Clinical and Histological Evaluations of Enlarged Facial Skin Pores After Low Energy Level Treatments With Fractional Carbon Dioxide Laser in Korean Patients

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BACKGROUND Enlarged facial pores can be an early manifestation of skin aging and they are a common aesthetic concern for Asians. However, studies of improving the appearance of enlarged pores have been limited.

OBJECTIVE The authors aimed to study the application of CO_2 fractional laser treatment in patients with enlarged facial pores.

METHODS A total of 32 patients with dilated facial pores completed 3 consecutive sessions of low energy level treatments with a fractional CO_2 laser at 4-week intervals. Image analysis was performed to calculate the number of enlarged pores before each treatment session and 12 weeks after the final treatment.

RESULTS After application of laser treatments, there was a significant decrease in the number of enlarged pores. The mean number of enlarged pores was decreased by 28.8% after the second session and by 54.5% at post-treatment evaluation. Post-treatment side effects were mild and transitory. Histological and immunohistochemical analyses demonstrated clear increases in the number of collagen fibers and the expression of transforming growth factor–β1.

CONCLUSION The short-term results showed that treatment with low energy level CO_2 fractional laser therapy could be a safe and effective option for patients with Fitzpatrick skin Types III and IV who are concerned with enlarged pores.

The authors have indicated no significant interest with commercial supporters.

Facial skin pores are the external openings of the pilosebaceous unit. Enlarged pore sizes are commonly associated with seborrhea, acne, aging, and skin laxity.[1,2] Enlarged facial pore size is a subjective characterization, but it is one of the most common aesthetic issues concerning Asian patients. Many patients desire treatment for the condition, which can be an early sign of skin aging. Few studies of techniques for improving the appearance of enlarged pores have been conducted. Histologically, enlarged pores appear as empty funnel-shaped structures or as cornified cylindrical plugs corresponding to comedones, which strongly suggest an increase in adjacent dermal fibers as a reasonable treatment mechanism.[1,3]

Limited evidence has suggested that various methods, including chemical peeling, Nd:YAG lasers, intense pulsed light, and nonablative fractional resurfacing, may help decrease dilated pore size. However, the studies did not generally focus on the treatment of only skin pores, did not provide objective data, and did not numerically count pore numbers.[4–6] Previous studies have validated fractional carbon dioxide (CO_2) laser therapy as an excellent treatment choice for atrophic acne scars and photoaging.[7,8] This laser combines the

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concept of fractional photothermolysis with an ablative wavelength of 10,600 nm, creating microthermal treatment zones with a confluent pattern of ablation that extends from the stratum corneum through the dermis.[9–11] Histologically, enhanced cutaneous architecture, including increased epidermal thickness and replacement of irregular dermal collagen bands with organized parallel novel collagen fibrils and elastins, were elucidated as the main mechanisms of effectiveness.[12] Based on this background, the authors designed this study to investigate the efficacy, safety, and histopathology of low energy level CO_2 fractional laser therapy for the treatment of enlarged facial skin pores in Asian patients using an image analysis system.

Methods

Study Design and Subjects

A prospective, single-arm, clinical study was conducted to investigate the application of low energy level CO_2 fractional laser for the treatment of facial skin pores. This study protocol was performed in accordance with the Declaration of Helsinki and approved by the institutional review board. Informed consents were acquired from all subjects before enrolment. Thirty-five subjects (12 men and 23 women, aged 29–45 years, 16 Fitzpatrick skin Type III and 19 Type IV) concerned with enlarged skin pores were enrolled. Patients were excluded from the study if they had more than few atrophic acne scars on the face (Echelle d'e'valuation clinique des cicatrices d'acne' [ECCA] scores >25) to prevent the image analyzer from detecting scar changing patterns or if they had received any other treatment for skin pores or textures including chemical or mechanical skin resurfacing within 3 months before the study. None of the patients underwent other treatments including chemical or laser resurfacing during study period. All subjects received a total 3 consecutive full-face treatments of fractional laser at 4-week intervals. Patients were also instructed to visit the clinic for post-treatment evaluation after 12-week lapse of the final treatment. At each visit, image analysis measurement, dermatologists' evaluations, and patients' subject assessments were performed. Skin biopsies were also conducted at both baseline and post-treatment evaluation.

