Ice Slurry Medical Protective Organ Cooling:
Buying Surgeons and Emergency Responders More Time

Prepared
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Surgical procedures are pushing the limits of technical excision and becoming less invasive through the development and use of laparoscopic procedures assisted by surgeon/machine robotic manipulations. There is an unmet need to protect critical organs and various tissue masses during the course of surgical manipulations. Multiple tissue sites and organ systems that require complex operative manipulations to cure disease are often exposed to ischemic, traumatic, and xenobiotic insults that can result in loss of function or life-threatening conditions. Ice slurry production and delivery equipment developed by Argonne National Laboratory (ANL) is being demonstrated in collaboration with the University of Chicago (UC) medical school as means for protectively cooling targeted vital organs for multiple surgical applications. This collaborative research is being conducted under a UC-ANL Bioengineering Institute for Advanced Surgery and Endoscopy (BIASE).

Ice slurry protective cooling is based on the premise that the ability of organs, tissue, and neurology to survive ischemia, reperfusion damage, and surgical insults is improved by cooling them 4-15°C, (depending on organ), below the normal temperature of 37°C rapidly in 5-15 minutes. Cooling slows metabolism and reduces the need for oxygen which slows cell death and provides more time for medical treatment. Presently cardiac and cardiovascular surgery often use bypass heat exchangers to induce protective cooling which is slow to implement and quite invasive (sometimes causing "bypass brain"). External cooling with ice packs, blankets, caps and jackets is also used for inducing protective or therapeutic hypothermia. However these methods cool very slowly (< 0.03°C/min) and similar to bypass methods cool the entire body often causing adverse secondary effects such as uncontrolled shivering and arrhythmias. They also frequently fail to protect a specific organ because of failure to achieve the temperature believed to be protective.

Chilled single-phase saline is starting to be used for medical cooling. However it is not capable of inducing the rapid targeted cooling that is possible with slurry. Slurry has the additional benefit of being able to absorb more than four times the heat than 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 characteristic of slurry greatly reduces the chances of upsetting bio-system chemistry resulting from coolant overload. Slurry also cools the target tissue faster than saline because the slurry remains at ~0°C until all the ice is melted; In contrast saline immediately from its entry into the delivery catheter starts increasing in temperature. Thus at the target, the temperature gradient between tissue and coolant is much larger for slurry than for saline and the tissue cools much faster. Additionally the very small ice particles flowing over the target tissue increase the convective heat transfer coefficient between coolant and tissue to higher levels than with single phase chilled saline. Figure 1 below shows how with proper production procedures ice slurry can be made which flows nearly as easy as water through very small medical deliver tubes.

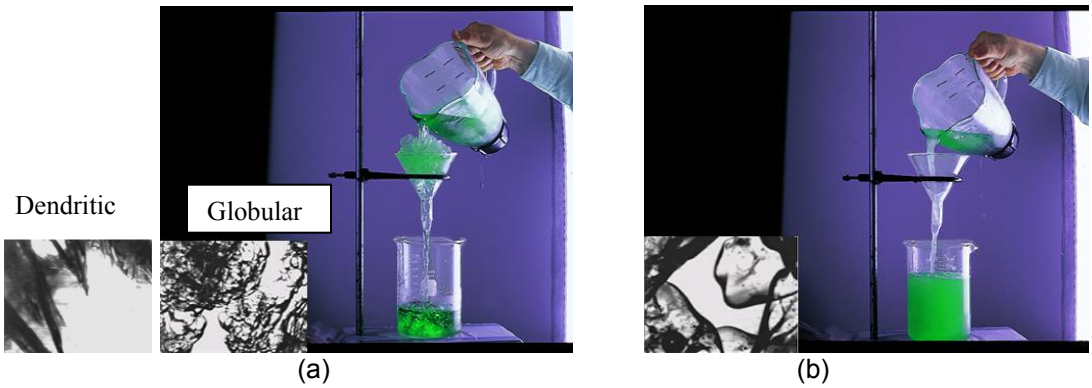

Figure 1. Argonne methods for chemical and thermal smoothing of ice particles in a slurry yields dramatic improvements in ice slurry behavior: (a) no smoothing; bad ice slurry; (b) with smoothing; good ice slurry which is deliverable by special medical injectors

