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Microneedling in All Skin Types: A Review

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ABSTRACT

INTRODUCTION: Microneedling procedures are growing in popularity for a wide variety of skin conditions. This paper comprehensively reviews the medical literature regarding skin needling efficacy and safety in all skin types and in multiple dermatologic conditions.

METHODS: A PubMed literature search was conducted in all languages without restriction and bibliographies of relevant articles reviewed. Search terms included: “microneedling,” “percutaneous collagen induction,” “needling,” “skin needling,” and “dermaroller.”

RESULTS: Microneedling is most commonly used for acne scars and cosmetic rejuvenation, however, treatment benefit has also been seen in varicella scars, burn scars, keloids, acne, alopecia, and periorbital melanosis, and has improved flap and graft survival, and enhanced transdermal delivery of topical products. Side effects were mild and self-limited, with few reports of post-inflammatory hyperpigmentation, and isolated reports of tram tracking, facial allergic granuloma, and systemic hypersensitivity.

DISCUSS: Microneedling represents a safe, cost-effective, and efficacious treatment option for a variety of dermatologic conditions in all skin types. More double-blinded, randomized, controlled trials are required to make more definitive conclusions.

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INTRODUCTION

Microneedling (MN), or percutaneous collagen induction therapy, was introduced in the 1990’s for the treatment of scars, striae, and laxity.[1] By rolling or gliding a needling device across the skin, thousands of vertical channels of injury are created, triggering a scarless healing cascade and neocollagenesis.[2] With lack of heat or chromophore target, MN offers an excellent safety profile in all skin types.

Mechanism of Action

Needles carry an electric potential that stimulates fibroblast proliferation.[3] MN-induced mechanical injury triggers the release of potassium and proteins that alter intercellular resting potential, drawing in fibroblasts and stimulating neocollagenesis and revascularization.[4] MN studies have shown up-regulation of TGFβ3, a cytokine that prevents aberrant scarring, increased gene expression for collagen type I, and elevated levels of vascular endothelial growth factor, fibroblast growth factor, and epidermal growth factor.[5,6,7] Histological studies have shown huge variation in epidermal thickness. Randomized murine studies have reported statistically significant epidermal thickening from 140% up to 685% after MN plus topical vitamins A and C when compared to control.[7,8] A human study of 480 patients treated with MN plus topical vitamins A and C reported 40% thickening of the stratum spinosum lasting up to 1-year later.[9] Increased collagen types I, III,

VII, and tropoelastin in human biopsies were found after 6 sessions of MN10 with elevated levels of collagen type I and elastin persisting at 6-months.11 Number of melanocytes was unchanged post-procedurally.[9]
Acne Scars *MN Monotherapy* Many studies have demonstrated statistically significant efficacy with MN monotherapy for acne scars in all skin types.[12-17] A randomized, evaluator blinded, clinical trial of 46 patients with atrophic acne scars, compared MN versus nonablative fractional Erbium 1,340-nm laser.[18] After 3 monthly sessions, there was no statistical difference between groups on the Quantitative Global Grading System for Post-Acne Scarring scale at 2 and 6 months post-treatment (P=0.264). Of note, 13.6% of laser patients experienced post-inflammatory hyperpigmentation (PIH), while the needling group had none. Another randomized, spit-face study of 30 patients with atrophic acne scars treated subjects with either fractional Erbium doped Yttrium Aluminum Garnet (Er:YAG) laser or MN over 5 monthly sessions.[19] Objective and subjective assessments at baseline and 3-months after post-treatment showed clinical and histological bene t in both treatment groups. However, the fractional Er:YAG group demonstrated 70% improvement, versus 30% in the MN group (P<0.001), and significantly lower pain scores with fractional Er:YAG. The MN group experienced shorter downtime. Another randomized, evaluator-blinded study of 30 patients with acne scars compared 4 monthly sessions of MN or 100% trichloracetic acid (TCA) chemical reconstruction of skin

