in best-corrected visual acuity and central macular thickness compared to the single-point mode. Additionally, the multipoint mode resulted in less laser damage. These findings suggest that multipoint scanning may be a preferred treatment approach for NPDR patients.

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INTRODUCTION

Diabetes is a comprehensive disease caused by absolute or relative insulin deficiency, leading to reduced sensitivity of target tissue cells to insulin, resulting in metabolic disturbances of proteins, fats, water, electrolytes, *etc*[1,2]. Data show that in recent years, with the improvement of residents' living standards, the prevalence of diabetes has been increasing year by year. In 2013, the prevalence of diabetes in adults in China was about 10.9%, with a total number of cases of approximately 110 million, ranking first in the world[3,4]. The most typical clinical manifestation of diabetes is elevated blood sugar, and long-term hyperglycemia can cause varying degrees of damage to multiple organs. Diabetic retinopathy (DR), caused by long-term hyperglycemia stimulation leading to retinal microvascular damage, is one of the common complications in the late stage of diabetes and the main cause of visual impairment and blindness in diabetic patients[5, 6]. Although global awareness of diabetes prevention and treatment has increased in recent years, the incidence of DR has not decreased, especially in low-income and middle-income countries.

Non-proliferative DR (NPDR) is a type of DR, accounting for approximately 19.1% of the total cases, which is significantly higher than the 2.8% of proliferative DR (PDR)[7]. The central macular thickness (CMT) refers to the thickness of the macula, which is the central part of the retina responsible for sharp, central vision. It's a crucial measure in assessing retinal health, especially in conditions like DR and age-related macular degeneration, where thickening of the macula can indicate disease progression. Clinical practice has indicated that early clinical symptoms of NPDR include bleeding and exudation, and it may progress to late stages with vascular proliferation and even blindness. Therefore, early treatment of NPDR is of great significance in improving the quality of life of diabetic patients[8]. Currently, treatment options for NPDR include medication intervention, laser photocoagulation, and vitrectomy. Among them, laser photocoagulation is widely used in clinical practice and has been proven in multiple studies to effectively improve clinical symptoms in NPDR patients[9,10]. However, there is still some controversy regarding the selection of laser treatment techniques for NPDR. Traditional laser photocoagulation for NPDR often uses single-spot or continuous single-spot emission, which, although effective, carries the risk of inducing visual field narrowing and decreased visual acuity [11]. In recent years, the clinical value of multi-spot scanning laser in the treatment of NPDR has been discovered. This study, through the establishment of a control group, found that compared to single-spot laser, the multi-spot scanning laser mode helps in the short-term visual recovery of NPDR patients after surgery, and the energy density is lower than that of single-spot scanning laser.

MATERIALS AND METHODS

General information

A total of 49 patients (86 eyes) diagnosed with NPDR and treated in our hospital from September 2020 to July 2022 were selected as the research subjects. They were randomly separated into the Single Spot Group (n = 23, 40 eyes) and the Multiple Spot Group (n = 26, 46 eyes). The approval of the Hospital Ethics Committee has been obtained for this study. The patients had given consent to participate in the study or treatment.

Inclusion criteria: (1) Age ≥ 18 years; (2) Type II diabetes patients; (3) Diagnosed with NPDR through fundus examination; and (4) Complete clinical data.

Exclusion criteria: (1) Patients with malignant tumors; (2) Patients with a history of laser photocoagulation therapy of the fundus; (3) Patients with poor dilation of the pupil or posterior synechiae that make laser photocoagulation therapy difficult; (4) Patients with coagulation disorders; (5) Patients already enrolled in other ongoing clinical studies; and (6) Pregnant or lactating women.

Intervention methods

The Single Spot Group received single-spot scanning laser photocoagulation therapy. The exposure time was set at 100-300 ms, and the total retinal photocoagulation was divided into four sessions, with each session targeting one quadrant starting from the inferior temporal quadrant. If the patient had concurrent macular edema, macular photocoagulation was performed first. The interval between the two photocoagulation sessions was 7 days, and the number of photocoagulated spots per session was approximately 300-500. The Multiple Spot Group received multiple-spot scanning laser photocoagulation therapy, using an approach from the periphery to the center. A total of six sessions were performed to complete the total retinal photocoagulation, with approximately 230 spots per session and a total of approximately 1500-2000 spots. The retinal photocoagulation procedures for both groups were performed by the same physician.

