Chapter

Tissue Induction in Plastic and Maxillo-facial Surgery

Simone La Padula, Rosita Pensato, Rebecca Sabban, Francesco D'Andrea, Edoardo Coiante, Giovanni Roccaro, Mounia SidAhmed-Mezi, Jean Paul Meningaud and Barbara Hersant

Abstract

Tissue induction is defined as the activation of cell regeneration to restore damaged tissue, which involves stimulating cell signaling and modifying the microenvironment. Tissue inducers therefore have the advantage of acting quickly and durably on treated tissues, alone or in combination with surgical procedures, in order to reduce iatrogeny and potentiate surgical results. The aim of this review was to detail the various current techniques for tissue regeneration in the field of plastic and maxillo-facial surgery. We conducted a systematic search on Pubmed, Google Scholar and Science Direct. Articles in English and French, published after 2012 and focusing on facial tissue induction were searched. Only prospective comparative studies assessing as many cases as possible were analyzed. The following keywords were used: "skin rejuvenation", "skin regeneration", "collagen induction", "skin enhancer", "aging rejuvenation", "oral mucosa rejuvenation", "oral mucosa regeneration", "buccal mucosa rejuvenation", "buccal mucosa regeneration", "oral bone regeneration", "alveolar bone regeneration". Fifty innovative articles published since 2012 dealing with tissue induction techniques with an interest in plastic and maxillo-facial surgery were identified and then selected. The most effective tissue inducers for skin and mucosal regeneration were lasers, radiofrequency, pulsed light, hyaluronic acid and PRP. Tissue induction allows collagen self-production leading to tissue regeneration. Many techniques can be used for tissue induction that represent an additional tool in the therapeutic arsenal available to plastic and maxillofacial surgeons to improve patient management.These inducers can be used alone or in combination to achieve synergistic effects and better clinical outcomes.

Keywords: skin rejuvenation, skin regeneration, oral mucosa regeneration, oral bone regeneration, skin enhancer

1. Introduction

Tissue induction is defined as the activation of collagen self-production allowing quantitative and qualitative tissue regeneration [1–15]. Many techniques are used for

tissue induction, especially in the field of skin, mucosa and bone healing and in the field of facial rejuvenation. Tissue inducers may be biological, physical, chemical or mechanical agents. Mechanotransduction is one of these tissue induction processes whose main techniques include needling, osteotensors, massage (LPG), HIFU ultrasound and radiofrequency. They act on dermal fibroblast mechanoreceptors by causing the release of growth factors and therefore an endogenous production of collagen. Tissue induction by photo-biomodulation is mainly based on two techniques, laser therapy and low-level light therapy (LLLT) and acts by modulating collagen production without adverse thermal effect. Cryotherapy is a mode of tissue induction based on the biophysical properties of cold to induce collagen production after short and repeated exposures to a cooling. Tissue induction by bio-induction may be performed by adipose tissue injection or lipofilling, mesenchymal stem cell-enriched and/or platelet-rich plasma (PRP)-enriched adipose tissue injection, filler injection with hyaluronic acid, direct PRP injection and mesotherapy. Resorbable and non-resorbable threads, commonly used as a non-surgical rejuvenation method, especially in the midface region, promote collagen production and can therefore be considered mechanical inducers. The aim of this review was to detail the techniques available for tissue regeneration in the field of plastic and maxillo-facial surgery.

2. Materials and methods

Articles in English or French, published after 2012 and focusing on facial tissue induction were searched on Pubmed Google Scholar and Science Direct. Only prospective comparative studies assessing as many cases as possible were analyzed. The following keywords were used: “skin rejuvenation”, “skin regeneration”, “collagen induction”, “skin enhancer”, “aging rejuvenation”, “oral mucosa rejuvenation”, “oral mucosa regeneration”, “buccal mucosa rejuvenation”, “buccal mucosa regeneration”, “oral bone regeneration”, “alveolar bone regeneration”. Articles were included if they dealt with one or more cutaneous and mucosal tissue induction techniques for rejuvenation or regeneration on at least five human patients after reading the abstract and the full article. Exclusion criteria: literature reviews, meta-analyses and case studies were excluded, as well as animal experiments and in vitro research. Articles not dealing with tissue induction after complete article reading were also excluded from the study.

