Intralesional Cryotherapy for Enhancing the Involution of Hypertrophic Scars and Keloids

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Although therapeutic management of hypertrophic scars and keloids using contact or spray cryosurgery has yielded significant improvement or complete regression of hypertrophic scars and keloids, it requires one to 20 treatment sessions. This study was designed to assess the clinical safety and efficacy of an intralesional needle cryoprobe method in the treatment of hypertrophic scars and keloids.

Ten patients, ranging in age from 3 to 54 years, with a total of 12 hypertrophic scars and keloids of more than 6 months duration and of diverse causes, were included in this study. The 18-month trial evaluated volume reduction of the hypertrophic scars and keloids after a single session of intralesional cryotherapy. Objective (hardness and color) and subjective (pain/tenderness and itchiness/discomfort) parameters were examined on a scale of 0 to 3 (low score was better). Pretreatment and posttreatment histomorphometric studies of the collagen fibers included spectral picrosirius red polarization and fast Fourier transformation orientation index. A specially designed cryoneedle was inserted into the long axis of the hypertrophic scars and keloids so as to maximize the volume of the hypertrophic scars and keloids to be frozen. The cryoneedle was connected by an adaptor to a cryogun filled with liquid nitrogen, which was introduced into the cryoprobe, thereby freezing the hypertrophic scars and keloids. After the hypertrophic scars and keloids were completely frozen, the cryoprobe defrosted and was withdrawn.

An average of 51.4 percent of scar volume reduction was achieved after one session of intralesional cryosurgery treatment (average preoperative hypertrophic scars and keloids volume, 1.82 ± 0.33; average posttreatment volume, 0.95 ± 0.21; \( p < 0.0022 \)). Significant alleviation of objective and subjective clinical symptoms was documented. Mild pain or discomfort during and after the procedure was easily managed. Only mild local edema and epidermolysis, followed by a short reepithelialization period, were evident. During the 18-month follow-up period, there was no evidence of bleeding, infection, adverse effects, recurrence, or permanent depigmentation. The histomorphometric analysis demonstrated rejuvenation of the treated scars (i.e., parallelization) and a more organized architecture of the collagen fibers compared with the pretreated scars.

This study demonstrated the increased efficacy of this method as a result of increased freezing area of deep scar material compared with that obtained with contact/spray probes. As a result, fewer treatment cycles are needed. Because the reepithelialization period is short, treatment intervals, if any, can be shortened to 2 to 3 weeks. This intralesional cryoneedle method is simple to operate and safe to use, it necessitates less postoperative care of the wound, and it can easily be added to any preexisting cryosurgical unit. (Plast. Reconstr. Surg. 111: 1841, 2003.)

The therapeutic management of hypertrophic scars and keloids remains a challenge. In 1982, Shepherd and Dawber were the first to apply cryosurgery as a monotherapy regimen for treating hypertrophic scars and keloids. Although this single cryosurgical session achieved 80 percent improvement, a high recurrence rate of 33 percent was observed. Additional monotherapy studies were lacking, perhaps delayed indefinitely by the rather disappointing relapse rate, until Mende, Zouboulis and Orfanos, and others showed that repeated surface/spray cryosurgical sessions can have a beneficial effect on hypertrophic scars and keloids (between 68 and 81 percent remission), with almost no recurrence (2 percent).

To achieve these results, one to 20 treatment sessions using the contact cryotherapy method were required. Thus, the problems that accompany commercially available application probes have been documented, and the need...
for improved devices has been recognized. This study was designed to assess the clinical safety and efficacy of an intralesional needle cryoprobe as a monotherapy method in the treatment of hypertrophic scars and keloids.

