Original Article

JHSMR Journal of Health Science and Medical Research

Long-term Efficacy of Q-switched 1064 nm Nd-YAG Laser for Treatment of Split-thickness Skin Graft: A Randomized Controlled Trial

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Received 19 May 2021 ● Revised 1 July 2021 ● Accepted 6 July 2021 ● Published online 20 September 2021

Abstract:

Objective: The aim of this study was to investigate the efficacy of the Q-switched 1064 nm Nd:YAG laser for reducing hyperpigmentation and erythema and increasing pliability in skin grafts.

Material and Methods: This was a prospective randomized controlled trial. Half of each skin graft was treated with a Q-switched 1064 nm Nd:YAG laser 4 times, and the other half was left untreated and collectively used as the controls. The treatment results were evaluated by clinical photographs, and assessment of the melanin index (MI), erythema index (EI), and elasticity parameters at baseline and at 2 weeks after each session and 1 month after the final treatment.

Results: Ten skin graft sites from 10 patients were included. Most patients had lesions at a lower extremity. After 4 sessions of treatment, average melanin index at the treated sites was non-significantly decreased compared to both baseline (p-value=0.232) and the untreated sites (p-value=0.770). The elasticity of the treated sites increased significantly when compared to baseline (p-value=0.039), but non-significantly when compared to the untreated sites (p-value=0.846). The EI at the treated sites non-significantly decreased compared to both baseline (p-value=0.432) and the untreated sites (p-value=0.164).

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J Health Sci Med Res 2022;40(3):309-316
doi: 10.31584/jhsmr.2021840
www.jhsmr.org

Conclusion: This study found the Q-switched 1064 nm Nd:YAG laser treatment to be a potentially promising modality for increasing the pliability of skin grafts, but reductions in hyperpigmentation and erythema were only clinically significant.

Keywords: long-term efficacy, Q-switched 1064 nm Nd-YAG laser, split-thickness skin graft, treatment

Introduction

Hyperpigmentation and poor skin texture are commonly observed side effects of split-thickness skin grafting (STSG) in Asian people. In addition to being difficult to treat, these adverse effects are often a source of patient self-consciousness and discomfort. Several hypotheses have been proposed that suggest a link between hyperpigmentation and the stimulation of melanogenesis; however, a definitive cause has not yet been conclusively established.[1-3] Many treatment options exist for hyper pigmentation, such as chemical peeling, bleaching creams, cryosurgery, and dermabrasion, but none of those treatment alternatives has provided good results.

Q-switched lasers are widely accepted and commonly used to treat abnormal pigmentation in the epidermis and dermis. The Q-switched 1064 nm Nd:YAG laser has a 1064 nm wavelength that can be absorbed by melanin. This laser produces a nanosecond pulse width that is shorter than the thermal relaxation time of melanosomes (about 1 millisecond), which reduces the chance of injury to surrounding tissue. By way of photomechanical reaction, the photo energy rapidly transforms to thermal energy inside the target, which causes breakage of target tissue into small particles that are then eliminated via lymphatic transport.[4]

This laser has been used to treat pigmentation abnormalities for decades, including abnormal pigmentation in the epidermis (e.g., freckles, solar lentigines, and seborrheic keratosis), abnormal pigmentation in the dermis (e.g., nevi of Ota, Hori's nevi), and abnormal pigmentation in both the epidermis and dermis (e.g., Becker's nevi and junctional melanocytic nevi).[5-7] This laser stimulates new collagen synthesis, which can improve skin texture, it inhibits collagen degradation, and it is used to treat skin problems, such as post-acne hyperpigmentation and post-acne erythema.[8-10]

Although the Q-switched 1064 nm Nd:YAG laser has been accepted and used as a standard treatment for hyperpigmented skin lesions, no previous study has investigated the use of this laser to prevent and treat hyperpigmented skin grafts or to improve skin texture in split-thickness skin grafts. Accordingly, the aim of this study was to investigate the efficacy of a Q-switched 1064 nm Nd:YAG laser for reducing hyperpigmentation, reducing erythema, and increasing pliability in Asian split-thickness skin grafts compared to untreated skin grafts and normal skin.