After finishing the initial protocol, the authors re-interviewed 26 participants by the telephone or e-mail and asked their facial pore states at 40 to 45 weeks after treatment. In addition, 1 participant revisited and took the picture in the identical condition.

Devices and Laser Treatment

The full face of each patient was treated with 10,600-nm CO_2 fractional laser (Fraxis; Ilooda, Suwon, Korea). For local anesthesia, the face was cleansed with a mild soap and 70% alcohol, and a topical eutectic mixture of 2.5% lidocaine hydrochloric acid and 2.5% prilocaine (AstraZeneca AB, Sodertalje, Sweden) was applied to the entire face under occlusion 1 hour before laser therapy. The treatment parameters were determined based on each patient's condition and availability as follows: 7.2 to 9.0 mJ, 240 to 300 μs duration, and 0.8 to 1.0 mm density in fractional CO_2 laser (coverage = 20%–25%, each pixel size ≈100 μm, and approximate depth = 1,100–1,400 μm, treatment density of 120–160 MTZ/cm^2). About total 1.0 to 1.5 kJ were administered on average per each patient. Each session of treatment was applied over the entire face for 2 passes, whereas additional 1 pass was added in patients who had markedly enlarged facial skin pores. Air-forced cooling was used to cool the skin during all laser treatments. For post-operative regimen, all patients were applied facial cooling mask with a soothing aloe gel just after finishing the procedure for several minutes. Oral antiviral prophylaxis (famciclovir 250 mg 3 times a day) was prescribed for subjects with documented histories of herpes labialis and was started the night before the treatment for a course of 3 days. Oral antibiotics (cefradine 500 mg twice a day) were given during the same time period as well. Then, they were instructed to use a mild cleanser and moisturizer several times daily for the first few days after each treatment session to promote wound healing and prevent dryness.

Clinical Outcome Assessment

At each visit, photodocumentation was performed with color imaging system (DermaVision-PRO; OptoBioMed Co., Wonju, Korea) to measure enlarged skin pores numerically. Global assessment of appearance for pores and skin texture of the face were assessed by 2 independent investigators and subjects, respectively. For

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assessments of the 2 investigators, arithmetic means of the 2 values were used for analysis. There were no baseline subjective assessments for each of them. The quartile improvement scale with values from 0 to 4 (Table 1) was used to assess any changes in the treated areas at each follow-up visit. Pain sensation during treatments was reported on a 1-to-10 scale. Subjects also recorded post-treatment responses including erythema, oozing, and edema using a 0-to-3 severity scale. Related side effects and changes (scarring, hyperpigmentation, hypopigmentation, and dryness) were documented during treatment in detail.

Image Analysis for Skin Pores

To detect photographic evidence of the appearance corresponding to clinically recognized enlarged pores, DermaVision-PRO uses analysis scripts based on information from structure, size, and color.[13,14] In the cross polarization image, which provides high-quality color images by removing reflection light and displays the distribution of skin pigmentation using an analysis algorithm, specifically designated pigmented areas larger than 3 pixels were counted as the enlarged skin pore (Figure 1). Enlarged skin pores were measured from 3 points: forehead (1.5×2.5 cm^2 central glabella area), nose (1.5×1.5 cm^2 central supratip area between alar side walls), and central areas of cheeks (each symmetrical 4.5×4.5 cm^2 central area). Specific numbers of enlarged skin pores were recorded during each visit.

Histopathology and Immunohistochemistry

Skin biopsies were performed from the cheek with a 2-mm punch to minimize scarring from 6 patients. Tissues acquired at typical skin pore lesions of zygomatic area at baseline and final visits were stained with both hematoxylin and eosin (H&E) and Masson's trichrome (MT) staining. For the investigation of molecular changes after laser therapies, samples were processed for immunohistochemical staining for Collagen-1, Collagen-3, and transforming growth factor (TGF)-β1 (Abcam, Cambridge, England). Relative intensity of staining of samples was assessed by an image analysis program (Leica QWin version 3.5.1; Leica Microsystems, Wetzlar, Germany).