An automated, computer-controlled, ice slurry production and delivery system shown in Figure 2 has been developed by Argonne for use in the operating room. The slurry system also monitors delivered dosage of coolant and tracks ice slurry loading and patient organ temperature to facilitate system control. This ice slurry production system is part of an application to obtain FDA approval for conducting human clinical trials involving ice slurry protective cooling for laparoscopic kidney surgery. The automated system has been used to make and deliver slurry through small cardiac catheters of the size shown in Figure 9. The system produces highly loaded ice slurry which can be reliably delivered through specially engineered injector tips for multiple surgical applications.

Figure 2. Argonne automated-portable ice slurry production and delivery system for OR patient cooling

The following ice slurry protective cooling surgery applications are under development with the UC using the above ice slurry system.

a) Minimally invasive laparoscopic kidney surgery cooling; (Arieh Shalhav-UC, Ken Kasza, Sergey Shikanov-UC, Yue Wu).

During kidney surgery the renal artery and vein are clamped prior to performing a partial nephrectomy to avoid blood loss, Fig. 3. To reduce ischemia damage from clamping in conventional open cavity kidney surgery, the surgeon uses a sterilized glove to hand pack ice chunks (slush) around the organ. Cooling allows the surgeon to reduce ischemic damage and extend surgery time significantly beyond thirty minutes. In recent years, minimally invasive laparoscopic procedures using from 3-5 very small access ports into the body (Fig. 4), are rapidly being developed to replace open-cavity surgery. Even though laparoscopic kidney surgery reduces scarring and post-surgical recovery time, the procedure is currently hindered by the inability to cool the organ due to lack of access for hand packing with ice. Argonne and UC are developing ice slurry cooling technology for use in laparoscopic surgeries. Slurry cooling involves using an engineered delivery tube inserted into a laparoscopic port for delivering, coating the outer surface of the kidney with slurry, and cooling the organ to 15°C for protection (see Figures 5-7).

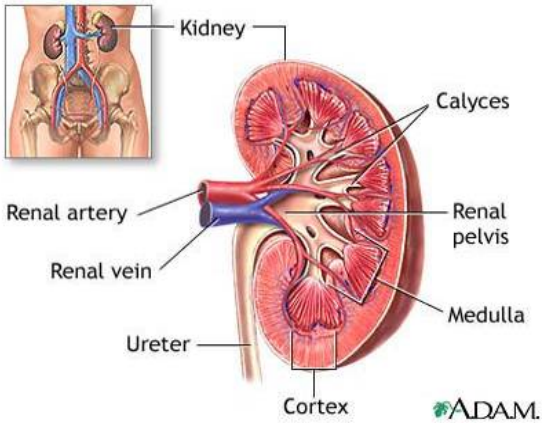

Figure 3. View of kidney

Figure 4. Laparoscopic surgery entry ports for surgical tools and ice slurry delivery tube

Figure 5. Large swine undergoing a laparoscopic partial kidney nephrectomy using ice slurry protective cooling