**Patients and Methods**

In this study, 10 white patients, ranging in age from 3 to 54 years, signed an informed consent. The patient group had a total of 12 hypertrophic scars and keloids of more than 6 months’ duration and from diverse causes (Table 1). The trial, which extended over an 18-month period, evaluated the volume reduction of hypertrophic scars and keloids using an Elite H-D Putty Vinyl polysiloxane high-precision (>99.5 percent) impression material (Zhermack, Badia Polesine, Italy) and water displacement method before and after a single intraleisional cryotherapy session. In addition, objective parameters (hardness and color) and subjective complaints of pain/tenderness and itchiness/discomfort were examined on a scale of 0 to 3 (a low score was better). Photographs were taken of all scars before and after treatment. This assessment was done before treatment and at 2 weeks and 1, 2, 3, 6, 12, and 18 months after treatment.

The novelty of this cryoprobe is its specially designed, elongated double-lumen uninsulated cryoneedle (U.S. patent 6,503,246) that has a cryogen vent and a sharp-cutting, sealed, distal tip so as to easily penetrate the often hard, rubbery, and dense hypertrophic scar and keloid tissue. The proximal end of the needle casing is attached to an adaptor that is connected to the cryogen source (the cryogun). Forcing liquid nitrogen to circulate through the needle produces an iceball around the needle, which freezes the adjacent hypertrophic scar and keloid tissue.

**Practical Procedure**

The skin surface of the hypertrophic scar and keloid is cleansed with disinfectant solution and draped. The area of penetration into the scar is locally anesthetized with lidocaine 1%. The sterile cryoneedle is forced into the long axis of the scar through the anesthetized area until the sharp distal end of the needle penetrates the opposite edge of the scar, thus maximizing the volume of scar to be frozen. Sterile gauzes are placed under the proximal and distal parts of the needle to prevent freezing of the normal surrounding skin. The proximal housing of the needle is connected by the adaptor to the cryogun (Brymill Cryogenic Systems, Ellington, Conn.), which is filled with liquid nitrogen. By activating the trigger, the valve opens and the cryogen fluid is introduced into the cryoprobe under a pressure of approximately 5 pounds per square inch, thereby freezing the hypertrophic scar and keloid (Fig. 1). Two iceballs appear at the opposite borders of the scar. The ice cylinder that forms around the embedded part of the needle is not visible. With time, the two iceballs at opposite ends of the scar gradually spread toward each other until complete freezing of the scar is achieved (Fig. 2).

After the scar becomes completely white and icy, regardless of the duration of the freezing process, the valve of the cryogun is closed and the cryoneedle is left to thaw for 2 to 3 minutes and is then withdrawn. After thawing, slight bleeding from the penetrating points of the needle requires the application of a sterile dressing. The patient is instructed to wash the treated scar daily and to apply antibiotic ointment until full recovery of the treated site is observed.

**Histomorphometry**

Biopsies for histomorphometric evaluation were taken from four patients, first from the pretreated scar and then 1 month and 3 months after the cryosurgical session. Deparaffinized hypertrophic scar and keloid tissue sections were histochemically stained by picrosirius red and examined by polarization microscopy. Staining of the collagenous matrix shows a mixture of red and green fibers of different proportions according to the particular spatial orientation levels. The red-stained fibers represent the thick and more tightly packed collagen fibers (mature), whereas the green-stained fibers represent the thin and loosely spaced collagen fibers (young). The ratio of red to green represents the relative amounts of the two types of collagen fibers. Images were captured by a three-chip (red-green-blue) video camera (Sony, Tokyo, Japan) and digitized with the aid of a frame grabber and an IBM-compatible personal computer equipped with a 17-inch, high-resolution screen.

