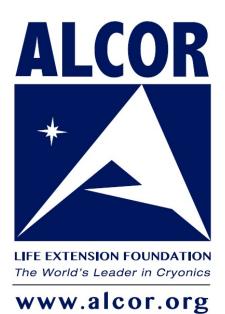
Alcor A-3656

Case Report



Prepared by:

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

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

A-3656 was a 54-year-old member with neuro cryopreservation arrangements. This was a postmortem notification. The death certificate gave the cause of death as probable acute cardiac event or pulmonary embolism. It did not become a coroner's case.

Cardiac arrest was estimated to be at 12:00 hrs on T-0 days and the member was pronounced legally deceased in Pennsylvania at 13:43 hrs on T-0 days in October of 2023.

After <u>field cryoprotection</u> (FCP), the patient was air transported on dry ice to Alcor for cryogenic cooldown. The patient arrived at Alcor on T+2 days at 00:22 hrs. The cryogenic cooldown was initiated on T+2 days at 00:35 hrs and terminated on T+5 days at 11:39 hrs. The patient was transferred to long-term care at liquid nitrogen temperature on T+36 days at 11:24 hrs.

2. Patient Assessment

T-0 days

This member suffered cardiac arrest at home at approximately 12:00 hrs from a presumed heart attack (the member had very common symptoms of heart attack). A family member started CPR and called 911. Paramedics attempted resuscitation; however, the member was pronounced legally deceased at 13:43 hrs, shortly after arriving in the ER. The patient was kept in the hospital morgue at refrigerator temperatures (typically 2°C to 4°C) until picked up by the funeral home.

Alcor's Medical Response Director (MRD) arranged by phone for a local funeral director to pick up the patient from the morgue at 04:30 hrs, and transport the patient to the funeral home with an estimated arrival time at the funeral home at 05:30 hrs. The plan was to attempt field cryoprotection (FCP) as soon as the Alcor DART team arrived on location. This would allow the procedure to take place at about 14/15 hrs post-pronouncement, or 16/17 hours post-estimated time of cardiac arrest.

Because this was a postmortem notification, no stabilization medications other than streptokinase (25,000 IU added to cryoprotectant bladder #1) would be administered, and no cardiopulmonary support (CPS) would be given.



3. Deployment

The Alcor Deployment Committee deployed two Deployment and Recovery Team (DART) members to depart Arizona on T-0 days, with a scheduled arrival time the next morning at an airport near the patient.

<u>T+1 days</u>

The DART team arrived at the destination airport at 04:00 hrs and began the 1hr 45m drive to the funeral home at 04:45 hrs.

4. Patient Recovery

The DART team arrived at the funeral home at 06:15 hrs and immediately began preparing for the delayed perfusion. The patient was placed in the ice bath to improve external cooling at 07:15 hrs (see the Discussion section) by placing ice around the patient's head and neck. The patient's left nasopharyngeal temperature (LNPT) was 13°C, and the right (RNPT) was 14°C, which was below the temperature needed to start perfusion.

5. Field Surgery and Cryoprotection

The first surgical cut was made at 07:37 hrs. The left and right carotid arteries were isolated. At 08:11 hrs the left carotid artery was cannulated with a 16 French (Fr) right angle cannula. At 08:15 hrs the right carotid artery was also cannulated with a 16 French (Fr) right angle cannula.

Using a scalpel to clear the tissues of the neck and expose the spine, the cephalic isolation was initiated at 08:16 hrs. The burr hole was completed at 08:17.hrs and a thermocouple was inserted to measure brain temperatures.

25,000 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 08:29 hrs with Bladder #1 containing nM22 cryoprotectant with a concentration of 0.05 concentration needed to vitrify (CNV), and a molarity of 0.47. See the Table of Concentrations (Brix), for the times the bladders were started, the precalculated concentrations of each bladder, and the refractive index of effluent samples taken.

Using a mallet and osteotome, the spine was severed, and the cephalic isolation was completed at 09:28 hrs. The vertebral arteries were severed during cephalic isolation and were both cannulated with 12 Fr red Robinson cannulae.

