Medical Ice Slurry Coolants for Inducing Targeted-Organ/Tissue Protective Cooling

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Introduction

Researchers at Argonne National Laboratory and the University of Chicago's (UC) Emergency Resuscitation Center (ERC) and the Urologic Surgery Section are developing a technology that could help in saving stroke and cardiac arrest victims and in performing various surgical procedures. The team has developed an ice slurry coolant — a saline-ice mixture that may be injected into a patient's body for rapid cooling of vital organs and tissues. One version of ice slurry is an equal mix of ultra-small (equivalent to the diameter of a human hair) ice particles and a salt water liquid carrier.

Recent research by others on inducing protective cooling has focused on single-phase coolants, such as chilled saline, and on external cold blankets.

Saline cooling is not capable of inducing the rapid targeted cooling that is possible with a slurry, which has the additional major benefit of absorbing more than four times the heat compared with chilled saline because of the ice particle melting (change of phase). Thus, a much smaller quantity of slurry is required to cool to the same temperature as a single-phase coolant, which relies only on sensible heat absorption. This slurry characteristic greatly reduces the chances of upsetting the patient's biochemistry resulting from coolant overload.

External cooling blankets, caps, and jackets for inducing protective hypothermia work very slowly and cool the entire body, often causing adverse effects such as uncontrolled shivering, and they may also fail to protect a specific organ from localized tissue damage.

The Argonne-UC slurry-induced protective cooling overcomes these shortcomings. It is very easy to administer, rapidly cools, and suppresses the effects of tissue damage, trauma, and infection and limits injury or organ cell death by slowing metabolism, which greatly reduces the needs for oxygen.

Our research to date has resulted in nine patents being granted or pending covering slurry production equipment (involving several methods for making slurry), various injector tips, and various medical applications. Argonne has also recently demonstrated the ability to make an ice slurry from a commercial blood substitute, which will provide oxygen and nutrients as well as cooling for protecting organs.

Background

Originally, under funding from the US Department of Energy (DOE) in the late 1980s and early 1990s, Argonne developed ice slurry technology for industrial and municipal applications, particularly to replace chilled-water cooling systems in building complexes.

In 2002, Argonne and UC received a joint five-year Bioengineering Research Partnership Grant from the National Institutes of Health (NIH) to develop ice slurry cooling for medical applications. Argonne performed the slurry development research, and UC conducted medical exploratory slurry tests with Argonne on animals simulating conditions such as emergency out-of-hospital cardiac arrest treatment and in-hospital kidney laparoscopic procedures. Argonne and UC over the last year and a half have worked on further broadening the slurry cooling research to develop other innovative medical procedures employing protective slurry cooling.

Technology Description

Figure 1 shows a research version of the Argonne-developed system for making an ice slurry. The produced slurry has the following attributes:

- Small ice particles (<0.1 millimeter),
- High ice concentration (>50 weight percent),
- Biologically compatible carrier liquid (saline solution plus other ingredients),
- Several times the cooling capacity of water (ice = 80 cal/gºC versus water = 1 cal/gºC),
- Excellent fluidity and storability obtained by altering ice particle size, shape, and surface roughness by using patented methods, and
- Slurry that can be pumped nearly as easily as water through very small, properly designed delivery devices.

Figure 1: Argonne-Developed Equipment for Making and Delivering Medical Slurry

The slurry production equipment in Figure 1:

- Produces slurry on-demand (< 2 min processing time),
- Is portable,
- Uses disposable sterile ingredient modules,
- Has a controllable dose and delivery rate,
- Is capable of continuous or intermittent delivery,
- Can maintain protective cooling for > 2 hours, and
- Includes special delivery injectors developed for various medical uses.

Application in Advanced Laparoscopic Procedures

Medical procedures are becoming less invasive through the development of laparoscopic procedures assisted by robotic manipulations. Critical organs and various tissue masses must be protected through the course of these manipulations, which often cause damage that results in loss of organ function and life-threatening infection. Those complications could be reduced if targeted cooling could be administered quickly and effectively.

We have conduced exploratory research with NIH funding on use of slurry-induced protective cooling under minimally invasive laparoscopic surgery to protect kidneys during “blood vessel clamp-off”. As indicated in Figure 2 a swine kidney was successfully cooled by using a specially designed slurry delivery tip compatible with standard laparoscopic ports.

