



Microneedling: Percutaneous Collagen Induction (PCI) Therapy for Management of Scars and Photoaged Skin—Scientific Evidence and Review of the Literature



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Abstract Demand for safe, less aggressive and cost-efficient treatment modality to improve skin quality and appearance following scarring or photoaging is increasing steadily. A treatment modality that preserves the epidermis while promoting regeneration rather than cicatrization would be ideal. Percutaneous collagen induction (PCI) therapy or microneedling is claimed to approach this ideal objective. The current comprehensive literature review is intended to analyze the scientific basis supporting this therapeutic modality and to evaluate the efficacy of PCI microneedling therapy versus no treatment of patients with photoaged skin and scars of various etiologies on aesthetic skin rejuvenation, skin tightening and scar quality in prospective, retrospective and experimental studies. Twenty-five published studies were identified and included in this review. Four publications are experimental animal studies; most clinical reports are case series or small cohort non-randomized studies or trials lacking methodological unity with a heterogenous mix of scars, wrinkles and skin laxity being treated. The majority are studies about management of scars of various etiologies while only 4 specifically investigated the effect of PCI on wrinkles and aging skin. One study compared burn scar erythema in the

treated area to the untreated area, and 5 studies included histologic evaluation of biopsies. Despite PCI promising therapeutic benefits and its increasing cosmetic applications, the current literature review unfortunately revealed a limited number of high-quality studies mostly experimental. Data and conclusions of clinical studies must be carefully interpreted before translating the evidence presented into clinical recommendations.

Level of Evidence IV This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Microneedling · Percutaneous collagen induction · Non-surgical cosmetic

Introduction

Demand for safe, less aggressive and cost-efficient treatment modality to improve skin quality and appearance following scarring or photoaging is increasing steadily. Available treatments such as laser resurfacing, considered the most effective option for skin rejuvenation, tightening and correcting textural defects, as well as chemical deep peelings are dermabrasive and result in significant damage to the epidermis and its basal membrane. Inflammatory response secondary to epidermal trauma stimulates fibroblasts to produce thick bundles of scar collagen; however, regenerated skin becomes more sensitive to photograph damage [1]. Moreover, due to their traumatic ablative nature, these modalities carry the risk of potential scarring in addition to post-inflammatory dyschromias, especially in dark skin individuals [2, 3].

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“Subcision” by skin needling to release fibrous strands responsible for depressed cutaneous scars and rhytides was first reported in 1994 by Orentreich et al. [4] as a way of building up connective tissue beneath retracted scars and wrinkles. In 1997, Camirand et al. [5] reported needle dermabrasion, a somewhat similar technique using a tattoo gun without ink to improve the clinical appearance and texture of surgical scars. However, this device never gained wide popularity due to the tight grouping of the needles causing over-treatment with potential scarring [6]. Management of facial rhytides and skin laxity with a micro-needle device was first reported in the early 2000s [7].

Preserving the epidermis while promoting regeneration rather than cicatrization would be ideal [1, 3]. Percutaneous collagen induction (PCI) therapy is a relatively recent concept of cutaneous remodeling designed to approach this ideal objective. PCI was presented in 1997 as a new promising mini-invasive therapeutic modality for the treatment of various skin alterations, and a simple alternative for the treatment of photo aged skin and scars to stimulate collagen deposition without the risk of dyspigmentation [1, 3, 7, 8]. After a period of 3 weeks to 3 months of skin preparation with daily topical vitamin A and C to maximize release of growth factors and further enhance collagen production [9], microneedling results in thousands of controlled fine epidermal pricks placed side by side together with micro-wounds in the papillary dermis. With a needle 1.5 mm in length, a confluent zone of superficial bleeding is created at a depth of 500–600 μm that stimulates a scarless healing cascade [10]. A multitude of various growth factors involved in the healing process including fibroblast growth factor, platelet-derived growth factor and transforming growth factor (TGF) β are released ultimately leading to neocollagenesis and elastin deposition at the epidermal/dermal junction with thickening of the epidermal stratum spinosum [3, 7, 10, 11, 13, 14]. A significant increase in collagen type I, III, and VII and tropoelastin has been demonstrated 6 months following clinical microneedling [15, 16]. It has been also proposed that the needles do not really create a wound; instead, when needles come near a cellular membrane whose resting electrical potential is -70 mV, the inner electrical potential increases quickly to -100 mV triggering an increased cellular activity with release of potassium and growth factors triggering fibroblast chemotaxis and subsequent collagen production [10].

Des Fernandes [11] described a simple drum-shaped device with very fine protruding 3-mm needles to puncture the skin and penetrate the dermis to a depth of about 1.5 mm reaching deep in the reticular layer. Subsequently, Zeitter et al. [2] demonstrated that 1-mm needles show similar results to 3-mm needles, with less downtime, swelling and pain. Modern automated microneedling

devices have replaced the dermal roller and the needle cylinder by single-use, sterile needle cartridges with a range of different needle configurations [17]. Ultimately, the choice of the device and needle length depends on the desired therapeutic intervention [6].

