Alcor A-1794
Internal Case

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Alcor A-1794 Case Report Contents:

1. Summary

Information was derived from multiple sources and was all converted to Mountain Standard Time (MST). For de-identification, dates are not shown. T-0 represents the date of pronouncement of legal death, T-X represents occurrences on dates before T-0, and T+X represents occurrences on dates following T-0.

A-1794 was a 78-year-old member with neuro cryopreservation arrangements who was pronounced legally deceased in California at 10:35 hrs in September on T-0 days.

After stabilization and field washout, the patient was driven to Alcor for cryoprotection. The patient arrived at Alcor on T-0 days at 22:41 hrs. The cryogenic cooldown was initiated on T+1 days at 04:53 hrs and terminated on T+4 days at 16:30 hrs. CT scans were made of the patient's brain at liquid nitrogen temperature on T+198 days after which the patient was transferred to long-term maintenance at liquid nitrogen temperature.

2. Patient Assessment and Pre-Deployment

This member was a paraplegic due to an accident that took place decades earlier. Throughout 2020 and 2021, Alcor's Medical Response Director (MRD) was in contact with the member periodically regarding both mental and physical health status. The member had been hospitalized several times but was always discharged. The member attempted to enroll in hospice multiple times before but was never successful due to not having a supporting terminal diagnosis.

T-17 days

The member was officially enrolled into in-home hospice with a diagnosis of vertebral osteomyelitis of the lumbosacral region and was given comfort medications (the specific medications were not recorded). The member inquired about Death with Dignity (DWD) and the hospice organization provided information about how to proceed.

Between T-16 and T-6 days

Alcor's MRD spoke to the member and the caretaker several times for status updates. The member's status was relatively unchanged but oral intake had begun to diminish. Hospice personnel and the member's caretaker had been instructed to notify Alcor immediately when legal death was deemed imminent.

3. Deployment and Standby

T-5 days

The member's caretaker reported at 12:07 hrs that hospice personnel had been at the home to assess the member and had estimated that clinical death could happen in a few hours to a few days. One of Alcor's strategic partners, Suspended Animation (SA), was deployed to the member's location to perform standby, stabilization, and transport (SST) as well as a remote blood washout procedure.

As the SA facility was located near the member, they had personnel on site at 13:42 hrs. The initial assessment was that the member, who was sleeping, had not been placed on oxygen, had taken in 0.25 cup of water the previous night and had no food for approximately three days. At 14:03 hrs the caretaker took the member's vital signs: capillary oxygen saturation (SpO_2) 99% on room air, heart rate (HR) 43 BPM, respiration rate (RR) 12-14/min. Vital signs taken earlier by the hospice nurse at 11:05 hrs were blood pressure (BP) 82/57 and HR 45 BPM. The member had produced 15 cc of urine in the last 16 hours.

The member's Medical Power of Attorney (MPOA) authorized hospice to give medical information to the SA team. At 17:30 hrs the portable ice bath (PIB) and all stabilization equipment and medications were moved into the member's home.

The member was agitated and in discomfort throughout the night. The caretaker contacted hospice at 20:30 hrs and was informed of the proper administration of the prescribed medication authorized by the hospice physician. The caretaker administered 0.25 mg morphine for pain management at 21:04 hrs and again at 21:34 hrs.

T-4 days

The hospice nurse took the member's vital signs at 10:45 hrs: temperature (T) 36°C, BP 154/91, HR 66/min, SpO_2 96%, RR 24/min, urine production had been 500 cc over the last 24 hours with one bowel movement.

The hospice nurse recommended 1mg Ativan/hour for anxiety. At 11:51 hrs the caretaker asked the SA team to leave during the day shifts until the member's end of life became more imminent. The team returned at 16:00 hrs and learned that the caretaker had given the member 1 mg Ativan at 11:00 hrs, 12:00 hrs, 15:00 hrs and 16:00 hrs. At 21:00 hrs the caretaker took the member's vital signs: SpO_2 89%, HR 65 BPM and RR 18/min.

T-3 days

The caretaker administered 1 mg Ativan and 0.125 mg hyoscyamine, also for anxiety, at 03:00 hrs and again at 07:53 hrs. The hospice nurse arrived at 10:00 hrs and advised that the member be given 10 mg morphine/hour, 1 mg Ativan/hour, and 0.125 mg hyoscyamine/2 hours as directed by the hospice physician. The member's vitals were: SpO_2 87%, HR 93 BPM, RR

20/min, BP 105/78 with 300 cc urine output. The member could respond to verbal commands but could not speak. The caretaker asked the SA team at 10:30 hrs to leave for the day.

The team returned at 19:00 hrs to find the member sleeping comfortably. The member had been receiving the advised medications since 11:00 hrs. At 19:15 hrs vitals per the caretaker were: SpO_2 90%, HR 85 BPM, RR 14/min, and BP 94/59. At 23:00 hrs the caretaker noticed the member's SpO_2 had dropped to 80%. The member was administered 2L/min of oxygen (O_2) via a nasal cannula connected to a hospice provided O_2 concentrator. At 23:54 hrs the member's SpO_2 had returned to 90%.

T-2 days

The hospice nurse arrived at 09:30 hrs. At 09:41 hrs the vitals were: temperature (T) 36°C, SpO_2 87%, HR 107 BPM, RR 12/min, BP 78/50 and 50cc amber urine output. The SA team left at 10:30 hrs and returned at 19:00 hrs. The caretaker stated that the same medications had been administered except for 12:00 hrs and 13:00 hrs. Per the caretaker the member's vitals were SpO_2 86%, HR 39 BPM, and RR 12/min.

At 20:00 hrs the member's BP was 104/69. The stabilization medications were drawn up and placed on ice. The member's vital signs at 20:30 hrs, as taken by the caregiver, were BP 104/69, HR 110/min, and SpO2 86%.

T-1 days

At 01:00 hrs the caretaker increased the member's morphine to 15 mg/30min due to the members' increased discomfort. The hospice nurse was requested by the caretaker to assess the patient at 04:00 hrs. The member's vitals were HR 98 BPM and thready, RR 12/min, and BP 52/38. The SpO_2 did not register. Also, at 04:00 hrs the caretaker increased the member's morphine to 20 mg/30min.

The vital signs taken by the caretaker at 08:40 hrs were T 37°C, SpO_2 84%, HR 109 BPM, RR 12/min, and BP 69/57. At 09:30 hrs the hospice nurse arrived and again took vitals: SpO_2 74%, HR 100 BPM, RR 12/min and shallow, and BP 48/36. A hospice nurse was present for a portion of the day in the event the member went into cardiac arrest. The member continued to receive 20 mg/30min morphine, 1 mg Ativan/1hr, and 0.125 mg hyoscyamine/2hr throughout the day and evening. The SA team members remained on site going forward.

4. Stabilization

T-0 days

At 09:05 hrs, as the caretaker was about to administer medications, he noticed that the member had stopped breathing. Hospice was immediately contacted, as were Alcor and the contract surgeon and perfusionist. At 09:10 hrs the caretaker positioned approximately 30 lbs. of water ice on and around the patient's head. The PIB and other equipment were placed near the member for a rapid start of stabilization procedures.

The hospice nurse arrived at 10:01 hrs and pronounced the member legally deceased at 10:03 hrs. The patient's temperature was 35°C. The patient was immediately placed in the PIB. No water had been put in the PIB due to modifications needed to shorten it to use the elevator for extraction. At 10:06 hrs the intraosseous (IO) access to the vasculature was placed in the tuberosity of the right leg, the AutoPulse device was applied, and mechanical chest compressions were initiated at 10:06 hrs to improve cooling of the patient and to circulate stabilization medications. Water ice was placed on and around the patient's head to assist with cooling.

At 10:07 hrs administration of the stabilization medications was initiated (see the Table of Medications Administered for the names of the medications, dosages, and times of administration). At 10:08 hrs vasopressin was administered in a single dose of 80 IU (see the Discussion section). Concurrently, with three team members working, the patient was intubated with a 37 French (Fr) CombiTube airway, a vent was attached, nasopharyngeal temperature (NPT) thermocouples were placed (left probe at 10:09 hrs and right probe at 10:10 hrs), and the CMI Health PC-900B capnograph device was started to measure the amount of expired carbon dioxide ($EtCO_2$), which assesses the efficacy of cardiopulmonary support. The NPT thermocouples were inserted to a depth of 10 cm and secured with an anchor knot, staples, and putty to prevent water from entering the nose and interfering with temperature measurement. The airway was covered with Tegaderm to deter water ingress into the oral cavity that could negatively affect the temperature measurements. At 10:11 hrs the IO needle had become dislodged. A new IO was placed into the tuberosity of the left leg at 10:12 hrs. Stabilization medication administration was then continued.

At 10:18 hrs the patient was transported to the mobile operating room (MOV) waiting outside the home. While the patient was being loaded into the MOV, the AutoPulse stopped functioning at 10:23 hrs due to shifting. At 10:25 hrs the fully extended PIB was secured inside the MOV, 5 gallons of water were added to the PIB and the water pump for the Surface Conduction Cooling Device (SCCD) in the PIB was activated to keep cold water circulating over and around the patient to optimize cooling. Manual chest compressions were started while troubleshooting how to restart the AutoPulse device.

