Alcor A-2924

Case Report

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January– 2024

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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 before T-0, and T+X represents occurrences following T-0.

A-2924 was a 73-year-old member with whole body cryopreservation arrangements. For lack of notification while the member was alive, this case was a post-mortem Field Cryopreservation (FCP), done as a neuro on whole body. The cause of death on the death certificate was sudden cardiac arrest, subsequent to coronary artery disease. The cardiac arrest which was estimated to be one hour before the pronouncement of legal death at 12:22 hrs. The member was pronounced legally deceased in Indiana at 13:22 hrs on T-0 days in 2022.

After field stabilization and cryoprotection, the patient was air transported on dry ice to Alcor for cryogenic cooldown. The patient arrived at Alcor on T+4 days at 08:31 hrs. The cryogenic cooldown was initiated on T+4 days at 09:22 hrs and terminated on T+9 days at 22:21 hrs. The patient was transferred to long-term maintenance at liquid nitrogen temperature on T+16 days at 12:30 hrs.

2. Deployment

T-0 days

Alcor received a call at 15:31 hrs from their medical answering service that this member had collapsed while playing tennis and was deceased upon arrival at a local hospital. This case took place before the time of cardiac arrest was being collected for the S-MIX data and therefore had to be estimated. It was estimated that the cardiac arrest took place at 12:22 hrs and the patient was pronounced legally deceased at 13:22 hrs. The patient was transferred to a local funeral home that agreed to cover the patient with water ice.

At 16:06 hrs Alcor's Medical Response Director (MRD) deployed International Cryomedicine Experts (ICE), one of Alcor's strategic partners. Delays of more than 18 hours (between clinical death and stabilization and cryoprotectant perfusion) can result in ischemic damage to the vasculature and potentially compromise successful perfusion. To prevent a straight freeze procedure (cryopreservation without cryoprotectant perfusion) for this patient, ICE would need to obtain air transportation to the patient's location and begin stabilization within that short time limit.

3. Stabilization

T+1 days

The ICE team, made up of two paramedics, was able to secure the necessary transportation and arrived at the funeral home in Indiana at 08:20 hrs. The patient had ice bags around the head and the hospital had placed bilateral IVs in the patient's arms and an IO (intraosseous device) in the right tuberosity of the patient's right leg, which allowed immediate access to the patient's

vasculature to administer the stabilization medications. The Abbreviated Medications Protocol was used due to the length of time since the patient went into cardiac arrest.

Mechanical cardiopulmonary support using the ROSC-U chest compression device was started at 08:50 hrs and the administration of stabilization medications was initiated at 08:56 hrs (see the below Table of Medications Administered for the names of the medications, the dosages, and the times of administration) and was completed at 09:09 hrs.

4. Field Surgery and Washout

The field bladder perfusion system was set up and the surgical trays opened and ready (see the Discussion section for details on this system). Cardiopulmonary support was terminated at 09:16 hrs to prepare the patient for surgery.

Field surgery was initiated at 09:18 hrs with an incision in the neck. The right carotid artery was raised at 09:28 hrs and cannulated with an 18-gauge rigid cannula at 09:32 hrs. The left carotid artery was cannulated at 09:43 hrs, also with an 18-gauge rigid cannula. As the cephalon had not been removed from the torso, the vertebral arteries could not be accessed for assessment of the Circle of Willis. The jugular veins were identified and allowed to drain to the table.

25,000 IU streptokinase, 10% of the dosage used for whole-body patients, a fibrinolytic, was added to Bladder #2 at 09:46 hrs, which would be the first bladder used for cryoprotectant perfusion (see the Table of Concentrations (Brix) of nM22 Solution, for the times the bladders were started, the precalculated concentrations of each bladder, and the refractive index of effluent samples taken.) To mitigate edema, perfusion was started with the lowest concentration of cryoprotectant.

The open circuit, gravity-induced cryoprotectant perfusion was initiated at 09:50 hrs using Bladder #2. The patient's scalp was prepped to establish the burr holes at 09:58 hrs. The right burr hole was opened at 10:03 hrs, using a Codman perforator. The left burr hole was made at 10:05 hrs. The burr holes were cleaned, and a thermocouple was placed in the right burr hole, secured to the scalp, and connected to a data logger at 10:10 hrs.

