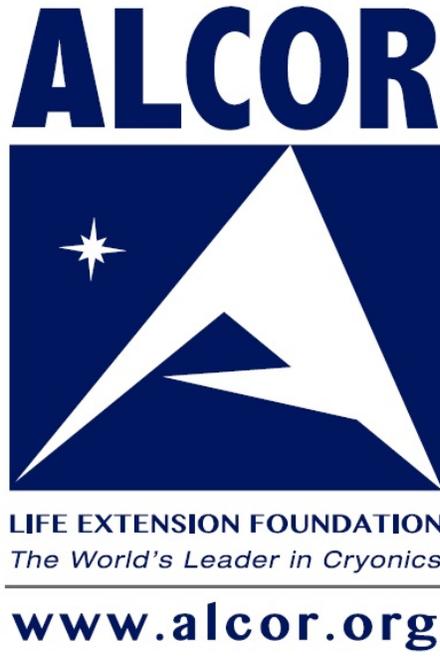


Alcor A-1395

Case Report



Prepared by:

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

Sources:

**Josh Lado, EMT; Alcor Medical Response Director
and Hugh Hixon, M.S. Biochemistry, Alcor Research Fellow,
Alcor Life Extension Foundation;
And Eric Vogt, EMT-P,
International Cryomedicine Experts**

Review and Editing:

**Christopher Divver, NREMT-P, Aschwin de Wolf,
Hugh Hixon, M.S. Biochemistry,
Marji Klima, and R. Michael Perry, Ph.D.,
of Alcor Life Extension Foundation**

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1. Personnel

Stabilization, Transport and Field Cryoprotection Team:

Josh Lado, Alcor Medical Response Director
Eric Vogt, EMT-P, International Cryomedicine Experts

Deployment Committee:

Max More, Ph.D., Alcor Chief Executive Officer
Steve Harris, M.D., Alcor Chief Medical Advisor
Josh Lado, Alcor Director of Medical Response

2. Overview

Information is derived from multiple sources and is all converted to Mountain Standard Time (MST).

Timothy Hubley was a 70-year-old male, a non-confidential, neurocryopreservation member who had joined Alcor in 1991. He had suffered a stroke in January of 2016. On Sunday, May 13, 2018, the member was pronounced legally deceased at a hospital in Jacksonville, Florida after choking on a piece of meat.

Alcor worked with the Medical Examiner and an autopsy was avoided. The Medical Examiner released the member to a local funeral home with no additional issues. Alcor made arrangements to fly to Jacksonville and perform a [field neurocryoprotection](#) (FNC). The procedure was initiated 17 hours after the member was pronounced legally deceased. The patient was flown to Alcor on May 15, 2018. Cryogenic cooldown was completed on May 19, 2018, and the patient was transferred to long-term maintenance at liquid nitrogen temperature on June 11, 2018.

On June 30, 2018, a CT scan was made. The CT scan showed non-uniform and incomplete cryoprotection, with extensive ice formation and notable symmetry (see CT scan at end of report).

3. Patient Assessment and Deployment

Information was derived from multiple sources and was all converted to Mountain Standard Time (MST).

Tim Hubley had been an Alcor member since 1991. After a stroke in January of 2016 the member had started to regain his speech and balance. He and his wife had moved to Jacksonville, Florida in 2018 to be closer to his wife's family so they would be able to help with his care.

On Sunday, May 13, 2018, the member and his family had just started dinner when a piece of steak became lodged in his throat. Heimlich abdominal thrusts and CPR were performed immediately by family members, however, when the member was taken to a nearby hospital he was pronounced legally deceased at 14:51 hrs.

Alcor received a Telemed alert at 15:03 hrs. After the Alcor Deployment Committee decided that a field neurocryoprotection would be done, the Medical Response Director (MRD) requested and obtained the assistance of a trained and experienced paramedic who had worked with Alcor on prior cases.

The Medical Examiner in Florida contacted Alcor and stated that an autopsy was required for two reasons. The first reason was that he did not have a primary physician in Florida to sign the death certificate and the second was due to the patient's cause of death. Alcor worked with the Medical Examiner and an autopsy was avoided. The Medical Examiner released the member to a local funeral home with no additional issues.