Material and Methods

This prospective randomized controlled trial was conducted from September 2017 to September 2018 at the outpatient unit of the Division of Plastic and Reconstructive Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

After receiving approval from the Siriraj Institutional Review Board (SIRB) (COA no. 535/2017), 10 patients (6 males, 4 females) with 10 lesions diagnosed as hyperpigmented split-thickness skin grafts were enrolled in this study. Written informed consent was obtained from all study participants. The inclusion criteria were patients aged 18-80 years who underwent split-thickness skin grafts which developed hyperpigmentation after the STSG healed. Patients having one or more of the following were excluded:

chemical peel, laser and/or intense pulsed light treatment within the previous year, coagulopathy, pregnancy, and/or diabetes mellitus.

Prior to the laser treatment, each patient's representative hyperpigmented split-thickness skin graft was identified and photographed for subsequent localization, pigmentation assessment, and elasticity assessment. Baseline melanin index measurements were then obtained at normal skin and the area of the STSG using a Mexameter® MX18 probe (Courage & Khazaka GmbH, Cologne, Germany), which has an arbitrary numeric scale of 0 to 999. Elasticity parameter measurements were then obtained at normal skin and the area of the STSG using a Cutometer® Dual MPA 580 probe (Courage & Khazaka GmbH, Cologne, Germany)

Before each laser treatment, topical lidocaine cream (a mixture of 2.5% lidocaine and 2.5% prilocaine; AstraZeneca AB, Sodertalje, Sweden) was applied to the hyperpigmented split-thickness skin graft. Low-fluence laser treatments were performed with a Q-switched 1064 nm Nd:YAG laser (SPECTRA XT) with a spot size of 6 mm for a total of 4 sessions that were performed at intervals of 2-4 weeks. The laser treatment was applied to 50.0% of the area of the STSG with appropriate overlap for a total of 8 passes or until the lesion showed mild erythema without petechiae or epidermal whitening. Each treatment session took about 15-20 minutes. The fluence of the laser treatment was set at 2-2.5 joules per square centimeter with adjustments according to the patient's response to the previous treatment session and the patient's sensitivity to pain. Objective assessments were performed using a Mexameter® and a Cutometer® to assess melanin content, erythema, and elasticity at baseline, at 2 weeks after each session, 1 month after the final treatment, and every month until the 1-year time point. The patients were instructed to avoid sun exposure. In instances where sun exposure was unavoidable, the patient was advised to apply sunscreen SPF 50 PA+++ 30 minutes before sun exposure, and to reapply the same product every 2 hours.

Assessment of treatment response

The patients were evaluated at baseline and assessed before treatment at every visit and at 1 month after the last visit by measurement of melanin and erythema indices by a Mexameter® and measurement of elasticity parameters by a Cutometer® at 3 areas (normal skin, the STSG area that was treated by Q-switched 1064 nm Nd:YAG laser, and the non-laser-treated STSG area that was the control). The averages of 3-5 melanin and erythema index readings and 3-5 elasticity parameter readings were computed as the final values.

The patients were asked to report any symptoms that developed after their treatments. Photographs were taken at every visit, and complications, including erythema, hyperpigmentation, and hypopigmentation, were recorded.

Results

Eleven patients with 11 lesions met the inclusion criteria, but 1 patient withdrew from the study, so the remaining 10 patients (6 males, 4 females) with 10 lesions were enrolled. The average age at presentation was 51.7 years (range: 29-73). Of the 10 split-thickness skin graft lesions, 5 were performed following by tumor excision, 2 were post-burn defects, 2 were donor sites from flap harvesting and 1 was a chronic wound. The average duration from operation to laser treatment was 57 days (range: 12-120) (Table 1).

There was no significant difference in the baseline melanin index scores between the control areas and the laser-treated areas of the STSGs (means: 385.7 and 369.1, respectively). There was also no significant difference in the erythema index scores between the control areas and the laser-treated areas of the STSGs (means: 413.3 and 408.2, respectively).