The height of the bladders above the patient was 39", providing a maximum perfusion pressure of 80 mmHg. 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 protect the vasculature. Ethylene glycol antifreeze at 50/50 concentration was added to the water in the heat exchanger at 09:10 hrs to produce temperatures below 0°C.



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. <u>On this case,</u> <u>bladders 5 & 6 represent the pause.</u> 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.

The field cryoprotectant perfusion was terminated at 10:40 hrs. The terminal refractive index reading was 52.9 Brix, with a molarity of 9.91.

6. Patient Transport to Alcor

The patient was moved into the neuro shipper at 10:45 hrs and covered with approximately 15 lbs. of dry ice. The patient was delivered to the airport cargo department at 20:00 hrs (see the Discussion section).

7. Cooling to Liquid Nitrogen Temperature

The neuro shipper arrived to Alcor's headquarters in Scottsdale, AZ at 00:22 hrs. Arrival temperatures were LNPT -44°C, RNPT -47°C, and BH -73°C.

Computer-controlled cryogenic cooldown was initiated at 00:35 hrs on T+2 days, plunging to -110° C and descending thereafter at -1° C/hour to liquid nitrogen temperature. On T+5 days at 11:39 hrs, an uneventful cooldown was terminated. On T+36 days at 11:24 hrs, the patient was transferred to long-term care at liquid nitrogen temperature.



8. Timeline and Time Summaries

Timeline

T-0	12:00	Estimated time of cardiac arrest					
T-0	13:43	Time of pronouncement of legal death					
T+1	07:15	Start of ice bath cooling (NPT = 57° C)					
T+1	07:37	Start field surgery					
T+1	08:17	Place burr hole and insert thermocouple					
T+1	08:29	Start of field cryoprotection (FCP)					
T+1	09:10	Start 30-minute pause for equilibration					
T+1	09:11	Start cannulation					
T+1	09:15	Completed cannulation					
T+1	09:16	Start cephalic isolation					
T+1	09:28	Completed cephalic isolation					
T+1	10:40	Termination of FCP (final RI reading was 52.9 Brix)					
T+1	10:45	Start dry ice cooling					
T+1	20:00	Patient delivered to airport cargo department					
T+2	00:22	Arrival of patient at Alcor					
T+2	00:35	Start of cryogenic cooldown					
T+5	11:39	End of cryogenic cooldown					
T+36	11:24	Transfer of patient into long-term care					





Time Summaries

Event Duration				
hr:min		days	time	
Stabilization				
01:43	From:	T-0	12:00	Estimated time of cardiac arrest
	Till:	T-0	13:43	Time of pronouncement of legal death
19:15	From:	T-0	12:00	Estimated time of cardiac arrest
	Till:	T+1	07:15	Start of ice bath cooling (NPT = 57° C)
19:37	From:	T-0	12:00	Estimated time of cardiac arrest
	Till:	T+1	07:37	Start field surgery
01:51	From:	T+1	07:37	Start field surgery
	Till:	T+1	09:28	Completed cephalic isolation
20:29	From:	T-0	12:00	Estimated time of cardiac arrest
	Till:	T+1	08:29	Start of field cryoprotection (FCP)
02:11	From:	T+1	08:29	Start of field cryoprotection (FCP)
	Till:	T+1	10:40	Termination of FCP (final RI reading was 52.9 Brix)
22:40	From:	T-0	12:00	Estimated time of cardiac arrest
	Till:	T+1	10:40	Termination of FCP (final RI reading was 52.9 Brix)
00:52	From:	T+1	07:37	Start field surgery
	Till:	T+1	08:29	Start of field cryoprotection (FCP)
03:03	From:	T+1	07:37	Start field surgery
	Till:	T+1	10:40	Termination of FCP (final RI reading was 52.9 Brix)
00:05	From:	T+1	10:40	Termination of FCP (final RI reading was 52.9 Brix)
	Till:	T+1	10:45	Start dry ice cooling
22:45	From:	T-0	12:00	Estimated time of cardiac arrest
	Till:	T+1	10:45	Start dry ice cooling
36:22	From:	T-0	12:00	Estimated time of cardiac arrest
	Till:	T+2	00:22	Arrival of patient at Alcor
00:13	From:	T+2	00:22	Arrival of patient at Alcor
	Till:	T+2	00:35	Start of cryogenic cooldown