PCI has now found its way into clinical practice, and a range of devices, manual, motorized, as well as radiofrequency coupled are available commercially [9, 10, 12, 14]. Innovative microneedling technology has shown promising results in minimizing acne scars, surgical scars, fine lines, wrinkles, stretch marks and cellulite, in addition to improving skin texture and firmness [18]. PCI is a simple treatment that can be carried under topical or local anesthesia; however, for needles longer than 2 mm general anesthesia is recommended [6]. It is also a safe treatment with mild and self-limited side effects and a low complication rate including post-inflammatory hyperpigmentation and tram tracking [12]. Nevertheless, inappropriate use could lead to more serious complications such as granulomas and allergic and systemic hypersensitivity reactions, particularly when the device has not been adequately sterilized or when antigenic or non-sterile topical products are applied before microneedling [18].

The current literature review is intended to analyze the scientific basis supporting this therapeutic modality without any other associated technology and to assess the available evidence regarding its clinical efficacy in the management of aging skin as well as scars of various etiologies.

Materials and Methods

A PubMed literature search was conducted to evaluate the efficacy of percutaneous collagen induction microneedling therapy versus no treatment of patients with photoaged skin and scars on skin rejuvenation, skin tightening and scar quality in prospective, retrospective and experimental studies. The search terms were “percutaneous collagen induction therapy,” “microneedling rejuvenation,” “microneedling scars,” “microneedling skin tightening” and “aesthetic microneedling.” A thorough PICO tool-based comprehensive search [19] for all possible published peer reviewed articles was also conducted with an additional PubMed advanced search builder. We first identified possible Mesh terms for every keyword, and only the keyword scar or scars had a Mesh term (Cicatrix) included. Other keywords had no identified Mesh words on PubMed. Then, we started the search with the keywords describing the patient population as those with scar OR scars OR “skin aging” with the intervention keyword as microneedl* OR micro-needl* with the outcome keywords used as “skin rejuvenat*” OR “scar qualit*” OR “skin tightening.” No

keywords search for the comparison group was conducted since the compared population was that who did not have an intervention. Reviews, expert opinions, letters to the editor, case reports, and studies about combination therapies or studies comparing microneedling to other therapeutic strategies were excluded as was microneedling for drug delivery or for indications other than aesthetic rejuvenation and scar treatment. Reports about radiofrequency needling that combines mechanical and thermal stimuli to the dermis were excluded. Reviewed articles were assessed regarding study design, treatment protocol, outcome parameters measurement and results as well as the strength of the evidence provided.

Results

A total of 326 publications were identified with the initial search (Table 1) and were screened on the basis of title and abstract. Publications with explicit titles indicating an exclusion category or without an abstract were readily dismissed. Abstracts and/or full texts of other publications were reviewed. In the final analysis, 25 published studies satisfying the inclusion criteria were selected for the review. On the other hand, the comprehensive PICO tool-based PubMed advanced search identified 37 publications. Titles of 15 publications indicated they were about radiofrequency microneedling, 6 literature review articles, and 8 combination therapies or microneedling for other than aesthetic indications. Out of the remaining 8 publications for which full texts were retrieved, 3 were reviews and the remaining were already included in the initial search.

Of the 25 manuscripts included in this review, 4 are about experimental animal studies (Fig. 1) designed to demonstrate the effect of PCI on cutaneous histology as well as on the profile of various cytokines and gene expressions involved in wound healing and cutaneous pigmentation. All 4 studies were randomized with a control group; however, they were not blinded. Moreover, researchers conducting 3 of these experimental studies

Table 1 Initial search terms and number of identified publications. Some publications were identified with more than 1 search term

Search terms	# Publications
Percutaneous collagen induction therapy	28
Microneedling rejuvenation	75
Microneedling skin tightening	13
Microneedling scars	141
Aesthetic microneedling	69

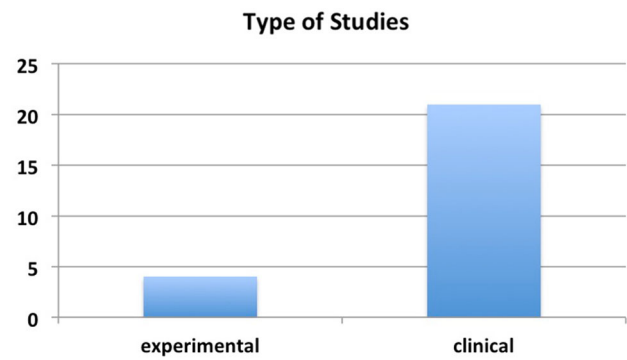


Fig. 1 Type of studies included in the review

have declared a conflict of interest. Most of the identified clinical reports are case series or small cohort non-randomized studies or trials lacking methodological unity with a heterogenous mix of scars, wrinkles and skin laxity being treated; there were also differences in treatment protocols and regimens as well as time to follow-up and outcome measures employed. The majority are studies about management of scars of various etiologies while only 3 specifically investigated the effect of this therapy modality on wrinkles and aging skin [1, 14, 16] (Fig. 2). Only one study by Busch et al. [20] compared burn scar erythema in the treated area to a non-treated area in the same patient, while all others were non-comparative case series comparing outcome to pretreatment status. Five studies included histologic evaluation of biopsies to document PCI effect [1, 14, 15, 21, 22]. One study was retrospective [1], and the rest were prospective. Independent or blinded observers evaluated the outcome in 7 studies [15, 22–27] (Fig. 3). For some objectivity to outcome measurements, standard scales were used by all clinical researchers; nevertheless, clinical assessment of changes by patients and observers was mostly subjective. Fabbrocini et al. [28, 29] evaluated outcome in both their studies with additional computerized digital image processing of silicone skin replicas. The authors of 2 clinical studies have declared