3. Results

Case reposts, reviews, animal studies, non-English/French language articles, and off topic papers were excluded (**Figure 1**).

Fifty innovative articles published since 2012 dealing with tissue induction techniques with an interest in plastic and maxillo-facial surgery were identified and then selected [1–10]. Of these articles, 23 dealt with induction techniques for *esthetic* facial rejuvenation and 27 dealt with oral mucosa regeneration techniques. Laser techniques for *esthetic* facial skin rejuvenation were addressed in the greatest number of articles, i.e. 10 articles published since 2012 including six that concluded that the technique was effective. Radiofrequency was addressed in eight articles published since 2012 including six that concluded that the technique was effective on skin rejuvenation. Light therapy was studied in five articles that all showed a significant inducing effect

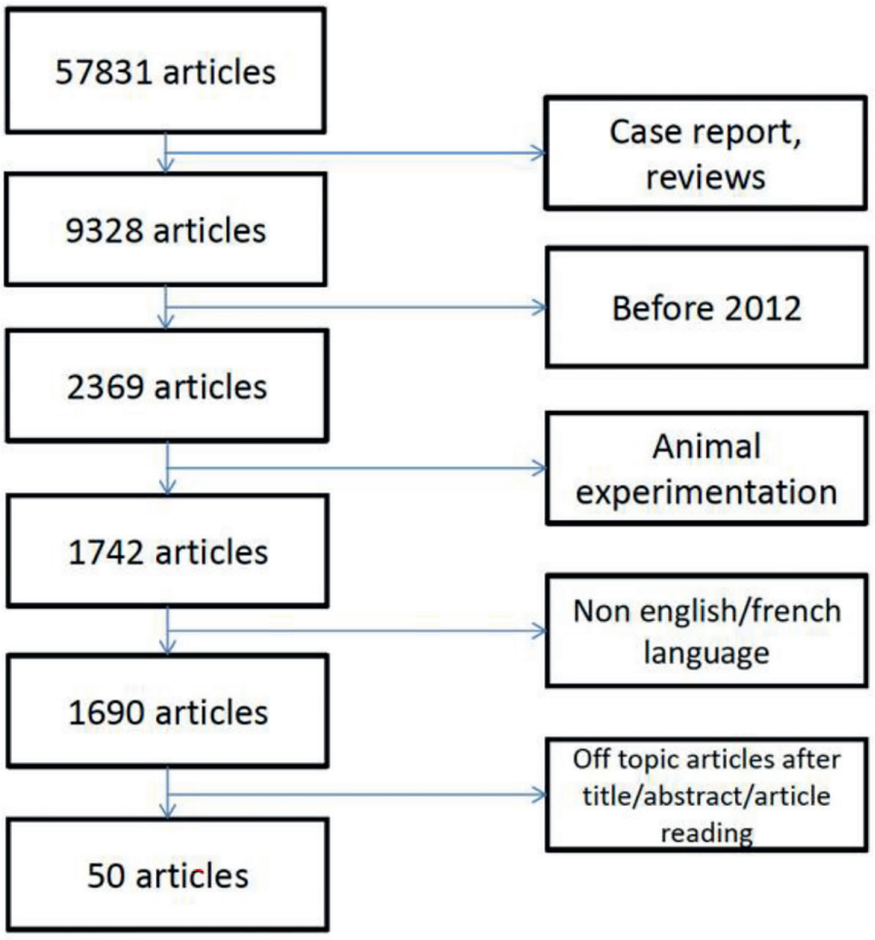

Figure 1.
Flow chart: articles selection.

on tissues. Lipofilling was studied in three articles but only one showed a significant inducing effect on tissues. Finally, mechanostimulation was only studied in one article that concluded to a tissue inducing effect on skin rejuvenation. In the field of facial mucosa and bone healing, the application of PRP or PRP derivatives such as fibrin-rich plasma (FRP) was the most studied technique with 20 articles published since 2012 that all showed an inducing effect on mucosa and bone tissues. The study of the impact of bone stem cell transplantation was more recent with three articles published since 2012 including two that showed positive results. The effect of laser phototherapy on bone regeneration was little studied with only one article published since 2012 but it showed a significant inducing effect on tissues. Similarly, the effect of osteotensors was only studied in one article that showed a non-significant inducing effect on bone tissues. The effect of laser phototherapy on oral mucosa regeneration was studied in one article that concluded to a significant effect on oral mucosa regeneration after surgery.

