# Alcor A-2976

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

A-2976 was a 77-year-old member with whole-body cryopreservation arrangements. The member had a cardiac arrest while on the Alcor Watchlist. Cardiac arrest was observed at 04:06 hrs on T-0 days and the member was pronounced legally deceased in Arizona at 04:50 hrs on T-0 days in March of 2024.

Stabilization was performed enroute to Alcor where cryoprotectant perfusion and cryogenic cooldown were to be performed. The patient arrived at Alcor on T-0 days at 09:18 hrs. The cryogenic cooldown was initiated on T+0 days at 15:17 hrs and terminated on T+5 days at 15:12 hrs. The patient was transferred to long-term care at liquid nitrogen temperature on T+9 days at 15:29 hrs.

## 2. Member Assessment

T-2 days

This member had in-home hospice care and had an in-home caregiver. The member had a history of multiple health problems including diabetes, hypertension, gout, heart blockage, hypercholesterolemia, hypothyroidism, heart palpitations, and kidney problems.

Upon learning about the member's cryopreservation agreement with Alcor, the hospice social worker called Alcor to learn more. Alcor's MRD returned the call to the social worker to explain the Alcor standby and stabilization procedures, and to obtain an update on the member's condition. The social worker stated that the member's death did not seem to be imminent and agreed to relay the Alcor information to all hospice staff members. The MRD then placed this member on the Alcor Watchlist.

At 13:08 hrs, the hospice nurse evaluated the member and called the MRD to provide the following:

Neurological status: The member had a possible stroke over the weekend. During the last visit on T-5 days, the member was responsive, alert and oriented, and was able to eat and turn self in bed, in spite of being bedbound for quite some time. Now the member was only opening eyes to voice, was not tracking, had facial droop, and had some resistance to gravity in the extremities.

Cardiopulmonary: There was no noticeable mottling, the capillary refill was normal, the pulse was weak, thready, and irregular. The lung sounds were clear, and breathing was non-labored and even.

Gastrointestinal and Genitourinary (GI/GU): The member was bedbound and used a brief. The brief had been changed twice that day with one being "not so wet" and the other being "very wet". The nurse placed a foley catheter. The member was made NPO (nothing by mouth) because medications and food from the prior night were still in the member's cheeks.

Skin: The member had scattered bruising, with a 1cm stasis ulcer (a wound caused by abnormal or damaged veins) on the back of the left calf and stage 2 moisture associated skin damage (MASD) to the coccyx (tailbone).

The vital signs were: blood pressure (BP) 122/72, capillary oxygen saturation (SpO2) 85% (the nurse placed the member on 2L/min oxygen, with a new reading of 95%), heart rate (HR) 86, respiratory rate (RR) 20, temperature (T) 37°C.

New medications ordered: morphine 5mg every 8 hours and every 2 hours if needed and lorazepam 0.5mg every 2 hours as needed.

General: The member was considered to be transitioning (a term used by end-of-life professionals to say that the person has transitioned to an actively dying state).

At 18:37 hrs the caregiver reported that the member was opening their eyes, attempting to speak, and responded with the caregiver's name. The caregiver also confirmed that the member's status was DNR (do not resuscitate).

T-1 days

Alcor's MRD spoke to the caregiver at 08:20 hrs to check on the member, who was about the same; still responsive. No vital signs had recently been taken.

The hospice nurse was scheduled to visit the member at 16:22 hrs but was turned away by the caregiver due to the member still being responsive. The nurse's next visit would be the following day at noon. The MRD coordinated with the nurse for a DART member to join her in her assessment so Alcor could have an eyes-on assessment of the member to decide on a plan regarding deployment (see the Discussion section).

At 19:43 hrs, the MRD requested that vitals be taken and reported. The caregiver responded with BP UTO (unable to obtain) due to member's pain and agitation, SPO2 98%, and HR 90.

## 3. Deployment

T-0 days

The member's caregiver called the MRD at 04:03 hrs and stated the member seemed close to cardiac arrest. Because of the severity of the situation, the MRD immediately deployed the DART team without first consulting the Alcor Deployment Committee. The MRD then notified the committee, and they agreed with the decision. At 04:06 hrs, the caregiver called the MRD and reported that the member had stopped breathing, and a pulse could not be found.

Two DART members then drove to Alcor to get the Medical Response Vehicle (MRV) and then to the member's location, approximately 1hr and 46min away. The MRD joined them at Alcor at 04:23 hrs.

## 4. Patient Recovery, Stabilization and Transport to Alcor

The member was pronounced legally deceased at 04:50 hrs by the on-call hospice nurse. The MRD asked the caregiver to surround the patient's body with bags of water ice, focusing on the head and neck. The caregiver agreed, but only had enough ice in the house to cover the head and neck.

DART arrived at the member's house at 07:00 hrs and started the digital audio recorder. DART planned that while enroute back to Alcor one team member would drive while the other two performed the initial stabilization protocols in the MRV.

The rectal occlusion device was placed at 07:06 hrs and the member was placed in the portable ice bath at 07:09 hrs to start external cooling. 200 lbs. of water ice was added. The MRV departed for Alcor at 07:12 hrs.

Manual chest compression was not performed as there were not enough team members. Mechanical chest compression with the Amoul device was started at 07:13 hrs. At 07:14 hrs the EZ-IO device was placed in the right tibial tuberosity for access to the vasculature to administer the stabilization medications. The first stabilization medication was administered at 07:16 hrs (see the below Table of Medications Administration for the names of the medications, the dosages, and the times of administration). The abbreviated set of Stabilization Medications was used because it had been more than one hour since pronouncement of legal death. A King airway, a Save ventilator, and a CO2 detector colorimeter (the color was orange) were placed at 07:16 hrs. The C02 detector changes from purple to orange in the presence of C02, affirming that the airway is in the lungs and not the esophagus.

At 07:19 hrs thermocouples were placed in the patient's nares. The initial temperature readings were: right nasopharyngeal temperature (R NPT) 28°C and left nasopharyngeal temperature (L NPT) 29°C. At 07:20 hrs a second EZ-IO was placed in the left tibial tuberosity to replace the original, which had become clogged. Medication administration continued. The surface conduction cooling device (SCCD) was started at 07:38 hrs to circulate ice water around the patient and improve external cooling.

