

Alcor A-1547

Case Report



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September - 2019

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1. Personnel

Standby, Stabilization, and Transport (SST) Team:

Josh Lado, EMT; Medical Response Director
Eric Vogt, EMT-P, International Cryomedicine Experts, LLC
Tim Freeman, Alcor member and volunteer
Jim Yount, volunteer and family friend

Surgery and Cryoprotective Perfusion Team:

Tom Wolvos, MD; General Surgeon
Steve Graber, Alcor Technical Coordinator;
 lead cryoprotection perfusionist, preparation, cooldown, and clean-up
Hugh Hixon, M.S. Biochemistry, Alcor Research Fellow; assistant cryoprotection
 perfusionist, cooldown, preparation, and clean up
Linda Chamberlain, scribe

Deployment Committee:

Max More, Ph.D., Chief Executive Officer
Steven B. Harris, M.D., Chief Medical Advisor
Josh Lado, EMT, Medical Response Director

2. Summary

Information was derived from multiple sources and was converted to Mountain Standard Time (MST). This report was written in 2019 but the case took place in 2018. As the Medical Response Director at that time is no longer with Alcor, some details are no longer available.

On February 20, 2018, Alcor was notified that Norma Peterson, a female, 85-year-old, non-confidential neurocryopreservation member, who had been an Alcor member since 1995, was in critical condition in a California hospice facility that specialized in patients with Alzheimer's disease and other forms of dementia. Alcor's Medical Response Director (MRD) and an experienced paramedic with International Cryonics Experts (ICE) flew to California to initiate standby, stabilization and transport (SST) procedures. The member was considered stable enough to transport to Arizona while still living.

The member was pronounced legally deceased on February 22, 2018, in Phoenix, AZ. Cryogenic cooldown was initiated on February 23, 2018, and was terminated on February 26, 2018. The patient went into long term maintenance on March 3, 2018.

Cryoprotection was non-uniform with large areas of the brain showing an M22 concentration below the concentration that is necessary for vitrification. An isotherm in the burr hole cooldown curve at approximately -7°C indicated ice formation as well.

3. Pre-Deployment and Patient Assessment

Tuesday, February 20, 2018

Alcor received a TeleMed alert at 22:48 hrs from a Redwood City, CA hospice facility. The hospice staff felt the member had entered into an active dying phase. The member was experiencing labored breathing, with a respiratory rate (RR) of 24 breaths per minute (/min). She had had episodes of apnea lasting 20-30 seconds per episode. She had an elevated heart rate (HR) of 124 beats/min, and her pulse felt erratic on palpation. The member was receiving 2 L/min of oxygen. The hospice nurse said she would call if there was any change in the member's status.

The Alcor Deployment Committee recommended that the MRD be deployed to the member's location as soon as possible as she could die suddenly due to respiratory problems. A paramedic from ICE was briefed on the case and asked to participate. This case was going to be an Alcor team response and a private jet would be chartered to fly the team to California as well as transport the patient back to Alcor. Noise restrictions at the airport made it impossible for them to fly out that evening so the fastest way to get the team to the patient was to take a commercial flight the next morning, departing at 07:30 hrs.

Shortly after midnight a California Alcor member who was a friend of the family and who had prior experience and an SST kit offered to assess the member and the situation, and be prepared to initiate the stabilization protocol if the member was declared legally deceased before the Alcor team could arrive. Around midnight there were no changes in the member's status. The member was on 2 L/min of oxygen. The hospice nurse said she would call if any changes occurred.

Wednesday, February 21, 2018

There were now three California Alcor members who were friends of the family and had deployed to the hospice facility as volunteers. One of the volunteer standby team called Alcor to report that the member still had labored breathing with periods of apnea and that her radial pulse could not be palpated for approximately one hour but had since returned.

Alcor's local funeral home was contacted and asked for help in finding a funeral home near the member in California should circumstances require it.

4. Standby

Wednesday, February 21, 2018

The Alcor team departed Phoenix Sky Harbor Airport and arrived at the member's bedside at 11:10 hrs. The member's daughter was at her bedside along with friends and the local Alcor

volunteers. The member's vitals were: Temperature (T) 37°C, heart rate (HR) 108 beats /min, respiratory rate (RR) 20 breaths/min, blood pressure (BP) 114/63, peripheral capillary oxygen Saturation (SpO₂) was 91% on 3.5 liters (L) of oxygen (O₂). Lung sounds on auscultation: slight rales were audible in the left lung; the right lung sounded clear. The member had received morphine (the dosage was not recorded) at 09:00 hrs. The member was moaning and able to cough but otherwise unresponsive to touch or voice.

Alcor's Chief Medical Advisor (CMA) suggested that the member be transported to Arizona for continued hospice care. The member's daughter agreed with the plan and arrangements were made to transfer the member to Arizona. The MRD called the Arizona hospice nurse to inform her about the arrangements to transport the member that night and to inquire about the progress in finding a skilled nursing facility (SNF) in Scottsdale, AZ.

The air ambulance company told the MRD that they would send both a nurse and a paramedic on the flight from Scottsdale, AZ to San Jose, CA and that they would send a non-emergency vehicle (an SUV) with two individuals to the nursing home to pick up the member. Once back in Scottsdale, a non-emergency vehicle would meet the plane and transport the member to the skilled nursing facility (SNF). The MRD inquired about using an ambulance for transport but was assured that a non-emergency vehicle was standard procedure for transporting patients of this type. A couple of hours later the air ambulance company called to say that a medical doctor would be on the flight instead of a nurse.

At 17:30 hrs the volunteer standby team (who had been with the member for over 17 hours) left the hospice facility due to exhaustion.

The Arizona hospice nurse called to inform the MRD that a skilled nursing facility in Scottsdale had been located but they required paperwork that included a tuberculosis (TB) skin test. The Arizona hospice nurse had contacted the nursing home in California, but they did not have the paperwork she needed, and the Scottsdale SNF would not take the member without the paperwork and the skin test. The MRD spoke to the SNF supervisor in California about these issues. She agreed to call the Arizona hospice nurse with the needed information.

That evening there were numerous calls between the MRD, the Arizona hospice nurse and the charter jet company to work out the final plan for transport and placement of the member into a facility in Arizona. It was determined that the SNF would not be a viable option due to their requirement for the TB skin test and paperwork. The Arizona hospice nurse reported that a local Scottsdale hospital would accept the member. The air ambulance was requested to leave Scottsdale and fly to California to transport the member back to Arizona.

At 19:21 hrs the air ambulance took off from Scottsdale. Strong headwinds caused the flight to be slower than anticipated. The air ambulance landed in San Jose at 21:17 hrs. At 21:34 hrs the member was transported to the San Jose International Airport in a non-emergency vehicle (an Escalade SUV) with the assistance of the staff from the memory care facility. At 21:55 hrs, they arrived at the airport and met the air ambulance crew.

The member's oxygen was removed, and she was transferred from the SUV to a gurney and then carried into the aircraft. The member was then placed back on 3 L/min of oxygen once aboard the aircraft. The air ambulance took off from San Jose, CA at 21:59 hrs.

During the flight, the medical flight crew, consisting of an M.D. and a paramedic, attended to the member. Since the member was unable to sit up at a 90° angle due to the cabin configuration, the member received light airway suction twice due to mouth secretions. Additionally, she became increasingly agitated, and the medical flight crew administered morphine sulfate to reduce her agitation (the dosage was not recorded).