We have also developed a three-dimensional computer model using the ABAQUS code that can be used for predictions of kidney ice slurry cooling during laparoscopic surgery. Figure 3 shows model calculations of kidney cooling temperature following kidney blood vessel clamp-off and application of slurry at time = 0 and for time > 20 min. when the slurry was removed and the blood vessels were unclamped compared with data from the large-animal model experiments at UC. The image on the left shows the four positions in the kidney for the model calculations of temperature.

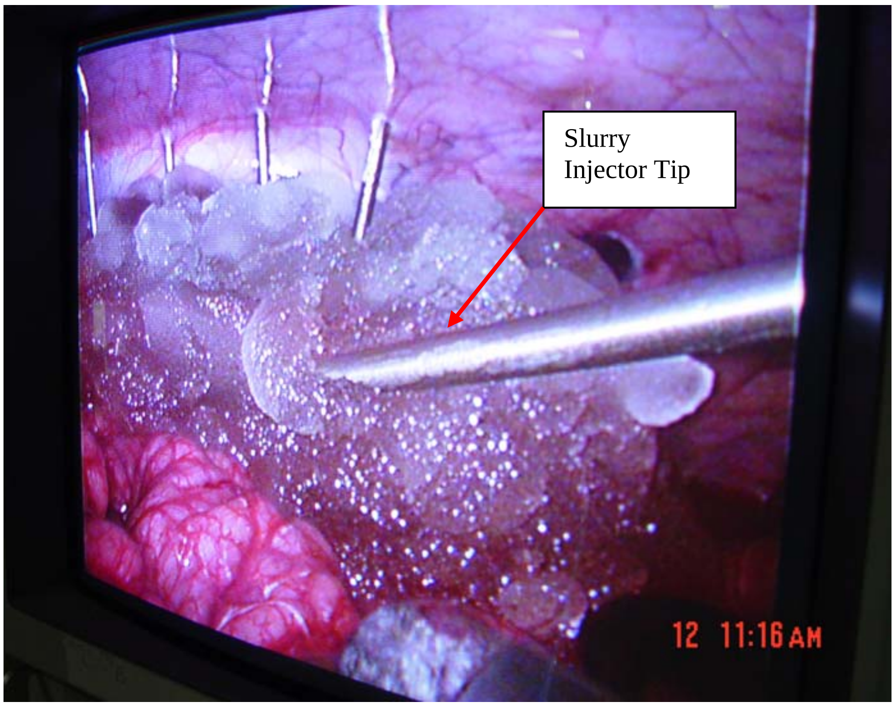
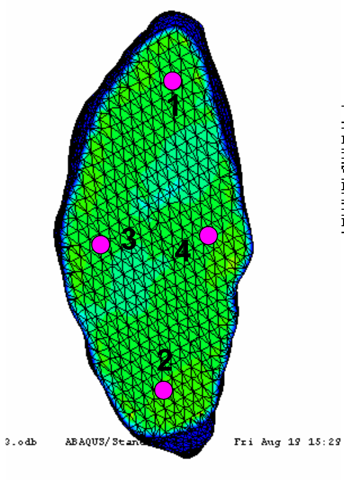
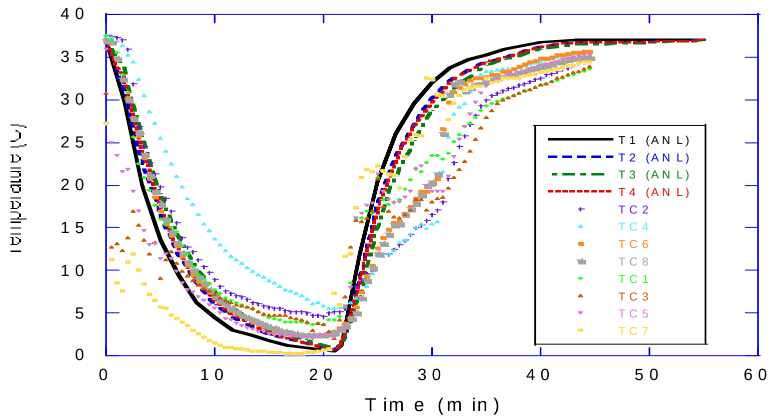