## 5. Cryoprotectant Surgery at Alcor

The DART team arrived at the back door to Alcor at 09:16 hrs. The patient was brought into the Alcor operating room (OR) at 09:18 hrs. The mechanical Amoul chest compression device was still operating. The initial nasopharyngeal temperature readings from the data logger at 09:19 hrs were RNPT = 21°C, LNPT = 20°C. At 09:22 hrs the chest compression device was discontinued.

Ice bags and equipment were removed at 09:27 hrs from around the patient, still in the PIB, to prepare for moving the patient to the OR table. Using a hoist, the patient was moved to the OR table at 09:35 hrs. The Megamover was still under the patient and crushed ice remained around the patient's neck and head.

Surgery (see the Discussion section) was initiated at 09:41 hrs with a single burr hole placed on the left forehead. A thermocouple was placed in the burr hole. The initial burr hole temperature (BT) reading was 23°C. Ice bags were placed back around the patient's head at 09:44 hrs. The median sternotomy surgery was started at 09:51 hrs. The sternum was cut with a sternal saw and the chest was opened at 09:56 hrs. Approximately 1" of adipose tissue needed to be removed to isolate the heart.

A purse string suture was started at 10:07 hrs to cannulate the inferior vena cava, which was cannulated through the purse string with a size 30 French (Fr) venous cannula and secured at 10:12 hrs. A purse string suture was started at 10:14 hrs to cannulate the ascending aorta, which was cannulated through the purse string with a size 20 Fr right angle arterial cannula and secured at 10:16 hrs.

The venous cannula was connected to the tubing circuit at 10:21 hrs. The arterial cannula was connected to the tubing circuit at 10:21 hrs. The bypass was closed, and open-circuit washout with B1 carrier solution was started at 10:22 hrs. The arterial pressure was 80 mmHg at 10:23 hrs. At 10:25 hrs the arterial pressure was lowered to 42 mmHg to re-suture the cannula in the aorta, The aorta was so large it required additional suturing for leakage control. The arterial pressure was decreased to 35 mmHg at 10:47 hrs. Enough return flow was leaking from the cannulae, and not being returned to the circuit, that suction was required. 250,000 IU of streptokinase was added to the mixing reservoir at 10:50 hrs to help break up blood clots in the vessels.

The cryoprotectant ramp was started at 10:54 hrs with M22 cryoprotectant and an arterial pressure of 37 mmHg. There was almost no return flow (see the Discussion section). The arterial refractive index (RI) was 13 Brix at 11:03 hrs. The circuit was placed in recirculation mode but was not yet on computer control. The flow rate was 0.65 L/min.

At 11:08 hrs the arterial pressure was increased to 30 mmHg, and the team watched to see if there would be additional leaks. The pump was set to 1.5 L/min, but there was no perfusion flow to the patient. The surgical team discussed the problem, and then decided to cannulate the carotid arteries and do a neuro-on-whole-body procedure in order to at least perfuse this patient's brain.

Preparation for carotid artery cannulation started at 11:18 hrs. The field bladder system was set up as the pump system was not set up for neuro-on-whole-body perfusion and would not provide sufficient perfusion control.

The surgery to isolate the right carotid artery was started at 11:19 hrs. The right carotid artery was isolated at 11:24 hrs and cannulated at 11:26 hrs with a 20 Fr right angle cannula. The left carotid artery was isolated at 11:31 hrs and cannulated at 11:34 hrs with a 20 Fr right angle cannula. The right jugular vein was cannulated at 11:37 hrs with a flexible, red Robinson cannula. The left jugular vein was cannulated at 11:40 hrs with a flexible, red Robinson cannula. As this was neuro-on-whole-body, the vertebral arteries could not be accessed or cannulated.

## 6. Cryoprotectant Perfusion at Alcor

The gravity-induced cryoprotectant perfusion flow (see the Discussion section) was initiated at 11:42 hrs with bladder #4 containing nM22 cryoprotectant with a concentration of 0.14 concentration needed for vitrification (CNV) and a molarity of 1.29. The perfusate temperature was 9°C. The OR pump system was turned off at 11:43hrs.

The right jugular effluent had a refractive index (RI) of 13.3 Brix at 11:44 hrs. The height of the bladders was 39 inches above cannulation site. See the below 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.

*Sidebar*
*Per the cryoprotection protocol, the ramp is to be paused at 30 Brix (approximately 50% of the desired terminal concentration of 52.5 Brix) to allow the patient to come to osmotic equilibrium. 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 (49.9 Brix x 105% = 52.5 Brix) and held between 102% and 105% concentration until the terminal concentration is obtained.*

Bladder #5, which represents the start of the 30-minute pause for equilibration (see the Discussion section) was opened to flow at 11:55 hrs. Per protocol, in order to limit toxic exposure to the cryoprotectant, perfusion was to be terminated after 3 hours from this point even if the terminal Brix (49.9) refractive index was not reached.

At 12:26 hrs, Bladder #7 was opened to flow, which represents the end of the 30-minute pause for equilibration, and the temperature of the patient enclosure was lowered from 3°C to -3°C.

The patient's chest was closed at 12:27 hrs and ice bags were placed over patient's head and face. Facial skin was beginning to tan at 12:51 hrs. This is a normal response to contact with the cryoprotectant and an indication that the cryoprotectant is replacing water in the cells. The eye lids were almost closed. Therefore, it was not possible to see if the eyes were concave (another indication of perfusion) or convex.

This patient weighed 300 lbs. At 13:09 hrs, tie straps were used to close the Megamover around the patient to make it possible to fix the patient into the cooldown dewar. This affected the Brix readings of the effluent (see the Discussion section). Skin tanning was uniform at 14:16 hrs and both eyes had collapsed.

Cryoprotectant perfusion was terminated at 14:55 hrs with bladder #10 due to the 3-hour perfusion limit. Bladder #10 had a concentration of 1.06 concentration needed to vitrify (CNV) and a molarity of 9.91. The final refractive index readings were 47.4 Brix from the left jugular, and 36.05 Brix from the right jugular. It was difficult to pull enough effluent from the left jugular to get a reading. The RI readings on this case didn't seem to make sense and were not understood (see the Discussion section).

