Alcor A-2999

Case Report

Prepared by:

Linda Chamberlain, Co-Founder and
Director of Special Projects,
Alcor Life Extension Foundation

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Alcor A-2999 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 cardiac arrest, T-X represents occurrences before T-0, and T+X represents occurrences following T-0.

A-2999 was a 91-year-old member with neuro cryopreservation arrangements. The medical examiner estimated the time of cardiac arrest to be 06:39 hrs. The member was pronounced legally deceased in Colorado at 07:39 hrs on T-0 days in November of 2021.

After stabilization and field cryoprotection (FCP), the patient was air transported to Alcor for cryogenic cooldown. The patient arrived at Alcor at 10:45 hrs on T+1 days. The cryogenic cooldown was initiated on T+1 days at 11:01 hrs and terminated on T+5 days at 10:44 hrs. CT scans were made of the patient's brain, while emersed in liquid nitrogen, on T+144 days; the patient was then transferred to long-term maintenance at liquid nitrogen temperature.

2. Patient Assessment and Pre-Deployment

T-4 days

The member's family called to notify Alcor that the member had been in and out of the hospital multiple times and would be enrolled into in-home hospice care. On a good day, the member did 30% of his own care. On a bad day, the member would not get out of bed. Hospice nurses had estimated the member had weeks to live and had prescribed 4 liters (L) of oxygen. The member was still taking in food and water.

T-1 days

Alcor's Medical Response Director (MRD) made several attempts to contact the member's family for an update but was not successful.

3. Deployment

T-0 days

The member's family called Alcor at 06:45 hrs to report that the member had gone into cardiac arrest and was found when the family woke in the morning. The patient was still warm to the touch. The family had not anticipated that this would happen and confirmed that even if the MRD had been able to have a conversation with the family the previous day there would have been no new indications for a deployment. The death certificate showed the estimated time of

cardiac arrest was 06:39 hrs and the cause of death was pulmonary hypertension subsequent to interstitial lung disease.

The family applied ice around the patient's head and neck (time not recorded). International Cryomedicine Experts (ICE), one of Alcor's strategic partners was immediately deployed to the patient's location for stabilization, transport, and field cryoprotection.

Personnel from the funeral home were at the patient's home for pickup at 08:45 hrs but said they had been advised by their legal counsel that they could not facilitate our procedures as originally agreed to by them due to insurance reasons. A new funeral home was contacted, and it was confirmed at 09:39 hrs that they would pick up the patient and pack additional water ice around the patient's head and neck.

4. Stabilization

Three ICE team members boarded a flight at 11:12 hrs and landed at 13:39 hrs. They arrived at the funeral home at 17:27 hrs after experiencing delays due to traffic and picking up dry ice. Dry ice was extremely limited in the area due to increased demand over Halloween (see the Discussion section). This caused a delay in getting to the funeral home as the only dry ice available was some distance away from the funeral home. After setting up the equipment for field cryoprotection, manual chest compressions were started on the patient at 17:32 hrs.

The first intraosseous device (IO) was placed in the tibial plateau of the patient's right leg at 17:38 hrs and the initiation of the abbreviated stabilization medications protocol for cases with more than an hour delay from cardiac arrest as begun at 17:39 hrs (see the below Table of Medications Administered for the list of medications, the dosages, and the times of administration). A second IO was placed in the tibial plateau of the patient's left leg at 17:42 hrs to make administration of medications by two team members more efficient. Manual chest compressions were terminated at 18:02 hrs.

5. Field Surgery and Cryoprotection

The first incision for the field surgery was made in the patient's neck at 18:17 hrs. The cannulation of the left carotid artery was completed at 18:24 hrs, using a 16-gauge catheter. The cannulation of the right carotid artery was completed at 18:37 hrs, using a 16-gauge catheter. An attempt was made to cannulate the vertebral arteries but there was no way to secure the cannulae and they would not stay in place (see the Discussion section). Both burr holes had been completed at 18:44 hrs. The cephalic isolation was started at 18:48 hrs and completed at 18:59 hrs. The cephalon weighed 4.67 kg prior to perfusion.