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. 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

At 11:12 hrs commercial antifreeze was added to the water in the heat exchanger to allow for temperatures below 0°C (see Discussion section). The one-hour countdown to the termination of perfusion started at 13:25 hrs. The refractive index reading from the left jugular vein was 50.0 Brix, 1.06 of the concentration needed to vitrify (CNV). The bladder system cryoprotectant perfusion was terminated at 14:26 hrs. The terminal refractive index reading was 51.1 Brix.

The patient was moved into the dry ice shipper and covered with approximately 200 lbs. of dry ice at 14:59 hrs.

T+2 days

The patient's temperature was checked to see if dry ice temperature (-80°C) had been reached, which it had not. Additional dry ice was added, and the patient continued to cool. The room temperature at the funeral home where the patient was temporarily stored was not recorded.

5. Patient Transport

T+3 days

Additional dry ice was added to the shipper at 09:20 hrs. The patient was transported to the airport starting at 17:34 hrs.

T+4 days

The patient left for the airport at 01:40 hrs and arrived at Alcor at 08:31 hrs. The patient's temperatures were -65°C nasopharyngeal temperature and burr hole temperature -70.8°C.

6. Cooling to Liquid Nitrogen Temperature

T+4 days

Computer controlled cryogenic cooldown was initiated at 09:22 hrs, starting from approximately -70°C and cooling at -1°C/hour to liquid nitrogen temperature. On T+9, an uneventful cooldown was terminated. On T+16 days at 12:30 hrs the patient was transferred to long-term maintenance at liquid nitrogen temperature.

7. Timeline and Time Summaries

Timeline

T-0 days	12:22	Estimated time of cardiac arrest
T-0 days	13:22	Pronouncement of legal death
T-0 days	13:25	Ice bags had been placed around head (estimated)
T-0 days	13:30	Bilateral IV and IO placed at hospital (estimated)
T+1 days	08:50	Start of mechanical chest compression
T+1 days	08:56	Admin of first med (20 g Sodium Citrate)
T+1 days	09:04	Admin of final med (200 ml Decaglycerol/THAM)
T+1 days	09:16	Stopped CPS (NPT)
T+1 days	09:18	Start field surgery
T+1 days	09:20	ICE team arrives at funeral home
T+1 days	09:45	End if surgery (estimated)
T+1 days	09:50	Start open circuit cryoprotection (FCP)
T+1 days	13:25	Start 1-hr countdown to termination of perfusion
T+1 days	14:26	End cryoprotection (terminal concentration 51.1 Brix, 1.06% CNV)
T+1 days	14:59	Start of dry ice cooling
T+3 days	17:34	Transport patient to airport
T+4 days	01:40	Departure of patient from airport to Alcor
T+4 days	08:31	Arrival of patient at Alcor OR (-65 deg C)
T+4 days	09:22	Start of cryogenic cooldown
T+9 days	22:21	End of cryogenic cooldown
T+16 days	12:30	Transfer of patient to long-term maintenance at LN2 temperature

Time Summaries

Event Duration hr:min		days	time	
FIELD STABILIZATION				
01:00	From:	T-0	12:22	Estimated time of cardiac arrest
	Till:	T-0	13:22	Pronouncement of legal death
20:28	From:	T-0	12:22	Estimated time of cardiac arrest
	Till:	T+1	08:50	Start of mechanical chest compression
20:34	From:	T-0	12:22	Estimated time of cardiac arrest
	Till:	T+1	08:56	Admin of first med (20 g Sodium Citrate)
FIELD SURGERY AND LIQUID NITROGEN COOLING				
00:14	From:	T+1	08:50	Start of mechanical chest compression
	Till:	T+1	09:04	Admin of final med (200 ml Decaglycerol/THAM)
20:56	From:	T-0	12:22	Estimated time of cardiac arrest
	Till:	T+1	09:18	Start field surgery
00:27	From:	T+1	09:18	Start field surgery
	Till:	T+1	09:45	End if surgery (estimated)
21:28	From:	T-0	12:22	Estimated time of cardiac arrest
	Till:	T+1	09:50	Start open circuit cryoprotection (FCP)
04:36	From:	T+1	09:50	Start open circuit cryoprotection (FCP)
	Till:	T+1	14:26	End cryoprotection (terminal concentration 51.1 Brix)
20:56	From:	T-0	12:22	Estimated time of cardiac arrest
	Till:	T+1	09:18	Start field surgery
00:32	From:	T+1	09:18	Start field surgery
	Till:	T+1	09:50	Start open circuit cryoprotection (FCP)
DRY ICE AND LIQUID NITROGEN COOLING				
05:08	From:	T+1	09:18	Start field surgery
	Till:	T+1	14:26	End cryoprotection (terminal concentration 51.1 Brix)
66:56	From:	T+1	14:26	End cryoprotection (terminal concentration 51.1 Brix)
	Till:	T+4	09:22	Start of cryogenic cooldown
93:00	From:	T-0	12:22	Estimated time of cardiac arrest
	Till:	T+4	09:22	Start of cryogenic cooldown
92:09	From:	T-0	12:22	Estimated time of cardiac arrest
	Till:	T+4	08:31	Arrival of patient at Alcor OR (-65 deg C)
00:51	From:	T+4	08:31	Arrival of patient at Alcor OR (-65 deg C)
	Till:	T+4	09:22	Start of cryogenic cooldown

