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CLINICAL REPORT

Evaluation of a Novel Dermal Cooling System for the Treatment of Benign Pigmented Lesions in Asians

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ABSTRACT

Objective: Our study aimed to evaluate the efficacy of this novel dermal cooling system (DCS) in reducing pigmentation in benign pigmented lesions in Asian patients and its potential side effects.

Methods: It was a prospective open-label single-center study. Asian patients, with the presence of benign pigmented lesions mainly including lentigines, melasma, nevus spilus, ephelides, café au lait, and seborrheic keratosis were recruited for a novel DCS. The DCS provided localized cooling of the epidermal layer below freezing but was less intense than cryotherapy. Each patient received DCS at Week 0 and repeated at 4-week intervals up to 10 sessions. Global aesthetic improvement scores (GAIS) by blinded physicians and subjects were recorded at 2, 6, and 12 months posttreatment follow-up.

Results: Eighty-one patients were recruited with a total of 305 sessions performed and 1716 lesion sites treated. At 2-month posttreatment, 76.5% and 58.6% treatment sites showed obvious to marked improvement respectively and the improvement sustained at 6 and 12 months. Only minor adverse events were reported. Erythema and edema were the most commonly anticipated effects immediately after treatment. The pain was minimal. Postinflammatory hyperpigmentation was only reported in 2.2% (38/1716) treated sites.

Conclusion: To our knowledge, this study was the first study to demonstrate that this novel DCS was an effective, safe, and well-tolerated treatment for benign pigmented lesions in Asians.

1 | Introduction

Hyperpigmentation of the skin is a common dermatological condition in which the color of the skin becomes darker as a result of various internal and external factors including hormonal changes, inflammation, injury, certain medications, and UV exposure. Various biological processes result in the production of skin pigment, melanin, which is produced by melanocytes in various layers of skin [1]. Dysregulation in melanin production or distribution of melanin results in skin pigmentation disorders [2]. Various common hyperpigmentation disorders include lentigines, ephelides/freckles, melasma, postinflammatory hyperpigmentation, and more. Most of these pigmentation disorders belong to acquired hypermelanosis skin conditions resulting in macules or patches of light to dark brown or gray-brown lesions, appearing most predominantly on sun-exposed parts of skin such as face and neck regions. While ephelides or freckles typically develop during childhood phase and are more prevalent in lighter and fairer skin persons, solar lentigines are often referred as “age spots” or “sun spots,” and melasma is predominantly observed in women.

Various lasers targeting melanin chromophores have proven efficacies in pigmentary reduction, but potential hyperpigmentation

does occur occasionally, especially in Asians or persons of skin type IV and above.

Cryotherapy has a long history of clinical use in the treatment of skin conditions since 1900s [3]. It is performed by using cryogen, typically liquid nitrogen, or other compressed gas such as carbon dioxide to freeze and destroy tissue in subzero temperatures. The boiling temperature of liquid nitrogen is −196°C, while that of carbon dioxide (CO_2) is −80°C. In daily practice, liquid nitrogen is the most commonly used cryogen and cryotherapy is applied directly to the skin through the use of an applicator, probe, or spray to create irreversible damage in the treated tissue. The target temperature to destroy benign cells is −20°C, and that for malignant cells is −50°C as cancerous cells are more resistant to thermal change. Of note, the melanocytes are very susceptible to thermal injury and undergo apoptosis or cell death at −5°C.

Conventional cryotherapy is uncontrolled, resulting in crusting and dyspigmentation. And its outcome is variable which are unsatisfied. One of the most common side effects of cryotherapy is hypopigmentation [4, 5], as a result of the melanocytes' sensitivity to freezing. This "side-effect" of direct cooling of the skin through cryotherapy forms the basis of a new treatment concept. By using a controlled, localized cooling, we could therapeutically lighten the areas of skin pigmentation. Previous studies have shown that dermal cooling resulted in a consistent reduction in pigmentation in subjects with normal skin with predetermined treatment parameters [6–8]. We hypothesized that such controlled localized cooling could be a potential alternative to laser treatment for benign pigmented lesions in Asians.

The novel dermal cooling system (DCS) has been developed to provide a noninvasive, localized controlled cooling for skin pigmentation reduction.

The essence of this new device is the controlled cooling. This cooling device uses temperatures that are much less intense than those applied for conventional cryosurgery. This would limit the effect of a response from the melanocytes while avoiding damage to other tissues.

We, therefore, aimed to assess the efficacy and safety of this novel DCS for the treatment of benign pigmented lesions in Asians.

2 | Methods and Materials

2.1 | Subjects

This was a prospective, open-label single-center study of this novel DCS conducted from August 1, 2017 to April 30, 2022. Subjects of Asian ethnicity aged 18–70 years old who have one or more benign pigmented lesions (such as solar lentigines, freckles/ephelides, seborrheic keratosis, melasma, and café au lait macules) were screened for recruitment to receive DCS for benign pigmented lesions.

Exclusion criteria included prior medical or surgical therapies on lesions, artificial tanning or over-the-counter products (such as hydroquinone, corticosteroid, retinoids) or laser surgery to alter skin color in the intended treatment area(s) in past 6 weeks. Subjects with a history of melanoma, scars or tattoos, vitiligo, abnormal wound healing or scarring, known history of illness or adverse reactions to cold insults (such as cryoglobulinemia, cold urticaria, paroxysmal cold hemoglobinemia, Raynaud's disease), current skin infection or inflammation, pregnancy or breastfeeding, consent refusal or noncompliance to treatment protocol were excluded.