Thursday, February 22, 2018

The air ambulance landed in Scottsdale, AZ just after midnight. At 00:28 hrs the member was transferred to non-emergency SUV for transport from the jet to the receiving hospital. The flight crew rode with the member to the hospital while the Alcor team took their equipment to Alcor. The MRD then went to the hospital and the other team member returned home. The member was admitted to an Arizona hospital through the Emergency Room (ER) at 00:58 hrs and was seen by the admitting staff in the ER at 01:00 hrs. She was in her assigned bed and by 01:07 hrs was being assessed by the hospital nurse.

At 01:09 hrs the member's vital signs were: T 37°C; HR 140 BPM, strong and regular; RR was 20/min on 3 L/min of oxygen; BP 146/88. At 01:14 hrs the MRD spoke with the nurse and explained the member's contractual arrangements to be cryopreserved. The nurse stated that the member would be placed on telemetry to monitor her vital signs.

The MRD left the hospital at 01:24 hrs and returned at 10:13 hrs. He then spoke to several members of the medical staff. The attending physician stated that she had put the member on 1 mg of morphine/hr I.V. continuous infusion and that the member had not had any changes during the morning. The MRD told the hospice nurse that he would return later with equipment for the standby and asked her to call if there were any changes or updates regarding the member's condition.

At 11:26 hrs the MRD called the CMA to give him an update and to report that he planned to return to Alcor for the standby and stabilization equipment before returning to the hospital. The CMA replied that the standby should start immediately since the member was not stable.

5. Stabilization

A hospital nurse called Alcor at 12:51 hrs to report that the patient was not doing well and a Code Blue, an emergency situation announced in a hospital in which a patient is in cardiopulmonary arrest, would soon be called.

The Alcor team deployed to the hospital and Alcor staff were asked to begin the operating room (OR) setup. A hospital nurse called to inform the MRD that the patient had been pronounced legally deceased at 13:02 hrs. The hospital had administered 50,000 units of heparin and had provided chest compressions for five minutes after legal death was declared in order to circulate the medication. The patient was then covered with ice for external cooling.

When the MRD arrived in the patient's room at 13:31 hrs the patient was moved to the portable ice bath (PIB). Additional ice and ten gallons of water were added to the PIB to improve external cooling. At 13:34 hrs the Lucas 2 mechanical cardiac compression device was placed around the patient to restore circulation. An attempt was made to turn it on, but an alarm sounded. The device could not be kept working.

Concurrently, the second team member arrived at the patient's bedside and prepared to draw the balance of the stabilization medications. The Lucas 2 was removed, and the hospital staff was asked to assist with manual chest compressions. At 13:41 hrs a nurse that teaches CPR training, assisted in helping monitor the rate and quality of compressions and the switching out of personnel when needed (the time when mechanical cardiopulmonary support was discontinued was not recorded).

Forty minutes after the patient was pronounced legally deceased, the infusion of the stabilization medications was begun through the existing hospital 20 g I.V. which had been placed in the right antecubital vein (see the Table of Medications Administered for the names, times and doses).

While the team administered the first two medications, additional ice was added to the ice bath and at 13:44 hrs the cooling mask for the surface conduction cooling device (SCCD) was placed over the patient's face and attached to the pump battery. Water flow was observed. The team did not have sufficient personnel to intubate the patient.

At 13:48 hrs a bone intraosseous (IO) needle was placed to improve the infusion of medications. The final stabilization medication was infused at 14:16 hrs.

6. Transport

The MRD called Alcor at 13:56 hrs to confirm that the operating room (OR) was ready for the patient and to report that the team would stay at the hospital and push more medications before leaving for Alcor. A hospital nurse was requested to prepare the paperwork in order to allow the team to depart with the patient. At 14:18 hrs the paperwork was signed and copies were made.

While still in the ice bath, at 14:24 hrs the patient was moved to the Alcor Response Vehicle (RV) and secured. Medication administration was terminated upon arrival at Alcor for reasons not stated in field notes, and that could not be determined as the MRD is no longer employed by Alcor. The field notes stated that not all the medications were administered but did not define what was omitted. However, per the Alcor Medications Protocol dated April 2014 (an assumption based on the fact that Ketorolac was used) the omitted medications might have been:

200 IU vasopressin, 500 mg niacinamide, 1.5 g kynurenine sulfate, 300 mg aspirin, 100 mL THAM (tromethamine), 250 mL Hetastarch, and 250 mL Maalox.

7. Cryoprotection Surgery

The patient arrived outside the Alcor facility and was brought into the OR at 14:51 hrs; there were no temperature probes in place on the patient.

At 14:54 hrs the SCCD was stopped. The surgeon marked the patient's face to show the left and right sides to avoid confusion while placing the cephalon into the cephalic enclosure and for cannulation. A nasopharyngeal (NP) thermocouple probe was inserted at 15:01 hrs and connected to the data acquisition system. The initial NP temperature was 8.4°C. The patient's shoulders were raised and propped up out of the ice and water with a 12" polyethylene support.

The easily accessible portion of the patient's head was shaved in preparation for the burr holes. At 15:12 hrs the first burr hole was started using a Codman perforator. The skull and perforator were cooled with normal saline. At 15:18 hrs the burr holes had both been completed. The NP temperature probe was not working and was replaced.

The patient's neck was prepped for accessing the carotid arteries for cannulation. The left carotid artery was raised, clamped, tied off and cut by 15:25 hrs. The right carotid artery was then raised, clamped, tied off and cut. The vertebral arteries were then clamped off. At 15:28 hrs the surgeon cut through the vertebra and by 15:30 hrs the cephalic isolation had been completed; the cephalon was inadvertently not weighed. The cephalon was moved into the cephalic halo and secured. At 15:31 hrs the right carotid artery was cannulated with a 14 French (Fr) red Robinson catheter.

Perfusion was started at 15:37 hrs. The reservoir volume was 1.85 liters (L), the pressure was set to 40 mmHg, and the pump pressure was building. At 15:41 hrs the bypass to the arterial line was clamped off and flow was detected two minutes later.

Cannulation of the left carotid artery was initiated at 15:45 hrs with a 14 French (Fr) Robinson catheter; it was completed one moment later. The pump ran slowly, was switched to manual control and was then stopped in order to open the circuit to calibrate the pump back to zero. At 15:50 hrs the pump was turned back on and open circuit washout commenced. The automatic perfusion pressure was set to 80 mmHg.

The volume in the mixing reservoir was 0.65 L; more B1 washout solution was added from the bladder via the circuit loop (amount not given to the scribe). The filter pressure was 5.5 psi. The refractometer pump was started. The burr hole thermocouple was placed (the scribe was not told which burr hole was used). Open circuit washout was started at 15:50 hrs. The initial temperature reading was 6.3°C. Clean-up was started and preparations were made to close the neuro enclosure.

8. Cryoprotectant Perfusion

At 16:07 hrs the circuit was still running to dump. At 16:09 hrs the volume of the patient's brain was observed to be notably decreased from dehydration. Brain volume reduction in the left burr hole was estimated to be 1.0 cm, and in the right burr hole, it was estimated to be 0.4 cm. The cause of the dehydration was not known. The patient had been diagnosed with Alzheimer's disease, and brain volume reduction can be a consequence. The reservoir volume was 0.9 L. The lid was placed on the cephalic enclosure to improve cooling.