Prior to moving the patient to the Patient Care Bay, lines and equipment were removed from around the patient starting at 15:01 hrs. The patient was relocated to the Patient Care Bay at 15:08 hrs. Cryogenic cooldown was initiated at 15:17 hrs.

## 7. Cooling to Liquid Nitrogen Temperature

Computer-controlled cryogenic cooldown was initiated at 15:17 hrs on T-0 days, plunging to -110°C and descending thereafter at -1°C/hour to liquid nitrogen temperature.

At T+87 hrs, the team discovered the solenoid valves making a continuous whining noise. While it was not impacting the cooldown, it was irritating. The team replaced the valve set with a dry manifold. The cooldown resumed with only minor temperature deviations (see the cooldown curve on the below graph).

On T+5 days at 15:12 hrs, an uneventful cooldown was terminated. On T+9 days at 15:29 hrs the patient was transferred to long-term care at liquid nitrogen temperature.

## 8. Timeline and Time Summaries

**Timeline**

| | | |
|---|---|---|
| T-0 | 04:06 | Estimated time of cardiac arrest |
| T-0 | 04:50 | Pronouncement of legal death |
| T-0 | 05:00 | Caregiver placed ice around head and neck |
| T-0 | 07:09 | Start of ice bath cooling |
| T-0 | 07:13 | Start of mechanical chest compressions |
| T-0 | 07:14 | Placement of intraosseous device |
| T-0 | 07:16 | Placement of airway |
| T-0 | 07:16 | Administration of first medication (citrate) |
| T-0 | 07:35 | Administration of final medication (antacid) |
| T-0 | 09:18 | Arrival of patient in OR at Alcor (NPT = 21°C) |
| T-0 | 09:27 | Termination of cardiopulmonary support |
| T-0 | 09:41 | Start of surgery (burr hole) |
| T-0 | 09:51 | Start cardiac cannulation |
| T-0 | 10:22 | Start of whole-body washout |
| T-0 | 10:54 | Start cryoprotection with chest cannulation |
| T-0 | 11:19 | Start carotid canulation |
| T-0 | 11:35 | Completion of carotid cannulation surgery |
| T-0 | 11:42 | Start cryoprotection with carotid cannulation |
| T-0 | 11:55 | Pause at 50% CNV achieved |
| T-0 | 12:26 | Start of sub-zero terminal concentration ramp (off pause) |
| T-0 | 14:55 | Termination of cryoprotection (final RI = 47.4 Brix) |
| T-0 | 15:17 | Start of patient cryogenic cooldown |
| T+5 | 15:12 | End of cooldown |
| T+9 | 15:29 | Transferred to long-term maintenance |

**Time Summaries**

| Event Duration hr:min | | days | time | |
|---|---|---|---|---|
| | | | | |
| | | | | |
| 00:44 | From:<br>Till: | T-0<br>T-0 | 04:06<br>04:50 | Estimated time of cardiac arrest<br>Pronouncement of legal death |
| 03:03 | From:<br>Till: | T-0<br>T-0 | 04:06<br>07:09 | Estimated time of cardiac arrest<br>Start of ice bath cooling |
| 03:07 | From:<br>Till: | T-0<br>T-0 | 04:06<br>07:13 | Estimated time of cardiac arrest<br>Start of mechanical chest compressions |
| 03:10 | From:<br>Till: | T-0<br>T-0 | 04:06<br>07:16 | Estimated time of cardiac arrest<br>Administration of first medication (citrate) |
| 00:19 | From:<br>Till: | T-0<br>T-0 | 07:16<br>07:35 | Administration of first medication (citrate)<br>Administration of final medication (antacid) |
| 05:12 | From:<br>Till: | T-0<br>T-0 | 04:06<br>09:18 | Estimated time of cardiac arrest<br>Arrival of patient in OR at Alcor (NPT = 21°C) |
| 00:23 | From:<br>Till: | T-0<br>T-0 | 09:18<br>09:41 | Arrival of patient in OR at Alcor (NPT = 21°C)<br>Start of surgery (burr hole) |
| 01:54 | From:<br>Till: | T-0<br>T-0 | 09:41<br>11:35 | Start of surgery (burr hole)<br>Completion of carotid cannulation surgery |
| 04:33 | From:<br>Till: | T-0<br>T-0 | 07:09<br>11:42 | Start of ice bath cooling<br>Start cryoprotection with carotid cannulation |
| 02:24 | From:<br>Till: | T-0<br>T-0 | 09:18<br>11:42 | Arrival of patient in OR at Alcor (NPT = 21°C)<br>Start cryoprotection with carotid cannulation |
| 02:01 | From:<br>Till: | T-0<br>T-0 | 09:41<br>11:42 | Start of surgery (burr hole)<br>Start cryoprotection with carotid cannulation |
| 05:14 | From:<br>Till: | T-0<br>T-0 | 09:41<br>14:55 | Start of surgery (burr hole)<br>Termination of cryoprotection (final RI = 47.4 Brix) |
| 03:13 | From:<br>Till: | T-0<br>T-0 | 11:42<br>14:55 | Start cryoprotection with carotid cannulation<br>Termination of cryoprotection (final RI = 47.4 Brix) |
| 00:22 | From:<br>Till: | T-0<br>T-0 | 14:55<br>15:17 | Termination of cryoprotection (final RI = 47.4 Brix)<br>Start of patient cryogenic cooldown |
| 11:11 | From:<br>Till: | T-0<br>T-0 | 04:06<br>15:17 | Estimated time of cardiac arrest<br>Start of patient cryogenic cooldown |
| 05:59 | From:<br>Till: | T-0<br>T-0 | 09:18<br>15:17 | Arrival of patient in OR at Alcor (NPT = 21°C)<br>Start of patient cryogenic cooldown |

## 9. Table of Medications Administered

**T-0 days**

| TIME | MEDICATION | DOSE | PURPOSE |
|---|---|---|---|
| 07:16 hrs | Sodium citrate | 20 g<br>Note 2 | Anticoagulant; prevents blood clot formation. |
| 07:17 hrs | Minocycline | 200 mg | Antibiotic; reduces microbial overgrowth during long transport times. |
| 07:19 hrs | Heparin | 50,000 IU | Anticoagulant; prevents blood clot formation. |
| 07:20 hrs | Tempol | 5 g | Low molecular weight superoxide scavenger used to mitigate ischemia-induced free radical damage. |
| 07:22 hrs | Decaglycerol/THAM | 200 ml<br>Note 3 | Decaglycerol inhibits cerebral edema. |
| 07:35 hrs | Antacid | 250 ml<br>Note 4 | A buffer used to neutralize stomach acid. |
| 10:50 hrs | Streptokinase | 250,000 IU<br>Note 5 | A thrombolytic used to break up existing blood clots. |

Notes:

1. The Abbreviated set of Stabilization Medications was used because it had been more than one hour past pronouncement of legal death before the medications could be administered.

