

# Alcor A-2821 Case Report



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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-2821 was a 78-year-old member with whole-body cryopreservation arrangements who suffered from diabetes. The member went into cardiac arrest at 07:43 hrs and was pronounced legally deceased in South Dakota at 07:47 hrs on T-0 days in August of 2022. The death certificate states the cause of death as natural causes. This was a Field Cryoprotection (FCP) in which only the head was cryoprotected.

After field cryoprotection the patient was driven to Alcor for cryopreservation. The patient arrived at Alcor on T+3 days at 12:05 hrs. The cryogenic cooldown was initiated on T+3 days at 12:52 hrs and terminated on T+9 days at 04:27 hrs. The patient was transferred to long-term maintenance at liquid nitrogen temperature on T+11 days at 16:56 hrs.

## 2. Patient Assessment

### T-12 days

The member was added to the Alcor Watch List for daily contact after Alcor's Medical Response Director (MRD) spoke with a full-time certified nursing assistant (CNA) who reported a decline in health and cessation of eating the day prior, and felt the member was suffering from failure to thrive. In elderly patients, failure to thrive is a state of decline that is multifactorial and may be caused by chronic concurrent diseases and functional impairments. The member also had diabetes but neither of these conditions were considered by the hospice organization to be sufficient to allow the member to be admitted into hospice care.

For the next week, the amount of food and water intake varied. The CNA understood that should the member decline before getting into hospice, she would call EMS if needed to pronounce legal death.

### T-5 days

The member was accepted into hospice primarily because no food or water were being taken. Alcor's Medical Response Director (MRD) attempted to be authorized to receive health information updates.

### T-3 days

A funeral home was contacted; they outlined several complications that would affect the transport of this patient: 1) there was no cargo company within the state that handled human remains, and this would increase the time needed to acquire permits prior to a flight, 2) it would be difficult to acquire transit permits on the weekends, and 3) there was no supplier of oversized Ziegler cases locally. This last issue prompted Alcor to ship a Ziegler case to the funeral service.

Alcor's Medical Advisor spoke with the hospice facility. The member was declining but not in imminent danger at that time. The hospice facility was giving supportive care, but not giving fluids.

### 3. Deployment

#### T-2 days

A hospice nurse reported that the member had stopped drinking and death could be within seven days. Alcor staff conferred and decided that due to the logistical challenges named above on T-3 days the best course of action was to cryoprotect the head in the field and then a 20-hour drive to transport the patient to Alcor.

At 11:00 hrs International Cryomedicine Experts (ICE), one of Alcor's strategic partners for providing standby, stabilization and transport (SST) as well as FCP, was informed about the pending situation. At 12:08 hrs a Level-1 deployment was called. The ICE team arrived at the member's residence at 22:47 hrs. Any reluctance to communicate directly with Alcor seemed to have faded as both the caretaker and the hospice personnel were cooperative with the ICE team members.

#### *Sidebar:*

*The medical personnel on the Alcor Deployment Committee have determined a list of medical indicators that have either a Level-1, or a high probability of death within seven days, or a Level-2, a medium probability of death within seven days. The Deployment Committee voting members use these criteria when considering if a deployment is necessary.*

### 4. Standby and Stabilization

#### T-1 days

The member's vital signs were: Pulse 111/min, Respiration 22/min, 125 cc urine output over the last 25 hours and concentrated, blood pressure 130/94, capillary oxygen saturation (SpO<sub>2</sub>) 81 to 82% on room air. The member would occasionally moan, lung sounds were course, had poor skin turgor, but no mottling.

The member was being given morphine for pain management, atropine to reduce excess mucus secretion and saliva production, and lorazepam for anxiety, all as needed. Hospice checks were done once per day and there was a 24-hour caregiver on site. All stabilization equipment and coolers of ice were pre-positioned near the member. 500 lbs. of dry ice was waiting at the funeral home.

### T-0 days

The member was pronounced legally deceased at 07:47 hrs by a hospice nurse. The ICE team leader, who was at the bedside, estimated that cardiac arrest took place at about 07:43 hrs. Since the full ICE team, consisting of four members, was at the bedside, stabilization procedures commenced immediately and many procedures could be accomplished simultaneously.

The patient was placed into a body bag with water ice and manual cardiac compressions were started at 07:47 hrs. The airway was placed at 07:48 hrs to provide ventilation. The nasogastric tube was placed at 07:50 hrs for introduction of an antacid to protect the stomach. To access the vasculature for the administration of stabilization medications, an intraosseous (IO) device was placed into the tibial plateau of the right leg at 07:51 hrs but it was not usable (see the Discussion section). A second IO was placed in the tuberosity of the left leg at 07:56 hrs and it was patent.