By hanging two bladders with different cryoprotectant concentrations on a teeter-totter atop an elevated tripod, a smoother transition of increasing concentrations of cryoprotectant can be achieved (see the Discussion section for a more detailed explanation of the field equipment).

The estimated height of the bladders on the teeter totter was 36 inches to 38 inches which is (36" x 2.054 mmHg per inch of height =) 74 to 78 maximum arterial pressure at the infusion site. The goal is to have the pressure between 70 and 80 mmHg and the bladders can be raised or lowered as needed to optimize flow and protection of the vasculature.

The gravity-induced perfusion flow was initiated at 19:12 hrs with Bladder #2 containing nM22 cryoprotectant with a concentration of 0.05 CNV). See the below Table of Concentrations (Brix) of nM22 Solution for the precalculated refractive index of the individual bladders, times when the bladders were started, and the refractive index of the effluent samples.

Refractive index (RI) readings were inconsistent; samples from the same bag produced several different readings, therefore, RI readings were not recorded (see the Discussion section).

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. When the bladder system is used, bladders 6 & 7 represent the pause. 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.

Bladder #6 was hung at 20:01 hrs and bladder #7 was hung at 20:14 hrs

Bladder #12 was hung at 21:24 hrs. The one-hour countdown to termination of cryoprotectant perfusion was started. The cryoprotection concentration of the bladder was 50.2 Brix.

Field cryoprotection was terminated at 22:30 hrs. The terminal cryoprotectant concentration as measured at the left jugular vein was still 50.3 Brix. The cephalon weighed 4.8 kg at 22:32 hrs which was a weight gain of 0.13 kg, or 2.8%. The patient was moved into the dry ice shipper at 22:35 hrs and the shipper was filled with approximately 5 lbs. .of dry ice to initiate dry ice cooling. (see the Discussion section)

6. Transport

T+1 days

The funeral home vehicle, with the patient, left for the airport at 07:00 hrs. The TSA inspection was lengthy (see the Discussion section), but the team managed to catch their flight, which departed at 08:36 hrs and arrived in Phoenix, AZ at 09:30 hrs. The patient arrived at Alcor at 10:45 hrs. The patient temperatures were: burr hole -65.2°C and NPT -68.0°C.

7. Cooling to Liquid Nitrogen Temperature

A computer program was used to initiate cryogenic cooldown at 11:01 hrs on T+1 days, plunging to -110°C and descending thereafter at -1°C/hour to liquid nitrogen temperature. On T+5 at 10:44 hrs, an uneventful cooldown was terminated. On T+144 days CT scans were made of the patient's brain while in liquid nitrogen; the patient was then transferred to long-term maintenance at liquid nitrogen temperature.

8. Timeline and Time Summaries

Timeline

T-0 days

06:39 Estimated time of cardiac arrest
------- Ice packed around patient's head by family (time not recorded)
07:39 Pronouncement of legal death
17:32 Start of manual chest compressions
17:38 Placement of first intraosseous device
17:39 Administration of first medication (20 g sodium citrate)
17:42 Placement of second intraosseous device
17:42 Administration of final medication (200 mL decaglycerol/THAM)
------ Pickup and Transport patient to mortuary (time not recorded)
18:02 Termination of cardiopulmonary support
18:17 Start of field surgery
18:48 Start of cephalic isolation
18:59 Weight of cephalon = 4.67 kg
19:04 Start of open circuit field cryoprotection (FCP)
22:30 End of FCP (final Brix reading = 50.3)
22:32 Weight of cephalon after perfusion = 4.8 kg (0.13 kg weight gain or 2.8%)
22:35 Start of dry ice cooling