At 10:28 hrs the AutoPulse was reinitiated, but stopped again, and manual compressions were begun. Within one minute the AutoPulse was started again and continued working. At 10:30 hrs the MOV was relocated to a predetermined operating location; permission to park at this location had been granted.

5. Field Surgery and Washout

The patient arrived at the operating location at 10:36 hrs. The AutoPulse battery was changed with no issue. The patient's NPT at 11:05 hrs was 25°C in both the left and right probes. The perfusion circuit was primed, and the AutoPulse was stopped to prepare the surgical area. At 11:09 hrs the first surgical incision was made for the median sternotomy. At 11:27 hrs the aorta was cannulated with a 6.5 mm aortic cannula and the inferior vena cava was cannulated with a 29/37 dual stage venous catheter.

At 11:31 hrs the cannulae were connected to the Sorin Centrifugal Pump Console (SCPC) for washout, and at 11:32 hrs the perfusionist added 250,000 units of Streptokinase through the 0.2-micron filter into the washout solution. The initial perfusion flow rate was 3L/min at 120 mmHg pressure to the head of the aortic cannula. When the patient's nasopharyngeal temperature (NPT) reached 20°C the arterial pressure was dropped to 100 mmHg for the washout procedure. At 11:46 hrs open-circuit washout was terminated and recirculation was initiated.

Electrical power in the MOV was temporarily lost at 12:44 hrs but restored at 12:47 hrs. The SCCD pump stopped at 12:54 hrs due to a low battery. The SCCD pump was turned back on with AC power at 12:56 hrs (see the Discussion section). Recirculation perfusion was terminated at 14:02 hrs, and closure of the patient's chest was begun. The cannulae were not removed. The sternum was closed with three #6 stainless steel wires, followed by staples for the skin.

Per the perfusionist's report, the patient's temperature at the start of surgery was 20°C and the lowest temperature recorded was 2.5°C. The lowest flow rate was 2.0 L/min, and the highest was 3.0 L/min. The highest line pressure was 100 mmHg.

During washout and recirculation SA was on the phone with the funeral home, Alcor, and the local coroner's office. The cause of death on the death certificate, vertebral osteomyelitis, was considered by the coroner's office to be an abnormal cause, and the coroner required that the patient be brought to the coroner's office for inspection and formal release. At 14:42 hrs the team started transport to the coroner's office.

6. Transport

At 15:17 hrs the patient arrived at the coroner's office. At 15:19 hrs the inspector required a physical inspection of the patient and the taking of photographs. While still in the PIB, the patient had to be rolled over to obtain pictures of the patient's posterior. At 15:29 hrs the inspector concluded his inspection and released the patient to SA for transport. After the inspector exited the vehicle, approximately 80 lbs. of water ice were applied to the patient with emphasis to the head, and water was again allowed to flow from the SCCD mask onto the patient at 15:30 hrs.

At 15:34 hrs the patient departed for the drive to Alcor. At 20:10 hrs the team stopped for fuel and placed approximately 30 lbs. of additional water ice on and around the patient's head. Arrival at Alcor was at 22:37 hrs.

7. Cryoprotectant Perfusion Surgery

T-0 days

As the cryoprotectant perfusion tubing was being set up and primed prior to the arrival of the patient, there was a failure of the serial port to the chiller dewar. A recirculating chiller designed for pet perfusions was used for this case without incident. The perfusion tubing system was primed at 22:32 hrs with 13.4 Brix, 7% nM22 perfusate (see the Discussion section).

The patient was brought into the operating room (OR) at Alcor at 22:41 hrs. The patient's right nasopharyngeal temperature (RNPT) was 0.3°C and the left nasopharyngeal temperature (LNPT) was 0.7°C. At 22:44 hrs resealable bags of water ice were placed on and around the patient's head and face. At 22:46 hrs the RNPT was 1.8°C and the LNPT was 1.2°C. The volume in the mixing reservoir at 22:47 hrs was 1.2 liters (L).

Surgery was initiated on the patient's neck to locate the left carotid artery. The first surgical cut was made at 22:49 hrs. The left carotid artery was isolated at 22:57 hrs. The right carotid artery was isolated at 23:01 hrs. Using a Codman craniotome fitted with a perforator bit, the right burr hole was started at 23:02 hrs and completed at 23:03 hrs. The left burr hole was both started and completed at 23:03 hrs. Thermocouples were placed in both burr holes at 23:08 hrs and secured to the scalp with sutures.

Using PVC pipe shears to separate the spinal cord, the cephalic isolation was complete at 23:12 hrs. The time when the cephalic isolation was initiated was not noted. The cephalon weighed 5.295 kg at 23:13 hrs and was secured in the neuro halo in the cephalic cooling enclosure at 23:15 hrs.

A purse string was placed in the right carotid artery at 23:16 hrs. The right carotid artery was cannulated, and the purse string was tightened around the cannulated artery at 23:18 hrs. The right carotid cannula slipped lose. It was re-cannulated, the purse string tightened, and open circuit perfusion was initiated through the right carotid artery at 23:19 hrs. Closed circuit perfusion was initiated at 23:23 hrs.

8. Cryoprotectant Perfusion

The cryoprotectant perfusion ramp was initiated at 23:25 hrs. The left carotid artery was cannulated at 23:26 hrs and perfusion through the left carotid artery was initiated at 23:27 hrs. The arterial pressure was still minimal at approximately 40 mmHg. The main pump was placed on automatic computer control at 23:28 hrs. The bypass was closed, and the arterial pressure was increased to 70 mmHg.

The computer determined arterial refractive index at 23:29 hrs was 16 Brix. At 23:37 it was noted that the flow rate was increasing while the arterial pressure remained constant (see the Discussion section). At 23:41 hrs the brain appeared to have retracted from the burr hole, but no measurement was made.

The left burr hole thermocouple was secured to the scalp with surgical staples at 23:42 hrs. The arterial refractive index (RI) reading was 18.8 Brix at 23:43 hrs and another reading at 23:44 hrs was 19.1 Brix. Concurrently, a jugular sampling line was placed into the right jugular vein and the arterial pressure dropped from 70 mmHg to 60 mmHg. At the same time, the left jugular sampling line was placed. The pre-filter line was over pressured, and the 0.2-micron filter failed. The filter was replaced in the tubing assembly at 23:47 hrs.

The left jugular vein sampling line was placed and secured at 23:48 hrs. The RI reading at the left jugular sampling line at 23:50 hrs was 15.8 Brix and the RI at the right jugular sampling line was 16.0 Brix. The arterial pressure returned to 70 mmHg at 23:52 hrs.The lid was placed on the neuro enclosure and cooling with nitrogen gas began at 23:53 hrs. The chiller temperature was set to 3°C.

T+1 days

The vertebral arteries were draining, which confirmed that the Circle of Willis was intact and there would be reasonable perfusion pressure at the back of the brain. The right vertebral artery was then clamped off. The left vertebral was only partially clamped at 00:01 hrs due to lack of clamps (see the Discussion section).

It was noted at 00:13 hrs that the 0.2-micron filter in the tubing assembly was again clogged. The arterial pressure was reduced to 40 mmHg, and it was replaced with a 0.45/0.2-micron filter. At 00:15 hrs the arterial pressure was restored to 70 mmHg (see the Discussion section). The addition pump speed was increased from 15 to 18 at 00:21 hrs.

The ramp pump was turned off at 01:01 hrs. The chiller and the neuro enclosure temperatures were both set to -3°C, and the 30-minute pause to allow equilibration was initiated.

Sidebar:
Per the cryoprotection protocol, the ramp is to be paused at 30 Brix (50% of the desired terminal concentration) to allow the patient to come to osmotic equilibrium. The cephalic enclosure 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 the terminal concentration is obtained.

It was noted at 01:24 hrs that the physical refractometers were not sampling the correct side of the patient. For example, the left refractometer was sampling from the right jugular vein (see the Discussion section). There was a pressure spike at 01:30 hrs to 150 mmHg when circuit tubing was incorrectly clamped off, but that was corrected, and the pressure went back to normal. The concentration of the nM22 in the cryoprotectant perfusate was increased to the terminal concentration and the equilibration pause was terminated.

Sidebar:
The 30-minute countdown to the termination of cryoprotection is initiated, after which the final sub-zero terminal concentration ramp is resumed. 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 addition pump speed is minimized, with frequent corrections, to compensate for latency.

There was a total loss of pressure for 10 minutes starting at approximately 02:30 hrs, accompanied by a loss of refractometer data (see the Discussion section). At 04.07 hrs the right venous RI was 49.9 Brix, and the left venous RI was 50.4 Brix. The cryoprotectant ramp was terminated when it was determined that the desired endpoint of over 49.9 Brix nM22 concentration from both jugulars for over 30 minutes was not going to be achieved without prolonging the cryoprotectant ramp. The post cryoprotection weight of the cephalon was 4.965 kg at 04:37. This represented a weight loss of 0.33 kg, or 6.2% due to shrinkage after exposure to the cryoprotectant.