The first stabilization medication (propofol) was administered at 07:57 hrs (see the below Table of Medications Administered for the names of the medications, the dosages, and the times of administration). The ROS-Q mechanical chest compression device was placed on the patient and activated at 08:02 hrs.

The administration of stabilization medications was complete at 08:35 hrs. Ice was placed around the patient's head. More ice was added when the patient was placed into the body bag for transport to the funeral home. Temperatures were not recorded during stabilization because of a faulty data logger. The logger did not function and had to be reset after the ICE team arrived at the funeral home. In order to reset the logger, a computer with a specific cable is required but was not available during SST. The funeral home had a compatible cable (see the Discussion section).

## **5. Field Surgery and Cryoprotection**

At 09:30 hrs the bladder system for cryoprotectant perfusion and the surgical trays had been set up and were ready for use. Cardiopulmonary support was terminated at 09:37 hrs in order to start surgery. The patient's scalp was prepped for establishing the burr holes.

Field surgery was initiated at 09:42 hrs. The right burr hole was completed at 09:45 hrs using a Codman perforator and chilled saline to cool the perforator and the skull. The left burr hole was similarly established at 09:50 hrs. The burr holes were cleaned of debris and a thermocouple was placed in the right burr hole to obtain temperatures and was secured to the scalp with surgical staples.

The right carotid artery was raised at 09:56 hrs and cannulated with an 18 French (Fr) rigid cannula at 09:58 hrs. The left carotid artery was raised at 10:07 hrs and cannulated at 10:09 hrs with an 18 Fr rigid cannula. Given that this was not an isolated cephalon cannulation, the vertebral arteries could not be accessed to determine if the Circle of Willis was intact.

At 10:18 hrs 250,000 IU of streptokinase, a thrombolytic used to break up existing blood clots, was added to the first cryoprotectant perfusion bladder. The gravity-induced perfusion flow was initiated at 10:20 hrs with Bladder #2 containing nM22 cryoprotectant with a concentration of 0.05 concentration needed to vitrify (CNV) (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).

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..

The gravity feed system for 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]. The height of the bladders on the teeter totter was 39 inches which is (39" x 2.054 mmHg per inch of height = a maximum arterial pressure of 80 mmHg 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.

This process allows for a smoother curve in the increasing concentrations of cryoprotectant. The gravity feed system for 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].

*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/patient 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 started at 11:30 hrs and ethylene glycol antifreeze was added to the water in the heat exchanger at 11:50 hrs to bring the perfusate below 0°C. The heat exchanger sump pump did not have a power adapter. One was repurposed from another piece of equipment that was located in the funeral home. At 14:10 hrs the refractive index (RI) of the effluent was 50 Brix, and the one-hour countdown to termination of cryoprotectant perfusion was started. Cryoprotectant perfusion was terminated at 15:26 hrs. The final RI concentration was 51.3 Brix.

The patient was moved to the dry ice shipper and covered with approximately 200 lbs. of dry ice at 15:55 hrs. Because this was a weekend the transit permit could not be obtained until T+2 days.

T+1 days

A trip was made to the funeral home to check on the dry ice level. 500 lbs. of dry ice were added to the shipper.

**6. Transport**T+2 days

The Transit Permit was obtained. After waiting for dry ice to be made in the quantity needed, 150 lbs. of dry ice were added to the shipper at approximately 11:42 hrs.. The patient was loaded and enroute to Alcor at 12:28 hrs.

**7. Cooling to Liquid Nitrogen Temperature**T+4 days

The patient arrived at Alcor at 12:05 hrs with a nasopharyngeal temperature (NPT) of -80°C. A computer program was used to initiate cryogenic cooldown at 12:52 hrs, plunging to -110°C and descending thereafter at -1°C/hour to liquid nitrogen temperature. The cooldown was terminated on T+9 days at 04:27 hrs. On T+X, the patient was transferred to long-term maintenance at liquid nitrogen temperature.