TABLE 1. Quartile Improvement Scale

Grade	*Description*
0	No improvement
1	Minor/mild improvement (1%–25%)
2	Moderate improvement (26%–50%)
3	Marked improvement (51%–75%)
4	Very marked improvement (76%–100%)

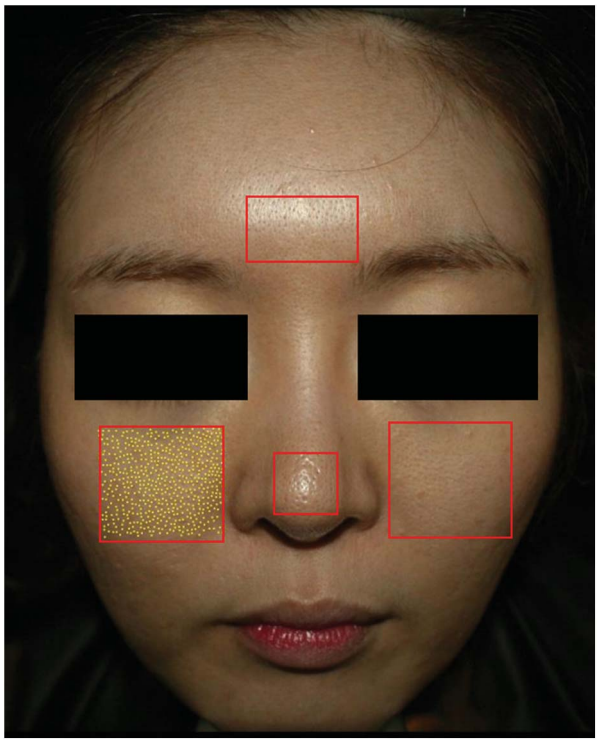


Figure 1. Measurement of enlarged facial pores using DermaVision-PRO imaging system. Red quadrangles indicate total enlarged pore measurement areas, and yellow dots indicate enlarged facial pores detected in the right cheek area. Total number of yellow dots from all areas was considered in the clinical assessment.

Statistical Analysis

The paired *t*-test or Wilcoxon-signed-rank test were used to compare the difference between the data obtained before and after treatment (SPSS, version 24; SPSS Inc., Chicago, IL). The statistical tests were 2-sided, and a *p*-value less than 5% was considered statistically significant.

Results

A total of 35 patients were initially enrolled in the study. Of these, 32 patients (11 men and 21 women;

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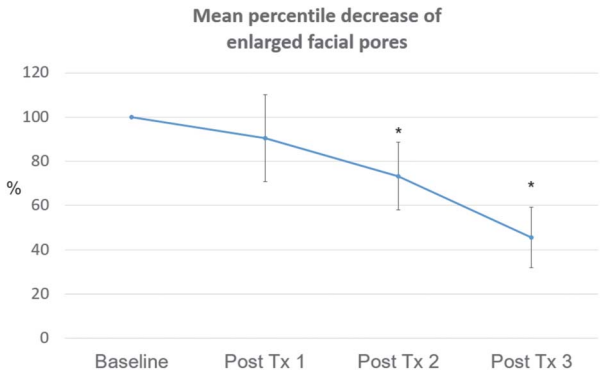


Figure 2. Mean percent changes of enlarged pore numbers measured by image analysis system from baseline to after 3 laser treatments. *$p < .05$ compared with baseline. The 95% confidence intervals are included.

ages 31–45 years; 14 Fitzpatrick skin Type III and 18 Type IV) completed the study. The 3 patients dropped out for personal reasons; none of them dropped out due to treatment-related adverse effects.

Image Analysis

Image analysis demonstrated progressive decreases in the mean number of enlarged pores after laser treatments. The average number of enlarged pores significantly decreased by 28.8% after the second session and by 54.5% 12 weeks after the third and final session compared with baseline measurements ($p < .05$ for both) (Figure 2). The paired differences from baseline to final visits of all facial areas evaluated (i.e., forehead, nose, and cheek) were statistically significant ($p < .05$ for all). Representative figures of patients after laser treatments are shown in Figures 3 and 4.

