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Intralesional cryosurgery for enhancing the involution of hypertrophic scars and keloids. A new effective technology based on experimental and clinical data

Although therapeutic management of hypertrophic scars and keloids (HSK) using contact or spray cryosurgery was shown to yield significant improvement or complete regression of HSK, it requires 1-20 treatment sessions and causes permanent hypopigmentation. Recently, an intralesional cryosurgery technology has been developed to treat HSK (CryoShape, Etgar Group International Ltd., Kefar Saba, Israel). This summary is aimed to provide the scientific and clinical data which has been obtained to date regarding the clinical safety and efficacy of the intralesional cryosurgery method in the treatment of HSK.

The intralesional cryosurgery technology: A specially designed cryoneedle[1] is inserted (under translesional local anesthesia with 0.5% Bupivacaine Hcl[7]) into the long axis and mid height of the HSK so as to maximize the volume of the HSK to be frozen. The cryoneedle is connected by an adaptor to a cryogun filled with liquid nitrogen, which is introduced into the cryoprobe thereby freezing the HSK. After the HSK is completely frozen, the cryoprobe defrosts and is withdrawn.

Clinical studies: 95 Caucasian patients (51 females; 44 males), ranging in age from 3 to 67 years, with a total of 112 HSKs (chest- 62; auricular and lobular- 26; shoulder- 7; neck- 4; abdomen- 4; breast- 4; nape- 3; arm and forearm- 2) of more than 6 months duration and of diverse causes were included in this study. The 18-month trial evaluated volume reduction of the HSK following a single session of intralesional cryosurgery. Objective (hardness and color) and subjective parameters (pain/tenderness and itchiness/discomfort) were examined on a scale of 0- 3 (low score was better).[1,2,3,4]

Scientific studies: Pre- and post-treatment biopsies were taken for histo-morphometric studies of the collagen fibers which included spectral Picrosirius red polarization, fractal analysis and Fast Fourier Transform algorithm orientation index. The histology examination of the pre- and post- treatment biopsies were evaluated for collagen structure with a confocal microscopy z-stacks, and 3-dimensional reconstruction with Imaris software. Mast cells and blood vessels were identified by immunohistochemistry, and cell proliferation was estimated by proliferating cell nuclear antigen antibodies. Surface thermal behavior measurements using thermocouples were executed in an ex-vivo model and during clinical treatments to measure the thermal history of the intralesional cryosurgery.[1,2,3]

Clinical results

An average of 51% of scar volume reduction was achieved following a single intralesional cryosurgery treatment. Specifically, for auricular and lobular HSK the average volume reduction was 67% and for upper back and shoulders HSK 60%. In 8 scars of the 112 no response to the intralesional treatment has been documented. Significant alleviation of objective and subjective clinical symptoms was documented, *i.e.* an average reduction of two levels of the scale. During the 18-month follow-up period there was no evidence of infection or permanent depigmentation *(Figure 1, 2)*.[1,2,4,5]

Scientific results

The histomorphometric analysis demonstrated rejuvenation of the treated scars, *i.e.*, parallelization, and a more organized architecture of the collagen fibers when compared to the pre-treated scars.[1,3]

The histological analysis revealed that after intralesional cryosurgery the collagen bundles lost their swirl structure, the thickness of the collagen layer decreased, and the bundles became more compact with less space between the fibers. A clear distinct transition zone separated the treated from the unaffected area. The frozen tissue was devoid of proliferating cells and of mast cells whereas the number of blood vessels remained unaltered. Most of the fibroblasts expressed all tested myofibroblast markers although some of them exclusively expressed one and not the other. Almost no mast cells were found following the cryo-treatment. Thus, intralesional cryosurgery treatment resulted in major changes in collagen structure and organization. In addition, the treatment reduced the numbers of proliferated cells in general and myofibroblasts and of mast cells in particular. These results may explain the significant reduction in no-response rate and the amelioration of the subjective and objective clinical symptoms after intralesional cryosurgery treatment.[6]

The surface thermal history during the intralesional cryosurgery procedure demonstrated a significant different pattern when compared with the contact technique. A slow cooling and thawing rates, and less pronounced end temperature, which is more "friendly" to the melanocytes, were doc-