2.2 | Study Device

The investigational device was the DCS (R2 Dermatology) which was designed for noninvasive, localized, and focused cooling of epidermal layers to reduce pigmentation. The system was comprised of a control unit which houses the system controller power source and a handpiece. The handpiece, used to apply cooling to the treatment site of a patient, was comprised of an aluminum contacting surface with a small, embedded thermistor for monitoring the treatment temperatures. This device can adjust the temperature from a range of −30°C to 40°C, which limits the effect of a response from the melanocytes and avoids damage to other tissues. The configuration shape (square or round) and size (5, 7, and 10 mm) of the aluminum cooling applicators were available to be chosen at the discretion of the clinician, for optimization of skin lightening.

2.3 | Treatment Protocol and Skin Preparation

The nontreatment area was covered with a thermally insulative material (foam tape) as needed to avoid exposure to nontargeted areas. A coupling medium was applied to the treatment area before the application of the DCS handpiece to ensure good thermal contact between the skin and the cooling applicator. No prior local anesthesia was required or provided. The cooling treatment was performed with various sizes and shapes of handpieces, which ranged from a 5/10 mm square-shaped handpiece, and 7 mm round-shaped handpieces. It was chosen at the discretion of investigators, depending on lesion size and shape. The cooling handpiece was removed at the end of the cooling treatment and repositioned at the next treatment site(s). The treatment parameters applied to each site were documented.

2.4 | Treatment Parameters (Durations and Temperature)

Previous study indicated that, to achieve the depigmentation effect, the treatment lesion should reach −7.5°C or cooler [8].

With reference to previous dosimetry performed on normal skin and then on area of pigmentation, the initial target temperature was set at −10°C to −12°C in our study. For thicker or deeper lesions, more intense cooling was needed. We adjusted the treatment regime by increasing the exposure time if the lesion

was deeper or thicker. More sessions would be applied if the lesion has not reached complete clearance and has shown pigmentation reduction compared with the last visit.

Therefore, DCS treatment parameters were selected based on the nature and thickness of lesions, anatomical location and skin type. The target temperatures used for treatment ranged between −10°C and −20°C, consisting of a single cooling cycle or multiple cooling-and-rewarming cycles. Treatment exposure duration was brief, up to 20 s of active cooling. The number of treatment sessions received by each subject depended on the thickness (epidermal, junctional, upper dermal) of the lesions to achieve pigmentation reduction or complete clearance. Treatment sessions were performed with DCS in Week 0 and repeated treatment at 4-week intervals up to 10 sessions. A maximum of 40 treatment sites were treated for each subject per session. The size of the handpiece was chosen depending on the size of the treated lesion. Digital photographs were taken in each treatment site at baseline, pre- and posttreatment.

2.5 | Follow-Up

Subjects were followed at 2, 6, and 12-month post-last treatment visits with visual assessment of treated areas, photographs, and documentation of any adverse events. Strict sun protection with the use of sunscreen SPF 50 or higher on the treated area(s) and sun avoidance were advised during the whole study period.

2.6 | Efficacy Evaluation

Standardized photography was obtained before and after each treatment session and at each follow-up visit using the Canfield VISIA®-CR system (Canfield Scientific). Photographs were captured with standard lighting, cross-polarization, parallel polarization, and ultraviolet light at right lateral 37°, left lateral 37°, and frontal views.

Subject and blinded investigators would rate the changes in the appearance of treated areas using the 5-point Global Aesthetic Improvement Scale (GAIS) compared with baseline photographs (Table 1: 0, worse; 1, no change; 2, improved; 3 much improved; 4, very much improved). Both the subject and the investigators were given a detailed introduction to the GAIS system before conducting the assessment. The GAIS assessments were recorded at baseline, 2-, 6-, and 12-month follow-up visits. Overall treatment satisfaction by the subject was also recorded at a 2-month follow-up visit.

2.7 | Safety Evaluation

A standard visual analog scale (VAS score 0–10, minimal to maximal) was provided to assess any pain and discomfort experienced and scored by the subject during treatment. Any adverse events (such as erythema, bruising, swelling, blistering, alternation in sensation/numbness, hypo/hyperchromia) during, immediately after, and posttreatment were documented.

2.8 | Statistics and Analysis

Data was summarized based on the nature of the data. Dichotomous (e.g., gender) and ordinal (e.g., Fitzpatrick Skin type) data were tabulated by category. The mean, standard deviation maximum and minimum was tabulated for continuous data (e.g., age). A two-sided p-value of less than 0.05 was considered statistically significant.

The primary efficacy endpoint of an improvement in the pigmentation of the treated area was assessed by blinded investigators as assessor, using the GAIS at the 2-, 6-, and 12-month follow-up visit. The primary safety endpoint was assessed by the tabulation of the frequency and proportion of any device- or procedure-related adverse events.

GAIS by subjects and investigators, procedure and treatment outcome satisfaction and pain VAS score by subjects were documented with mean or median value ± standard deviation or interquartile range and percentage compared with baseline value as appropriate.