Figure 2: Endoscope View of Swine Kidney Being Covered with Ice Slurry During Laparoscopic Procedure (with Dr. Arieh Shalhav, Section Chief UC-Urologic Surgery)





Comparison between Argonne predicted kidney cooling and experimental data from laparoscopic procedure

Figure 3: Argonne 3-D Computer Model Simulation Using ABAQUS Code of Kidney Cooling for Laparoscopic Procedure Along with Experimental Data (Jimmy Chang, Argonne)

Application in Emergency Response

Another ice slurry application is cooling of organs such as the brain and heart during medical emergencies such as cardiac arrest, stroke, hemorrhagic trauma, and heat stroke, where easily administered rapid slurry cooling can be used to protect vital organs, giving doctors more time to treat the injury.

Figure 4 shows slurry being delivered into the lungs of a large animal by way of an Argonne-developed squeeze bottle and a special endotrachea tube. The test procedure followed a model for cardiac arrest testing developed at the UC and a protective cooling protocol for emergency use.

Figure 4: Argonne Slurry Delivery to Lungs of Large Swine (50 kg) Using Squeeze Bottle and Endotracheal Tube under Cardiac Arrest Conditions in which Chest Compressions Circulate Blood (with UC-ERC)

Current Research on Medical Slurry Cooling

Argonne engineers/scientists and UC medical doctors are continuing research on ice-slurry protective cooling. One of the near-term goals is to obtain Federal Drug Administration approval of the ice slurry production and delivery equipment so it can be used to conduct clinical trials. Current research includes the following tasks:

- Continue to refine controls for delivery of the ice slurry and to establish its medical efficacy for laparoscopic kidney manipulations. This study will support the near-term start of human clinical trials.

- Demonstrate the use of targeted ice slurry cooling during various cardiac/cardiovascular procedures for primary target cooling, as well as for protective cooling of secondary organs such as the kidney, brain, and intestinal tract. The proposed research will build upon Argonne's recently demonstrated ability to make ice slurry from a blood substitute.

- Determine whether a subset of heart care procedures can be performed off-bypass and with cooling protection furnished only by targeted slurry cooling.

- Determine the efficacy of using slurry cooling to prevent reperfusion damage during arterial dilatation to open a blocked blood vessel via a catheter prior to insertion of a stent. Argonne has recently demonstrated the ability to deliver highly loaded ice slurry through small-diameter catheters longer than 1 meter, as illustrated in Figure 5.

Figure 5: Slurry Delivered Through Argonne Catheter (1-mm Inside Diameter, 1-m Length); Being Developed for Surgical Applications

The preceding research involves making further improvements in the slurries and the production/delivery equipment. We are also working on developing:

- methods for intentionally adding micro-bubbles of therapeutic gases,
- slurry equipment upgrades for real-time monitoring/display of percent ice loading/inventory and feedback control safety features regarding avoiding slurry delivery over pressurization and maintaining required protective temperature,
- capability for multiple routes/streams for slurry delivery, and
- slurries that have different carrier liquids such as blood substitutes.

Development of Medical Simulation Computer Models

We are also developing technologies for real-time visualization of tissue viability and function based on computer simulations that will provide a new tool for doctors to help them in planning for and using protective cooling. This work further advances the development effort already started by Argonne for modeling the cooling of organs such as the kidney (see Figures 2 and 3). We are improving our whole organ thermal modeling by developing an improved understanding of tissue perfusion, metabolism, and vasculature blood flow under surgical or emergency conditions. We are also improving our 3-D simulation models employing computational fluid dynamics (CFD) calculations of flow in blood vessels. Figure 6 shows a 3-D computer simulation using Argonne's NEK5000 CFD code of blood flow at a vessel bifurcation. The computer simulation research also involves coupling CFD and bio-structural models that will allow simultaneous simulation of bio-fluid interactions with confining blood vessels and organ structures.

