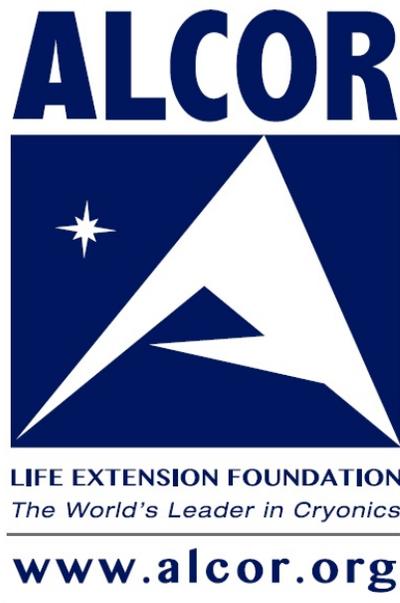


# **Alcor A-1990 Case Report**



## **Prepared by:**

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## **Sources:**

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## 1. Personnel

### Standby, Stabilization and Transport:

Christopher Divver, NRP, MPA, CPM, Alcor Medical Response Director  
 Ryan Levesque, Donor Recovery Manager, Suspended Animation, Inc.  
 Sayer Johanson, NREMT, Operations Manager, Suspended Animation, Inc.

### Cryoprotective Surgery and Perfusion Team:

Tom Wolvos, M.D., General Surgeon  
 Christopher Divver, NRP, MPA, CPM, Alcor Medical Response Director, Assistant Surgeon  
 Hugh Hixon, Jr., Alcor Research Fellow, Lead Cryoprotection Perfusionist,  
 cooldown, data reduction  
 Steve Graber, Alcor Technical Coordinator, Assistant Cryoprotection  
 Perfusionist; setup, cooldown, data reduction  
 Sandra Russell, readiness, supplies, cleanup  
 Linda Chamberlain, scribe

### Deployment Committee:

Max More, Ph.D., Alcor Chief Executive Officer  
 Steve Harris, M.D., Alcor Chief Medical Advisor

## 2. Summary

*Information is derived from multiple sources and is all converted to Mountain Standard Time (MST).*

Norman Hardy, a non-confidential, neurocryopreservation Alcor member was pronounced legally dead on October 30, 2018, in Mountain View, CA. This case was the first time the newly enacted California End of Life Option Act (EOLOA) was used to reduce the potential ischemic damage that can result from a prolonged dying process.

Alcor's Medical Response Director (MRD), Alcor's Chief Medical Advisor (CMA), and other Alcor staff worked for over a week after being notified of the member's end of life choice to make sure that all legal requirements were in place. The hospice facility and the family members were all cooperating with Alcor to make this case as flawless as possible, legally, logistically and technically.

The cryoprotective perfusion was relatively successful. Perfusion flow rates were high throughout the procedure. However, the post-cryopreservation CT scan showed poor cryoprotection and extensive CT-visible ice formation in the cerebellum, and incomplete cryoprotection with a small amount of CT-visible ice formation in the frontal lobes.

### 3. Patient Assessment and Pre-Deployment

The member was an 85-year old Caucasian male, 6'4" in height and weighing approximately 160 lbs. He had been diagnosed with Stage IV prostate cancer that had metastasized to his bones and lungs. While living with his daughter and ex-wife, he had been admitted into an in-home hospice program. The member had been on Alcor's Watch List for several months but failed to notify Alcor that he planned to end his life by using the newly enacted EOLOA (End of Life Option Act; <https://www.cdph.ca.gov/Programs/CHSI/Pages/End-of-Life-Option-Act.aspx>).

Monday, October 22, 2018

Alcor received a call from a northern California Alcor member who stated that his friend planned to use the EOLOA to legally end his life. He further stated that the member had received his aid-in-dying (AID) medications from the State of California and was planning to take those medications on Wednesday, October 24, 2018, just two days later.

This created a logistical problem for Alcor. It would be the first time an Alcor member used EOLOA in conjunction with their arrangements for cryopreservation. It was imperative that Alcor make sure the laws were followed exactly and two days was not enough time to do that proficiently. The member agreed to postpone taking his AID medications but only for a few days. Additional time would have given Alcor more confidence that no legal requirements had been overlooked.

### 4. Preparation and Deployment

Tuesday, October 23, 2018

There was extensive discussion on Slack (Alcor's internal communication system for the team members) about making sure that all legalities were handled properly and sufficiently. That included having Suspended Animation (SA) do the Standby, Stabilization and Transport (SST) since this case took place in California and having Alcor's new Medical Response Director (MRD) involved for additional training and experience. It was also decided that the MRD would deploy the next day to evaluate the situation and the member's condition and to collect Health Insurance Portability and Accountability Act (HIPAA), Advance Directive and end of life paperwork.

There was also discussion about how to best time the arrival of SA with the member taking his prescribed AID medications, the fact that SA and Alcor personnel could not be in the room with the member when he took the AID medications, and how long after ingestion before the medications would take effect. Several northern California Alcor members volunteered to assist with this case. Alcor's MRD spoke with the family in an attempt to get a signed HIPAA form to enable Alcor to obtain the member's medical records and to ensure that the member was fully compliant with the legal requirements pertaining to the EOLOA legislation.

Wednesday, October 24, 2018

Alcor's Chief Medical Advisor (CMA) sent two citations to the team, one of which was the legislation itself and the other contained two required forms. There was a discussion about the need to acquire: 1) a signed form from the two physicians who confirmed that they interviewed the member and approved him to use the EOLOA, 2) documentation that the member had made two requests 15 days apart, and 3) documentation from the physician who prescribed the AID medications.

The member had earlier planned to take the AID medications on Thursday, November 01, 2018, but had gone for blood work that morning and had a near-syncopal episode. That caused him to become agitated and he voiced his desire to take his AID medications earlier than planned. His family gave him some prescribed Dilaudid for his pain which subsequently calmed him and allowed him to sleep.

Alcor's CMA requested information about the member's then current pain medication and dose, requested a phone number for hospice and asked if a signed HIPAA form was in place so that he could speak with them. The MRD was still en route to California but replied that as soon as he got off the plane, he would try to get more information; the hospice staff was supposed to have gotten the HIPAA form signed the previous day.

SA requested contact information for the member's physicians as this would be needed in order to expedite the death certificate and the transit permit. They also requested a copy of any form to be signed by the designated power of attorney (DPOA).

The MRD arrived at the member's home that afternoon and met with the member and his ex-wife. They spoke briefly as the hospice nurse (RN) and the home health aide (HHA) were changing the member's dressings on two kidney shunts. One of the shunts was constantly draining and caused him discomfort.

There was a discussion between the RN, the HHA and the family about the member's Dilaudid, how much he could receive over each four-hour period and the importance of maintaining the narcotic log, which had not been filled out prior to that conversation. All entries onto that log prior to October 24, 2018, at 15:00 hrs were an estimate of time and dosage. All entries after that were accurate for dosage and administration time. The hospice RN gave the MRD a copy of the Authorization for Use and/or Disclosure of Member/Patient Health Information form.

During this meeting with the family, several outstanding concerns were addressed regarding the AID medications. The main concern was that the member had no access to any of his medications. He also needed to, per the laws of the State of California, provide a 48-hour notice prior to ingesting the AID medications and he needed to sign a letter of attestation stating that he was of sound mind and body. The law stipulated that no food and only a little liquid was to be ingested within 12 hours of taking the AID medications. The member had chosen the following AID protocol: diazepam 1 gram (to relieve anxiety), digoxin 50 mg (to decrease HR), morphine 15 grams (to relieve pain) and propranolol 2 grams (to decrease HR).

That same afternoon SA had spoken with the San Jose coroner's office and because the member was in home hospice the case would not go to the coroner as long as all the proper documentation was on hand, the member's physician had signed the death certificate, and the designated Power of Attorney (DPOA) had signed off to release the remains to Alcor.

The member's daughter was identified as being the DPOA, which was helpful with making various aspects of this case come together well.

Alcor's CMA worked with the hospice staff to better control the member's pain. Concurrently, Alcor staff urged the SST team to inform Alcor and all team members as soon as a time and date were chosen by the member and his family for ingestion of the AID medications.

There were planning discussions about which air ambulance company to use and the type of aircraft to use. There was also a discussion about whether or not to do the neuroseparation in California or wait until the patient arrived in Arizona. It was decided that except for unforeseen circumstances there would be no need to do the procedure in California.

#### Thursday, October 25, 2018

The MRD spent many hours working to obtain the needed HIPAA and EOLOA paperwork. In spite of being given inappropriate paperwork and being sent to incorrect locations, requiring additional trips, he finally accomplished the task. Upon returning to the member's home he found that the member had gone to the emergency department (ED) to have a draining shunt repaired. The member was comfortable and had no pain that morning. The hospice RN supervisor told the MRD that the AID medications should take effect within an hour after ingestion and hospice could be called to pronounce as soon as the member ingested the medications.