scars (CROSS).[20] All patients saw clinical improvement on a scar severity scale at 2-month follow-up, without statistically significant difference in percent improvement between treatment groups. No major adverse events were reported. *MN Plus Platelet Rich Plasma* In a split-face trial of 12 patients with acne scars, investigators compared MN alone versus MN with topical platelet-rich plasma (PRP).[21] Both groups saw reduced acne scar severity scores, but the MN plus PRP group had an overall mean lower score. Another split-face study of 50 patients with acne scars evaluated MN of the entire face followed by topical and intradermal injection of PRP or distilled water.[22] MN plus topical and intradermal PRP showed 62.20% clinical improvement compared to 45.84% improvement with MN plus distilled water. In the MN plus PRP group, 40% of subjects reported an excellent response and 60% reported a good response. In the MN plus distilled water group, 10% saw excellent response and 6% reported good response. A split-face study of 30 patients compared MN plus topical PRP versus MN plus topical vitamin C for the treatment of acne scars.[23] The MN plus PRP group had 22% poor responders versus 36% poor responders in the MN plus vitamin C group. Of note, no statistically significant difference was noted in a randomized study of 45 patients with acne scars treated with 3 bi-weekly sessions of either MN plus topical PRP, intradermal injection of PRP, or the CROSS technique with 100%TCA.[24] *MN Plus Chemical Peel* Sixty acne scar patients of Indian background with Fitzpatrick skin type (FST) III-IV underwent MN alone or MN followed by 35% glycolic acid peels 3 weeks later.[25] After 5 treatment sessions, the combined treatment group demonstrated 62% clinical improvement on the Echelle d'Evaluation clinique des Cicatrices d'acné scale when compared to the 31% improvement seen in the MN monotherapy group at 3-months (P=0.001). MN plus 15% TCA peel was evaluated in a non-controlled study of 50 patients with acne scars and FST III-V.26 Of those with grade-2 scars on the Goodman and Baron Global Acne Scarring System (GBGASS), 100% had complete resolution. Of those with grade-4 scars, 63% improved to grade-2 scars and 38% improved to grade-3 scars. Results persisted at 1-year follow-up. PIH occurred in 6% of patients but resolved after 5 months of tretinoin, hydroquinone, and mometasone. *MN Plus Energy Devices* A randomized, controlled trial of 39 patients with atrophic acne scars were treated with either MN plus 20% TCA, MN plus 1,540-nm nonablative fractionated laser, or alternating sessions of both regimens.[27] The group receiving both regimens showed superior clinical response when compared to those receiving only one. A randomized, open-label, pilot study of 60 patients with ice pick acne scars treated subjects with pinpoint irradiation technique by ablative CO2 laser.[28] The laser procedure was followed by 1mm MN with a 26-gauge needle or not, for 4 sessions at 3-week intervals. According to the acne scar severity index, GBGASS, and patient satisfaction scores, both groups demonstrated clinical improvement (P<0.05) but without significant difference in efficacy between groups (P greater than 0.05). No adverse events were reported. Fractional radiofrequency microneedling (FRFM) delivers thermal energy via insulated or uninsulated microneedles, causing coagulation and resultant neocollagenesis. The use of FRFM for acne scars was evaluated in a retrospective study of 31 patients with FST III-V and grade 3-4 facial acne scars on the GBGASS.[29] After 4 treatments every 6 weeks, 80% of patients showed a 2-grade improvement and 19% had a 1-grade improvement. All adverse events were transient, including erythema, edema, and hyperpigmentation.

Varicella Scars

One patient of FST V with varicella scars underwent 3 MN treatments and reported significant improvement.[30] Another study reported 34 of 36 patients with varicella scars, acne scars, and post-traumatic scars improved after MN on the GBGASS, with 80% achieving "excellent" results on a 10-point scale.[17] PIH

occurred in 1 patient.

Burn Scars

One patient with facial burn scar underwent 5 treatments of ablative CO2 laser followed by MN and reported smoother scar texture and less contracture.[31] In a non-randomized trial of 16 patients with post-burn scars affecting 20% body surface area, 1 month of topical vitamin A and C preceded 1-4 MN treatments.[9] Patients reported 80% improvement on average when compared to baseline on the visual analog scale ($P<0.005$), with normalized collagen and elastin at 1-year. Hypopigmented burn scars in a 20-patient study were divided into 3 distinct treatment zones, receiving either 3mm needling plus a topical non-cultured autologous skin cell suspension (NCASCS), 3mm needling alone, or no treatment.[32] The NCASCS is harvested from a split thickness skin sample and digested by enzymes. The suspension is then sprayed onto a hypopigmented scar that was prepped beforehand via dermabrasion. After 12 months, 17 of 20 patients rated the needling plus NCASCS portion 50% improved in color on the Patient and Observer Scar Assessment Scale (P less than 0.05), while observers not- ed 37.5% improvement (P less than 0.05). At 1-year, the Melanin Index

score increased by 29.3% in the needling plus NCASCS group versus 8.4% in the needling only group (P less than 0.05).