2. 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 weighed 136 kg and therefore received 20 grams of sodium citrate.

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). It is a fixed dose of 400 ml to be given in two separate doses.

4. An antacid can be given in several doses, totaling 250 mL, and inserted through the nasogastric tube in an airway.

5. 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.

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

| A-2976 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** | **L. Jugular Eff. Conc., Brix** | **R. Jugular Eff. Conc., Brix** |
| 4 | 0.14 | 1.29 | 15.35 | 11:42 | 7.60 | 153.8 | | 11:44 | 13.3 | 0 |
| 5 | 0.50 | 4.67 | 29.85 | 11:55 | 7.82 | 153.8 | | 11:54 | 16.3 | 0 |
| 6 | 0.50 | 4.67 | 29.85 | 12:08 | 8.03 | 222.2 | | 12:05 | 20.4 | 0 |
| 7 | 1.06 | 9.91 | 52.31 | 12:17 | 8.18 | 48.8 | | 12:30 | 25 | 0 |
| 8 | 1.06 | 9.91 | 52.31 | 12:58 | 8.87 | 62.5 | | 12:42 | 29.3 | 0 |
| 9 | 1.06 | 9.91 | 52.31 | 13:30 | 9.40 | 32.3 | | 12:58 | 32.5 | 32.7 |
| 10 | 1.06 | 9.91 | 52.31 | 14:32 | 10.43 | 87.0 | | 13:11 | 32.2 | 29.8 |
| END | | | | 14:55 | 10.82 | | | 13:58 | 37 | 38.7 |
| | | | | | | | | 14:16 | 44.9 | 34.4 |
| | | | | | | | | 14:27 | 49.5 | 33.8 |
| | | | | | | | | 14:41 | 50.7 | 32.8 |
| | | | | | | | | 14:55 | 48.4 | 36.1 |
| * does not account for concentration of non-penetrating CPAs | | | | | | | | | | |

## 11. Discussion

Standby and Stabilization

During the standby, the Deployment Committee decided to dispatch a DART member to obtain an eyes-on assessment of the member to decide on a plan regarding deployment. Before the assessment could be made, the member unexpectedly went into cardiac arrest. Alcor is updating the deployment criteria used by the Deployment Committee to avoid this happening in the future.

Due to misconfiguration of a new style of temperature logger, the device was not logging data during the transport and cryoprotection. The team recorded periodic manual measurements from the logger display which were graphed with dotted lines indicating non-continuous data.

Cryoprotectant Surgery and Perfusion at Alcor

*Sidebar:*
*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 refractive index (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.*

*The height of the bladders on the teeter totter was 39 inches which produced (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.*

Alcor's normal surgeon was not available for this case due to this being on duty at his hospital. The backup surgeon was not available due to a recent back surgery which put him out of work for a time. No other backup surgeons were available. Alcor management discussed this situation and agreed that Alcor's Medical Response Director (MRD), assisted by two DART members (all of whom had been previously trained by Alcor's surgeon for this procedure) would be allowed to attempt the median sternotomy. The surgery was successful.

The cryoprotection required the team to rapidly transition from pump-based perfusion of the whole body to step-ramp perfusion of the cephalon (neuro-on-whole-body) in response to irreparable leakage around the cardiac cannulae. Due to the amount of perfusate that had already been pumped into the patient, the team decided to start the step ramp with bladder #4 (15.35 Brix).

Because the operating room system was arranged for whole body cryoprotection, effluent concentrations were taken manually. The computer system was never fully connected to the patient and was taken offline once the call was made to switch to the step ramp perfusion procedure. As a result, the patient's temperature probes were never transferred to the computer, and the recorded data was lost with the data logger configuration issue discussed above. Manual temperature readings are plotted with dotted lines indicating non-continuous data.

Midway through the cryoprotection the team shifted the patient to place a Megamover lifting sling beneath him. After this, the right jugular appeared to be occluded for an unknown reason, and effluent flow out of the right jugular almost completely ceased. The team continued to attempt manual effluent sampling from the right jugular, but the flow never returned to original levels and the sampled values may be erroneous.

The cryoprotectant perfusion ramp was started with an arterial pressure of 37 mmHg. There was almost no return flow. This could have been due to damaged veins or arteries resulting in leak after leak inside the patient's chest as more appeared with every attempt to increase the arterial pressure to the patient. The damage could have occurred prior to cannulation, such as thumper damage, as there was a lot of bleeding in the chest cavity when it was opened. This same problem was seen within the last year on a patient who was obese and was a smoker.
When the decision was made to switch to the neuro-on-whole-body procedure, a field-cryoprotection (FCP) step ramp system was set up as the OR whole-body perfusion tubing/recirculation system was not compatible with the neuro recirculating reservoir cryoprotectant ramp procedures. This was due to several reasons.

First, the use of whole-body M22 perfusate already in the recirculating system was contraindicated for neuro-only nM22 perfusion. Second, the tubing circuit design, pump shoe size, and filtration systems were not intended for the vastly lower flow and pressure control requirements. Third, because the whole-body system is designed to use arterial pressure for pump control and the entire tubing system is sized for whole-body perfusion, the whole-body system is incapable of adequate pump control to make neuro perfusion via arterial pressure control possible. Further, after the most recent OR neuro case, just 10 days prior, the OR neuro system was still completely torn down for cleaning and re-assembly since the team focused on the whole-body system for this patient. Therefore, when perfusion of the whole-body was not possible, the only option available to prevent this case from turning into a straight-freeze procedure was the step ramp bladder system for a neuro-on-whole-body procedure.