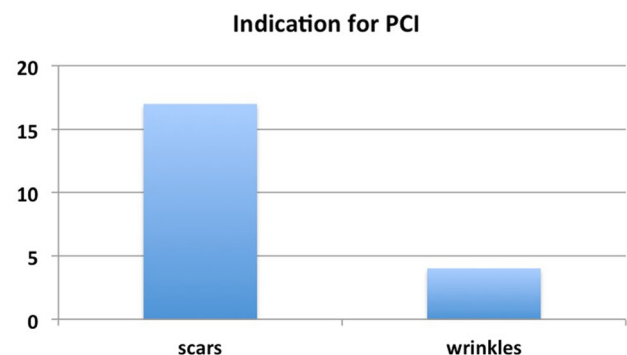


Fig. 2 Indication for microneedling

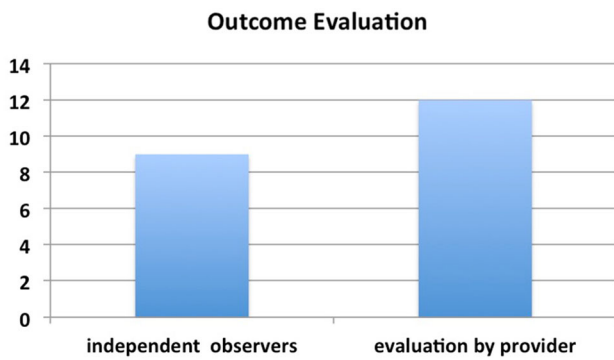


Fig. 3 Evaluators of intervention outcome

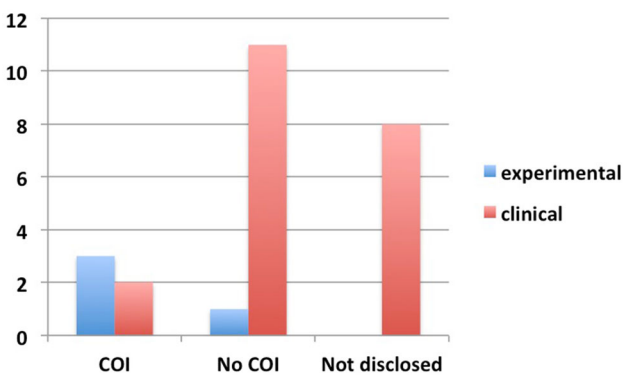


Fig. 4 Conflict of interest of authors whose publications are included in the review

having a conflict of interest while declaration of no conflict of interest was available for 11 publications only (Fig. 4).

Study design, outcome measurements and level of evidence of all reports included in this review are detailed in Tables 2, 3, 4 and Fig. 5.

Discussion

PCI therapy effect on collagen production was confirmed by 4 experimental well-conducted comparative animal studies with clearly defined objectives and outcome measures [2, 3, 30, 31]. Aust et al. have conducted 3 of these studies [3, 30, 31]. The first rat experimental study [3] demonstrated that the needling device punctures the epidermis without damaging any of its layers and without ablation of the basal membrane and its melanocytes. It causes also bleeding in the papillary dermis. The epidermis heals completely within 48 h. The authors demonstrated also that interleukin-10 is two times up-regulated in treated skin after 2 weeks; it returns to normal levels after 4 weeks. MC1R (melanocyte-stimulating hormone) is slightly down-regulated 2 weeks after needling but increases 3.5 times after 8 weeks; melanocytes in the skin

of the treated skin were unchanged and remained similar in number and distribution to the untreated skin. In the post-inflammatory response, and in contrast to ablative laser treatment, PCI therapy does not induce reepithelialization nor regeneration of basal membrane and melanocytes. In a subsequent experimental study [31], it was demonstrated that PCI with topical vitamins results in 140% increase in epidermal thickness with increased gene and protein expression of collagen I, glycosaminoglycans (GAGs), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF)-7 and epidermal growth factor (EGF). Moreover, collagen fiber bundles increase in number and become thickened and more loosely woven in both the papillary and reticular dermis. In another study [30], initial up-regulation of TGF- β 1 and TGF- β 2 at 4 weeks after treatment was demonstrated, followed by strong down-regulation at 8 weeks. There was also strong up-regulation of TGF- β 3 at 2 weeks, an essential marker for preventing scarring, without any down-regulation at 4 and 8 weeks, suggesting that the skin could be regenerated by PCI without scar formation.

For their part, Zeitter et al. [2] noticed that medical needling by 3-mm needles necessitated general anesthesia and resulted in bleeding post-operatively with excessive inflammation and swelling as well as prolonged downtime. They evaluated the benefits and risks of singular and repetitive skin microneedling by a device with 1-mm needle length in the rat experimental model. The authors demonstrated that shorter needles had a comparable effect on collagen production, and that the effect of repetitive needling every 3 weeks was additive with an increase in epidermal thickness of 115% after 1 needling session to 205% after 4 sessions and to 658% when combined with skin care consisting of topical application of high-level vitamin A oil (retinyl palmitate) and vitamin C oil (ascorbyl tetra-isopalmitate 10%). The authors concluded that the effects and benefits of singular medical needling with 3-mm needles can be achieved by singular microneedling with 1-mm needles with less pain, risks and costs; by repeating the treatment epidermal thickening might even be superseded.