## 8. Timeline and Time Summaries

### Timeline

T-0	07:43	Estimated time of cardiac arrest
T-0	07:47	Pronouncement of legal death
T-0	07:47	Start of ice in body bag cooling (estimated)
T-0	07:47	Start of manual chest compressions
T-0	07:48	Placement of airway
T-0	07:56	Placement of intraosseous device (IO)
T-0	07:57	Administration of first medication (200 mg propofol)
T-0	08:02	Start of mechanical chest compressions
T-0	08:35	Administration of final medication (100 ml decaglycerol/THAM)
T-0	08:38	Transport patient to mortuary for surgery/cryoprotection
T-0	09:30	Arrival at funeral home
T-0	09:37	Termination of cardiopulmonary support
T-0	09:42	Start of field surgery
T-0	10:19	End of field surgery (estimated)
T-0	10:20	Start of open circuit cryoprotection
T-0	11:30	Start 30-minute pause for equilibration
T-0	14:10	Start of one hour countdown to termination of perfusion
T-0	15:26	End of open circuit cryoprotection (final Brix = 51.3)
T-0	15:55	Start of dry ice cooling
T+2	12:28	Departure of patient from airport
T+4	12:05	Arrival of patient at Alcor
T+4	12:52	Start of patient cryogenic cooldown
T+9	04:27	End of cooldown
T+11	16:56	Transfer of patient to long-term maintenance at LN2 temperature



**Time Summaries**

Event Duration hr:min		days	time	
<b>FIELD STABILIZATION</b>				
00:04	From:	T-0	07:43	Estimated time of cardiac arrest
	Till:	T-0	07:47	Pronouncement of legal death
00:04	From:	T-0	07:43	Estimated time of cardiac arrest
	Till:	T-0	07:47	Start of manual chest compressions
00:14	From:	T-0	07:43	Estimated time of cardiac arrest
	Till:	T-0	07:57	Administration of first medication (200 mg propofol)
00:38	From:	T-0	07:57	Administration of first medication (200 mg propofol)
	Till:	T-0	08:35	Administration of final medication (100 ml decaglycerol/THAM)
<b>FIELD SURGERY AND CRYOPROTECTION</b>				
01:59	From:	T-0	07:43	Estimated time of cardiac arrest
	Till:	T-0	09:42	Start of field surgery
00:37	From:	T-0	09:42	Start of field surgery
	Till:	T-0	10:19	End of field surgery (estimated)
02:33	From:	T-0	07:47	Start of manual chest compressions
	Till:	T-0	10:20	Start of open circuit cryoprotection
05:06	From:	T-0	10:20	Start of open circuit cryoprotection
	Till:	T-0	15:26	End of open circuit cryoprotection (final Brix = 51.3)
07:43	From:	T-0	07:43	Estimated time of cardiac arrest
	Till:	T-0	15:26	End of open circuit cryoprotection (final Brix = 51.3)
00:38	From:	T-0	09:42	Start of field surgery
	Till:	T-0	10:20	Start of open circuit cryoprotection
05:44	From:	T-0	09:42	Start of field surgery
	Till:	T-0	15:26	End of open circuit cryoprotection (final Brix = 51.3)
<b>DRY ICE AND CRYOGENIC COOLDOWN</b>				
00:29	From:	T-0	15:26	End of open circuit cryoprotection (final Brix = 51.3)
	Till:	T-0	15:55	Start of dry ice cooling
08:12	From:	T-0	07:43	Estimated time of cardiac arrest
	Till:	T-0	15:55	Start of dry ice cooling
100:22	From:	T-0	07:43	Estimated time of cardiac arrest
	Till:	T+4	12:05	Arrival of patient at Alcor
00:47	From:	T+4	12:05	Arrival of patient at Alcor
	Till:	T+4	12:52	Start of patient cryogenic cooldown

## 9. Table of Medications Administered

### T-0 days

TIME	MEDICATION	DOSE	PURPOSE
07:56 hrs	Propofol	200 mg	Anesthetic; reduces cerebral metabolic demand; reduces the theoretic possibility of increased awareness during aggressive CPS.
07:57 hrs	Heparin	50,000 IU	Anticoagulant; prevents blood clot formation.
08:06 hrs	SMT (S-methyl-isothiourea)	400 mg Note 1	Neuroprotectant (iNOS inhibitor); protects the brain from ischemic injury; raises blood pressure.
08:13 hrs	Antacid	250 cc Note 2	A buffer used to protect the stomach from acid erosion.
08:15 hrs	Vital Oxy (w/ saline)	70 ml Note 3	Antioxidants: melatonin, vitamin E (D-alpha tocopherol), PBN (alpha Phenyl t-Butyl Nitron) and anti-inflammatory carprofen.
08:20 hrs	Sodium citrate	20 gm Note 4	Anticoagulant; prevents blood clot formation.
08:22 hrs	Decaglycerol/THAM	100 ml Total 1 <sup>st</sup> dose Note 5	Decaglycerol inhibits cerebral edema.
08:25 hrs	Streptokinase	250,000 IU Note 6	A thrombolytic used to break up existing blood clots.
08:32 hrs	Minocycline	200 mg	Antibiotic; reduces microbial overgrowth during long transport times.
08:33 hrs	Hetastarch	250 mL	Restore volume in dehydrated patients and increase cerebral perfusion during CPS.
08:35 hrs	Decaglycerol/THAM	100 ml Total 2 <sup>nd</sup> dose Note 5	Decaglycerol inhibits cerebral edema.
10:18 hrs	Streptokinase	25,000 IU Note 6	A thrombolytic used to break up existing blood clots.

