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ORIGINAL ARTICLE

A split-face study: comparison of picosecond alexandrite laser and Q-switched Nd:YAG laser in the treatment of melasma in Asians

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Abstract

To evaluate efficacy and safety of picosecond 755 nm alexandrite laser as compared to 1064 nm QS-Nd:YAG laser for melasma treatment in Asians. Twelve patients received 4 sessions of treatments at 1-month interval in a split-face manner. The right side of each patient's face received 755 nm picosecond laser, and the other side received 1064 nm QS-Nd:YAG laser. Zoom handpiece of 755 nm picosecond laser at fluence of 0.88–1.18 J/cm^2 was applied. The treatment protocol used for 1064 nm QS-Nd:YAG laser was 8 mm spot size at fluence of 2.0 J/cm^2 initially followed by 6 mm spot size at fluence of 3.5 J/cm^2, and finishing with 4 mm spot size at 3.2 J/cm^2. For both 755 nm picosecond laser and 1064 nm QS-Nd:YAG laser, the endpoint was mild erythema and swelling without petechiae. Objective evaluation with visual analogue score was conducted by two independent physicians. Subject self-assessment for each patient was conducted as well. Statistical results showed that higher pigmentation clearance rate was achieved at the 755 nm picosecond laser side after the second treatment. At the 3 months follow-up, greater clearance was observed at the 755 nm picosecond laser side compared to the 1064 nm QS-Nd:YAG side. 755 nm alexandrite picosecond laser has been observed to achieve a faster and better clearance rate for melasma compared to 1064 nm QS-Nd:YAG laser. We conclude that the 755 nm picosecond laser could be a safe and effective modality for melasma treatment in Asians.

Keywords Melasma · 755 nm picosecond alexandrite laser · 1064 nm QS-Nd:YAG laser

Introduction

Melasma is a recalcitrant pigmentation disorder that has a high incidence rate in Asians, primarily in child-bearing women [1]. It presents as light to dark brown patches with indistinct borders typically located on the cheeks and forehead. While this predominance in Asian populations has been a historically recognized issue and has been thoroughly studied [2], there are still instances of exacerbation, indicating that there is no single cure or protocol that consistently addresses the disorder. The use of low-fluence 1064 nm QS-Nd: YAG laser in the treatment of melasma in Asian patients has historically been the high prevalence rate and has been reported in several studies [3–7]. Over the past few years, we have seen the introduction of the picosecond pulsed laser systems, shortening pulse durations from a billionth of a second to a trillionth of a second. The picosecond laser device we used has 5 modes of pulse duration with 750, 700, 650, 600, and 550 ps. The target chromophore of the device with 755 nm is mainly melanin. Picosecond laser pulses create a largely photomechanical effect on the targeted tissue, accompanied by a diminished photothermal effect. The laser-tissue interaction of a picosecond laser is primarily the photodisruption. The physical effects associated with optical breakdown are plasma formation and shock wave generation in the photodisruption. In picosecond lasers, we know the photomechanical effect increases while the pulse duration decreases. Overall, the shorter the pulse

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duration, the more the photomechanical effect than longer pulse duration in picosecond the regime. This allows for more safety during treatment as the major effect on the tissue does not rely on simply heating it to a high degree and accepting the risks involved [8–11]. We believe that applying a picosecond laser to treat melasma should achieve better result compared to QS-Nd:YAG based on the increased photomechanical effect and decreased thermal component. There are picosecond laser systems with wavelengths of 755, 532, and 1064 nm commercially available now. Because of the specificity of 755 nm in melanin absorption and proper penetration depth, 755 nm picosecond laser was chosen to be used. In this study, we compared the efficacy of 755 nm picosecond alexandrite laser and 1064 nm QS-Nd:YAG laser in treatment of melasma in Asians.

Materials and Methods

Subjects

This study was conducted in compliance with the Declaration of Helsinki. Institutional Review Board (IRB) approval was granted by the Chang Gung Memorial Hospital medical research ethics committee (IRB 104-1730A3). Twelve patients (11 female and 1 male), age 32–52, with Fitzpatrick skin type III–IV, and presenting with dermal or mixed-type melasma were enrolled in this split-face study to compare the efficacy of 755 nm picosecond laser and 1064 nm QS-Nd:YAG laser. The exclusion criteria include a history of any cosmetic treatments including laser, IPL, and chemical peels within 1 year prior to the study commencement, recent severe sun exposure, and the use of oral retinoid or other photosensitive medications. All patients' history was examined, and informed consent was obtained before they were enrolled.