Despite obvious histologic benefits demonstrated experimentally, evidence provided by clinical studies about effectiveness and aesthetic outcome of PCI is, however, less robust. Aust et al. [1] reported a retrospective analysis of 480 patients treated for fine wrinkles, acne or burn scars, and stretch marks or lax skin of the abdomen or arms. In another report [21] the authors investigated dermal scar remodeling with PCI in 16 patients with post-burn scarring. In both reports, visual analogue scale (VAS) and Vancouver Scar Scale (VSS), in addition to punch biopsies 6 and 12 months after intervention, were used to assess outcome. Improved scores were reported in addition to

Table 2 PCI experimental studies

Authors	Study design	#	Outcome	Level of evidence
Zeitter et al. [2]	Experimental comparative; animals were euthanized after 10 weeks. Skin specimens stained with HE and Masson's trichrome; gene expression analysis with microarray technique for various TGF β 1-3, FGF, EGF, VEGF, TNF- α and real-time reverse transcription PCR for collagen I and III	30 rats	Increase in epidermal thickness (up to 658%) and dermal connective tissue; juvenile collagen I d up-regulated in all groups, while collagen III was down-regulated. 1-mm needles resulted in similar outcome as 3-mm needles. Effect of repetitive needling with 1-mm needle was additive. Effect is amplified with Vit A and C	II
Aust et al. [31] ^a	Experimental comparative study; to determine the effects of PCI on skin both qualitatively and quantitatively; histology and immunofluorescence; changes in gene expression of vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF)-7, epidermal growth factor (EGF) and extracellular matrix molecules collagen type I and type III	60 rats	PCI with topical vitamins resulted in a 140% increase in epidermal thickness; an increase in gene and protein expression of collagen I, glycosaminoglycans (GAGs) and growth factors such as VEGF, EGF and FGF7. The collagen fiber bundles were increased, thickened and more loosely woven in both the papillary and reticular dermis.	II
Aust et al. [30] ^a	Experimental comparative study; assess immediate effects on the skin: systemic inflammatory response, production and gene expression of TGF isoforms beta1, beta2 and beta3	80 rats	TGF-beta3, an essential marker for preventing scarring, was up-regulated and expressed for 2 weeks	II
Aust et al. [1] ^a	Experimental comparative study; evaluate effect on epidermis, melanocytes, and pigmentation markers interleukin-10 and melanocyte-stimulating hormone	56 rats	Therapy left epidermis intact without damage to the stratum corneum or basal membrane; no signs of dermabrasive reduction in epidermal thickness; melanocytes neither increased nor decreased; interleukin-10 was increased after 2 weeks; melanocyte-stimulating hormone gene expression showed faint down-regulation at both 24 h and 2 weeks; no risk of dyspigmentation	II

^aAuthors disclosed a conflict of interest

normalization of the collagen/elastin bundles in addition to 40% thickened epidermal stratum granulosum with normal rete ridges 1 year post-operatively. In both reports, the authors admitted that some patients requested additional treatments to improve outcome and strangely mention that no treated patient underwent any open surgical procedure because PCI did not meet her or his expectation, shedding some doubts about objectivity of their observations.

Further studies about clinical application of PCI for the treatment of scars of various etiologies were reported [8, 12, 14, 20, 23–26, 28, 32–37] with similar results. In one study labeled as a prospective randomized study [36], results of PCI in 50 patients with facial acne scars, traumatic scars, hypertrophic scars and scars with skin discoloration were assessed by three evaluators comparing preoperative and postoperative clinical photographs. Unfortunately, validity of evaluating skin appearance and texture based on 2D clinical photographs is highly questionable due to inconsistent quality of photographs that may vary by image composition (magnification, angle, perspective) or exposure (luminance, contrast, white balance, focus/depth of field) responsible for low reproducibility of clinical outcome. Medical photography is not only limited by technical proficiency but also by the

arbitrary approach in deciding which specific areas to document [38]. Skin quality and appearance are best measured by skin replicas and optical image analyses. Unfortunately, these require access to costly technical equipment that limits their utility in clinical practice [39]. Such assessment methodology has been applied by Fabrocini et al. [28] for documenting the efficacy of PCI in the treatment of acne scarring in different skin phototypes. Computerized image analysis of data from the silicone cutaneous casts was conducted, and irregularities of the surface micro-reliefs were quantified with fast Fourier transformation (FFT) demonstrating objectively evident aesthetic improvement with net decrease in the degree of skin texture irregularity in all patients.

In the single clinical study comparing treated to none treated areas, Busch et al. [20] investigated whether PCI improves erythema in hypertrophic burn scars. Erythema measurement was performed objectively with the Mexameter that determines the amount of hemoglobin in the vascular system of the affected area. A modest 19% improvement was reported after 6 months in treated areas compared to only 1% in none treated areas, suggesting that PCI could represent a controlled and relatively simple method for the targeted treatment of persistent scar