2.9 | Ethics Approval

This study was conducted in full compliance with the ICH E6 guideline for Good Clinical Practice (ICH-GCP) and the principles of the Declaration of Helsinki. Informed consent was obtained from all subjects. Ethics approval was granted by the Quorum Review Institutional Review Board, Washington.

3 | Results

A total of 81 patients of Asian ethnicity were recruited (mean age 48.3 ± 9.8, range 25–69) (Figure 1); 95.1% (77/81) were female; 43.2% (35/81) had skin type III, 56.8% (46/81) skin type IV.

TABLE 1 | Global Aesthetic Improvement Scale Assessment (GAIS).

Score	Rating	Definition
4	Very much improved	Optimal cosmetic result; would not benefit from additional treatment
3	Much improved	Marked improvement in appearance, but might benefit from additional treatment
2	Improved	Obvious improvement in appearance, but additional treatment is indicated
1	No change	The appearance is essentially the same as baseline
0	Worse	The appearance is worse than the original condition

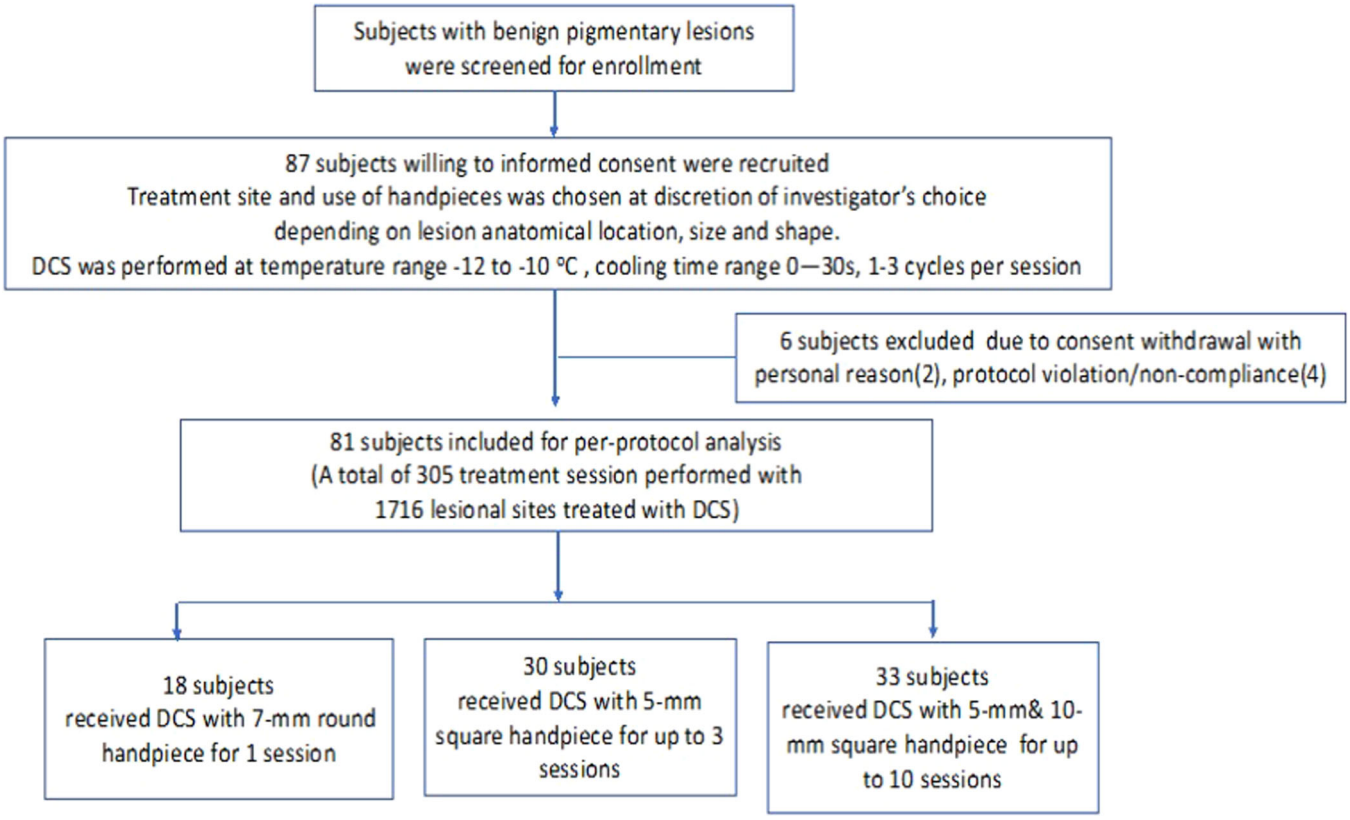

FIGURE 1 | Subject recruitment process.