A-3656 step-r	amp, nM22	2						
Preferred en	dpoint is ov	/er 49.9 Brix f	rom both jug	gulars for 1/2	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
1	0.05	0.47	11.81	8:29	20.48	333.3	8:57	15.5
2	0.08	0.78	13.14	8:35	20.58	153.8	9:05	18.9
3	0.14	1.29	15.35	8:48	20.80	200.0	9:19	31.8
4	0.23	2.15	19.03	8:58	20.97	166.7	9:40	48.7
5	0.50	4.67	29.85	9:10	21.17	500.0	10:10	51.5
6	0.50	4.67	29.85	9:14	21.23	105.3	10:40	52.9
7	1.06	9.91	52.306	9:33	21.55	29.9		
END				10:40	22.67			
* does not account for concentration of non-penetrating CPAs								

9. Table of Concentrations (Brix) of nM22 Solution

10. Discussion

Patient Recovery

There was approximately 1 hour between when the DART team arrived at the funeral home and when the patient was placed into the ice bath for cooling. There was approximately another half hour before surgery began. This was due to the funeral home waiting to receive paperwork from Alcor. It was also the result of being an early case for the DART team. However, the patient was placed in the ice bath to improve external cooling and the patient's left nasopharyngeal temperature (LNPT) was 13°C, and the right (RNPT) was 14°C, which were below the needed temperature to start perfusion, when DART arrived. Since then, a Deployment Binder has been created with detailed instructions to prevent another occurrence such as this.

Field Cryoprotectant Perfusion (FCP)

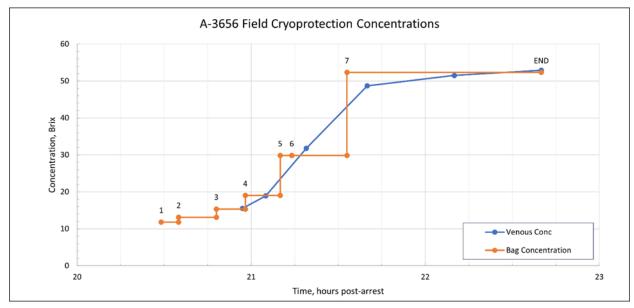
It is suspected that measurements of venous effluent were contaminated by perfusate bypassing the cannulas, as the measured concentrations were extremely close to the calibrated concentrations of the step ramp bladders. Furthermore, flow through the patient was nearly zero by the end of the procedure. This patient experienced approximately 2 hours of normothermic ischemia before being pronounced, followed by multiple hours of ischemia in the hospital morgue, and no stabilization was performed. Poor flow was to be expected based on similar cases, and it is possible that the perfusion was unsuccessful or only partially successful. Analysis of post-cryoprotection CT scans will provide more insight.



Patient Transport

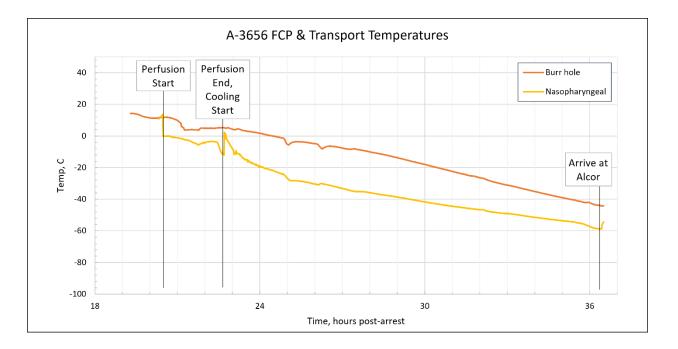
The protocol for how long to wait once a patient is placed on dry ice before they are left at an airport cargo department has recently been changed to: wait 24 hours before leaving the patient shipper at cargo, so that the patient will equilibrate to dry ice temperature (-80°C), and additional dry ice can replace any that sublimated away while waiting, making it less likely that the patient would warm up if there was any kind of a delay in the shipment.

