Received: 24 January 2020 | Accepted: 10 February 2020

DOI: 10.1002/der2.13

INVITED REVIEW

Dermatological Reviews WILEY

Current concepts on how to optimise skin needling 2020: A personal experience: Part 1

Desmond Fernandes MB, BCh, FRCS (Edin)

Department of Plastic and Reconstructive Surgery, Faculty of Medicine, University of Cape Town, Cape Town, South Africa

Correspondence
Desmond Fernandes, MB, BCh, FRCS (Edin), The Cosmetic Surgery Institute, 183 Bree St, Cape Town 8001, South Africa.
Email: private@drdes.co.za

Funding information
Vivida SA cc; Environ Skin Care (Pty) Ltd

Abstract

This is a brief history of the skin needling treatment (collagen induction therapy), and it covers the original clinical work that was validated by research of Matthias Aust and the team at Hanover Medical School, Germany. Skin needling became the very first medical procedure to induce regeneration instead of scar formation, as it employs TGFB3 and IL10. The methods to optimise the effects of skin needling are examined. The depth of penetration into the skin will depend upon the condition treated. Wrinkles, stretch marks and so forth only require 1.0 mm, whereas burn scars, acne scars and so on require a deeper penetration, that is, about 3.0 mm. The use of topicals both before and after skin needling also needs to be considered. Vitamins A and C are scientifically proven to almost quadruple the effects of needling. Selected peptides seem to further enhance the results. Hyaluronic acid is best induced naturally, but it may be used topically for comfort. Finally, the rationale of the intervals between needling is examined. To take advantage of the increased titres of TGFB3 and IL10, the best clinical results seem to come from treatments at 4- to 10-day intervals. For better results, other modalities such as red and infrared LED, platelet rich plasma and mild peeling are receiving attention. Skin needling is the safest and the most effective method to treat photoageing, lax skin, stretch marks, acne scars and burn scars.

KEYWORDS

CIT, IL10, needling, platelet-derived growth factors, regeneration, TGFB3

1 | INTRODUCTION

I started skin needling in 1994 in Cape Town with deep dermal needling, parallel to the skin surface of the upper lip skin, to treat upper lip lines. This technique is not similar to the one described by Orentreich and Orentreich,[1] which transects scars subcutaneously. After Camirand's[2] lecture about piercing the skin vertically with a tattoo device to treat facelift scars, I was convinced to change the direction of the needle penetration and then I extended skin needling into the realms of burn scars as well as photoageing and wrinkles. In 1997, I started skin needling on photoageing and burn scars in larger areas, through the skin surface (just as we know it today), on at least 20 volunteers. I used a tattoo artist's instrument (equivalent to the common pen-style needling done nowadays) to do skin needling but found the technique to be too laborious and the needles could not penetrate as deeply as I felt they should. I also felt that the holes were too close to each other. Therefore, I designed a roller tool and a stamping device that I believed would be easier to use and give better and safer results. To obtain the best penetration of the needle, the important point is that the needles need to be spaced so that there is not much resistance from the skin.

The first paper on skin needling was presented at the International Plastic, Reconstructive and Aesthetic Society (IPRAS) congress in San Francisco in 1999, and it was hailed as a paradigm shift in the treatment of scars. However, it was soon forgotten, because the doctors doing the needling did not do it intensively enough and

the patients were not prepared for the use of vitamin A. In fact, one doctor said that the use of vitamin A cosmeceuticals was a stupid idea, and he further remarked, "come on, we all know that cosmetics do not work." I think that is a common error and needs correction.

Right from the beginning, I believed that growth factors, probably from keratinocytes or fibroblasts, must be responsible for the rejuvenation that results from the use of topical vitamin A, either as retinoic acid or as its precursors.[3] Vitamin A, even as a cosmetic, definitely speeds up the repair of any wound in my experience, so I used this to prepare my cases and then kept them on topical vitamin A cosmetics.

I soon realised that skin needling caused changes in skin because it sets up a cascade of growth factors derived from platelets. As we are trying to create healthy collagen in much greater quantities, we additionally also need much more vitamin C.