Alcor's Chief Medical Advisor (CMA) was informed that no heparin had been administered to the patient as the member's physician had not returned a call to the MRD before he had to deploy. The two Alcor team members departed for Orlando, FL at 22:30 hrs (estimate) and arrived in Orlando, FL on Monday morning, May 14, 2018. They drove to the destination in Jacksonville, FL in the previously arranged rental vehicle.

4. Field Surgery and Washout

Upon arrival at the funeral home at 06:00 hrs (estimate) on Monday, May 14, 2018, the team unpacked their equipment. The bilge pump for the the heat exchanger was not in the kit. The team went to a local hardware store to purchase the needed pump and hoses.

The patient's neck was prepared for surgery. The first incision to expose the right carotid artery was made at 08:06 hrs. The burr holes were established at 08:36 hrs and the neuro isolation was completed at 08:41 hrs.

The field neuro cryoprotectant perfusion was started at 08:50 hrs. This protocol utilized a series of individual bladders made up in advance with different and gradually increasing concentrations of nM22 cryoprotectant (see the below Table of Concentrations (Brix) of nM22 Solution). Gravity was used to infuse the perfusate into the patient as an open circuit procedure.

The concentration of nM22 was 48.8 Brix from the left jugular vein and 48.7 Brix from the right jugular vein. Per the cryoprotection protocol, the normal endpoint criterion for neuro patients is over 100% (49.9 Brix) concentration from both jugular veins. The final concentration set in the cryoprotectant bags was 104% of the desired final concentration and was clearly inadequate to produce the desired endpoint of 49.9 Brix. (The concentration of the final step has subsequently been set to 106%) Field cryoprotection was completed at 13:15, after which the patient was packed in dry ice.

5. Transport

At 13:27 hrs the patient was secured into a neuro shipping container with dry ice for cooling to dry ice temperature. The cooldown record showed an isotherm, which is an indication of ice formation, at about -10°C in the burr hole temperature descent, but not in the nasopharyngeal plot.

The team departed the funeral home at 13:30 hrs en route to the hotel with the patient cooling on dry ice. There was a break in the temperature recording between 34 and 44.5 hours post-mortem, probably because the batteries of the Reed thermocouple froze inside the closed shipping case due to cold CO_2 emission. The temperature record for the shipment from Jacksonville to Scottsdale was unremarkable.

On Tuesday, May 15, 2018, at 20:30 hrs the patient and the two Alcor team members arrived at Phoenix Sky Harbor airport and at 22:08 hrs they arrived at Alcor. No manual temperature measurement was made upon arrival but the datalogger did later confirm that the patient was at dry ice temperature (-79°C).

6. Cooling to Liquid Nitrogen Temperature

On May 15, 2018, an eyebolt was placed in the patient's vertebra for ease of handling and the patient was placed into the cooldown dewar. At 22:23 hrs the program "cryoprotected neuro" was started, plunging the patient from -78°C to -110°C and then cooling more slowly to minimize thermomechanical stress during passage through the temperature range where tissue is solid. An uneventful cooldown was terminated on May 19, 2018. A CT scan was made of the patient's brain and the patient was placed in long-term maintenance at liquid nitrogen (LN_2) temperature on June 30, 2018.

7. Timeline and Time Summary

May 13, 2018

14:51 Pronouncement of legal death

May 14, 2018

Note: The cephalon was not weighed either before or after cryoprotection

08:06 Start of field surgery

08:36 Burr holes established

08:41 Cephalic isolation completed

08:50 (Estimate from video) Field cryoprotection started

11:21 Data logger stopped recording

13:15 Completed field neuro cryoprotection, venous Brix readings:
Left = 48.8, right = 48.7

13:15 Start dry ice cooldown

13:30 Team and patient left funeral home

May 15, 2018

16:41 Departure of patient from Orlando Airport for Scottsdale, AZ on American Airlines