This major limitation in the existing OR whole-body perfusion circuit will be solved with the upcoming OR perfusion system redesign by Alcor engineers so that future cases of this type of conversion to neuro-on-whole-body will be possible using the whole-body perfusion system.

During the mid-stages of the cryoprotectant perfusion (~ 30 Brix point), it was noted that due to the considerable girth of the patient, it was possible that the patient would not fit into the cooldown system after perfusion. Indeed, the patient was large enough to spill over the edges of the OR table which also functions as the whole-body patient forming tray for fitment into the cooldown system. It was decided by the team at that point that additional pre-forming of the patient could be accomplished by further binding the patient's torso and pulling the arms tightly against the body under the Megamover.

It is possible that this constriction of the patient torso caused the lower concentration perfusate (the refractive index, or RI), already present in the circulatory system of the torso from the earlier median sternotomy attempt to flow towards the head via the jugular veins and other vasculature. This lower concentration of perfusate then drained out of the patient via the jugular sampling system, causing the drop in refractive index readings initially, and the fluctuation of readings for the rest of the cryoprotectant perfusion.

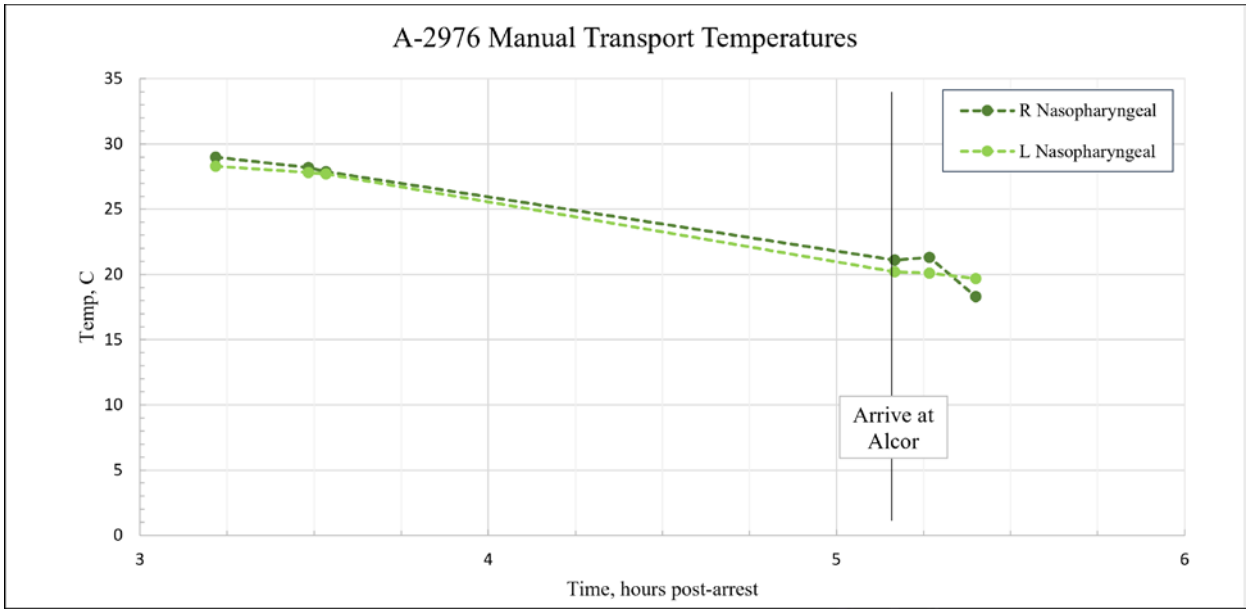
It is assumed that the patient's brain vasculature was already compromised at this point in the procedure due to either edema, clotting (during cannulation many large clots were in the effluent), vasculature disease or otherwise. This was noted by the low flow rate from the step ramp perfusion system prior to any torso manipulations.

The patient cephalon was perfused at the carotid arteries cannulated toward the head, with drainage provided through the jugular veins that were cannulated toward the head. It seems unlikely that fluid from the body would leak past fully cannulated jugulars and/or carotids to then flow through the brain, but it is possible that fluids from the circulatory system would travel up into the cephalon through other internal vasculature. Which vasculature, or whether this actually happened, is purely conjecture.

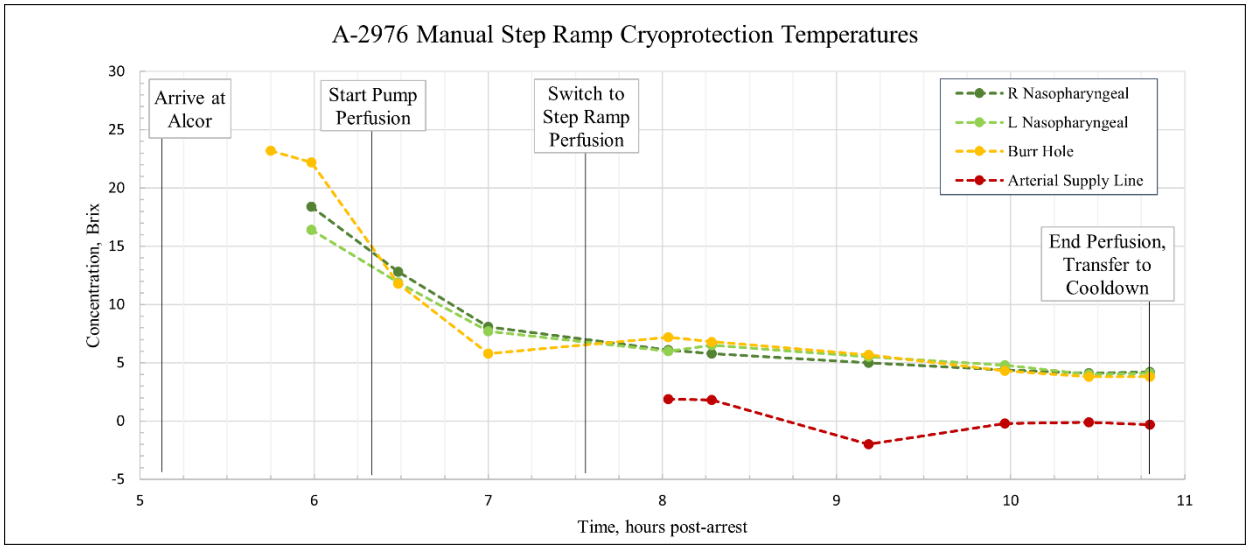
Additionally, while the step ramp system was functionally perfusing the brain at approximately 80 mmHg pressure via the carotid arteries, due to massive internal leaking, it was never possible to generate more than 35 mmHg pressure into the patient during the whole-body median sternotomy. Upon removal of the cannulae from the heart, those cannula incisions remained open, and it makes more sense that reforming the torso would cause fluid to leak directly out of those incisions into the heart, with fluid leaking into the chest cavity rather than flowing up into the brain. Again, this is conjecture and an attempt to explain the potential arguments against fluid flowing from the torso into the brain.