Dermatologists' Overall Assessments

Study investigators noted a significant improvement in evaluated facial areas after completion of the first treatment (Figure 5A). The improvement in the appearance of pores and overall skin texture continued to increase after the first treatment ($p < .05$). At the last visit, 12 weeks after the final treatment, dermatologists rated the appearance of pores and overall appearance as moderate to marked improvement. On the 0-to-4 scale, the means ± standard errors of assessment scores were 2.9 ± 0.4 for improvement in the appearance of pores and 3.1 ± 0.4 for improvement in overall skin texture, corresponding to moderate (26%–50%) to marked (51%–75%) improvement.

Participants' Overall Assessments and Adverse Effects

Participants also rated clinical improvements in the appearance of pores and overall skin texture (Figure 5B). Similar to the dermatologists' scores, participants' assessments for the improvement of skin pores and textures continued to increase as the treatment series progressed ($p < .05$). At the last visit, the means ± standard



Figure 3. Representative figures of improvement for enlarged pore appearance: a 45-year-old woman with photographs at baseline, 12-week follow-up, and 43-week follow-up visits after treatment.

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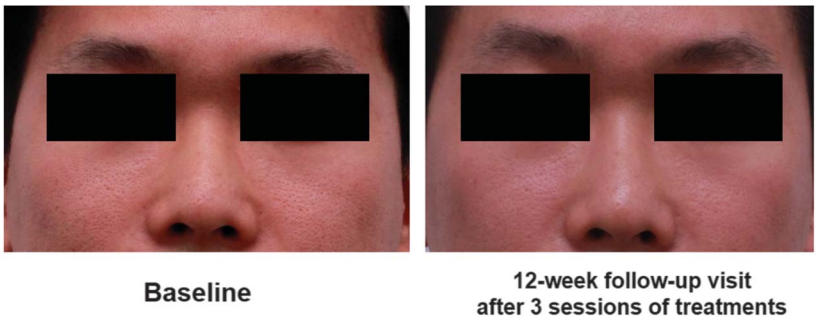


Figure 4. Close up views of a 31-year-old man at baseline and 12-week after 3 treatments.

errors of clinical improvement scales were 3.2 ± 0.5 for the appearance of pores and 3.3 ± 0.3 for skin textures. At 40 to 45 weeks after treatment, 26 participants were interviewed again by telephone or e-mail. Most of the participants (n = 19; 69%) stated that their pore status remained improved compared with baseline.

Average pain sensation during treatments was reported to be 3.1 ± 0.2 on a 1-to-10 scale. The means ± standard errors of scores (0–3 scale) for erythema, oozing, and edema were 1.4 ± 0.5, 0.9 ± 0.4, and 0.7 ± 0.2, respectively, corresponding to mild-to-moderate degrees of adverse effects. Most of the lesions improved spontaneously within 1 week of treatment. Mild crust formation was observed in some patients, but lesions were completely resolved in less than 1 week for all cases. Neither scarring nor pigment changes were observed.

Histopathology and Immunohistochemistry

A comparative investigation of histological changes before and after treatments was conducted. In H&E and MT staining, increased numbers of thick collagen fibers were observed throughout the dermis after treatments (Figure 6A–D). Specifically, both Collagen-1 and Collagen-3 molecules, representative collagens produced quickly by activated fibroblasts, increased significantly based on immunohistochemical staining (Figure 6E–H). Consistent with these data, high-intensity levels of TGF-β1 in the epidermis and dermis were observed after successive treatments (Figure 6I,J).