#### Notes:

1. 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.

2. An antacid is inserted through the nasogastric tube in an airway.

3. 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.

4. 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.

5. 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). The fixed dose of 200 ml had to be split between two syringes. The times on the table indicate when each syringe was administered.

6. Streptokinase is not administered with the stabilization medications but is put in the first batch of washout solution. The standard administration of streptokinase is 250,000 IU dissolved in 5 mL of 9% sodium chloride, and 25,000 IU for the abbreviated medications protocol. This medication previously needed to be infused through a 0.2  $\mu$  filter. The medication now in use is already sterile filtered and can be reconstituted in the vial.

## 10. Table of Concentrations (Brix) of nM22 Solution

A-2821 step-ramp, nM22						
Preferred endpoint is effluent over 49.9 Brix for 1/2 hr						
2-liter bag called #	[nM22], CNV	Brix (calc)	bag started, hr:min MST	bag started, hr:min post-pro-nouncement	bag flow rate, ml/min	effluent, Brix
1	0.05	11.81	10:20	2:33		
2	0.08	13.14	10:32	2:45	167	15.5
3	0.14	15.35	10:47	3:00	133	
4	0.23	19.03	11:01	3:14	143	
5	0.50	29.85	11:18	3:31	118	
6	0.50	29.85	11:30	3:43	167	
7	1.06	52.31	11:49	4:02	106	
8	1.06	52.31	12:04	4:17	133	42.1
9	1.06	52.31	12:17	4:30	154	44.1
10	1.06	52.31	12:36	4:49	105	48.9
11	1.06	52.31	12:55	5:08	105	
12	1.06	52.31	13:29	5:42	59	49.5
13	1.06	52.31	14:10	6:23	49	50.1
14	1.06	52.31	14:23	6:36	154	50.4
15	1.06	52.31	14:40	6:53	118	50.7
END			14:46	6:59		50.7

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. 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 and Stabilization

The first attempt to place an intraosseous device to access the vasculature for the administration of stabilization medications was not successful. Attempting vascular access through any route, IV, IO, etc., is not always successful on the first attempt. In this case, the trocar needle apparently glanced off of the plateau, when injected, and did not enter the bone. These IOs are a one-attempt-only device, so a second attempt with the same IO could not be made. As the kit has numerous IOs for this very reason, another one was used, and the second attempt was successful.

## Field Surgery and Field Cryoprotection (FCP)

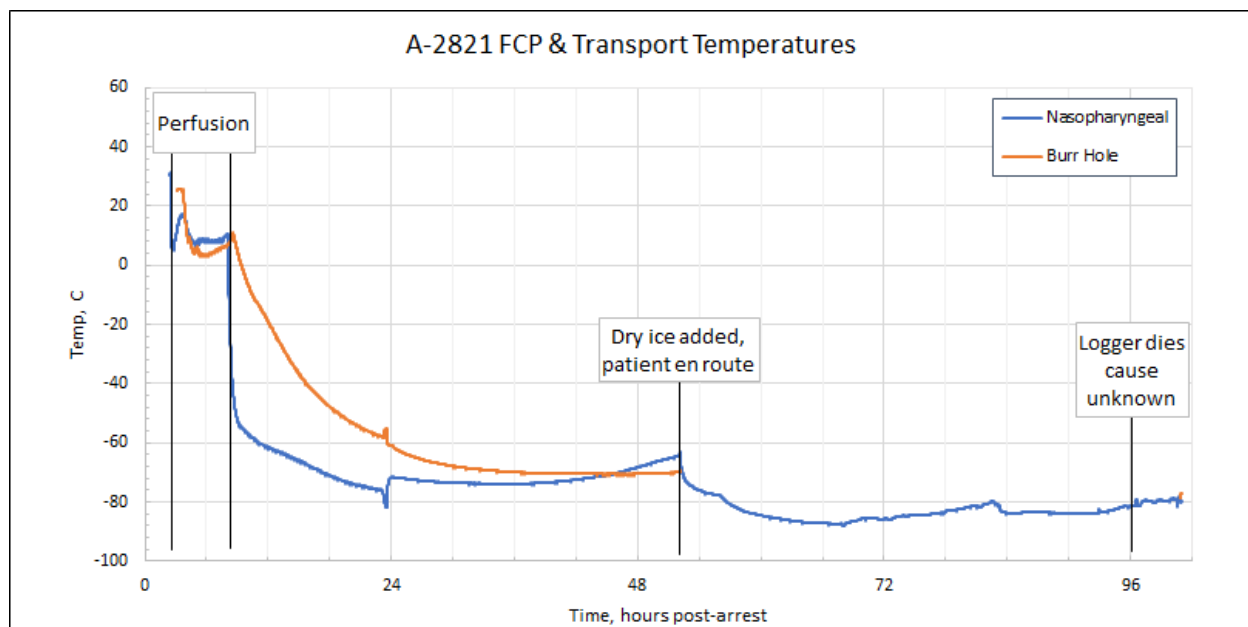
The gravity feed system for FCP uses a tripod that can be adjusted for height to control the arterial pressure. The pre-mixed cryoprotectant was in a series of bladders with graduated concentrations [measured by the refractive index (RI) in Brix units].