At 16:11 hrs the open circuit washout was complete. The system was switched to recirculation mode and the cryoprotective ramp pump was started using nM22, the cryoprotectant formulation for neuro patients. The pump was halted in order to repair a thermistor plug (part of the enclosure temperature control) which had shorted and the enclosure temperature was manually dropped by injecting nitrogen gas. This was needed because the enclosure was too warm (see note at 21:21 hrs below). At 16:16 hrs the ramp pump was restarted.

At 16:24 hrs there was observable tanning of the skin in the patient's cheeks. Perfusate effluent was observable in both jugular veins. The mixing reservoir level was 1.1 L and the volume of the nM22 reservoir was 8.5 L. At 17:00 hrs perfusate was flowing from the burr holes while the brain retraction detection device (BRDD) was inserted into a burr hole.

At 17:13 it was determined that the pump rate was unreasonably high, and this was traced to an air leak between the isolator and all the pressure sensors. (This was a leak of air out of the normal air-filled lines between the isolator and sensors, not an air leak into the perfusion circuit.) The isolator diaphragm had reached its limit and the pump control was almost completely uncoupled from the arterial pressure, resulting in a gradual but relentless increase in the pump speed. The problem was corrected by tightening the leaking connection and injecting air into the isolator to restore it to normal function.

Looking at the pressure and pump speed graph, this problem had been developing for at least an hour, exacerbated by a continuing increase in vascular resistance. The over-pressurization could be the cause of the poor perfusion in this case.

At 17:15 hrs the pump was stopped while the computer system pressure was tared back to 0 mmHg to produce correct readings. The pump was again started in manual mode and the pump speed was raised slowly to prevent overpressure. The pump was returned to automatic mode, and everything worked correctly. This had been the cause of the pump speed increase and not edema.

At 18:22 hrs the ramp was paused, 50% concentration necessary for vitrification (CNV) had been achieved. The arterial concentration of nM22 was 43 Brix, the right venous concentration was 30 Brix and the left venous concentration was 27.5 Brix. The cephalic enclosure temperature and the chiller temperature were both set to -3.0 °C.

Sidebar:

Per the cryoprotection protocol, the ramp is to be paused at 30 Brix (50% of the desired end concentration) to allow the patient to come to osmotic equilibrium. The reservoir box, table and chiller are switched from +3°C operation to -3°C. At the end of the 30-minute pause, the ramp is resumed at the maximum addition rate (maximum without losing total volume in the circuit) to go to 105% of the desired end concentration (52.5 Brix) and held between 102% and 105% concentration until the goal is obtained. The main pump is turned on and off repeatedly to compensate for latency.

At 18:25 hrs, it was noted that the patient's eyes had not yet collapsed from dehydration as would typically be expected.

At 18:53 hrs the cryoprotective ramp was re-started and set to full speed to start the sub-zero terminal concentration ramp. The mixing reservoir volume was 1.02 L, the effluent volume was 2.7 L, and the concentrate volume was 6.4 L. At 19:03 hrs the mixing reservoir volume was 1.86 L. The reservoir was drained down to 1.0 L. The concentrate volume was 3.6 L.

It was noted that the mixing reservoir did not have the typical foaming of the cryoprotectant.

At 19:22 hrs the main pump speed was running so slowly that the brain was barely being perfused. Both the uptake and the rate of perfusion were slow. The ramp pump speed was reduced to 50 (approximately 65 mL/min) down from 90 (approximately 118 mL/min) to keep from overwhelming the main pump. The mixing reservoir volume was drained from 1.7 L to 0.7 L.

At 21:21 hrs the enclosure cooling solenoid appeared to be failing. It had been operating somewhat erratically during the entire procedure. It would need to be replaced before the next case.

At 21:28 hrs the ramp was turned off to keep the nM22 concentration less than 105% of the desired terminal concentration.

Sidebar:

Per the cryoprotection protocol, the normal endpoint criterion for whole body patients is over 100% for over 30 minutes from the venous return and for neuro patients, it is over 100% for over 30 minutes from both jugular veins. The main pump is turned on and off repeatedly to compensate for latency.

At 21:46 hrs the ramp was turned on at speed 50 (approximately 65 mL/min). The arterial concentration was 52.6 Brix, the right jugular was 45.11 Brix and the left jugular was 41.7 Brix.

At 22:33 hrs the mixing reservoir level was 0.83 L. The arterial concentration was 54.45 Brix, the right jugular was 46.25 and the left jugular was 42.9 Brix.

At 23:48 hrs the decision was made to terminate cryoprotectant perfusion based on the combination of diminishing returns and team exhaustion after approximately nine hours of

cryoprotectant perfusion. The right jugular effluent was at 52.98 Brix, and the left jugular was at 45.16 Brix against a desired terminal nM22 concentration of 49.90 Brix.

The cephalon was not weighed.

9. Cooling to Liquid Nitrogen Temperature

Cryogenic cooldown was initiated at 00:07 hrs on February 23, 2018, plunging to -110°C and descending thereafter at -1°C /hour to liquid nitrogen (LN₂) temperature. The cooldown was terminated on February 26, 2018, and was uneventful. The patient was transferred to long-term maintenance at LN₂ temperature on March 3, 2018.

10. Timeline and Time Summaries

Timeline

February 22, 2018

- 13:02 Pronouncement of legal death
- 13:21 Hospital staff administered 50,000 units of heparin through existing hospital 20 g I.V. and circulated it with manual chest compressions for five minutes after the pronouncement
- 13:34 Hospital staff started compressions after Lucas2 failed (time of termination not recorded)
- 13:42 Administration of first medication (200 mg propofol)
- 13:44 Start of ice bath cooling
- 13:48 Intraosseous (IO) needle placed in the patient's right tibia
- 14:16 Administration of final medication given (200 mL of 20% Mannitol)
- 14:24 Patient moved to Alcor's Response Vehicle
- 14:51 Patient moved into the operating room; there were no temperature probes in place
- 14:54 Ice bath circulation device (SCCD) was stopped
- 15:01 Nasopharyngeal temperature (NPT) probe attached to the data acquisition system; initial temperature was 8.4°C

15:12 Start burr hole surgery

15:18 Completed burr hole surgery

15:30 Surgical procedures and cephalic isolation completed

15:50 Start open circuit washout

16:11 Completion of washout and start of the cryoprotectant perfusion

17:09 Problem detected; pump speed rising to maintain pressure. Meanwhile, pressure remained steady at 80 mmHg

17:13 Problem found in tubing, air leak in the pressure sensing system; corrected

18:22 50% of concentration necessary for vitrification (CNV) achieved

18:53 Start of sub-zero terminal concentration ramp

19:22 Pump speed so low that brain barely being perfused

21:21 The box cooling solenoid appeared to be failing

23:48 Termination of cryoprotection; arterial Brix was 54.45, right venous Brix was 52.98, left venous Brix 45.16

February 23, 2018

00:07 Cryogenic cooldown initiated

February 26, 2018

Cryogenic cooldown terminated

March 3, 2018

Transfer of patient to long-term maintenance at LN₂ temperature

Time Summaries

Stabilization

hrs:min

- 00:32** From pronouncement of legal death to start of cardiopulmonary support:
13:02 hrs to 13:34 hrs
- 00:40** From pronouncement to start of medication administration: 13:02 to 13:42 hrs
- 00:34** From the start to the end of medication administration: 13:42 to 14:16 hrs
- 01:49** From pronouncement of legal death to patient arrival at Alcor: 13:02 to 14:51 hrs