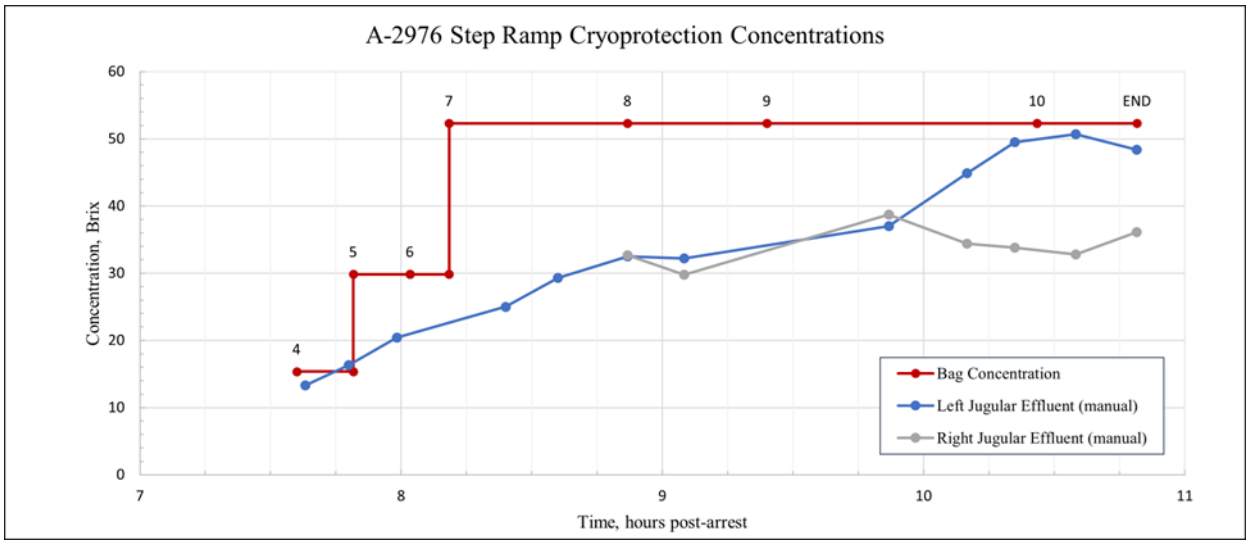
Toward the end of the cryoprotectant perfusion, it became increasingly difficult to obtain refractive index (RI) samples from the left jugular vein. This loss of flow out of one jugular has been noted in previous cases as well, mainly when patients have significant poor health in general as in this case. Flow could be blocked due to edema, clotting, pre-existing vascular constriction, etc. Or, it might have happened due to the patient torso binding as an attempt to ensure the patient would fit into the cooldown dewar. The actual cause is unknown without direct inspection of the brain, which is impossible, so only speculation and previous experience is left to guide a conclusion.

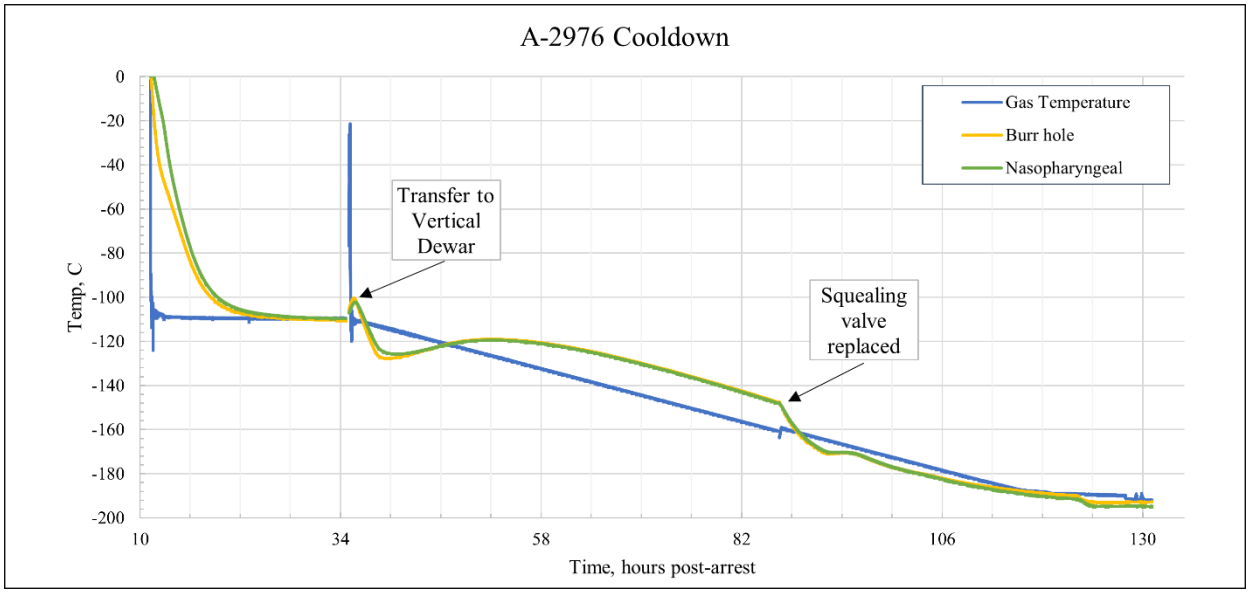
## 12. Cryoprotection and Temperature Graphs