A major pool of fluid was noted on the floor, underneath the perfusion equipment located under the operating table (see the Discussion section). There was also blood drippage from the neuro enclosure.

The patient was moved into the patient care bay for cryogenic cooldown.

9. Cooling to Liquid Nitrogen Temperature

A computer program was used to initiate cryogenic cooldown at 04:53 hrs on T+1 days, plunging to -110°C and descending thereafter at -1°C/hour to liquid nitrogen temperature. An isotherm was observed in the nasopharyngeal cooldown record at approximately -35°C.

Sidebar 1:
An isotherm (freezing event) is a period of interrupted temperature descent observed on the time vs. temperature graph of a specimen as the specimen undergoes a phase transition, for example when freezing a liquid to a solid. An isotherm occurs as energy is exchanged to rearrange molecules into the new phase. In the context of cryonics, an isotherm is undesirable because it is an indicator of ice formation, and therefore incomplete vitrification. The formation of a glassy solid by vitrification, which involves no crystallization, does not express an isotherm.

T+4 days

At 03:20 hrs the #2 valve-set froze in the open position and the system defaulted to the backup valve. At 04:24 hrs it was discovered that the cooldown system was in alarm mode (see the Discussion section). With the primary valve stuck in the open position, this resulted in the temperature plunging from -178°C to -196°C. The valve was successfully replaced at 05:10 hrs. The cooldown system control profile was advanced 10 hours to reduce the target temperature and prevent a large temperature rise. At approximately 06:00 hrs a pool of nitrogen in the patient dewar had boiled away and the temperature rose from -196°C to -189°C. The cooldown system resumed control at -189°C. At 16:30 hrs the cooldown was terminated.

On T+198 days, CT scans were made of the patient's brain at liquid nitrogen temperature and the patient was then transferred to long-term maintenance at liquid nitrogen temperature.

10. Timeline and Time Summaries

Timeline

T-0 days

09:05 Estimated time of cardiac arrest
09:10 Placement of water ice around patient's head
10:03 Pronouncement of legal death
10:05 Start of ice bath cooling
10:06 Start of mechanical chest compressions
10:06 Placement of intraosseous (IO) device in the right leg
10:07 Placement of CombiTube airway
10:07 Administration of first medication (200 mg propofol)
10:09 Left nasopharyngeal thermocouple placed in patient's nare
10:10 Right nasopharyngeal thermocouple placed in patient's nare
10:11 IO dislodged
10:12 IO reset in left leg
10:23 Patient loaded into mobile operating vehicle (MOV)
10:30 Transport patient to location of surgery
10:34 Administration of final stabilization medication (50 mL hetastarch)
10:36 Patient on MOV arrived at location of surgery
11:05 Termination of cardiopulmonary support (LNPT 29.2°C, RNPT 29.6°C)
11:09 Start of field surgery
11:31 Start of open circuit washout
11:32 Administration of 250,000 IU streptokinase in washout perfusate
11:46 Start of closed-circuit perfusion
14:02 Completion of closed-circuit perfusion
14:42 Begin transport of the patient to Coroner's office
15:29 Coroner's release of the patient
15:30 80 lbs. of water ice applied to patient's body and head
15:34 Departure of transport vehicle to Alcor
20:10 30 lbs. water ice applied to patient's head
22:41 Arrival of patient at Alcor OR (RNPT 0.3°C, LNPT 0.7°C)
22:49 Start of surgery
23:02 Start of burr hole surgery
23:03 Completion of burr hole surgery
23:12 Completion of cephalic isolation
23:13 Cephalon weighed (5.295 kg)
23:19 Start of open-circuit perfusion to the right carotid artery
23:25 Start of cryoprotectant ramp

T+1 days

01:01 Pause at 50% of concentration necessary for vitrification (CNV) achieved
01:30 Start of sub-zero terminal concentration ramp (off pause)
04:07 Termination of cryoprotection (49.9 Brix in both jugulars for over 30 minutes)
04:37 Weight of cephalon after perfusion (4.965 kg, weight loss of 0.33 kg or 6.2%)
04:53 Start of cryogenic cooldown to LN_2 temperature

T+4 days

03:20 Failure of cooldown system
05:10 Cooldown system reinitiated
16:30 Completion of cryogenic cooldown at LN_2 temperature

T+198 days

CT scans made post-cooldown at LN_2 temperature and transfer of patient to long-term maintenance at LN_2 temperature

Time Summaries

Stabilization

Event Duration
hrs: mins

00:58 From the estimated time of cardiac arrest (ETCA) to pronouncement of legal death: 09:05 hrs to 10:03 hrs
01:01 From ETCA to start of cardiopulmonary support: 09:05 hrs to 10:06 hrs
01:02 From ETCA to start of medication administration: 09:05 hrs to 10:07 hrs
00:27 From start to the end of medication administration: 10:07 hrs to 10:34 hrs

Field Surgery and Washout

Event Duration
hrs: mins

02:04 From ETCA to start of surgery: 09:05 hrs to 11:09 hrs
00:20 From the start of surgery to end of surgery: 11:09 hrs to 11:29 hrs
02:26 From ETCA to start of washout: 09:05 hrs to 11:31 hrs
02:31 From the start of washout to end of washout: 11:31 hrs to 14:02 hrs
04:57 From ETCA to end of washout: 09:05 hrs to 14:02 hrs

Cryoprotectant Surgery at Alcor

Event Duration
hrs: mins

13:36 From the ETCA to the patient's arrival at Alcor OR: 09:05 hrs to 22:41 hrs
00:08 From arrival at Alcor OR to the start of surgery: 22:41 hrs to 22:49 hrs
00:23 From the start of surgery to the end of the cephalic isolation: 22:49 hrs to 23:12 hrs
00:36 From the start of surgery to the start of the cryoprotection: 22:49 hrs to 23:25 hrs
05:18 From the start of surgery to the end of the cryoprotection: 22:49 hrs on T-0 to 04:07 hrs on T+1

Cryoprotectant Perfusion and Cryogenic Cooldown

Event Duration
hrs: mins

38:20 From ETCA to start of cryoprotection: 09:05 hrs on T-0 to 23:25 hrs on T+1
00:44 From arrival at Alcor OR to the start of cryoprotection: 22:41 hrs to 23:25 hrs
04:42 From start to the end of cryoprotection: 23:25 hrs on T-0 to 04:07 hrs on T+1
00:46 From the end of cryoprotection to the start of cooldown: 04:07 hrs to 04:53 hrs
19:48 From ETCA to start of cooldown: 09:05 hrs on T-0 to 04:53 hrs on T+1
06:12 From arrival at Alcor OR to the start of cooldown: 22:41 hrs on T-0 to 04:53 hrs on T+1

11. Table of Medications Administered

T-0 days

TIME	MEDICATION	DOSE	PURPOSE
10:07 hrs	Propofol	200 mg	Anesthetic; reduces cerebral metabolic demand; reduces the theoretic possibility of increased awareness during aggressive CPS.
10:07 hrs	Sodium citrate	100 mL Note 1	Anticoagulant; prevents blood clot formation.
10:08 hrs	Heparin	50,000 IU	Anticoagulant; prevents blood clot formation.
10:08 hrs	Vasopressin	80 IU total Note 2	Vasopressor; increases blood pressure during CPS.
10:09 hrs	SMT (S-methyl-isothiourea)	400 mg Note 3	Neuroprotectant (iNOS inhibitor); protects the brain from ischemic injury; raises blood pressure.
10:10 hrs	Minocycline	200 mg	Antibiotic and neuroprotectant.
10:13 hrs	Decaglycerol/THAM [tris(hydroxymethyl) aminomethane]	200 mL (first dose) Note 4	Decaglycerol inhibits cerebral edema. THAM is a buffer to mitigate acidosis.
10:13 hrs	Vital Oxy	43 mL Note 5	Antioxidants: melatonin, vitamin E (D-alpha tocopherol), PBN (alpha Phenyl t-Butyl Nitrone) and anti-inflammatory carprofen.
10:13 hrs	Antacid	60 mL Note 6	A buffer used to protect the stomach from acid erosion.
10:14 hrs	Antacid	60 mL Note 6	A buffer used to protect the stomach from acid erosion.
10:14 hrs	Antacid	70 mL Note 6	A buffer used to protect the stomach from acid erosion.
10:15 hrs	Decaglycerol/THAM [tris(hydroxymethyl) aminomethane]	200 mL (second dose) Note 5	Decaglycerol inhibits cerebral edema. THAM is a buffer to mitigate acidosis.
10:15 hrs	Antacid	60 mL Note 6	A buffer used to protect the stomach from acid erosion.
10:31 hrs	Hetastarch (Hespan)	50 mL Note 7	Volume expander: increases cerebral perfusion during CPS, replaces volume loss.
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10:34 hrs	Hetastarch (Hespan)	50 mL Note 7	Volume expander: increases cerebral perfusion during CPS, replaces volume loss.
11:32 hrs	Streptokinase	250,000 IU Note 8	A thrombolytic used to break up existing blood clots.