Observation indicators and evaluation criteria

Clinical data, including sex, age, body mass index, smoking, drinking, alanine aminotransferase (ALT) level, aspartate aminotransferase (AST) level, *etc*, were collected for both groups. The laser energy used during the therapies was recorded for both groups, and the energy density was calculated. Follow-up evaluations were conducted 12 months after therapy to assess the effectiveness rate, based on improvements of ≥ 2 Lines in best-corrected visual acuity (BCVA) indicating improvement, improvements of ≥ 2 Lines indicating worsening, and no change. BCVA and CMT were measured before therapy, 1 month, 6 months, and 12 months after therapy for inter-group comparisons. The incidence of adverse reactions such as iritis and vitreous hemorrhage within 12 months of follow-up after therapy was also analyzed.

Statistical analysis

Normality was assessed for continuous variables using Shapiro-Wilk test. The t-test utilized in this study was one-tailed. Continuous data are presented as mean ± SD, and comparisons between groups were made using one-tailed t-tests. Data collection was performed using Excel 2021. Data processing and analysis were conducted using SPSS 19.0. Categorical data are presented as percentages (%), and comparisons between groups were made using χ^2 tests. A significance level of $P < 0.05$ was used to determine statistical significance.

RESULTS

Comparison of baseline clinical data

A total of 46 patients were included in this study, including 26 patients in the multipoint group and 23 patients in the single point group. The baseline clinical data of the enrolled patients, such as sex, age, body mass index, ALT, AST, serum creatinine, and creatine kinase levels, were included in the study, and intergroup distinctions were compared. The comparison showed no obvious distinctions in baseline clinical data of patients ($P > 0.05$), indicating good comparability (Table 1). There was no obvious distinction in laser energy ($P > 0.05$), but the energy density of the multipoint group was lower than that of the single point group, and the distinction was obvious ($P < 0.05$) (Table 2 and Figure 1).

The effective rate was different

In the multipoint group, the visual acuity improved in 17 cases, remained unchanged in 26 cases, and decreased in 3 cases. There was no obvious distinction in the change of visual acuity ($P > 0.05$) (Table 3 and Figure 2).

Comparison of LogMAR BCVA before and after therapy

Before therapy, there was no obvious distinction in LogMAR BCVA ($P > 0.05$). After 1 month of therapy, the LogMAR BCVA in the multipoint group was lower than the single point group, and the distinction was obvious ($P < 0.05$). However, there was no obvious distinction in LogMAR BCVA after 6 months and 12 months of therapy ($P > 0.05$) (Table 4, Figure 3A).

Table 1 Comparison of baseline clinical data, *n* (%)

Clinical parameters	Multi-point mode, *n* = 26	Single point mode, *n* = 23	t/χ^2	*P* value
Male sex	16 (61.64)	12 (52.17)	0.437	0.509
Average age in years	44.92 ± 6.35	44.22 ± 6.40	0.384	0.703
Average body mass index in kg/m^2	22.80 ± 2.87	23.95 ± 2.50	1.486	0.144
Smoking	3 (11.54)	4 (17.39)	0.341	0.559
Alcohol drinker	3 (11.54)	3 (13.04)	0.026	0.873
ALT in U/L	29.11 ± 14.54	29.83 ± 14.13	0.175	0.862
AST in U/L	34.22 ± 16.64	36.20 ± 17.02	0.411	0.683
FBG in mmol/L	5.20 ± 0.85	5.30 ± 1.01	0.376	0.708
Creatinine in μmol/L	72.48 ± 14.73	63.26 ± 17.67	1.992	0.052
Creatine kinase in U/L	181.87 ± 135.88	177.37 ± 114.54	0.124	0.902
Uric acid in μmol/L	373.43 ± 95.80	389.90 ± 96.51	0.599	0.552
Concurrent diseases				
Hypertension	2 (7.69)	4 (17.39)	1.068	0.301
Nonalcoholic fatty liver disease	2 (7.69)	1 (4.35)	0.238	0.626
Liver cirrhosis	1 (3.85)	0 (0.00)	0.903	0.342

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; FBG: Fasting blood glucose.