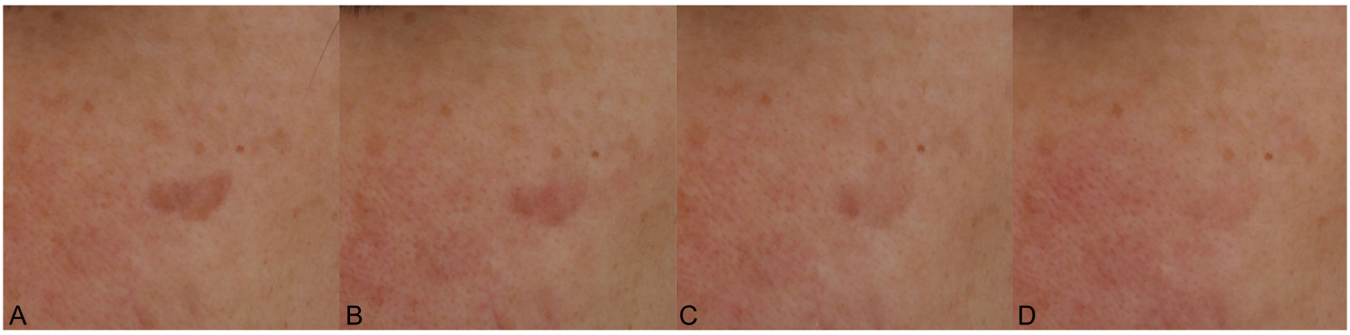

FIGURE 2 | Facial lentigines. (A) Baseline, (B)–(D) 2, 6, 12 months after two treatment sessions. Global Aesthetic improvement scale (IGAS): improved on 2-month follow up, much improved on 6-month follow up, and very much improved on 12-month follow up.

A total of 305 sessions were performed with 1716 lesion sites treated. The median number of treatment sites per subject per session was 5 (range 1–20). The benign pigmented lesions treated in this study included solar lentigines (40.7%, Figure 2), ephelides (25.9%, Figure 3), and other benign pigmented lesions (33.4%), such as seborrheic keratosis (Figure 4), melasma, cafe aul ait, and nevus spilus (Table 2).

3.1 | Treatment Outcome

Overall, 58.6%, 63.3% and 65.1% of treatment sites showed'Improved to Very Much Improved' at 2, 6 and 12 months posttreatment by investigator GAIS (Figure 5); while 76.5%, 69.1% and 69.9% rated'Improved to Very Much Improved' by subject GAIS at 2, 6 and 12-month posttreatment respectively (Figure 6).

With repeated treatment using the type of HP based on lesion size, 28% of treated sites showed pigmentation improvement after a single DCS, while 83.2% and 91.8% of treated lesions achieved pigmentation improvement after repeated treatment, up to 3 sessions versus repeated treatment up to 10 sessions respectively. The pigmentation improvement was sustained in approximately two-third to three quarters of the subjects at 6- and 12-month follow-up (Table 3).

Subject feedback on procedure length, comfort, side effects, and outcomes were collected in this pilot study. Most participants (94%) rated the procedure length as expected or shorter than expected,

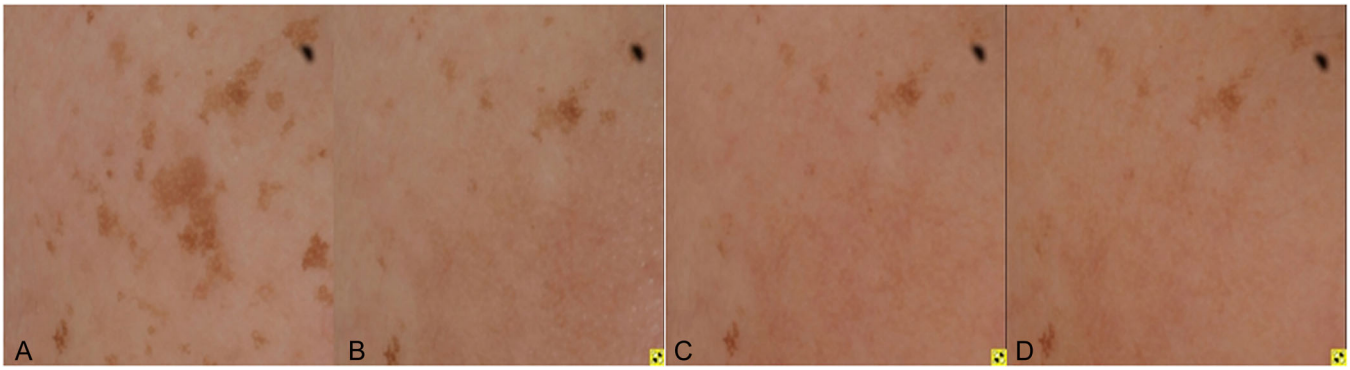

FIGURE 3 | Facial freckles. (A) Baseline, (B)–(D) 2, 6, 12 months after three treatment sessions. Global Aesthetic improvement scale (IGAS): much improved at 2-month follow up and very much improved on 6-, 12-month follow up.