T+1 days

07:00 Departure of patient from funeral home
08:36 Patient flight leaves the airport
10:45 Arrival of patient at Alcor (BHT = -65°C, NPT = -68°C)
11:01 Start of patient cryogenic cooldown to LN_2 temperature

T+5 days

10:44 End of cooldown to LN_2 temperature

T+144 days

CT scans were made of the patient's brain at LN_2 temperature; the patient was then transferred to long-term maintenance at LN_2 temperature

Time Summaries

Stabilization

Event Duration
hrs: mins

01:00 From the estimated time of cardiac arrest (ETCA) to pronouncement of legal death: 06:39 hrs to 07:39 hrs
28:06 From ETCA to the patient's arrival at Alcor: 06:39 hrs on T-0 to 10:45 hrs on T+1
10:53 From ETCA to start of cardiopulmonary support: 06:39 hrs to 17:32 hrs
11:00 From ETCA to start of medication administration: 06:39 hrs to 17:39 hrs
00:03 From start to the end of medication administration: 17:39 hrs to 17:42 hrs

Field Surgery and Cryoprotection

Event Duration
hrs: mins

11:38 From ETCA to start of field surgery: 06:39 hrs to 18:17 hrs
00:43 From the start of surgery to end of surgery: 18:17 hrs to 19:00 hrs
12:25 From ETCA to start of field cryoprotection (FCP): 06:39 hrs to 19:04 hrs
03:26 From the start of FCP to end of FCP: 19:04 hrs to 22:30 hrs
15:51 From ETCA to end of FCP: 06:39 hrs to 22:30 hrs
00:42 From the start of surgery to end of the cephalic isolation: 18:17 hrs to 18:59 hrs
00:47 From the start of surgery to the start of the FCP: 18:17 hrs to 19:04 hrs
04:13 From the start of surgery to the end of the FCP: 18:17 hrs to 22:30 hrs

Cryogenic Cooldown

Event Duration
hrs: mins

12:31 From the end of FCP to the start of cooldown: 22:30 hrs on T-0 to 11:01 hrs on T+1
28:22 From ETCA to start of cooldown: 06:39 hrs on T-0 to 11:01 hrs on T+1
00:16 From arrival at Alcor to the start of cooldown: 10:45 hrs to 11:01 hrs

9. Table of Medications Administered

TIME	MEDICATION	DOSE	PURPOSE
17:39 hrs	Sodium citrate	20 g Note 1	Anticoagulant; prevents blood clot formation.
17:40 hrs	Streptokinase	250,000 IU Note 2	A thrombolytic used to break up existing blood clots.
17:42 hrs	Heparin	50,000 IU	Anticoagulant; prevents blood clot formation.
17:44 hrs	Tempol	5 g	Low molecular weight superoxide scavenger used to mitigate ischemia-induced free radical damage.
17:48 hrs	Minocycline	200 mg	Antibiotic; reduces microbial overgrowth during long transport times.
17:50 hrs	Decaglycerol/THAM	200 ml Note 3	Decaglycerol inhibits cerebral edema.

Notes:

1. The standard formulation for sodium citrate is 20% w/v, in sterile packaging provided by the manufacturer. This patient received 20 grams of sodium citrate as per protocol because his weight was over 40 kg.

2. The standard administration of streptokinase is 250,000 IU dissolved in 5 mL of 9% sodium chloride and sterile packaged by the manufacturer.

3. Decaglycerol/THAM is administered as a custom formulation of 20% w/v decaglycerol and 4.5% w/v THAM (tromethamine) in water.