Table 2 Comparison of surgical indicators

Groups	Eyes	Laser energy in mW	Energy density in mW·ms/μm^2
Multipoint group	46	551.93 ± 64.25	0.51 ± 0.08
Single point group	40	540.64 ± 73.77	2.02 ± 0.92
t	-	0.759	11.094
P value	-	0.450	0.000

Table 3 Distinctions in therapy response rates, *n* (%)

Groups	Eyes	Changes in vision		
		Improve	Unchanged	Decline
Multipoint group	46	17 (36.96)	26 (56.52)	3 (6.52)
Single point group	40	8 (20.00)	25 (62.50)	7 (17.50)
χ^2	-	2.983	0.574	2.509
P value	-	0.084	0.317	0.113

Comparison of CMT before and after therapy

Before therapy, there was no obvious distinction in CMT ($P > 0.05$). After 1 month of therapy, the CMT in the multipoint group was lower than the single point group, and the distinction was obvious ($P < 0.05$). However, there was no obvious distinction in CMT after 6 months and 12 months of therapy ($P > 0.05$) (Table 5, Figure 3B).

Comparison of the incidence rates of adverse reactions

In the multipoint group, there was 1 case of iritis and 1 case of vitreous hemorrhage. The overall occurrence rate of adverse reactions is 7.69% (2/26). There was no obvious distinction in comparison to the single point group, which had an incidence rate of 17.39% (4/23) (Table 6, Figure 4).

Table 4 Comparison of LogMAR best-corrected visual acuity before and after therapy

Groups	Eyes	Pre-therapy	1 month after surgery	6 months after surgery	12 months after surgery
Multipoint group	46	0.65 ± 0.08	0.54 ± 0.10	0.49 ± 0.11	0.51 ± 0.10
Single point group	40	0.68 ± 0.09	0.60 ± 0.10	0.48 ± 0.09	0.53 ± 0.06
t	-	1.637	2.775	0.457	1.103
P value	-	0.105	0.007	0.649	0.273

Table 5 Comparison of central macular thickness before and after therapy

Groups	Eyes	Pre-therapy	1 month after surgery	6 months after surgery	12 months after surgery
Multipoint group	46	446.36 ± 175.99	366.74 ± 102.17	346.41 ± 85.47	345.72 ± 82.03
Single point group	40	455.08 ± 118.94	423.35 ± 94.54	359.14 ± 76.18	349.35 ± 86.54
t	-	0.265	2.653	0.724	0.200
P value	-	0.792	0.010	0.471	0.842

Table 6 Comparison of the incidence of adverse reactions, *n* (%)

Groups	Cases	Iritis	Vitreous hemorrhage	Tractional retinal detachment	Overall incidence
Multipoint group	26	1 (3.85)	1 (3.85)	0 (0.00)	2 (7.69)
Single point group	23	2 (8.70)	1 (4.35)	1 (4.35)	4 (17.39)
Fisher	-	-	-	-	1.068
P value	-	-	-	-	0.301

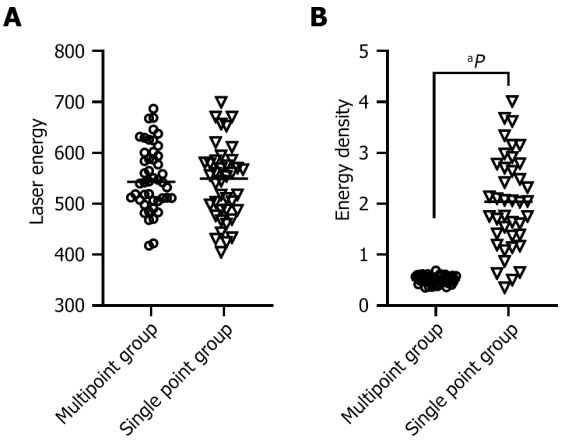

Figure 1 The laser energy in the multipoint group and single point group. A: The difference of laser energy between multi-point group and single-point group was not statistically significant ($P > 0.05$); B: The energy density of multi-point group was lower than that of single-point group, and the difference was statistically significant ($P < 0.05$). $^aP < 0.05$.