For some reason, clinicians doing needling do not believe this simple, logical advice to use topical vitamins A and C, despite research, first by Aust et al[4] and then later by Zeitter et al,[5] confirming that vitamin A preparation and maintenance after needling caused almost four times greater thickening of the skin.

According to me, the results of needling stemmed from the "inflammatory" cascade of platelet-derived growth factors, particularly TGFB3, which had been described by Fergusson and his team as the most important regenerating factor.[6] I was heavily influenced by the excellent research of Ferguson and his team who were trying to prevent the formation of scars.[7] In the case of skin needling, the release of growth factors from platelets is much more intense than the growth factors released by the action of vitamin A on keratinocytes and dermal fibroblasts.[3] The most important weakness of skin needling is that we cannot predict the answers to the following questions: how many circulating platelets does a particular patient have and how rich are these platelets in TGFB3? This may explain why the results of needling can be so variable. Some people obtain very mild changes, whereas others get impressive results.

At that stage, I used the terms related to the induction of the "inflammatory" phase after wounding as the best way to describe the concatenation of chemical events. Today I would not use those terms, because needling does not cause significant inflammation. It causes a healing cascade of growth factors totally unrelated to the inflammation caused by prostaglandins.

The first paper on skin needling as an alternative to laser treatments of skin in the *Aesthetic Surgery Journal* in 2002[8] was followed by invitations to write a chapter in *Clinics of North America Maxilla-facial Surgery* in 2005.[9] Matthias Aust and I published our joint multicentre experience with needling in over 480 patients,[10] and then Massimo Signorini and I were able to publish our combined experience.[11]

Aust and his team in Hannover, Germany, subsequently confirmed that platelet-derived growth factors were the drivers for skin changes from skin needling and produced collagen I and elastin.[4]

This paper by Aust and team is one of the most important papers in the history of scar treatment, because for the very first time ever, a medical procedure was proven to cause regeneration instead of scar formation. Until then, all other treatments had focussed on scarring skin to tighten and smoothen out skin. In fact, skin needling, also known as percutaneous collagen induction therapy (CIT), opened up a new paradigm in treating scars, which is due to the automatic production of TGFB3 and IL10 (see Figure 1).

After treating several hundred people, I realised that we were not always getting good results, and that is when I realised that we need to discover several things:

1. The ideal length of penetration into the skin.
2. The ideal interval between sessions of skin needling.
3. What topical or injected products would help us to get even better results.

2 | NEEDLE LENGTH

In the beginning, I used needles in a pen-type tattoo device with needles in various arrays that penetrated only about 1.0 mm into the upper papillary dermis. I have been professionally trained to do tattooing, so I never experienced any problems of over-needling, which is a real risk of mechanical needling. After about a year, I felt that the needles needed to be longer so that they would prick not only the vessels of the upper papillary dermal loops but also the plexus of deeper vessels in the reticular dermis. For safety, and also to reduce skin resistance to penetration, the needles need to be more widely spaced apart in a roller type of device. I thought that we needed needles that would penetrate about 1.0–3.00 mm into the dermis,

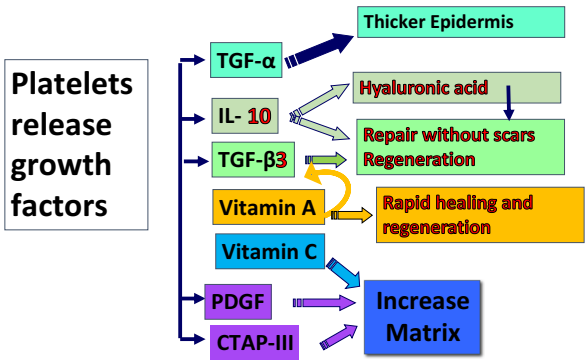

FIGURE 1 The cascade of platelet-derived growth factors released from platelets after puncturing a vessel: transforming growth factor-alpha (TGF-α) and transforming growth factor beta-1, 2 and 3 (TGF-β). TGFB3 has been shown to be the dominant growth factor responsible for the regeneration of tissue and is the most important growth factor in needling, as we understand it today. Interleukin-10 (IL10) also plays a part and stimulates hyaluronic acid. Vitamin A also stimulates TGFB3. As we increase the production of collagen and elastin, we need more vitamin C to ensure healthy collagen. Connective tissue growth factor (CTGF) is derived from neutrophils, and it also contributes to increased matrix production. Vitamin C is essential for the production of collagen

with the aim of getting into the reticular dermis which is a little more than 1.5 mm below the surface of the skin on the face.