8. Table of Medications Administered

T-0 days

TIME	MEDICATION	DOSE	PURPOSE
08:56 hrs	Sodium citrate	20 g Note 1	Anticoagulant; prevents blood clot formation.
08:59 hrs	Streptokinase	250,000 IU Note 2	A thrombolytic used to break up existing blood clots.
09:00 hrs	Heparin	50,000 IU	Anticoagulant; prevents blood clot formation.
09:01 hrs	Minocycline	200 mg	Antibiotic; reduces microbial overgrowth during long transport times.
09:04 hrs	Tempol	5 g Note 3	Low molecular weight superoxide scavenger used to mitigate ischemia-induced free radical damage.
09:04 hrs	Decaglycerol/THAM	200 ml Note 4	Decaglycerol inhibits cerebral edema.
09:46 hrs	Streptokinase	25,000 IU Note 2	A thrombolytic used to break up existing blood clots.

Notes:

1. The standard formulation for sodium citrate is 20% w/v, in sterile packaging provided by the manufacturer. 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 the patient's weight was over 40 kg.

2. If there is a delay of more than one hour after cardiac arrest, an abbreviated list of medications should be administered. The standard administration of streptokinase is 250,000 IU fixed dose, dissolved in 5 mL of 9% sodium chloride, to be added to the blood washout solution prior to remote blood washout, or to the first cryoprotection flush in the OR. The dosage is reduced to 25,000 IU in field neuro (FCP) cases and added to the first bladder). 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.

3. 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).

9. Table of Concentrations (Brix) of nM22 Solution

A-2924 step-ramp, nM22								
Preferred endpoint is over 49.9 Brix from both jugulars for 1/2hr								
2L Bag label number	[nM22], CNV	Molarity of penetrating CPAs*	Brix (calc)	Bag start hh:mm, MST	hrs post pronounc-ement	Bag avg. flow rate, mL/min	Sample time hh:mm, MST	Effluent Conc., Brix
2	0.05	0.47	11.81	9:50	20.47	100.0	11:27	40.6
3	0.08	0.78	13.14	10:10	20.80	200.0	11:36	44.1
4	0.14	1.29	15.35	10:20	20.97	166.7	12:00	48.8
5	0.23	2.15	19.03	10:32	21.17	153.8	12:48	49.7
6	0.50	4.67	29.85	10:45	21.38	200.0	13:25	50
7	0.50	4.67	29.85	10:55	21.55	117.6	13:50	50.4
8	1.06	9.91	52.306	11:12	21.83	200.0	14:22	50.7
9	1.06	9.91	52.306	11:22	22.00	117.6		
10	1.06	9.91	52.306	11:39	22.28	100.0		
11	1.06	9.91	52.306	11:59	22.62	64.5		
12	1.06	9.91	52.306	12:30	23.13	117.6		
13	1.06	9.91	52.306	12:47	23.42	64.5		
14	1.06	9.91	52.306	13:18	23.93	76.9		
15	1.06	9.91	52.306	13:44	24.37	181.8		
16	1.06	9.91	52.306	13:55	24.55	111.1		
17	1.06	9.91	52.306	14:13	24.85	153.8		
END				14:26	25.07			
* does not account for concentration of non-penetrating CPAs								

Note: 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. Bladder #2 contains the lowest concentration of cryoprotectant. 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.