DISCUSSION

Diabetes is a metabolic-related disease characterized by high blood sugar levels. DR is one of the common complications of diabetes, and with the progression of the disease, almost every diabetic patient will develop different manifestations of complications. Among them, DR is the most common[12-15]. From a clinical perspective, DR can be categorized into two forms based on the development of new blood vessels: PDR and NPDR. NPDR is an initial indication, while PDR is a more advanced stage[13]. The early clinical symptoms of NPDR are not obvious, and patients' vision does not obviously change. However, as the condition worsens, patients may experience an obvious reduction in vision, along with manifestations such as retinal capillary dilation, and the presence of hemorrhages, exudates, and cotton wool spots[14]. Early intervention is crucial in NPDR, and proactive surgery can help to seal retinal vascular leaks, prevent new bleeding, and

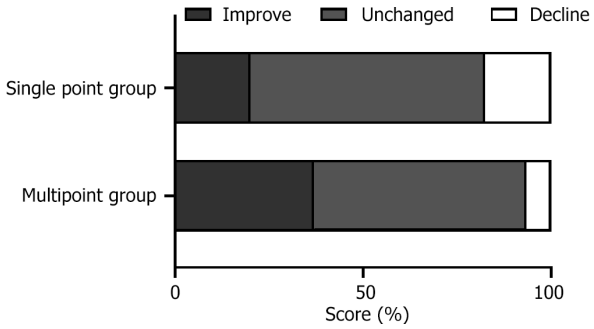

Figure 2 Distinction in therapy effectiveness.

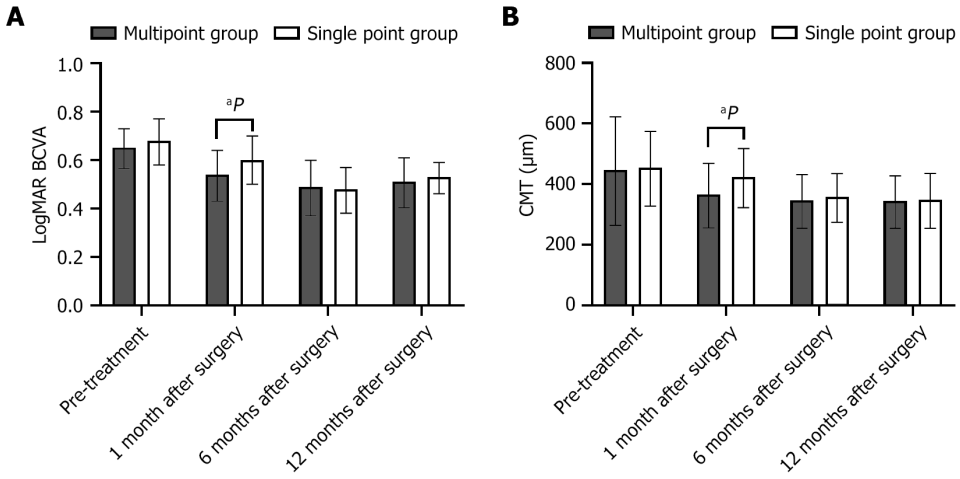

Figure 3 Comparison of LogMAR best-corrected visual acuity between the two groups before and after treatment. A: LogMAR best-corrected visual acuity; B: Central macular thickness. There was no significant difference between the multi-point group and the single-point group before treatment ($P > 0.05$), and the multi-point group was lower than the single-point group 1 month after treatment ($P < 0.05$), and there was no significant difference between the multi-point group and the single-point group 6 months and 12 months after treatment ($P > 0.05$). $^aP < 0.05$. CMT: Central macular thickness.