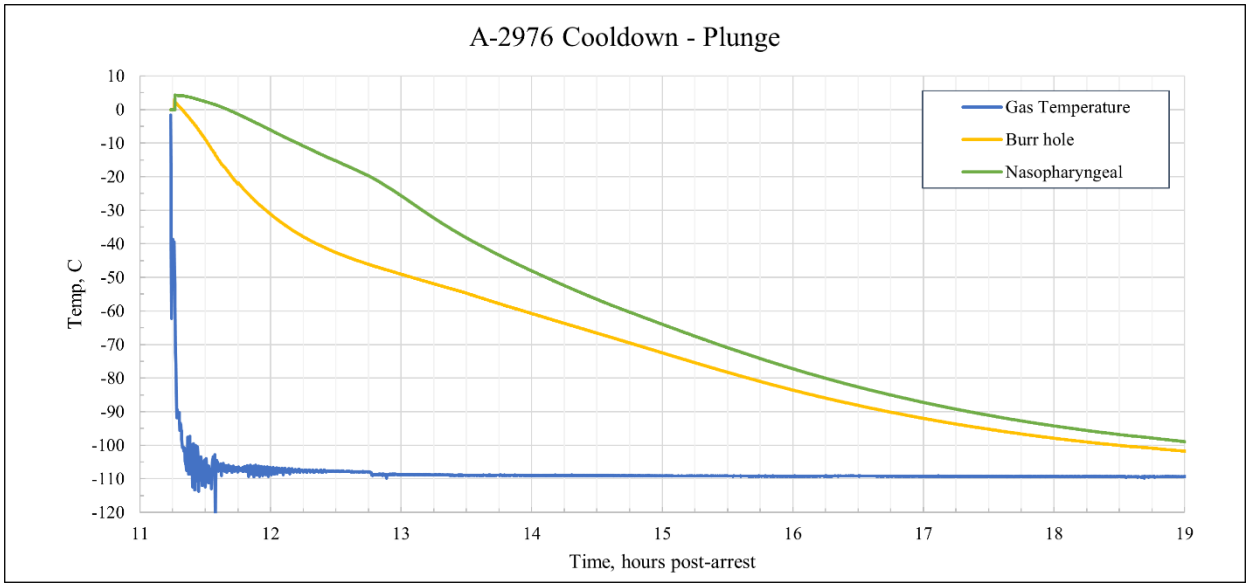



Due to misconfiguration of a new style of temperature logger, the device was not logging data during the transport and cryoprotection. The team recorded periodic manual measurements from the logger display which have been graphed with dotted lines indicating non-continuous data.




A-2976 Step Ramp Cryoprotection Concentrations
Concentration, Brix
Time, hours post-arrest
4
5
6
7
8
9
10
END
Bag Concentration
Left Jugular Effluent (manual)
Right Jugular Effluent (manual)


A-2976 Cooldown
Temp, C
Time, hours post-arrest
Gas Temperature
Burr hole
Nasopharyngeal
Transfer to Vertical Dewar
Squealing valve replaced

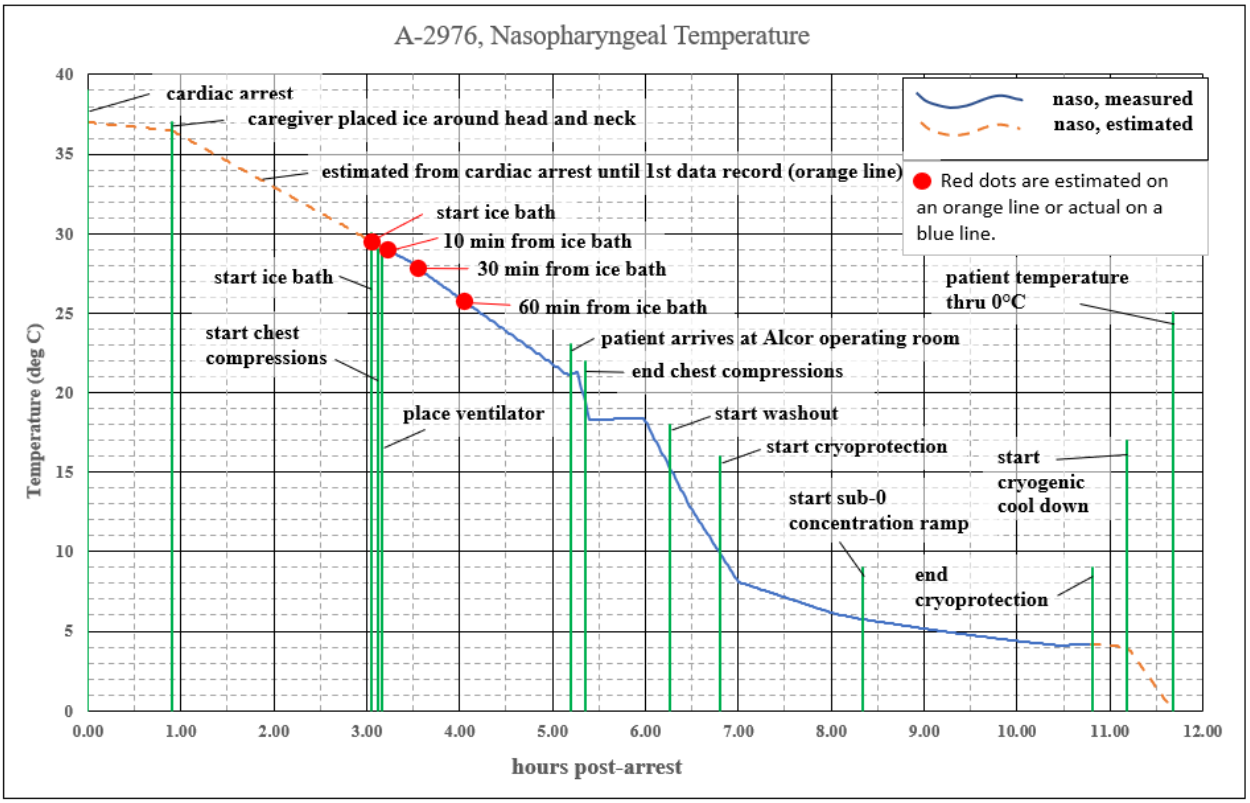

A-2976 Cooldown - Plunge
Temp, C
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
11
12
13
14
15
16
17
18
19
Time, hours post-arrest
Gas Temperature
Burr hole
Nasopharyngeal

