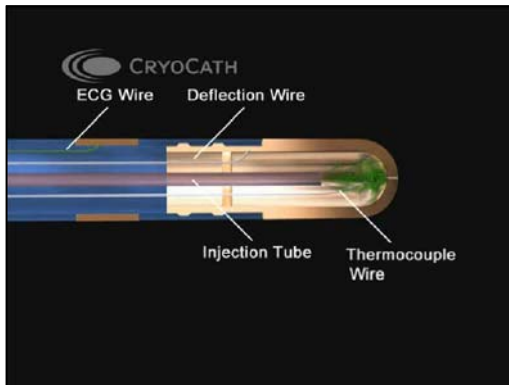


Notes for Videos located in the Electrophysiology Knowledge Center

<http://www.cryocath.com/en/1.medical.professionals/1.1.6.3.presentation.materials.asp>

How the Technology Works



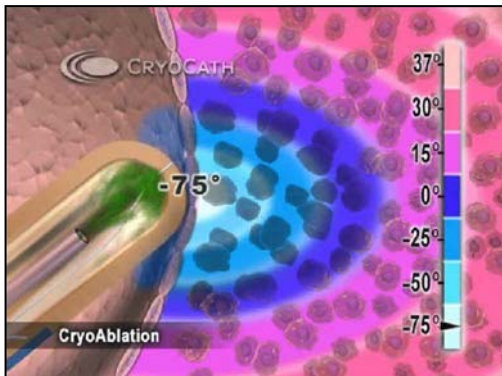
- Pressurized liquid nitrous oxide is delivered to the tip of catheter from the cryoconsole through an ultra fine, robust injection tube
- Before it is released into the tip expansion chamber, it is further pressurized when it encounters a restriction tube at the distal end of the injection tube
- The restriction tube is designed to maximize the temperature drop of the refrigerant prior to entering the expansion chamber
- The Joule Thompson effect (as refrigerants are subjected to a decrease in pressure, they cool down)
- As the refrigerant enters the tip expansion chamber (maintained under vacuum) and comes in contact with the tip surface, a liquid-to-gas phase change occurs when the cold liquid refrigerant evaporates as it absorbs heat from the tip that is in contact with the tissue
- Phase change (fluid changes phase, at a constant temperature and pressure as it exchanges heat)
- The warmed vapor is returned to the console through a lumen maintained under vacuum
- Tip-embedded thermocouple in a copper tip which is very conductive so represents tip tissue temperature

Fundamentals of CryoTherapy



- Observe two cells (one: centered, two: bottom right-hand corner), at top: temperature dropping, time increasing
- As the temperature cools the cell on the bottom right freezes at approximately -6°C/17 seconds
- The center cell freezes and ruptures at approximately -20°C/40 seconds

A Thermal Gradient



- Where the cryocatheter is applied, cooling creates a temperature gradient across the CryoTherapy zone
- At the tip/tissue interface of the catheter, the cryotherapy temperature can range between -30°C and -75°C, depending on type of cryo intervention (CryoMapping/CryoAblation)
- Tip-embedded thermocouple in a copper tip, which is very conductive, so represents tip tissue temperature
- As you move away from the tip across the CryoTherapy zone, the temperature ranges from the subzero cryogenic temperature to body temperature
- The zone is “dynamic” because it expands (during freezing) and shrinks (upon rewarming) with time

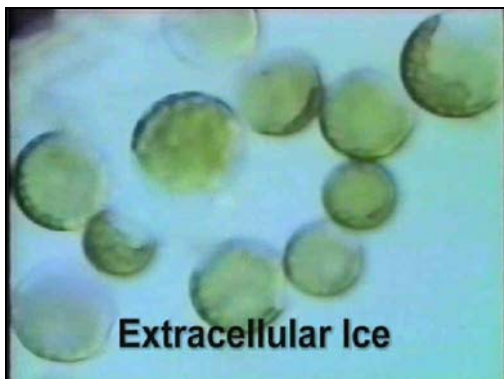
- The zone is also thermally ‘dynamic’ over time – cells remaining above zero sustain a transient electrical effect, cells reaching and remaining at subzero temperatures are ablated
- In living tissue the vascularity is always providing a heat source and will cause local variations
- In living tissue, you will never have all of the tissue at a homogeneous (same) temperature because of the vascular nature of the tissue

Hypothermia Chills Cardiac Cells



- This movie shows a single beating cell that is cooled and then warmed back up again
- It illustrates the hypothermic effects of CryoMapping
- The temperature is shown numerically and graphically at left and a sample ECG signal is shown
- As the temperature cools from body temperature down to 23°C observe how the beating cell slows down as it is cooled,
- Then the cell is re-warmed and returns to its original rate
- This is a good illustration to show that the cells in the range of 37°C to 5°C may demonstrate a transient hypothermic effect and upon re-warming often return to normal function