Table 1 Demographic and clinical characteristics of included patients

Characteristic	Maximum	Minimum	Mean	S.D.
Age (years)	29.0	73.0	51.7	14.33
Body mass index (kg/m^2)	18.3	31.3	24.0	3.59
Hematocrit (%)	24.8	49.0	39.7	7.91
Albumin (g/dL)	2.5	5.0	4.0	0.91
Fasting blood sugar (mg%)	103.0	117.0	110.0	9.89
Blood urea nitrogen (mg%)	7.8	16.4	11.5	3.25
Creatinine (mg/dL)	0.7	1.1	0.9	0.14
Time to intervention (days)	120	12	57.1	45.19
Size (cm^2)	330	15	135.6	104.35

S.D.=standard deviation

Table 2 Mean, median percentage change, and p-value in each study group

Parameter	Mean±standard deviation		% Change from baseline to month 12		No laser vs. laser
	Baseline	Month 12	Median (min, max)	p-value	p-value
Melanin					
No laser	386±146	460±167	14 (-38, 138)	0.232	0.770
Laser	369±109	441±149	10 (-18, 101)	0.232	
Normal skin	391±149	365±127	-4 (-42, 65)		
Erythema					
No laser	413±97	396±135	-2 (-40, 42)	0.625	0.846
Laser	408±94	386±98	-4 (-35, 28)	0.432	
Normal skin	368±117	378±126	2 (-41, 45)		
Elasticity					
No laser	0.62±0.14	0.62±0.12	0 (-44, 46)	1	0.164
Laser	0.64±0.13	0.73±0.15	20 (-21, 50)	0.039	
Normal skin	0.79±0.11	0.77±0.11	-1 (-6, 0)		

A p-value<0.050 indicates statistical significance

Objective melanin index measurement

We compared differences in the mean melanin index between baseline and after laser treatment in normal skin and in the control and laser-treated areas of the STSGs (Figure 1). That analysis revealed a clinically significant, but not statistically significant (p-value=0.232), decrease in pigmentation at the laser-treated areas at the 12th visit (after 4 sessions of laser treatment). There was also no statistically significant difference between the non-laser-treated STSGs and the laser-treated STSGs (p-value =0.770) (Table 2 and Figures 1, 4).

Objective erythema index measurement

We compared differences in the mean erythema indexes between baseline and after laser treatment in normal skin and in the control and laser-treated areas of the STSGs (Figure 2). We observed a clinically significant, but not statistically significant (p-value=0.432), decrease in

erythema at the laser-treated areas at the 12th visit (after 4 sessions of laser treatment). No significant difference was observed between the non-laser-treated STSG areas and the laser-treated STSG areas (p-value=0.846) (Table 2 and Figure 2, 4).