That afternoon there had been no change in the member's plan to ingest the medications on Monday, which was four days away. Once all the paperwork was in hand and verified, Alcor could then officially call a deployment that would give SA ample time to deploy.

#### Friday, October 26, 2018

That afternoon the MRD received documents from the hospice and there was extensive discussion on Slack about being sure that all the required paperwork had been gathered, who could act as witnesses, whether family members with an interest in the member's will could witness, and if not, that disinterested local Alcor members could fill that role.

#### Saturday, October 27, 2018

SA confirmed that their contract surgeon and perfusionist were flying to California on Sunday afternoon, and SA team members would drive from southern California to northern California in their mobile operating vehicle (MOV) on Sunday.

Alcor reminded the team that a video recording was needed that showed that no one from Alcor or

SA was in the room with the member when he took the AID medications and not before he was pronounced legally dead. There was also a discussion about making sure all details were covered for obtaining the death certificate and moving the member from California to Arizona.

The member's ex-wife had asked the member to delay his ingestion of the AID medications since he was having less pain; the member was considering the request. That evening the member's daughter told the team that the date of ingestion had been officially changed from Monday to Tuesday. SA moved the arrival of the surgeon and perfusionist from Sunday to Monday.

#### Sunday, October 28, 2018

The member had slept well the previous night with little discomfort and was in good spirits. The member was still planning to take the EOL medications on Tuesday.

#### Monday, October 29, 2018

SA confirmed in the morning that they were leaving their southern California facility and on their way to the member's location. Stabilization operations were still scheduled for Tuesday. The MRD had spoken with the hospice supervisor; she informed him that due to a mandatory meeting from 9:00 hrs to 11:30 hrs on Tuesday no one from hospice would be able to respond and pronounce during that time frame. The MRD got the name of the hospice physician that would be on duty and forwarded that to SA as well as to the member's family. The member's daughter informed the MRD that she had informed her father about the time constraints and he planned to take his medications at 11:00 hrs on Tuesday.

Hospice personnel had made assurances that they were going to cooperate in every way possible. The CMA advised the team that the law specified that in cases using the EOLOA, for statistical purposes the death certificate should *not* state that the cause of death was either homicide or suicide. He asked that the physicians be advised of this since this legislation in California was new and the member's physicians may not already be aware of this.

### **5. Standby**

SA reported that they had just arrived in Mountain View and were with Alcor's MRD. Alcor's Arizona mortician had been updated on the status of this case and his staff was ready.

#### Tuesday, October 30, 2018

The MRD reported at 08:12 hrs that they were on schedule for medication ingestion at 11:00 hrs. The air ambulance had been scheduled to depart from Moffett Field. SA began setting up their equipment and drawing up the medications in preparation for the stabilization procedure.

The Alcor MRD and the SA team arrived at the member's house at 09:48 hrs. They set up the stabilization equipment in a part of the home separate from where the member was located. There was a locked door between the team and the patient. The rectal occluder and the nasopharyngeal wax were not in the vehicle and therefore not available to use on this patient.

Alcor's CMA instructed the team at 10:01 hrs that propofol, a standard part of the stabilization medications, would not be needed in this case since the AID drugs would accomplish the reduction in cerebral metabolism and suggested that the stabilization protocol begin with the infusion of sodium citrate or heparin. SA agreed to make the change to the protocol. At 10:30 hrs the member's friend informed the team that the member had taken a dose of Zofran which was to prevent the possibility of vomiting once the AID medications were ingested.

At approximately 11:20 hrs the MRD, SA and the hospice RN reviewed Alcor's post-mortem procedures and verified that all necessary paperwork was in place. Once the hospice staff was satisfied that the documentation was all in order, they said they would send a nurse out to the patient's bedside to pronounce. This information was relayed to the family. At 11:30 hrs the AID medications were administered by the family.

At 11:50 hrs the member's friend informed the team that the member had taken his AID medications. An hour later no hospice nurse had yet arrived; they were one hour into the wait and there was no update yet from the family. Shortly thereafter the hospice nurse arrived at the house. The member was still breathing but unresponsive. The hospice nurse reported that there was no blood pressure, respirations were shallow, and the heart rate was low.

## 6. Stabilization

The member was pronounced at 13:14 hrs. After the family left the patient's room, using his bed sheet, the team lifted the patient and carried him into the garage; the doors between the team and the family were closed behind the team. The patient was placed into the portable ice bath (PIB).

Ice was placed around the patient's head and over his body. At 13:20 hrs, the AutoPulse mechanical chest compression device was turned on to circulate the medications through the vasculature. The mask of the surface conduction cooling device (SCCD) was placed over the patient's face at 13:21 hrs to increase cooling efficiency.

Concurrently, #9 nasopharyngeal temperature (NPT) probes were placed in the patient's left and right nares along with therapy putty in lieu of the missing nasal wax, and an intraosseous (IO) needle was placed in the left tibial tuberosity for infusion of the stabilization medications. At 13:23 hrs the endotracheal tube was placed and ventilation was initiated. At 13:27 hrs the patient was covered with additional crushed ice and the portable ice bath was moved to the mobile operating vehicle (MOV).

All the stabilization medications were infused between 13:30 hrs and 13:44 hrs (see the below Table of Medications Administered for the specific medications and the times of infusion).

Upon administering the first medication into the IO line, it was noticed that there was substantial resistance. A second IO line was placed in the same area. This line too was not adequately infusing the medications. A third IO was placed into the left humeral head and flushed to ensure patency. At 13:44 hrs all the high-volume medications had been infused.

While transferring the patient to the MOV, and due to the steep incline on which the vehicle was parked in the driveway, the patient shifted in the ice bath during transport causing the AutoPulse to shut off briefly. Manual cardiopulmonary support was initiated until the Autopulse could be restarted two minutes later. During transport in the MOV to a location away from the patient's home, topical cooling, ventilation and cardiopulmonary support were continued.

## 7. Field Surgery and Washout

The contract surgeon and perfusionist were in the MOV and ready to begin the cardiopulmonary bypass procedure when the patient arrived. The procedure was performed with the patient in the portable ice bath with the SCCD pump and face mask running, but cardiopulmonary support was discontinued at 13:50 hrs. The NPT in the right nare was 25.8°C and in the left nare, it was 27.3°C.

Per the reports from the contract surgeon and the perfusionist, the chest was prepped and sterile drapes were placed. A standard median sternotomy incision was made at 13:55 hrs and deepened to the level of the sternum, which was divided with an oscillating saw. The pericardium was opened and the cardiac structures were noted to appear grossly normal. Purse-string sutures of 2-0 Prolene were placed in the distal ascending aorta and the right atrial appendage, and appropriate small cannulae were inserted and connected to the cardiopulmonary bypass circuit at 14:12 hrs.

Flow was initiated immediately, and streptokinase was infused during the open circuit washout three minutes later. Cooling continued until the patient reached an eventual NPT of 4°C to 5°C. A good washout resulted, although there remained a faint tinge of blood in the effluent.

At this point, SA received an email from the southern California funeral home with an attached death certificate and transit permit. With these two documents obtained, the member would have no obstacles to transport.

The closed-circuit perfusion was initiated at 14:26 hrs. The remainder of the Vital-Oxy was added to the closed circuit. The closed-circuit procedure was terminated at 14:59 hrs and took 33 minutes. The highest flow rate was 2.3 L/min.

The cannulae were removed and the cannulation sites were oversewn. The sternum was closed with two #5 stainless steel wires. The subcutaneous tissues were closed with running 2-0 Vicryl, followed by staples for the skin.

## 8. Transport

At 15:43 hrs the team departed for Moffett Field where the private air ambulance was waiting. The patient and team arrived within 15 minutes. During transit, double-bagged water ice had been placed around the patient's head for cooling during air transport. Upon arrival at the airfield, the SCCD pump was turned off and the mask was removed.

The patient was moved from the PIB to a body bag and double-bagged water ice was placed around the patient's head. While transporting the member to the body bag it was noted that there was a heavy-duty body bag missing that would normally be used to prevent leakage from the ice bags. Since ice bags were only placed around the member's head, instead of around the whole body, there was no leakage during transport.

The patient was officially handed off to Alcor's MRD and the patient was loaded into the aircraft to be transported to Alcor in Scottsdale, AZ. Arrival time was estimated to be approximately two hours later. The SA team returned to their California facility.

Alcor staff met the plane upon arrival in Scottsdale. The patient was offloaded from the aircraft onto a gurney and then loaded into Alcor's rescue vehicle and secured. The team was approximately one minute from Alcor.

## 9. Cryoprotective Surgery

In preparation for the arrival of the patient, the OR staff connected and checked out the perfusion circuit and the data being sent to the large wall screen in the operating room (OR). Upon checking out the cephalic enclosure, the red rubber Robinson catheters had not been clamped off when placed into the box. Approximately 30 mL of B1 perfusate was lost into the packaging when the pump was again switched on.