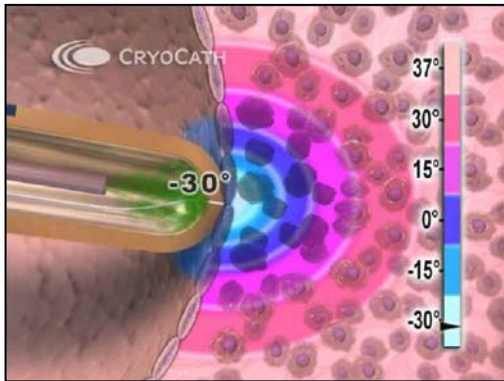
Ice Formation Kills Cardiac Cells



- Extracellular ice occurs when the “fingers” enter the movie from the top left to the bottom right

- Intracellular ice occurs when the cells start to turn gray
- The movie also illustrates the variability of effect that is observed as the cells are subjected to ice formation at different times

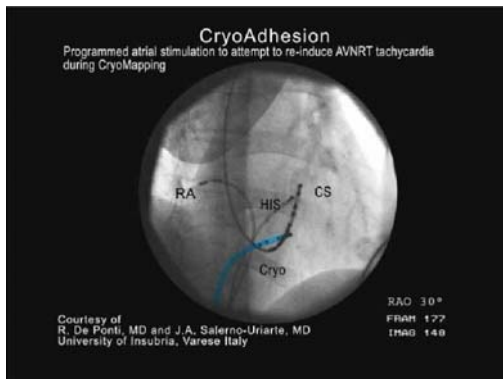
CryoMapping



Animation Notes (for illustration purposes only):

- This animation illustrates how the temperature isotherms radiate from the point of contact with the catheter during the CryoMapping procedure
- Notice the range of temperatures that the cells experience depending on their proximity to the cryocatheter
- Notice that as the cells are cooled below body temperature their activity slows down
- On the termination of the CryoMapping procedure, the frozen tissue zone retreats
- The activity of the cells that were subjected to non-subzero temperatures returns to normal and the cells that were subjected to the subzero temperatures may stop (depends on time and exposed temperature)
- In the animation, some of the endothelial cells and some of the cells very close to the probe/subzero isotherm are killed; however, the extracellular matrix is left intact
- Note the thermal gradients through the CryoMapping Zone: not all cells are subjected to -30°C tip/tissue temperature
- The CryoCath CryoMapping procedure involves applying temperatures of -30°C at the **tip** of the CryoCatheter for up to 60 seconds
- -30°C is the temperature recorded at the tip only
- Up to 60 seconds is allowed for cooling the tip of the catheter to achieve -25°C
- Once the CryoCatheter has adhered to the tissue (when noise appears on electrograms), pacing to test for the desired effect (for up to 60 seconds) can be performed (described on subsequent slides)

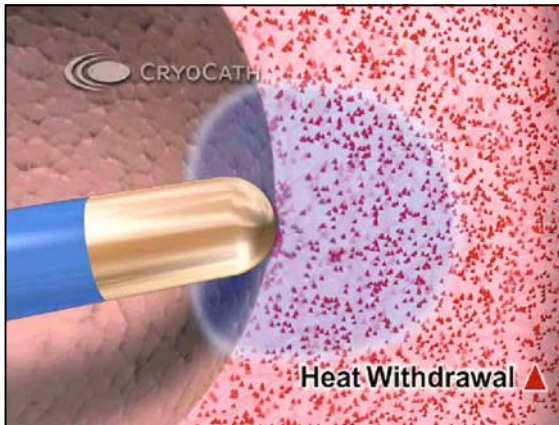
CryoAdhesion



There are 4 sequences of movies in this movie (titles are at the top of each sequence):

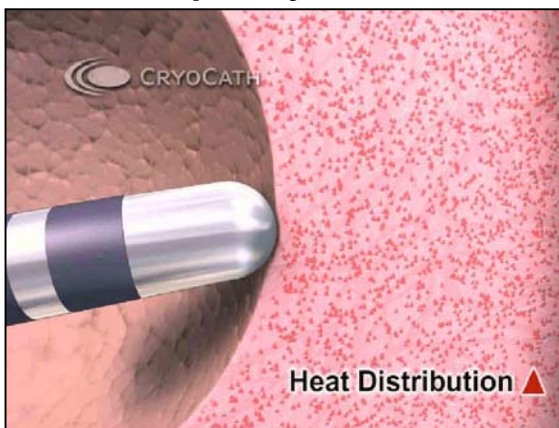
1. Programmed atrial stimulation to attempt to re-induce AVNRT tachycardia during CryoMapping
 - ▶ Demonstrates how the catheter stays adhered during a cryo application, even during pacing
2. AVNRT arrhythmia termination during Slow Pathway CryoAblation
 - ▶ Demonstrates how the catheter stays adhered during a cryo application, even during abrupt rhythm changes
3. Release of Freezor® catheter after Slow Pathway CryoAblation
 - ▶ Demonstrates how the catheter releases quickly after a cryo application
4. (Best sequence) Arrhythmia termination during CryoAblation of Anteroseptal Accessory Pathway
 - ▶ Demonstrates how the catheter stays adhered during a cryo application very close to the HIS
 - ▶ Note all of the movement on the HIS catheter