3.1 Soft tissue induction

Several techniques have been used in the last years to improve the skin aging signs and the soft tissues quality, especially in burn patients [1, 2] The most studied technique is non-ablative Nd:YAG laser. The article by Hong published in 2015 has histologically assessed the efficacy of Nd:YAG laser (1064 nm) on the signs of skin

aging such as wrinkles and skin laxity and on the production of dermal collagen in a series of 20 cases [1]. It has shown that after three monthly sessions including three passages on the treated hemiface, with a delivered energy of 20–24 J/cm^3, the number of wrinkles was significantly improved with a 45.1% decrease ($p < 0.001$). The histological assessment corroborated the clinical results with a marked increase in dermal collagen and elastic fibers. Charles-de-Sá et al. [2] have compared the effects of trophic (and non-volumizing) adipose transplantation to those of adipose-derived stem cell transplantation on facial skin rejuvenation. Their protocol was based on the reinjection of autologous fat taken from the abdomen in a hemiface and the reinjection of adipose-derived stem cells, previously isolated and then cultured in the presence of growth factors, in the other hemiface. The final assessment, including a 3-month histological analysis of the reticular dermis arrangement and the number of elastic and collagen fibers, showed an increased density of the collagen and elastin network, the presence of a richer microvascular bed without showing any difference between the two treated areas. Thus, the lipofilling technique appeared to have the same rejuvenating effect as stem cell transplantation without its associated technical complexities. This effect could be explained by the high concentration of mesenchymal stem cells contained in the adipose tissue. Humbert [3] has studied the effect of mechanotransduction on the expression of genes involved in skin regeneration. After a total of 24 sessions of standardized massage on a randomly chosen hemiface in 30 subjects, there was an increase in histological criteria for tissue induction such as the fibroblast migration capacity, showing their activation, an increased synthesis of elastin fibers, endogenous hyaluronic acid and metalloproteases, including MMP9, MMP1 and TIMP1. This study has also shown a 100% patient satisfaction with the anti-aging effect of mechanostimulation with an absence of side effects such as pain. Seo et al. [4] have analyzed the effect of radiofrequency, combined or not with the injection of adipose-derived stem cells, on facial anti-aging rejuvenation. The care protocol included three radiofrequency sessions 1 month apart. The authors have shown an improvement in skin thickness in both groups, which was confirmed by the histological analysis. The latter showed a significant increase in the dermis thickness associated with an increase in collagen fibers and type I pro-collagen after three radiofrequency sessions.

3.2 Bone induction

In his study, Hauser [5] has shown the impact of platelet rich fibrin (PRF) on alveolar bone regeneration. The protocol was based on the addition of autologous PRF in the dental extraction cavity of 23 patients and then a histological analysis of the newly formed alveolar bone 8 weeks after treatment. The microscopic examination showed the creation of a significant bone micro-trabeculation and the maintenance of a bone height significantly higher than in the control group. The results obtained were substantially identical to those obtained with a mucosal coverage flap. This technique could therefore be an alternative to mucosal coverage flaps that are necessary in certain circumstances but could lead to morbidity on the sampling sites. The 2013 study by Kaigler [6] has examined the benefit of bone stem cell transplantation on facial bone defects. Iliac crest bone marrow-derived stem cells were collected, isolated, cultured and reimplanted in areas of mandibular bone defects such as dental extraction cavities. Bone regeneration was measured radiologically and histologically. It showed a better healing with a lesser need for subsequent bone grafting and a significantly greater radiological bone gain in the test group. Histologically, the newly formed bone

was denser and more voluminous in the test group. This technique could replace bone transplantation in maxillo-facial surgery in the context of bone defects, a fortiori in case of debilitated backgrounds including after irradiation, while decreasing the morbidity and sequelae of donor sites. In 2015, Odin et al. have studied pre-implant bone tissue induction by mechanotransduction with a protocol of osteotensors in a patient with ectodermal dysplasia [7]. The protocol was based on mechanotherapy sessions for 3–6 weeks before placing dental implants. This technique, through the creation of a transmatricial canal between the periosteum and the endoste with a manual or rotary instrument could activate osteogenesis and angiogenesis through the recruitment of bone stem cells. The 3-year clinical assessment showed a perfect integration of implants and the radiological assessment by Cone-Beam showed a gain in maxillary and mandibular bone height and thickness.