Notes:

1. The standard formulation for sodium citrate is 20% w/v. 10 grams of sodium citrate are given to patients who weigh less than 40 kg, and 20 grams are given to patients who weigh over 40 kg. This patient received 20 grams of sodium citrate because his weight was over 40 kg.

2. The standard protocol for administering Vasopressin is as a fixed dosage of 40 IU, per dose for two doses. The second 40 IU dose is to be administered concurrently with Vital-Oxy, IV/IO. This patient received one dose of 80 IU (see the Discussion section). Vasopressin is to be administered only if the patient's temperature is above 20°C as it is ineffective at cold temperatures.

3. SMT (S-methyl isothiourea) is a fixed-dose and is a powder, (1 vial = 400 mg) dissolved in 10 mL of saline and injected through a 0.2 µ filter. SMT is unstable in solution with a useful life of approximately six hours.

4. Decaglycerol/THAM is administered as a custom formulation of 20% w/v decaglycerol and 4.5% w/v THAM (tromethamine) in water (pH = 10.4 and pKa = 8.3).

5. The medications protocol dilutes 70 mL or less, based on body weight, of Vital-Oxy into 150 mL of saline for a total of 220 cc of diluted Vital-Oxy 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.

6. Antacid was given in four doses and was inserted through the CombiTube airway. A total of 250 mL was inserted.

7. Hetastarch is a volume expander used to restore volume in dehydrated patients and increase cerebral perfusion during CPS. It is administered 250 mL as a fixed dosage by IV/IO. due to the patient's dehydrated condition.

8. The standard administration of streptokinase is 250,000 IU dissolved in 5 mL of 9% sodium chloride. This medication previously needed to be infused through a 0.2 µ filter. The medication now in use is already sterile filtered and can be reconstituted in the vial. This medication was administered at the start of the blood washout.

12. Discussion

Standby, Stabilization and Transport

During the administration of the stabilization medications, Vasopressin was administered in a single dose of 80 IU. The standard protocol for administering Vasopressin is a fixed dosage of 40 IU, per dose for two doses. The second 40 IU dose is to be administered concurrently with Vital-Oxy by IV/IO. Continued education will be provided to SA team members for administering the medications in the proper order and using the proper protocol.

The AutoPulse mechanical chest compression device stopped working while loading the patient into the mobile operating vehicle (MOV). This had been a reoccurring issue when jostling the patient in the portable ice bath (PIB). All SA team members are trained on how to troubleshoot the AutoPulse. The quick reaction to its stopping by providing manual compressions and the quick correction of the malfunction showed that this is an issue that will need to be dealt with occasionally on a case-by-case basis.

Electric power was lost in the MOV for 3 minutes (12:44 hrs to 12:47 hrs) during the recirculation portion of the blood washout. This was a time of maximum load on the vehicle power output. The AC unit was restarted, and power was restored to the inverter. All major equipment is backed up with batteries except for the perfusion circuit heat exchanger pump. SA will purchase an auxiliary battery for this pump.

On a recent case (A-2798), Suspended Animation had reintroduced the use of $EtCO_2$ readings during stabilization procedures to see if these could help determine the effectiveness of cardiopulmonary support (CPS. The data obtained (see below) in this case are significantly lower than in case A-2798 and would not be associated with successful recovery of spontaneous circulation and neurological recovery in a clinical out-of-hospital cardiac arrest case. This result should not be surprising given that there was a 1-hour delay between estimated time of circulatory arrest and start of cardiopulmonary support. With only two recent data sets, it is challenging to draw any significant conclusions. We should attempt to continue to obtain this data and continue to make analyses. However, at this point, it is too difficult to definitively declare what the standard should be with our equipment and procedures.

Due to the delay between circulatory arrest and start of procedures, this case was on the cusp between doing standard protocol and doing Alcor's Abbreviated Protocol, in which only a small portion of medications are administered and CPS is only provided to assist in medications circulation. $EtCO_2$ data and CT scan results reflect this delay. Alcor's 1 hour criterion for doing the Abbreviated Protocol is based on our best judgement about the risk of perfusion injury outweighing the benefits of cardiopulmonary support and the efficacy of medications administration. As we collect more experimental and clinical data (such as the $EtCO_2$ data and CT scans) it is conceivable that the criterion for doing the Abbreviated Protocol needs to be further tightened.

Cryoprotectant Surgery and Perfusion

Due to Covid-19 precautions, the primary Alcor scribe took notes via a virtual medium that did not allow good observation of the operating room (OR). A second scribe was in the OR to assist but good scribe notes require that the primary scribe be inside the OR for the best documentation to occur. For future cases, every effort will be made to accomplish this.

The OR at Alcor had not been used for almost two years due to the pandemic. Now that vaccinations made it possible for the OR to be used routinely again, the practice of holding dry-run drills when the OR has not been used in at least three months will again be put in place when possible, subject to changing pandemic conditions.

There was only one functional camera in the OR, and it stopped functioning. There have typically been two functional cameras for OR cases, the room camera, and the overhead surgical light camera. During the pandemic the room was cleared multiple times for deep cleaning and organization. It is not known where the room camera went after these cleaning sessions. A new room camera has been purchased and installed.

As the perfusion tubing circuit in the OR was being set up, the National Instruments 2-port USB connected to the RS-232 converter failed to work, as did available replacements. As a result, the LN_2-driven chiller could not be used. The chiller for pet neuro cryopreservation was substituted and performed adequately for this neuro patient. These converters have a record of failure and are expensive. Their function could be directly replaced with something much simpler, and this is being pursued.

The "balanced" dual pump shoe system seemed less balanced than normal, as perfusate built up in the collector tray during pre-perfusion circulation and the addition line had to be clamped several times to move the cryoprotectant back into the mixing reservoir. In the future, the dual Masterflex-16 silicone tubing pump shoes in the main pump will need to be replaced. Solutions to this problem are being investigated. Normally the perfusion system is not primed too far in advance of the surgical procedure, but in this case, priming took place hours before the surgery.

The expectation is that vertebral cannulation/perfusion should at least be attempted for OR-based neuro cases. Vertebral cannulation is not a mainstream medical application, so custom cannulas are being developed in-house specifically for this purpose.

While a blood washout was done in the field before the patient arrived at Alcor, there were still enough red blood cells in the vasculature to load both installed 0.2-micron filters and a larger 0.45/0.2-micron filter as well as loading a second 0.45/0.2-micron filter. Two filter swaps had to be performed during the cryoprotection. In addition, the filter loading blew the filter back-pressure monitor line off its gauge holder resulting in fluid losses from the neuro enclosure onto the floor of the OR. Back-pressure rose above 30 psi during this incident. Since the only current notification of back-pressure problems is visual inspection, a pressure gauge alarm will be added to the filter pressure gauge.

To stay ahead of perfusion flow restrictions that are typically noted after travel-induced cold ischemic delays, the patient cryoprotection was started at 7% nM22. This modification to spike the perfusate concentration at the onset of perfusion is in keeping with the recent revision to the field-neuro protocol during cases with edematous flow restrictions. In this case it appears that field washout did not completely flush the patient vasculature prior to transport, probably due to ischemia-induced no-reflow. The filters had to be replaced during the procedure due to building back pressure.

During cryoprotectant perfusion, at approximately 23:37 hrs, it was noted that the flow rate was increasing while the arterial pressure remained constant. Vascular resistance appeared to be dropping. The reason for this was not clear but this could have been due to blood washout with 7% nM22, shrinking the edematous brain tissue and opening the capillaries.

The main pump speed was not recorded during the cryoprotection. The pump was properly hooked up to the computer as is required for functional pressure control. The cause of the data loss is unknown.

Also, during cryoprotectant perfusion (see the graph A-1794 Cryoprotectant Pressure) not only was there a total loss of pressure for 10 minutes starting at approximately 16.5 hrs post-arrest, accompanied by loss of refractometer data, but there was also a period after this event where arterial pressure was only 60 mmHg. This was the result of the perfusionist manually setting the pressure to 60 mmHg during the pump shoe replacement. The perfusionist returned the pressure setting to 70 mmHg 30 minutes later.

The replacement of the long flex line (LFL) pump shoes was done in haste with larger diameter LFL tubing (-17 Tygon LFL, which is a big difference from -16), and this resulted in a concentration spike to approximately 110% nM22 being perfused. Except for the problems noted, perfusion was done at 70 mmHg.

After noticing an inconsistency between what was seen on the big screen in the OR and the manual refractive index readings from the refractometers, it was noted that the refractometer designated as being on the left side of the patient was sampling from the right jugular vein. The readings were reversed/corrected for this report. This probably resulted during the cannulation and a clearer labeling system will be developed to prevent this error in the future.