Cryoprotective Surgery

hrs:mins

- 00:21** From arrival at Alcor to start of surgery (burr hole #1): 14:51 hrs to 15:12 hrs
- 00:18** From start of surgery to end of the cephalic isolation: 15:12 hrs to 15:30 hrs
- 00:59** From the start of surgery to the start of the cryoprotection: 15:12 hrs to 16:11 hrs
- 08:36** From the start of surgery to the end of the cryoprotection: 15:12 hrs to 23:48 hrs

Cryoprotectant Perfusion

hrs:mins

- 07:37** From start to end of cryoprotection: 16:11 hrs to 23:48 hrs
- 00:19** From the end of cryoprotection to the start of cooldown: 23:48 hrs to 00:07 hrs
- 09:16** From arrival at Alcor to the start of cooldown: 14:51 hrs to 00:07 hrs
- 11:05** From pronouncement of legal death to start of cooldown: 13:02 hrs on 2-22-18 to 00:07 hrs on 2-23-18

11. Table of Medications Administered

TIME	MEDICATION	DOSE	PURPOSE
13:02 hrs	Heparin (administered by hospital staff)	50,000 IU Note 3	Anticoagulant; prevents blood clot formation.
13:42 hrs	Propofol	200 mg	Anaesthetic; reduces cerebral metabolic demand; reduces the theoretic possibility of increased awareness during aggressive CPS.
13:46 hrs	Sodium citrate	10 g Note 4	Anticoagulant; prevents blood clot formation.

13:48 hrs	Epinephrine (via Baxa pump)	30 mg	Vasopressor; increases blood pressure during CPS.
13:51 hrs	Heparin	100,000 IU Note 3	Anticoagulant; prevents blood clot formation.
13:52 hrs	SMT (S-methyl-isothiourea)	400 mg Note 5	Neuroprotectant (iNOS inhibitor); protects the brain from ischemic injury; raises blood pressure.
13:56 hrs	Vital-Oxy	40 mL Note 6	Antioxidants: melatonin, vitamin E (D-alpha tocopherol), PBN (alpha Phenyl t-Butyl Nitron) and anti-inflammatory carprofen.
13:59 hrs	Ketorolac	15 mg Note 7	Non-steroidal anti-inflammatory; inhibits ischemia-induced inflammation.
14:05 hrs	Gentamicin	80 mg	Antibiotic; reduces microbial overgrowth during long transport times.
14:16 hrs	Mannitol 20%	200 mL	Osmotic diuretic, decreases pressure in the brain and eyes, reducing swelling.

Notes:

1. The medications used were per the protocol dated April 2014.
2. The times shown in the above chart are estimates based on the video.
3. The team was not able to confirm whether the hospital had given the initial dose of heparin. Therefore, it was felt that an overdose of heparin would not be harmful, and an extra dose would be better than for the patient to receive no heparin.
4. The standard formulation for citrate is 50 mL vials of 20% w/v = 10 grams sodium citrate, with a maximum of two vials being administered depending on patient weight. This patient received 10 grams of sodium citrate as per protocol because his weight was under 40 kg.
5. SMT (S-methyl-isothiourea) is a fixed dose of 400 mg dissolved in 10 mL of saline.
6. The standard formulation for Vital-Oxy (0.7 ml/kg up to 70 mL, I.V., dissolved in 150 mL saline) Each mL of Vital-Oxy contains 194 mg Sigma Cremophor EL (or Sigma Kolliphor EL), 155 mg ethanol, 19.4 mg PBN, 3.24 mg carprofen, 1.55 mg melatonin, and 198 IU vitamin E.
7. The ketorolac was administered as a custom formulation of 2 mL at 30 mg/mL and must be adjusted for patient weight. For patients 50 kg to 100 kg: draw and use only 0.25 mL. For patients over 100 kg: draw 0.5 mL into a 3 mL syringe and use that amount.
8. Streptokinase was inadvertently not added to the open-circuit washout.

12. Discussion

1. At 16:09 hrs the volume of the patient's brain was observed to be notably decreased from dehydration. Brain volume reduction in the left burr hole was estimated to be 1.0 cm, and in the right burr hole, it was estimated to be 0.4 cm. The patient had been diagnosed with Alzheimer's disease, and brain volume reduction can be a consequence.
2. At 17:13 hrs an air leak was observed in the pressure sensing system in the manometer line tubing near the pressure gauge. The leak was in the line between the isolator and the pressure transducer causing the isolator diaphragm to reach its internal travel limit. The connections were checked and tightened to prevent further leaking. An extension of the luer fitting would be useful for making an easier connection.
3. There was an isotherm in the burr hole cooldown curve at approximately -7°C , indicating incomplete cryoprotection and the formation of ice.
4. The CT scan reveals large areas with M22 concentrations that are below the concentration that is necessary for vitrification, with some areas substantially lower ($<60\%$). While it has been observed that in ideal, non-ischemic, cases vitrification is possible at lower than 100% M22 concentrations, it is not likely that this occurred in this case because vitrification was not assisted by strong CPA-induced brain shrinking.

The blood-brain barrier seemed to have been compromised. As a result of the (ischemia-induced) swelling of the brain, the perfusion rate declined rapidly from around 220 mL/min to 25 mL/min, accounting for the slow rise in the jugular concentration of nM22 and incomplete cryoprotection.

It has been some time since Alcor has cryopreserved an Alzheimer's patient. In one prior Alzheimer's case (A-1894 in 2001) the brain retracted so dramatically that the bottom of the braincase could be observed. That was not true in this case. In the CT scan, the spongiform brain was floating in cryoprotectant with lower amounts in the brain itself.

13. Issues and Actions

A debriefing meeting was held on February 27, 2018, and the following issues and corrective actions were identified.

Insufficient planning

There was no clear understanding between the members of the SST team about whether the member should be transported to Arizona and then be placed in a hospital, a skilled nursing facility or in a hospice facility. This resulted in confusion and could have resulted in compromised care for the member. The following solutions have been implemented to improve planning in the future:

1. The CMA will be called earlier in cases like this so he can help determine the best course of action and then help make it happen.
2. Oximetry readings could help with better assessment of our members. Baseline medical information is also essential for assessing whether the member is well enough to transport while living.

SST kit not completely stocked

The camera was not in the standby, stabilization and transport (SST) kit. The kits must be ready at all times. Extra recording equipment and batteries should be kept in the vehicle. A battery station has been set up and a standard operating procedure (SOP) written for how and how often batteries are to be charged.

Insufficient number of team members

There were only two members on the SST team and this resulted in several deficiencies: 1) Despite the urgency of transporting the member from California to Arizona the member was left alone once she was admitted to the hospital in Arizona, 2) there were no temperatures recorded during stabilization, 3) the member was not intubated, and 4) there was a delay in getting the patient to Alcor while stabilization was being completed.