The osteotensor is a flapless mechanotherapy, with creation of a transmatrix channel ranging in size from 200 to 500 μm that sets up communication pathways between the endosteum, the bone marrow, and the periosteum. The resultant bone distraction phenomenon leads to modification of internal bone matrix tensions. This activation causes cell mobilization locally, in the periosteum, endosteum, bone marrow, and along the vascular walls where progenitor cells are recruited. Formation of a blot clot followed by a bony callus reinforces the local architecture. In the sinus regions, where bone is initially type IV, this generally results in transformation into active type II bone. Bleeding under the Schneiderian membrane has a balloon-like effect that elevates the membrane, allowing formation of a callus and a bone gain of 2 to 6 mm.

Romão et al. have studied the effect of laser phototherapy on alveolar bone repair in 20 patients after dental extraction through a radiological and histological assessment [8]. At 40 days, it has been shown both radiologically and histologically that laser phototherapy significantly increased bone thickness and volume after dental extraction and therefore improved bone healing in pre-implant contexts.

4. Discussion

Various tissue induction techniques have been studied and developed in plastic and maxillo-facial surgery. In facial rejuvenation, the most relevant tissue inducers appear to be Nd:YAG laser, trophic lipofilling, mechanostimulation and radiofrequency. Regarding bone induction in maxillo-facial surgery for acquired or congenital defects, the inducers with a proven efficacy are the PRF and the reinjection of bone stem cells. The use of osteotensors should be more carefully studied before being added to the therapeutic arsenal of maxillo-facial surgeons. Many other induction methods are known, but their efficacy has not yet been proved in the plastic and maxillo-facial surgery field [1–15]. Radiofrequency and the plasma (a physical agent) are for example being assessed in non-surgical blepharoplasty. The authors have identified and resumed two main tissue induction mechanisms that act directly and indirectly (**Figures 2** and **3**).

5. Conclusions

Tissue induction allows collagen self-production leading to tissue regeneration. Many techniques can be used for tissue induction that represent an additional tool in the therapeutic arsenal available to plastic and maxillofacial surgeons to improve patient management.