The addition pump shoe of the ramp generator fractured toward the end of the cryoprotectant ramp, pumping several liters of 1.25 x nM22 onto the pump, the pump cart, and the floor, requiring extensive cleanup time. The shoe was -16 Tygon LFL formulation PVC, which does not become hardened with cold temperatures as quickly as the normal S-50HL PVC formulation and is cheaper than silicone. Silicone pump shoes will become standard for future cases. The conversion will begin by replacing the LFL shoes in perfusion circuits already made up before new circuit construction. This may affect the indicated ramp pump speed, and this should be considered.

Cryogenic Cooldown

There was a failure of the cryogenic cooldown system at 03:20 hrs but the alarm was not noticed by personnel until 04:24 hrs. The completion of a cooldown failure alarm system, and its implementation, are a priority.

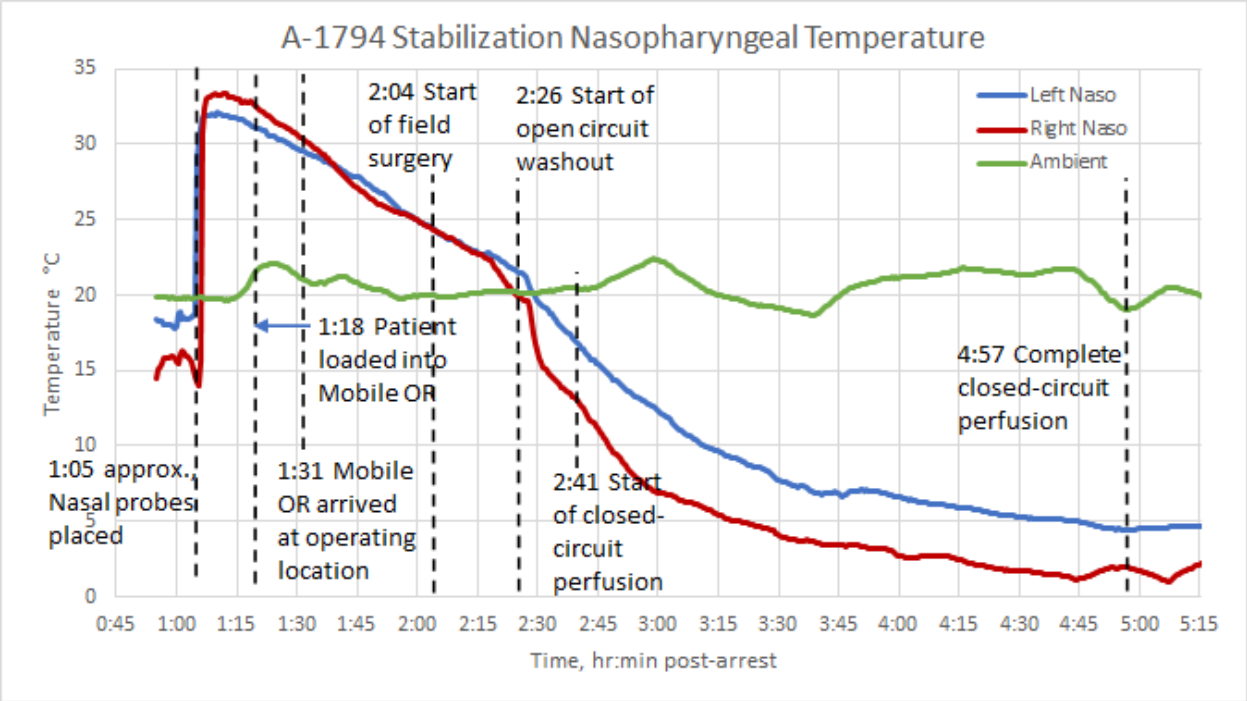
An isotherm, which results when ice forms, was observed in the nasopharyngeal cooldown record at approximately -35°C, indicating incomplete cryoprotection.

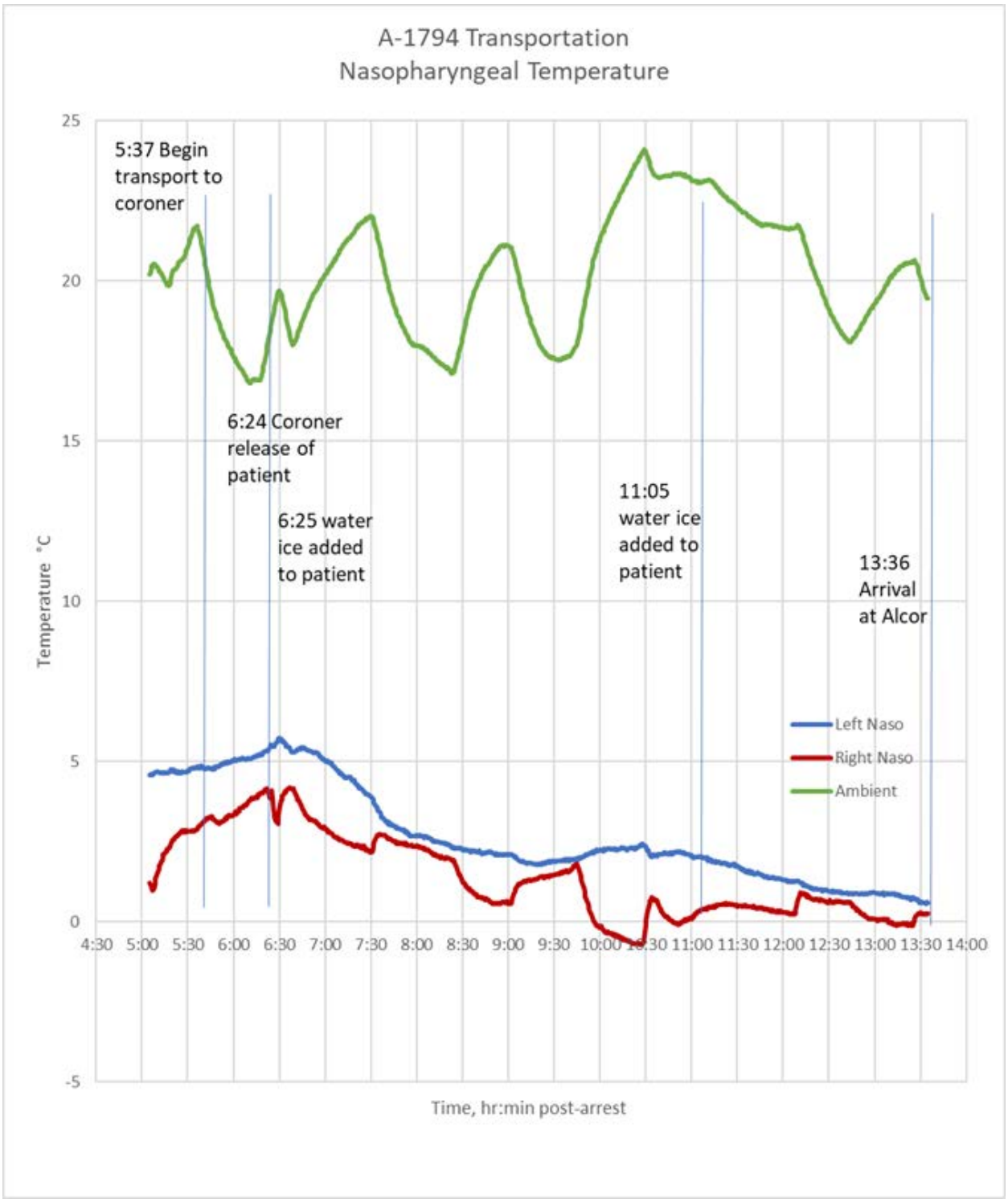
The below graph titled *A-1794 Cryoprotection Temperatures* shows the patient's neuro temperatures varied from those of the neuro enclosure. The neuro enclosure temperature settings had not been calibrated for an extended period, so the neuro enclosure temperature differed from the nominal values. This calibration was completed before the publication of this report.