22:08 Patient arrived at Alcor

22:23 Start of cryogenic cooldown at Alcor

May 19, 2018 – Termination of cryogenic cooldown

June 30, 2018 - A CT scan was made of the patient's brain and the patient was then placed into long-term maintenance at liquid nitrogen (LN₂) temperature

Time Summary

Field Surgery and Washout

May 14, 2018

hrs:min

17:15 From pronouncement to start of field surgery: 14:51 hrs on 5-13-18 to 08:06 hrs on 5-14-18

00:35 From start of surgery to end of surgery: 08:06 hrs to 08:41 hrs

17:59 From pronouncement to start of cryoprotection: 14:51 hrs on 5-13-18 to 08:50 hrs on 5-14-18

04:25 From start of cryoprotection to end of cryoprotection: 08:50 hrs to 13:15 hrs

22:24 From pronouncement to start of dry ice cooldown: 14:51 hrs on 5-13-18 to 13:15 hrs on 5-14-18 (dry ice cool down started at the end cryoprotection)

40:17 From pronouncement to patient arrival at Alcor: 14:51 hrs on 5-13-18 to 07:08 hrs on 5-15-18

8. Discussion

1. For greater inter-operability, quick release connections should be added to the pumps, using a pre-made adapter. This feature will be considered.

2. The instrument pocket in the neuro shipper is currently not too well insulated and this will continue to be a problem for anything with batteries. The instrument pocket could be moved outside the wall of the shipper case, where it will be warmer. Another alternative is to leave the instrument outside the shipper during the cooldown, if possible. In addition, a blind thermocouple plug could go into one of the sockets to record the temperature in the instrument pocket. Redesign and replacement will be considered.

3. The field kits used to have soft dividers but that wasted space. The elimination of the dividers allowed us to reduce the number of Pelican cases needed, which is an advantage. Nonetheless, the cases are not well organized at this time. Organization schemes change with personnel changes. Everyone has their own preferences, and every scheme has its own problems and advantages.

Options discussed included the use of Ziploc bags to separate items inside the Pelican case and the use of a vacuum sealer to eliminate air from the bags. The technical staff will work together to find a way to better organize the cases. Two folding bed tables have been added to the kits for holding items during a case.

4. The data logger had stopped recording at 11:21 hrs. Alcor texted the team and asked if 1) the data logger had gotten too cold, 2) the buttons on the data logger had gotten pressed across the panel inside the case, and 3) if the team could check the SD card to verify the data. The team replied that they did not understand why it had stopped and that the SD card could not be checked in the field.

At 11:29 hrs Alcor texted and asked if the team had tried recording data again. The team responded that 1) they had switched batteries, 2) there was no room for additional dry ice, and 3) they had taken a short video showing the data logger was recording. Alcor responded that a better data logger would be sought.

5. At 09:57 hrs pictures of the tubing and heat exchanger were sent to Alcor personnel together with a request for assistance with the problematic flow to the patient. Alcor staff responded with a question about whether or not there was a stopcock between the isolator and the pressure gauge. The team sent a picture of the pressure gauge with the cover removed. Alcor staff texted back that they had received the picture and would confer with another staff member with more familiarity with the tubing when he arrived at the office. At 10:15 hrs the B1 perfusate had flowed into the patient well, but none of the nM22 cryoprotectant had flowed into the patient.

Alcor requested that the team bring the heat exchanger back to Alcor so it could be examined as the possible cause of the flow restriction. At that time the refractive index was 10.6 Brix on the left carotid artery and 10.1 Brix from the right carotid artery. Alcor staff texted that the Brix

readings were reasonable and requested a pressure reading. At 10:37 hrs the arterial pressure was 68 mmHg and was steady, which was low but acceptable.

6. The CT scans showed erratic and incomplete cryoprotection, with extensive ice formation and notable symmetry. This confirms the isotherm in the cooldown plunge to dry ice temperature. Discussion among technical staff and advisors was initiated about whether increasing the colloid content of vitrification solutions for cases with long ischemic times might improve brain perfusion. Administration of streptokinase during the first flush of cryoprotection may also improve perfusion.

9. Issues and Actions

A debriefing meeting was held on May 30, 2018. The following issues and actions were identified.