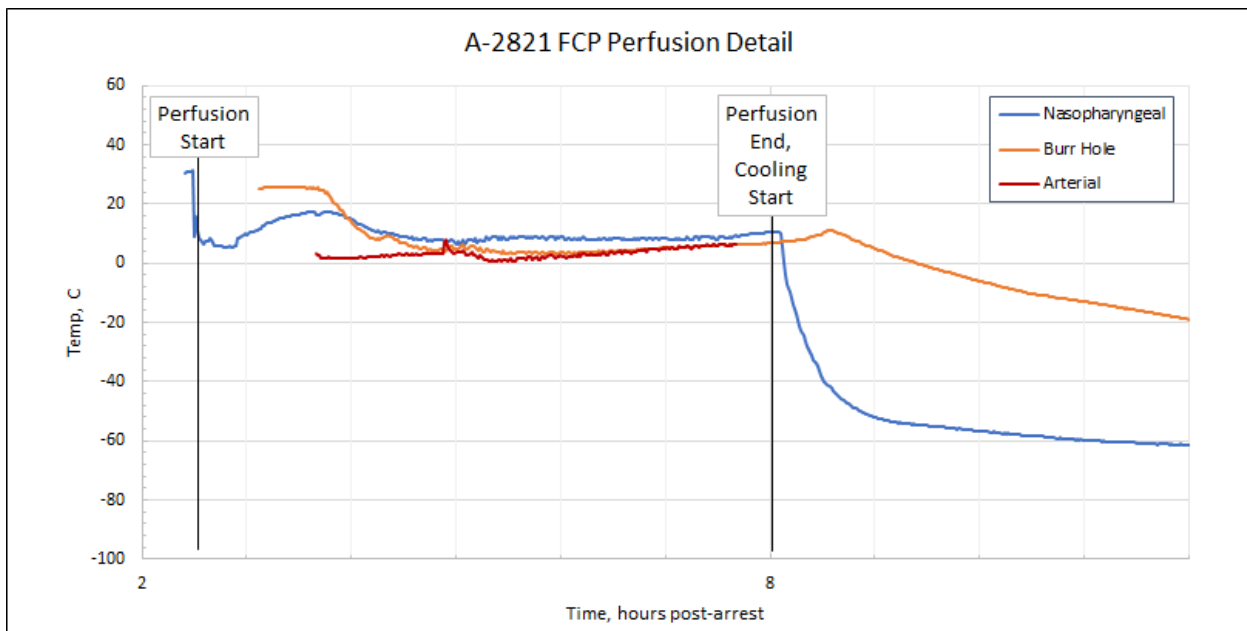
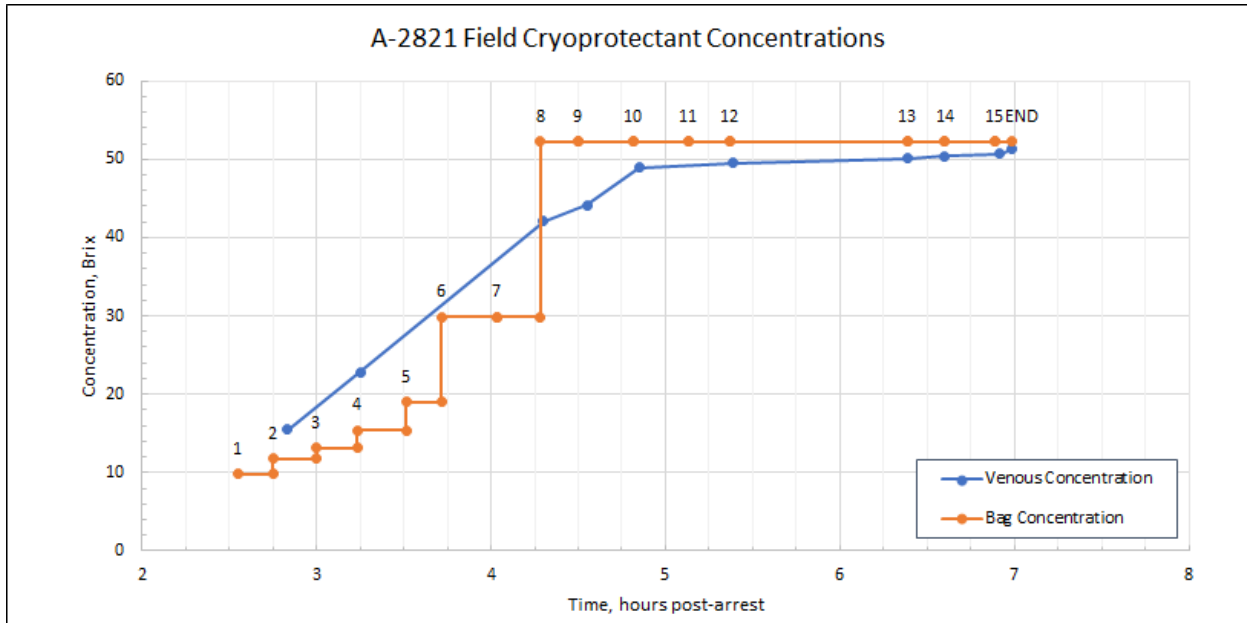
By hanging two bladders with different RI concentrations on a teeter-totter atop the tripod, the bladder with the lower RI runs out and becomes lighter. At the mid-way point, the teeter-totter will allow both bladders to flow, mixing the two concentrations and creating a smoother transition from one 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.