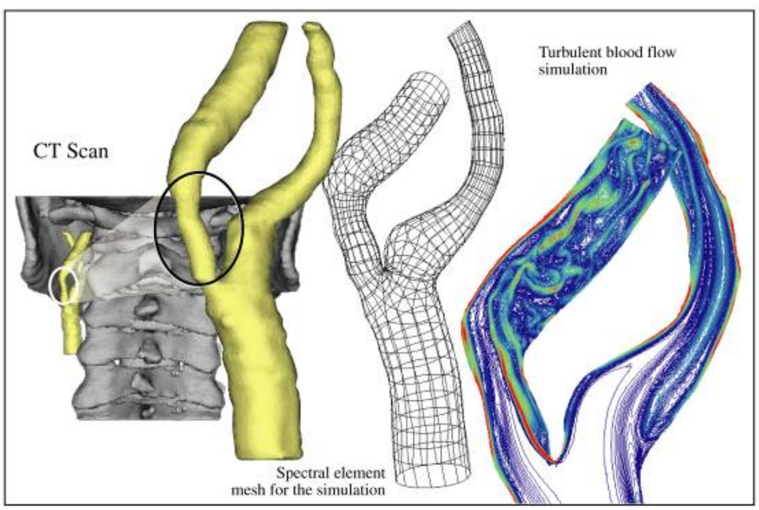


Figure 6: Computer Simulation Using NEK5000 CFD Code for Blood Flow at a Vessel Bifurcation (Paul Fischer, Argonne)

Under many medical treatments, activities performed on the target organ/tissue often illicit responses of adjacent organs or subsystems which complicate treatment. Being able to model, understand, and prevent or mitigate these secondary sometimes detrimental feed back responses will improve treatment. Figure 7 shows a schematic of an Argonne computer simulation model being developed for modeling the complex interaction of multiple organs and bio-subsystems.

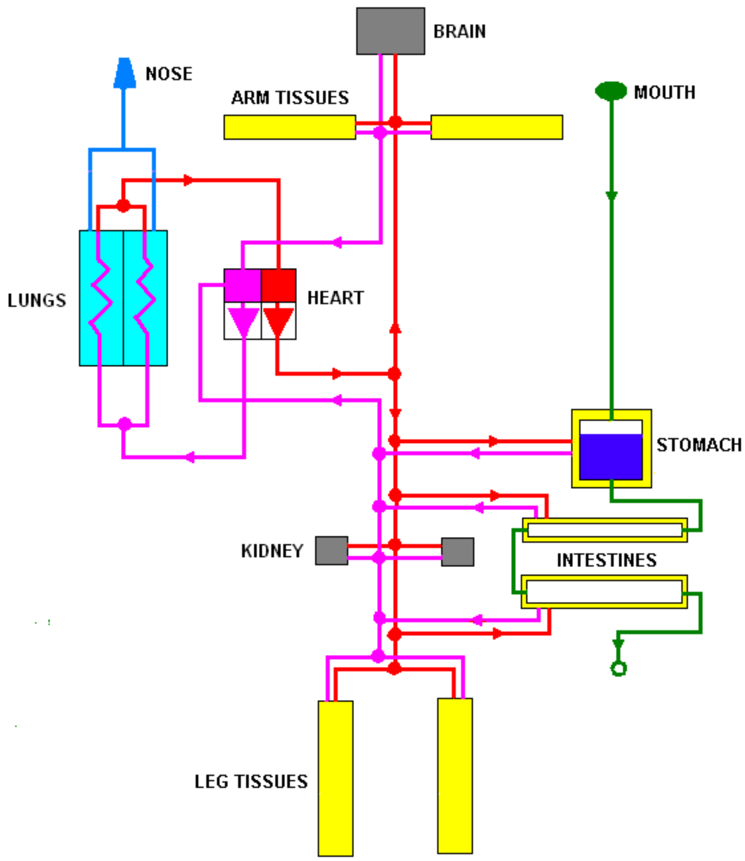


Figure 7: Argonne Computer Simulation Model under Developed for Modeling the Complex Interaction of Multiple Organs and Bio-Subsystems (Adrian Tentner, Argonne)

With continued research and success in slurry development, broadening medical applications, and human clinical trials, a technology originally developed for industrial and municipal cooling may some day find medical applications by both emergency first responders and surgeons.