Computerized morphometric analysis of collagen fibers was then performed using the Image Pro Plus 4.5 software (MediaCybernetics, Carlsbad, Calif.). Five representative micro-
### TABLE I

Patient Parameters*

<table>
<thead>
<tr>
<th>Patient Initials</th>
<th>Age (yr)</th>
<th>Sex (M/F)</th>
<th>Duration (yr)</th>
<th>Location</th>
<th>Clinical Symptoms Score (0–3)†</th>
<th>Objective</th>
<th>Subjective</th>
<th>Scar Volume (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Hardness</td>
<td>Redness</td>
<td>Pain/Tenderness</td>
<td>Itching/Discomfort</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>1 R.E.</td>
<td>3</td>
<td>M</td>
<td>1.5</td>
<td>Rt. cheek</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>2 I.T.</td>
<td>14</td>
<td>M</td>
<td>1</td>
<td>Back</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>3 A.M.</td>
<td>20</td>
<td>M</td>
<td>0.5</td>
<td>Lt. helix</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>0</td>
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<tr>
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<td>M</td>
<td>2.5</td>
<td>Rt. upper post auricle</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
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<tr>
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<td>M</td>
<td>2.5</td>
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<td>2</td>
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<tr>
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<td>M</td>
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<td>Chest</td>
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<td>1</td>
<td>3</td>
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<td>7 E.P.</td>
<td>30</td>
<td>M</td>
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<td>Chest</td>
<td>3</td>
<td>1</td>
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<td>8 H.V.</td>
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<td>F</td>
<td>10</td>
<td>Rt. lobule</td>
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<td>9 H.V.</td>
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<td>F</td>
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<td>0</td>
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<td>F</td>
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<td>1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>11 K.Y.</td>
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<td>M</td>
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<td>Chest</td>
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<td>2</td>
<td>3</td>
<td>3</td>
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<tr>
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<td>M</td>
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<td>Lt. post auricle</td>
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<tr>
<td>Mean ± SEM</td>
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<td>4.1 ± 1.0</td>
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<td>p values</td>
<td>0.0022</td>
<td>0.011</td>
<td>0.0051</td>
<td>0.0051</td>
<td>1.82 ± 0.33</td>
<td>0.95 ± 0.21</td>
<td>51.4 ± 5.2</td>
<td>0.0022</td>
</tr>
</tbody>
</table>

* Rt., right; Lt., left.
† Hardness: 3, very hard, like cartilage; 2, rubbery hard; 1, partially soft; 0, soft (like normal skin).
Redness: 3, severe redness; 2, redness disappears with pressure; 1, no redness, but alteration in skin tone; 0, normal skin color.
Itching/discomfort: 3, severe itching sensation or constant itch with signs of scratching; 2, occasional itchy sensation, moderate and tolerable; 1, sometimes itchy; 0, no itchy sensation.
Previous therapy: ST, intralesional steroids; EXC, surgical excision; PE, pressure earring; CRYO, surface spray cryotherapy; SIL, silicone gel/sheeting.
scopic fields were scanned at a magnification of ×100. After establishment of the appropriate thresholds, the relative areas of green and red collagen fibers were stained separately and calculated by the program. Then, the average green-to-red ratio was computed for each scar.

The orientation index of the collagen fibers in the hypertrophic scars and keloids before and after cryotherapy was evaluated using the fast Fourier transformation algorithm. To compute the orientation index, the Auto-Pro environment of the Image Pro-Plus 4.5 software was used. A macro algorithm was developed that automatically traces, thickens, and singles out the longest diameter of the fibers. Subsequently, the fast Fourier transformation algorithm was applied to obtain two-dimensional power-scattergrams of the histological images. A median filter was applied to homogenize close pixels. A scar with randomly oriented collagen fibers exhibited a circular scattergram, compared with a scar with well-oriented fibers, which showed an elongated (elliptically shaped) scattergram. The larger the index value, the greater the degree of collagen fiber orientation in the scar.

### Statistical Analysis

The average and standard error of the mean were calculated and presented for each group. The clinical scores and scar volumes before and after treatments were compared using the Wilcoxon test for pairs. A receiver operating curve analysis was performed, and sensitivity and specificities were computed to detect the best cutoff point of the initial scar volume for predicting treatment success of 50 percent scar reduction.