## 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 11:41. As shown below, and due to lowering of the body temperature, S-MIX duration is shorter, at 03:58.

| 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 | 04:06 | 00:00 | 37.0 | | | |
| | seg 1 | | 00:54 | 00:54 | -0.5 | no | no | 00:53 |
| Caregiver placed ice around head and neck | | T-0 | 05:00 | 00:54 | 36.5 | | | |
| | seg 2 | | 02:09 | 02:09 | -7.0 | no | no | 01:39 |
| Start ice bath cooling | | T-0 | 07:09 | 03:03 | 29.5 | | | |
| | seg 3 | | 00:04 | 00:04 | -0.2 | no | no | 00:02 |
| Start of mechanical chest compressions | | T-0 | 07:13 | 03:07 | 29.3 | | | |
| | seg 4 | | 00:03 | 00:03 | -0.2 | no | no | 00:02 |
| Placement of airway & ventilator | | T-0 | 07:16 | 03:10 | 29.2 | | | |
| | seg 5 | | 02:02 | 02:02 | -8.0 | yes | no | 00:27 |
| Arrival of patient in OR at Alcor | | T-0 | 09:18 | 05:12 | 21.2 | | | |
| | seg 6 | | 00:09 | 00:09 | -1.7 | yes | no | 00:01 |
| End cardiopulmonary support | | T-0 | 09:27 | 05:21 | 19.4 | | | |
| | seg 7 | | 00:55 | 00:55 | -4.2 | no | no | 00:15 |
| Start whole-body washout | | T-0 | 10:22 | 06:16 | 15.2 | | | |
| | seg 8 | | 00:32 | 00:32 | -5.3 | no | no | 00:06 |
| Start cryoprotection with chest cannulation | | T-0 | 10:54 | 06:48 | 9.9 | | | |
| | seg 9 | | 01:32 | 01:32 | -4.2 | no | no | 00:12 |
| Start of sub-zero concentration ramp | | T-0 | 12:26 | 08:20 | 5.8 | | | |
| | seg 10 | | 02:29 | 02:29 | -1.6 | no | no | 00:16 |
| End cryoprotection (final RI = 47.4 Brix) | | T-0 | 14:55 | 10:49 | 4.2 | | | |
| | seg 11 | | 00:22 | 00:22 | -0.2 | no | no | 00:02 |
| Start patient cryogenic cooldown | | T-0 | 15:17 | 11:11 | 4.0 | | | |
| | seg 12 | | 00:30 | 00:30 | -4.0 | no | no | 00:03 |
| Patient temperature thru 0°C | | T-0 | 15:47 | 11:41 | 0.0 | | | |
| totals: | | | 11:41 | 11:41 | -37.0 | | | 03:58 |

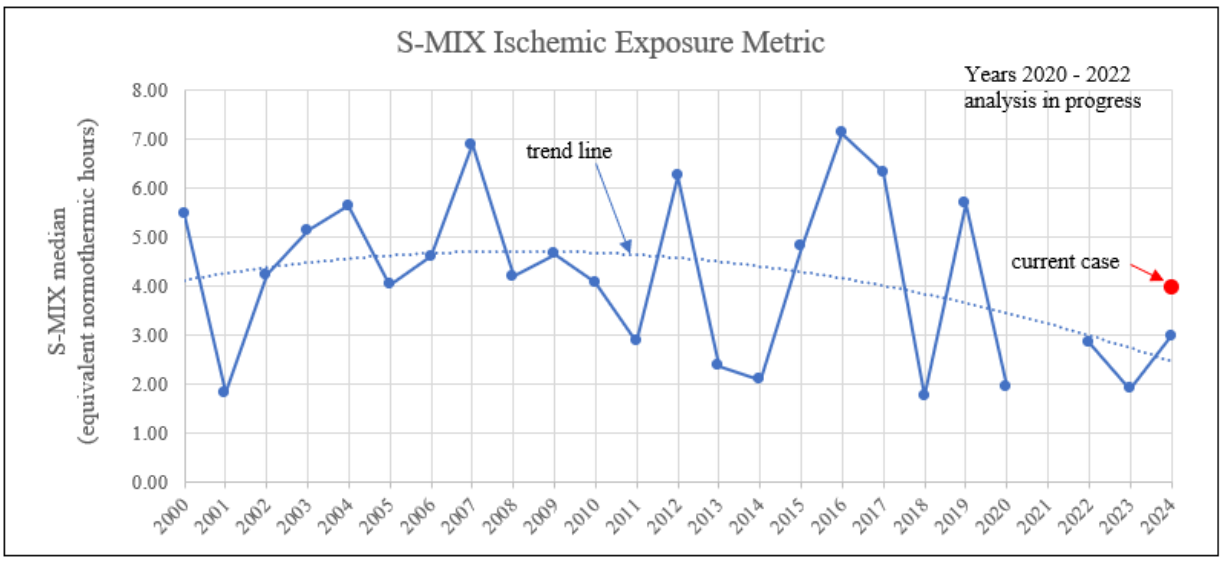
The plot below shows events related to the S-MIX calculation. The red dots can be used to construct a metric for how fast the patient is initially cooled (see the Patient Cooling Rate table below). This is a critical period since body temperature is highest and ischemic damage most rapid.




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

| **Patient Cooling Rate** | | | (patient weight 136 kg; 300 lb) | |
|---|---|---|---|---|
| Note: time = 0 at start of ice bath | 0 min elapsed | 10 min elapsed | 30 min elapsed | 60 min elapsed |
| Naso temperature (°C) | 29.5 | 29.0 | 27.8 | 25.7 |
| Temperature drop (°C) from t = 0 | 0.0 | -0.5 | -1.7 | -3.8 |
| Cooling rate (°C/min) from t = 0 | N/A | -0.05 | -0.06 | -0.06 |

The following plot shows the trend of S-MIX achieved since 2000.




## 14. 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.