Flap and Graft Survival

A randomized murine study on skin aps evaluated MN plus PRP, MN plus platelet poor plasma, MN alone, PRP alone, sham, and control.[33] The MN plus PRP group demonstrated the longest increase in ap survival and most reduced Substance P (P A controlled, sham murine study on fat graft survival evaluated MN of a recipient site 1-week prior to fat graft transfer.[34] After 15 weeks, MN-treated fat grafts maintained larger volume when compared to control (P less than 0.05), with better integrity and uniformity of adipocytes (P less than 0.01), less inflammation (P less than 0.05), better vascularity (P less than 0.01), less brosis and vacuolization (P less than 0.01).

Striae

A study of 16 patients with striae distensae underwent 3 monthly treatments of MN.[35] Seven patients (43.8%) had excellent improvement on histologic and photographic grading scales, while 9 patients showed minimal to moderate improvement. Only 6 patients (37.5%) were highly satisfied. Side effects included mild pain, erythema, and spotty bleeding. Forty striae patients treated with MN or microdermabrasion with sonophoresis reported significant clinical improvement after MN, when compared to microdermabrasion.[36] Increased collagen, fibroblasts and epidermal thickness was seen in 90% of MN-treated specimens versus 50% of microdermabrasion specimens. A randomized, evaluator-blinded trial of 20 striae patients compared MN versus fractional CO2 laser.[37] Ninety percent of MN patients achieved significant improvement by photograph on a quartile scale, versus only 50% in the laser group (P less than 0.001). Both groups showed increased epidermal thickness and fibroblasts at 6 months, but patient satisfaction was higher in the MN group.

Acne

FRFM creates coagulation zones that damage sebaceous glands. After 1 treatment, 20 acne patients of Asian ethnicity achieved reduced sebum level and excretion rate by 30-60% and 70-80% respectively from weeks 2-8 (P less than 0.01).[38] Physician global improvement scores peaked at 2-weeks and returned to baseline at 8-weeks. A study of 25 moderate to severe acne patients with FST III-V reported a 76% reduction in number of lesions and a 37% reduction in sebum excretion after 3 FRFM treatments.[39] Subject satisfaction improved with each visit (P less than 0.05). A similar study of 18 moderate to severe acne patients with FST IV reported a 26-50% mean reduction in in ammatory lesion count after 2 FRFM treatments.[40] No PIH was reported in either study. A split-face study comparing FRFM versus bipolar radio-frequency alone in 20 mild to moderate acne and acne scar patients, reported superior efficacy after 2 monthly FRFM treatments when compared to bipolar radiofrequency alone.[41] A retrospective study on acne-related post-inflammatory erythema (PIE) compared the outcomes of 2 monthly FRFM treatments versus oral antibiotics and topical agents.42 After 8 weeks, computer-aided erythema evaluation software reported that 25 of 25 FRFM patients improved by about 45%, while only 5 of 27 antibiotic and topical patients improved by about 7.5% (P less

than 0.001). Histology showed reduced vascular markers and lower in ammation in the FRFM group.

Hyperhidrosis

A pilot study of 20 patients treated with 2 monthly sessions of FRFM reported Hyperhidrosis Disease Severity Scale (HDSS) scores reduce from 3.3 to 1.5 at 1-month, and 1.8 at 2-months.[43] At least 50% improvement was reported in 70% of subjects and 95% of patients improved on the starch iodine test. Histology showed reduced number and size of apocrine and eccrine glands, indicating a mechanism of action that works directly on glandular structures. Side effects included mild discomfort, transient swelling, and PIH for 2 weeks. Compensatory hyperhidrosis occurred on the chin and upper lip of 2 patients.

MN-assisted Drug Delivery

Keloids and Hypertrophic Scars In a non-controlled study of 13 patients with keloids and hypertrophic scars, topical bleomycin was followed by 25-gauge manual needling.[44] "Complete" or "highly significant" attening was seen in 12 patients and "significant attening" in 1 patient. Two patients developed recurrence at 10 and 12 months. *Plantar Warts* Three patients with refractory plantar warts achieved complete cure after 2mm MN plus topical bleomycin for 3 treatments every 2-4 weeks.[45] There was minimal pain and no necrosis. *Androgenetic Alopecia* A randomized, evaluator-blinded, pilot study of 100 androgenetic alopecia (AGA) patients compared weekly MN plus twice daily minoxidil 5% lotion, versus minoxidil lotion alone.[46] The MN group saw significantly greater mean change in hair count when compared to minoxidil monotherapy at 12 weeks. New hair growth began earlier in the MN group at 6 weeks, versus 10-weeks in the minoxidil alone group. Subjectively, 82% of MN patients reported over 50% improvement, whereas 4.5% of minoxidil monotherapy patients reported similarly.