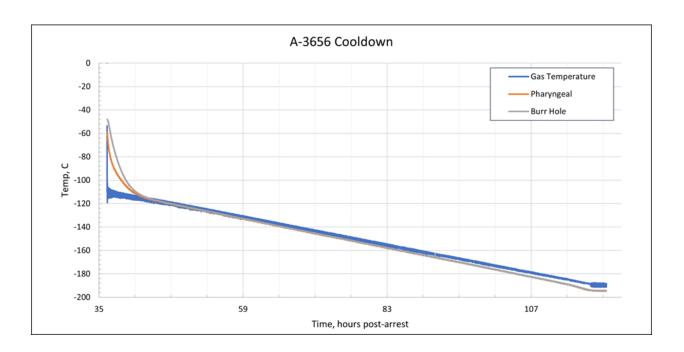
On this case the shipper was left at the airline cargo department before the 24-hour wait because the DART team was trying to get to the patient within the 24-hour cut-off for a potentially success cryoprotectant perfusion. The only other flight option would have been the evening of the next day, which would have been beyond the 24-hour limit for perfusion.



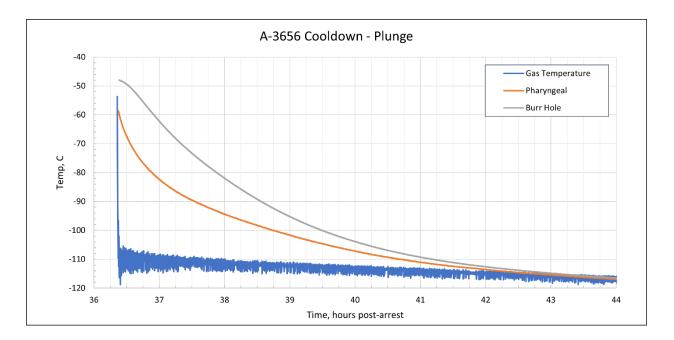
11. Cryoprotection and Temperature Graphs













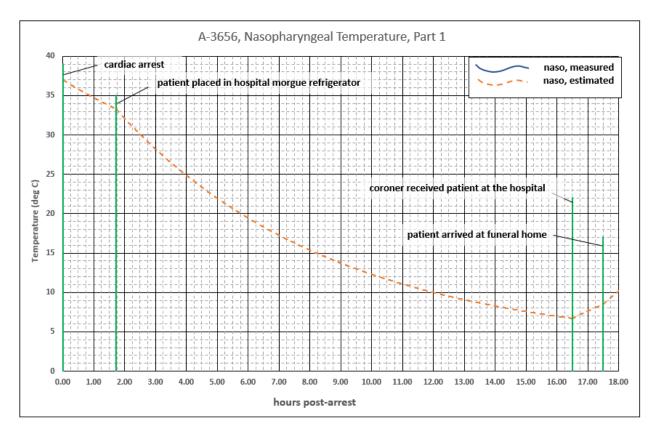
12. S-MIX

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 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 24:27. As shown below, and due to lowering of the body temperature, S-MIX duration is shorter, at 06:29.