10. Discussion

Field Surgery and Cryoprotectant Perfusion

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 is 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.

The height of the bladders on the teeter totter is usually 36 inches to 38 inches which is (36” x 2.054 mmHg per inch of height =) 74 to 78 mmHg 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.

More concerning is that all parts of cryoprotectant perfusion were conducted between +15°C and +10°C, which is much higher than recommended FCP temperature. As a consequence, this patient was exposed to increased cryoprotectant toxicity. FCP Protocol is to introduce all steps of M22 perfusion between 0°C and 5°C. The contractor used on this case is no longer providing services for Alcor.

The contractor did not provide the type of commercial antifreeze that was used in the heat exchanger but will do so in the future. Most consumer antifreeze is made from ethylene glycol, but it may have been propylene glycol, ethanol, methanol, and isopropyl alcohol. Looking at the perfusion graph, it seems the anti-freeze, which is intended to cool the arterial perfusate supply to sub-zero after the pause at 30 Brix, did not cool the perfusate below 0°C.

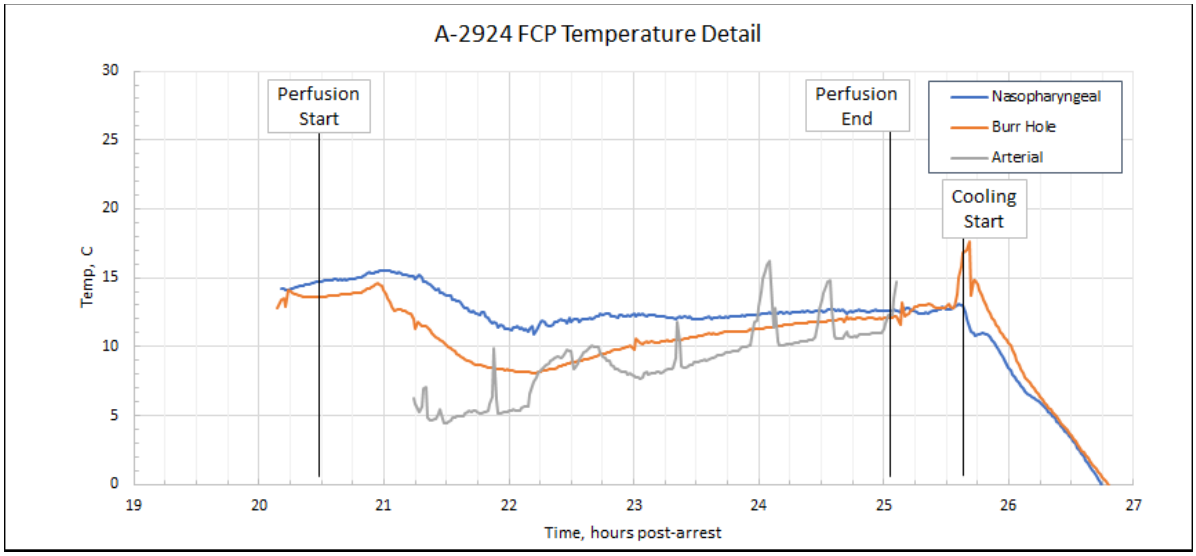
The power adapter for the heat exchanger sump pump was not in the kit. One was repurposed from another piece of equipment that was located in the funeral home. More attention will be given to checking that each kit has a full inventory of supplies.