10. Table of Concentrations (Brix) of nM22 Solution

A-2999 step-ramp, nM22						
Endpoint is over 49.9 Brix from both jugulars for 1/2 hr						
2-liter bag labeled	[nM22], CNV	Brix (calc)	bag started, hr:min post-pro-nouncement	bag flow rate, ml/min	Brix, effluent	Comments
			13:18			start cryoprotection
2	0.05	11.81	13:26			
3	0.08	13.14	13:37	182		
4	0.14	15.35	13:50	154		
5	0.23	19.03	14:03	154		
6	0.50	29.85	14:15	167		
7	0.50	29.85	14:28	154		
8	1.06	52.31	14:40	167		
9	1.06	52.31	14:54	143		
10	1.06	52.31	15:09	133		
11	1.06	52.31	15:25	125		
12	1.06	52.31	15:38	154	50.3	starting 1 hr countdown
13	1.06	52.31	15:52	143		
14	1.06	52.31	16:19	74		
			16:44	80	50.3	end cryoprotection

When the bladders with precalculated concentrations of cryoprotectant are made up in the lab, the first bladder in the series contains only the B1 carrier solution with no cryoprotectant and was intended to be used for purging air bubbles. Limited experience with the bladder system, however, has shown that better edema control is provided when the initial perfusion is done with cryoprotectant. As a result, cryoprotectant perfusion is initiated with Bladder #2. When there is sufficient experience to make this the standard protocol, the lab procedure for creating the Bladders will be changed so that Bladder #1 will contain cryoprotectant.

11. Discussion

Standby, Stabilization and Transport

The original funeral home agreed to assist Alcor with the case, but after arriving at the patient's home for pickup, declined assistance citing insurance problems. This is not anticipated to be a frequent issue in the future. Most funeral homes will openly decline to be involved upfront rather than accepting and then changing their mind.

Upon arriving in the area, the team experienced problems with finding dry ice which was extremely limited due to Halloween having just occurred, and suppliers had not yet restocked. All the dry ice suppliers called were closing or closed. One seller who was closing requested $1000.00 to stay late.. All grocery stores in the area were completely sold out of dry ice. If a future case occurs near this holiday, Alcor should anticipate a possible shortage of dry ice and the fact that dry ice suppliers may not be open for late cases.

The temperature logger was not functioning properly as it was reading 55.55 degrees on all channels when the patient was placed in the dry ice shipper and during the early part of the transport, but it was operating normally upon arrival at Alcor. The reason for the malfunction is not known. Alcor will ensure that there are multiple loggers in each kit and always keep the loggers plugged in even if it appears as though they are not functional.

When the neuro shipper was x-rayed by TSA, the inspector saw the thermocouple wires and thought it might be a bomb. ICE personnel explained, but the inspector delayed ICE until they almost missed the flight. ICE will work on a carry-on, itemized list of why Alcor teams are allowed to do what they do to hopefully prevent a recurrence of this situation.

Field Cryoproptectant surgery and Perfusion

This case took place in 2021 and this report is being finalized in 2023. It was not practical to have cannulae of every size in the field kits and that resulted in occasionally not having the size needed, which then resulted in cannulae that would back out of the vessel, even after being tied off. Alcor now has specially designed, 3-D printed cannulae that will work with all vessel sizes.

The gravity feed system for field cryoprotection (FCP) uses a tripod that can be adjusted for height to control the arterial pressure. The pre-mixed cryoprotectant was in a series of bladders with graduated concentrations [measured by the refractive index (RI) in Brix units]. By hanging two bladders with different RI concentrations on a teeter-totter atop the tripod, as the bladder with the lower RI runs out and becomes lighter, at the mid-way point the teeter-totter will allow both bladders to flow, essentially mixing the two concentrations and creating a smoother transition from one concentration to the next. When the bladder with the lower RI runs out, the full concentration of the bladder with higher RI is then flowing exclusively. This process allows for a smoother curve in the increasing concentrations of cryoprotectant.