To prevent problems such as the team members becoming fatigued and stretched too thinly, deployment should consist of a minimum of six team members to be rotated for sleeping, eating and other activities, as well as having sufficient team members to properly carry out the protocols. The fact that telemetry was used by the hospital staff should not be an excuse to leave a member unsupervised. The member should never be left alone, especially when in critical condition. Carotid cannulation at Alcor usually takes less than 15 minutes to perform, so there would have been no reason to delay transporting the member to Alcor if there had been sufficient team members.

The Lucas 2 interruption

The Lucas 2 mechanical cardiac compression device stopped and could not be used. The cause of this will be determined. That specific unit is not to be used until the problem is resolved. An extra Lucas 2 unit is to be kept in the rescue vehicle as a back-up. (Note: At the time of writing this report the Lucas 2 has been replaced with the ROSC-U device which is more reliable.)

Ice entered the patient's nose and mouth

Ice got into the patient's nose and mouth from the portable ice bath. This could have resulted in inaccurate temperature readings from the nasopharyngeal probes. To prevent this occurrence, cover the patient's face, use wax around the thermistor probes, and use a King airway to block off the mouth along with packing with paper towels and/or gluing the lips around the airway.

Generator not working

The generator on the vehicle did not work due to lack of sufficient fuel. Always make sure the gas tank is at least one-half full for local cases. An orange sticker will be placed over the fuel gauge saying *Fill when ½ full*.

Medical personnel not provided by the air transport company

Alcor had requested an ambulance with medical personnel to transport the patient on the ground, but the charter air company did not provide either. If the patient had died in transport, it could have been a medical examiner's case and resulted in an autopsy. In the future, do not use that air ambulance company. Always use an ambulance to transport critical patients. Impress the non-negotiability of this to the air transport broker. Specify the below level of need:

Level 1: Patient is ambulatory and non-emergent:

This would require a wheelchair and a van.

Level 2: Basic Life Support: Two EMTs with a gurney.

Level 3: Advanced Life Support: Two Paramedics with a gurney.

OR Camera not turned on

The camera in the operating room (OR) was not turned on. In the future, multiple individuals will be tasked with checking to make sure the camera has been turned on at the beginning of the procedure.

Need for OR team training

It had been too long between cases and mistakes were made. Dry runs will be scheduled at least quarterly if there have been no cases. Training tubing will be used to string the pumps. The first dry run was scheduled.

Lack of familiarity with surgical trays

People were not familiar with the contents of the surgical trays and had to ask where to find instruments. Again, this relates to it being too long between cases. Simplify the contents of the various trays and have any seldom used instruments on a separate tray. Ask the surgeon for his input about what he wants to see on the main surgical tray.

Burr hole placement was not uniform

The placement of the burr holes was not done in the standard way. A template for burr hole placement was made and will be kept on the instrument tray to ensure uniformity of burr hole placement in the future.

Cannulation time was excessive

The cannulation took too long to complete. The red Robinson catheters were too long and difficult to handle. In the future, they will be trimmed for easier handling.

Anatomical anomaly

A picture was taken of the right carotid with an unusual structure next to it, perhaps a *sub-carotid*, but this unusual anatomy was not discussed during the cannulation. If the wrong carotid were to have been cannulated, it could explain ice formation in the brain. Remind our surgeons to point out, during surgery, anything that is unusual so that we can help make decisions about how to proceed.

Better team communication needed

Team members need to be kept better informed during a case, and separate emails to everyone is problematic. All team members will be invited to join Alcor's new internal communication system (ICS) which is a cell phone application where team members can view and participate in an on-going text stream.

Cephalon not weighed

The cephalon was not weighed either before or after cryoprotection. This needs to be done on all neuro cases. A procedure for doing this in the field will be created and necessary equipment will be added to the field neurocryoprotection kits.

Streptokinase not added to open-circuit washout

Streptokinase must always be added to the blood washout solution prior to the remote blood washout or the first cryoprotection flush in the OR. The OR staff have been given a review of this essential step.

Perfusion termination criteria

This perfusion continued at terminal concentration for five hours, with the staff exhaustion being one of the stated reasons for not continuing it even longer. There is no data showing what M22 does to a brain after more than 60 minutes of exposure at -3°C . There needs to be a policy limit set for terminal concentration perfusion time. The research committee will be asked to address this issue.

High pump speed and perfusion pressure

Perfusion was not optimal on this case because the arterial pump speed increased to a grossly abnormal high speed for over 20 minutes. This exposed the patient's brain to an abnormally high perfusion pressure, possibly damaging the vascular system so that the remainder of the perfusion was compromised. 200 mL/min is a typical starting rate for neuro perfusions and the 50%

flow drop rate at 25 Brix was atypical. This could be due to vascular damage from over-pressurization. There are three parts to remediation of this issue, each with easily implemented solutions.

The first part of the solution is that the OR staff will be trained to understand the correlation between the pump speed trace and the arterial pressure signal trace on the computer monitor. They will be trained on what to look for in those traces at the onset of every OR case. A copy of 'nearly nominal' pump traces will be printed and available for review in the OR.