TABLE 1.

Commonly Used Medical Microneedling Devices

Device	Manufacturer	Device type	Motorized or Manual	Other features	Needle number	Needle length	FDA status
Aquagold Fine Touch	Aquavit Pharmaceuticals, Inc, NewYork, NY USA	Gliding Stamper	Motorized	Product infusion, 0.13mm width needles	24	0.6mm	FDA registered
Collagen PI.N.	Induction Therapies, Brookings, SD USA	Gliding Stamper	Motorized	Cordless or with cord	12 or 36	0-3.0mm	FDA registered
Cosmopen	CosmoFrance Inc, Miami, FL USA	Gliding stamper	Motorized	N/A	12	0.25-2.5mm	FDA registered
Dermafrac	Genesis Biosystems, Lewisville, TX USA	Roller	Motorized	Product infusion, vacuum assisted	180	0.25-0.50mm	FDA registered
Dermaroller MC4, MC9	Dermaroller GmbH, Wolfenbüttel, Lower Saxony, Germany	Roller	Manual	N/A	MC4: 72 MC9: 162	0.2-2.5mm	FDA registered
Dermastamp	Dermaroller GmbH, Wolfenbüttel, Lower Saxony, Germany	Stamper	Manual	N/A	6	2.0mm	FDA registered
eDermastamp	Dermaroller GmbH, Wolfenbüttel, Lower Saxony, Germany	Gliding Stamper	Motorized	Product infusion, foot pedal	6	0-1.5mm	FDA registered
Dermapen 3MD	Equipmed, Sydney, Australia	Gliding stamper	Motorized	N/A	12	0-2.5mm	FDA registered
Eclipse MicroPen	Eclipse Aesthetics, LLC, TX USA	Stamper	Motorized	Cordless, Lithium Battery	12	0-2.0mm	FDA registered
Infini	Lutronic, Fremont, CA, USA	Gliding Stamper	Motorized	Bipolar FRFM, insulated needles	49	0.5-3.5mm	FDA cleared
Intracel	Jeisys Medical, Seoul, South Korea	Gliding stamper	Motorized	Bipolar FRFM, insulated needles	49	0.5-2.0mm	FDA cleared
Intensif	EndyMed, New York, NY, USA	Gliding stamper	Motorized	3DEEP® FRFM, non-insulated needles	25	0.5-5.0mm	FDA cleared
Profound	Syneron, Irvine, CA, USA	Gliding stamper	Motorized	Bipolar FRFM, insulated needles, enter at 75o angle	10	6.0mm	FDA cleared
Rejuvapen	Refine USA, LLC, Jacksonville Beach, FL, USA	Gliding Stamper	Motorized	N/A	9	0.2-2.5mm	FDA registered
Skinpen	Bellus Medical, Dallas, TX USA	Gliding Stamper	Motorized	N/A	12	0.25-2.5mm	FDA registered
Vivace	Aesthetics Biomedical, Phoenix, AZ, USA	Gliding Stamper	Motorized	Bipolar FRFM, insulated or non-insulated needles	36	0.5-3.5mm	FDA cleared

N/A, Not Applicable;
FRFM, Fractional radiofrequency microneedling;
FDA, U.S. Food and Drug Administration

Another study of 4 males with refractory AGA to minoxidil and nasteride reported thicker hair after 1-month of MN, with results lasting 18-months.[47] *Alopecia Areata* Two patients with alopecia areata (AA) refractory to topical minoxidil, intralesional triamcinolone, and topical corticosteroids, underwent MN with topical triamcinolone acetonide (10mg/ml) applied pre- and post-treatment.[48] After 3 sessions at 3-week intervals, both patients showed excellent hair growth at 9 weeks without recurrence at 3-months. Another study of 3 patients with corticosteroid resistant AA, underwent MN followed by a mixture of 1mL triamcinolone acetonide