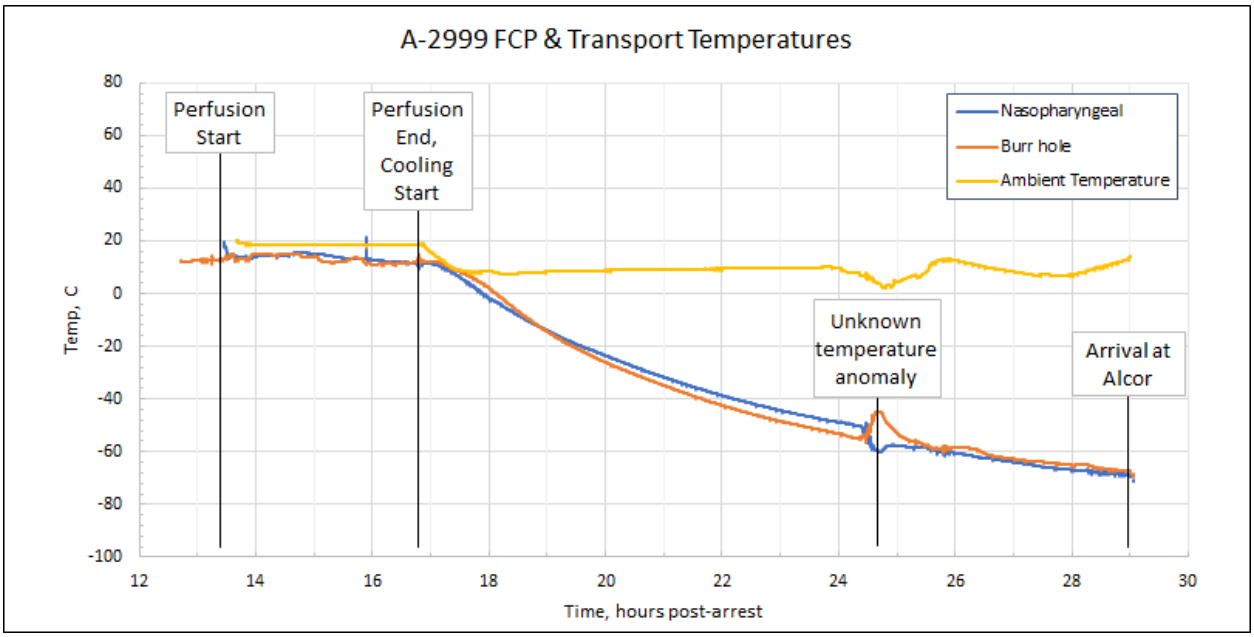
Refractive index (RI) readings were inconsistent; samples from the same bladder produced several different readings, therefore, RI readings were not recorded. The refractometer was determined to work properly upon arrival at Alcor. It is possible that some samples were taken outside of the temperature range that RI readings are usually measured, producing discrepancies. It is important to measure samples at a uniform temperature.

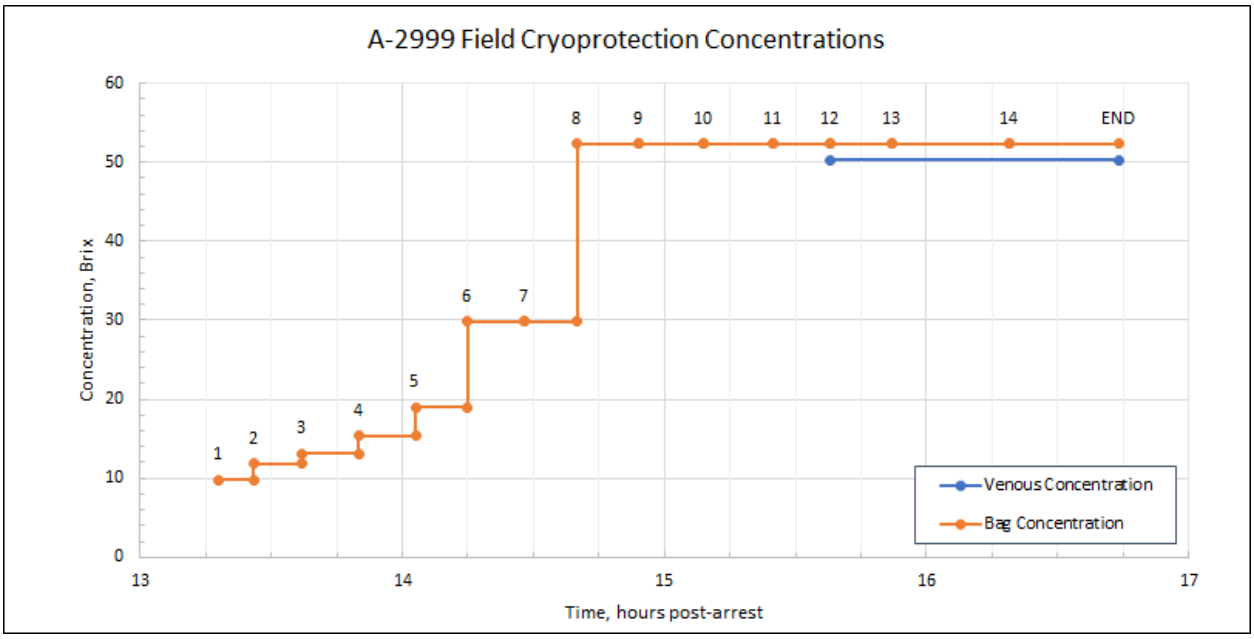
Refractive index readings can vary if the sample temperature is outside the automated temperature calibration range (ATC) of the refractometer unit. To prevent this, wait several minutes for the sample to warm up before taking a reading.