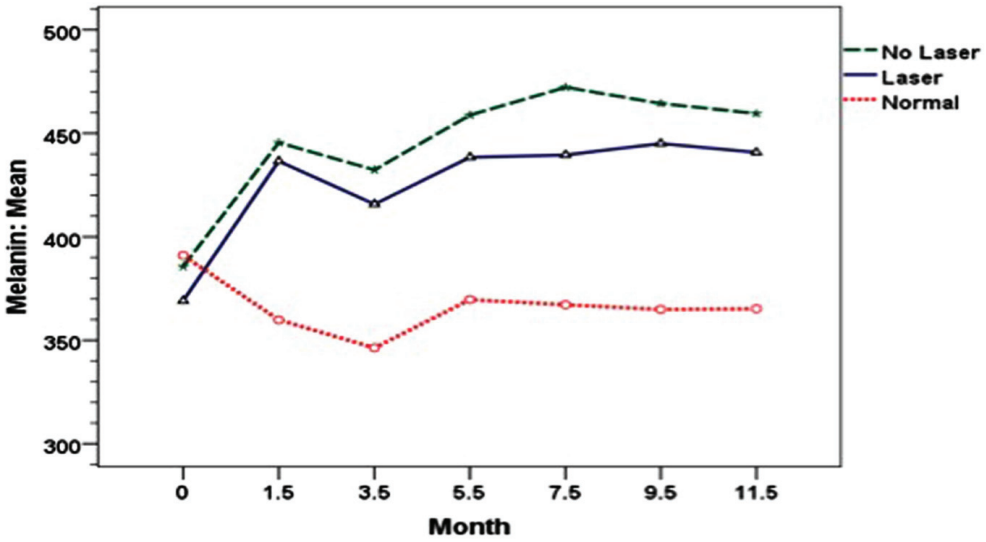

Figure 1 Mean melanin index compared among the no laser treatment, laser treatment, and normal skin groups at different time points

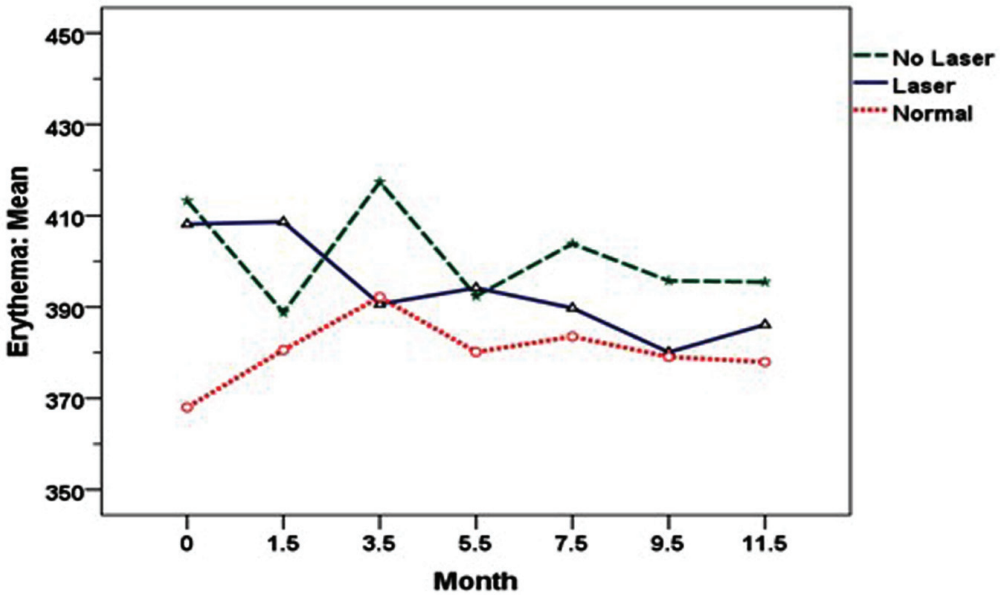

Figure 2 Mean erythema index compared among the no laser treatment, laser treatment, and normal skin groups at different time points