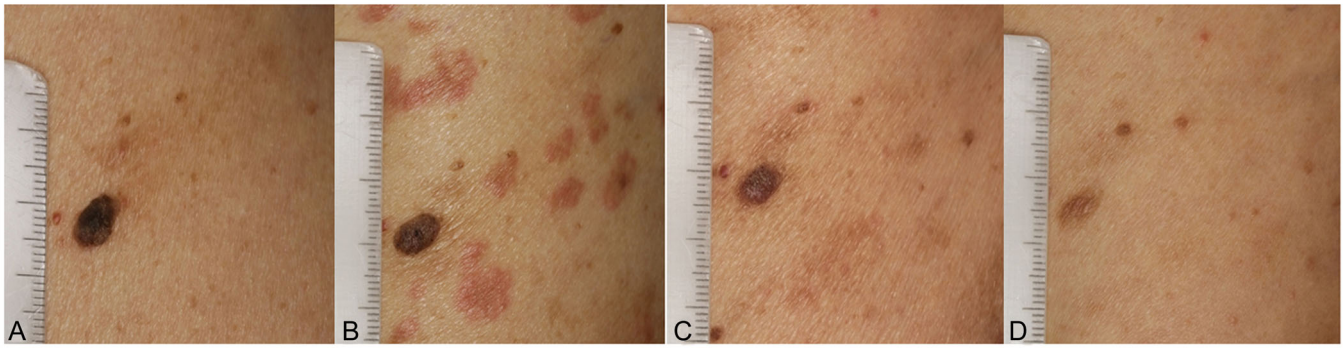

FIGURE 4 | Seborrheic keratosis. (A) Baseline, (B)–(D) 2, 6, 12 months after one treatment session. Global Aesthetic improvement scale (IGAS): improved on 2, 6 months follow up, and much improved on 12 months follow up.

and only 1 case reported the treatment procedure as uncomfortable. The majority of participants (77.8%) rated side effects as equal to or less than expected, and 44.5% rated procedure outcomes as expected to more than expected. In addition, 74.1% (60/81) of the subjects would recommend the treatment to friends or relatives, and 66.7% would like to receive the treatment again in future. Three subjects expressed that they would not receive the treatment again, because the lesions were completely resolved, therefore, they perceived that they no longer required the treatment.

3.2 | Adverse Events

There were no major or serious adverse events. Mild erythema and edema were the most commonly anticipated effects immediately after treatment (Table 2). Pain experienced was minimal (VAS 4.2 ± 2.2 during treatment, and 1.2 ± 1.7 immediately posttreatment). Postinflammatory hyperpigmentation was only reported in 2.2% (38/1716) treated sites.

4 | Discussion

According to a previous study, the epidermal melanocytes could be selectively destroyed in swine skin by topical application of cold [8]. In that, swine skin tissue was cooled at a temperature of −7.5°C or lower, which successfully resulted in epidermal depigmentation. The longer the duration of cold application and the lower the freezing temperature, the more complete depigmentation of the treated skin surface was observed. No skin ulceration or scarring was observed. The depigmentation was hypothesized as a result of the apoptosis of melanocytes in the basal layer of the epidermis observed around 2 weeks after cold application [8]. Skin necrosis, scarring and inflammation were absent or minimal.

Our study was the first study applying DCS to Asian skin, and has demonstrated that this novel controlled cooling—DCS was effective in improving benign pigmented lesions in Asians.

4.1 | Hyperpigmentation Risk Was Reduced in DCS Compared With Laser Treatment

Using DCS, hyperpigmentation risk has been significantly reduced compared with conventional cryotherapy and laser treatment for benign pigmented lesions in Asians.

Various laser treatments have shown clinical improvement in benign pigmented lesions like Q-switch 532 nm Nd: YAG laser, Q-switch alexandrite laser, Q-switch ruby laser, long-pulsed 532-nm Nd: YAG laser, and picosecond laser [9–11]. However, laser treatment on pigmented skin lesions in patients with skin of color remained challenging. As a previous study showed, the use of Q-

TABLE 2 | Subjects' demographics and anticipated effects after treatment.

	Overall	1 session	Up to 3 sessions	Up to 10 sessions
Subject, *n*	81	18	30	33
Age, mean ± SD (min, max)	48.3 ± 9.8 (25, 69)	52.1 ± 10.8 (27, 69)	46.2 ± 9.1 (25, 67)	48.1 ± 9.5 (28, 64)
Gender				
Female	77 (95.1%)	16 (88.9%)	30 (100%)	31 (93.9%)
Skin type (I–VI)				
III	35 (43.2%)	8 (44.4%)	15 (50.0%)	12 (36.4%)
IV	46 (56.8%)	10 (55.6%)	15 (50.0%)	21 (63.6%)
Handpiece (HP)		7-mm round	5-mm square	5- and 10-mm square
Lesion type				
Only lentigines	33 (40.7%)	17 (94.4%)	7 (23.3%)	9 (27.3%)
Only ephelides	21 (25.9%)	—	13 (43.3%)	8 (24.2%)
Lentigines and ephelides	21 (25.9%)	—	9 (30.0%)	12 (36.4%)
Lentigines and melasma	1 (1.2%)	—	1 (3.3%)	—
Lentigines and SK	2 (2.5%)	—	—	2 (6.1%)
Café Au Lait Macule	1 (1.2%)	—	—	1 (3.0%)
Nevus Spilus	1 (1.2%)	—	—	1 (3.0%)
Seborrheic keratosis	1 (1.2%)	1 (5.6%)	—	—
Treatment session/Subject	—	1	Up to 3[a]	Up to 10[b]
Sessions (total delivered)	305	18	83	204
Treatment site/Subject	5 (1,20)	5 (1,18)	6 (2,12)	5 (1,20)
Pain score (VAS)				
During treatment	4.2 ± 2.2 (0, 9)	1.6 ± 1.5 (0, 6)	5.3 ± 2.1 (1, 9)	3.9 ± 2.0 (0, 8)
Immediate posttreatment	1.2 ± 1.7 (0, 8)	0.0 ± 0.3 (0, 3)	2.5 ± 2.0 (0, 8)	0.7 ± 1.1 (0, 7)
Adverse events (by sessions)	(*n* = 305)	(*n* = 18)	(*n* = 83)	(*n* = 204)
Immediate after treatment				
Erythema				
Mild	238/305 (78.0%)	6/18 (33.3%)	61/83 (73.5%)	171/204 (83.8%)
Moderate	34/305 (11.1%)	0	20/83 (24.1%)	14/204 (6.9%)
Severe	1/305 (0.3%)	0	1/83 (1.2%)	0
Edema (mild)	17/305 (5.6%)	1/18 (5.6%)	11/83 (13.3%)	5/204 (2.5%)
Erythema				
PIH (by sites)	(*n* = 1716)	(*n* = 110)	(*n* = 531)	(*n* = 1075)
	38/1716 (2.21%)	0	35/531 (6.60%)	3/1075 (0.28%)