Four attempts were made to weigh the cephalon using a mesh bag and the hanging scale in the kit, but the mesh always ripped. The cephalon was finally weighed on a mortuary scale, but because the scale was not considered to be very accurate, the weight is only an estimate.

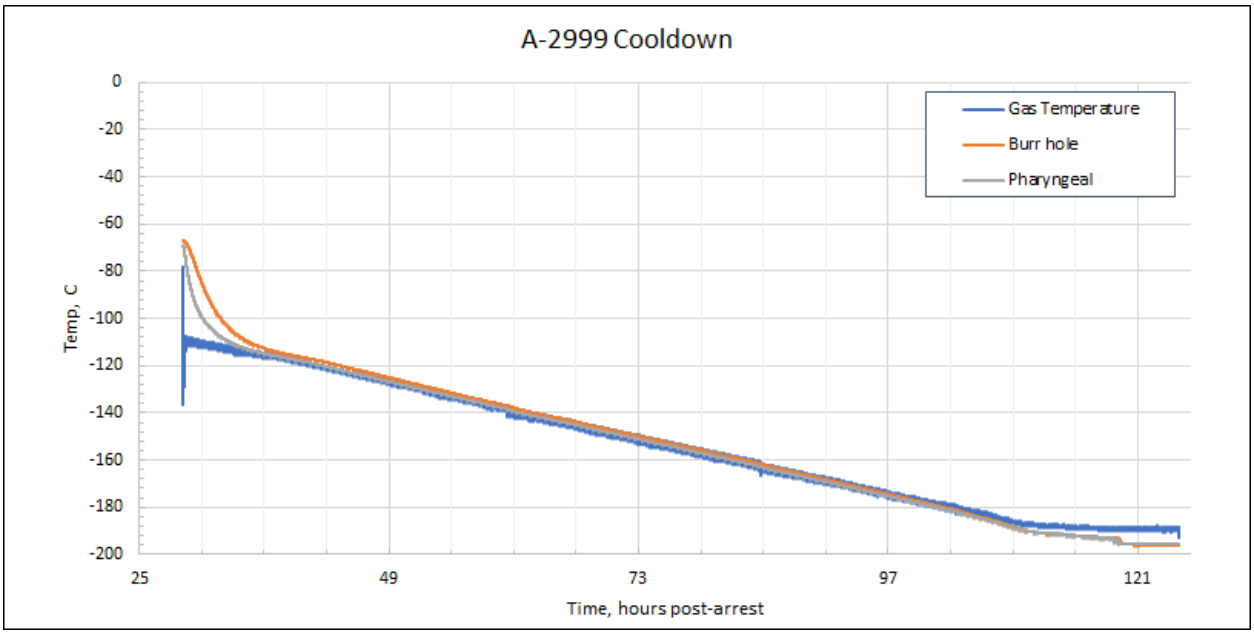
When the patient was moved into dry ice shipper it was filled with approximately 5 lbs. of dry ice to initiate cooling. As much dry ice as possible was added without preventing the internal Styrofoam lid from being closed. This can be limited based on the size of the cephalon.