Study design

The study was designed to compare the efficacy of the picosecond alexandrite laser with that of the QS-Nd:YAG laser in the treatment of melasma in Asian skin types. Patients received a total of four laser treatments at 1-month intervals. We shaved all vellus hair before application of topical anesthesia. Five percent lidocaine cream was applied topically 40 min before all treatments. The entire right side of the face of each patient was treated with a 755 nm picosecond laser (PicoSure, Cynosure, MA), and the left side of the face was treated with a 1064 nm QS-Nd:YAG laser (MedLite C6, Cynosure, MA). The settings used for the 755 nm picosecond laser were fluences of 0.88–1.18 J/cm^2, with spot sizes of 4.4–5.1 mm and a pulse duration of 650 ps. There are 5 modes of pulse duration with 750, 700, 650, 600, and 550 ps in the 755 nm picosecond laser device. Under the same pulse duration mode, the fluence decreases while the spot size increases. Actually, we preferred the shortest pulse duration then we could utilize primarily the photomechanical effect. However, we had to also consider the proper spot size and the fluence. Thus, we found that when we utilized the boost mode with pulse duration of 650 ps, the spot size and fluence setting of the device were not sufficient to reach a proper clinical endpoint. That was the reason why the boost mode with the pulse duration of 650 ps was chosen in this study. The pulse duration of 650 ps was applied in this study to match the appropriate spot size and fluence. For melasma treatment, the spot size and fluence were chosen carefully. An average of 1000 pulses within 3 passes totally were delivered on the right side of the face. On the left side of the face, three sets of parameters were applied: first, an 8 mm spot size with 2.0 J/cm^2 was used for one pass followed by a pass a 6 mm spot size with 3.5 J/cm^2, and finally a pass with a 4 mm spot size with 3.2 J/cm^2. Additional passes were delivered to the more pigmented areas until the proper endpoint was observed. The endpoint for both side of the face was mild erythema and swelling without petechiae. All patients received cooling for the treated area with ice packs for 15 min immediately post laser treatments. To reduce the risk of post-inflammatory hyperpigmentation, all the subjects were instructed to take oral tranexamic acid 250 mg 3 times 1 day for 1 week after each treatment. All patients were also instructed to use the same sunscreen SPF 50 during the daytime and the same 3% topical tranexamic acid whitening essence at night on both side of face. All patients did not use any topical steroid or hydroquinone.

Evaluation of efficacy and safety

Evaluation of pigmentation clearance was conducted by two independent physicians (one dermatologist and one plastic surgeon). Our evaluators were blinded while conducting the evaluation. Subjects were not blinded. Digital photographs were taken at (T1) Baseline; (T2) 1 week after the first treatment; (T3) 1 month after the first treatment; (T4) 1 week after the second treatment; (T5) 1 month after the second treatment; (T6) 1 week after the third treatment; (T7) 1 month after the third treatment; (T8) 1 week after the fourth treatment; (T9) 1 month after the fourth treatment, and (T10) 3 months after the fourth treatment. Objective evaluation was conducted by using a 5-point visual analogue scale (VAS). VAS assessment for both side of the face was designed to compare photographs taken at each time point with the baseline photograph (T1): (1) excellent, clearance of melasma > 81%; (2) good, clearance between 61 and 80%; (3) moderate, clearance between 41 and 60%; (4) mild, clearance between 21 and 40%; (5) minimal, clearance less than 20% or no change/getting worse.

Statistical analysis

The statistical analysis was conducted with Statistical Package for Social Sciences (SPSS) software version 17.0 (IBM Corporation, NY, USA). Paired *t* test was used to compare the mean of physicians' assessment and patients' self-assessment. The level of significance was defined as $P < 0.05$. Interobserver reliability of VAS score of both physicians was tested with Cronbach α.