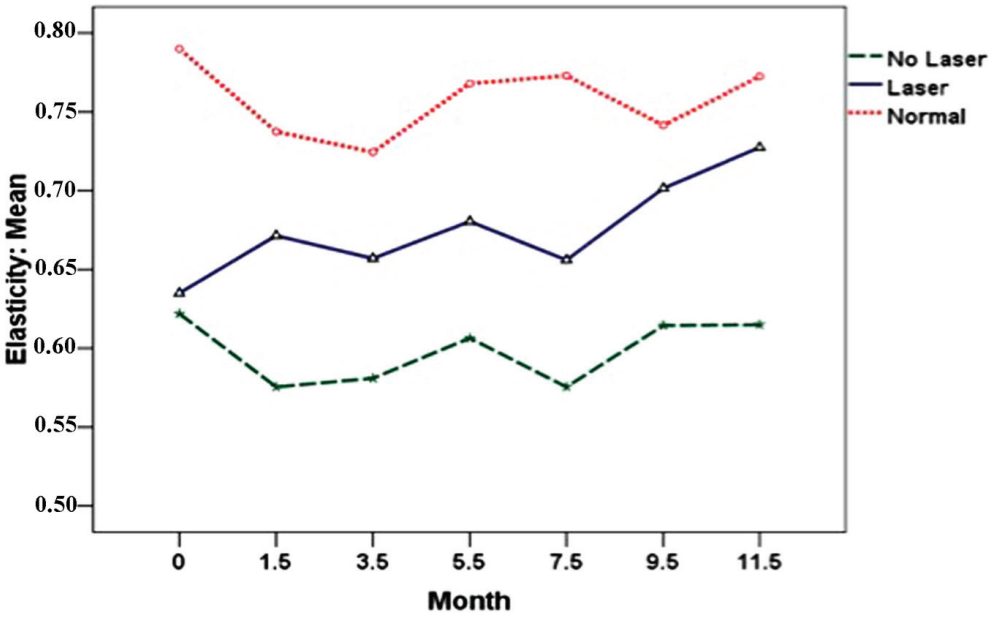

Figure 3 Mean elasticity index compared among the no laser treatment, laser treatment, and normal skin groups at different time points

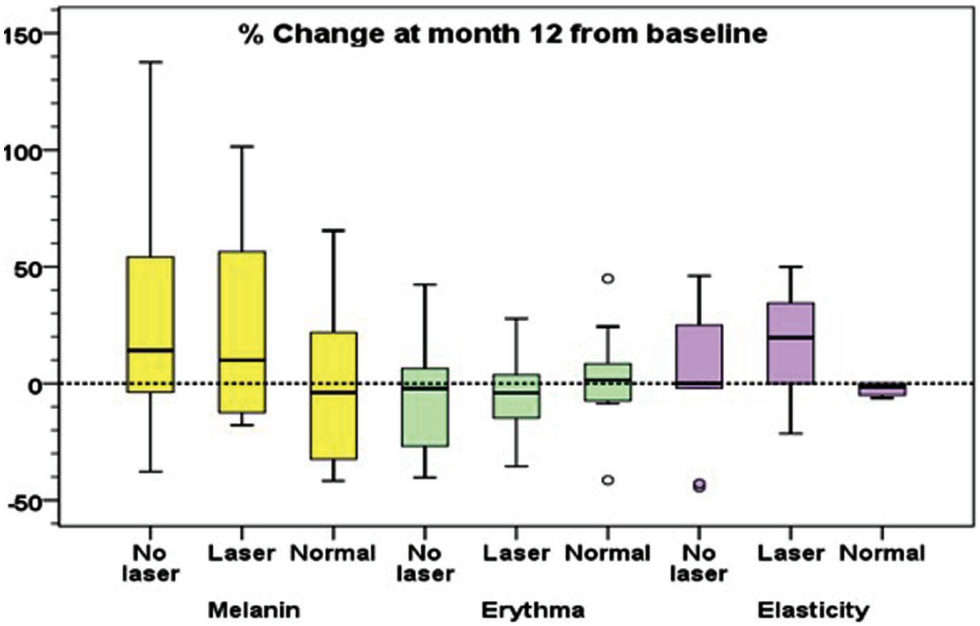

Figure 4 Median percentage change from baseline to month 12 for melanin, erythema, and elasticity compared among the no laser treatment, laser treatment, and normal skin groups

Objective elasticity index measurement

We compared differences in the mean elasticity index between baseline and after laser treatment in normal skin and in the control and laser-treated areas of the STSGs (Figure 3). Our findings revealed clinically significant and statistically significant (p-value=0.039) improvement in elasticity in the laser-treated areas at the 12th visit (after 4 sessions of laser treatment). However, no statistically significant improvement was found when we compared between the non-laser-treated and laser-treated areas of the STSGs (p-value=0.164) (Table 2 and Figure 3, 4).

Discussion

Hyperpigmentation after split-thickness skin grafting is a common problem that is caused by increased activity of melanocytes, which become larger in size, highly dendritic, and crowded with melanin granules.[1] It is also caused by the distribution, degradation pattern, and size of the melanosomes within keratinocytes.[2] All of these factors may contribute to the hyperpigmentation of a skin graft. In addition to hyperpigmentation, reduced elasticity after the skin grafting procedure can lead to patient discomfort.