(10mg/ml), 0.5mL of growth factors, copper tripeptide-1, multivitamins, amino acids, and minerals, and minoxidil 2.5% spray.[49] Patients showed 50, 75, and 90% improvement after 4-6 treatments. A split-scalp study of 6 patients with refractory AA or alopecia totalis evaluated MN plus methyl 5-aminolevulinate (MAL) versus only MAL, before red light exposure.[50] After 3 monthly sessions, photograph and phototrichogram analyses showed no hair regrowth in either group. Authors proposed that MN-induced bleeding may have hindered photosensitizer absorption. *Melasma* A randomized study of 60 patients with FST IV-V and moderate to severe melasma, compared MN plus tranexamic acid, an antibrinolytic that inhibits melanogenesis, versus tranexamic acid microinjections.[51] After 3 sessions, there was 44.41% improvement in the MN group (P<0.001) versus 35.72% improvement in the microinjection group (P<0.01) as per the Melasma Area Severity Index score. Fifty percent improvement was seen in 41% of MN patients versus 26% of microinjection patients. No adverse effects were reported. A split-face trial of 20 melasma patients with FST III-V investigated MN plus rucinol, which inhibits tyrosinase activity, and sophora-alpha, which blocks alpha-MSH activity versus the depigmentation serum alone.[52] After 2 months, the MN group improved by 10.1 points on the Melasma Area Severity Index score (PI less than 0.001), while the non-MN group improved by 7.1 points (P less than 0.05). *Periorbital Melanosis* A 48-year old male with FST V and idiopathic periorbital melanosis underwent MN-assisted delivery of a lightening serum.[53] Physician Global Assessment scores revealed 50-75% improvement after 4 sessions and 75-90% improvement after 12 sessions with no side effects. *Actinic Damage* A split-face, pilot study of 10 patients with actinic keratosis (AK's) compared conventional photodynamic therapy (PDT) with methyl aminolevulinate (MAL) versus MN-assisted PDT with MAL.[54] Results showed no difference in AK count and equivalent reduction in photodamage, dyschromia, roughness, and sallowness. However, the MN group reported improved appearance of fine lines (P=0.004) and course wrinkles (P=0.002). The MN group also reported more pain, erythema, edema, and crusting, with 1 secondary bacterial infection reported. A larger split-face study of 20 patients with at least 4 AK's on each side, randomized subjects to receive PDT with MN-assisted delivery of levulan or PDT with just levulan.[55] At 4-month follow-up, mean percentage reduction in AK's was 89.3% in the MN PDT group versus 69.5% in the PDT alone group. Physician global assessment showed cosmetic improvement in 15 of 19 patients who completed the study. Of these, 13 showed more improvement on the MN side.

Rejuvenation

A 9-year study of 480 patients with rhytides, laxity, and photodamage, who underwent 1-4 MN sessions, achieved 60-80% clinical improvement when compared to baseline.[9] Increased collagen and elastin was seen at 6 months, with 40% thicker stratum spinosum and normal rete ridges at 1-year. MN rejuvenation for neck and upper lip has also been reported in small trials of 8 and 10 patients respectively.[56,57] MN-assisted delivery of secretory factors from endothelial precursors of human embryonic stem cells (hESC-EPC) was studied in a randomized, controlled, split-face trial of 25 Asian females.[58] After 5 bi-weekly treatments, results showed statistically significant improvement in wrinkles and pigmentation on the Physician's Global Assessment Scale after MN plus hESC- EPC versus MN alone (P less than 0.05). FRFM plus topical growth factors and cytokines was studied in a split-face trial of 15 female patients with FST III-IV.59 After 3 monthly treatments, overall appearance and reduction of fine wrinkles was more significant with FRFM plus the topicals versus FRFM alone (P less than 0.05), with increased levels of collagen and brillin-1.

Safety

The most common adverse events reported were procedural pain and bleeding, transient erythema and edema, and serous drainage.[12,14,15,16,17,20,21,25] Seven cases of PIH exist after MN monotherapy[16,17,25] yet overall risk for PIH is low.[60] There were two cases of "tram-track" scarring with 1.5mm and 2mm MN for acne scarring.[17,61] Bruising and hematoma were reported over bony prominences[15,62] and one case exists of secondary bacterial infection.[54] Three cases of foreign body granuloma and systemic hypersensitivity exist after MN treatment and microinjection of vitamin C serum.[63] Both patients had patch test positivity to the vitamin C

serum, indicating that MN may introduce immunogenic particles systemically, particularly if the product is not approved for intradermal injection.

CONCLUSION

MN is most commonly used for acne scars, anti-aging, and transdermal delivery of topical products.

Histological and biochemical evidence support its use in myriad conditions as monotherapy or in combination with other modalities. There is need for more randomized, controlled trials with larger patient populations and longer-term follow-up to evaluate the efficacy of MN and in comparison to other therapies.

DISCLOSURES

Lauren Meshkov Bonati and Gorana Kuka Epstein have no con icts. Tamara Lazic Strugar is on the advisory board for La Roche Posay and is a consultant for Valeant.

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