Abbreviations: HP, handpiece; *n*, number.
[a]Number of sessions delivered pre-set at a minimal of one session and maximal of three sessions.
[b]Number of sessions delivered at a minimal of one session to a maximal of 10 sessions.

switched lasers for the treatment of cutaneous pigmented lesions in Asians was associated with a high risk of postinflammatory hyperpigmentation of up to 25% [11]. Patients with darker skin tones were more prone to hyperpigmentation due to the higher melanin level. The excessive heat generated by the laser could stimulate the production of melanin in the skin. The laser treatment could also cause inflammation and damage to skin cells, triggering melanin production as a natural response to protect the skin.

By controlled cooling, DCS has minimized the risk of postinflammatory hyperpigmentation to only 2.2% in this study, which was at least twofold less than that observed in picosecond laser treatment (4.8%–20%) [9–11] among Asian patients with darker skin tone.

4.2 | With Controlled Cooling, DCS has Shown Satisfactory Pigmentation Reduction and Fewer Side Effects Compared With Conventional Cryotherapy

As the melanocytes are particularly sensitive to thermal damage, most benign pigmented lesions could be treated with conventional cryotherapy with some success. However,

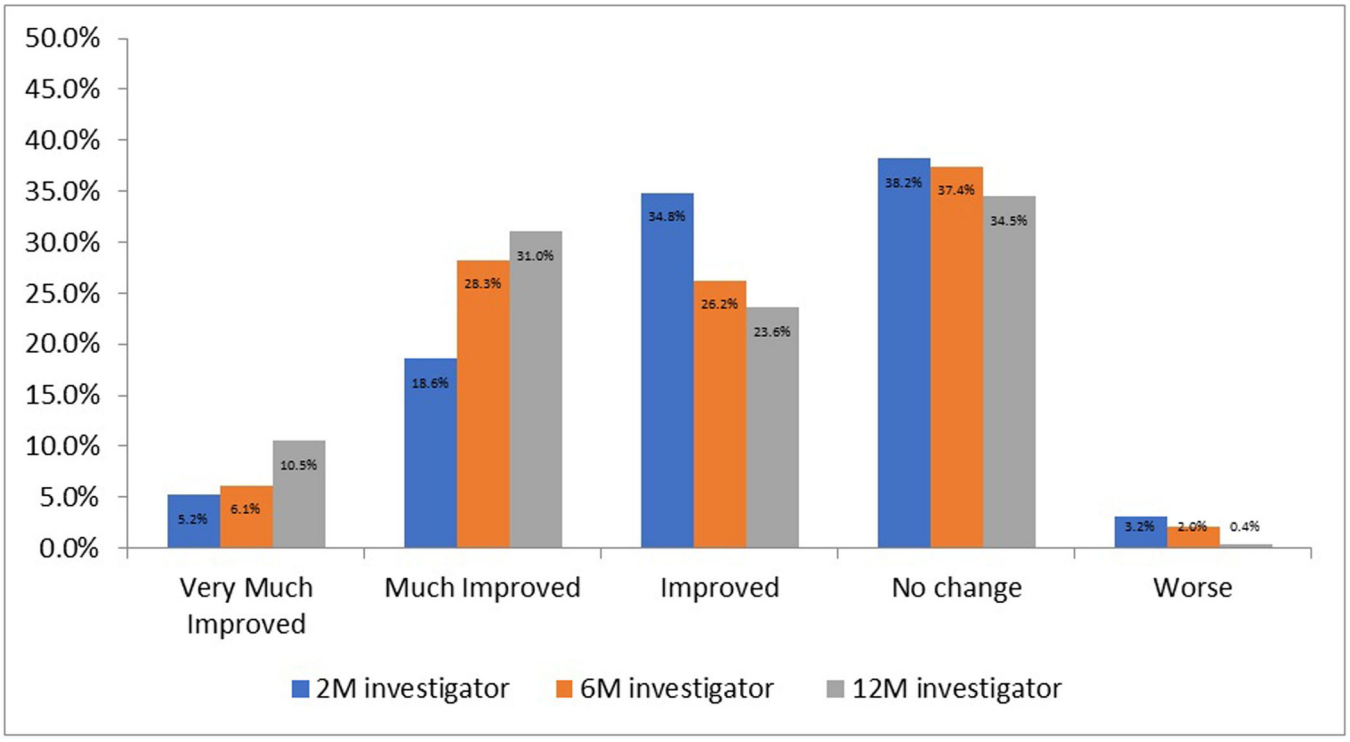

FIGURE 5 | The overall Global Aesthetic Improvement Scale (GAIS) by Investigator at 2-, 6-, and 12-month posttreatment follow-up.