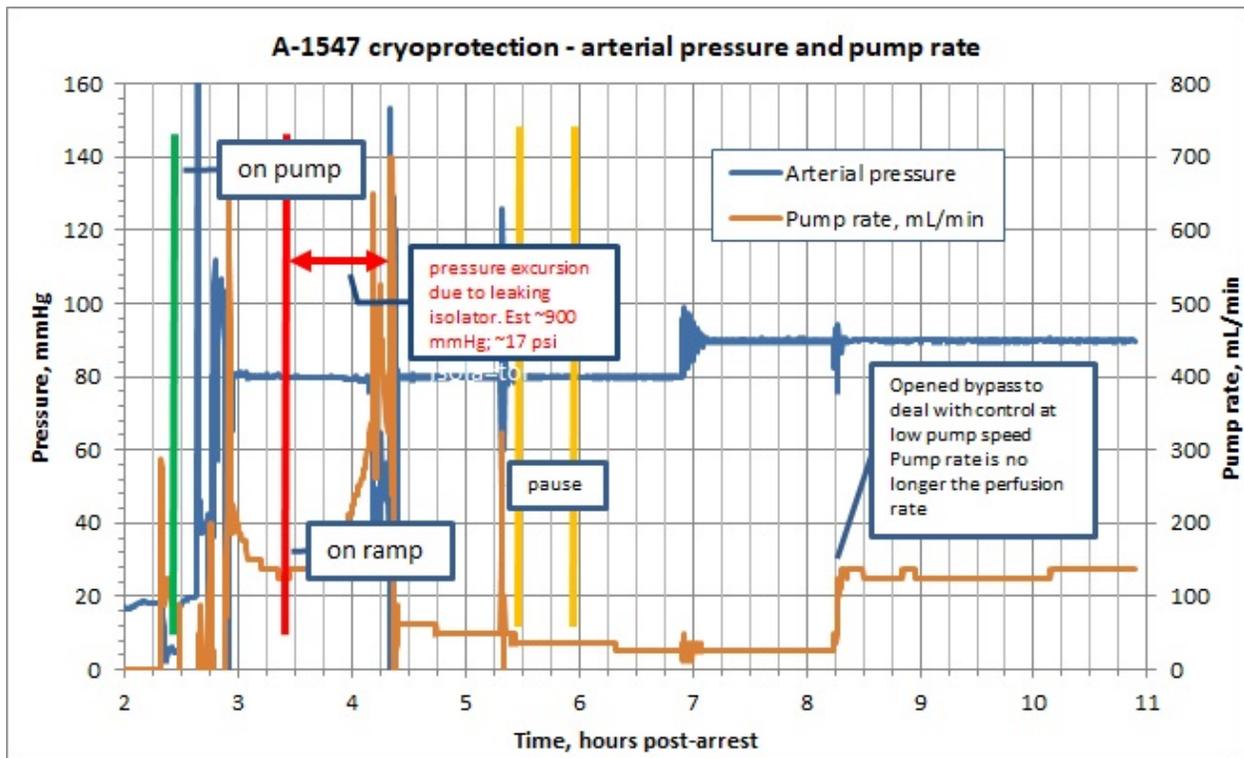
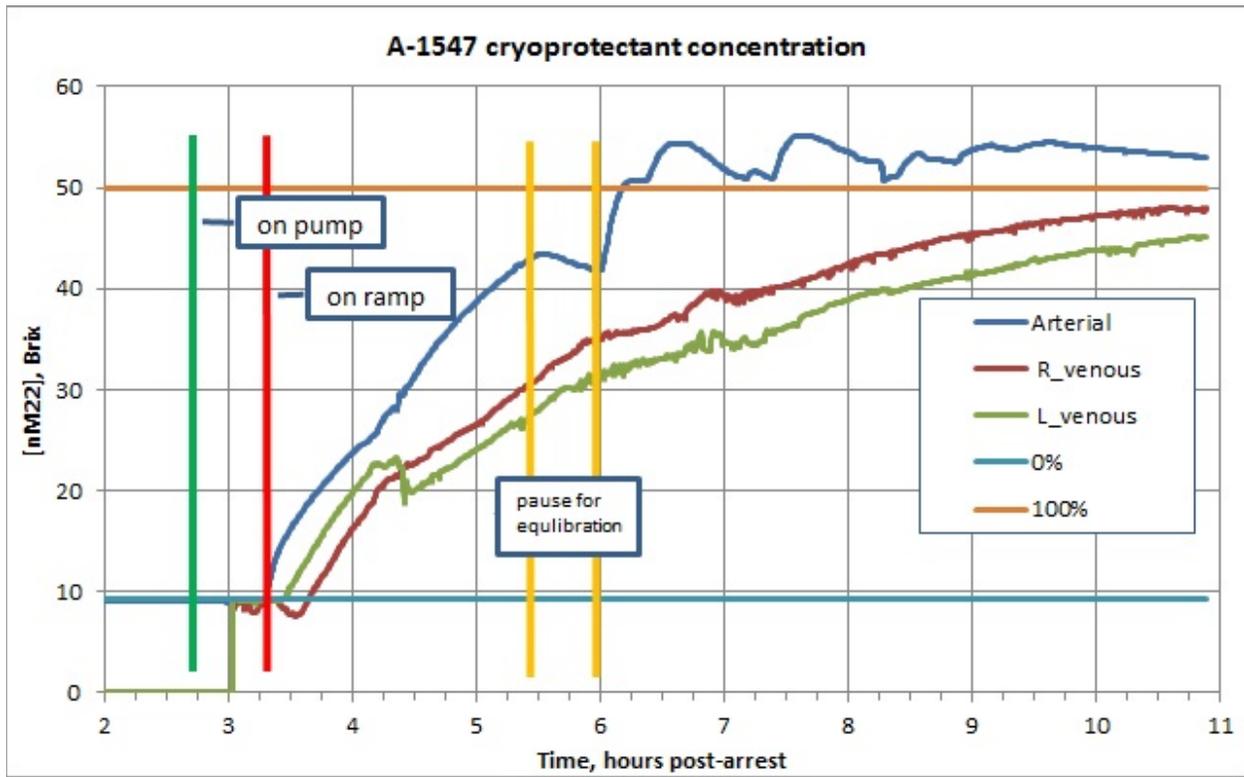
The second seems almost too simple to be considered an issue, but indeed it was a big problem on this case, and still is a problem as of the writing of this report. The pump head turning is a good indicator of pump speed. During the heat of the moment in a case there are many issues vying for the perfusionists attention. Having better equipment layout with the entire circuit and pumps visible to personnel would be beneficial. A legacy effect of incremental improvements made over time to the existing system without a major overhaul means that we are still using an original pump cart from the era when a human being sat for hours in front of the pump cart observing an analog gauge and controlling the arterial pump speed manually.