Results

Evaluation of efficacy

Physician VAS assessment

The mean score of the physician graders VAS assessment for the right and left sides of the face at T5 was 2.50 ± 0.52 and 3.21 ± 0.92, respectively. This indicates the average improvement of the right side of the face in terms of melasma clearance of 41–60% (VAS = 3, moderate clearance) and the left side of the face achieved clearance of 21–40% (VAS = 4, mild clearance) after two laser treatment sessions.

Further improvement was observed at T10 with the mean score of physicians VAS assessment of the right and left sides of face were 1.38 ± 0.48 and 2.04 ± 0.75, respectively. This indicates the average improvement after completing four treatment sessions on the right side of the face achieved "good" melasma clearance of 60–80% (VAS = 2, good clearance) and on the left side of the face achieved "moderate" melasma clearance of 40–60% (VAS = 3, moderate clearance).

The method of errors showed good inter-rater reliability with Cronbach alpha at T2 = 0.89, T3 = 0.90, T4 = 0.85, T5 = 0.94, T6 = 0.90, T7 = 0.92, T8 = 0.85, T9 = 0.96, and T10 = 0.96 on patient's left side of the face. Fair to good inter-rater reliability was detected with the same method for the right side of the face at T2 = 0.79, T3 = 0.90, T4 = 0.91, T5 = 0.69, T6 = 0.94, T7 = 0.58, T8 = 0.76, T9 = 0.92, and T10 = 0.95.

Respectively, the physician VAS scores for the right and left sides of the face were 3.42 ± 0.47 and 3.87 ± 0.77 (P = 0.067); 3.13 ± 0.38 and 3.33 ± 0.69 (P = 0.241) at T3; 2.75 ± 0.66 and 3.29 ± 0.66 (P = 0.020) at T4; 2.50 ± 0.52 and 3.21 ± 0.92 (P = 0.014) at T5; 2.21 ± 0.58 and 2.88 ± 0.83 (P = 0.005) at T6; 2.04 ± 0.40 and 2.58 ± 0.70 (P = 0.005) at T7; 1.75 ± 0.40 and 2.29 ± 0.66 (P = 0.002) at T8; 1.46 ± 0.50 and 2.13 ± 0.74 (P = 0.003) at T9; 1.38 ± 0.48 and 2.04 ± 0.75(P = 0.005) at T10. Figure 1a shows the result of physician VAS assessment at various timepoints.

Patient self-assessment

Respectively, the patient VAS score for the right and left sides of the face were 4.58 ± 0.51 and 4.41 ± 0.67 (P = 0.220) at T2; 3.58 ± 0.51 and 3.91 ± 0.90 (P = 0.166) at T3; 3.17 ± 0.58 and 3.50 ± 0.80 (P = 0.053) at T4; 2.75 ± 0.62 and 3.25 ± 0.86 (P = 0.025) at T5; 2.41 ± 0.66 and 3.08 ± 0.90 (P = 0.026) at T6; 2.17 ± 0.58 and 2.67 ± 0.78 (P = 0.002) at T7; 1.92 ± 0.29 and 2.50 ± 0.68 (P = 0.007) at T8; 1.75 ± 0.62 and 2.25 ± 0.62 (P = 0.002) at T9; 1.41 ± 0.51 and 2.08 ± 0.79 (P = 0.005) at T10. Figure 1b shows the result of patients' self-assessment at various timepoints.

The result of patients' VAS self-assessment was aligned with physician VAS assessment. 3 months after the fourth treatment, the melasma clearance rate of 61–80% (VAS = 2, good clearance) was achieved on the right side of the face treated by 755 nm picosecond laser; while 41–60% (VAS = 3, moderate clearance) of melasma clearance rate was achieved on the left side of the face treated by 1064 nm QS-Nd:YAG laser.

In this study, the statistical analysis showed that significant improvement on the right side of the face treated by 755 nm picosecond laser compared to the mild-moderate improvement the left side of the face treated by 1064 nm QS-Nd:YAG laser based on both physician and patient assessments ($P < 0.05$ at T5~T10). Based on physician assessment results, 755 nm picosecond laser can achieve a faster, statistically significant pigmentation clearance rate when compared to 1064 nm QS-Nd:YAG laser in two treatment sessions. As treatments progressed, the 755 nm picosecond laser was continually superior in terms of improvement when compared to the 1064 nm QS-Nd:YAG laser and at the final 3-month follow-up, the results were consistent with findings throughout the study; the 755 nm picosecond laser was superior. The only adverse effect observed is temporary erythema which was resolved within 24 h after the treatment. We applied air cooling system to manage the discomfort while treating the patients. All subjects did not complain about any pain or discomfort. No rebound melasma, dyspigmentation, or post-inflammatory hyperpigmentation was observed throughout the study.