CryoTherapy Removes Heat



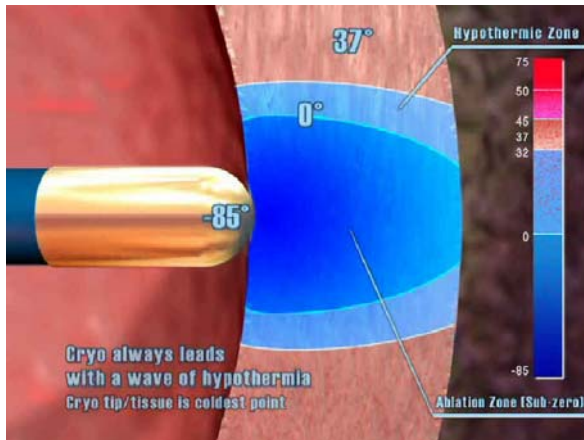
- The small red triangles represent heat molecules at body temperature
- As the cooling/freezing process is started heat is removed from the tissue (red triangles disappear)

Radio Frequency Generates Heat



- The small red triangles represent heat molecules at body temperature
- As heat is added (larger red triangles) heat is added to the tissue and the tissue is “cooked”

The Biophysics of CryoTherapy

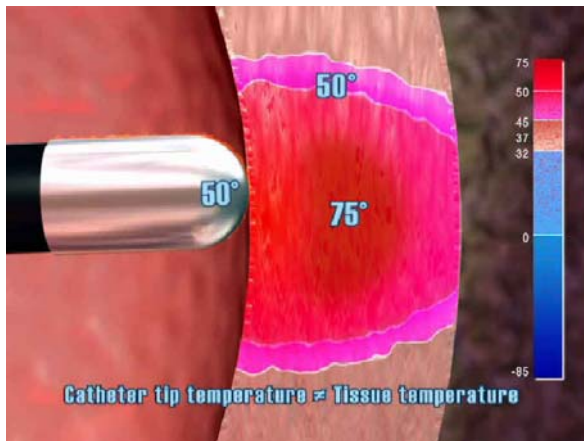


Total play time 0:50

- CryoAdhesion provides catheter stability
- CryoTherapy removes heat from the tissue at the point of tip tissue contact
- Because heat is removed/absorbed by the catheter, the corresponding coldest spot when ablating with cryo is directly at the tip^{1,2}
- Cryo always leads with a wave of hypothermia as the tissue is subjected to a thermal from Body Temperature, through transient hypothermic temperatures, through subzero ablative temperatures. Therefore as cooling is initiated the temperature in the tissue cools before being frozen
- Cells that are subjected to hypothermic temperatures in the range of 0°C may experience transient loss of electrical function. Cells typically die when temperatures are colder than 0°C^{1,2}
- Because heat is removed, as soon as the injection stops, the tissue starts to warm up because it is vascularized

1. John G. Baust, Ph. D. Cryotherapeutic Intervention in Cardiovascular Disease. White paper, 2002.
2. John G. Baust, Ph.D., A.A Gage. The molecular basis of cryosurgery, BJU International, 95 , 11 8 7 – 11 91. June 2005.

The Biophysics of Radio Frequency Ablation



Total play time 0:50

- The RF catheter does not adhere therefore less control of lesion placement
- RF generates heat in the tissue through resistive and conductive heating
- Because the tissue offers the highest resistance, it is the tissue that is heated by RF current flow
- The hottest spot may be deeper into the tissue^{1,2,3}
- When tissue temperatures exceed 50°C, cardiac tissue is permanently injured²
- When the energy is terminated the tissue may stay warm for seconds²

1. G. Keith Bruce, MD; T. Jared Bunch, MD; Mark A. Milton, MD; Alvaro Sarabanda, MD, PhD; Susan B. Johnson, BS; Douglas L. Packer, MD. Discrepancies Between Catheter Tip and Tissue Temperature in Cooled-Tip Ablation Relevance to Guiding Left Atrial Ablation. *Circulation*. 2005;112:954-960.
2. T. Jared Bunch, MD; G. Keith Bruce, MD; Susan B. Johnson, BS; Alvaro Sarabanda, MD, PhD; Mark A. Milton, MD; Douglas L. Packer, MD. Analysis of Catheter-Tip (8-mm) and Actual Tissue Temperatures Achieved During Radiofrequency Ablation at the Orifice of the Pulmonary Vein. *Circulation*. 2004;110:2988-2995.
3. Mark A. Wood, MD, Katherine M. Shaffer, Amy L. Ellenbogen, Evan D. Ownby, BA. Microbubbles during radiofrequency catheter ablation: Composition and formation. *Heart Rhythm* 2005;2:397– 403.