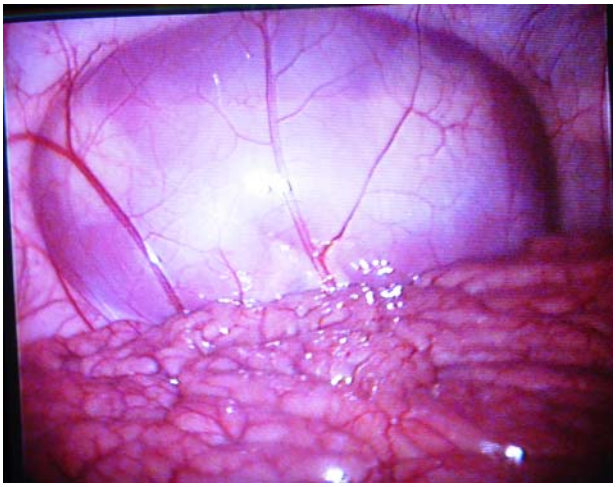

Figure 6. Kidney prior to coating with ice slurry: endoscope view

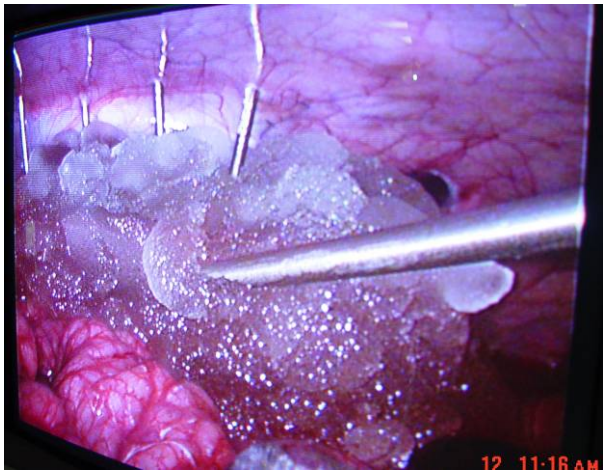

Figure 7. Kidney covered with ice slurry coolant

Kidney protection during surgery using ice slurry is the most developed application. Efforts are underway to obtain FDA approval for conducting human clinical trials.

b) Cardiac surgery cooling; (Jai Raman-UC, Neeraj Jolly-UC, Ken Kasza, Yue Wu, Adrian Tentner-ANL, Paul Fischer-ANL).

Studies under BIASE have highlighted that the cardiac surgical treatment scenario involving the use of balloon angioplasty to open a blocked artery, and which occasionally results in heart muscle reperfusion damage, can be improved by using ice slurry targeted cooling to prevent damage (see Figure 8). In the longer range heart slurry cooling will be explored for a broader range of surgical procedures which jeopardize heart tissue. BIASE animal testing of heart cooling with slurry will start in 2009.

The balloon angioplasty heart protection slurry cooling scenario shown pictorially in Figure 8 involves the following treatment protocol which is under development:

- left coronary artery is blocked; (denoted by X);
- slurry delivery catheter enters body through femoral artery and is routed to the coronary artery;
- slurry is delivered in the coronary artery upstream of the blockage for pre-cooling;
- blood flow carries slurry toward the blocked area inducing protective heart muscle cooling (37°C to 33°C);
- a balloon catheter is inserted opening the blockage
- cooling is maintained for an additional period of time after opening the blockage to mitigate damage

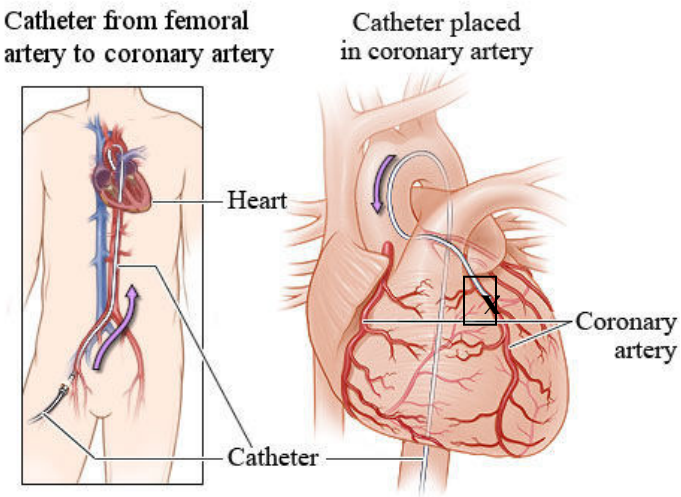

Figure 8. Catheter delivery of slurry to a blocked artery during balloon angioplasty reduces reperfusion damage

Argonne scoping calculations show that cooling and maintaining the heart myocardium at a protective temperature with ice slurry requires ~1/3 the volume of chilled saline. This gives slurry cooling a significant advantage over cooling with chilled saline during a long surgical procedure since we do not need to infuse as great a volume to maintain the desired protective temperature which reduces the chance of bio-system overload. Argonne has established the ability to reliably deliver ice slurry with out plugging through 100 cm long cardiac catheters (internal diameter < 1mm) as shown in Figure 9.