Discussion

To the best of our knowledge, this is the first report of low energy level CO_2 fractional laser application for the treatment of enlarged skin pores. The phrase "enlarged skin pore" is usually applied to the visible topographic features at the skin surface corresponding to enlarged openings of pilosebaceous follicles.[1,3] Horny impacted pores are normally seen in the facial skin, especially on the nose and cheeks, and the appearance of pores differs among individuals.[15] Although strict measurement of enlarged pore number

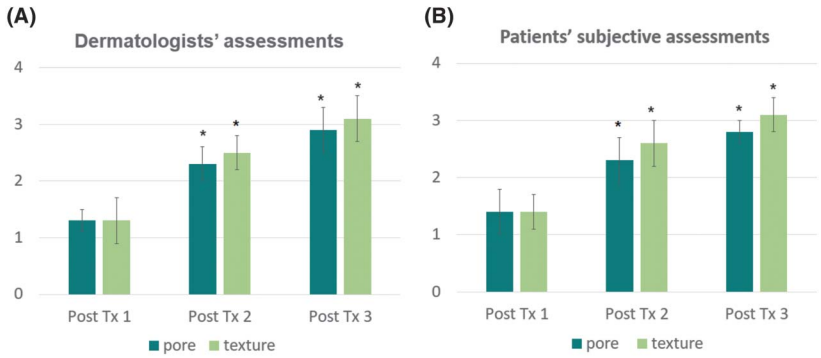


Figure 5. (A) Dermatologists' assessments. Means and 95% confidence intervals of the dermatologist-rated clinical improvement scales in appearance of pores and overall skin texture at the follow-up visit of each 3 treatment. (B) Patients' subjective assessments. Means and 95% confidence intervals of the subject-rated clinical improvement in appearance of pores, and overall skin texture at baseline and 12-week follow-up. Both of them by 0 to 4 severity scale. *$p < .05$ compared with post Tx 1 for both assessments.

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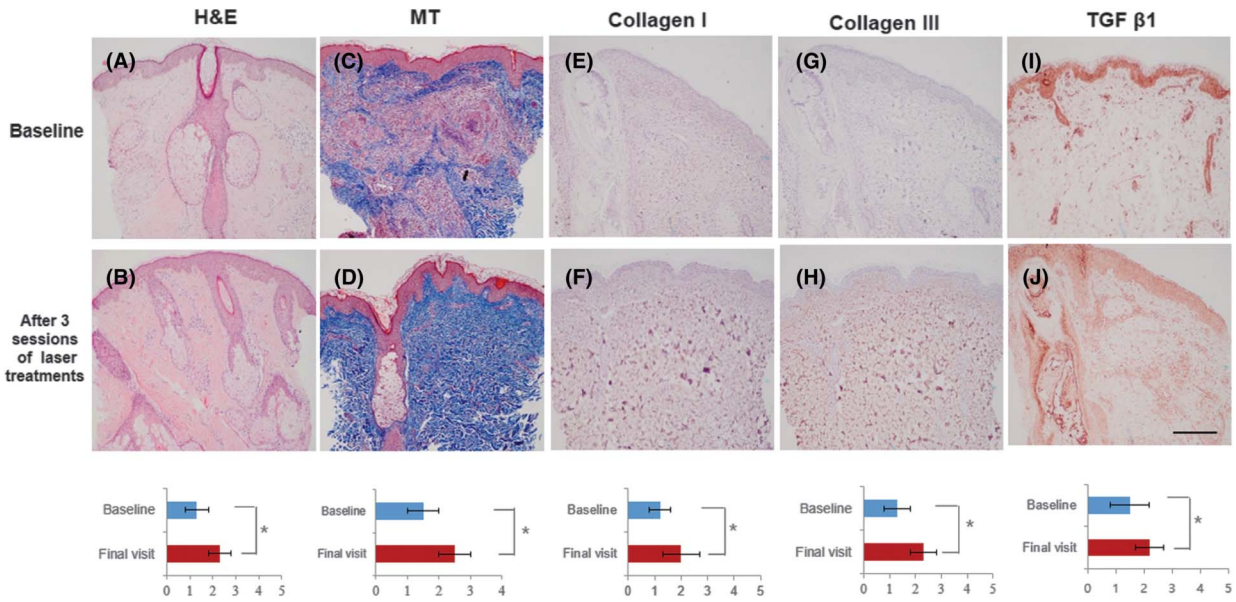