SCDD bilge pump not in field kit

The 360-110 GPH Bilge pump was not taken on the trip because the MRD thought it was a duplicate. There are two bilge pumps in the kits for two different uses (one for the surface conduction cooling device (SCCD) and one for the heat exchanger). We could use the SCCD pump to replace a missing bilge pump if there were a malfunction, but it is better to always have both pumps in the kit. Further, we should always have an extra backup pump along, they only cost about \$20 each. Additional pumps have been purchased.

Heat exchanger hose kinked

The way the heat exchanger was positioned inside the bucket, and once ice was added, the flexible hose at the bottom of the heat exchanger had become kinked. The flexible hose at the bottom of the heat exchanger was replaced with a 90-degree, 1/4" elbow and a holder for the heat exchanger has been designed, printed and added to the current kits.

Heat exchanger instability

The heat exchanger flopped around in the enclosure. The enclosure has been redesigned with a pocket that holds the heat exchanger in place.

Datalogger too noisy

The pressure record was too noisy to be useful. The interior of the shipper can be cold enough to freeze the logger batteries. The logger needs to be kept outside the shipper during cooldown, and its pocket in the shipper needs to be moved to out to the shipper case wall for shipment.

Need for training

It has been too long since our last neuro case and a lot of things were forgotten. If we have not had a case within the last three months, the team will do mock-up trial runs quarterly, alternating with OR simulations. The team will go through every step and collect all the data. The first dry run was scheduled for June 5, 2018.

Communication problem

One of the deployed team members did not see an email from Alcor's CEO putting him in charge of this case until well into the case. The team was not yet accustomed to using Alcor's internal communication system (ICS) as a means of keeping the group updated but will use it in the future.

Insufficient number of team members

An insufficient number of team members was used on this standby, stabilization and transport (SST). There should always be at least four people on a case, preferably six, so that staff can be rotated and there are enough team members to carry out the entire protocol.

Cephalon not weighed

The cephalon was not weighed either before or after cryoprotection. This needs to be done on all neuro cases. The OR team will receive training to make sure this is not omitted in the future.

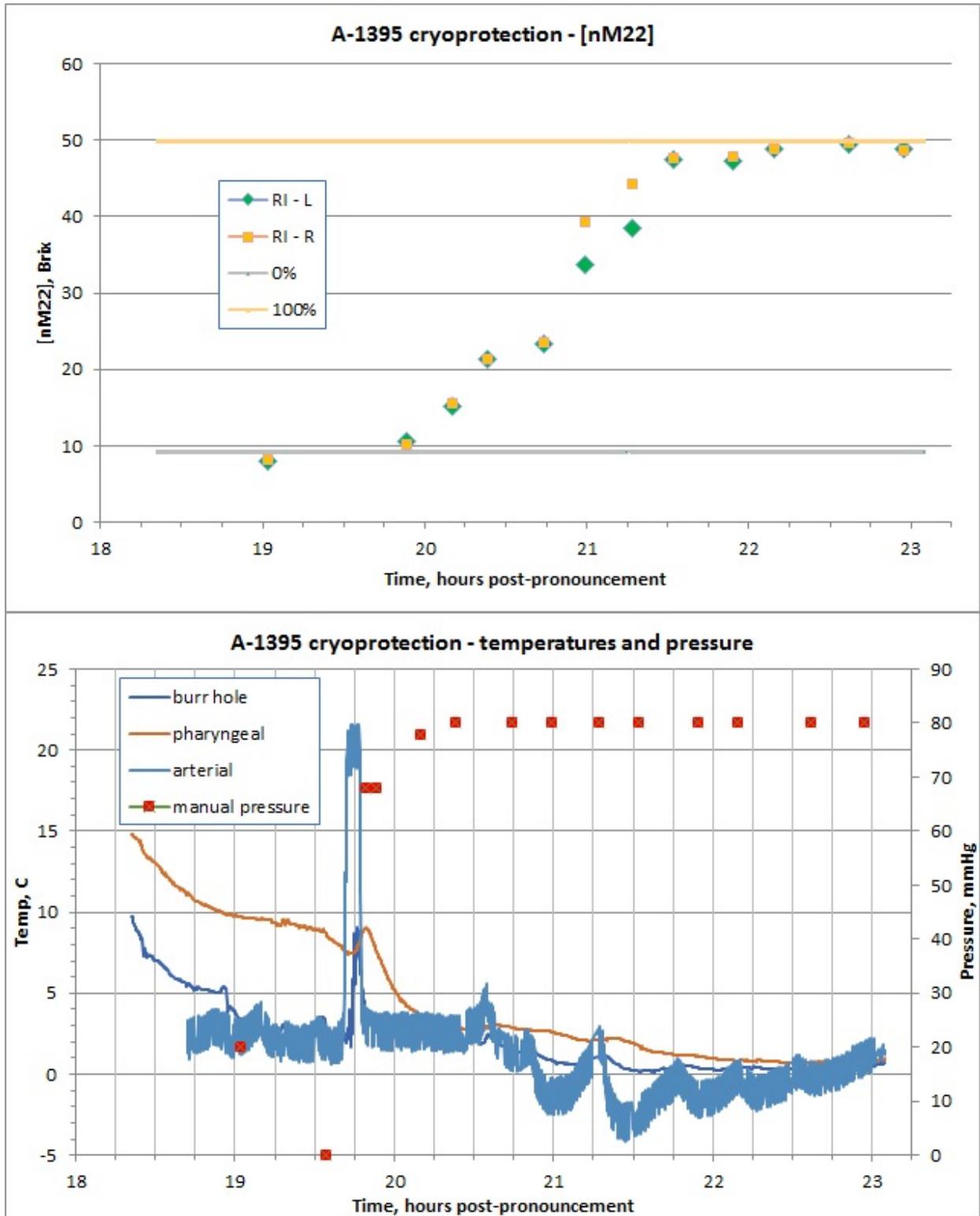
No temperature recorded upon arrival at Alcor