The red-to-green ratios were compared in the three groups (pretreated and 1 and 3 months after treatment) using the Wilcoxon rank sum test for paired data, with adjustments...
for multiple group comparisons. Two-tailed values of $p \leq 0.05$ were considered to be statistically significant.

**RESULTS**

The time needed to achieve a complete freezing of the hypertrophic scars and keloids was between 7 and 24 minutes, depending on the volume of the pretreated hypertrophic scars and keloids.

A significant reduction in objective parameters (hardness and redness) and alleviation of the subjective complaints of pain/tenderness and itchiness/discomfort were achieved. The average hardness and redness of the hypertrophic scars and keloids before treatment were $2.8 \pm 0.1$ and $2.9 \pm 0.1$, respectively, and at 18 months after treatment, $0.8 \pm 0.2$, $p = 0.0022$ and $1.4 \pm 0.3$, $p = 0.011$, respectively. The average levels of pretreatment pain/tenderness and itchiness/discomfort were $2.3 \pm 0.3$ and $2.6 \pm 0.2$, compared with $0.5 \pm 0.2$, $p = 0.0051$ and $1.0 \pm 0.3$, $p = 0.0051$, respectively, at 18 months after cryotherapy (Table I; Figs. 3 and 4). The average volume of the preoperative hypertrophic scars and keloids was $1.82 \pm 0.33$ cm$^3$ (range, 0.3 to 3.8 cm$^3$), compared with the average posttreatment volume of $0.95 \pm 0.21$ cm$^3$ after one session of intraleisonal cryosurgery treatment. The average volume reduction, therefore, was $51.4 \pm 3.2$ percent (range, 33 to 67 percent; $p < 0.0022$; Table I; Figs. 5 through 9).

The patients complained of very mild pain or discomfort during and after the procedure, which was easily managed. Only mild local edema and epidermolysis were evident. Neither active bleeding from the penetration points nor infection was documented. No adverse reactions, including permanent depigmentation at the cryosurgical site or scar recurrence, were noted during the 18-month follow-up period.

The receiver operating curve analysis revealed that the best cutoff point of the pretreated scar volume for predicting a 50 percent scar reduction was $1.5$ cm$^3$. Pretreated scar values of less than $1.5$ cm$^3$ correlated with successful scar reduction (sensitivity, 100 percent; specificity, 57 percent). The ratio of red (mature) collagen fibers to green (young) collagen fibers obtained by the picrosirius red color spectral analysis and the subsequent polarization microscopy revealed the following red-to-green ra-

![Fig. 3. A significant reduction of scar volume is achieved after a single intraleisonal cryotherapy session.](image)

![Fig. 4. Significant alleviation of objective parameters (hardness and redness) and subjective complaints (pain/tenderness; itchiness/discomfort) was achieved after a single intraleisonal cryotherapy session, rated on a scale of 0 to 3 (a low score is better). A, Before treatment; B, after treatment.](image)
tios; in the pretreated scar, $1.4 \pm 0.15$; at 1 month after treatment, $1.14 \pm 0.15$; at 3 months after treatment, $1.06 \pm 0.2$. All differences were statistically significant ($p < 0.001$; Fig. 10).

The orientation index was significantly higher in the posttreated scar ($2.06 \pm 0.7$) than in the untreated keloid ($1.40 \pm 0.2$, $p = 0.044$, Fig. 11). Hence, the architectural pattern of the collagen is more organized in the treated scar, i.e., the parallel organization of the collagen fibers in the treated scar is similar to that in the normal dermis, in contrast to the disorientation of the collagenous network seen in the nontreated scar (Fig. 12).
Normal and keloidal fibroblasts, which are somewhat resistant to freezing and cryosurgery, were shown to significantly increase their proliferation in vivo\textsuperscript{9} and in vitro\textsuperscript{10,11} after cryotherapy. In addition, Shepherd and Dawber\textsuperscript{12} showed that after freeze-thaw cycles, an absence of damage to collagen was noticed, and it was proposed that this phenomenon explains the lack of scarring. Furthermore, significant thinning of pig skin was documented at 6 months after cryosurgery.\textsuperscript{12}