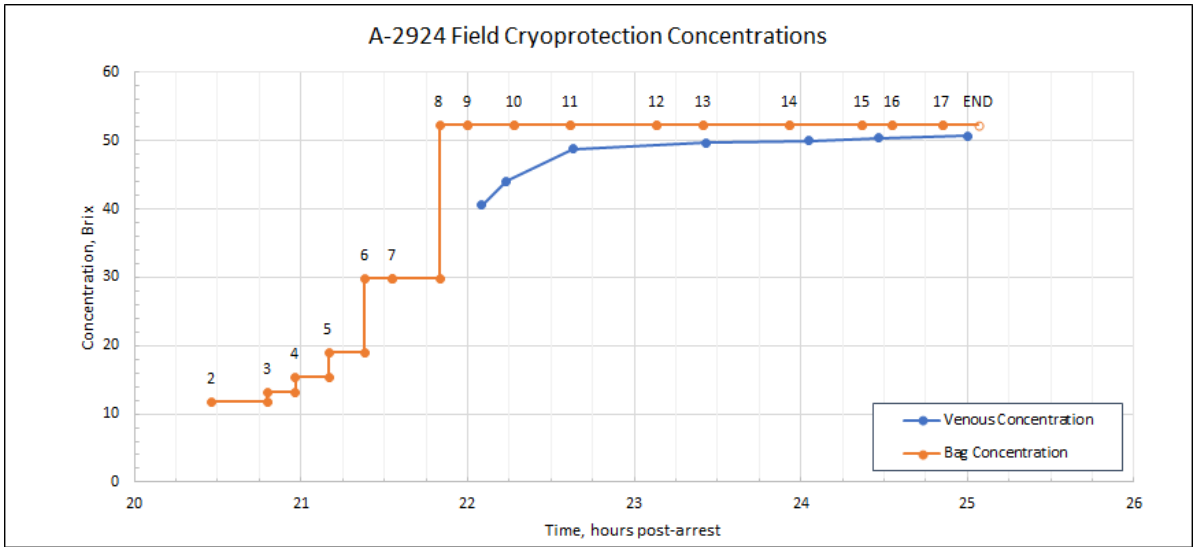
Performing a head-only cryoprotection on whole-body patients with extensive post-mortem time is expected to yield better outcomes than permitting more cold ischemic damage to accumulate. However, the current protocol for such cases is known to produce poorer results than true whole-body field cryoprotection because it only permits two-vessel cannulation, which causes back flow through the vertebrals and decreased perfusion pressure in the brain.

