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Original article

Humans histological evaluation of regenerative activity using Subdermal Induced Heat (S.I.H.) Technology®

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Abstract. *Introduction:* The use of radiofrequency (RF) in aesthetic medicine is widely appreciated for its ability to heat cutaneous and muscular tissues, leading to collagen denaturation and stimulating new collagen and elastin production, alongside improved blood flow. However, precise temperature control is essential to avoid surface skin damage. Subdermal Induced Heat (S.I.H.) Technology® represents an advancement in RF application, delivering targeted heat to subcutaneous tissue while preserving skin surface integrity. This technique may improve tissue tone and elasticity, provide analgesic benefits, and accelerate tissue repair. *Materials and Methods:* The study involved five female patients aged 30 to 58, treated with endodermic RF using S.I.H. technology in the abdominal (two cases), gluteal (two cases), and inner thigh (one case) regions. Three patients were treated at 50°C under Klein's solution, and two at 48°C under local anesthesia, with each session lasting 25 minutes per side. Biopsies were collected pre-treatment (T0), at 1 month (two patients), at 3 months (T1), and at 6 months (T2) post-treatment. Histological analysis was performed using hematoxylin-eosin and orcein staining to assess connective tissue and elastic fibers. *Results:* Histology revealed significant skin improvements in all patients at six months. Initially, the epidermis was thin, with reduced dermal papillae and deep-seated elastic fibers. At three months, increased vascularization and superficial migration of elastic fibers were noted. By six months, dermal papillae elongation, dermal thickening, and further reorganization and proliferation of elastic fibers were evident, without pathological changes. *Discussion:* RF is known for its regenerative effects. This study highlights how subcutaneous RF via S.I.H. technology promotes tissue regeneration without inducing elastosis or fibrosis. Significant improvements were observed, especially in younger subjects, including enhanced dermal structure and elastic fiber organization. *Conclusions:* Endodermic RF using S.I.H. technology stimulates the regeneration of essential skin components safely, ensuring effective results without adverse tissue reactions.

Key words: Subdermal Radiofrequency, histological evaluation, human regenerative response

Introduction

In the past decades, radiofrequency (RF) has gained significant interest in the medical field, particularly in aesthetic medicine, because of its application on cutaneous, subcutaneous, fascial, and muscular tissues.

The effectiveness of the method is due to the production of heat as the radio frequency waves pass through the tissues (diathermy). Heat immediately denatures collagen and later stimulates the fibroblasts to produce neo-collagen and elastin by increasing vascularization. The results depend on the distribution, the temperature reached in the target tissue, and the timing[1-6].

Several studies support the effectiveness of radiofrequency technology in aesthetic medicine. In a

transcutaneous treatment the main limitation is posed in the risk of damaging the skin, caused by variations in the temperature that can be reached in the subcutis[7-14].

Constant scientific development has made it possible to obtain a new way of generating radiofrequency that allows the heat produced to reach the subcutaneous tissue in a constant and very precise manner, avoiding the overt increase in skin temperature.

Subdermal induced heat (S.I.H.) technology® is a latest generation radiofrequency with a continuous or pulsed emission of energy and opens the way to the innovation of endodermal radiofrequency which allows for a restructuring of the dermis of the treated tissue with remarkable precision.

Radiofrequency is administered with external handpieces or with micro-needles that deliver energy percutaneously into the subcutaneous tissue, producing the desired effects: an improvement in the tone and elasticity of the tissues and a general analgesic effect, along with an acceleration of reparative processes in the presence of damaged tissues.

The main effect radiofrequencies have on tissues is the increase in tissue temperature, however a direct effect of radiofrequency at both cellular and interstitial levels cannot be excluded.

This study was designed to evaluate the histological effects produced on human cells and extracellular tissues by S.I.H. technology applied to tissues through special cannulas which are covered with an insulating coating that allows the delivery of energy only in the last 10 mm of the device, thus avoiding unwanted contact with other areas and ensuring the integrity of the skin, while observing brilliant results of this treatment from a clinical point of view[15-18].