The pump and circuit were working properly and the B1 bladder was switched to recirculation to await the arrival of the patient. The back pressure on the pump was 7 psi; the flow rate was high at nearly 300 mL/min. Alcor's surgeon arrived in the OR and started to prepare the surgical table.

The patient was brought into the OR at 18:28 hrs. No stress loops had been used for the temperature probes when stapled in place. The OR cameras were turned on. The patient's head and shoulders were raised with a 12" polyethylene support. The NPT probe was attached to the data acquisition system at 18:31 hrs and the initial NPT was 4.4°C.

The patient's face was marked designating the left and right sides to prevent errors once the cephalon was placed into the cephalic enclosure. The easily accessible portion of the patient's head was shaved and incisions were made in the scalp for the burr holes. At 18:38 hrs the first incision was made to identify and raise the carotid arteries. The left carotid artery was isolated first, cut and tied off, then the right carotid artery was isolated, cut and tied off.

Concurrently with the surgery to raise the carotid arteries, the burr holes were made using a Codman perforator that was cooled with normal saline. While drilling the left burr hole the perforator clutch stopped before the burr hole was sufficiently deep. Several minutes were spent trying to correct the problem before others in the OR were available to help. Additional skin was cleared from around the burr holes in order to make them deeper and success was obtained when a slower speed setting and more pressure was used.

Using an osteotome and mallet, the vertebra was incised and the cephalic separation was completed at 18:51 hrs. The cephalon weighed 5.56 kg (12.26 lbs.). The cephalon was placed in the cephalic halo and it was observed that the vertebral arteries were large and visible. The NPT probes were again connected to the data acquisition system.

The surgeon trimmed the catheter and placed a purse-string in the right carotid artery using 3.0 silk. The main pump was started at 83 rpm in order to fill the catheters with B1 perfusate. The right carotid artery was cannulated with an 18 Fr red Robinson catheter and tied off. An additional purse-string was placed to better secure the catheter. Open circuit perfusion was initiated at 19:01 hrs, the NPT was 5.0°C.

The left carotid artery was cannulated with an 18 Fr red Robinson catheter and a 3.0 silk purse-string was placed to secure the cannula. The catheter was filled with B1 perfusate and the cannulation of the left carotid artery was tied off.

Perfusion was clamped off and was held at 80 mmHg and 59 rpm (210 mL/min). The right sampling line was secured and cryoprotective surgery was complete at 19:19 hrs.

## 10. Cryoprotectant Perfusion

At 19:19 hrs the cryoprotective ramp was initiated using nM22 perfusate; the NPT was 2.5°C. The starting ramp pump speed was set to 15 (~20 mL/min). The mixing reservoir volume was 1.01 L. The left sampling line was secured and the cephalon was rotated in the cephalic enclosure to provide better flow. Both vertebral arteries were clamped off. The brain retraction detection device (BRDD) was placed in the right burr hole.

The main pump rate was over 300 mL/min, the mixing reservoir volume was 1.1 L, and the refractive readings were noted to be increasing (see the Cryoprotection graph at the end of this report).

The cephalic enclosure was closed, cleaning of the OR was begun, and the remains were prepared for pickup by the funeral home.

At 19:42 hrs the mixing reservoir volume was 1.25 L and two minutes later the arterial pressure was dropped to 70 mmHg, the main pump was still running at 94 rpm (335mL/min) and the main pump pressure 9.5 psi. A few minutes later it was noted that the sampling system was not drawing air bubbles as is normal.

Ten minutes later, the mixing reservoir volume was 1.44 L, the main pump speed was 100 rpm (356 mL/min). The perfusate concentration in the right venous sampling line was 14.5 Brix and in the left venous sampling line, it was 15.3 Brix. Three minutes later the right venous concentration was 15.3 Brix and the left venous was 15.9 Brix.

At about the same time the ramp pump rate was approximately 16, the arterial concentration was 19.3 Brix. The patient's face had started to darken uniformly, the patient's vasculature was large and open resulting in rapid perfusion, but the corneas and eyeballs had not yet been affected.

Perfusate was flowing forcefully from the neck stump at 20:06 hrs. The arterial perfusion was turned down to a pressure of 50 mmHg. The cephalic enclosure was opened, and the affected vessels were clamped with a hemostat. The enclosure lid was put back in place.

The left burr hole edges were cleaned away at 20:20 hrs with a rongeur to insert the borescope camera to photograph the brain surface. The borescope camera was placed in the burr hole and the bottom of the brain casing could be seen.

The brain had continued to shrink (see Brain Shrink Distance and Perfusate Concentration graph at the end of this report) and it was noted that the skin was uniformly tanned, but the eyeballs had not yet shrunken. All systems were functioning properly.

*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 neuroperfusion box and the chiller are switched from +3°C to -3°C operation. 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, hopefully, the goal is obtained.*

At 21:18 hrs the ramp pump was stopped for the standard 30-minute pause because the nM22 concentration was over 30 Brix in both the left and the right venous sampling lines. The arterial refractive index reading was 32.7 Brix, the right jugular was 30.1 Brix and the left jugular was 30.5 Brix. The ramp was turned off and the cephalic enclosure and the main chiller were both set to -3°C. The mixing reservoir volume was lowered from 1.76 L to 1.2 L because the reservoir was too full to start the ramp at the end of the 30-minute pause.

The borescope camera was used to look into the burr hole. Substantial brain retraction was observed. The main pump pressure was 29 psi, the main pump output pressure was 5.5 psi and the arterial pressures was 50 mmHg. A second filter was brought into the system.

The 30-minute pause was ended at 21:48 hrs. The ramp pump was turned on full at speed 92 (330 mL/min). A normal amount of foam was observed in the mixing reservoir.

At 21:51 hrs the right cornea had collapsed from dehydration of the eye. (This is a normal response to cryoprotective perfusion.) It was noted that both times when the cephalic enclosure was opened to observe the brain through the borescope camera, the BRDD reading fluctuated with a spike.

The flow slowed due to the pump speed declining. The arterial pressure was increased to 60 mmHg. The chiller temperature was changed to  $-2^{\circ}\text{C}$  to increase cooling.

The arterial refractive index reading was 51 Brix. The ramp pump was stopped and started several times to compensate for latency. Cleanup of the surgical instruments was begun and the setup of the cooldown system was started. The ramp pump was turned off at 52 Brix arterial. The right venous concentration was 47.45 Brix and the left venous was 48.23 Brix.

At 22:48 hrs the left cornea had not collapsed, it was even somewhat convex. Measurements were made to ensure the cephalon would fit into the neuro can.

The 30-minute countdown to termination of perfusion was started at 23:09 hrs, holding between the limits of 52 to 55 Brix and compensating for latency. Cryoprotective perfusion was terminated at 23:41 hrs. The arterial refractive index reading was 51.96 Brix, the right venous was 51.00 Brix and the left venous was 50.73 Brix.

*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.*

At 23:43 hrs, in preparation for moving the cephalon into the patient care bay for cooldown, the catheters were cut and it was noted that the left eyeball had become more convex. It was also noted that the right sampling line was about 2" into the right jugular vein and the left sampling line was about 1.25" into the left jugular vein. A hole was drilled and an eyebolt was put into the vertebra stump for handling the cephalon and the rest of the monitoring lines were removed.

The borescope camera was inserted one last time for photos of the brain. The overhead surgical camera was found to not be functioning but after viewing the video, all critical operations had been captured. A card failure had caused the camera to malfunction.

At 23:52 hrs the cephalon was removed from the halo. The weight of the cephalon was 4.425 kg and the weight loss was  $(5.56 - 4.425) = 1.135$  kg.

The cooldown Dewar was precooled with liquid nitrogen ( $\text{LN}_2$ ). The thermocouple extension was connected and the cephalon was lowered into the precooled dewar. The thermocouple probes were taped to the side of the cooldown dewar and the lid was put in place. The lines were connected to the cooldown computer and the lid was secured with duct tape. The cooldown dewar was connected to the  $\text{LN}_2$  source and the  $\text{LN}_2$  was turned on.

## 11. Cooling to Liquid Nitrogen Temperature

The computer program “Cryoprotected Neuro” was initiated and cooldown was initiated at 23:59 hrs on October 30, 2018, plunging to  $-110^{\circ}\text{C}$  and descending thereafter at  $-1^{\circ}\text{C}/\text{hour}$  to  $\text{LN}_2$  temperature. On November 4, 2018, an uneventful cooldown was terminated. On November 15, 2018, the patient was transferred to long-term maintenance at  $\text{LN}_2$  temperature.