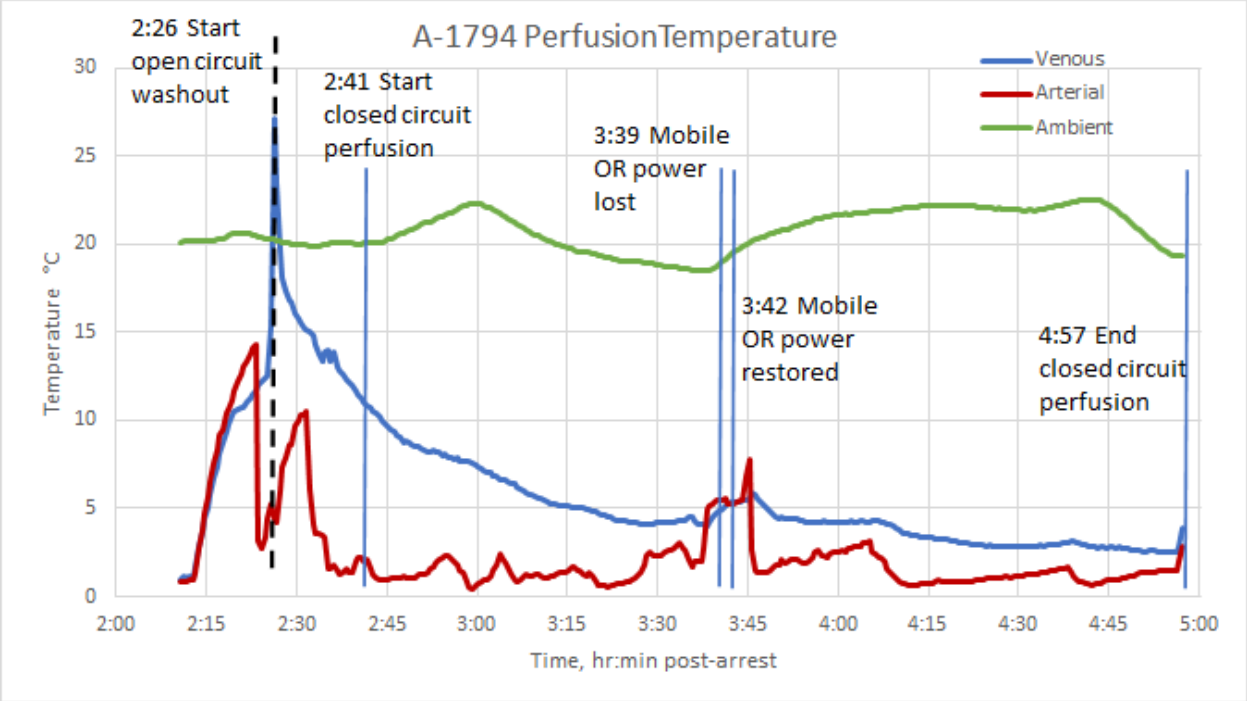
The CT scan indicates that the majority of the brain received insufficient concentration of M22 to inhibit ice formation. Some areas appear to be straight frozen blood. This outcome, most likely, reflects the extensive delay between pronouncement of legal death and the start of stabilization procedures, which may be further aggravated by the cold ischemic transport time. Sub-optimal cryoprotection co-existed with loss of cephalon weight after perfusion, which indicates that CPA-induced weight loss does not necessarily correspond to sufficient cryoprotection in all areas of the brain. The CT scan does not show evidence of CPA-induced brain shrinking, which further confirms that total ischemic exposure time was extensive, despite rapid stabilization efforts as soon as access to the patient was obtained. Starting with a higher concentration of CPA seems sensible but the CT scan still shows evidence of extensive perfusion impairment.

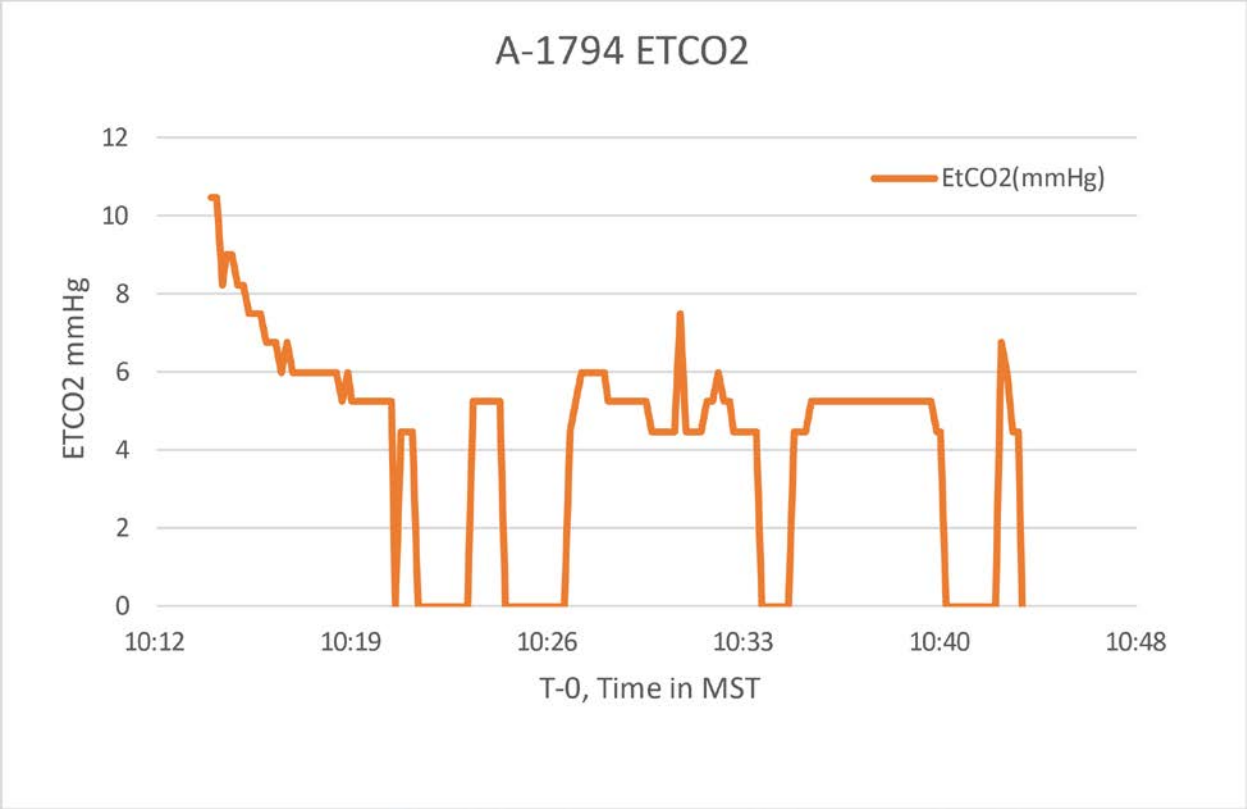
13. Graphs and CT Scans

Graphs provided by SA:



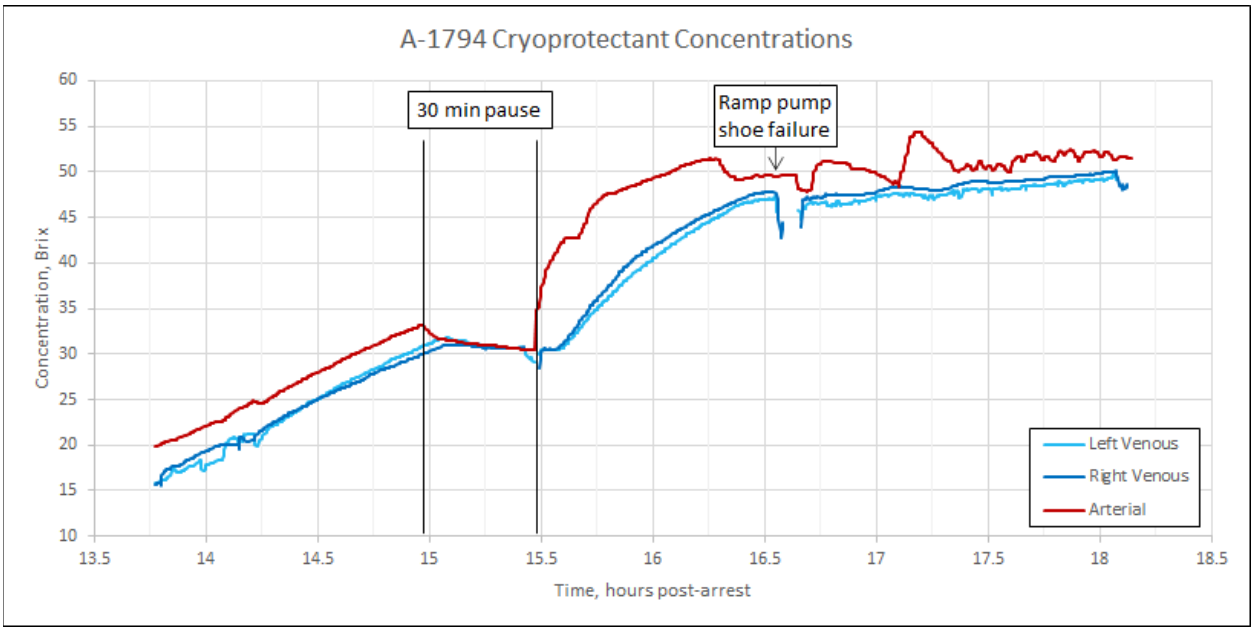

A-1794 Transportation
Nasopharyngeal Temperature
5:37 Begin transport to coroner
6:24 Coroner release of patient
6:25 water ice added to patient
11:05 water ice added to patient
13:36 Arrival at Alcor
Left Naso
Right Naso
Ambient
Temperature °C
Time, hr:min post-arrest
25
20
15
10
5
0
-5
4:30 5:00 5:30 6:00 6:30 7:00 7:30 8:00 8:30 9:00 9:30 10:00 10:30 11:00 11:30 12:00 12:30 13:00 13:30 14:00