For this purpose, volunteers were recruited to undergo a biopsy sampling before and after treatment. The biopsies were examined using light microscopy.

Materials and Methods

Five female patients aged 30, 46, 48, 56, and 58 years were recruited to undergo biopsy sampling before and after treatment; three of these women were of fertile age with regular menstrual cycles, while the last two were in menopause.

Type 1 'Early Wrinkles'	20s - 30s	Early photo-aging, Mild pigment changes Minimal wrinkles, No 'age spots'
Type 2 'Wrinkle in Motion'	30s - 40s	Early to moderate photo-aging Appearance of smile lines, Early brown 'age spots' Skin pores more prominent, Early changes in skin texture
Type 3 'Wrinkles at Rest'	50s & older	Advanced photo-aging, Prominent brown-pigmentation, Visible brown 'age spots' Prominent, small blood vessels Wrinkles, even at rest
Type 4 'Only Wrinkles'	60s or 70s	Severe photo-aging, Yellow-gray skin color Prior skin cancers, Pre-cancerous skin changes (actinic keratosis), Wrinkles everywhere

Figure 1. Glogau Skin Classification.

Patients with an ongoing anticoagulant treatment, implanted pacemakers or defibrillator were not included, since this is an absolute contraindication for RF therapy. Patients with the presence of acute systemic infections, local infections such as herpes simplex or impetigo, and those with open wounds in the area of treatment, were excluded. Patients with genetic disorders of connective tissue, like cutis laxa, were excluded from this trial.

All participants were of normal weight and had a skin quality classified as type 2 or 3 on the Glogau scale (Figure 1)[19].

The patients received an endodermic radiofrequency treatment with 15 cm long cannulas, for a duration of 25 minutes for each side; two patients were treated in the abdominal region, two in the gluteal area, and one in the inner thigh region.

The treatment was performed with the S.I.H technology device.

In three patients, 200 ml of Klein's solution was infiltrated, and the treatment was conducted at a temperature of 50°C (degrees Celsius); two of the patients only had local anesthesia at the cannula insertion site, and the treatment was performed at 48°C without infiltrating the anesthetic solution. All patients underwent a biopsy with a 3mm puncher before the intervention (T0), repeated at an analogous site after 3 months (T1) and after 6 months (T2). Two patients also underwent a further biopsy one month after treatment (Table 1).

Histological examinations were performed using hematoxylin-eosin staining to evaluate the structural

Table 1. Data of the case series.

	Age	Glogau Classification	Treatment Site	Treatment Temperature	Biopsies
Patient 1	46	3	Buttocks	50°C	N. 4
Patient 2	30	2	Abdomen	50°C	N. 3
Patient 3	58	3	Abdomen	50°C	N.4
Patient 4	48	3	Buttocks	48°C	N. 3
Patient 5	56	3	Inner thigh	48°C	N. 3

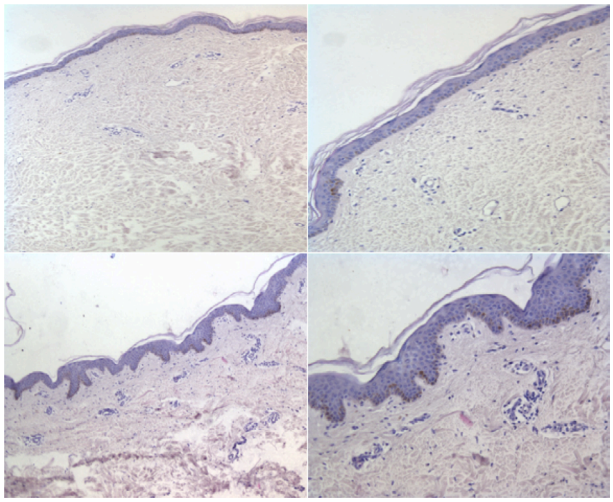

Figure 2. T0, pretreatment. 4X (left) and 10X (right). Hematoxylin Eosin. A thin epithelium with reduced or almost absent dermal papillae is observed.