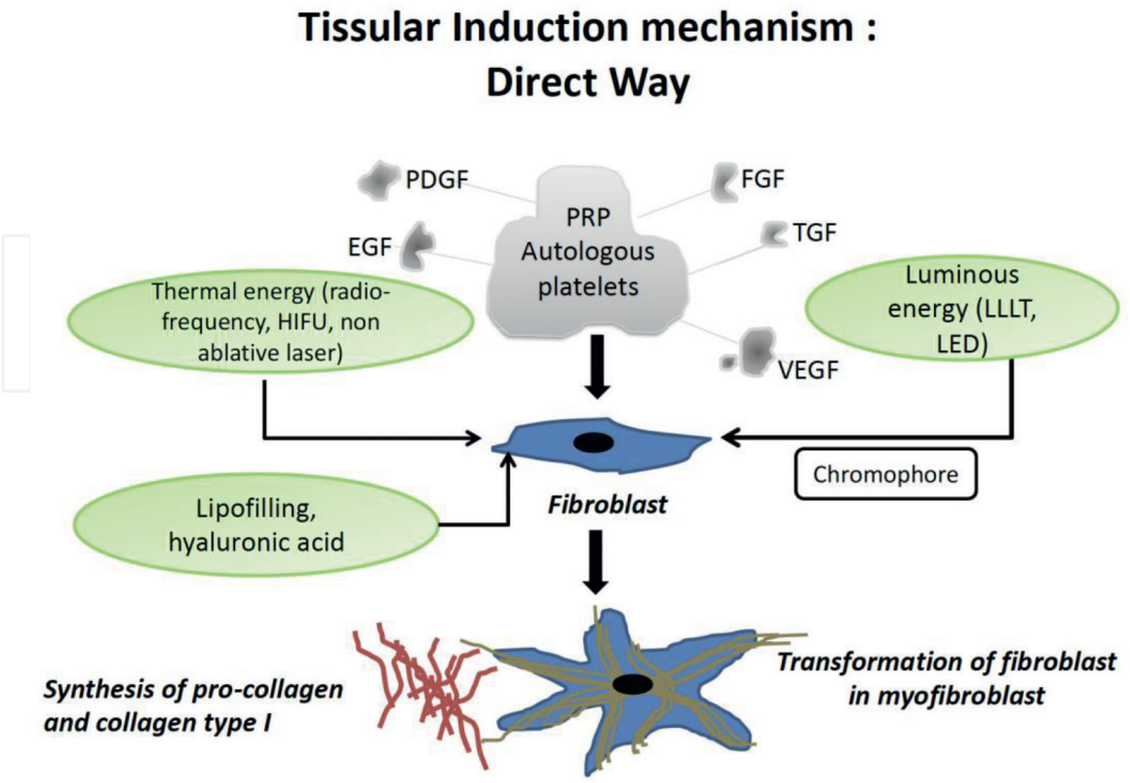

Figure 2.
Activation of fibroblast via PRP after releasing of TGF, EGF, VEGF and FGF thanks to the PDGF. Activation of fibroblast via luminous energy by activation of fibroblastic chromophore and increase synthesis of FGF by macrophages. The peak of efficiency is reached with a wave length including 680 and 840 nm.

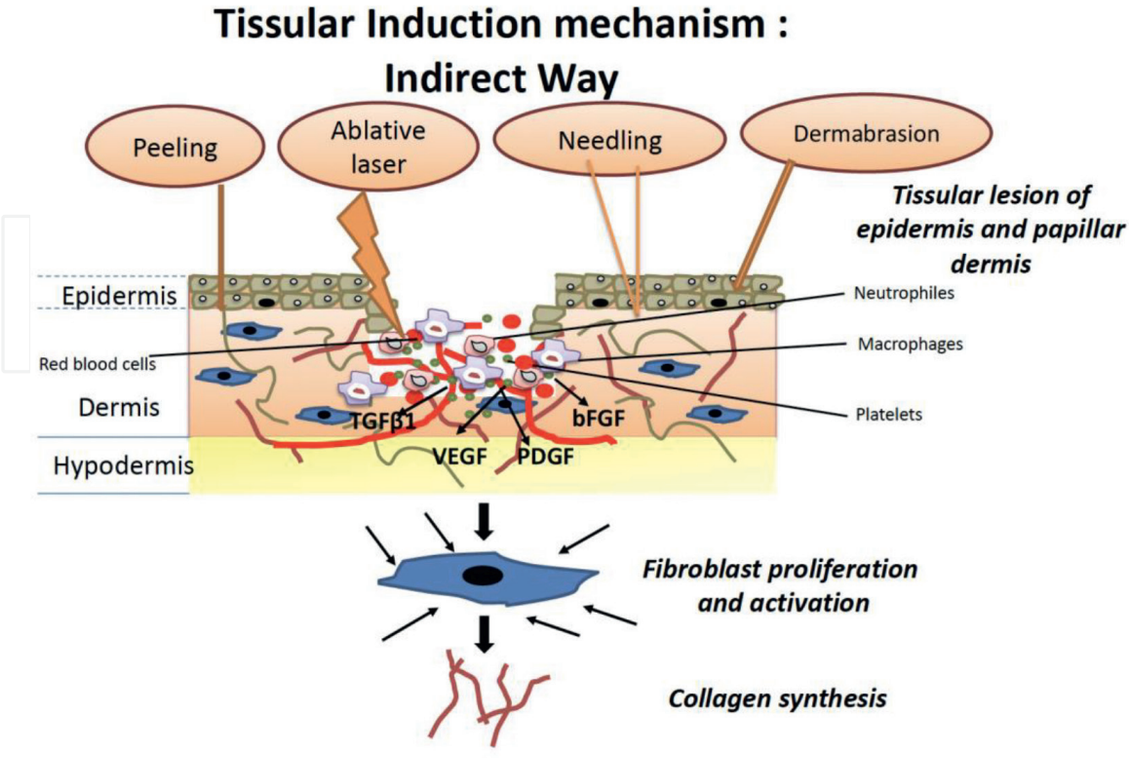

Figure 3.
Tissular lesion of the skin: wound healing process, releasing of growth factors and activation of fibroblasts and collagen synthesis.

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Conflicts of interest

The authors declare no conflict of interest.

Data availability statement

Pubmed Google Scholar and Science Direct. No copyright needed.

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