Intralesional Cryosurgery – a new effective technology for the treatment of hypertrophic scars and keloids

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Financial Interest in the Intralesional Cryosurgery Technology
Cryosurgical Treatment of Hypertrophic Scars and Keloids

- The Contact Technique
- Intrallesional Cryosurgery
The Contact Technique
Cryosurgical Treatment of Hypertrophic Scars and Keloids

- The Contact Technique
- Intrallesional Cryosurgery
Principles of Cutaneous Cryosurgery:
Ch.C.Zouboulis
Department of Dermatology, University Medical Center Benjamin Franklin, The Free University of Berlin

Dermatology 198:111-117, 1999

Intralesional cryosurgery using lumbar puncture and/or hypodermic needles for large, bulky, recalcitrant keloids

Somesh Gupta, MD, DNB, and Bhushan Kumar, MD, MNAMS

Cryoneedle Probe

Occluded Cutting Tip

Safety Vent

U.S Patent # 6,503,246   European Patent # 1299043

Contact Vs. Intralesional Cryosurgery Techniques

Contact

Intralesional

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Patients

95 Caucasian patients (51 female: 44 males) with total of 112 hypertrophic scars and keloids

- Ages: 3 to 67 years
- Chest: 62
- Auricular: 26
- Shoulder: 7
- Neck: 4
- Abdominal: 4
- Breast: 4
- Nape: 3
- Arm and Forearm: 2
Method

- Intralesional Cryosurgery using a cryoneedle
- Freezing achieved using Liquid Nitrogen
- One cryo-session
- No additional therapy
Method

- Volume reduction using impression material
- Objective parameters: hardness, elevation, redness
- Subjective parameters: itching, pain, tendernessness
- Scale 1 to 3 (low score is better)
- Follow-up 18 months to 3 years
Freezing Sequence
Demonstrative Case
Demonstrative Video
Clinical Results

Before

After

1 cryo-session

1.5 years

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pre – 1cc

1 cryo-session

2 years
pre - 1cc

post - 0.4cc

1 cryo-session
pre – 3.8cc  
18 months  
1 cryo-session  
post – 1.5cc
pre – 3.8cc

1 cryo-session

post – 0cc
1 cryo-session
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Pre

1 cryo-session

Post
1 cryo-session
1 cryo-session
1 cryo-session
1 cryo-session  18 months
Neck

Pre

Post

4.5 years

1 cryo-session

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Shoulder

Pre                               Post

1 cryo-session

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Chest

7 days

1 cryo-session

2.5 years

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Chest

Pre

Post

1 cryo-session

18 months

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Chest

Pre

Post

1 cryo-session

2.5 years

Yaron Har-Shai MD
Chest

1 cryo-session
Chest

Pre

Post

2 cryo-sessions

3.5 years

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2 cryo-sessions
Average Volume

Reduction 51.4%

P < 0.001 (ANOVA for repetitive measurements)
Multiple comparisons: Baseline vs 6 months:  p=0.006
Baseline vs 12 months:  p=0.009
6 months vs 12 months:  p>0.050
Volume Reduction of Auricular Keloids

67.4 ± 23% (± SE)  p < 0.005
Freezing Time (min)

5-30 min (until a complete freezing of the treated scar is clinically evident)

No need for time taking
Clinical Score

Clinical score 0-3 (a low score was better)

A – pre-treatment; B – post-treatment

- Hardness: p=0.0022
- Redness: p=0.011
- Pain/tenderness: p=0.0051
- Itching/discomfort: p=0.0051
Elevation

\[ p < 0.0001 \]

Redness

\[ p = 0.004 \]

Hardness

\[ p = 0.002 \]

(Means ± SEM)

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Itching

Tenderness

Pain

(Means ± SEM)

p = 0.004

p = 0.056

0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8

0
0.5
1
1.5
2
2.5

Baseline 6 months 18 months

Baseline 6 months 18 months

Baseline 6 months 18 months
Spectral Analysis of Keloid Scars Collagen Following Intralesional Cryotherapy

Red to green ratio

Sirius red polarization

P < 0.01 (between all groups)
Fast Fourier Transform (FFT)

- Collagen fibers, non-treated
  - FFT power-plot
  - Orientation index = 1.2

- Collagen fibers, post cryotherapy
  - FFT power-plot
  - Orientation index = 4.5
Keloid (histological image, Picro Sirius Red)

Fast Fourier Transform Power Plot (3D View)

Fast Fourier Transform Power Plot (Top View)