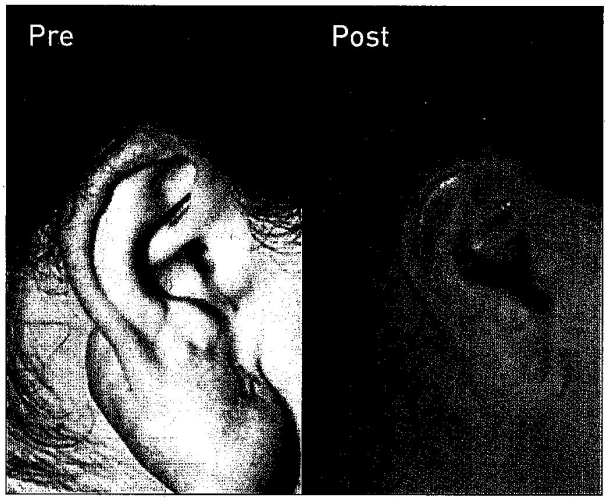

Figure 1. Left: Pre-op view of a keloid on the right lobule following piercing. Right: Post-op view 6 years following a single intralesional cryo-treatment.

umented. In addition, a significantly long hold time, until complete freezing is achieved clinically during the intralesional treatment, might explain the effectiveness of this new technology and the absence of permanent hypopigmentation. Furthermore, lower temperatures are present at the core of the HSK (abutting the cryoneedle) which increase the freezing area of deep scar material causing cryoinjury which is more effective than the contact method.[2,3]

Pain control protocol: Skin cryosurgery inevitably entails pain. Therefore, pain experienced by the patient could limit the wide-ranging application of this effective technology, and it is of great importance that the procedure be as painless, pleasant, and comfortable as possible, for the patient. Therefore, a pain control protocol has been developed and applied clinically during the intralesional cryosurgery treatment. The protocol involved oral pain-relief tablets (Dipyrone) and translesional local anesthesia with Bupivacaine hydrochloride 0.5%. The pain-control protocol significantly reduced pain severity to tolerable levels (VAS ≤ 3 cm) during and following intralesional cryosurgery.[7]

The treatment of keloids and hypertrophic scars following aesthetic surgery: It has been demonstrated that intralesional cryosurgery technique provides the plastic surgeon with an effective and proper instrument to reduce, in a relative short time, the dissatisfaction of patients who have developed problematic and unsightly hypertrophic scars and keloids following aesthetic surgery. Thus, the patient confidence in the plastic surgeon is maintained which creates a positive attitude for a successful solution for those challenging scars.[4]

In conclusion, the clinical and scientific studies have demonstrated increased efficacy of the intralesional cryosurgery technique due to increased freezing area of deep scar tissue compared with that obtained with contact/spray probes. As a result, fewer treatment cycles are needed. This technique is simple to operate and requires a short learning curve, safe to use, consumes less liquid nitrogen fluid per treatment, avoids the need for time taking during the freezing process, is almost painles, necessitates less postoperative wound care, and can easily be added to any preexisting cryosurgical unit. ■

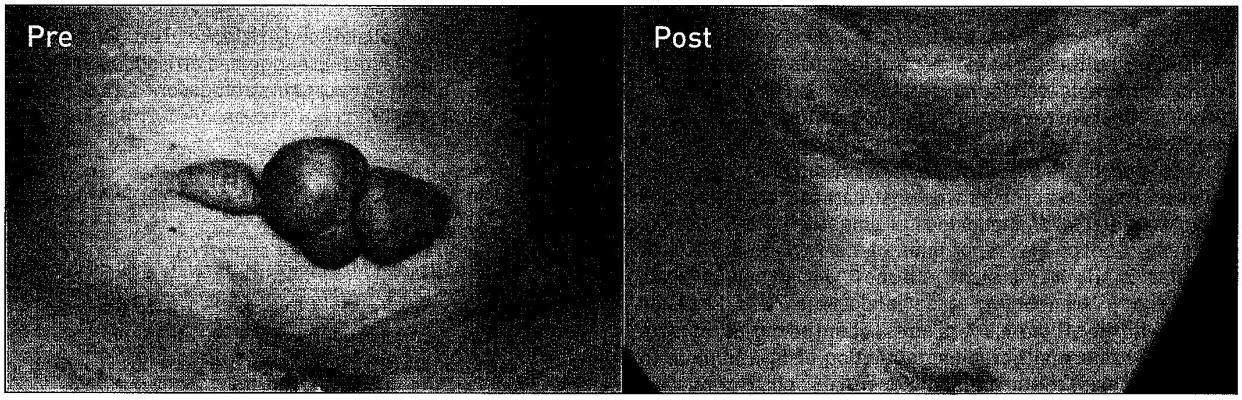

Figure 2. Left: Pre-op view of a keloid on the anterior base of the neck following thyroidectomy. Right: Post-op view 12 months following a single intralesional cryo-treatment.

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