Cryotherapy

Thomas J. Vogl, B. Panahi

ID I R: Institute of Diagnostic and Interventional Radiology
Goethe University Frankfurt, Germany
Disclosure

Speaker name:
Thomas Vogl

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other: travel grant
- I do not have any potential conflict of interest

Institute of Diagnostic and Interventional Radiology, Goethe University, Frankfurt/Main
What is Cryoablation?

Cryoablation is a minimally invasive image-guided US / CT treatment that uses extreme cold to freeze and accurately destroy diseased tissue within the tumor zone.
What is Cryoablation?

**Intracellular ice crystallization:**
- Contact with extremely cold cryoprobe
- Intracellular ice crystals form causing cell lysis/death.

**Extracellular ice crystallization:**
- Freeze, thaw, freeze cycle
- Repeated, rapid osmotic shifts of fluid into and out of the cell weakens the cell membrane causing membrane rupture and cell death.

**Platelet aggregation in capillaries surrounding the tumor:**
- Lack of blood supply to tumor starves any remaining cells.
- Prevents regrowth

**Post cryoablation & cryoimmunology:**
- Area becomes an irregular accumulation of hypoechoic necrotic debris
- Elimination of debris over time
- No artifact that would adversely affect interpretation
- Clinical studies suggest anti-tumoral response are generated through cryoablation.
Mechanism of Action - Direct

1. During the freeze: Intracellular ice crystallization

- Contact with extremely cold cryoprobe (~-170°C on the probe shaft)
- Intracellular ice crystals form causing cell rupture --> lysis/death

Kaufman, 2004
Mechanism of Action - Direct

2. During the thaw:
Extracellular ice crystallization

- Freeze, thaw, freeze cycle
- Repeated, rapid osmotic shifts of fluid into and out of the cell weakens the cell membrane causing membrane rupture and cell death
Mechanism of Action – Indirect/Delayed

3. Delayed Cell Destruction: Vascular stasis

- Endothelial damage leads to platelet aggregation, vascular stasis => thrombosis and target-tissue anoxia in capillaries surrounding the tumor
- Lack of blood supply to tissue starves any remaining cells.
- Prevents regrowth

Kaufman, 2004
Summary of Killing Mechanisms

Necrosis versus Apoptosis = Stimulation versus Suppression

- **Direct Damage:**
  - intracellular ice formation
  - osmotic dehydration
- **Indirect damage:**
  - ischemia / vascular injury
  - immunologic response

**HIGH freeze rate** → immune stimulation / significant increase in tumor-specific T cells / reduction of metastases / improved survival

**LOW freeze rate** → may alter the immune response from stimulatory to suppressive

Cryoablation with IceCure

**System:**
- Optimized for comfortable treatment of various tumors
- Can be done in the physician’s office or O.R.
- System utilizes LN2 for cost effective, fast and efficient treatment with stable & low temperature

**Probe:**
- Disposable component
- Various models
- Easy probe placement

**Console:**
- Intuitive & flexible touch screen
- Simple operation
An unfrozen hypothermic zone. A transient effect.
Timeline Post-Ablation

- **Hemorrhagic and inflammatory phase:**
  - 30 minutes: Immediate post-thaw phase: cells become swelling and irreversible damage occur.
  - 8-12 hours: Apoptosis progressively increases.
  - 48 hours: Coagulation necrosis, characterized by hemorrhage, edema, and inflammation.

- **Replacement phase:**
  - 1 week: Infiltrates of inflammatory cells, fibrin and collagen stranding, and capillary ingrowth sharply demarcate the periphery of the lesion. Endothelial layers remain intact, and thrombus formation is uncommon.
  - 4 weeks: Necrotic tissue is largely cleared up, new blood vessels reestablishing at the periphery.
  - 3 months: Small fibrotic scar with an intact endothelial layer and a well-demarcated boundary is formed.
Cryoablation Overview

- The cooling rate and the lowest achieved temperature are the most important factors that affect the effectiveness and efficacy of the cryoablation.