The extremely low temperature of freezing causes vascular damage and blood stasis within the keloid tissue that, in itself, leads to cell anoxia. As blood flow becomes increasingly sluggish, white thrombi form, occluding the lumen of the capillaries and leading to tissue necrosis and sloughing.\textsuperscript{3} Using an in vivo microvascular preparation, Hoffmann and Bischof\textsuperscript{13} showed experimentally a complete destruction of the vasculature in the center of normal skin after cryoinjury and a gradual return to normal patency moving radially outward. Histological examination revealed a band of inflammation near the edges of the large necrotic region up to 7 days after cryosurgery. These results are consistent with the hypothesis that cryotherapy causes cellular destruction by a vascular-mediated injury that activates the shrinkage of hypertrophic scar tissue.

Previous histological and immunohistological studies indicate that cryosurgery can induce in keloids changes that are compatible with scar rejuvenation. After cryosurgery, the collagen fibers are generally flat and normal in quantity, and their axes are parallel to the skin surface, with no signs of the vorticose and nodular arrangement typical of keloids. Sizov et
al.14 studied the biochemical and microstructural changes of the collagen molecule in postburn scars before and after cryosurgery. It was demonstrated that a tendency to normalization of the collagen structure as well as the presence of type III collagen was found in the treated scars. In the present study, both the red-to-

green ratio of the picrosirius red staining and the orientation index confirm these histological findings, i.e., young normal collagen fibers are found in hypertrophic scars and keloids treated by cryotherapy.

The common therapeutic cryogen applications include the contact and spray techniques.

**Fig. 9.** Patient 12. (Left) Preoperative view of the left posterior auricular sulcus of a keloid with a volume of 1.5 cm³. (Center) Intralesional cryotherapy of the keloid. (Right) Eighteen months after a single session of intralesional cryotherapy of the keloid. Its volume was reduced to 0.6 cm³ with no recurrence or depigmentation.

**Fig. 10.** Spectral analysis (red-to-green ratio) as visualized with picrosirius red polarization of scar collagen before treatment, after intralesional cryotherapy, and after partial (1 month) and complete (3 months) healing. A significant rejuvenation of the treated scars is evident.
These methods freeze the scar surface, whereas the depth and lateral spread within the lethal zone are limited to 20 mm and depend primarily on the cryoprobe tip configuration and the shape of the frozen tissue.15,16 The contact method using flat metallic probes is indicated in regular and flat lesions, whereas the spray technique is particularly useful for irregular and curved surface scars. The clinical course of cryoreaction following these two therapeutic techniques is peripheral erythema, edema, bulla formation, exudation, crust formation, and final healing with a flat, slightly atrophic scar that usually is complete after approximately 1 month.

There are some drawbacks to the surface techniques. The application can cause pain, and the postoperative phase may be disturbing to the patient because cryotherapy produces an open, oozing wound that usually takes several weeks to heal. In addition, a certain degree of skin atrophy and permanent hypopigmentation is also inevitable with this approach because of melanocyte sensitivity to low temperatures. Therefore, this characteristic probably renders surface cryotherapy in dark-skinned patients less than optimal.

Fig. 11. Orientation index of collagen fibers in the untreated and posttreated scars using the fast Fourier transformation. In the treated scars, the orientation index is significantly higher, i.e., parallel organization of the young collagen fibers is noticeable compared with the pretreated scars.

Fig. 12. Fast Fourier transformation (FFT) power plots and orientation indices of the collagen fibers demonstrating a highly oriented architecture of a treated scar (higher index) versus a disoriented architecture of the untreated scar (lower index).
It has been documented that to achieve complete hypertrophic scar and keloid regression, up to 20 cryosessions are required, whereas the combination of surface/spray cryosurgery with intralesional steroid injections renders results that are neither faster than nor superior to those obtained by cryotherapy alone. In light of these considerations, the need for improved cryoprobes is advocated.