A roller device with a 3-mm needle has an interesting voyage into the skin. The needle approaches the surface at an oblique angle, piercing the skin, and then as the roller is pushed forwards, the skin is pushed backwards and the needle becomes vertical and penetrates to its maximum. Then, as the roller is further pushed forwards, the needle starts to exit the skin, and if one examines this with a slow-motion video, the skin is tented up as the needle exits, but the needle, contrary to the popular myth, does not cut the skin. The needle hole on magnification may look slightly oval, but within a few hours, it becomes difficult to see any needle holes. They never leave scars. However, one has to recognise that in the arc of its transit through the skin, the individual needle does break more blood vessels as compared with simple vertical puncturing. This is compounded as each needle does this rotation in the skin, and most likely the tension involved may explain why the roller is less comfortable than vertical needling (see Figure 2).

Vertical puncturing through the skin is more comfortable, but it also punctures the blood vessels in the needle pathway.

The work with this roller has been in continuation since 1998. Experience in this field has shown that this roller is the safest way to treat skin laxity, especially thicker scars. Instances of "over-needling" or "post-needling hyperpigmentation" have never been reported with a roller. In contrast, pen-style needling on many occasions has had complications of excessive needling and post-inflammatory hyperpigmentation. Pen-style needling cannot penetrate the skin and scar tissue properly, and it may cause damage to the epidermis when trying to do deep needling.

The problem with deeper 3.0-mm needling is that it generally needs to be done with infiltrative local anaesthesia or general anaesthesia, which limits its availability; however, the results are very impressive and worth the added trouble of receiving anaesthesia.

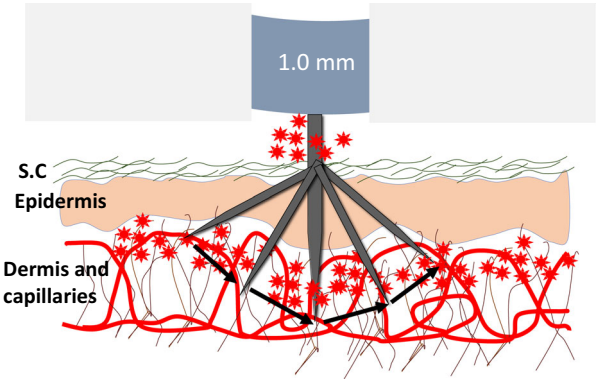

FIGURE 2 The diagram shows how the needle penetrates through a single puncture hole and is then rotated from left to right as the roller moves until the needle slips out without cutting the skin. In its path, it damages more blood vessels than vertical needling, and at the same time, there is only one hole through which the blood may escape, and it is believed that more blood and more platelets remain in the skin to give better results

In summary, the needle has to be long enough to prick blood vessels in the papillary dermis. Shorter needles into the epidermis cannot produce equivalent results because bleeding and the release of platelet-derived growth factors are the driving force for the changes created by skin needling, and no bleeding essentially means no results.

