Cryopreservation Case Summary:

The Cryopreservation of Patient A 2071

By Tanya Jones, *Director of Technical Operations*

Background

When member A 2071 entered the application process in May 2004, his medical history included diabetes and colon cancer. His diabetes was controlled, but he was receiving aggressive treatment for his cancer. He was 79 years old, and he had no remaining family except a godson. His membership was approved on July 16, 2004.

Our emergency response system was initially activated on July 11, 2005, when the member's godson called us to say that the cancer treatments had proved ineffective. We provided him with emergency instructions for his physician and a funeral director (both in case of sudden death). A week later, we launched a standby reconnaissance of the area.

Our reconnaissance team flew to San Antonio, Texas, on July 19 with the intent of scouting the member's home, answering questions for the member and his godson, and making arrangements with a local funeral home for post pronouncement assistance.

We were hoping to deploy our new transport vehicle, in its first operational test, and immediately encountered a slight logistical problem. The member lived on the second floor of an apartment complex. To get to the front door, we had to walk through an open courtyard, and the stairs up did not have a foyer that was large enough to hold the mobile rescue cart.

The member's godson was a gracious and caring individual. He briefed us on the member's condition before we went in to meet him. We introduced ourselves, explained the procedure and answered all questions thrown our way. A brief patient assessment indicated that it would still be weeks before we would be needed.

We went with the godson to visit the funeral home they had found on our behalf. It was fortunate this was a reconnaissance mission and not the actual case, because we got terribly lost trying to find the mortuary. When we finally arrived, we negotiated with the local funeral home for priority access when called at pronouncement; we arranged for a funeral director to perform the femoral cannulation, and for assistance with obtaining the death certificate and the necessary permits to leave the state. This negotiation went well, as the funeral home was affiliated with a group that we had worked with on a previous case.

Flying home, we were confident that this case was well positioned to proceed smoothly, depending upon what kind of notice we received. The godson understood the urgency of keeping us informed of the member's condition, and he promised to brief hospice personnel, once they began 24 hour care. As with previous patients, we left monitoring equipment for the family and hospice nurses, so they could keep us informed of any changes in vital signs.

Standby and Pronouncement

The member took a sudden turn for the worse on August 10. At 8:00 that morning, his vital signs were blood pressure of 80/54, pulse tachycardic at 105, oxygen saturation of 70 percent, and his mental state was confused. To ensure we would be prepared to provide the best service, half the team flew out carrying a transport kit; and the second half of the team began the 1,000 mile drive in the new transport vehicle.

While our team was deploying, hospice personnel arranged to have a liter of saline administered to the member, in the hopes of prolonging his life long enough for the team to arrive and set up. Due to hospice limitations, the saline had not been fully administered by the time the flight team arrived; but the remaining saline was still administered in the hopes that the member would be sustained until such time as the transport vehicle arrived.

We arrived at the member's home at 17:12 local time and found the patient still conscious and feeling better. He was conversing coherently, even joking with us.

Once the emergency transport vehicle arrived on the scene, we began preparing it for the stabilization. Despite not having time to organize the supplies before leaving Arizona, it took the team only a half hour to prepare. With the patient's condition being much improved after his morning decline, we settled in for what would ultimately be a five day standby.

During the standby, we monitored the patient's condition closely. We knew from general monitoring that his tachycardia was normal, as his pulse had registered below 90 beats per minute only twice in the intervening month. His level of consciousness was fairly good, and he responded appropriately to questions. There were no signs that he was suffering from kidney failure. He did not become confused and was not obviously in pain until a couple days before cardiac arrest. In many ways, this was an unusual agonal decline, in that the patient was not dehydrating and his vital signs resembled none we have on record. Our timing for the standby was not too far off. Cardiac arrest occurred at 23:25 local time on August 15, 2005, with two team members nearby.