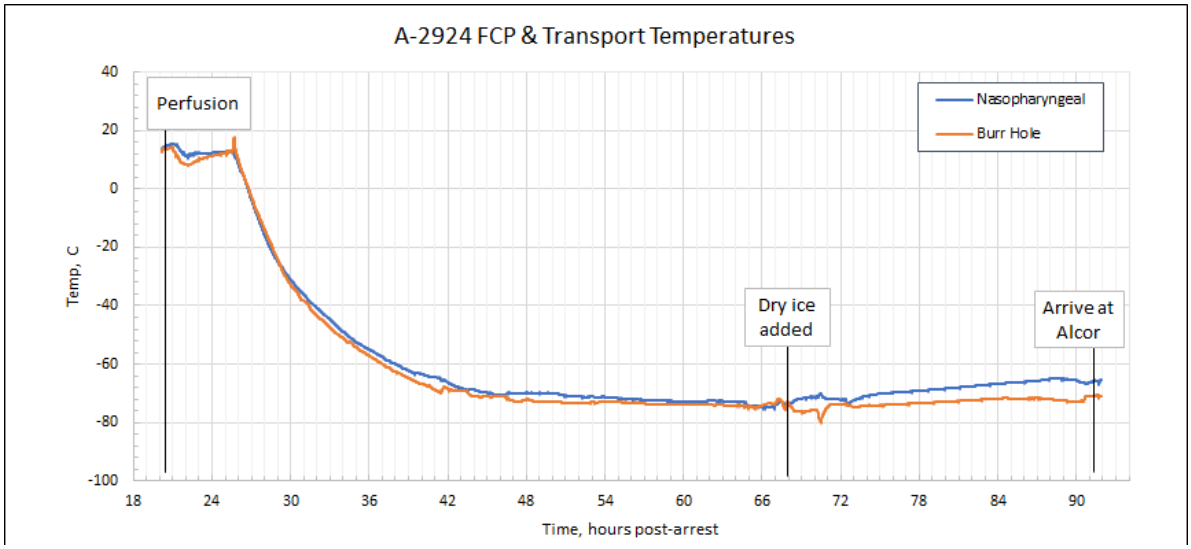
Patient Transport

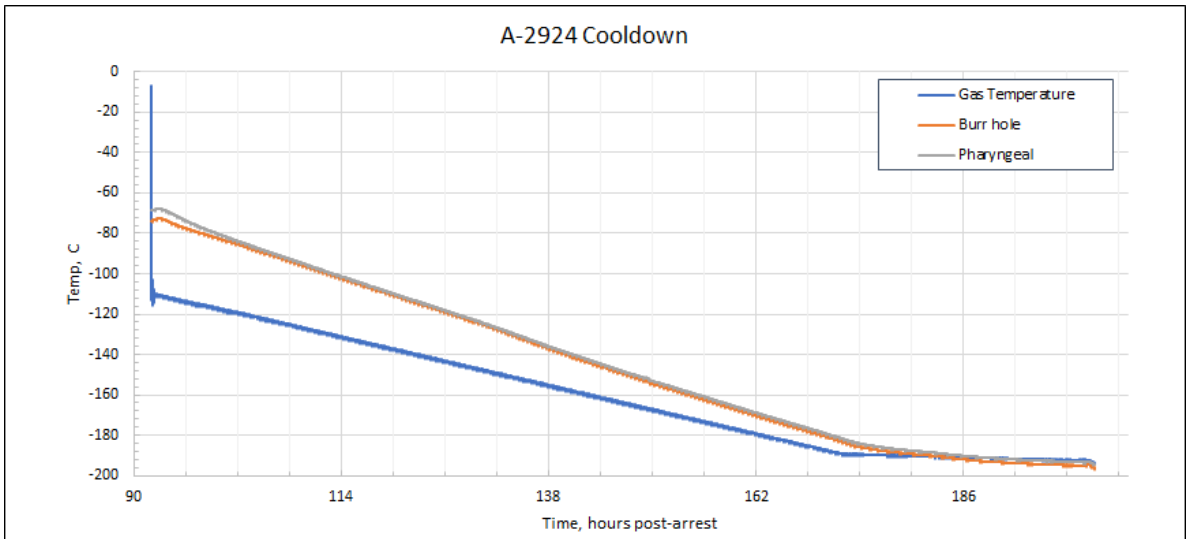
On T+2 days the whole-body patient was still being cooled to dry ice temperature (-80°C) before being taken to the airport. Alcor requires patients to be at dry ice temperature before transport to Alcor to ensure they do not warm up during transport, which would cause a damaging cryopreservation/thaw cycle.