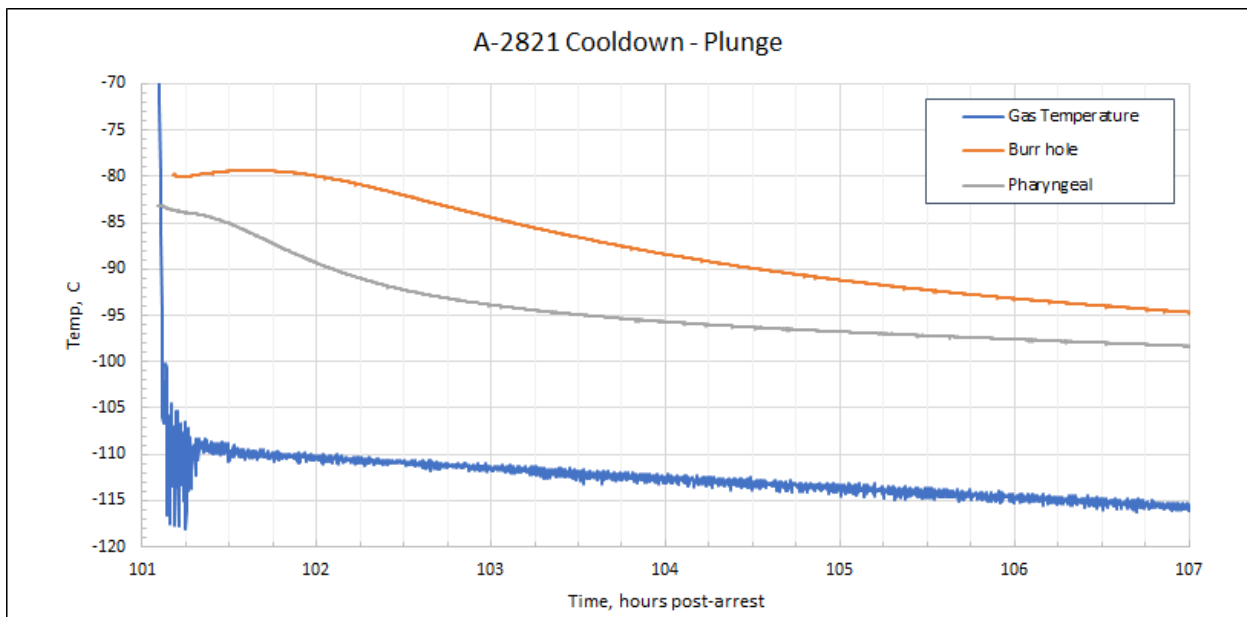
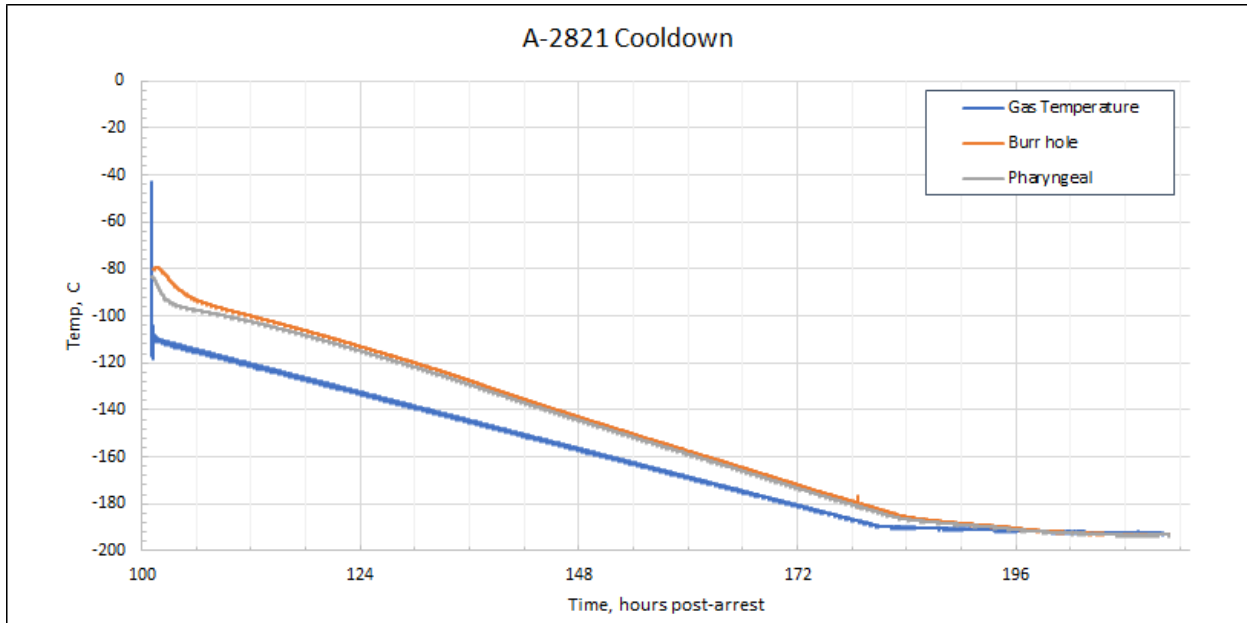
This process allows for a smoother curve in the increasing concentrations of cryoprotectant. The gravity feed system for FCP uses a tripod that can be adjusted for height to control the arterial pressure. The pre-mixed cryoprotectant was in a series of bladders with graduated concentrations [measured by the refractive index (RI) in Brix units].