Stabilization

Following pronouncement, the patient was transferred to the living room using a new sling. The mobile rescue cart (MRC) was being moved from the vehicle to the front door and the patient's head was packed in ice to start the cooling process. The first medications were administered and circulated using manual chest compressions. An airway was placed and standard ventilation protocols applied. (Because of tumors in the throat, the Combi tube could not be inserted, and standard endotracheal intubation was used.) Once the medications had circulated sufficiently, the patient was transferred to the MRC.

By 23:42, the patient had been transferred to the emergency transport vehicle. Mechanical cardiopulmonary support using the LUCAS was initiated, and the patient was covered with more ice. Oxygen support, in concentrations

higher than room air, failed at this time. This highlighted that our team needs additional training on using the MRC.

Medications were still being administered. By 00:04, we had placed our new respiratory monitor, and the patient's oxygen saturation levels read 85 percent, his "pulse" was 85, and his temperature was 34.5°C. Priming of the circuit was done simultaneously, and all but the last large volume medications had been administered when the funeral director arrived to perform the femoral cut down.

The funeral director began operating at 00:31, and mechanical CPS was terminated. By this time, the patient's temperature had dropped to 31.6°C. The funeral director took longer than anticipated completing the cannulation. Blood washout began at 01:05. No clots were visible at this time, indicating that the early medications had been administered and circulated properly.

We lost volume in the early part of the washout due to a cannula leak. Closed circuit perfusion began at 01:14 with the patient's temperature at 19.7°C. This cooling rate was slower than expected. After examining the heat exchange portion of the circuit, we discovered that the pump in the ice bath had formed a shell of ice. By breaking up the shell and replacing the pump, cooling rates improved.

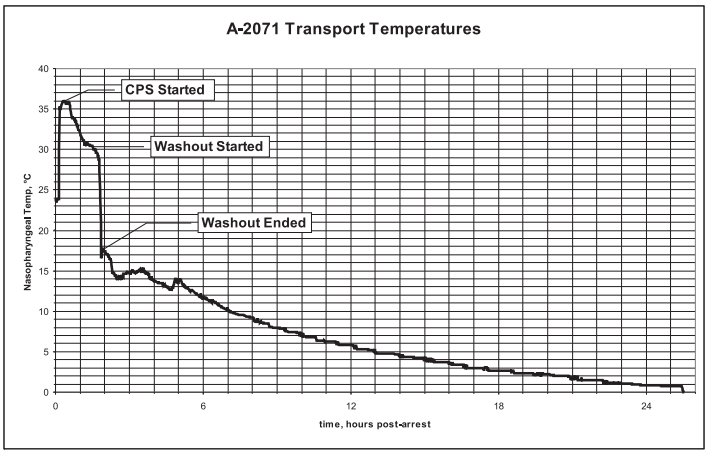
Washout switched from continuous perfusion to intermittent at 01:46 in an attempt to eke out additional cooling. The typical volume loss seen in a circuit was problematic in this case, but we were able to recover enough volume in the circuit by letting it rest for a few minutes before turning on the pumps again.

Because of the heat exchange difficulties, the patient's temperature was only lowered to 12.8°C when washout concluded at 02:15. Our goal is a maximum of 10°C with the desired temperature being closer to 5°C. Washout was stopped because of a combination of volume loss and a new member of the team stepping on the circuit, causing a breach. When we next deploy the MRC, we will be sure to raise all parts of the circuit off the floor to eliminate this hazard.

With the patient stabilized, we headed to the funeral home to arrange for paperwork processing and shipment to Alcor. We had previously established the general guidelines of driving a patient to Scottsdale when they are within a five or six hour radius of the facility, and continuing perfusion during that drive. For this patient, with a 20 hour distance, flying was the preferred option, especially given that we already had to wait until 08:00 to obtain the transit permit.

Upon arriving at the funeral home, we packed the patient for shipment to Alcor using our new ice bath liner for insulation. The patient was ready by 05:15; and the team waited for the Office of Vital Statistics to open and for the death certificate to be signed.