Zouboulis and Orfanos were the first to describe intralesional cryotherapy for the treatment of keloids and hypertrophic scars. Gupta and Kumar described their experience with intralesional cryosurgery for the treatment of large, bulky keloids unresponsive to intralesional corticosteroid injections. The main advantage of intralesional cryotherapy compared with contact and spray techniques is minimal surface destruction and enlarged volume of frozen scar tissue.

The area frozen by cryosurgery can be divided into a lethal zone, in which the temperature is lower than −22°C, and a recovery zone, with temperatures between 22°C and 0°C. Cells within the lethal zone undergo cryonecrosis, whereas cells situated in the recovery zone generally survive the freeze. In surface cryosurgery, the lethal zone includes the surface epithelium but not the dermis, which is the domain of the main pathological disorder. In this manner, the dermis is in the recovery zone and thus survives freezing. In contrast, the intralesional cryoneedle is inserted directly into the dermis of the pathological scar, where the ice cylinder surrounding the length of the needle produces a 360° lethal zone. The recovery zone is situated toward the epithelium and the subcutaneous tissue. Thus, the surface reactions are minimal and the maximal destruction occurs deep in the lesion, increasing the chances of therapeutic success with less depigmentation because of survival of melanocytes in the recovery zone.

The method of intralesional cryotherapy described is based on the technique developed by Weshahy, in which a curved hypodermic needle is introduced into the skin and through the deeper part of a cutaneous lesion. Liquid nitrogen is then passed through the needle, thus freezing the base of the skin lesion. Zouboulis and Gupta and Kumar modified this technique to treat hypertrophic scars and keloids by using a 20- to 18-gauge hypodermal/lumbar puncture needle.

The cryoneedle used in this study is a further refinement of the intralesional freezing needle. This 14-gauge, stainless steel needle has a sharp-cutting, sealed, distal tip that enhances penetration into the hard, rubbery hypertrophic scar without the need for a stylet and causes less tissue trauma than might occur with an open cutting tip. The inbuilt cryogen safety vent situated at the proximal end of the needle enables the creation of a uniform ice cylinder along the entire length of the needle and prevents direct spillage of liquid nitrogen onto the surrounding normal skin, which might occur with open-tip needles.

The 14-gauge needle creates a larger iceball around it compared with the 18- to 20-gauge needles. In addition, it was demonstrated by Popken et al. that the iceball and lethal-zone diameters produced with an 8-mm cryoneedle were significantly larger than those produced with the 3-mm cryoprobe. Therefore, the efficacy of cryotherapy can be enhanced by use of the cryoneedle presented in this study, an improvement that helps reduce the number of treatment cycles.

Because of the fair skin color of the patients included in the present study, permanent hypopigmentation/depigmentation was not noticed over the 18-month follow-up period. However, in the report by Gupta and Kumar, hypopigmentation/depigmentation was noted along the needle tracks in all hypertrophic scars and keloids treated with the intralesional cryosurgery technique, a condition that improved during the follow-up period. This temporary pigmentation disorder was noticed in 10 of the 12 treated scars and was explained by the survival of islands of normally pigmented skin that resisted the freezing process and gradually spread. However, the skin color of the patients in that article was not reported. Nevertheless, this temporary hypopigmentation/depigmentation might encourage the use of the intralesional cryotherapy method for dark-skinned individuals, especially compared with the permanent loss of pigment that occurs with contact/spray cryosurgery.