Table 3 PCI clinical studies

Authors	# patients	Treated condition	Outcome	Level of evidence
Alster et al. [35] ^a	120	Various scars	All scars improved at least 50% after 2.5 treatments. Over 80% of patients had 50–75% improvement, and 65% of patients demonstrated over 75% improvement	IV
Vijaya Lakshmi et al. [33] ^b	14	Facial scars: cleft lip, acne scars	Statistically significant improvement observed with patient satisfaction scale (PSS) and observed satisfaction scale	IV
Bhargava et al. [24]	45	Acne scars	Overall improvement seen in 95.6% of patients; majority of the patients (55.5%) perceived an improvement of 25–49%	II
Afzal et al. [25] ^b	50	Acne scars	Post-treatment grading improvement was statistically significant	II
Bandral et al. [36]	50	Facial scars	14% showed excellent response to PCI treatment, 52% had a good response, 28% had fair response, and 6% had poor response	IV
Minh et al. [26]	31	Acne scars	Goodman and Barron's grade decreased from 3.29 ± 0.59 at baseline, to 1.77 ± 0.57 two months after the completion of therapy; Lipper and Perez score dropped significantly from 36.48 ± 12.07 to 16.37 ± 7.29 at two months after the final treatment; 83.3% of patients were satisfied	II
Ablon [16]	48	Facial skin aging	Statistically significant mean improvements in global wrinkle score, skin laxity, and skin texture observed at Day 90 and 150; Improvements in wrinkle grading and skin texture were confirmed by the PRIMOS profilometry	IV
Al Qargaz et al. [34]	39	Acne scars	PAHPI and Goodman–Baron scales showed statistically significant improvement	IV
Busch et al. [20]	20	2-y-old burn scars healed by secondary intention	Scars showed significant reduction in erythema. Objective measurements demonstrated normalization of the skin color	II
Amer et al. [27] ^b	40	Facial wrinkles	2 blinded dermatologists evaluated the photographs taken before treatment and after completion of the treatment. Physicians assessed the results using quartile grading scale which categorizes the improvement as follows: excellent improvement > 75%; very good improvement of 50–74%; good improvement of 25–49% and poor improvement < 25%. A questionnaire was given to patients at the end of treatment to assess their degree of improvement	IV
Šuca et al. [8] ^b	6	STSG scars Burns	Subjective improvement. Objective evaluation with the Vancouver Scar Score showed improvement in an average of two points and more even distribution of pigment	IV
Kubiak et al. [23]	47	Post-burn scars	All patients reported subjective improvement and were satisfied; overall VSS scores improved post-treatment in all patients; scar vascularity, pliability and height all improved; there was no statistically significant effect on pigmentation	II
El-Domyati et al. [14] ^b	10	Wrinkles	Increased collagen production; multiple sessions are usually needed to maintain the improvement achieved	II
El-Domyati et al. [15] ^b	10	Acne scars	Noticeable clinical improvement; significant increase in collagen types I, III, and VII, while total elastin was significantly decreased	IV
Dogra et al. [37] ^b	36	Acne scars	Significant decrease in mean acne scar assessment score from 11.73 ± 3.12 at baseline to 6.5 ± 2.71 after five sittings of dermaroller; results on visual analog scale (VAS) showed “good response” in 22 patients and “excellent response” in 4 patients; post-inflammatory hyperpigmentation in 5 patients and tram-trek scarring in 2	IV
Fabbrocini G, et al. [28]	60	Acne scars	Statistically significant ($p < 0.05$) reduction in severity grade of acne scars; surface micro-relief analysis of skin replicas showed decrease in the degree of irregularity of skin texture in all three phototype groups of patients without risk of dyspigmentation	IV
Park et al. [22] ^b	16	Stretch marks	Marked to excellent improvement was noted 43.8% patients; patient satisfaction scores showed 37.5% were highly satisfied, 50.0% were somewhat satisfied	II

Table 3 continued

Authors	# patients	Treated condition	Outcome	Level of evidence
Aust MC, et al. [21] ^a	16	Post-burn scarring	Patients rated improvement as a mean of 80% better. Histology: considerable increase in collagen and elastin deposition at 12 months; 45% epidermis thickening of stratum spinosum and normal rete ridges; normalization of the collagen/elastin matrix in the reticular dermis	IV
Majid [32]	37	Atrophic facial scars	34 patients achieved a reduction in the severity of their scarring by one or two grades; more than 80% of patients assessed treatment as “excellent”	IV
Fabbrocini et al. [29]	60	Acne scars	Severity grade of rolling scars in all patients was greatly reduced and there was an overall aesthetic improvement	IV
Aust MC, et al. [1] ^a	480	Fine wrinkles, lax skin, scarring, and stretch marks	Patients rated improvement between 60 and 80% better; Histologic examination o 20 patients showed considerable increase in collagen and elastin deposition at 6 months; epidermis 40% thickening of stratum spinosum and normal rete ridges at 1 year	III

^aAuthors disclosed a conflict of interest

^bConflict of interest not disclosed

erythema. However, superiority of PCI over other treatment modalities such as compression with or without silicone patches remains to be determined.

In addition to the initial report by Aust et al. [1], 2 more reports addressed management of wrinkles and aging skin [14, 16]. Among 350 patients with fine wrinkles and 58 with stretch marks or lax skin of the abdomen or arms included in the retrospective study of Aust et al. [1], 35 and 15 patients, respectively, were treated in Germany. The average preoperative patient satisfaction score using a visual analogue scale improved from 4.5 to 8.5 post-operatively for fine wrinkles and from 3.5 to 8.0 for skin laxity. However, improvement in the other patients treated in South Africa if any was not reported. Based on histology of skin biopsies taken one and three months after the start of six skin microneedling sessions at 2-week intervals, El-Domyati et al. [14] noted that PCI is a promising minimally invasive treatment option for increasing dermal collagen production. While it is recommended that multiple sessions are usually needed to maintain the improvement achieved, little data about objective assessment of aesthetic outcome were provided. The main interest of Ablon [16] for his part was to evaluate the efficacy and safety of an automated microneedling device for the rejuvenation of facial skin. Efficacy of the device was made by evaluating improvement in wrinkles in nine separate facial areas using the Lempeler grading scale [40]. Improvement in pigmentation, wrinkle lines, skin texture and pores was reported in 98% of patients 90 and 150 days after treatment without, however, providing clear objective measurement of this improvement and how significant is this improvement aesthetically. Ablon’s main conclusion was that the device is cost-effective, with the only real recurring cost to the operator being the single-use microneedling cartridges.