## 12. Timeline and Time Summaries

### October 30, 2018

- 13:14 Pronouncement of legal death
- 13:20 Start of mechanical cardiopulmonary support
- 13:21 Start of ice bath cooling
- 13:21 Placement of the intraosseous device
- 13:23 Placement of an endotracheal tube
- 13:27 The patient was moved to SA’s mobile operating vehicle
- 13:30 Administration of the first medication (20 g sodium citrate)
- 13:50 Termination of cardiopulmonary support: right NPT =  $25.8^{\circ}\text{C}$ , left NPT =  $27.3^{\circ}\text{C}$
- 13:55 Start of field surgery
- 14:12 End of surgery and start of open circuit washout
- 14:26 Start of closed-circuit perfusion
- 14:27 Administration of the final medication (27 mL Vital-Oxy IV)
- 14:59 End of closed-circuit perfusion
- 15:43 Departure of transport vehicle to airport
- 18:28 Arrival of patient at Alcor; no NPTs with patient
- 18:31 NPT probes attached to data acquisition system; initial temp  $4.4^{\circ}\text{C}$

18:38 Start of surgery (burr holes, cannulation, vertebrals, sampling lines, cephalic isolation)

18:51 The cephalon weighed 5.56 kg when isolated

19:01 Open circuit started with B1; NPT 5.0°C

19:19 Completion of surgery

19:19 Start of cryoprotection; NPT 2.5°C

21:18 50% of concentration necessary for vitrification (CNV) achieved

23:09 Start of sub-zero terminal concentration ramp

23:41 Termination of cryoprotection; final Brix readings: arterial 51.96, right venous 51.00,  
left venous 50.73

23:52 The weight of the cephalon was 5.56 kg and the weight loss was  $(5.56 - 4.425) = 1.135$  kg.

23:59 Start of patient cryogenic cooldown

The patient reached LN<sub>2</sub> temperature and the cooldown ended November 4, 2018. The patient was transferred to long-term maintenance at LN<sub>2</sub> temperature on November 15, 2018.

## Time Summaries

### Stabilization

hrs: mins

00:06 From pronouncement to start of cardiopulmonary support: 13:14 to 13:20  
 00:16 From pronouncement to start of meds administration: 13:14 hrs to 13:30 hrs  
 00:57 From start to end of medication administration: 13:30 hrs to 14:27 hrs  
 05:14 From pronouncement to patient arrival at Alcor: 13:14 hrs to 18:28 hrs

### Field Surgery and Washout

hrs: mins

00:41 From pronouncement to start of surgery: 13:14 hrs to 13:55 hrs  
 00:16 From start of surgery to end of surgery: 13:55 hrs to 14:11 hrs  
 00:58 From pronouncement to start of washout: 13:14 hrs to 14:12 hrs  
 00:47 From start of washout to end of closed-circuit cooldown: 14:12 hrs to 14:59 hrs  
 01:45 From pronouncement to end of closed-circuit cooldown: 13:14 hrs to 14:59 hrs

### Cryoprotective Surgery

hrs:mins

00:10 From arrival at Alcor to the start of surgery: 18:28 hrs to 18:38 hrs  
 00:13 From start of surgery to end of the cephalic isolation: 18:38 hrs to 18:51 hrs  
 00:41 From the start of surgery to the start of the cryoprotective ramp: 18:38 hrs to 19:19 hrs  
 05:03 From the start of surgery to the end of the cryoprotective ramp: 18:38 hrs to 23:41hrs

### Cryoprotectant Perfusion

hrs:mins

04:22 From start to end of cryoprotective ramp: 19:19 hrs to 23:41 hrs  
 00:18 From the end of cryoprotective ramp to start of cooldown: 23:41 hrs to 23:59 hrs  
 05:31 From arrival at Alcor to the start of cooldown: 18:28 hrs to 23:59 hrs  
 10:45 From pronouncement to start of cooldown: 13:14 hrs to 23:59 hrs

### 13. Tables of Medications Administered and Temperatures

TIME	MEDICATION	DOSE	PURPOSE
13:30 hrs	Sodium citrate	65 mL (1st dose)	Anticoagulant; prevents blood clot formation.
13:32 hrs	Sodium citrate	65 mL (2nd dose)	Anticoagulant; prevents blood clot formation.
13:33 hrs	Sodium citrate	65 mL (3rd dose)	Anticoagulant; prevents blood clot formation.
13:35 hrs	Heparin	50,000 IU	Anticoagulant; prevents blood clot formation.
13:36 hrs	Vasopressin (first dose)	40 IU	Vasopressor; increases blood pressure during CPS.
13:37 hrs	SMT (S-methyl-isothiourrea)	400 mg	Neuroprotectant (iNOS inhibitor); protects the brain from ischemic injury; raises blood pressure.
13:37 hrs	Minocycline	200 mg	Antibiotic; reduces microbial overgrowth during long transport times.
13:37 hrs	Decaglycerol/THAM [tris(hydroxymethyl) aminomethane]	60 mL (1st dose)	Decaglycerol inhibits cerebral edema. THAM is a buffer to mitigate acidosis.
13:38 hrs	Decaglycerol/THAM [tris(hydroxymethyl) aminomethane]	60 mL (2nd dose)	Decaglycerol inhibits cerebral edema. THAM is a buffer to mitigate acidosis.
13:39 hrs	Decaglycerol/THAM [tris(hydroxymethyl) aminomethane]	60 mL (3rd dose)	Decaglycerol inhibits cerebral edema. THAM is a buffer to mitigate acidosis.
13:40 hrs	Decaglycerol/THAM [tris(hydroxymethyl) aminomethane]	60 mL (4th dose)	Decaglycerol inhibits cerebral edema. THAM is a buffer to mitigate acidosis.
13:41 hrs	Decaglycerol/THAM [tris(hydroxymethyl) aminomethane]	60 mL (5th dose)	Decaglycerol inhibits cerebral edema. THAM is a buffer to mitigate acidosis.
13:41 hrs	Decaglycerol/THAM [tris(hydroxymethyl) aminomethane]	60 mL (6th dose)	Decaglycerol inhibits cerebral edema. THAM is a buffer to mitigate acidosis.
13:42 hrs	Decaglycerol/THAM [tris(hydroxymethyl) aminomethane]	40 mL (7th dose)	Decaglycerol inhibits cerebral edema. THAM is a buffer to mitigate acidosis.

13:43 hrs	Vasopressin (second dose)	40 IU	Vasopressor; increases blood pressure during CPS.
13:44 hrs	Vital Oxy	27 mL (1st dose)	Antioxidants: melatonin, vitamin E (D-alpha tocopherol), PBN (alpha Phenyl t-Butyl Nitron) and anti-inflammatory carprofen.
14:15 hrs	Streptokinase	250,000 IU	A thrombolytic used to break up existing blood clots. <i>This was added to the open circuit washout.</i>
14:27 hrs	Vital Oxy	27 mL (2nd dose)	Antioxidants: melatonin, vitamin E (D-alpha tocopherol), PBN (alpha Phenyl t-Butyl Nitron) and anti-inflammatory carprofen.

## Notes:

1. Per the recommendation of Alcor's Chief Medical Advisor, propofol was not administered.
2. Based on this patient's weight, 54 mL of Vital-Oxy were drawn up into a 250 mL IV saline bag. The first infusion was approximately 1/2 the total bag volume, so 27 mL of Vital-Oxy with 125 mL saline or 152 mL diluted Vital-Oxy/saline solution. The second was the same, 27 mL of Vital-Oxy with 125 mL saline or 152 mL diluted Vital-Oxy/saline solution into the closed-circuit perfusion. 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.
3. Hetastarch was not given as the patient was well hydrated.
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 20 grams of sodium citrate as per protocol because his weight was over 40 kg. The 20 grams was administered in three divided doses of 65 mL each with the extra solution volume provided by saline removed from a 250cc bag of sodium chloride to make room for the Vital-Oxy in the bag.
5. Decaglycerol/THAM is administered as a custom formulation of 20% w/v decaglycerol and 4.5% w/v THAM (tromethamine) in water.

**Table of Nasopharyngeal Temperatures during Field Surgery and Washout**

Time	Temp	Time	Temp	Time	Temp	Time	Temp
13:37	25.7°C R	14:11	23.0°C R	14:36	13.4°C R	14:51	5.2°C R
13:37	28.2°C L	14:11	24.0°C L	14:36	13.9°C L	14:51	7.5°C L
13:48	25.8°C R	14:19	21.5°C R	14:40	11.8°C R	14:53	5.2°C R
13:48	27.8°C L	14:19	21.7°C L	14:40	11.8°C L	14:53	7.5°C L
14:06	25.0°C R	14:33	15.8°C R	14:45	10.0°C R	14:54	4.4°C R
14:06	25.0°C L	14:33	14.6°C L	14:45	7.9°C L	14:54	5.3°C L

## 14. Discussion

### Transport

1. Two items of new equipment worked very well. First, the brain retraction detection device (BRDD) is now functional and providing useful information. The previously noticed brain re-expansion is no longer theoretical.

Second, the new gurney loading system engineered for use with the black Sprinter rescue vehicle also worked well. This is important when loading a portable ice bath with a patient and ice water into the back of the vehicle.

