Cryothermal energy for surgical ablation

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Disclosures

• Medtronic Inc. : Speaker
• LivaNova : Speaker and Proctor
• Atricure Inc. : Consultant
• NidoSurgical : Advisory Board
• LAA Occlusion LLC. : Co-Owner
6: Which surgical ablation devices are associated with reliable transmural lesions?

Recommendation #9:

- The best evidence exists for the use of bipolar radiofrequency clamps (off and on Pump) and cryoablation devices (on Pump), which have become an integral part of many procedures including pulmonary vein isolation and the Cox maze IV procedure.

- We do not recommend the use of unipolar or unidirectional radiofrequency ablation devices outside of clinical trials, as its efficacy is questionable.
Cryolesions, the mechanism of tissue damage

The molecular basis of cryosurgery

JOHN G. BAUST and ANDREW A. GAGE*

2005 BJU INTERNATIONAL | 95, 1187–119
Cryolesions, the mechanism of tissue damage

Mechanism of Injury:

• The direct injury to cells caused by ice crystal formation.

• The microcirculatory failure which occurs in the thawing period (Necrosis)

• Apoptosis
Cryolesions, the mechanism of tissue damage

Temperature-dependent activation of differential apoptotic pathways during cryoablation in a human prostate cancer model

A T Robilotto, J M Baust, R G Van Buskirk, A A Gage and J G Baust
Cryolesions, the mechanism of tissue damage

- Exposure to $<-30^\circ C$ significant early apoptotic process:
  - Within 30 min of thawing, peaking at 90 min (~40%), and by 6 h, only necrosis was observed.

- In samples only reaching temperatures $>-30^\circ C$, apoptosis was delayed until 6–24 h post thaw.
  - The levels of apoptosis at 6 h post thaw:
    - $\sim 10\% (-15^\circ C)$
    - $\sim 25\% (-30^\circ C)$
Apoptosis

- Early-onset apoptosis progressed through a membrane-mediated mechanism,
- Delayed apoptosis progressed through a mitochondrial path.
Apoptosis

• The more severe cryogenic stress activated the extrinsic, membrane-regulated pathway, whereas less severe freezing activated the intrinsic, mitochondrial-mediated path.

• The rapid induction and progression of apoptosis at ultra-low temperatures provides an explanation as to why such results have not previously been identified following freezing.
Apoptosis

- The understanding of the events and signaling pathways involved in triggering apoptosis following freezing may provide a path for selective induction of the rapid-onset and delayed programmed cell death pathways in an effort to improve the overall cryoablation efficacy.
Cell Survival Profile of Human Cardiomyocytes in Response to Freezing.

HCM Samples were frozen to various temperatures and held for 30 or 60 seconds. Metabolic activity was assessed at 1 and 2 days post-treatment. The data illustrate that temperatures of -25°C or lower were necessary to achieve complete cell destruction. Thermal exposures between -15°C and -18°C resulted in a precipitous reduction in cell survival from 60% to 20% likely due to increased intracellular ice formation. Comparison of hold time at a given temperature revealed no significant differences.
Principles of Cryoablation

• Direct probe tissue interphase
  – No blood
  – No folds

• Duration of freezing?
  – 120 seconds
  – Longer duration for thicker temperature
Should we approach devices differently?
Should we approach devices differently?

**Atricure Cryo2 vs. Medtronic CryoFlex, Rate of Cooling (6mm Tissue)**

- **Atricure Cryo2 Avg Rate of Cooling °C/Sec**
- **Medtronic CryoFlex Avg Rate of Cooling °C/Sec**

<table>
<thead>
<tr>
<th>Time Segments, 2 min Ablation</th>
<th>Rate of Cooling °C per sec.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - :15</td>
<td>0.71</td>
</tr>
<tr>
<td>:15 - :30</td>
<td>0.66</td>
</tr>
<tr>
<td>:30 - :45</td>
<td>0.55</td>
</tr>
<tr>
<td>:45 - :60</td>
<td>0.38</td>
</tr>
<tr>
<td>:60 - :75</td>
<td>1.07</td>
</tr>
<tr>
<td>:75 - :90</td>
<td>0.88</td>
</tr>
<tr>
<td>:90 - 1:05</td>
<td>0.74</td>
</tr>
<tr>
<td>1:05 - 1:30</td>
<td>0.20</td>
</tr>
<tr>
<td>1:30 - 1:45</td>
<td>0.81</td>
</tr>
<tr>
<td>1:45 - 2:0</td>
<td>0.44</td>
</tr>
</tbody>
</table>
Should we approach devices differently?

**Atricure Cryo2 vs. Medtronic CryoFlex, Rate of Cooling (8mm Tissue)**

- Atricure Cryo2 Avg Rate of Cooling °C/Sec
- Medtronic CryoFlex Avg Rate of Cooling °C/Sec

![Graph showing rate of cooling comparison between Atricure Cryo2 and Medtronic CryoFlex](chart.png)
Pulse Cryoablation

• In thicker tissue (over 4mm)
  – Longer duration (>2 min) is required
  – 1+1+1 may be > 3 minutes

• Following the freeze
  – Active defrost
  – Stay for 20 more second (Argon)
  – Tissue temperature – rewarming equal
Efficacy

- Cryoablation may be a more consistent energy source
  - Thicker tissue
  - More severe remodeling
  - There is some evidence that
    
    Cryo Only > Combined Bipolar RF and Cryo
## Variables Associated with Long Term Failure

<table>
<thead>
<tr>
<th>Type of AF</th>
<th>LA Size</th>
<th>Duration</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>X</strong></td>
<td><strong>X</strong></td>
<td></td>
<td><strong>X</strong></td>
</tr>
</tbody>
</table>
New Paradigm for Long Term Failure

- Ablation Technology
- Duration
- Surgeon
Thank You