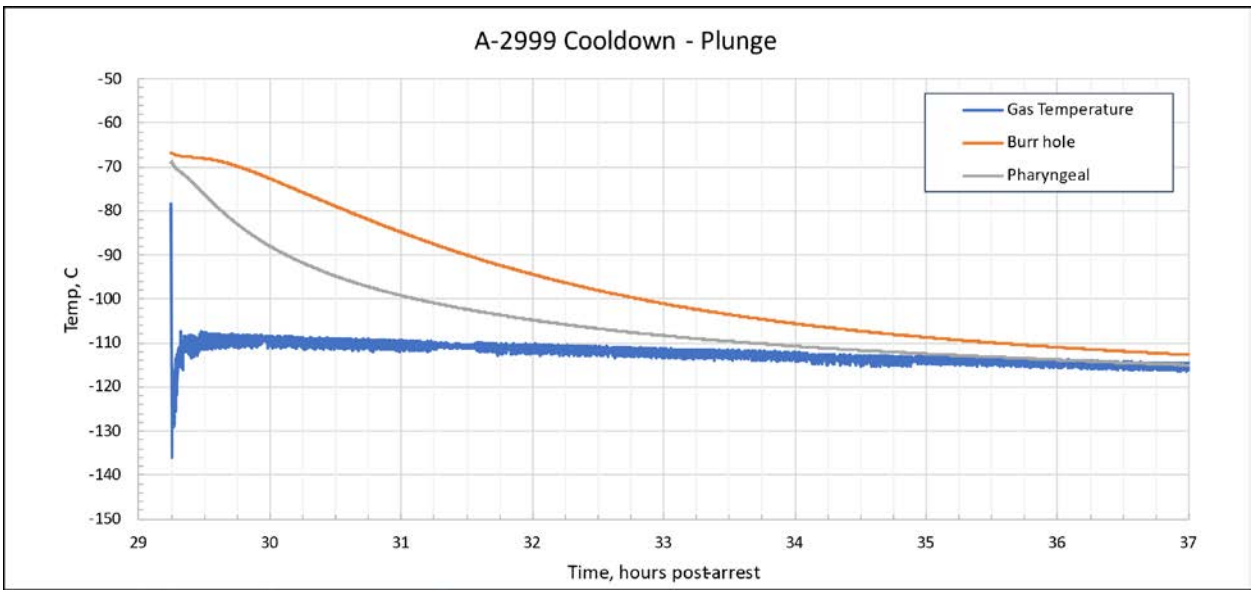
12. Graphs and CT Scans



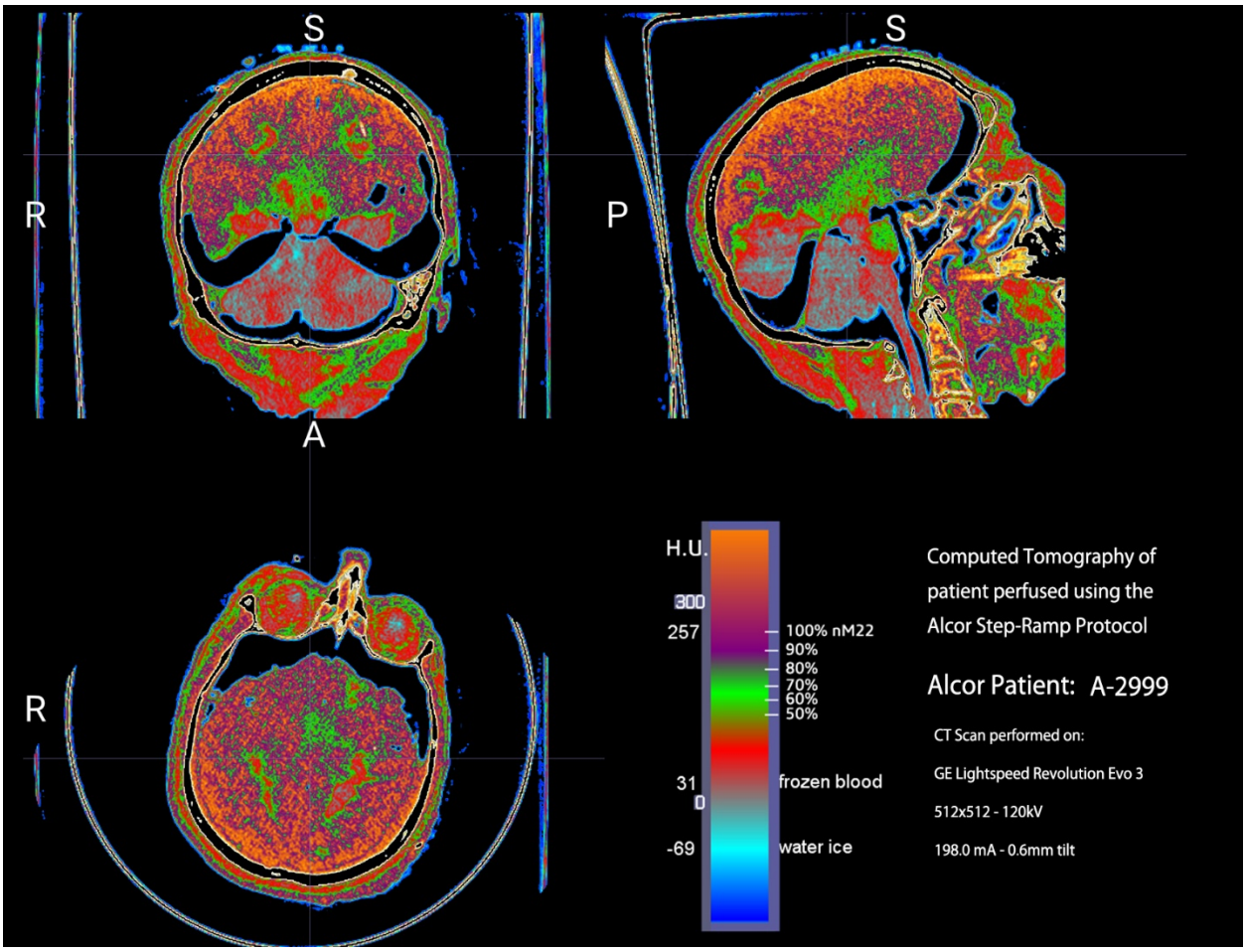


Note: The numbers (1-14) are bladder numbers and refer to the earlier Table of Brix Concentrations.




A-2999 Cooldown - Plunge
Gas Temperature
Burr hole
Pharyngeal
Temp, C
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
29
30
31
32
33
34
35
36
37
Time, hours post-arrest

Cryoprotectant Distribution (Post-cryopreservation CT scan)



The post-cryogenic cooldown CT scans were obtained on T+144 days; the patient was at liquid nitrogen temperature (-196°C).

Despite the extensive ischemia this patient sustained, the frontal and parietal lobes show good cryoprotection. In fact, the areas close to the edge of the cranium indicate concentrations of M22 that seem higher than the 100% concentration necessary to vitrify, an unusual phenomenon, especially in ischemic brains. Given this was also the where the thermocouple was placed, this could also explain why no isotherm was detected in the cooling graph. Other areas of the brain, most notably the cerebellum, look frozen, and are more consistent with the post-mortem delays in this patient.