FFT

High frequency

Medium frequency

Low frequency

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Berlin – Haifa Cooperation (Prof. C.C. Zouboulis)
T = Temperature
\( t = \text{ time} \)

\( T_1 / t_1 = \text{ Freezing Rate} \)
\( T_2 / t_2 = \text{ End Temperature} \)
\( T_3 / t_3 = \text{ Hold Time} \)
\( T_4 / t_4 = \text{ Thawing Rate} \)
Isolated Contact Probe
Isolated cryoneedle
Comparison of Thermal History Between Isolated Contact Probe and Cryoneedle
Contact Probe - Ex-Vivo Swine Model

6 mm deep

3 mm deep

Surface

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Cryoneedle - Ex-Vivo Swine Model

3 mm deep

6 mm deep

Surface

Cryoneedle
Comparison of Thermal History Between Contact Probe and Cryoneedle (Ex-vivo)

Har-Shai et al, Wound Repair and Regeneration, 14:18-27, January 2006
Comparison of the Thermal History of Skin Surface Temperature During the Treatment of Hypertrophic Scars and Keloids Using Contact and Intralesional Cryosurgery and its Effect on Skin Pigmentation

- 30 caucasian patients with 45 Hypertrophic scars and Keloids (HSK), older than 6 months
- 21 HSK were treated by the contact method
- 24 scars were managed with intralesional cryosurgery technique
Cryoneedle Surface Temperature (In-Vivo)
# Skin Surface Thermal History

## Contact Vs. Intralesional (In-Vivo)

<table>
<thead>
<tr>
<th></th>
<th>Cooling rate* (C/min)</th>
<th>End Temperature* (C)</th>
<th>Hold time* (sec)</th>
<th>Thawing rate* (C/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contact</strong></td>
<td>54.52±32.17</td>
<td>-46.77±14.74</td>
<td>16.86±23.49</td>
<td>89.00±86.42</td>
</tr>
<tr>
<td>(n=21)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Intralesional</strong></td>
<td>6.09±4.56</td>
<td>-15.55±6.77</td>
<td>82.67±138.03</td>
<td>13.47±9.04</td>
</tr>
<tr>
<td>(n=24)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P-value</strong></td>
<td>&lt;0.00001</td>
<td>&lt;0.00001</td>
<td>&lt;0.05949</td>
<td>&lt;0.00001</td>
</tr>
</tbody>
</table>

*mean value ± STD, ** t-test (2-tailed)
Hypopigmentation Score Following Contact Vs Intralesional Cryosurgery

<table>
<thead>
<tr>
<th>Hypopigmentation Score</th>
<th>Contact</th>
<th>Intralesional</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>8.3%</td>
<td>72.7%</td>
<td>50.0%</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>0%</td>
<td>27.3%</td>
<td>17.6%</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>75.0%</td>
<td>0%</td>
<td>26.5%</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>16.7%</td>
<td>0%</td>
<td>5.9%</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>22</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

p<0.0001 (Mann-Whitney)
0 - Skin color with no significant hypopigmentation changes
1 - Skin with pink pigmentation
2 - Skin color pal, with pigment islets
3 - Skin color white, with no pigmentation

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Hypopigmentation Scoring Following Contact Vs Intralesional Cryosurgery

- Skin color with no significant hypopigmentation changes
- Skin with pink pigmentation
- Skin color pail, with pigment islets
- Skin color white, with no pigmentation

n = 34
Contact 12
Intralesional 22

p<0.0001
Post Cryosurgery Skin Hypopigmentation - Fair Skin Contact Technique
Chest (Dark Skin) - Intralesional

Pre

Post

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Intralesional Cryosurgery - Side Effects and Complications

- **Immediate**
  - Mild pain / discomfort during penetration and freezing
  - Local edema
  - Epidermolysis (vesiculobullous formation)

- **No delayed complications**
Intralesional Cryosurgery - Contraindications

- Cryoglobulinopathy
- Collagen and Autoimmune Diseases
- Immunosuppressive Drugs
- Blood Dyscrasias
- Adjacent Vital Organs
Intralesional Cryosurgery - Conclusions

- Increase efficiency of freezing
- Less treatment cycles are needed
- Shortened treatment intervals (3-4 w)
- 8/ 112 did not respond
- Significantly reduced hypopigmentation
- Simple, safe and a short learning curve
- Fits to existing cryosurgical unit
- Consumes less LN$_2$ and does not need time measurements
CryoShape
Intralesional Cryosurgery Technology

New

Har-Shai et al, Wound Repair and Regeneration, 14:18-27, January 2006

U.S Patent # 6,503,246   European Patent # 1299043

Har Shai MD
Thank you