3 | THE INTERVALS BETWEEN NEEDLING

To develop reasonable concepts for the frequency of needling, we need to understand about scarless healing, as much as possible, which we find either in the early foetus or in animals that regenerate tissue, for example, salamanders. Then we should inspect the details of the laboratory research work done on skin needling, which should help us in working out the most effective regime for skin needling. The value of vitamin A in regeneration may be derived from the understanding that salamanders and axolotls depend very heavily on vitamin A concentrations at the site of amputation to determine regeneration of the missing limb.[12]

3.1 | Laboratory work with growth factors TGFB3 and IL10

Ferguson's work demonstrated that the higher the level of TGFB3, the better is the regeneration.[13] Research has also shown that IL10 seems to work with TGFB3 to cause regeneration of damaged tissues.[14] IL10 is anti-inflammatory; it stimulates hyaluronic acid and is essential for normal foetal healing without scars.[15] IL10 glycosaminoglycan scars also induce higher levels of hyaluronic acid.[16,17]

With the finding of Aust et al[4] that TGFB3 remains upregulated for about 2 weeks, it has become important to know whether needling again before 2 weeks will affect the TGFB3 titre positively or negatively. Zeitter et al[5] have addressed this point and have shown that needling at weekly intervals gave almost four times thicker skin when the skin was needled four times in 3 weeks with the use of topical vitamins A and C.

By 2004, I had reviewed the long-term results of my earlier work done with 1.0-mm needling and recognised its value for superficial scars, wrinkles and stretch marks. I tried 0.5-mm needling without topical anaesthesia, and it did not cause enough bleeding into the papillary dermis. Then, with 1.0-mm needle length and topical anaesthetics, for example, EMLA, treatments were possible using 1.0-mm needling but with much less bleeding than with infiltrative anaesthesia. To obtain the effects of more bleeding, I suggested that six needlings be done in 5 weeks to take advantage of the increase in TGFB3 and IL10, and prolong their influence on the skin.

Many people do needling at intervals of 2–3 months as I did when I first started, but my results from that period do not match the results obtained from shorter intervals.

3.2 | Clinical experience with humans

There is a lot of controversy about the frequency with which needling should be done. When I first started needling, I used 1-mm penetration and did it once in a month. I then thought that the sessions should be conducted with wide intervals because this would obviate the need for repeated treatments, as the final results from needling only truly become evident about 6–8 months after needling. However, I soon recognised that one session of skin needling is very rarely enough, and as I started to understand the growth factor cascade and the role of TGFB3, I realised that we need to understand the specific details about the three types of TGFB.

Ferguson and the team started researching TGF from about 1980 and by about the mid-1990s, they realised that TGFB3 caused scarless healing in utero, whereas TGFB1 and TGFB2 were involved in normal healing with scar formation. Their work demonstrated that after an injury, TGFB1, TGFB2 and TGFB3 are released, but the TGFB3 is a transient molecule and it disappears within 24 hours, whereas TGFB1 and TGFB2 remain upregulated for several weeks and are responsible for scar formation. The disappearance of TGFB3 within 24 hours explains why we cannot regenerate tissue after injury. In the foetus, TGFB3 and IL10 dominate, resulting in tissue regeneration without scars.[13] Their team did amazing work to show that one could prevent scarring by using TGFB3.[18,19]

Aust and team have shown in the laboratory that histologically there is a regeneration of the collagen latticework after skin needling[20] even when the collagen network has been destroyed by photoageing or scar tissue.[21] Their work demonstrated that TGFB3 remains upregulated for about 10–14 days, whereas TGFB1 and TGFB2 are transient molecules after skin needling.[4] This is exactly the opposite of what happens in normal wound healing. We do not understand why needling causes this response. I postulate that open wounds are exposed to much higher concentrations of oxygen, which favours TGFB1 and TGFB2, whereas the much lower normal oxygen tensions of tissue in needled skin favour TGFB3. The more anoxic the skin, that is, the bluer the skin looks after skin needling, the better are the results, as anoxia enhances growth factors[22] and possibly the effects of TGFB3 and also IL10.[23–25]

Currently, this regime of treatments at weekly intervals has become more popular because patients want the best possible results. In 2014, Matthias Aust and Zeitter pointed out that four 1.0-mm needlings done in 3 weeks gave better results than four 3.0-mm needlings done in 3 months.[5] This seems to confirm that TGFB3 and IL10 have a more profound effect when the needling sessions are closer. I believe that the titre of TGFB3 is raised higher and for a longer period when needling is done at intervals of 7 days. IL10 has not been tested this way. Clinically, the results can easily match and even surpass the results achieved with partial or full resurfacing laser treatments.