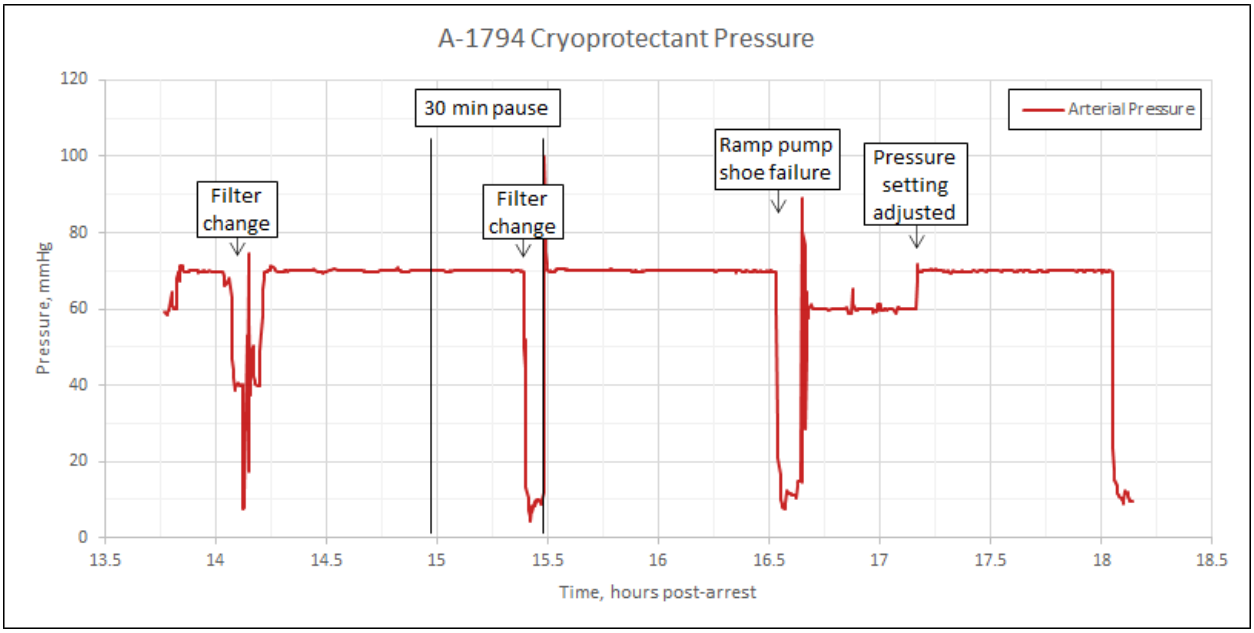

A-1794 PerfusionTemperature
2:26 Start open circuit washout
2:41 Start closed circuit perfusion
3:39 Mobile OR power lost
3:42 Mobile OR power restored
4:57 End closed circuit perfusion
Venous
Arterial
Ambient
Temperature °C
Time, hr:min post-arrest
30
25
20
15
10
5
0
2:00
2:15
2:30
2:45
3:00
3:15
3:30
3:45
4:00
4:15
4:30
4:45
5:00

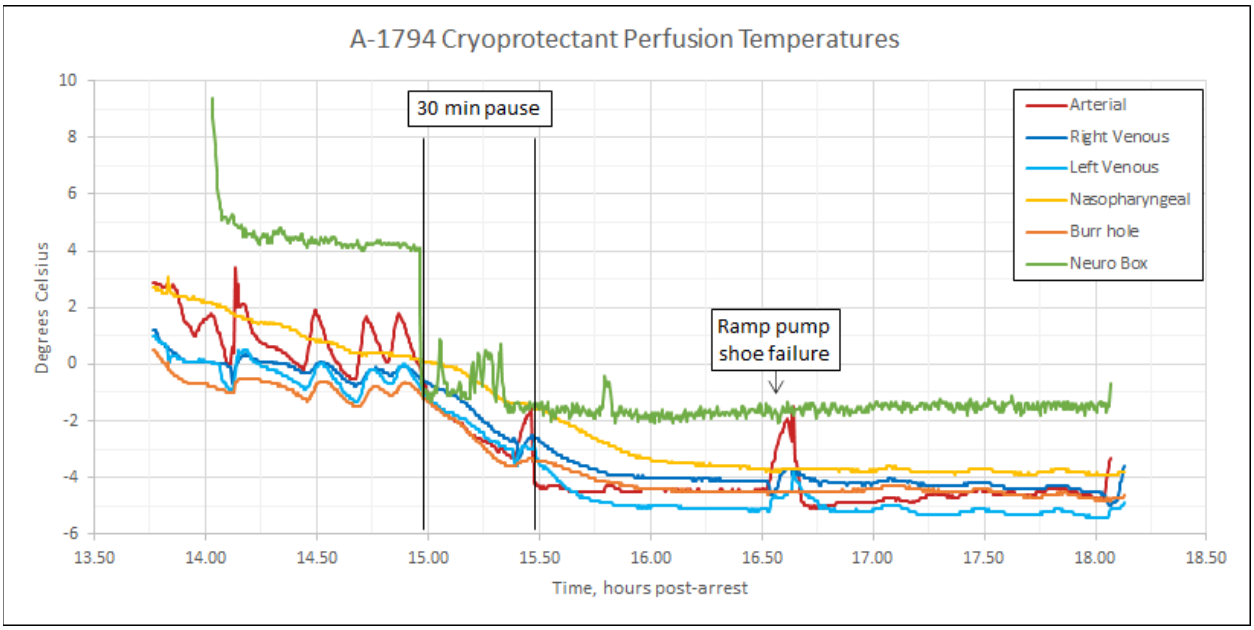


$ETCO_2$ Pressures are averaged out over 12-second intervals and not displayed in real-time.

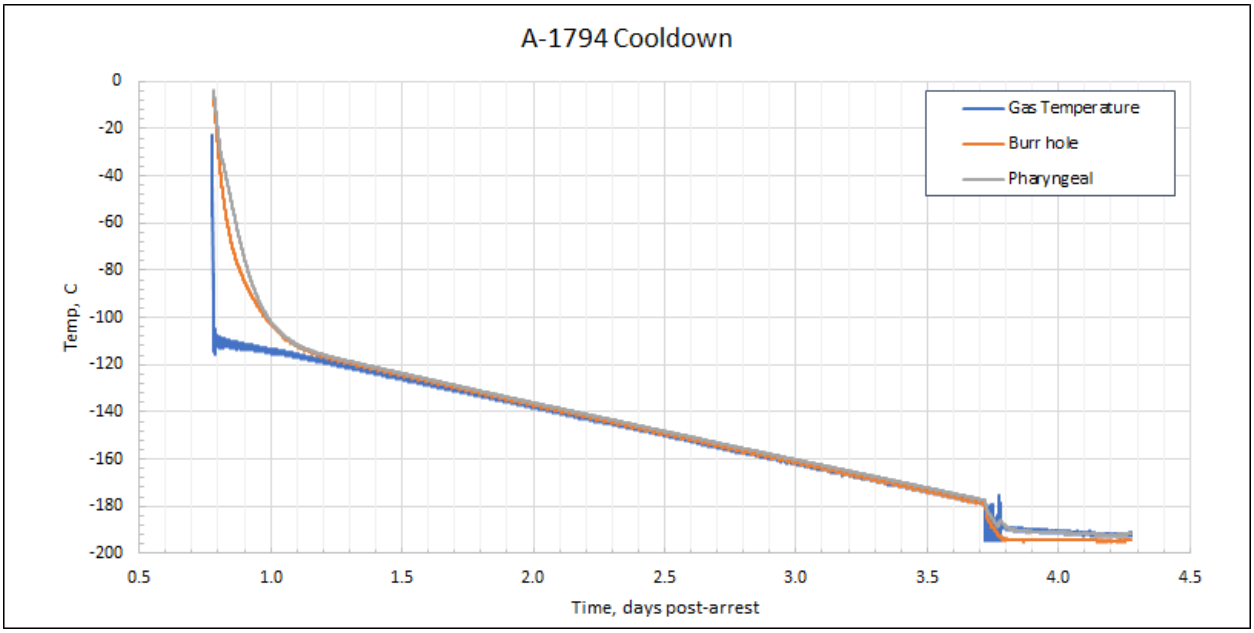
Graphs provided by Alcor:

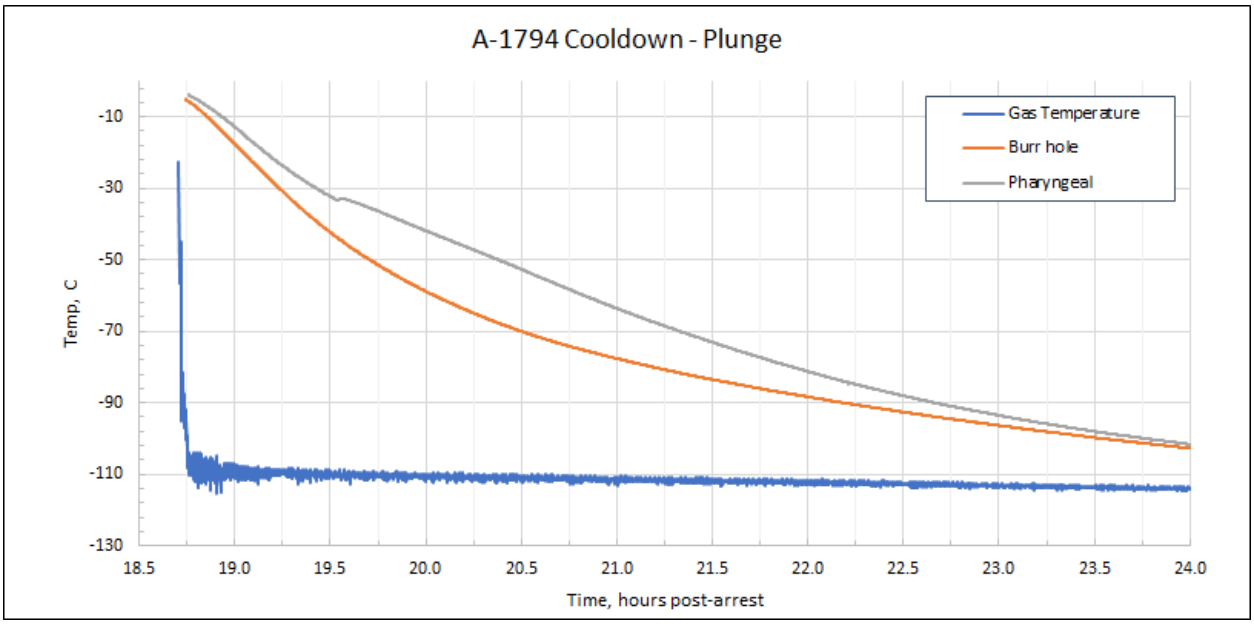


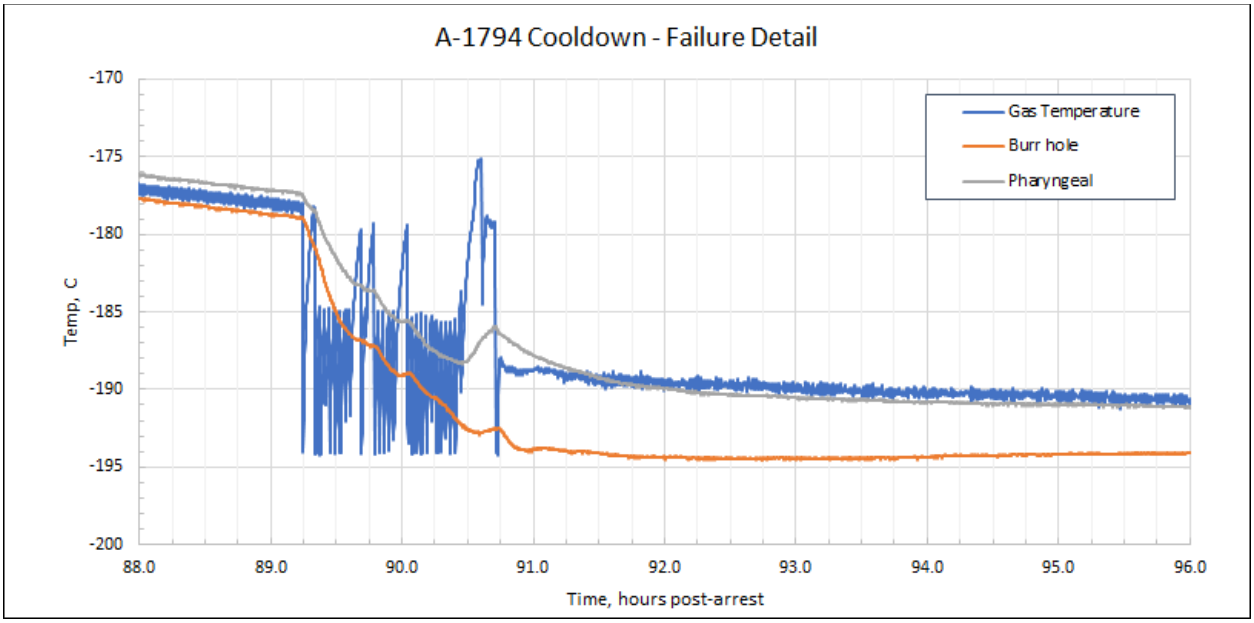




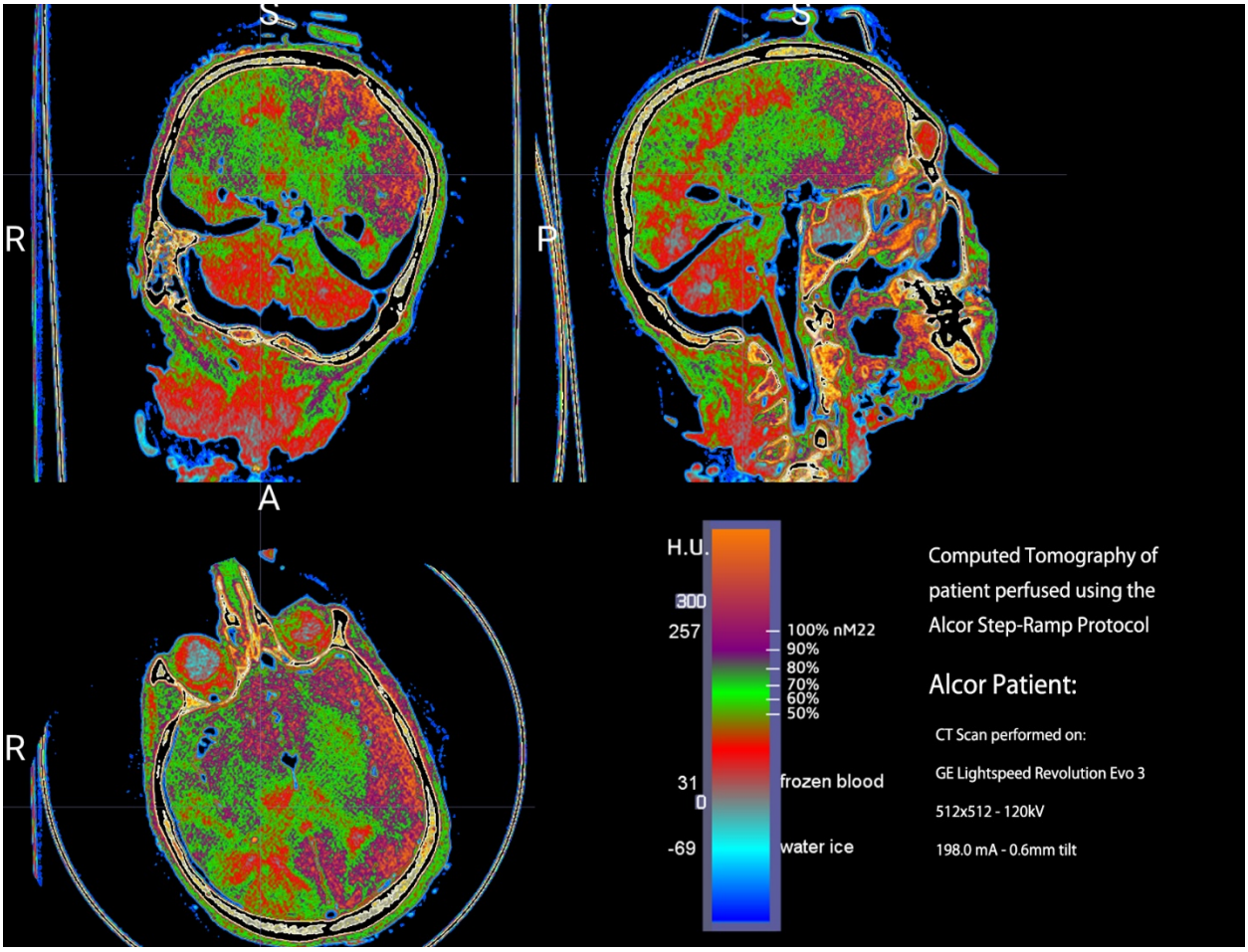
Note: The neuro enclosure temperature settings had not been calibrated for an extended period, so the neuro enclosure temperature differed from the nominal values.




A-1794 Cooldown - Plunge
Gas Temperature
Burr hole
Pharyngeal
Temp, C
-10
-30
-50
-70
-90
-110
-130
18.5
19.0
19.5
20.0
20.5
21.0
21.5
22.0
22.5
23.0
23.5
24.0
Time, hours post-arrest


A-1794 Cooldown - Failure Detail
Gas Temperature
Burr hole
Pharyngeal
Temp, C
-170
-175
-180
-185
-190
-195
-200
88.0
89.0
90.0
91.0
92.0
93.0
94.0
95.0
96.0
Time, hours post-arrest

Cryoprotectant Distribution (Post-cryopreservation CT scan)



Note: The post-cryogenic cooldown CT scans were obtained on T+198 days; the patient was at liquid nitrogen temperature (-196°C).