11. Graphs and CT Scans





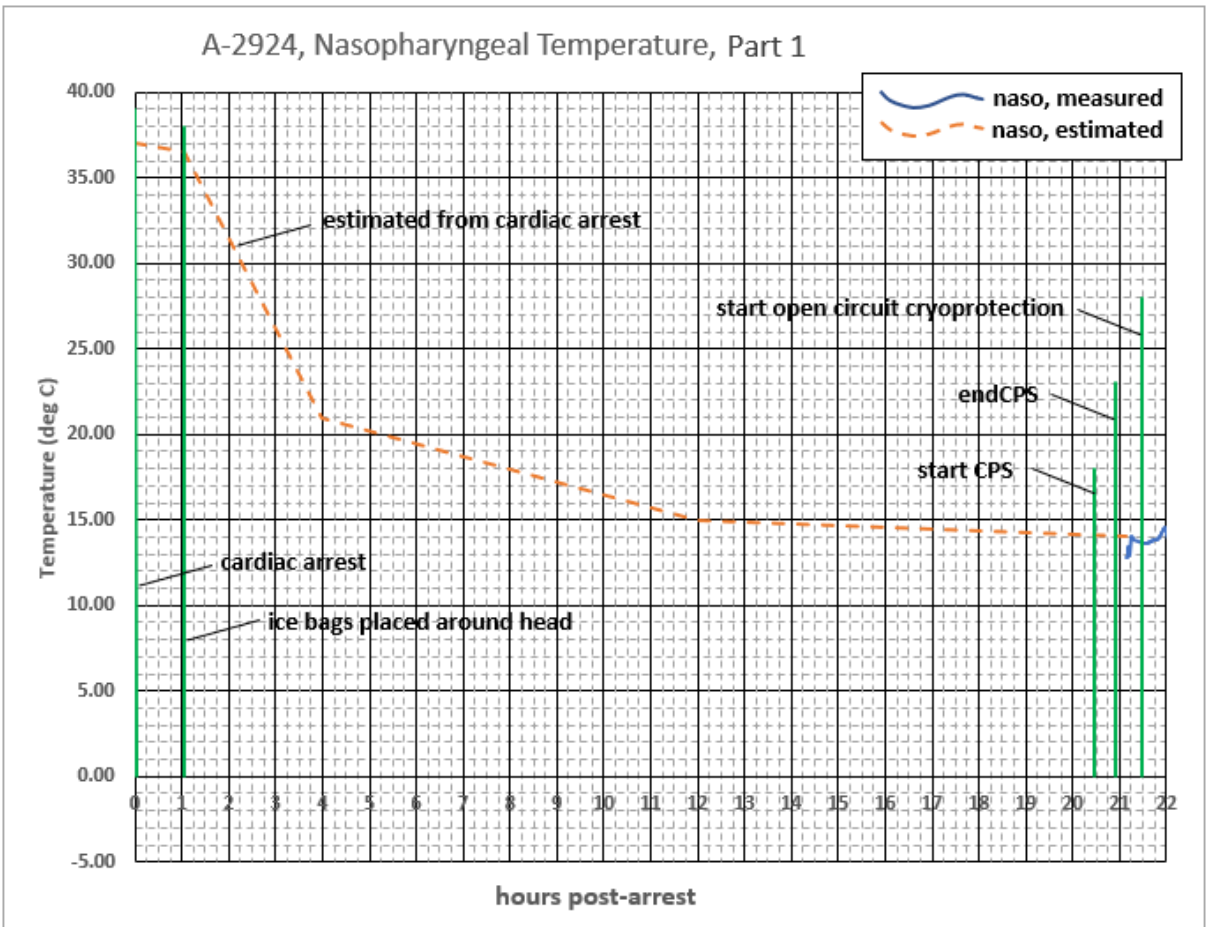

A-2924 FCP & Transport Temperatures
Perfusion
Dry ice added
Arrive at Alcor
Nasopharyngeal
Burr Hole
Temp, C
Time, hours post-arrest
40
20
0
-20
-40
-60
-80
-100
18
24
30
36
42
48
54
60
66
72
78
84
90


A-2924 Cooldown
Gas Temperature
Burr hole
Pharyngeal
Temp, C
Time, hours post-arrest
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
90
114
138
162
186

12. S-MIX

The Standardized Measure of Ischemic Exposure (S-MIX) expresses the total ischemic exposure prior to the start of cryogenic cooling as the equivalent duration of normothermic ischemia. An S-MIX of 00:00 (hh:mm) is the ideal case of no ischemic damage. The higher the S-MIX time, the more ischemic damage to the brain. Factors that improve the S-MIX, and that are quantitatively accounted for in the below table are: shorter times at higher temperatures, ventilation during cardiopulmonary support (CPS), and oxygenation during blood washout. As calculated below, S-MIX duration for this case is 07:53.

event	segment #	days (T+X)	time (MST) duration	post-arrest	Tnaso (deg C)	CPS w/ ventil.	washout oxygen.	S-MIX (hh:mm)
Cardiac arrest estimate		T-0	12:22	00:00	37.0			
	seg 1		01:03	01:03	-0.5	no	no	01:02
Ice bags had been placed around head		T-0	13:25	01:03	36.5			
	seg 2		19:25	19:25	-22.3	no	no	05:42
Start of mechanical chest compression		T+1	08:50	20:28	14.1			
	seg 3		00:26	00:26	0.0	no	no	00:05
Stop CPS		T+1	09:16	20:54	14.1			
	seg 4		00:34	00:34	-0.5	no	no	00:07
Start open circuit cryoprotection		T+1	09:50	21:28	13.6			
	seg 5		04:36	04:36	-1.5	no	no	00:42
End cryoprotection		T+1	14:26	26:04	12.1			
	seg 6		00:33	00:33	3.3	no	no	00:06
Start of dry ice cooling		T+1	14:59	26:37	15.4			
	seg 7		01:11	01:11	-15.3	no	no	00:010
Temperature drops through 0 C		T+1	16:10	27:48	0.1			
totals:			27:48	27:48	-36.9			07:53