Data logger reliability has consistently been a problem. Alcor staff are developing a Universal Data Logger (UDL) that will solve the problems with commercially available data loggers. The UDL is expected to be available early in 2023 and it is hoped that these problems will be a thing of the past.

## 12. Cryoprotection and Temperature Graphs







### 13. 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 damage. 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. The duration from cardiac arrest to 0 C is 08:12. As shown below, and due to lowering of the body temperature, S-MIX duration is shorter, at 02:30.

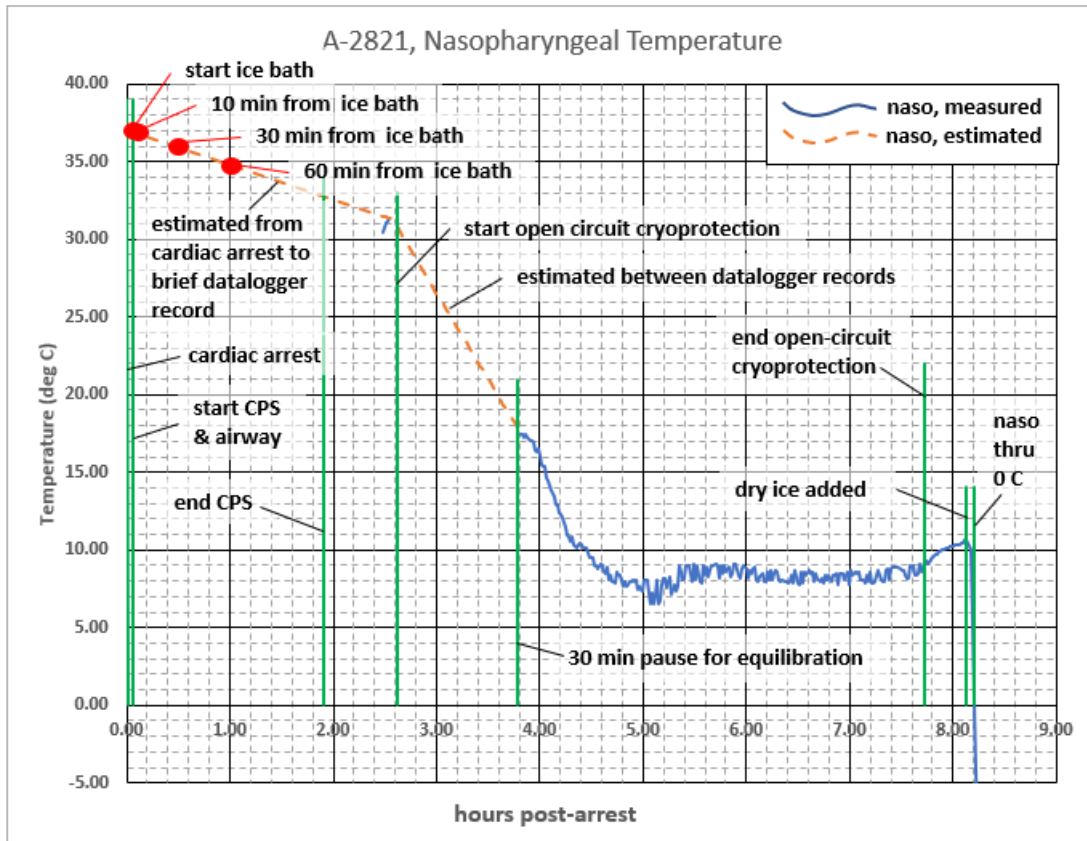
event	seg- ment #	days (T+X)	time (MST) duration	post- arrest	Tnaso (deg C)	CPS w/ ventil.	washout oxygen.	S-MIX (hh:mm)
Estimated time of cardiac arrest		T-0	07:43	00:00	37.0			
	seg 1		00:04	00:04	-0.1	no	no	00:04
Apply ice to body bag, manual CPS, & airway		T-0	07:47	00:04	36.9			
	seg 2		01:50	01:50	-4.1	yes	no	00:47
End CPS		T-0	09:37	01:54	32.8			
	seg 3		00:43	00:43	-2.0	no	no	00:30
Start of open circuit cryoprotection		T-0	10:20	02:37	30.8			
	seg 4		01:10	01:10	-12.9	no	no	00:30
Start 30-minute pause for equilibration		T-0	11:30	03:47	17.8			