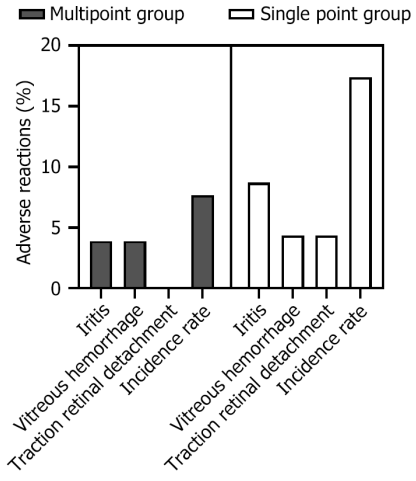

Figure 4 Comparison of adverse reaction rates.

suppress the development of neovascularization, thereby achieving therapy goals[15]. In this study, the clinical value of multi-point scanning laser photocoagulation and single-point scanning laser photocoagulation in NPDR patients was analyzed using a control group. The results showed no obvious distinction in the therapy efficacy between multi-point scanning laser photocoagulation and single-point scanning laser photocoagulation, suggesting similar effectiveness of both procedures. The mechanism of laser photocoagulation in the therapy of NPDR can be summarized as follows: (1) The thermal coagulation effect of laser can transform high oxygen-consuming photoreceptors into low oxygen-consuming glial components, thereby redistributing oxygen to other retinal tissues and improving retinal blood circulation[16]; (2)

Laser can destroy the ischemic areas of the retina, preventing neovascularization within those regions[17]; (3) By disrupting the outer barrier of the retina, laser allows oxygen previously trapped in the outer retina to reach the inner retina, thus improving oxygen supply to the inner retina[18]; and (4) Photocoagulation helps to inhibit the overexpression of cyclooxygenase-2 and vascular endothelial growth factor in NPDR patients, preventing the occurrence of neovascularization[19]. The manner in which laser photocoagulation is applied does not obviously affect its effectiveness, and therefore, there is no obvious distinction in the clinical efficacy.

Furthermore, follow-up was conducted on patients in the single-point and multipoint groups. The results showed that at 1 month after therapy, the LogMAR BCVA and CMT were obviously lower in the multipoint group in comparison to the single point group. The authors of this study analyzed the reasons as follows: Although single-point scanning laser has less powerful laser energy, it has higher energy density. After absorption by the target tissue, it produces a high-temperature effect in a short period of time, causing greater damage to the choroid and retina, resulting in a higher risk of reactive macular edema[20]. On the other hand, multi-point scanning laser utilizes a pre-designed short pulse sequence to rapidly complete pan-retinal photocoagulation, keeping the exposure time below 50 ms. The reduction in energy density and shorter laser irradiation time effectively limit the range of thermal conduction, minimizing damage to the retinal pigment epithelium and photoreceptor layer, and obviously reducing CMT in patients after surgery[21,22]. At 6 months and 12 months of follow-up, there was no obvious distinction in LogMAR BCVA and CMT. The reason for this is that both single-point and multi-point scanning laser photocoagulation can effectively control the exacerbation of diabetic macular edema, which is consistent with the similar therapy efficacy observed. Finally, the study compared the occurrence of complications during follow-up, and found no obvious distinction in the incidence of adverse reactions, indicating that both single-point scanning laser photocoagulation and multi-point scanning laser photocoagulation are safe in the therapy of NPDR.

CONCLUSION

Multi-point and single-point scanning laser photocoagulation have similar therapeutic effects on NPDR, with similar laser energy intensity and safety. However, multi-point scanning has lower energy density in comparison to single-point scanning, and in the short term after therapy, the multi-point approach shows better improvement in BCVA and CMT for NPDR patients, with less laser-induced damage. Although this study compared the distinctions in the effectiveness of multi-point scanning laser photocoagulation and single-point scanning laser photocoagulation in the therapy of NPDR, it has limitations such as a small sample size and relatively short follow-up time. Adding laboratory examination results to the study would help further compare the advantages and disadvantages of the two.

FOOTNOTES

Author contributions: Zhang YZ, Gong H, Yang J, Bu JP, and Yang HL designed the research study; Zhang YZ, Gong H, and Bu JP performed the research; Zhang YZ, Gong H, and Yang J contributed new reagents and analytic tools; Zhang YZ, Bu JP, and Yang HL analyzed the data and wrote the manuscript; All authors have read and approved the final manuscript.

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Clinical trial registration statement: This study has not yet been registered with clinical trials.

Informed consent statement: All research participants or their legal guardians provided written informed consent prior to study registration.

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