Discussion

Melasma is a very common hyperpigmented disorder in the Asian population, especially in middle-aged women and usually presents as symmetrical, irregular hypermelanosis on face, majorly on bilateral central cheek [12, 13]. The pathogenesis of melasma is unclear and could be related to many factors, e.g., genetic, sun exposure, hormonal factor, and subclinical inflammation [13]. Because of the aesthetic desire of lighter skin tone in Asia and higher prevalence rate of

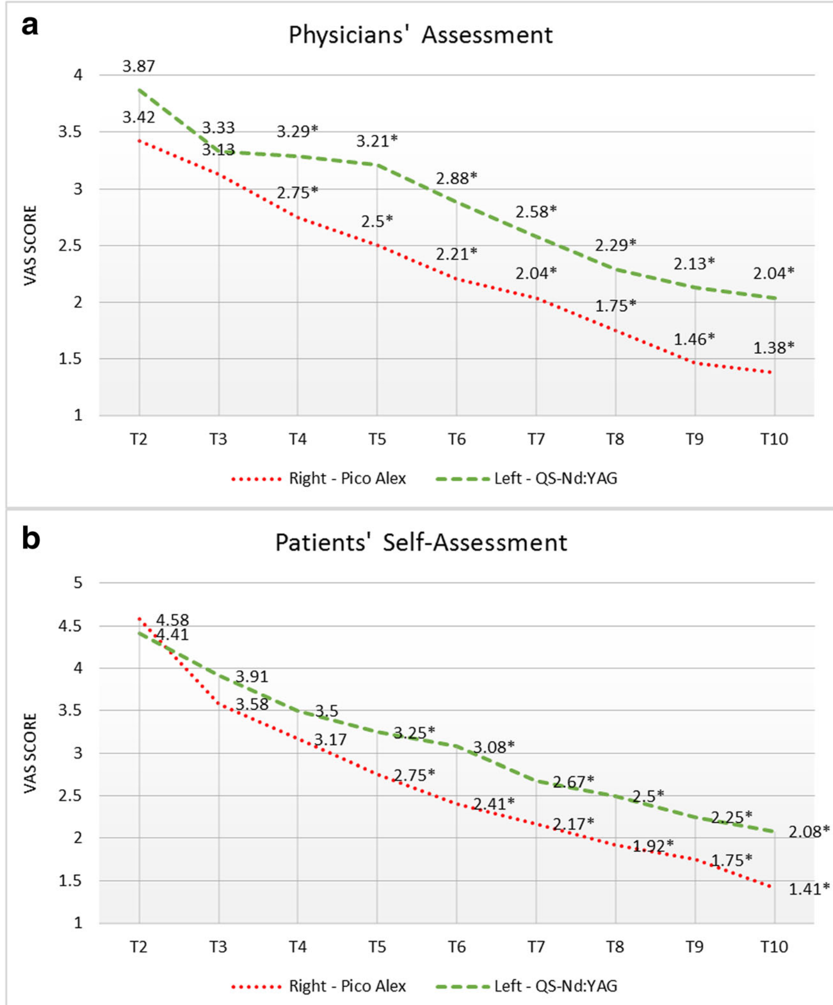

Fig. 1 **a**, **b** A diagram of mean of physicians'(**a**) and patients'(**b**) assessments using the visual analog scale (VAS) of four laser treatments given at 1-month intervals for facial melasma on the right face with 755 nm picosecond alexandrite laser and left face with 1064 nm QS-Nd:YAG laser ($n = 12$ patients). VAS = 5, minimal response (< 20% melasma clearance); VAS = 4, mild response (21–40% melasma fading); VAS = 3, moderate response (41–60% melasma clearance);VAS = 2, good response (61–80% measma clearance) and VAS = 1, excellent response (> 80% melasma clearance). (*indicates $P < 0.05$)