The receiver operating curve analysis indicated a volume of 1.5 cm³ or less for predicting a 50 percent reduction in hypertrophic scar and keloid volume after a single cryotherapy session. These data may highlight a critical relationship between cryoneedle diameter, size of the ice cylinder formed around it, and the volume of the scar affected. For hypertrophic scars and keloids with volumes larger than 1.5
cm³, more freezing cycles are needed until the entire scar volume is reduced to 1.5 cm³; thereafter, using the same cryoneedle, the cryotherapy can be completed effectively. This may explain the relatively small response in volume reduction observed in the larger scars in this study, which were submitted to a single session of cryotherapy. In a very large scar, a number of cryoneedles can be applied simultaneously to maximize the freezing area of the scar.\textsuperscript{18}

The degree of collagen fiber orientation was assessed by computing a fast Fourier transformation-based orientation index. Fast Fourier transformation comprises a family of mathematical techniques based on converting signals into sinusoids.\textsuperscript{21} It is a powerful tool for analyzing phenomena that take the form of waves, such as light, sound, vibrations, and heat.\textsuperscript{22} Digitized images are composed of two-dimensional arrays of pixels, each having a light intensity value (gray level) ranging from 0 (black) through different shades of gray to 255 (white). Every row or column in this two-dimensional array represents a signal in the form of a wave and therefore can be analyzed by Fourier mathematics. Fast Fourier transformation is an efficient computer algorithm for calculating the Fourier transform of a discrete (digital) signal.\textsuperscript{21}

The periodicity and orientation of structures can be represented as a power plot of the fast Fourier transformation of an image. De Vries et al.\textsuperscript{23} applied the fast Fourier transformation algorithm to histological images of the skin in scleroderma patients and computed an orientation index of the dermal collagen fibers. We used the same principles to compute an orientation index of the collagen fibers in hypertrophic scars and keloids before and after cryosurgery. The orientation index was higher in the posttreated scar specimens than in the pretreated samples. This finding suggests recovery of normal collagen synthesis after application of cryotherapy. Furthermore, analysis of the collagen using the picrosirius red staining spectrum and polarized light microscopy revealed a shift in the red-to-green ratio between the pretreatment and posttreatment groups, thus supporting the spatial and conformational differences between them.

Hence, the methods of fast Fourier transformation algorithm and spectral analysis of the collagen bundles, in addition to confirming the effects of cryotherapy on the hypertrophic scars and keloids, may also serve as objective tools for assessing the cryotherapy efficacy, because they contribute to a better understanding of the structural changes of the collagen molecules in hypertrophic scars and keloids after cryosurgery. Van Zuilen et al.\textsuperscript{24} reinforce this observation by establishing a poor correlation between the laser-scattering results, the observer assessment, and the fast Fourier transformation. It was postulated that the Fourier analysis has a perfect reliability and accuracy, because the calculation of the same images will always produce the same outcome.

**Conclusions**

This study demonstrates a more efficient method of freezing scars because of a greater internal freezing area, which causes greater destruction of deep scar material than is achieved with the use of contact/spray probes. Given this advantage, it is assumed that fewer treatment cycles will be necessary. The minimal superficial ulceration or dermal–epidermal separation noticed after the procedure requires a short reepithelialization period. Thus, the treatment intervals can be shortened to a period of 2 to 3 weeks. During the 18-month follow-up period, no recurrence or permanent hypopigmentation was noticed. The small residual volume of hypertrophic scars and keloids remaining after the intralesional cryosurgery can be further eliminated with appropriate therapy (e.g., silicone sheets, intralesional corticosteroids, pressure garments, earrings).

This simple-to-operate intralesional cryoneedle method can be applied to every scar shape or contour with a sufficient volume into which the cryoneedle can be introduced. It is safe to use, consumes less cryofluid, necessitates less postoperative care of the wound, can easily be added to a preexisting cryosurgical unit, and enables the surgeon to freeze any hypertrophic scars and keloids to an adequate depth. These promising results encourage further investigational work comparing this technique with previous well-established cryosurgical methods to ascertain its merits in the treatment of hypertrophic scars and keloids.

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REFERENCES