- Two ways to achieve low temperature:
  - Using expansion of high-pressure gas ("Joule-Thompson" method):
    - **Argon** can reach -120-150°C. Argon is being used by BTG (Galil Medical) and Healthronics (Endocare).
    - **Nitrogen** reaches the "near-critical-point" at -147°C. This system was developed by CryoDynamics, and is being used by Endocare.
  - Boiling liquefied gas:
    - **Nitrous Oxide**, boils at -88°C, is used by Medtronic (CryoCath) for Atrial Fibrillation.
    - **Liquid Nitrogen** ($\text{LN}_2$), boils at -196°C, is used by Sanarus and IceCure.
IceCure Superior Liquid Nitrogen (LN2) Technology for Optimum Tumor Destruction

Lower stable temperature and faster cooling rate for larger lethal zone.
IceCure Iceball Growth During Bench Testing

Prosense System: Freeze of 8 minutes
IceCure Prosense™
Ice Ball Diameter Comparison

Prosense™ versus Sanarus Visica 2™
Prosense™ versus Galil Medical
# IceCure Competitive Advantage

<table>
<thead>
<tr>
<th>Feature</th>
<th>3rd Generation IceCure ProSense™</th>
<th>2nd generation Sanarus Visica 2™</th>
<th>1st Generation Galil Medical EndoCare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor destruction method</td>
<td>Liquid nitrogen</td>
<td>Liquid nitrogen</td>
<td>Argon gas</td>
</tr>
<tr>
<td>Office setting</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Procedure time</td>
<td>5-40 minutes</td>
<td>10-30 mins</td>
<td>30-60 mins</td>
</tr>
<tr>
<td>Cooling rate</td>
<td>Fast</td>
<td>Medium</td>
<td>Slow</td>
</tr>
<tr>
<td>Pressure</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Single operator</td>
<td>✓</td>
<td>2 operators</td>
<td>2 operators</td>
</tr>
<tr>
<td>Compact disposable</td>
<td>✓</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Intuitive, flexible user interface</td>
<td>✓</td>
<td>Limited</td>
<td>Limited</td>
</tr>
<tr>
<td>Customizable procedure</td>
<td>✓</td>
<td>Limited</td>
<td>Limited</td>
</tr>
<tr>
<td>Probe positioning</td>
<td>Focused</td>
<td>Focused</td>
<td>Penetrates beyond the tumor</td>
</tr>
<tr>
<td>Procedure release</td>
<td>Heated Nitrogen</td>
<td>Electricity in needle</td>
<td>Electricity in needle</td>
</tr>
<tr>
<td>Temperature</td>
<td>Constantly low (-160°C)</td>
<td>Not constant</td>
<td>Constantly medium (-120°C)</td>
</tr>
<tr>
<td>Cost of procedure</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>
# IceCure is Superior to Thermal Ablation Therapies (RF and Microwave)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Cryoablation IceCure ProSense™</th>
<th>Thermal Ablation (RF &amp; MW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Minimal or no pain</td>
<td>Very painful</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>Local</td>
<td>High amount to general</td>
</tr>
<tr>
<td>Visualization</td>
<td>Ultrasound &amp; CT</td>
<td>MRI only</td>
</tr>
<tr>
<td>Accuracy</td>
<td>Very high</td>
<td>Low</td>
</tr>
<tr>
<td>Immune response</td>
<td>Positive effect</td>
<td>None</td>
</tr>
<tr>
<td>Procedure time</td>
<td>5-40 minutes</td>
<td>30 – 60 minutes</td>
</tr>
<tr>
<td>Equipment size</td>
<td>Floor top console</td>
<td>Tabletop</td>
</tr>
</tbody>
</table>

---

Institute of Diagnostic and Interventional Radiology, Goethe University, Frankfurt/Main
IceCure Indications for Use – in Europe

- **Urology:**
  - The system may be used to ablate prostatic tissue.
  - The system may be used to ablate kidney tissue including renal cell carcinoma.
  - The system may be used for the ablation of prostate tissue in cases of prostate cancer and benign prostatic hyperplasia.