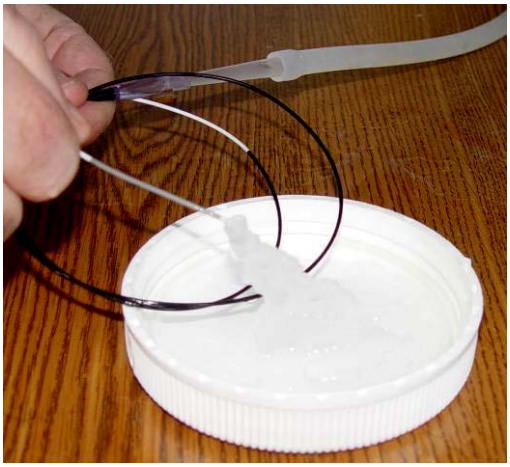

Figure 9. Argonne's highly loaded ice slurry being delivered through 100 cm long cardiac catheter

c) Spinal cord and brain neurological cooling; (Jeffrey Frank-UC, Ken Kasza, Agnieszka Ardelt-UC, Yue Wu).

Under BIASE, we are also exploring how ice slurry cooling can be used to provide spinal cord and brain neurological protection. An evaluation of the recent literature on cooling research employing cold saline, suggests that there is considerable merit in using targeted delivery of slurry for inducing neurological protection. Argonne and UC are currently developing the ability to deliver slurry to the brain or spinal cord via arterial and cerebrospinal-fluid routes using catheters.

d) Improving organ recovery viability for transplantation by cooling; (Robert Harland-UC, Ken Kasza, Yue Wu).

Under BIASE, ANL is working with the UC Director of Kidney and Pancreas Transplant Surgery to develop slurry cooling for improving recovery of donor organs to increase the quantity and improve the quality of organs obtained from donors after cardiac death (DCD) by using targeted ice slurry cooling. The reduction in warm ischemia time, is anticipated to significantly increase the number of renal and non-renal transplants performed using organs from this class of donors. Since the window for successful recovery of DCD organs is relatively narrow, even a modest decrease in the warm ischemic time through more rapid and efficient slurry cooling is anticipated to increase the number of kidney, liver and pancreas transplants performed. Slurry coolant delivery by various routes is being explored and each evaluated regarding the ability to rapidly and easily reduce ischemia damage during organ recovery from DCD.

e) Development of science-base computer simulations and patient data management surgical tools; (Ken Kasza, John Christiansen-UC, Adrian Tentner, Paul Fischer, Yue Wu).

This task involves development of improved models and science-based computer simulations of blood flow and organ/tissue cooling and integrating/managing this information along with other patient information using a visualization based surgical operating room video display tool; an example is shown in Figure 10. The improved data management and simulation tools will revolutionize how patient information is handled and used both for planning and during actual surgery.