2. An important aspect of cryonics stabilization is that cardiopulmonary support (CPS) goes on for a long time, sometimes 60 minutes or more, before it is possible for logistical or temperature reasons to stop CPS before the surgery required for cooling by washout. This is especially true for Scottsdale cases. That differs from cardiopulmonary resuscitation (CPR) in which hopefully the patient can be defibrillated in only a few minutes. Prolonged CPS makes a cryonics patient analogous to an unconscious, living patient with a heartbeat (the heartbeat being the thumper that the patient is going to depend on for the next hour or more). It is just as important for a cryonics patient receiving CPS after a standby to have a patent airway as it is for a living patient.

### Perfusion

3. Three (instead of the usual one) filters were used both in this case and the one before it. In view of the filter loading and the fact that three filters were used, more blood should have been washed out. Also, the filter loading was not linear; the filters loaded up with more material in the jump to 100% concentration. The perfusate in the mixing reservoir remained cherry-red throughout the first half of the perfusion, clearing up only in the second half, probably due to massive dilution with the concentrate, so the loading and the color came from hemolyzed red blood cells that were still being released from the vasculature.

A better understanding of cellular release from the vascular system is needed. The protocol for field washout is for SA to use 30 L of MHP-2. Research should be done to determine whether more B1 solution is needed in the field, if additional B1 should be used for washout in the OR, or for both procedures.

4. At 19:42 hrs, during the cryoprotective perfusion, the mixing reservoir volume was 1.25 L and two minutes later the arterial pressure was dropped to 70 mmHg. It was speculated that the patient's vasculature was so unobstructed that the pump could not keep up. This situation had never been seen before. A few minutes later it was noted that the sampling system was not drawing air bubbles as is normal; this also could have been due to the fast flow rate.

5. The left burr hole edges were cleaned away at 20:20 hrs with a rongeur to insert the borescope camera to photograph the brain surface; this was the first time this equipment was experimentally used. The borescope camera was placed in the burr hole and the bottom of the brain casing could be seen.

6. At 21:51 hrs the right cornea had collapsed. It was noted that both times when the box was opened to observe the brain through the borescope camera, the BRDD reading fluctuated with a spike. This could have been the result of vibrations from handling the enclosure and the cephalon, but the reason is not definitively understood.

7. At approximately 21:51 hrs the box temperature controller appeared to be running at  $-7^{\circ}\text{C}$  rather than the  $-3^{\circ}\text{C}$  called for in the protocol. This was corrected before the next case. It was of no practical consequence because the freezing point of the cryoprotectant being perfused at that time

## 15. Issues & Actions

A debrief meeting was held on November 7, 2018, and attended by all persons involved in this case. The following issues and actions were identified.

### Standby, Stabilization, and Transport

#### **Mobile operating vehicle (MOV) not in a secure location**

The MOV was parked in a pharmacy parking lot while the blood substitution was done. This could have potentially become a negative and dangerous situation. In future cases, the Alcor Medical Response Director (MRD) or person in charge will arrange with prior permission to have the MOV parked either 1) in a medical facility parking lot, 2) a local mortician's parking lot, 3) some other private parking situation such as at the home or business of another Alcor member [in this instance, there were a lot of northern California members who would have been willing to assist and would have had appropriate parking locations], or 4) some other legal way or location for the mobile operating vehicle to be parked during surgery and washout procedures.

**Field kit not complete**

Three items were not in the field kit or in the mobile operating vehicle (MOV): the rectal occluder (necessitating field improvisation), wax for the nasopharyngeal probes, and a second heavy duty body bag. Always take time to ensure that the vehicle and/or all supplies are properly stocked and ready to go immediately after a case is concluded. The time to discover an item is missing is *not* when it is needed. A miscommunication between the team members about the location or existence of additional waste containers resulted in improper disposal of bio-hazardous waste. This resulted in part due to a new team member who lacked familiarity but who has since been further trained.

**Bone intraosseous (IO) gun not placed correctly**

The bone intraosseous (IO) gun was not placed correctly and had to be reset twice. The IO cannot be reset in the same extremity. Team members need frequent re-training of all skills. SA will make this a priority on their next annual recertification training.

**Successful establishment of an IO line by a new team member was verified by injection of 5 mL of ice bath water due to perceived lack of availability of saline.**

External team members unfamiliar with team procedures and supplies will be counseled to refrain from performing parenteral administration of agents unless at the specific direction of the team leader. Unless at the direction of Alcor's Chief Medical Advisor, team members will be counseled to never parenterally administer material that they would not administer to a legally living patient, including any non-sterile liquid.

**Miscommunication between Alcor and SA**

The hospice facility was not given the cryonics documents from Alcor until just before stabilization was to begin. This could have resulted in a delay in procedures. Due to miscommunication between Alcor and SA about who was in charge of this case and therefore who was responsible for providing the appropriate cryonics-related documents to the hospice personnel, the hospice legal department became involved at the last minute. In the future, the cryonics documentation must be delivered as early as possible and it will be the responsibility of the team leader of the team assigned the case to see that this is done.

**Water entered the patient's nose**

Some cooling water may have entered the nose before the endotracheal tube was placed. In future cases, start cardiopulmonary support (CPS), secure the airway and nasal temperature probe(s) before starting the surface conduction cooling device (SCCD).

## Field Washout

### **Surgeon Availability**

The timing of this case could have conflicted with the availability of our preferred surgeon. Alcor does have several back-up surgeons but they have not been used recently. Observation and training sessions will be set up so that in the event the preferred surgeon is not available, other surgeons can be called who have current training.

### **New nasopharyngeal plugs**

The nasopharyngeal plugs made of “therapy putty” worked well on this case. Alcor would like to use this putty instead of the “swimmer’s wax” currently being used. SA will send Alcor information to purchase this product.

## Cryoprotective Surgery and Perfusion

### **OR setup error**

When the red rubber Robinson catheters were placed in the cephalic halo during the OR setup, they were not clamped shut. When the pump was turned on during the testing of equipment prior to the arrival of the patient, approximately 30 mL of B1 was lost. This has been added to the OR Setup standard operating procedure to make sure these clamps are closed.