In my personal series, I have found that 4–6 sessions of needling done at 4–10-day intervals provide the most reliable results and the happiest patients. This seems to be supported by research work by Zeitter and Aust's team who showed that if 1.0-mm needling is done four times in 3 weeks, then the results are superior to 3-mm needling done four times in 3 months.[5] One can safely assume that when skin needling is done at weekly intervals, the level of TGFB3 will be higher and influence tissue responses for longer. Ferguson has shown that the higher the level of TGFB3 and the longer it is kept active, the better are the results.[19] Whereas 20 years ago, the concept that TGFB3 and IL10 should be a major determinant of regeneration instead of scar formation was a revolutionary idea, today we are seeing more and more research concentrating on promoting TGFB3 and IL10 through various procedures.[26,27] The chances are that new research will also highlight the use of new molecules in conjunction with skin needling to get better results. We also have to ask ourselves how many times we should repeat treatments in a series: Four times or six times? At this stage, this remains unknown.

ACKNOWLEDGEMENTS

The work was funded by Environ Skin Care (Pty) Ltd., manufacturer of the cosmetic creams used in the study, and by Vivida SA cc, the manufacturer of the rolling devices used on all the patients in author's studies.

CONFLICT OF INTERESTS

I personally formulated and developed the Environ Skin Care cosmeceutical products that I use specifically for skin needling. I am paid as the scientific director of Environ Skin Care and I serve on the Board of Directors. I also designed and developed the needling devices (Environ Roll-CIT and Focus-CIT), and I own shares in this company. I patented the technology of combined iontophoresis and low-frequency sonophoresis for skincare (Environ DF Electrosonic).

ORCID

Desmond Fernandes http://orcid.org/0000-0002-3100-1212

REFERENCES

1. Orentreich DS, Orentreich N. Subcutaneous incisionless (subcision) surgery for the correction of depressed scars and wrinkles. *Dermatol Surg*. 1995;21(6):543-549.
2. Camirand A, Doucet J. Needle dermabrasion. *Aesthetic Plast Surg*. 1997;21(1):48-51.
3. Shao Y, He T, Fisher GJ, Voorhees JJ, Quan T. Molecular basis of retinol anti-ageing properties in naturally aged human skin in vivo. *Int J Cosmet Sci*. 2017;39(1):56-65.
4. Aust MC, Reimers K, Gohritz A, et al. Percutaneous collagen induction. Scarless skin rejuvenation: fact or fiction? *Clin Exp Dermatol*. 2010;35(4):437-439.
5. Zeitter S, Sikora Z, Jahn S, et al. Microneedling: matching the results of medical needling and repetitive treatments to maximize potential for skin regeneration. *Burns*. 2014;40(5):966-973.
6. O'Kane S, Ferguson MW. Transforming growth factor beta S and wound healing. *Int J Biochem Cell Biol*. 1997;29(1):63-78.
7. Shah M, Foreman DM, Ferguson MW. Neutralisation of TGF-beta 1 and TGF-beta 2 or exogenous addition of TGF-beta 3 to cutaneous rat wounds reduces scarring. *J Cell Sci*. 1995;108(pt 3):985-1002.
8. Fernandes D. Percutaneous collagen induction: an alternative to laser resurfacing. *Aesthet Surg J*. 2002;22(3):307-309.
9. Fernandes D. Minimally invasive percutaneous collagen induction. *Oral Maxillofac Surg Clin North Am*. 2005;17(1):51-63.
10. Aust MC, Fernandes D, Kolokythas P, Kaplan HM, Vogt PM. Percutaneous collagen induction therapy: an alternative treatment for scars, wrinkles, and skin laxity. *Plast Reconstr Surg*. 2008;121(4):1421-1429.