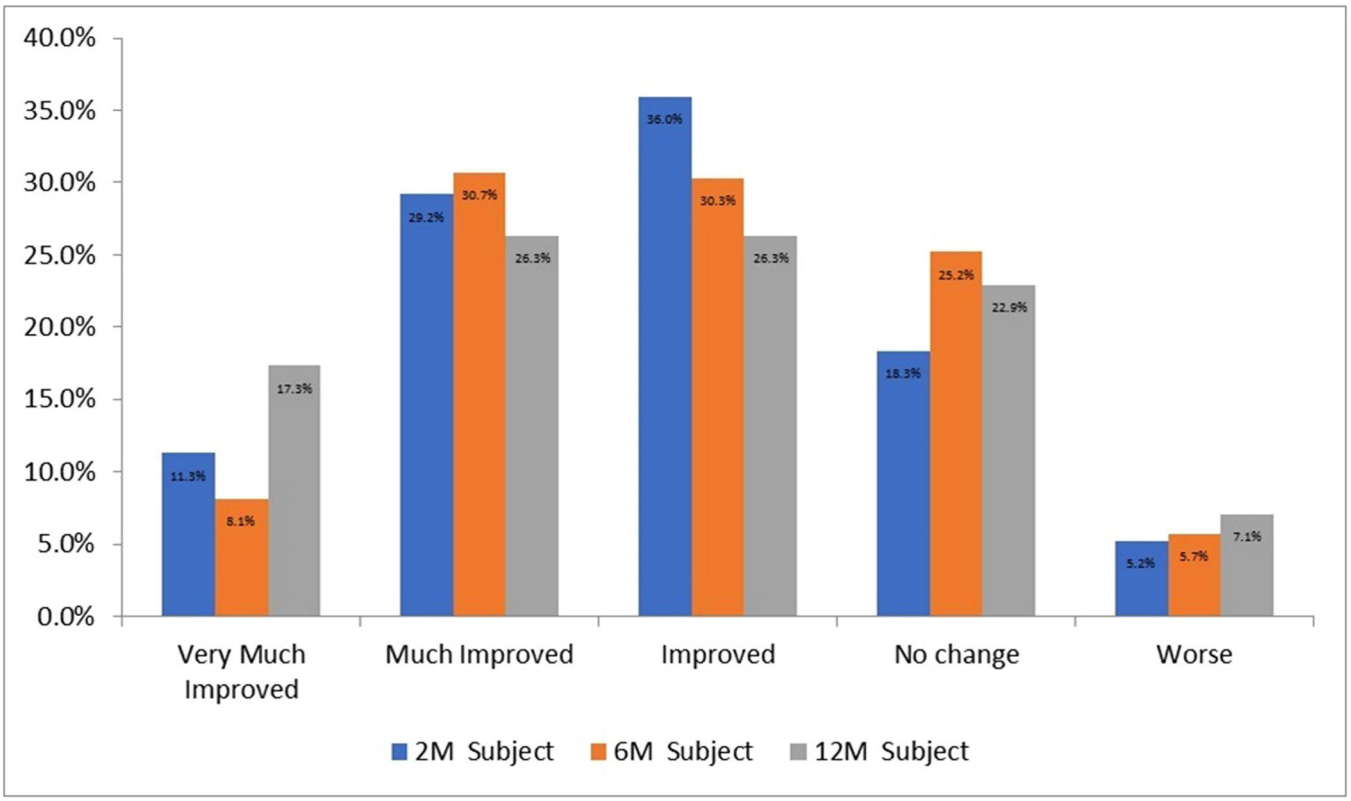

FIGURE 6 | The overall Global Aesthetic Improvement Scale (GAIS) by Subject at 2-, 6-, and 12-month posttreatment follow-up.

conventional cryotherapy has caused several complications which include pain, blister formation, erythema, and dyspigmentation; less commonly, hemorrhage, infection, systemic reactions, hair loss, tissue destruction and scarring [12–15].

Of note, pain was one of the adverse effects commonly reported. Some patients reported migraines or headaches after cryotherapy treatment lesions located on the forehead, temples and scalp. This pain was usually transient. But sometimes, patients

TABLE 3 | Treatment efficacy of dermal cooling system.

Session performed	1 session	Up to 3 sessions	Up to 10 sessions
Subject number, *n*	18	30	33
Handpiece (HP)	7-mm round	5-mm square	5- and 10-mm square
2-month posttreatment			
Improvement	28.2%	83.1%	91.8%
No improvement	71.8%	16.9%	8.2%
6-month posttreatment			
Improvement	27.3%	76.0%	64.3%
No improvement	72.7%	24.0%	37.7%
12-month posttreatment			
Improvement	39.0%	77.5%	65.8%
No improvement	61.0%	22.5%	34.2%

Abbreviations: HP, handpiece of cooling applicator of dermal cooling system chosen based on lesion size; Improvement, improved, much improved and very much improved in GAIS (by investigator); No improvement, no improvement or worsen in GAIS (by investigator).

required moderate analgesia to settle the pain [4, 16, 17]. No headache or migraine was reported in this study nor did patients use of analgesics after this DCS.