A striking difference was observed among reviewed clinical studies in the time to follow-up, which varied between 1 and 12 months. Studies have observed that effects of microneedling changed over several months to reach a maximum at 3–6 months [6]. Time to follow-up was not specified in 4 clinical studies [8, 25, 33, 36], and 4 others reported a follow-up period shorter than 3 months [15, 23, 32, 37]. It must be noted though that multiple sittings were performed in many studies and the time to follow-up was from the last sitting. Though the follow-up time of both studies reported by El-Domyati et al. [14, 15] was only 1 month, patients had 6 sittings at 2-week interval; thus, it was in fact 3 months from the first sitting, though it was too short to fully evaluate the cumulative effect of the authors’ treatment protocol.

Outcome measurement in plastic surgery relies mostly on clinical expertise and is often surgeon centered and clinician derived [41] even more so when a given intervention is primarily for aesthetic purposes. Similar to all reports about aesthetic outcome, the primary dilemma faced with the clinical studies included in this review is how outcome was measured. Traditionally, aesthetic outcomes are assessed through the use of photographs with a natural inclination to the provider’s perspective [42]. Besides general genuine reservations regarding medical photography alluded to earlier, key elements to a valid assessment based on photographic documentation must include multiple expert evaluators blinded to the procedure with high degree of agreement among raters [43]. Having only one expert, usually the treating physician to assess outcome, introduces bias into the study design [43]. In only 8 clinical studies reviewed, independent observers have evaluated the intervention outcome [14, 22–26, 35, 36]. In 3 of these studies [24–26], there was only 1 observer and in

Table 4 Study design and outcome of clinical studies

Authors	Device	Intervention protocol	Control	FU	Observer-reported outcome	Patient-reported outcome	Bx
Alster et al. [35]	Hand-held motorized (Collagen P.I.N.; Induction Therapies, Louisville, Ky.) Disposable needle cartridges (30-gauge, 36-needle array) needle depths 2.5 to 3 mm	1 to 6 consecutive monthly treatments till desired clinical improvement attained. Rolled until uniform pinpoint bleeding (4 to 10 passes) Photographs of scars at baseline, before each treatment and 1, 3, 6 and 12 months after final PCI	–	12 months	2 blinded assessors to treatment protocol. Comparing photographs. Five-point scale: Global Assessment Score	Subjects' own assessments of scar improvement	–
Vijaya Lakshmi et al. [33] ^b	Dermaroller	Minimum of 2 sittings, with minimum interval of 30 days	–	–	Observer satisfaction scale (OSS) + Scale for scar height and color	Patient satisfaction scale (PSS)	–
Bhargava et al. [24]	Subcision performed with 18-gauge, tribeveled, hypodermic needle. PCI performed using a dermaroller (2-mm needle size, 192 needles)	4 sittings 4 weeks apart. Rolled until uniform ne pinpoint bleeding points appeared. Digital photographs	–	3 months	Scar grading by a blinded dermatologist. Clinical scar assessment with Goodman and Baron scale	Patient response graded as poor (0–24% improvement), good (25–49%), very good (50–74%) or excellent (75–100%)	–
Afzal et al. [25] ^b	Dermapen at speed of 60–90 cycles per sec with 33-gauge 12 micro-sized needle cartridge used with depth of 1.5–2.0 mm. 10–12 passes	4 sittings 3 weeks apart. Photographs	–	–	Independent observer with 10 years of experience; procedure was kept double blind. Scar assessment with Goodman and Baron scale	–	–
Bandral et al. [36]	Dermaroller [®] with barrel 20 mm wide with 540 needles in 8 rows. Movement 4 times in 4 directions.	1 session Photographs analyzed by 3 evaluators	–	–	3 evaluators comparing preoperative and postoperative clinical photographs	–	–
Minh et al. [26]	Microneedle derma roller (MTS Roller, 192 needles in 8 rows, 0.25 mm diameter and 1.5-mm-long needles)	Every week for 3 months. Rolled in 4 directions and repeated 4–10 times. Photographs	–	3 months	Blinded dermatologist. Assessment with Goodman and Baron scale	Patient response graded as poor (0–24% improvement), good (25–49%), very good (50–74%) or excellent (75–100%)	–