11. Fernandes D, Signorini M. Combating photoaging with percutaneous collagen induction. *Clin Dermatol*. 2008;26(2):192-199.
12. Maden M, Ong DE, Summerbell D, Chytil F. The role of retinoid-binding proteins in the generation of pattern in the developing limb, the regenerating limb and the nervous system. *Development*. 1989; 107(suppl):109-119.
13. Ferguson MW, O'Kane S. Scar-free healing: from embryonic mechanisms to adult therapeutic intervention. *Philos Trans R Soc Lond B Biol Sci*. 2004;359(1445):839-50.
14. Mofikoya BO, Adeyemo WL, Ugburo AO. An overview of biological basis of pathologic scarring. *Niger Postgrad Med J*. 2012;19(1):40-45.
15. Moore AL, Marshall CD, Barnes LA, Murphy MP, Ransom RC, Longaker MT. Scarless wound healing: transitioning from fetal research to regenerative healing. *Wiley Interdiscip Rev Dev Biol*. 2018;7(2):e309.
16. Balaji S, Wang X, King A, et al. Interleukin-10-mediated regenerative postnatal tissue repair is dependent on regulation of hyaluronan metabolism via fibroblast-specific STAT3 signaling. *FASEB J*. 2017;31(3): 868-881.
17. King A, Balaji S, Le LD, Marsh E, Crombleholme TM, Keswani SG. Interleukin-10 regulates fetal extracellular matrix hyaluronan production. *J Pediatr Surg*. 2013;48(6):1211-1217.
18. So K, McGrouther DA, Bush JA, et al. Avotermin for scar improvement following scar revision surgery: a randomized, double-blind, within-patient, placebo-controlled, phase II clinical trial. *Plast Reconstr Surg*. 2011;128(1):163-172.
19. Occleston NL, Laverty HG, O'Kane S, Ferguson MWJ. Prevention and reduction of scarring in the skin by transforming growth factor beta 3 (TGFbeta3): from laboratory discovery to clinical pharmaceutical. *J Biomater Sci Polym Ed*. 2008;19(8):1047-1063.
20. Aust MC, Reimers K, Kaplan HM, et al. Percutaneous collagen induction-regeneration in place of cicatrisation? *J Plast Reconstr Aesthet Surg*. 2011;64(1):97-107.
21. Aust MC, Knobloch K, Reimers K, et al. Percutaneous collagen induction therapy: an alternative treatment for burn scars. *Burns*. 2010; 36(6):836-843.
22. Lee EY, Xia Y, Kim WS, et al. Hypoxia-enhanced wound-healing function of adipose-derived stem cells: increase in stem cell proliferation and up-regulation of VEGF and bFGF. *Wound Repair Regen*. 2009;17(4):540-547.
23. Du L, Lv R, Yang X, Cheng S, Ma T, Xu J. Hypoxic conditioned medium of placenta-derived mesenchymal stem cells protects against scar formation. *Life Sci*. 2016;149:51-57.
24. Zhao B, Guan H, Liu JQ, et al. Hypoxia drives the transition of human dermal fibroblasts to a myofibroblast-like phenotype via the TGF-beta1/Smad3 pathway. *Int J Mol Med*. 2017;39(1):153-159.
25. Namazi MR, Fallahzadeh MK, Schwartz RA. Strategies for prevention of scars: what can we learn from fetal skin? *Int J Dermatol*. 2011;50(1):85-93.
26. Wang L, Hu L, Zhou X, et al. Exosomes secreted by human adipose mesenchymal stem cells promote scarless cutaneous repair by regulating extracellular matrix remodelling. *Sci Rep*. 2017;7(1):13321.
27. Samadikuchaksaraei A, Mehdipour A, Habibi Roudkenar M, et al. A dermal equivalent engineered with TGF-β3 expressing bone marrow stromal cells and amniotic membrane: cosmetic healing of full-thickness skin wounds in rats. *Artif Organs*. 2016;40(12):E266-E279.

How to cite this article: Fernandes D. Current concepts on how to optimise skin needling 2020: A personal experience: Part 1. *Dermatological Reviews*. 2020;1:5–9.
https://doi.org/10.1002/der2.13