	seg 5		03:56	03:56	-8.6	no	no	00:35
End of open circuit cryoprotection		T-0	15:26	07:43	9.2			
	seg 6		00:25	00:25	1.4	no	no	00:04
Start of dry ice cooling		T-0	15:51	08:08	10.6			
	seg 7		00:04	00:04	-10.6	no	no	00:01
naso passes thru 0 C		T-0	15:55	08:12	0.1			
<b>totals:</b>			<b>08:12</b>	<b>08:12</b>	<b>-36.9</b>			<b>02:30</b>

The below plot shows events related to the S-MIX calculation. The orange dashed lines show estimated data for intervals without datalogger data.

The red dots provide a metric for how fast the patient is initially cooled. This is a critical period since body temperature is highest and ischemic damage most rapid. The below table provides cooling data for 10, 30, and 60 minutes after the team first applies water ice.

Patient Cooling Rate				
Note: time = 0 at start of ice bath	0 min elapsed	10 min elapsed	30 min elapsed	60 min elapsed
Naso temperature (°C)	36.9	36.6	35.9	34.8
Temperature drop (°C) from t = 0	0.0	-0.3	-1.0	-2.1
Cooling rate (°C/min) from t = 0	N/A	-0.03	-0.03	-0.04





## 14. CT Scans

### Cryoprotectant Distribution (Post-cryopreservation CT scan)

As this was a neuro-on-whole-body cryopreservation, no post-cryopreservation CT scans were obtained.