Figure 6. Histological analysis of facial skin tissues after laser treatments. Dermal remodeling and neocollagenesis after fractional CO_2 laser treatment was observed. Note greater numbers of and thicker collagen bundles in the dermis than at baseline (A–D) (hematoxylin and eosin and Masson trichrome stain; ×100). Higher expression of Collagen-I, Collagen-III, and transforming growth factor–β1 (×100) after combination treatments compared with baseline (E–J) are definitely shown in the whole dermis according to immunohistochemistry (scale bar = 50 μm). Quantification was performed for each picture. *$p < .05$ compared with baseline.

is difficult, degree of improvement assessed by detecting pore number changes based on image analysis of pixel size, as in this study, is a rational criterion compared with other technological methods including scanning reflectance spectrophotometer, tristimulus colorimeter, and SIAscopy.[16–19]

Many Asian patients are concerned with enlarged facial pores, but the treatment of this cosmetic issue has not been thoroughly covered in the field of dermatology. One sophisticated prospective study included 6 sessions of treatments with a single nonablative fractional laser; this treatment led to mild reductions of pore sizes.[6] However, the therapeutic regimen in this study showed greater efficacy in decreasing the number of enlarged skin pores with only half the number of treatment sessions according to both subjective evaluations and objective measurements. Significant improvement was also observed earlier in the treatment regimen, with improvements observed after the second session. The authors applied lower energy levels than those usually used in atrophic acne scar treatments in Asian skin,[20–23] so the incidences of commonly observed side effects were also lower. These findings support the intrinsic efficacy of CO_2 fractional laser treatments. Severe side effects, including hyperpigmentation and long-lasting crust formation, were not observed. Adequate laser settings for the treatment of enlarged pores and scars using a CO_2 fractional laser, especially for Asian skin, should be further investigated.[20,24]

Compared with previous studies that applied other devices or used other techniques to improve skin pores, including intense-focused ultrasound, Q-switched and long-pulsed 1,064-nm Nd:YAG laser, chemical peeling, and topical retinoic acid, the results demonstrated better results with respect to degrees of improvement.[4,5,25,26] Mean improvements of 3 sessions of Q-switched or long-pulsed 1,064-nm Nd:YAG were moderate (26%–50%).[4] Marked improvements (>50%) after 6 weeks of intense-focused ultrasound with 3.0-mm focal transducer were observed in less than 25% of patients.[22] No significant differences were observed in the safety profiles of the techniques included in the studies. However, further well-designed, direct comparative studies should be conducted because the protocols differed greatly among studies.

By depositing a pixilated pattern of microscopic ablative wounds surrounded by healthy tissue, the

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fractional laser offers the ability to ablate the epidermis and heat the dermal tissue at a deeper level, without significant risks of adverse sequelae.[21] Although no direct comparisons were performed in this study, superior efficacy of CO_2 fractional laser treatment compared with nonablative fractional laser treatment would be explained by differential levels of dermal stimulation for perifollicular collagen formation, and direct effects on the wall of the pore by tightening the surrounding dermal connective tissues. In fact, previous studies demonstrated that ablative fractional laser treatment, including CO_2 fractional laser, has more robust effects than nonablative fractional laser treatment for both immediate skin tightness and shrinkage through dermal stimulation and gradual collagen production to the deeper target,[9,27] which are required for effective treatment when the aforementioned anatomical structure of the skin pore is considered.

Two major phenomena seem to affect skin pores when CO_2 fractional laser is applied[27–30]: the first involves the shrinkage of collagen fibers surrounding skin pores due to the conformational changes of its 3-dimensional helical structure by fractional reticular dermal ablation, which compacts and firms skin tissues; the second, which has a long-term effect, is based on the activation of fibroblasts. Parallel and continuous patterns of collagen fibers arranged in this way results in textural improvement of the skin and lessens the prominence of pores.