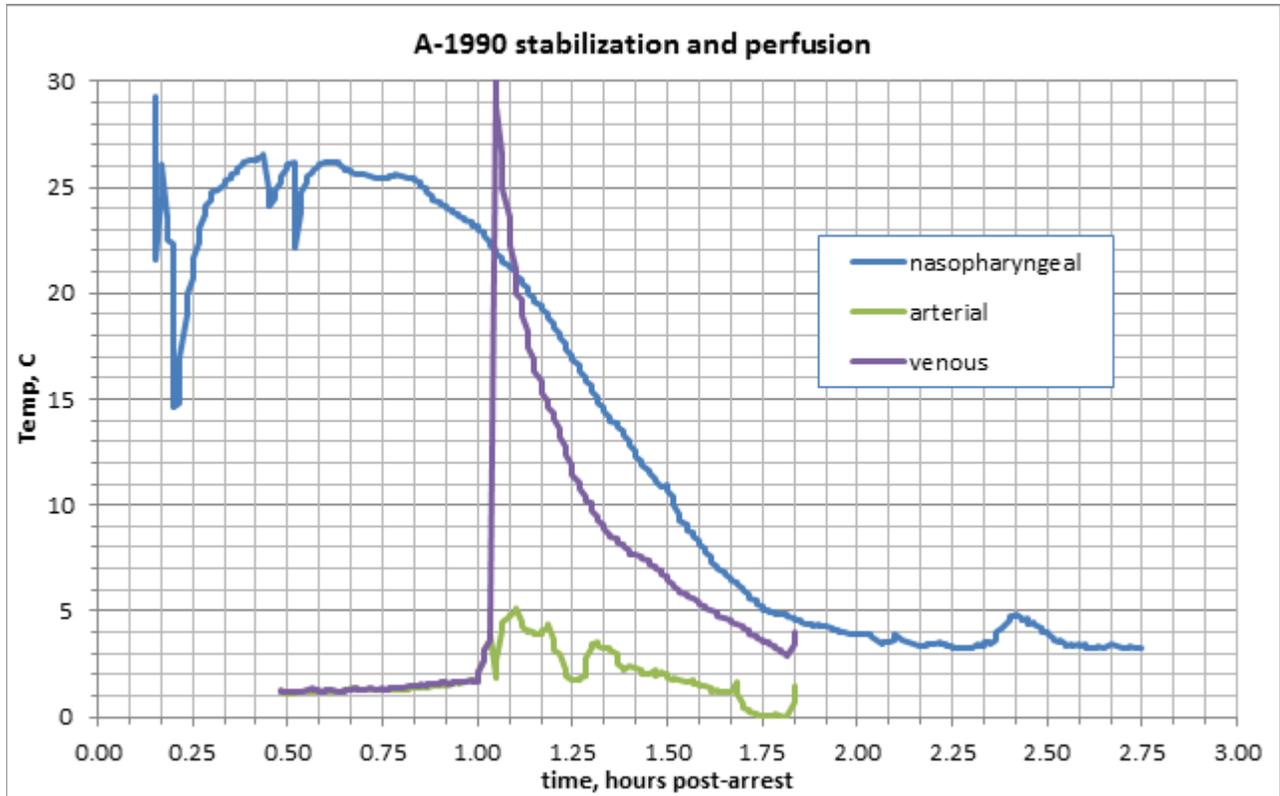
### **Perforator declutched**

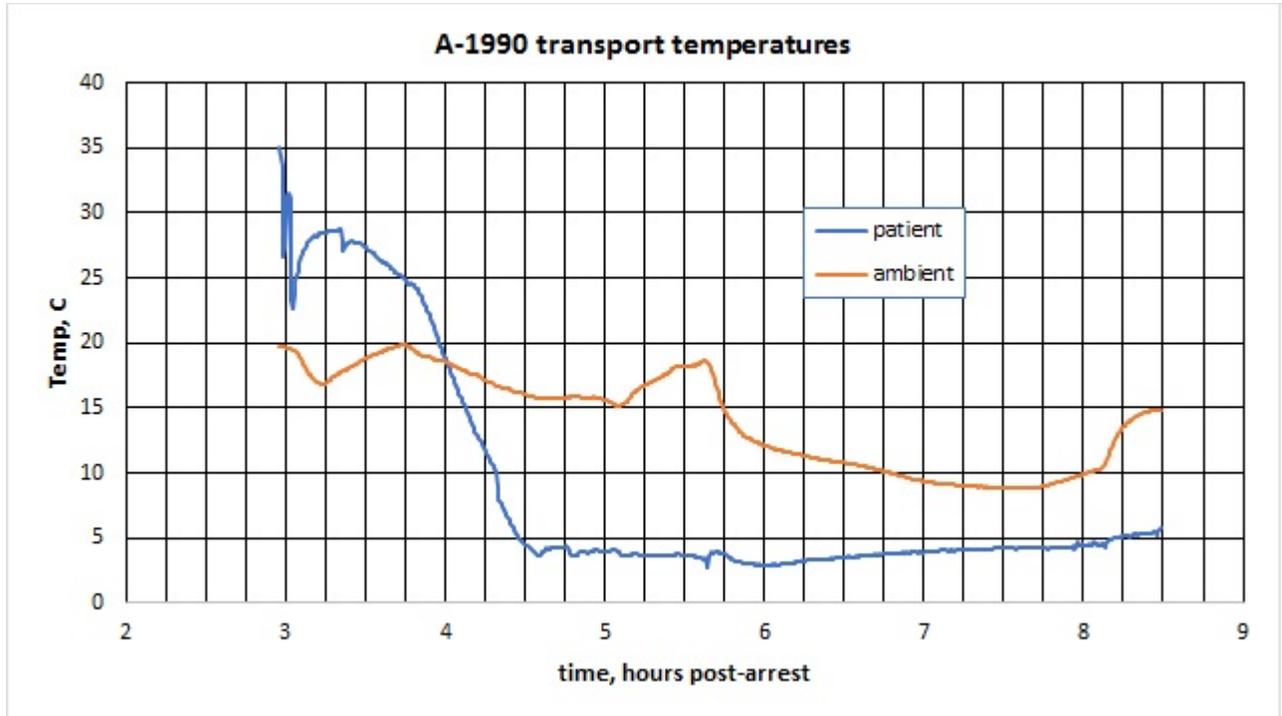
The clutch shut off the perforator before the burr hole was deep enough. Some finesse is required with this equipment. For best results, the user should push harder against the drill, use a lower speed and use a rocking motion.

### **Temperature controller malfunction**

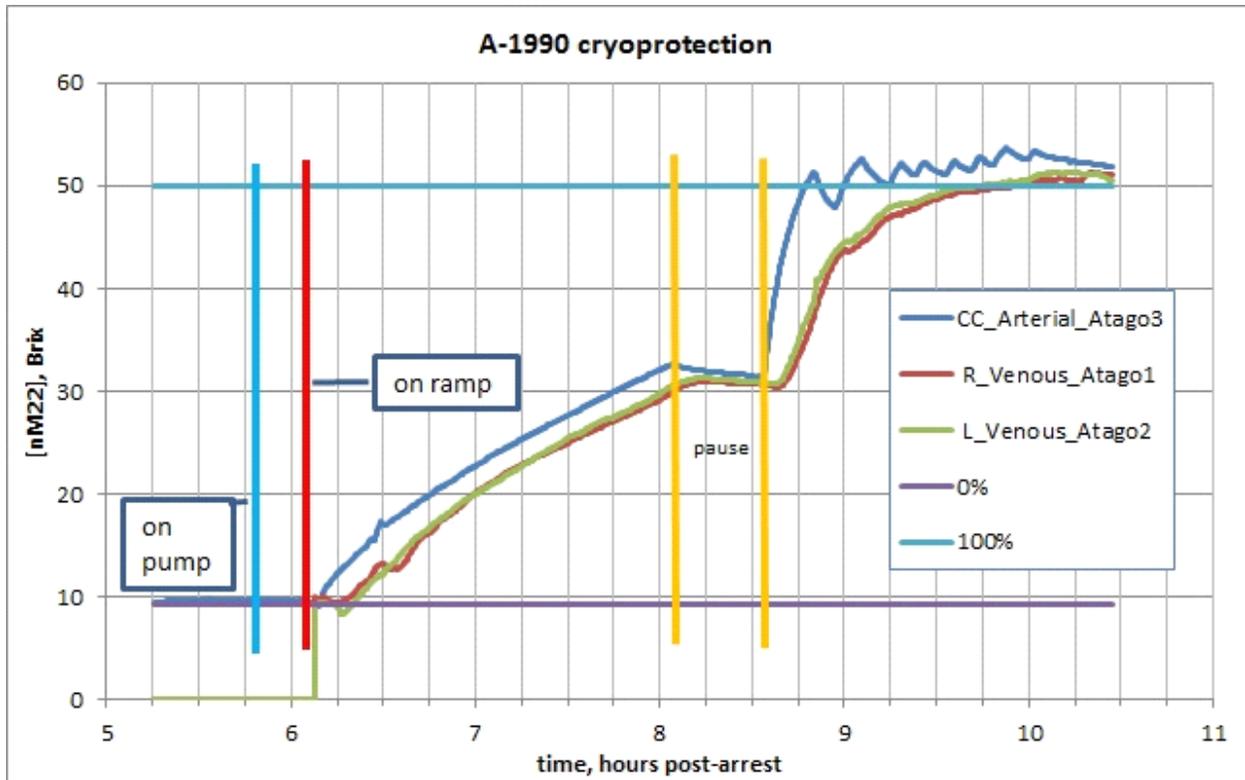
The cephalic box temperature controller appeared to be running at  $-7^{\circ}\text{C}$  rather than the protocol mandated  $-3^{\circ}\text{C}$ . The set point on the chiller will be corrected before the next case.