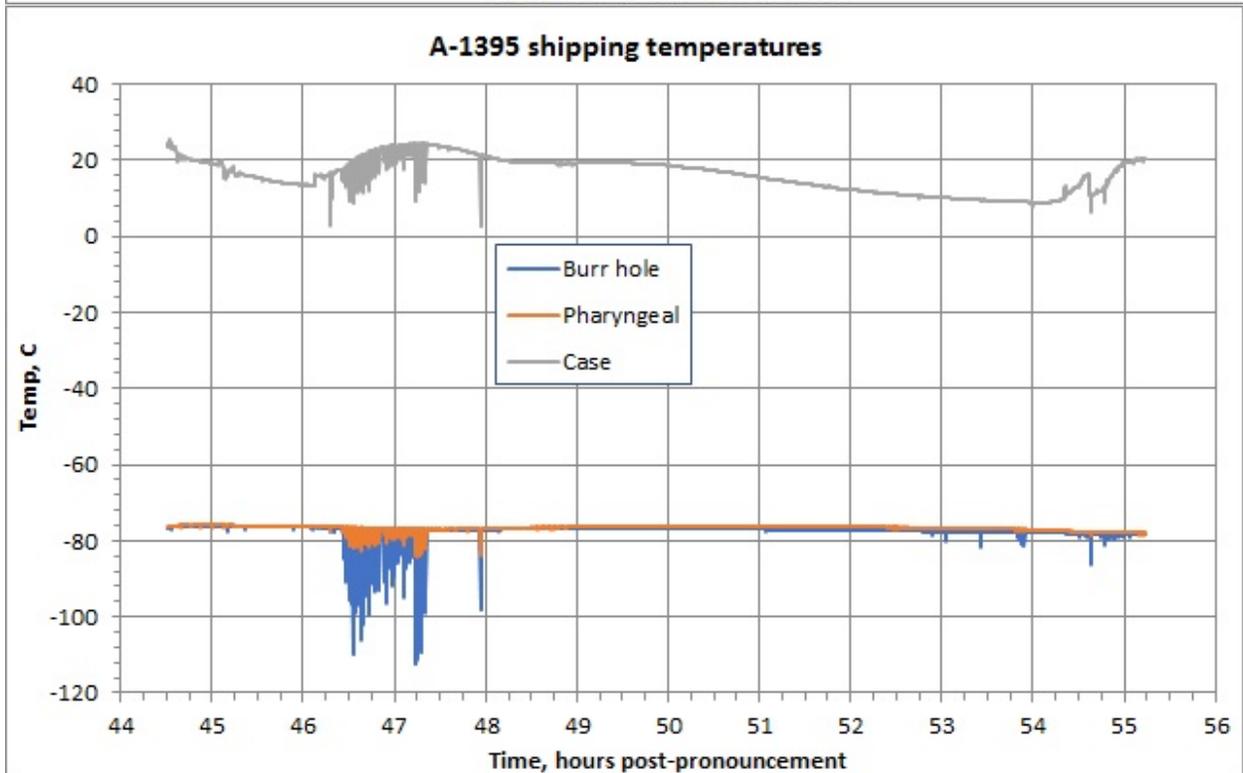
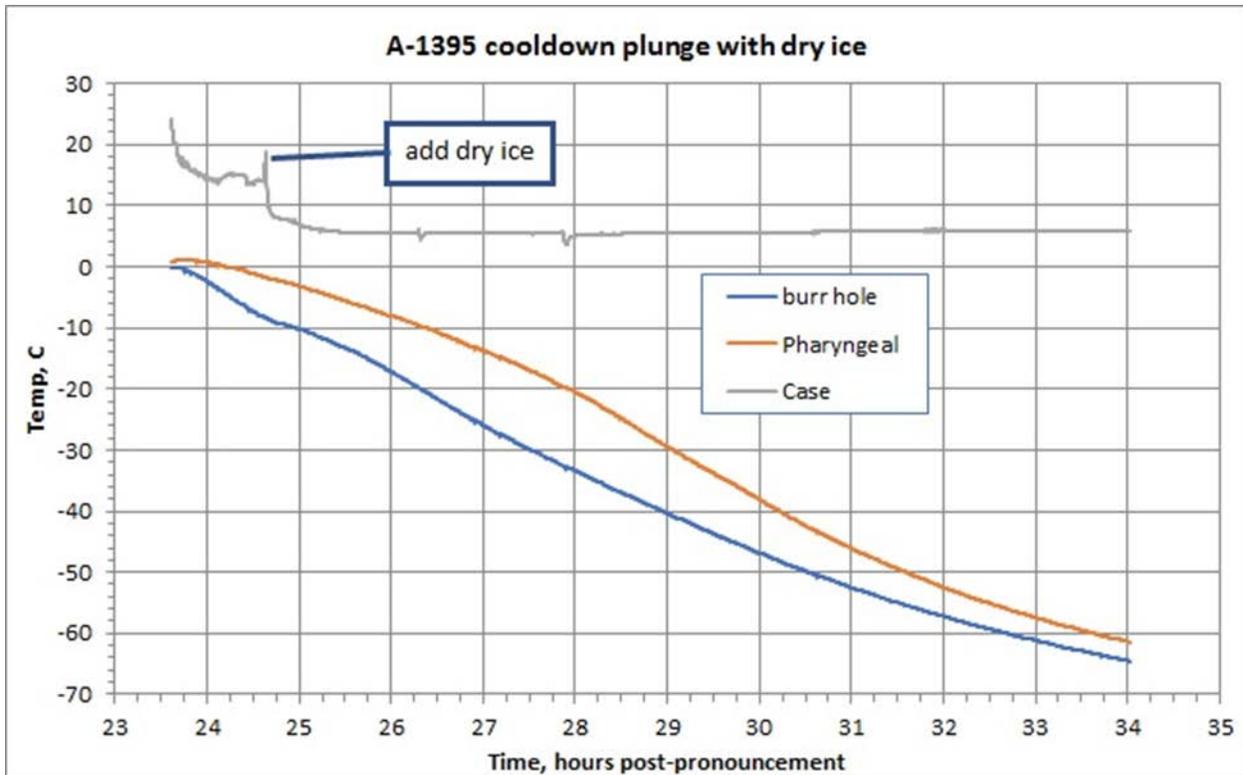
No manual temperature measurement was made upon arrival at Alcor. The datalogger did later confirm that the patient was at dry ice temperature (-79°C), but a manual temperature measurement should always be made when the patient first arrives at Alcor in case the datalogger has malfunctioned.