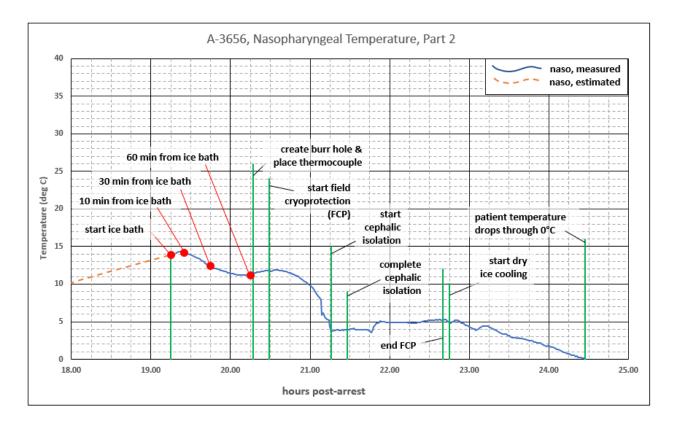
	seg-	days	time (MST)	post-	Naso	CPS w/	washout	S-MIX
event	ment#	(T+X)	duration	arrest	(deg C)	ventil.	oxygen.	(hh:mm)
Estimated time of cardiac arrest		T-0	12:00	00:00	37.0			
	seg 1		01:43	01:43	-3.7	no	no	01:30
Pronouncement of legal death & put in		T-0	13:43	01:43	33.3			
	seg 2		14:47	14:47	-26.6	no	no	03:53
Coroner received patient at the hospital		T+1	04:30	16:30	6.7			
	seg 3		00:60	00:60	1.8	no	no	00:08
Patient arrived at funeral home		T+1	05:30	17:30	8.5			
	seg 4		01:45	01:45	5.4	no	no	00:18
Start of ice bath cooling (NPT = 14°C)		T+1	07:15	19:15	13.9			
	seg 5		01:02	01:02	-2.5	no	no	00:11
Place burr hole and insert thermocouple		T+1	08:17	20:17	11.4			
	seg 6		00:12	00:12	0.4	no	no	00:02
Start of field cryoprotection (FCP)		T+1	08:29	20:29	11.8			
	seg 7		00:47	00:47	-8.0	no	no	00:07
Start cephalic isolation		T+1	09:16	21:16	3.8			
	seg 8		00:12	00:12	0.1	no	no	00:01
Completed cephalic isolation		T+1	09:28	21:28	3.9			
	seg 9		01:12	01:12	1.3	no	no	00:08
Termination of FCP (final RI reading was 52.9		T+1	10:40	22:40	5.2			
	seg 10		00:05	00:05	-0.4	no	no	00:01
Start dry ice cooling		T+1	10:45	22:45	4.9			
	seg 11		01:42	01:42	-4.8	no	no	00:010
Patient passes through 0°C		T+1	12:27	24:27	0.1			
totals:			24:27	24:27	-36.9			06:29



The below plots show events related to the S-MIX calculation. The red dots can be used to construct a metric for how fast the patient is initially cooled (see the Patient Cooling Rate table below). This is a critical period since body temperature is highest and ischemic damage most rapid.



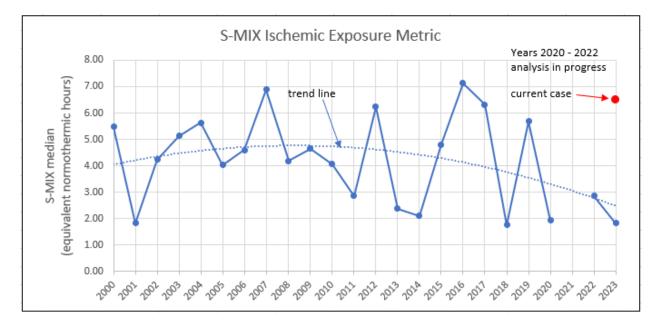




The below table provides cooling data for 10, 30, and 60 minutes after the team first applies water ice.

Patient Cooling Rate			
0 min	10 min	30 min	60 min
elapsed	elapsed	elapsed	elapsed
13.9	14.2	12.4	11.2
0.0	0.3	-1.5	-2.7
N/A	0.03	-0.05	-0.04
	0 min elapsed 13.9 0.0	0 min 10 min elapsed elapsed 13.9 14.2 0.0 0.3	0 min 10 min 30 min elapsed elapsed elapsed 13.9 14.2 12.4 0.0 0.3 -1.5





The following plot shows the trend of S-MIX achieved since 2020.

13. CT Scans

Cryoprotectant Distribution (Post-cryopreservation CT scan)

When the in-house scanner is functional and whole-body patients are being scanned, additional information will be added to this report.