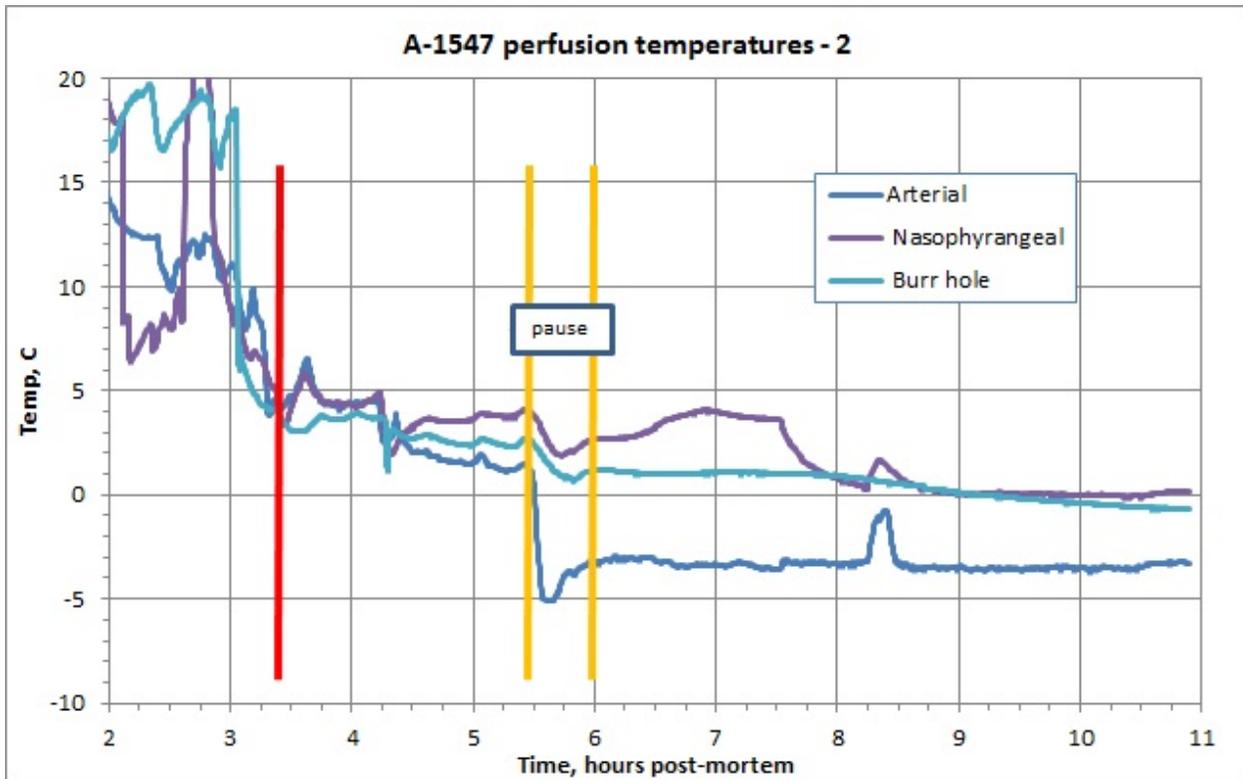
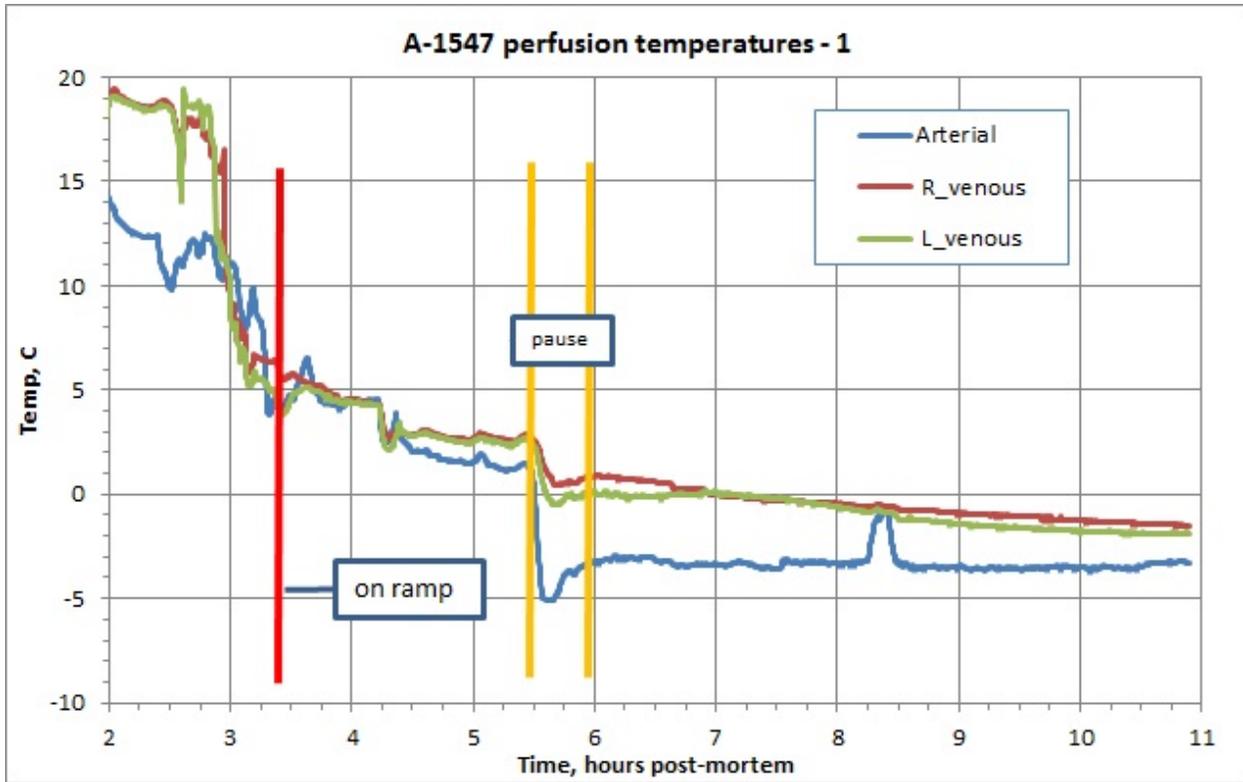
Those days are now long gone as the computer is capable of doing a much better job of controlling pump speed than a human being ever could, but the pump location has not changed. The pump is located in such a place where it is not easily visible from the main area of the OR. You cannot visibly observe the pump rotation unless you walk completely behind the cart. This problem has been apparent for a long time and it has been very low priority issue which will ultimately be fixed when the whole body and the neuro perfusion systems are split into two discrete products.

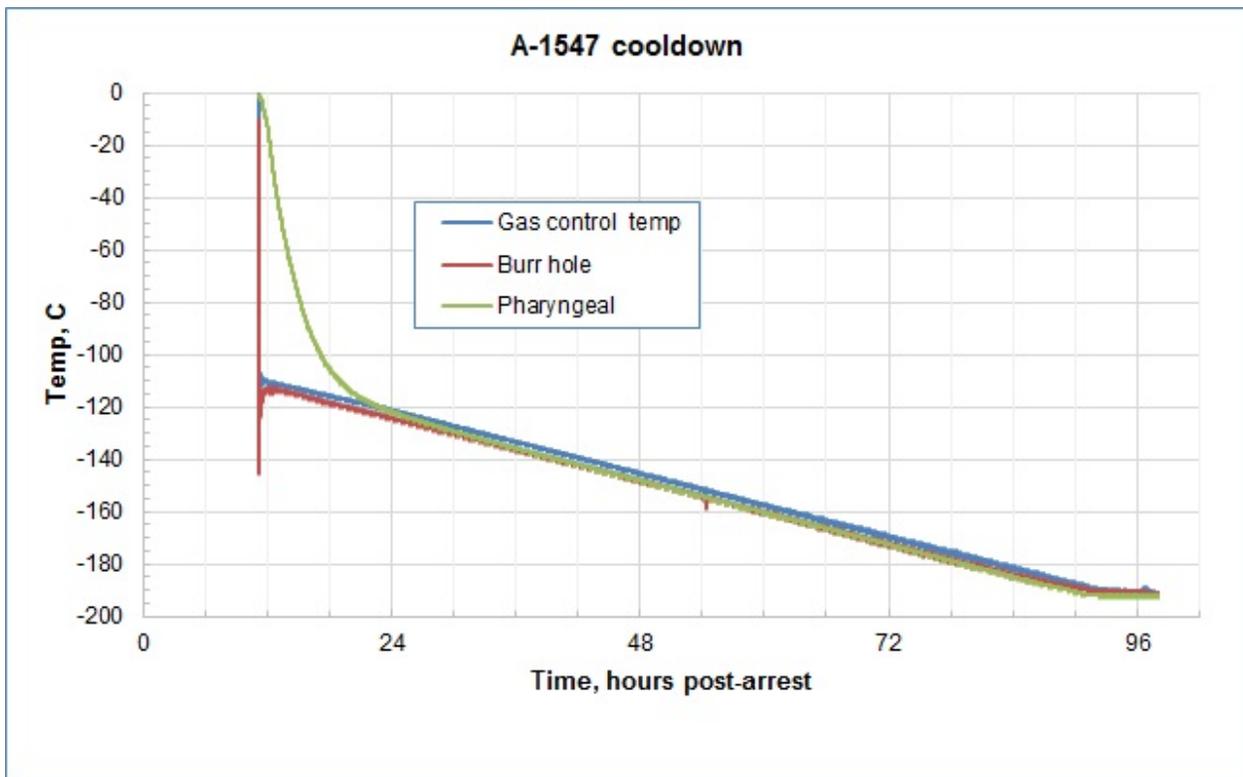
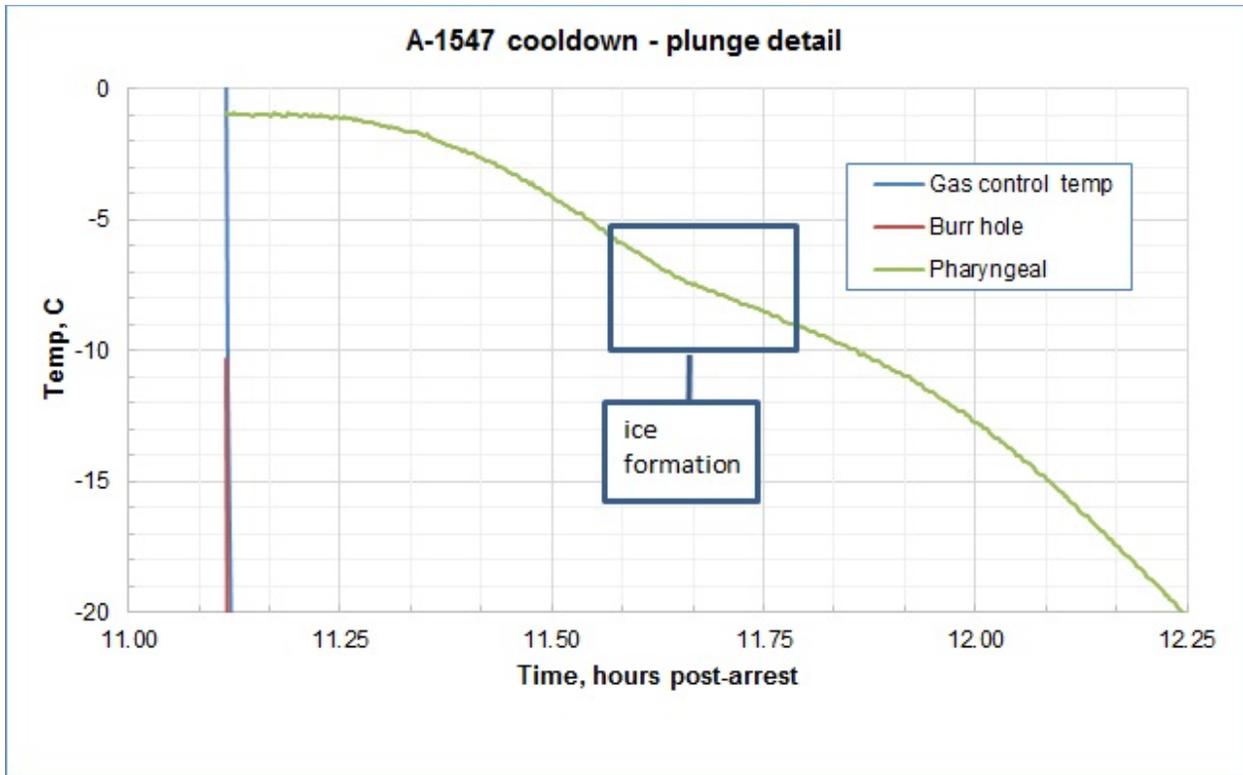
Right now, both whole body and neuro systems share data acquisition and control. Until that happens (probably early 2020) it will still be necessary to walk behind the pump cart to directly observe the pump rotation. As a solution in the interim, a small video camera and small composite monitor (car backup camera) will be placed on the cart which will display the pump head video onscreen in a prominent location next to the main Perfusion Process Computer (PPC) control panel screen.