The histological analysis supports these mechanisms and demonstrated marked increases in the number and thickness of collagen fibers. Greater expression of TGF-β1 may be responsible for the accumulation and thickening of collagen fibers in the dermis. TGF-β1 plays important roles in optimal wound healing during the early phase of laser treatment, leading to stimulation of fibroblasts in a dose-dependent manner.[31,32] These findings further support that reproduction of collagen surrounding dilated pores through the TGF-β pathway tightens dilated pores. Further studies focusing on concomitant changes of other microstructures such as sebaceous glands are also required.

There are some limitations to this study. First, the follow-up period is rather short. Although some patients reported their pore statuses in this study, it would be ideal to systematically follow all patients for 12 or even 18 months after the last treatment. This long-term follow-up may provide clues whether the improvements are structural reformations or simply temporary alterations in the 2-dimensional appearance of the pores. Second, all enrolled patients had identical ethnic backgrounds. Third, no internal control arm existed in this study. However, from a clinical perspective, significant changes in skin pore sizes during the study period would not be expected in a hypothetical control group.

In conclusion, enlarged skin pore is an under-studied subject and its clinical significance is overlooked. This is the first clinical and histopathological study of CO_2 fractional laser therapy treatment of dilated facial pores. The authors determined that 3 sessions of low energy level CO_2 fractional laser treatments could be a viable option for patients concerned with enlarged skin pores.

References

1. Uhoda E, Pierard-Franchimont C, Petit L, Pierard GE. The conundrum of skin pores in dermocosmetology. Dermatology 2005;210:3–7.
2. Pierard GE, Pierard-Franchimont C, Marks R, Paye M, et al. EEMCO guidance for the in vivo assessment of skin greasiness. The EEMCO Group. Skin Pharmacol Appl Skin Physiol 2000;13:372–89.
3. Roh M, Han M, Kim D, Chung K. Sebum output as a factor contributing to the size of facial pores. Br J Dermatol 2006;155:890–4.
4. Lee CN, Kim YJ, Lee HS, Kim HS. Effects of Q-switched and long-pulsed 1064 nm Nd:YAG laser on enlarged facial pores. Photodermatol Photoimmunol Photomed 2009;25:328–30.
5. Grimes PE. The safety and efficacy of salicylic acid chemical peels in darker racial-ethnic groups. Dermatol Surg 1999;25:18–22.
6. Saedi N, Petrell K, Arndt K, Dover J. Evaluating facial pores and skin texture after low-energy nonablative fractional 1,440-nm laser treatments. J Am Acad Dermatol 2013;68:113–8.
7. Cameli N, Mariano M, Serio M, Ardigo M. Preliminary comparison of fractional laser with fractional laser plus radiofrequency for the treatment of acne scars and photoaging. Dermatol Surg 2014;40:553–61.
8. Taub AF, Garretson CB. Treatment of acne scars of skin types II to V by sublative fractional bipolar radiofrequency and bipolar radiofrequency combined with diode laser. J Clin Aesthet Dermatol 2011;4:18–27.
9. Alajlan AM, Alsuwaidan SN. Acne scars in ethnic skin treated with both non-ablative fractional 1,550 nm and ablative fractional CO2 lasers: comparative retrospective analysis with recommended guidelines. Lasers Surg Med 2011;43:787–91.
10. Magnani LR, Schweiger ES. Fractional CO2 lasers for the treatment of atrophic acne scars: a review of the literature. J Cosmet Laser Ther 2014;16:48–56.

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11. Tierney EP, Eisen RF, Hanke CW. Fractionated CO2 laser skin rejuvenation. Dermatol Ther 2011;24:41–53.

12. Serowka KL, Saedi N, Dover JS, Zachary CB. Fractionated ablative carbon dioxide laser for the treatment of rhinophyma. Lasers Surg Med 2014;46:8–12.

13. Kang H, Jung B, Nelson JS. Polarization color imaging system for on-line quantitative evaluation of facial skin lesions. Dermatol Surg 2007; 33:1350–6.

14. Bae Y, Son T, Stuart Nelson J, Kim JH, et al. Dermatological feasibility of multimodal facial color imaging modality for cross-evaluation of facial actinic keratosis. Skin Res Technol 2011;17:4–10.