Post-cryotherapy pigmentation changes could cause cosmetic concerns. In conventional cryotherapy, greater than 50% of patients reported hypopigmentation in the cryotherapy-treated sites, especially after longer freeze times. These hypochromia could last more than 6 months [18]. Rarely, scarring has been reported after cryotherapy on benign pigmentation lesions [19]. Treatment of the hair-bearing areas could also cause permanent hair loss. Sensory nerve damage was rare, but it was reported occasionally in large case series and it might take 12–18 months to recover [12, 13]. In this study, none of these adverse events (such hypopigmentation, scarring, hair loss or sensory damage) was reported.

This DCS delivered controlled cooling that was less intense than the freezing used in conventional cryotherapy. This resulted in lower adverse effects. Besides, this DCS focuses on the treatment site, sparing adjacent normal tissue for potential side effects, such as in skin irritation and postinflammatory pigmentation.

Although only one-quarter of treated lesions showed obvious pigmentation reduction after a single treatment (with the 7 mm HP), this was likely due to the single treatment applied. As mentioned in the method, the type of handpiece was chosen based on lesion size. With repeated treatment to enhance cooling-induced melanocyte apoptosis, more than 90% of treated sites showed significant improvement in pigment reduction in combination of HP used (5 or 10 mm). This showed that the residual pigmentation could be further cleared with subsequent sessions performed. Of note, the improvement was sustained at 2-, 6- and 12-month posttreatment. The anticipated side effects after treatment were mild. In this study, only erythema and mild edema were reported.

With more challenging cases like mixed type with melasma, café au lait macules (CALM), the pigmentation was expected at slightly deeper site, beyond basal layer, the pigmentation reduction was not very obvious after single treatment. With repeated treatment, the pigmentation reduction was observed in nevus spilus, but not in melasma or CALM. We believed the cooling beyond the basal layer has to be further adjusted to reach the temperature low enough to induce melanocyte apoptosis, and at the same time, avoid unnecessary injury to induce PIH.

For these cases, the lesion response to DCS was variable. The patient with nevus spilus reported unresponsiveness to previous laser treatment on the lesion before study enrollment. However, the pigmentation of the nevus spilus has moderate reduction (25%–50%) after 10-session of this DCS as assessed by investigator.

However, the CALM lesion developed PIH after two DCS treatment session, while melasma (lentigo mixed melasma) lesion developed PIH after three treatment session and these patients were noncompliant to strict sun avoidance.

4.3 | Less Downtime in the Treated Area and a More Comfortable Treatment Journey

The controlled dermal cooling method in this device not only proved effective in lowering the risk of PIH, but also, the patient experienced less downtime, and the controlled cooling method was more comfortable. According to our study result, without local anesthetics, low pain scores were reported from the participants during and after controlled cooling treatment. This study showed similar results, as in Murray et al. study [20], with high patient satisfaction during and after the procedure. In Murray et al study, cryomodulation or a controlled cooling device was used immediately after non-ablative skin resurfacing. The controlled cooling device was effective in the reduction of pain, erythema and edema as in this device [20].

Notably, for this controlled cooling system, there were no extra local anesthetics required. It was not necessary for post-treatment observation as the anticipated effect of DCS would be mild. Compared with treatment requiring local anesthetics,

such as laser treatment, if one chose to use DCS on benign pigmented lesions, the patient could save 45–60 min for local anesthetics application and save another 15 min for post-treatment cleansing and care.

Besides, the cost of topical anesthesia can be saved. In particular, the cost would be slightly lower in DCS as DCS did not require topical anesthetics application. Generally, the cost of topical anesthetics for skin preparation varies in laser pigmentary treatment, depending on the area of the face applied. In our center, four to six tubes of 5 g 5% EMLA cream (containing mixed lidocaine 2.5% and prilocaine 2.5%) are used for the whole face laser treatment. The cost is estimated to be around USD 400-500 per laser session together with topical anesthesia and nursing care. Thus, DCS is relatively more convenient and economical as an office-based procedure with no spare room and extra time, or cost required before the procedure.

4.4 | Limitation

One of the disadvantages of this controlled cooling system was the amount of time it might take for multiple lesions (e.g., multiple freckles or SKs) in one session. In fact, the amount of time to perform the procedure on each lesion would be as brief as several few seconds, or up to 20 s per session. Factors which influence the lesion to achieve the target temperature, including the epidermal thickness of the target lesion, might influence the outcome of the pigment clearance.

The diameter of the handpiece could tailor the size or area of lesions to be covered. It might take a longer time for those resistant cases. The subject would need to be followed up to assess the treatment response if further treatment was required. Similar to laser therapy on benign pigmented lesions such as lentigines or ephelides, the majority of the cases would achieve complete or near clearance within two to three sessions. More destructive techniques such as laser treatment could achieve faster outcomes, but Asians or subjects of darker skin types might bear a higher risk of side effects, in particular PIH, and scarring. No scarring was observed in this controlled cooling system. For cases with melasma, café au lair, nevus spilus, as the case number is limited, it was hard to further comment on this response.

For those thicker or deeper lesions, more sessions were usually required in DCS, compared with laser treatment, however, the downtime and PIH were minimal compared to laser treatment.

5 | Conclusion

To our knowledge, this study was the first study to demonstrate that the novel DCS was an effective, safe and cost-effective treatment for benign pigmented lesions in Asians. The performance of this controlled cooling procedure was satisfactory with minimal side effects and tolerable to our patients. Further randomized studies in delineating the optimal parameter for individual benign pigmentation disorders would be warranted.

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