The third issue was the incorrect placement of the pressure isolator ahead of the pressure transducers in the arterial pressure monitoring line. When the pressure isolator leaked and bottomed out, the transducers were on the wrong side of the isolator. This issue has been corrected. The arterial pressure transducers are now placed ahead of the isolator, followed by the analog pressure gauge at the end of the line.

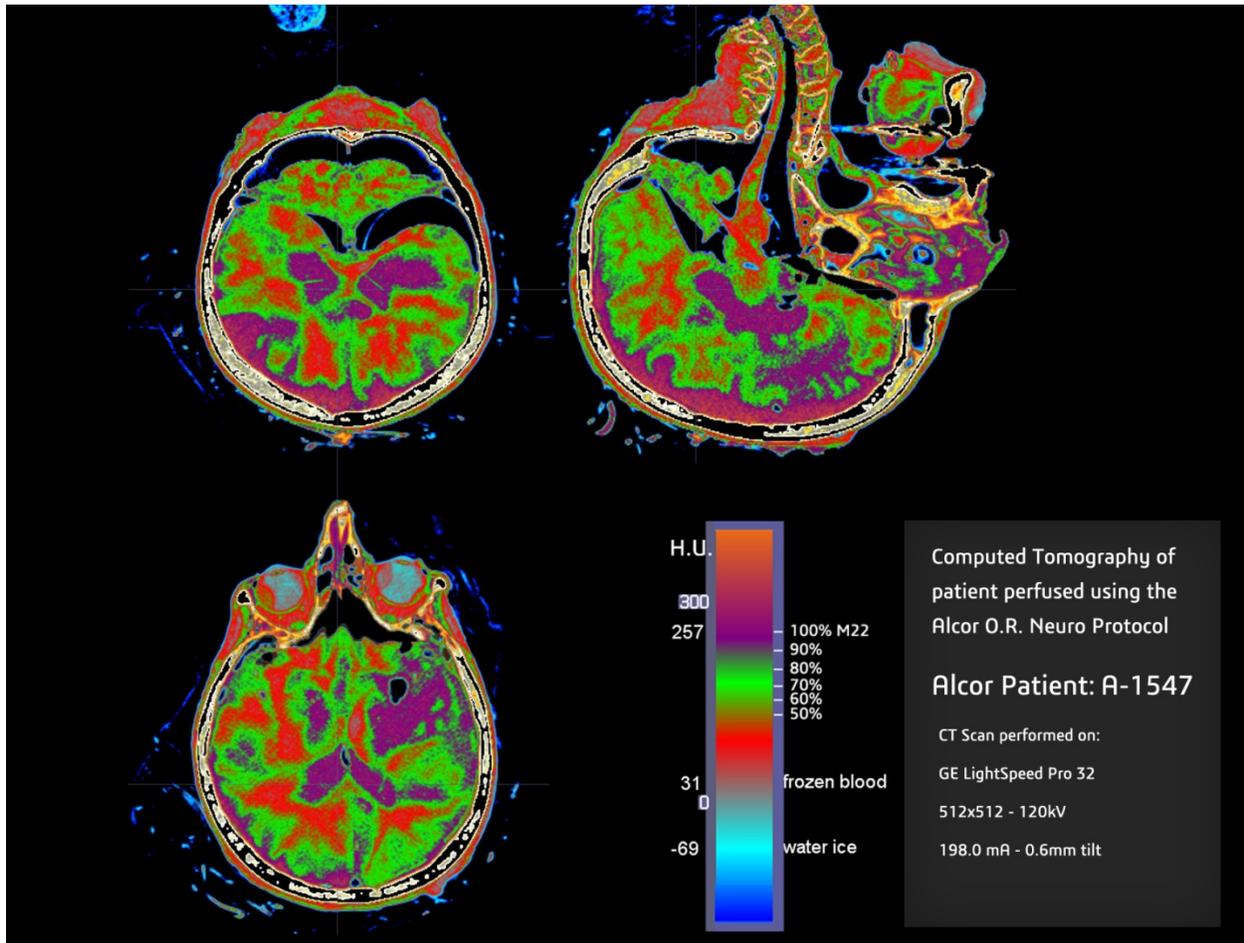
14. Graphs and CT Scans







Cryoprotectant Distribution



Note: The CT scan was made on March 3, 2018. The patient was in liquid nitrogen (-196°C).