Unfortunately, the hospice physician who pronounced legal death was unwilling to sign the death certificate, and we had to track down the patient's personal physician. This was not an easy task, and we eventually enlisted the aid of the patient's godson. Furthermore, all flights to Phoenix were completely booked. Though we were able to secure a flight for the patient once the paperwork was prepared, he traveled unescorted. Two team members took a different flight on an airline that does not accept human remains and arrived a few hours in advance of the patient, while the two remaining team members drove the vehicle back to Arizona.



Temperature descent in patient from time of cardiac arrest to arrival at Alcor.

CRYOPROTECTION

The patient arrived at Alcor at 22:35 MST on August 16, 2005 (approximately 25 hours after cardiac arrest), in a 525 lb. container with ice bags intact and still cold. The new liner had worked extremely well.

For this case, Alcor was attempting its first whole body cryoprotection using the cryoprotectant M22 and was attempting to vitrify the brain without separation from the rest of the body. The surgery was standard, but the patient enclosure, perfusion equipment, and cryoprotectant were all being used for the first time.

When the patient was transferred to the operating room table, we found the patient sling worked well. The Teflon we had placed on the base of the table worked too well. We had hoped the Teflon would help us slide the patient into the enclosure easily, and that part worked; but later, the patient slid around too much and had to be held in place.

The first incision was made at 22:55, and pleural additions were found in the chest cavity. The patient's colon cancer had spread throughout his body, and tumors were in his lungs. When the atrium was located and a temperature probe and monitor with display functions were placed, the patient's nasopharyngeal temperature was 0.97°C.

Cannulation was completed by 00:09 on August 17, and the patient was prepped for burr holes. Once bubbles had been removed from the circuit, bypass began at 00:21. We immediately saw leakage in the chest and had to find the source and repair it. By 00:37, we saw good perfusion in the extremities. We also observed edema in the lungs and retraction in the left brain hemisphere.

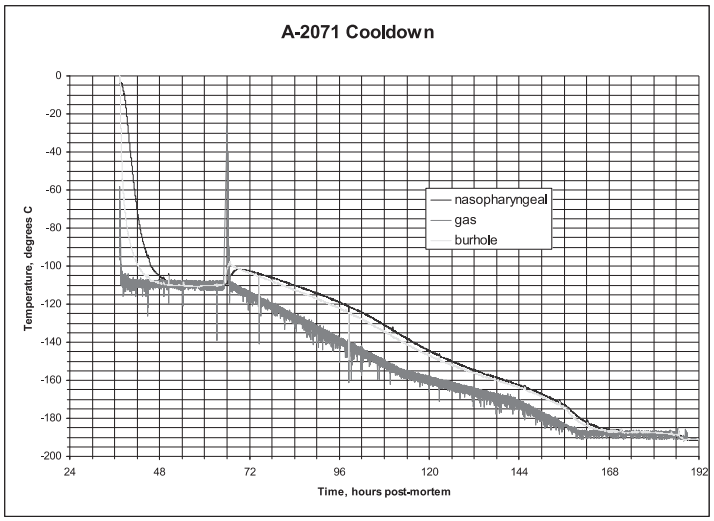
The cooling system on the patient enclosure initially caused some visibility problems. When nitrogen vapor was being circulated to maintain the external environment around the patient, the clouds impaired visibility. External cooling was turned off for the surgery but re started later.

Cryoprotection proceeded smoothly until 02:01, at which time an arterial air embolism occurred while the

perfusionist was away from his station and remaining staff had difficulty monitoring the recirculating reservoir level. One of the components in the M22 cryoprotectant has very strong foaming properties, causing the recirculating reservoir to fill with foam, obscuring the fluid level. Foam was pumped into the patient in unknown volume, and we then spent 90 minutes removing the bubbles from the aorta prior to resuming the cryoprotection. Based on this experience, the perfusion circuit will be modified to prevent foam formation in future cases.