15. Jacobsen E, Billings JK, Frantz RA, Kinney CK, et al. Age-related changes in sebaceous wax ester secretion rates in men and women. J Invest Dermatol 1985;85:483–5.

16. Jung B, Choi B, Shin Y, Durkin AJ, et al. Determination of optimal view angles for quantitative facial image analysis. J Biomed Opt 2005;10:024002.

17. Zhang R, Verkruysse W, Choi B, Viator JA, et al. Determination of human skin optical properties from spectrophotometric measurements based on optimization by genetic algorithms. J Biomed Opt 2005;10:024030.

18. Bogaerts W, Taillaert D, Dumon P, Van Thourhout D, et al. A polarization-diversity wavelength duplexer circuit in silicon-on-insulator photonic wires. Opt Express 2007;15:1567–78.

19. Kim CS, Kim MK, Jung B, Choi B, et al. Determination of an optimized conversion matrix for device independent skin color image analysis. Lasers Surg Med 2005;37:138–43.

20. Chan NP, Ho SG, Yeung CK, Shek SY, et al. Fractional ablative carbon dioxide laser resurfacing for skin rejuvenation and acne scars in Asians. Lasers Surg Med 2010;42:615–23.

21. Manuskiatti W, Triwongwaranat D, Varothai S, Eimpunth S, et al. Efficacy and safety of a carbon-dioxide ablative fractional resurfacing device for treatment of atrophic acne scars in Asians. J Am Acad Dermatol 2010;63:274–83.

22. Cho SB, Lee JH, Choi MJ, Lee KY, et al. Efficacy of the fractional photothermolysis system with dynamic operating mode on acne scars and enlarged facial pores. Dermatol Surg 2009;35:108–14.

23. Kim S, Cho KH. Clinical trial of dual treatment with an ablative fractional laser and a nonablative laser for the treatment of acne scars in Asian patients. Dermatol Surg 2009;35:1089–98.

24. Jung JY, Lee JH, Ryu DJ, Lee SJ, et al. Lower-fluence, higher-density versus higher-fluence, lower-density treatment with a 10,600-nm carbon dioxide fractional laser system: a split-face, evaluator-blinded study. Dermatol Surg 2010;36:2022–9.

25. Lee HJ, Lee KR, Park JY, Yoon MS, et al. The efficacy and safety of intense focused ultrasound in the treatment of enlarged facial pores in Asian skin. J Dermatolog Treat 2015;26:73–7.

26. Phillips TJ, Gottlieb AB, Leyden JJ, Lowe NJ, et al. Efficacy of 0. 1% tazarotene cream for the treatment of photodamage: a 12-month multicenter, randomized trial. Arch Dermatol 2002; 138:1486–93.

27. Park SH, Kim DW, Jeong T. Skin-tightening effect of fractional lasers: comparison of non-ablative and ablative fractional lasers in animal models. J Plast Reconstr Aesthet Surg 2012;65: 1305–11.

28. Hantash BM, Bedi VP, Chan KF, Zachary CB. Ex vivo histological characterization of a novel ablative fractional resurfacing device. Lasers Surg Med 2007;39:87–95.

29. Rahman Z, MacFalls H, Jiang K, Chan KF, et al. Fractional deep dermal ablation induces tissue tightening. Lasers Surg Med 2009;41: 78–86.

30. Hantash BM, Bedi VP, Kapadia B, Rahman Z, et al. In vivo histological evaluation of a novel ablative fractional resurfacing device. Lasers Surg Med 2007;39:96–107.

31. Cordeiro MF, Bhattacharya SS, Schultz GS, Khaw PT. TGF-beta1, -beta2, and -beta3 in vitro: biphasic effects on Tenon's fibroblast contraction, proliferation, and migration. Invest Ophthalmol Vis Sci 2000;41:756–63.

32. Lu L, Saulis AS, Liu WR, Roy NK, et al. The temporal effects of anti-TGF-beta1, 2, and 3 monoclonal antibody on wound healing and hypertrophic scar formation. J Am Coll Surg 2005;201: 391–7.

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