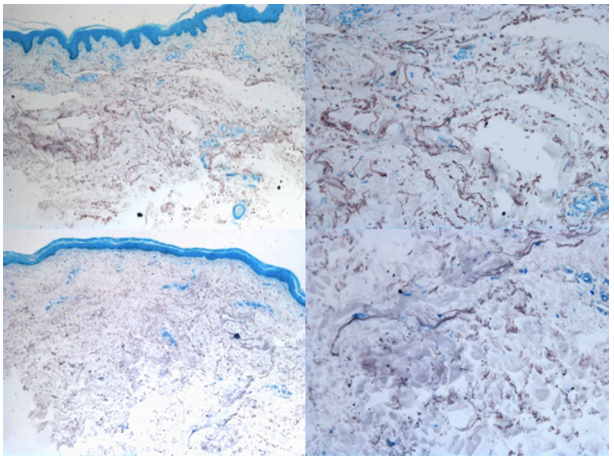

Figure 3. T0, pretreatment. 4X (left) and 10X (right). Orcein. The specific coloring for elastin highlights the presence of elastic fibers, more evident at the dermal-hypodermic level than in the superficial dermis.

and vascular components of the connective tissue and orcein to highlight the elastic fibers.

Results

At six-months post treatment, an evident histological improvement is demonstrated in all treated patients.

The histological evaluation at time zero (before treatment) shows a slightly thinned epithelium in the patients, with dermal papillae of reduced height, or in some cases almost absent, and a normal cellular component for site and age (Figure 2).

Orcein staining highlights the presence of elastic fibers abundant in the dermo-hypodermal layer and less represented in the superficial dermis, as is normally the case in cutaneous aging (Figure 3).

Three months after treatment (T1), the epithelium presents more developed dermal papillae, and remodeling of the dermis is noted with an increase in capillary vessels (Figure 4).

There is a greater expression of hypodermal elastic fibers and a migration of those present at time T0 from the deep dermis and hypodermis to the reticular and superficial dermis, indicating that cutaneous rejuvenation processes have been activated (Figure 5).

Six months after treatment (T2), a further improvement of the characteristics observed at time T1 is observed, with an elongation of epithelial papillae at the level of the papillary dermis so that the dermo-epidermal junction presents a marked festooning while the reticular dermis appears thickened (Figure 6).

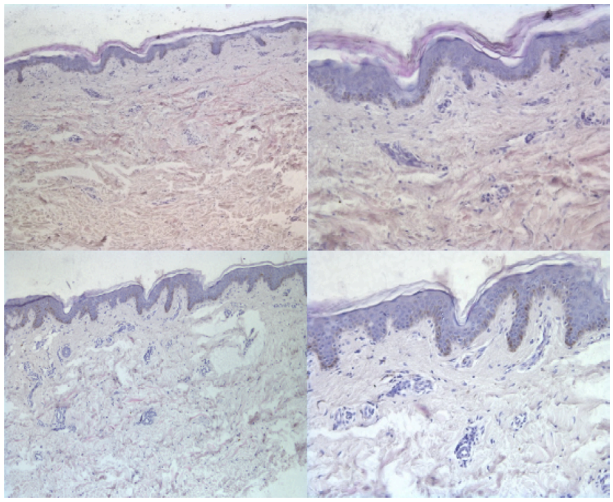

Figure 4. T1, 3 months after treatment. 4X (left) and 10X (right). Hematoxylin Eosin. At the epithelial level, more developed dermal papillae are noted compared to T0 and a remodeling of the dermis is observed, with an increase in capillary vessels.