During the later stages of the cryoprotection, we found ourselves losing volume from an unknown source. The chest leakage was controlled via cardiotomy suction, but there were additional losses that required time to locate. The source proved to be the femoral vessels, which had been jostled loose during transit.

Cryoprotection was concluded at 09:20, with the patient achieving target concentrations. Serious edema in the torso made closing difficult, but the patient was prepped and transferred for deep cooling at 10:22.



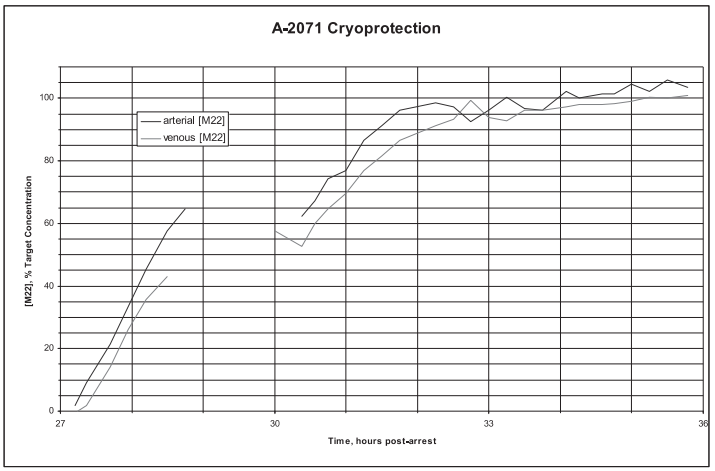
Cryoprotectant uptake during the vitrification procedure in patient A 2071, the gap represents a portion of the procedure during which samples were not being taken.

COOLING

Cooling occurred in accordance with usual protocols, a plunge to just above the glass transition temperature for the cryoprotectant followed by slower cooling at 1°C per hour. The cooling was changed to 0.5°C per hour for the interval from 155 to 170°C because of delays in our liquid nitrogen delivery schedule. Fifteen acoustic events were observed, with the first occurring at 121.9°C and the last at 171.4°C. Halving the cooling rate did not prevent cracks, nor did resuming the 1°C per hour cause additional events to occur.

CONCLUSION

This case, like all, had its good points and bad. On the positive side, the new transport vehicle performed well, with the exception of a generator problem that was fixed in the field. Use of the transport vehicle highlighted design deficiencies in the older equipment, which will be added to the list of things to improve. The entire stabilization was performed within the vehicle, and the funeral director had no concerns about performing femoral cannulation in it. Communication with the patient and his family was good throughout, from preliminary emergency activation to the resolution of paperwork problems.



Cooling curve and patient temperature, the spike in the gas represents the transfer of the patient to the single person dewar for the final stage cooling, when the gas line was temporarily disconnected.

This was the world's first attempt at vitrification in a whole body patient, and we are confident the brain was vitrified for the first time without separation. Some of the engineering done to implement the new whole body cryoprotection protocol needs to be re thought in light of the foaming properties of the cryoprotectant and vapor visibility issues, but overall the system performed as anticipated. We know how to solve these problems and plan to have implemented the necessary changes before our next whole body case.

Edema was an issue, and we believe it also reflects some interesting physical properties of the cryoprotectant; but this swelling was also the direct result of a long transit time between stabilization and cryoprotection. More investigation is needed on this issue, but we have made a couple modifications to the protocol that might be sufficient to reduce or eliminate edema in patients with less cold ischemia.

On the less positive side, we had paperwork problems again. Plus, the perfusionist left his station unattended, which resulted in foam being introduced to the patient's circulatory system. Field perfusion had heat exchange problems, and perfusion was stopped because the lines were breached. Transport teams need training on using the MRC, which has not been used for several years.

It was not until we were beginning to assemble and share the case data that we realized the operating room computer had not been set up properly. Cryoprotection data, aside from what was collected manually, was lost, hence the gap in refractive readings in the cryoprotection graph above. LabView has proven problematic in the past, and we are looking into placing it with something more user friendly. ▲