- **Oncology:**
  - The system may be used for ablation of cancerous or malignant tissue.
  - The system may be used for ablation of benign and malignant breast tumors.
  - The system may be used for ablation of benign and malignant lung tumors.
  - The system may be used for ablation of benign and malignant bone tumors.
  - The system may be used for ablation of benign and malignant liver tumors.
  - The system may be used for ablation of benign tumors.
  - The system may be used for palliative intervention.
IceCure Breast Application

12 month follow up

Institute of Diagnostic and Interventional Radiology, Goethe University, Frankfurt/Main
IceCure Indications for Use – in Europe

- **Dermatology:**
  - The system may be used for the ablation or freezing of skin cancers and other cutaneous disorders.

- **Gynecology:**
  - The system may be used for the ablation of malignant neoplasia or benign dysplasia of the female genitalia.

- **General surgery:**
  - The system may be used for the ablation of leukoplakia of mouth, angiomas, sebaceous hyperplasia, basal cell tumors of the eyelid or canthus area, ulcerated basal cell tumors, dermatofibromas, small hemangiomas, mucocele cysts, multiple warts, plantar warts, hemorrhoids, anal fissures, perianal condylomata, pilonidal cysts actinic and seborrheic keratoses, cavernous hemangiomas, recurrent cancerous lesions. The system may be used for the destruction of warts or lesions. The system may be used for the palliation of tumors of the oral cavity, rectum, and skin. The system may be used for ablation of breast fibroadenomas and breast tumors.
IceCure Indications for Use – in Europe

**Thoracic surgery:**
- The system may be used for the ablation of arrhythmic cardiac tissue.
- The system may be used for the ablation of cancerous lesions, including lung tissue.

**Proctology:**
- The system may be used for the ablation of benign or malignant growths of the anus and rectum.
- The system may be used for the ablation of hemorrhoids.
IceCure Indications for Use – in the U.S.A.

ProSense™ cryoablation system is indicated for use as a cryosurgical tool in the fields of general surgery, dermatology, thoracic surgery, gynecology, oncology, proctology, and urology as detailed below. The ProSense™ cryoablation system may be used with an ultrasound device to provide real-time visualization of the cryosurgical procedure.

Urology:
- The system may be used to ablate prostatic tissue.
- The system may be used for the ablation of prostate tissue in cases of prostate cancer and benign prostatic hyperplasia.

Oncology:
- The system may be used for ablation of cancerous or malignant tissue.
- The system may be used for ablation of benign tumors.
- The system may be used for palliative intervention.

Dermatology:
The system may be used for the ablation or freezing of skin cancers and other cutaneous disorders.
IceCure Indications for Use – in the U.S.A.

Gynecology:
The system may be used for the ablation of malignant neoplasia or benign dysplasia of the female genitalia.

General surgery:
• The system may be used for the ablation of leukoplakia of mouth, angiomas, sebaceous hyperplasia, basal cell tumors of the eyelid or canthus area, ulcerated basal cell tumors, dermatofibromas, small hemangiomas, mucocele cysts, multiple warts, plantar warts, hemorrhoids, anal fissures, perianal condylomata, pilonidal cysts, actinic and seborrheic keratoses, cavernous hemangiomas, recurrent cancerous lesions.
• The system may be used for the destruction of warts or lesions.
• The system may be used for the palliation of tumors of the oral cavity, rectum, and skin.

The system may be used for ablation of breast fibroadenomas.
IceCure Indications for Use – in the U.S.A.

Thoracic surgery:
- The system may be used for the ablation of arrhythmic cardiac tissue.
- The system may be used for the ablation of cancerous lesions.

Proctology:
- The system may be used for the ablation of benign or malignant growths of the anus and rectum.
- The system may be used for the ablation of hemorrhoids.
- The ProSense™ cryoablation system is indicated for patients whom the surgeon has designated as eligible for cryotherapy.
Cryotherapy

Thomas J. Vogl, B. Panahi

ID IR: Institute of Diagnostic and Interventional Radiology
Goethe University Frankfurt, Germany