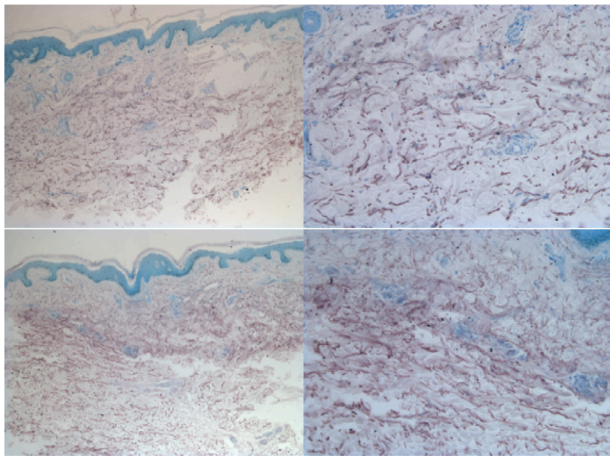

Figure 5. T1, 3 months after treatment. 4X (left) and 10X (right). Orcein. Compared to T0, a greater expression of elastic fibers in the dermis and a migration from the dermo-hypodermis to the dermis of those present in the pre-treatment samples are observed, indicating that skin rejuvenation processes have been activated.

With specific staining, the restructuring of elastic fibers is most evident, and the migration of more elastic fibers towards the superficial dermis is observed. There is no evidence of elastosis, such as the aberrant production of elastin, which would lead to a stiffer and more fibrotic tissue; on the contrary, the tissue is more nourished by small-caliber blood vessels, and the restructuring of the dermis is observed with the appearance of sebaceous glands and the initial restructuring of the hypodermis (Figure 7).

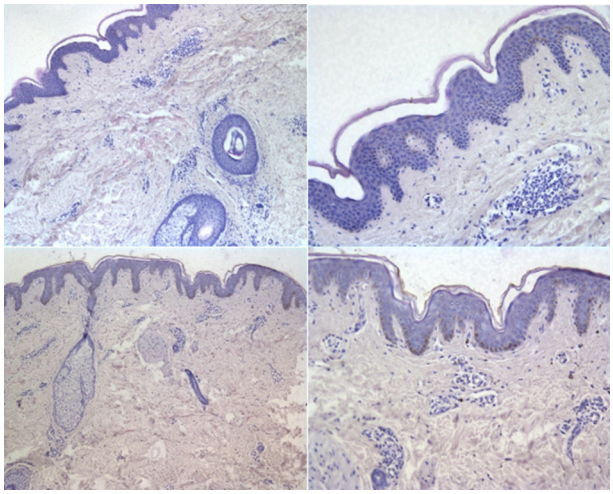

Figure 6. T2, 6 months after treatment. 4X (left) and 10X (right). Hematoxylin Eosin. A further improvement of the epithelium is observed, with lengthening of the epithelial papillae at the level of the papillary dermis, so that the dermal-epidermal junction presents a marked scalloping, while the reticular dermis appears thickened. The tissue is supplied with more blood vessels of a smaller caliber and the restructuring of the dermis can be appreciated with the appearance of sebaceous glands.

It should be noted that in the oldest patient who presented a more fibrotic tissue at time zero, the modifications at time T1 were less noticeable, although still present; however, after six months, a remodeling of the dermis is evident even in this case, although newly formed glandular structures are not observed (Figure 8).

Discussion

In aesthetic medicine, the effectiveness of RF is well known. A histological evaluation of a fractional RF-induced coagulation demonstrated a mixed cellular infiltration, neovascularization and granulation tissue formation, blood vessel response, increase in mid to deep dermal GAGs, increased epidermal mitotic

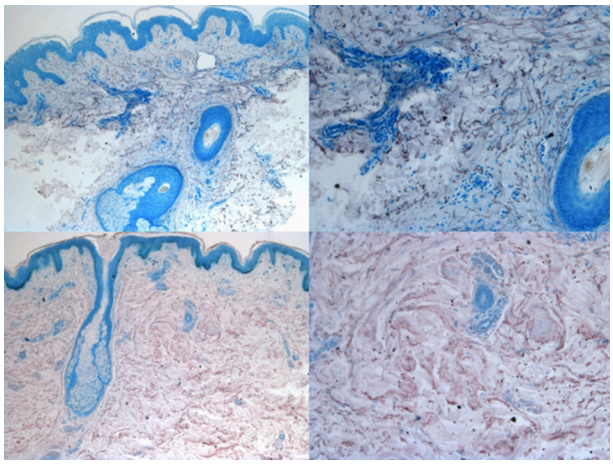

Figure 7. T2, 6 months after treatment. 4X (left) and 10X (right). Orcein. The specific color highlights the restructuring of the elastic fibers and the migration of more elastic fibers from the deeper layers towards the superficial dermis. There is no evidence of elastosis.