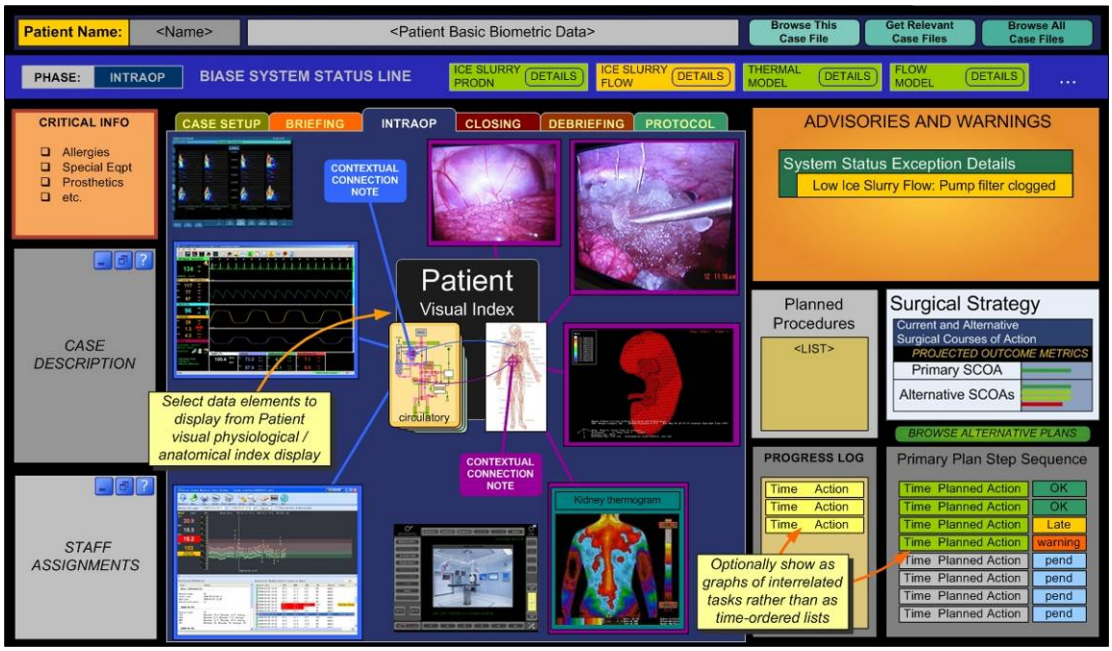

Figure 10. Future operating room medical information visual display monitor being developed (depicts kidney surgery)

The initial focus is on simulation of protective cooling; in the longer range, the focus will broaden to other surgical treatments. This research is a common foundational element of all of the ice slurry cooling surgical applications. Predictions of kidney cooling with ice slurry during laparoscopic surgery made using an Argonne developed 3-D computer model are shown in Figure 11.

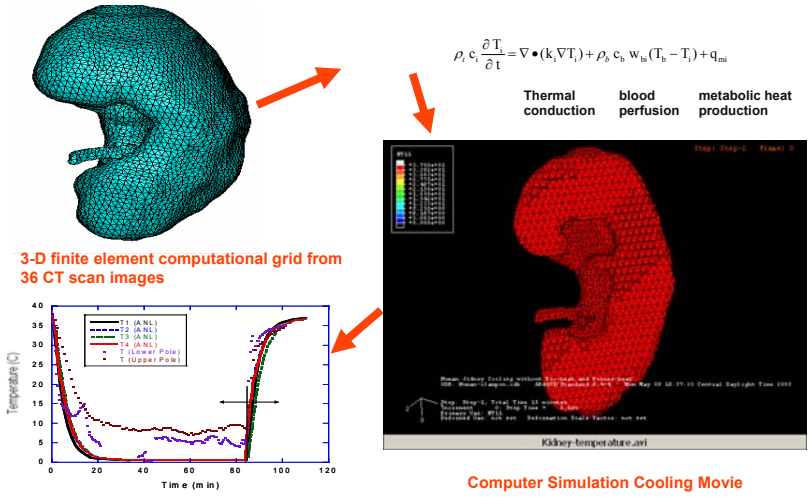

Figure 11. Argonne 3-D kidney cooling computer simulation of laparoscopic surgery kidney cooling with slurry

The development of much more complex simulation tools for predicting heart cooling (see Figures 12-13) as well as interactions between multiple organs and software for patient data management are part of our longer range research plan.

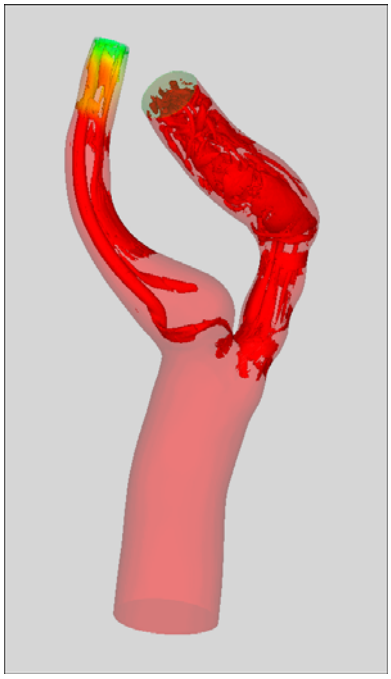

Figure 12. Argonne simulation of vascular flows

Figure 13. Argonne heart blood flow simulation