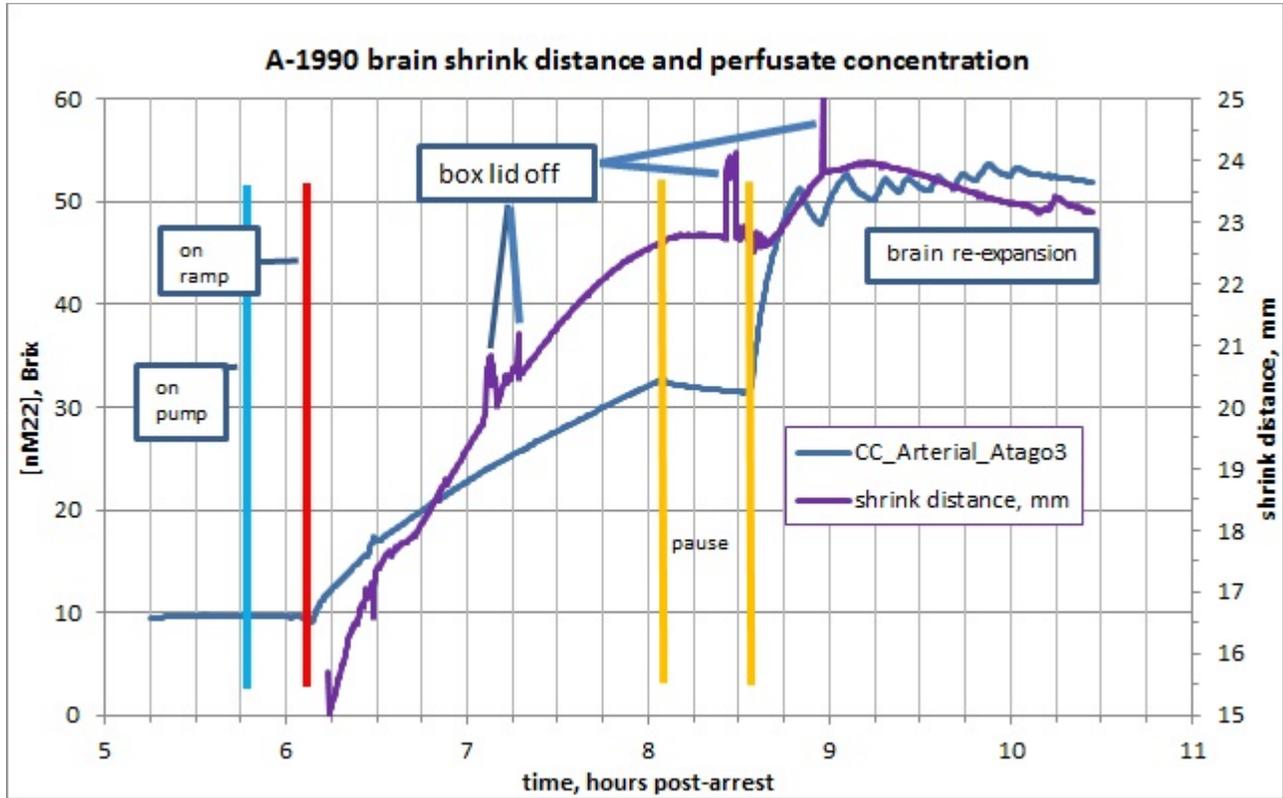
## 16. Graphs



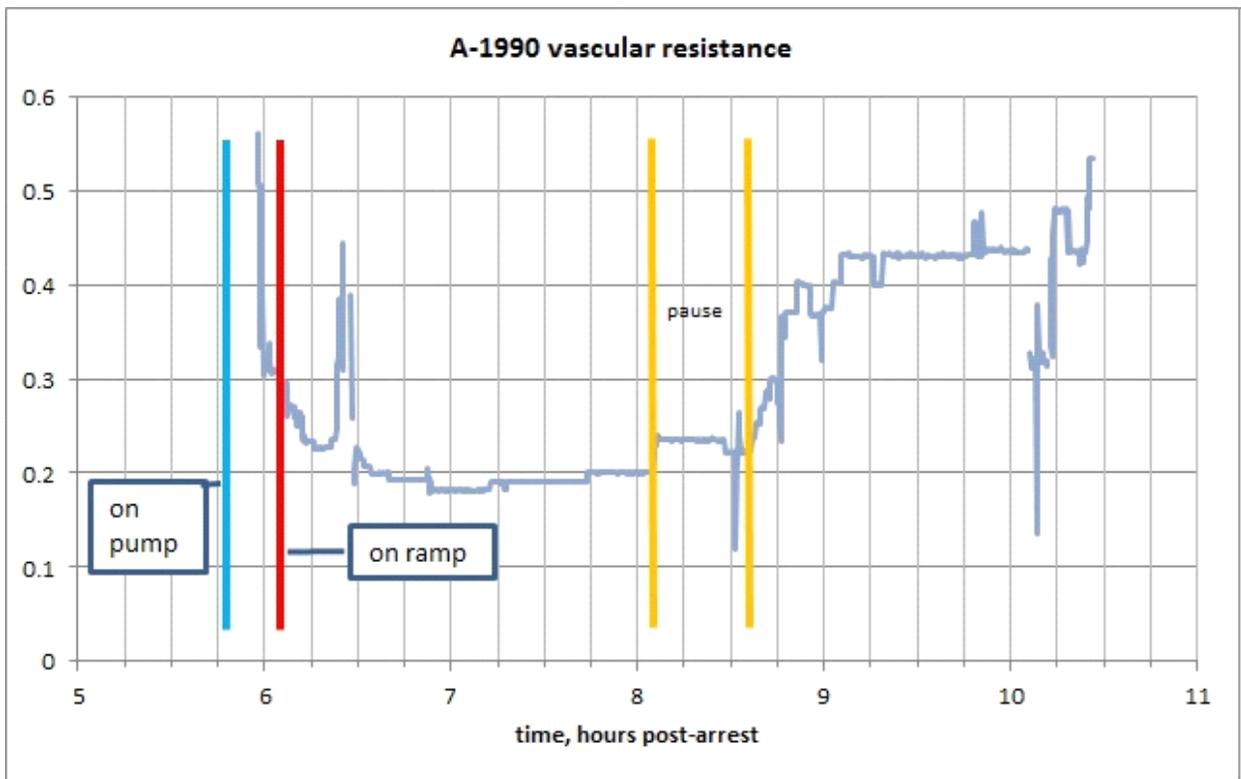
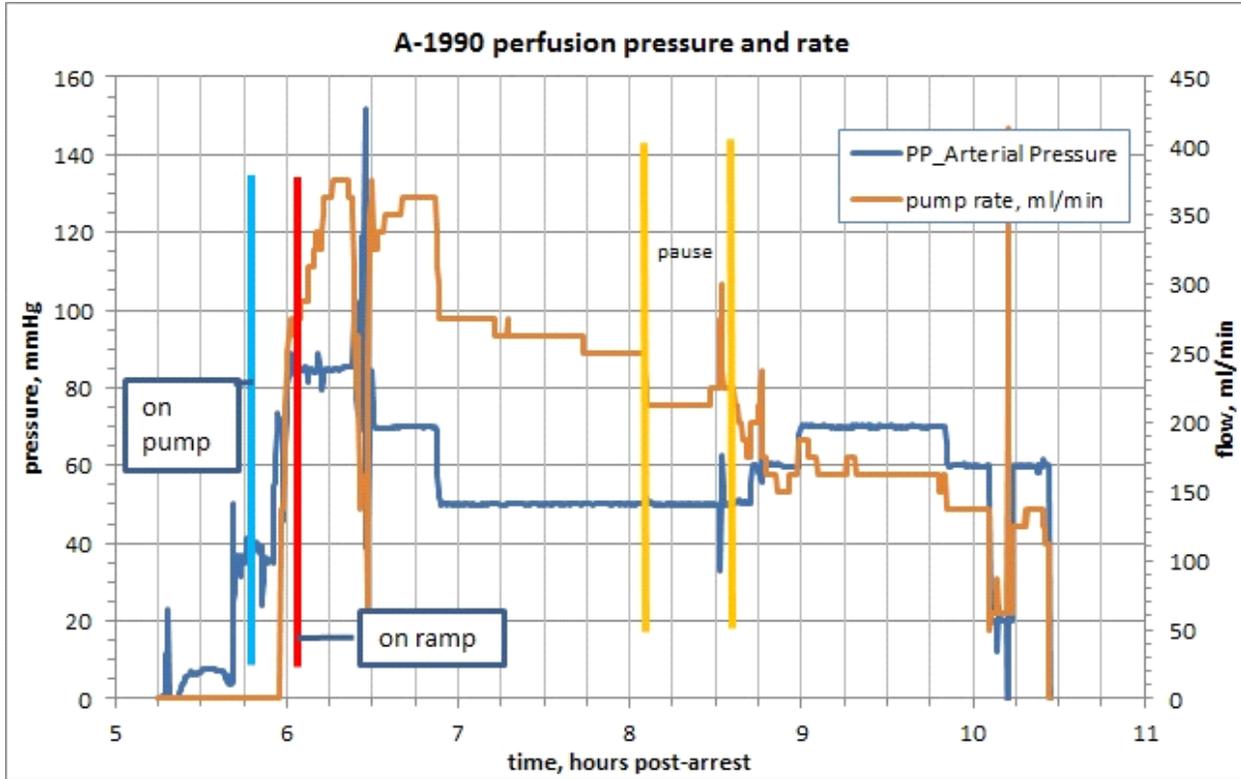


Note: The anomalously low nasopharyngeal temperature readings until 0.6 hrs post-arrest are believed to be due to ice water entering the nasal passages due to the absence of wax sealant normally used around the nasopharyngeal probe wire. The airway was protected by an endotracheal tube during this time. The venous and arterial temperature loggers are not activated until 30 minutes into the case to conserve battery life; data before priming the patient circuit for perfusion would be inconsequential.