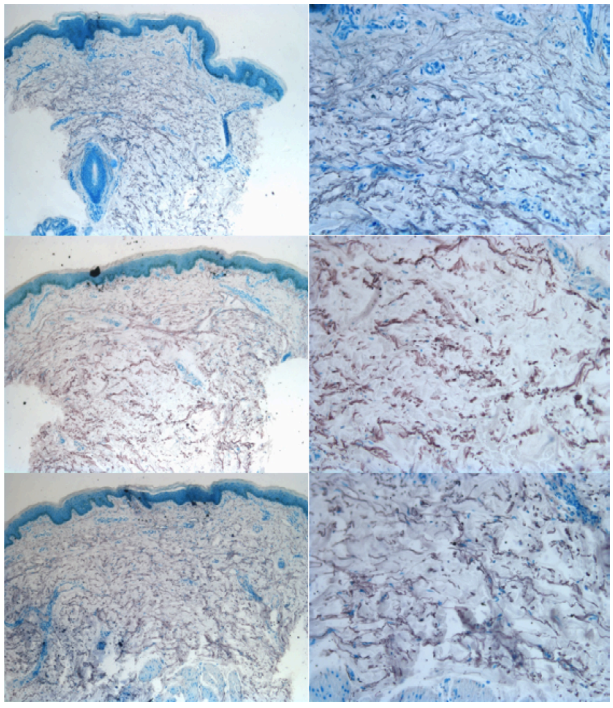

Figure 8. 4X (left) and 10X (right). Orcein. From top to bottom T0, T1 and T2. In the samples coming from the older subject, a more fibrotic starting tissue (T0) is observed. At time T1 the tissue improvement is less evident than in other cases, although still present. After 6 months (T2) a remodeling of the dermis becomes evident in this case too.

index, and elevated epidermal hyaluronan and CD44 expression[20-23].

There isn't literature on in vivo studies using sequential subcutaneous RF.

The results highlighted by the histological examinations performed in our case series allow us to affirm, despite having examined a limited number of cases, that subcutaneous radiofrequency presents a clear regenerative action.

The possibility of using minimally invasive and controlled technology has made it possible to highlight the absence of elastosis and fibrosis phenomena in all cases in our series, an unequivocal sign that temperatures between 44°C and 50°C administered for a total time not exceeding 25 minutes induce a structural regeneration of the entire extracellular matrix and not only of fibroblasts, without producing areas of necrosis or tissue suffering.

A remodeling and restructuring of connective tissues including its vascular and glandular components were evident; these aspects were clearer in younger subjects of fertile age, where it was possible to better appreciate the improvement of the epithelium, elongation of dermal papillae with marked festooning of the dermo-epidermal junction, neovascularization, and greater evidence of sebaceous glands. It seems important to emphasize that, although not previously reported in the literature, radiofrequency improves the quantity and organization of elastic fibers in treated patients. This data significantly supports the clinical findings of aesthetic improvements observed in patients. Although the results were less evident in menopausal subjects, the structural improvements observed were still noteable, especially in biopsies taken at six months compared to those at three months.

In our opinion, these results could be largely attributed to the direct and inverse piezoelectric effect that the technology is able to produce in the connective system. In fact, the introduction of the cannula into the tissue occurs very slowly, so it mechanically deforms the connective fibers of the treated area (direct piezoelectric effect), while the constant release of energy converted into constant heat alters the electron orbitals of the cellular magnetic field, inducing a structural modification that translates into anabolic activity (inverse piezoelectric effect).

Conclusions

Based on these initial clinical and biopsy findings, it can be stated that this endodermic radiofrequency (S.I.H. technology) used at temperatures of 48°C and 50°C is able to stimulate the regeneration of elastic fibers, fibroblasts, and the components of the extracellular matrix without secondary signs of elastosis and fibrosis.

Note: The authors declare that they have no conflict of interest.

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