Several modalities have been proposed and studied for the treatment of hyperpigmented skin grafts. One study used cryopreservation with trehalose treat hyperpigmented skin grafts in mice[3], but no similar studies have been performed in humans.

The advent of Q-switched lasers, which facilitates selective destruction of target melanocytes, has resulted in safe and effective treatment for pigmented lesions. The mechanism of Q-switched 1064 nm Nd:YAG laser in the treatment of pigmented lesions is based on the principle of selective photothermolysis. Thermal damage limited to dermal melanocytes can treat pigmented lesions with minimal thermal damage to surrounding tissue and less scarring.[4]

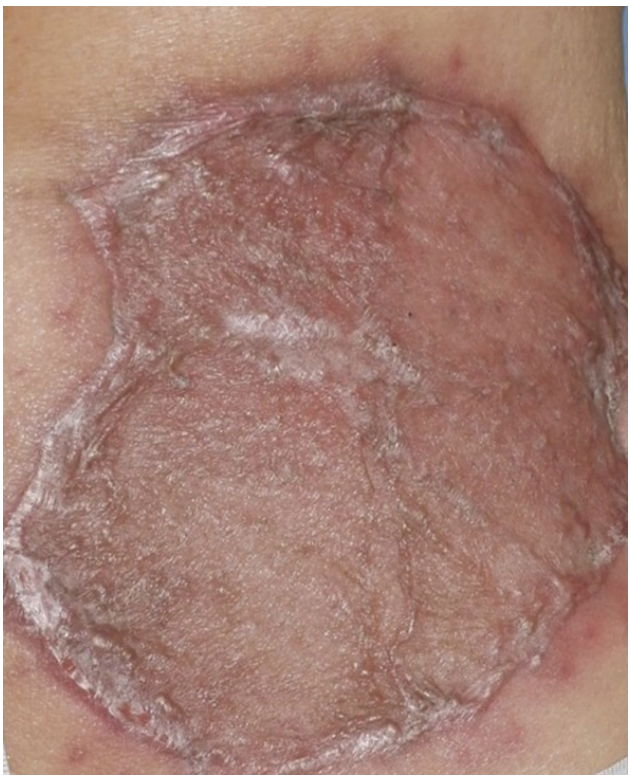

Figure 5 The split thickness skin graft after treatment with Nd-YAG and non-Nd-YAG at 12-month follow-up

The Q-switched 1064 nm Nd:YAG laser treatment used in this study showed clinically significant decreases in melanin indexes after 4 sessions of treatment. Repeated treatment with the Q-switched 1064 nm Nd:YAG laser also showed significant decreases in melanin indexes when compared to the control areas. However, when we compared between untreated STSG and the Nd:YAG-treated STSG areas, no statistically significant difference was observed, which meant that no hypopigmentation occurred in the Nd:YAG-treated STSG areas. Moreover, when we observed the clinical presentation of the treated areas, we found no hypopigmentation. Regarding the mean erythema index, we found no statistically significant difference between the control and treatment areas. In

contrast, our analysis revealed a statistically significant difference between the Nd:YAG-treated STSG area at the first visit and the Nd:YAG-treated STSG area at the last visit. No complications were observed in this study because we used low fluence, which helped to minimize complications. Overall, better quality of skin was observed at the laser-treated areas, and this may be due to stimulation of new collagen synthesis by the laser treatment (Figure 5).

Conclusion

This study found the Q-switched 1064 nm Nd:YAG laser treatment to be a potentially promising modality for increasing the pliability of skin grafts, but reductions in hyperpigmentation and erythema were only clinically significant.

Acknowledgement

The authors gratefully acknowledge the patients who agreed to participate in this study.

Funding sources

This research project was supported by a grant from the Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.

Conflict of interest

All authors declare no personal or professional conflicts of interest, and no financial support from the companies that produce and/or distribute the drugs, devices, or materials described in this report.

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