Table 4 continued

Authors	Device	Intervention protocol	Control	FU	Observer-reported outcome	Patient-reported outcome	Bx
Ablon [16]	Needle incision from 0 to 1.5 mm. Frequency of the needle stroke 100 to 150 Hz. Safety needle cartridge with 6 single-use, stainless steel microneedles (maximum 1.5 mm length, 0.35 mm gauge)	4 sessions 30 d apart. Photographs and rhytides and skin laxity scores	–	150 days	Assessment of routine VISIA photograph and PRIMOS digital fringe projection technology to assess skin topography. Facial rhytides (Lemperle Wrinkle Scale) and skin laxity (Alexiandes Armenakas Laxity Scale)	Subject evaluation of pain and discomfort	–
Al Qargaz et al. [34]	Electric microneedling device (e Dermastamp, Dermalroller GmbH, Germany)	PCI performed until pinpoint bleeding and uniform erythema of treated skin obtained	–	14 weeks	Assessment with Goodman–Baron and PAHPI scores	VAS score: not satisfied less than 25% (0), mild improvement 25–49% (1), good 50–75% (2) or excellent > 75% (3)	–
Busch et al. [20]	Needling device with 3-mm-long needles rolled over scar in three directions under constant pressure	1 PCI session. Target scar areas: 2 subareas randomly selected for positive (medical needling) and negative control (no treatment). Photography	+ Patient is his own control	12 months	Patient and observer scar assessments (POSAS). Mexameter to quantify presence of melanin and hemoglobin	Patient and observer scar assessments (POSAS)	–
Amer et al. [27] ^b	Dermapen with needle tip containing 12 needles	6 sessions of treatment with two-week interval between the sessions. Photographs of patients were obtained at every session	–	At end of Rx	Analysis of patients photographs and patients' questionnaire	Questionnaire to rate scars as poor, good, very good and excellent. Photographs graded by quartile grading scale	–
Šuca et al. [8] ^b	Dermalroller [®] with 2.5 mm needles	3 sessions 6–8 weeks apart. Photographs	–	–	Vancouver Scar Score. Average improvement of 2 points. More uniform pigment distribution and the hypertrophic and unstable areas reported to be flatter and more stable	Patient rating. Subjective improvement in the final scar quality, improved pain profiles and reduced tension	–
Kubiak et al. [23]	Dermalroller, Dermalroller GmbH, Wolfenbüttel, Germany 2.5 mm needles	1 PCI session under general anesthesia. Rolled multiple times in multiple directions with pressure over the scar. Photographs	–	4 weeks	Images graded independently by 3 investigators according to Vancouver Scar Scale (VSS)	Patient satisfaction outcomes	–

Table 4 continued

Authors	Device	Intervention protocol	Control	FU	Observer-reported outcome	Patient-reported outcome	Bx
El-Domyati et al. [14] ^b	Dermaroller with a needle length of 1 mm (Directive MDD 93/42 EEU. DERMAROLLER Deutschland S.a.r.l. Lindener Strasse15, D38300 Wolfenbüttel, Germany; Model MF8, 192 needles in eight rows, needle diameter at penetration point of 0.25 mm, width and diameter of the roller head, 20 mm)	6 sessions a t 2 weeks interval. 6 passes per area treated carried in 8 directions. Photographs	–	3 months	2 dermatologists, and 2 independent observers evaluated wrinkle improvement, skin texture and overall satisfaction, based on a 5-point scale. Histopathology and Immunofluorescence studies. Quantitative evaluation of immune-stained tissues with computer-based software	Patients evaluated wrinkle improvement, skin texture, and overall satisfaction, based on a 5-point scale. (none = 0%; mild = 1–25%; moderate = 26–50%; good = 51–75%; and very good = 76–100%)	+
El-Domyati et al. [15] ^b	Dermaroller with 1.5-mm-long needles (Directive MDD 93/42 EEU, Dermaroller Deutschland S.a.r.l., Germany, 192 needles in 8 rows, needle diameter at penetration point: 0.25 mm, width and diameter of the roller head: 20 mm)	6 sessions a t 2-week interval. Rolled in 8 directions with minimal pressure till presence of uniform bleeding points	–	1 month	Histopathology and Immunofluorescence studies + Clinical assessment based on 5 point scale	Clinical assessment based on 5 point scale	+
Dogra et al. [37] ^b	Drum-shaped roller studded with 192 fine microneedles (1.5 mm in length and 0.1 mm in diameter) in eight rows	PCI monthly for five sittings. 16–20 passes made in different directions. Photographs	–	1 month	Assessment of improvement based on quartile score (1: < 25%, 2: 25–50%, 3: 50–75%, 4: > 75% improvement)	10-points VAS. above 6 points was graded as “excellent,” between 4 and 6 as “good” and below 4 as “poor”	–
Fabbrocini et al. [28]	Dermaroller, model MS4; Horst Liebl CEO, Fresenheim, France, rolling barrel 10 mm wide with 96 needles (length 1.5 mm, diameter 0.25 mm) in 4 rows	3 settings at monthly intervals. Rolling 4 times in 4 different directions. Depending on the applied pressure, needles penetrate the scar tissue up to a 1.5 mm. Photographs	–	10 months	Aesthetic improvement was evaluated with Global Aesthetic Improvement Scale (GAIS) + computerized image analysis of skin replicas using silicone molds in 10 patients		–
Park et al. [22] ^b	DTS roller; DTS-MG, Inc., Seoul, Korea. Plastic body and head cylinder with 540 needles protruding 1.5 mm from the surface	3 treatments 4 weeks apart. Rolling 4 times in 4 directions. Photographs	–	3 months	Evaluation of photographs using a quartile grading system (0 = no change [1 = minimal [< 25%], 2 = moderate t [26–50%], 3 = marked [51–75%], 4 = excellent [76–100%])	Patients rated their satisfaction after treatment completion (A = unsatisfied, B = some-what satisfied, C = highly satisfied)	+