melasma in Asian skin type [1], the demand for the treatment of melasma has been very high. Different modalities of phototherapy including intense pulsed light (IPL) [14, 15], QS ruby laser (694 nm) [16, 17], non-ablative fractional 1540 nm [18], and QS-Nd:YAG laser (1064 nm) [19–21] have been used to treat melasma, However, some of results of these treatments were disappointing. Post-inflammatory hyperpigmentation, hypopigmentation, and dyschromia were common. Until now, there is no many curative treatment for melasma. Rebound and recurrence were frustrating. In the past decade, the use of 1064 nm QS-Nd:YAG laser with a flat-top beam profile for melasma treatment has been reported by various authors [5–7, 19–22]. Although the use of 1064 nm QS-Nd:YAG laser for the treatment of melasma has showed promising clinical results, post-laser hypopigmentation with insufficient recovery time due to short treatment interval or over treatment involving high fluence were reported [23, 24]. Repeated laser treatments at 1-week intervals may reduce hyperactive melanocytes, but may eventually increase the risk of spotty hypopigmentation [23, 24] because of the lack of recovery time.

The goal of the treatment for melasma with lasers is to reduce hyperpigmentation to a normal level of pigmentation. The mechanism of the picosecond laser primarily relies on photomechanical effect to destroy the targeted tissue, accompanied by a diminished photothermal effect (relative to nanosecond or millisecond pulses) [10]. With the recently commercialized picosecond alexandrite laser technology, a new opportunity has been presented for the selective reduction of abnormal melanins. The extremely short picosecond pulse, for the first time, has provided physicians a novel method to manage both melanin and melanocytes selectively [9].

Compared to the QS-Nd:YAG laser, the picosecond laser has the advantage of a higher safety profile due to the limited photothermal effect. There are 532, 755, and 1064 nm picosecond laser devices available on the aesthetic laser market now. Although 532 nm has much higher absorption coefficient than 755 nm for melanin, 532 nm also has relatively high absorption for hemosiderin. Furthermore, 1064 nm has lower absorption coefficient for melanin and higher absorption coefficient for hemosiderin than 755 nm. Thus, 755 nm has

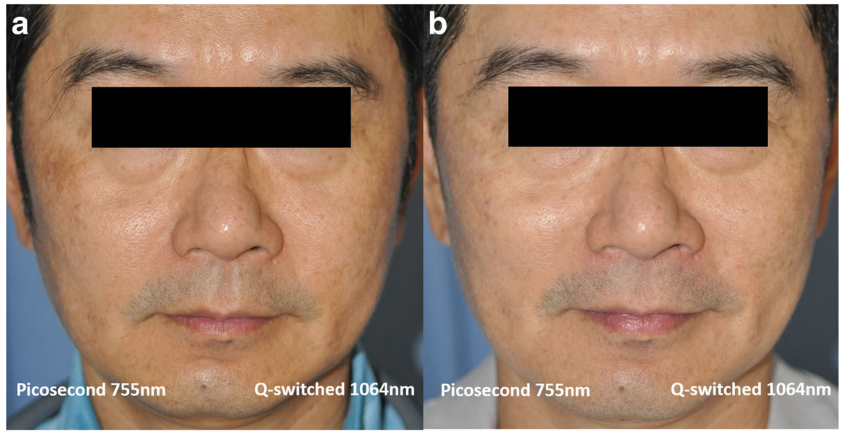

Fig. 2 Severe melasma in a 50-year-old man with Fitzpatrick skin type IV. **a** Baseline. **b** 3 months after four sessions of treatments; the clearance rate of right side of face treated with 755 nm picosecond alexandrite laser is higher than left side of face treated with 1064 nm QS-Nd:YAG laser

better selectivity targeting on melanin over 532 nm and 1064 nm. Because of the high selectivity in melanin absorption and proper penetration depth, we chose a 755 nm picosecond laser to perform this split face study.

In our study, the statistical analysis showed that significant improvement on the right side of the face treated by 755 nm picosecond laser compared to the left side of the face treated by 1064 nm QS-Nd:YAG laser based on both physician and patient assessments ($p < 0.05$ at T5~T10). Both patients' and physicians' assessments showed obvious improvement after the first treatment, with continuously diminishing pigmentation throughout the following treatments and follow-up visits. The right side of the face treated with the 755 nm picosecond laser had achieved a faster, statistically significant pigmentation clearance rate than the left side of face treated with the 1064 nm QS-Nd:YAG laser after two treatment sessions. No relapse on either side of the face was observed within 3-month follow-up (Figs. 2, 3, 4). The present study is limited by the small sample size and a relatively short follow-up. Future studies with larger sample size and longer period of follow-up may be required.