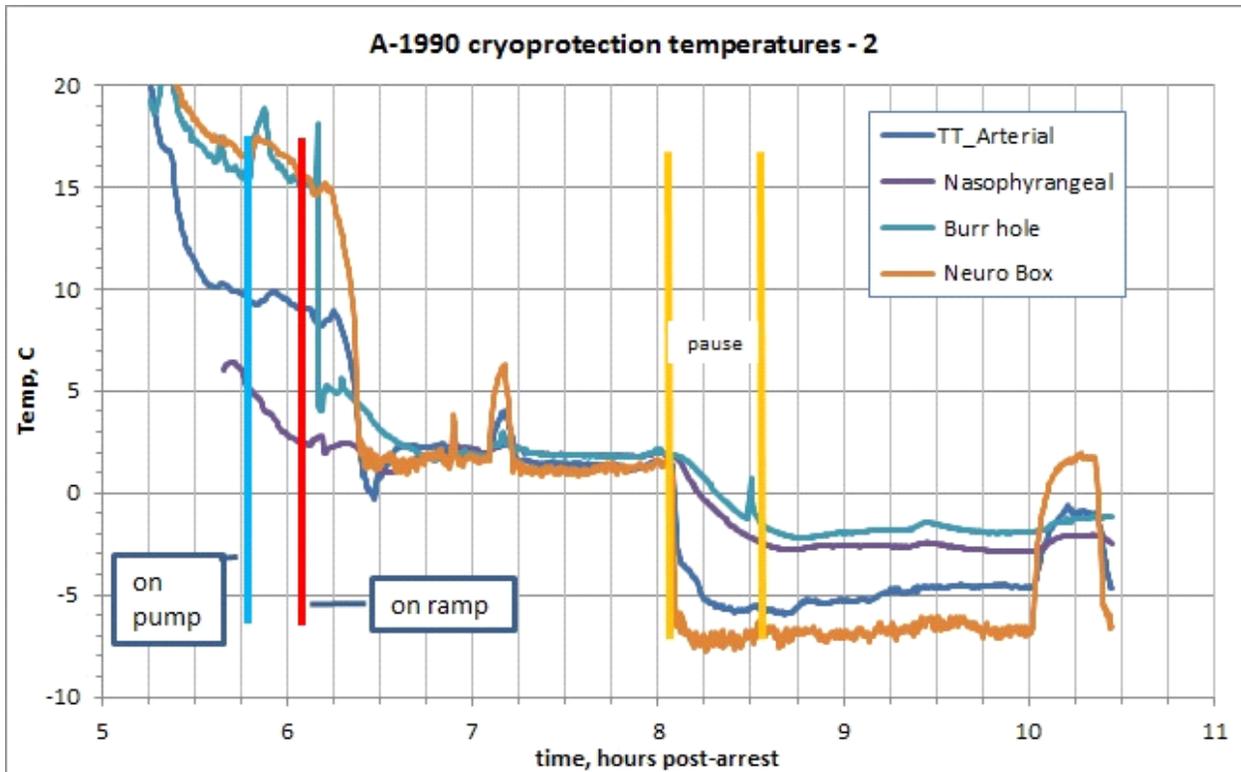
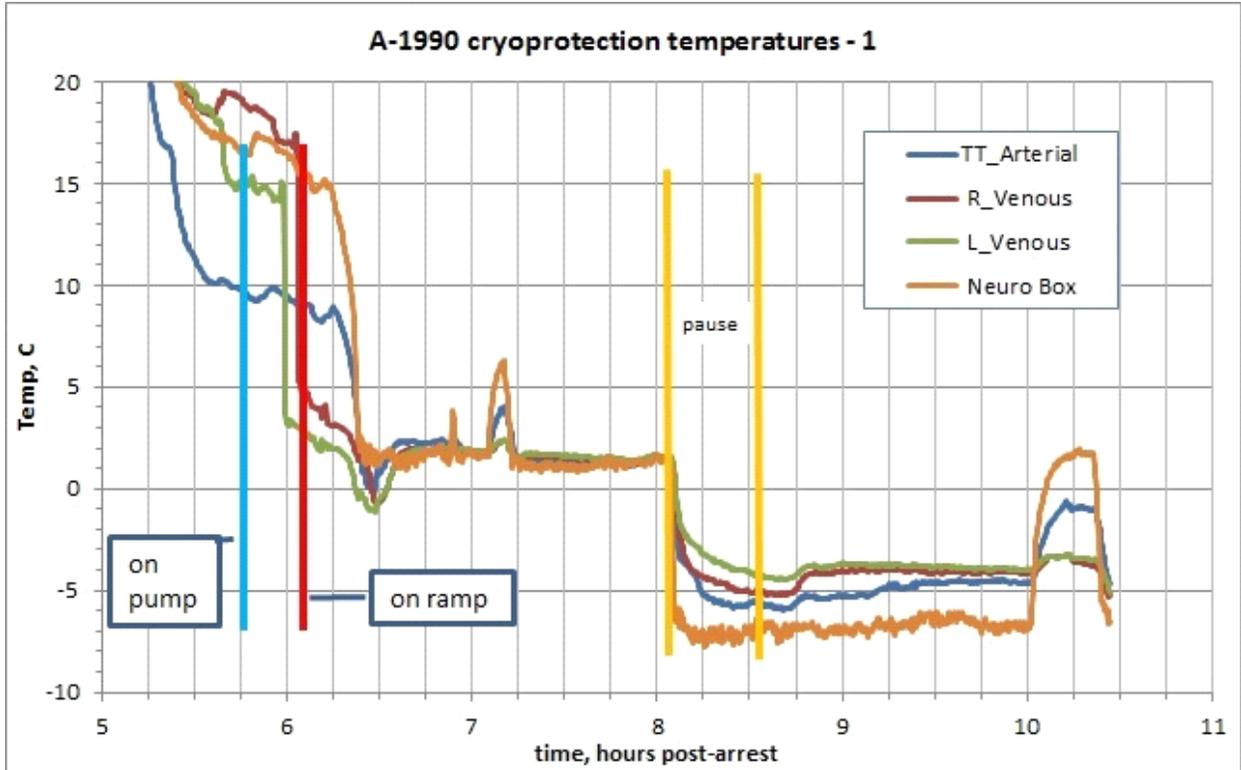


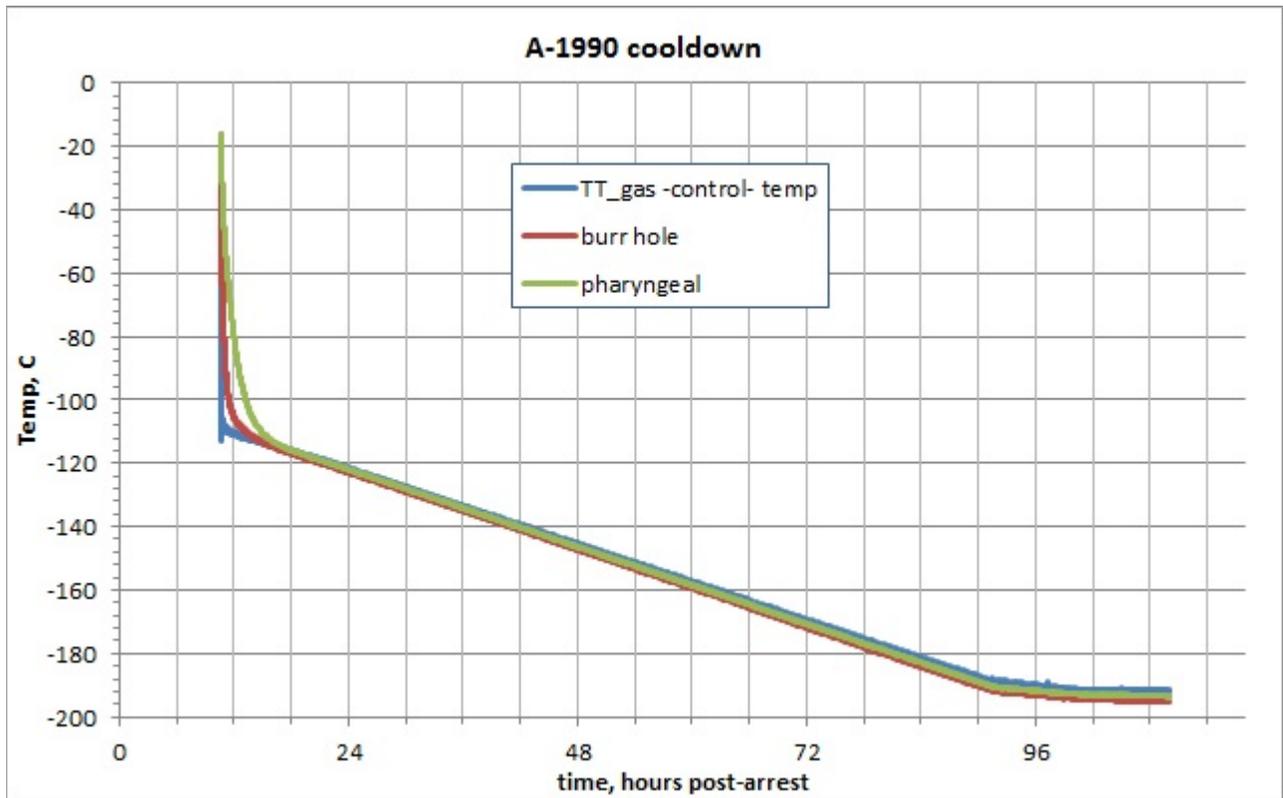


Note: Using a laser, the Brain Retraction Detection Device (BRDD) measures the contraction and expansion of the brain surface directly below a burr hole during cryoprotection. The output from the device is calibrated to derive a standardized reading in millimeters.



Note: pressure mmHg / flow mL/min





### Cryoprotectant Distribution (CT scan)