Table 4 continued

Authors	Device	Intervention protocol	Control	FU	Observer-reported outcome	Patient-reported outcome	Bx
Aust et al. [21] ^a	Medical Roll-CIT (Vivida, Cape Town, South Africa)	1–4 treatments	–	12 months	Rating on questionnaires (visual analogue scale (VAS), Vancouver Scar Scale (VSS) and patient and observer Scar Assessment Scales)	Patient and observer Scar Assessment Scales	+
Majid [32]	Derma-rollers with 1.5-mm-long needles	PCI at monthly intervals till satisfactory outcome for a maximum of 4 sittings. Rolled till presence of uniform bleeding points. Photographs	–	2 months	Scar grading scale	Questionnaire to rate scars on 10-point scale	–
Fabbrocini et al. [29]	Derma-roller, model MS4; Horst Liebl CEO, Fresenheim, France, rolling barrel 10 mm wide with 96 needles (length 1.5 mm, diameter 0.25 mm) in 4 rows	2 sessions at 8 weeks interval. Rolled 4 times in 4 directions resulting in 250–300 pricks/cm ² Needles penetrated scar tissue to a depth of 0.1–1.3 mm depending on pressure applied. Photographs taken by dermatologist not involved in the study; micro-relief impression of scars in 5 patients e	–	8 weeks	Analysis of the patient photographs + degree of irregularity of the surface micro-relief by computerized digital image processing		–
Aust et al. [1] ^a	Environ Medical Roll-CIT (Vivida-SA cc, Renaissance Body Science Institute, Cape Town, South Africa)	Group I: Wrinkles (<i>n</i> 350) Group II: Scarring (<i>n</i> 72) Group III: Lax Skin/Striae (<i>n</i> 58)	–	6 months	Vancouver Scar Scale, and the Patient and Observer Scar Assessment Scales + observer scale considering 5 parameters (vascularization, pliability, pigmentation, thickness and relief). Histology	Visual analogue scale (0 absolutely dissatisfied and 10 completely satisfied) + patient scale, considering 6 parameters (color, pliability, thickness, relief, itching and pain)	+

^aAuthors disclosed a conflict of interest

^bConflict of interest not disclosed

3 studies [14, 22, 35] 2 observers. Independent observers were blinded in only 4 studies [24–26, 35], implying that the risk of bias in the other studies was high. For the remaining studies, the providers have personally assessed the outcome or have asked their patients if they are satisfied that is a seriously flawed methodology [43]. Patients' and surgeons' concept of beauty as well as degree of improvement may vary dramatically, and measuring

satisfaction is a very complex endeavor [43]. Moreover, evaluating outcome from the patient's perspective depends on the accuracy and reliability of the questions asked, whether ad hoc, generic, domain specific or condition specific. Unfortunately, previously validated condition-specific measures are limited for aesthetic procedures. Limited scientific rigor in development, content and validation characterizes most patient-reported outcome

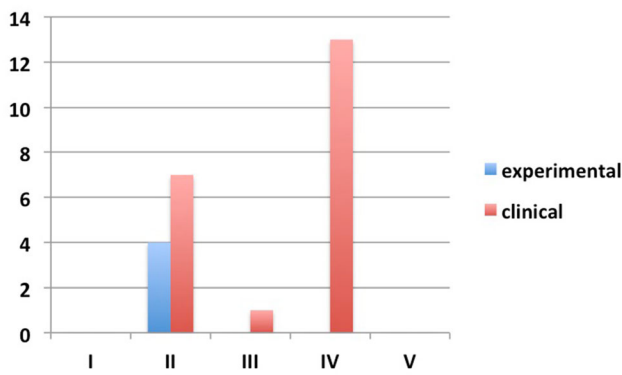


Fig. 5 Levels of evidence determined according to the American Society of Plastic Surgeons Levels of Evidence for Therapeutic Studies. I: High-quality or single-centered, randomized controlled trials with adequate power or systematic reviews of these studies. II: Lesser-quality, randomized controlled trials, prospective cohort studies or systematic reviews of these studies. III: Retrospective comparative study, case–control study or systematic review of these studies. IV: Case series. V: Expert opinions, case reports or clinical examples, or evidence-based studies on physiology, bench research or “first principles”

measures for facial cosmetic interventions [42, 43]. It must be kept in mind also that satisfaction with surgical outcomes can change over time [43].

Conclusion

Several methods and combined approaches to enhance collagen formation, skin rejuvenation and scar improvement are currently available; nevertheless, the most optimal technique striking an appropriate benefit–risk–cost balance is yet to be determined. Compared to other ablative resurfacing modalities, advantages of PCI by simple microneedling in addition to maintaining the epidermal layer integrity and increasing dermal thickness and collagen formation include non-specialized equipment required and versatility as well as low risk of side effects and complications [9]. The technique, however, is operator dependent with depth of penetration determined by pressure exerted and the number of roller movements over the same skin area; moreover, what is considered as effective treatment relies on good clinical judgment regarding visible microbleeding [12]. Despite PCI promising therapeutic benefits and its increasing cosmetic applications, the current literature review unfortunately revealed a limited number of high-quality studies mostly experimental. Data and conclusions of most clinical studies must be carefully interpreted before translating the evidence presented into clinical recommendations. PCI clinical relevance regarding aesthetic efficacy is yet to be demonstrated. Even though choosing the suitable and valid outcome measurement can

be nebulous [41], current evidence, as recently stressed [6], needs to be strengthened by more qualitative, randomized, controlled, double-blinded, comparative clinical trials with standardized validated measurement tools and longer follow-up times.

Compliance with Ethical Standards

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

Human and Animal Rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent For this type of study, informed consent is not required.

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