Though 755 nm picosecond laser treatment is not curative for melasma. According to the results in this study, the 755 nm alexandrite picosecond laser was observed to achieve a faster

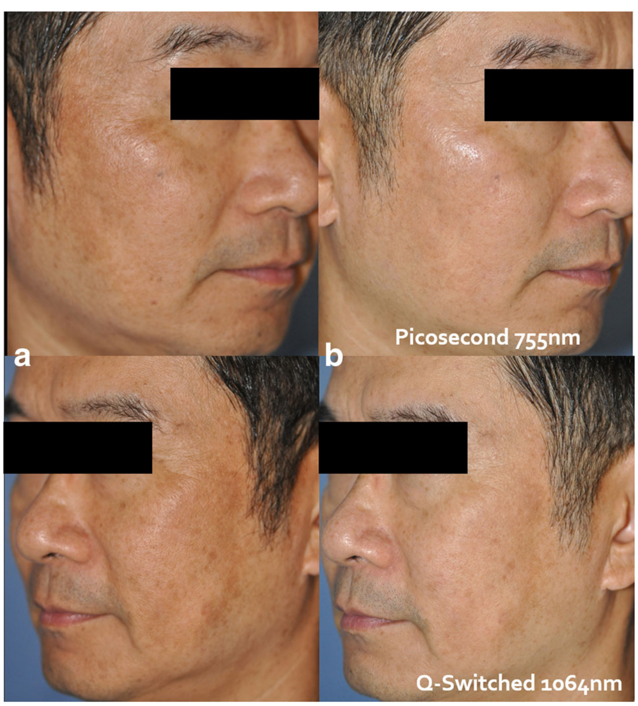

Fig. 3 Severe melasma in a 50-year-old man with Fitzpatrick skin type IV. **a** Baseline. **b** 3 months after four sessions of treatments; right side of face treated with 755 nm picosecond alexandrite laser (clearance rate over 80%); left side of face treated with 1064 nm QS-Nd:YAG laser (clearance rate over 60%)

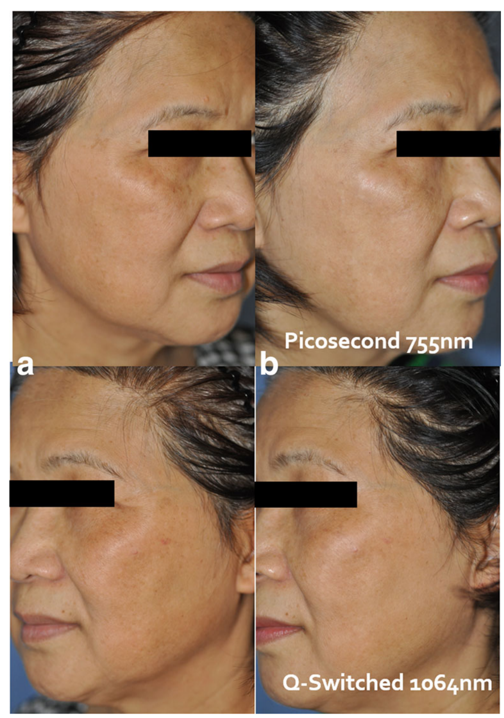

Fig. 4 Melasma in a 48-year-old women with Fitzpatrick skin type IV. **a** Baseline. **b** 3 months after four sessions of treatment; right side of face treated with 755 nm picosecond alexandrite laser (clearance rate over 70%); left side of face treated with 1064 nm QS-Nd:YAG laser (clearance rate over 50%)

and higher clearance rate for melasma than 1064-nm QS-Nd:YAG laser in Asian patients. We conclude that the 755-nm picosecond laser can be a safe and effective option for melasma treatment.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Institutional Review Board (IRB) approval was granted by the Chang Gung Memorial Hospital medical research ethics committee (IRB 104-1730A3).

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