A-2924, Nasopharyngeal Temperature, Part 1
naso, measured
naso, estimated
estimated from cardiac arrest
start open circuit cryoprotection
endCPS
start CPS
cardiac arrest
ice bags placed around head
Temperature (deg C)
hours post-arrest
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
-5.00
0
1
2
3
4
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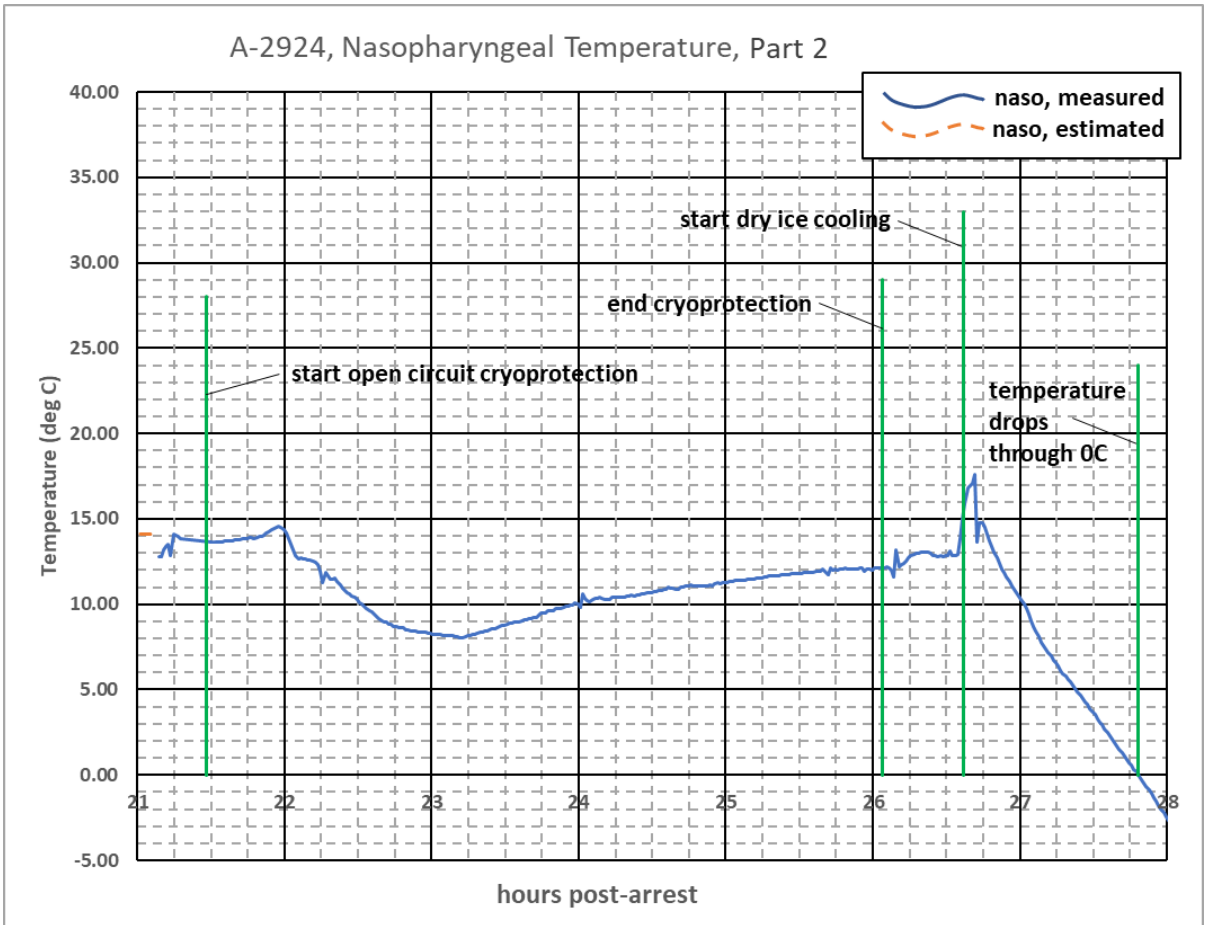

13. CT Scans

Cryoprotectant Distribution (Post-cryopreservation CT scan)

As this was a neuro-cryoprotection on a whole-body patient, no CT scans were obtained. When the Alcor CT scanner is operational, scans will be done and added to this report.