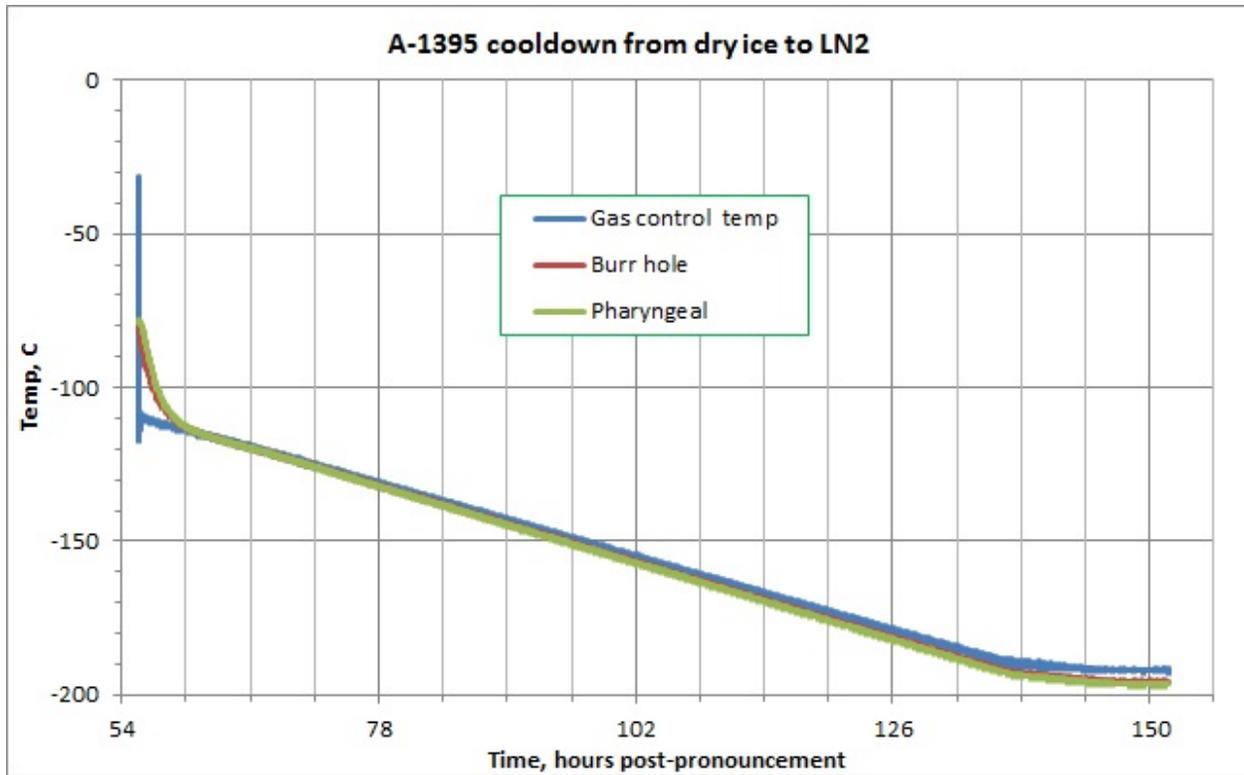
10. Table of Concentrations (Brix) of nM22 Solutions

Step-ramp calculator, nM22			
sixth root of [% CNV]/5 =		1.6584	step ratio
bag #	contents	[nM22], CNV	Brix (calc)
1	washout	0.00	9.80
2	0.05	0.05	11.81
3	0.08	0.08	13.12
4	0.14	0.14	15.31
5	0.23	0.23	18.94
6	0.38	0.50	29.85
7	0.63	0.50	29.85
8	1.04	1.04	51.50
9	1.04	1.04	51.50
10	1.04	1.04	51.50
11	1.04	1.04	51.50
12	1.04	1.04	51.50

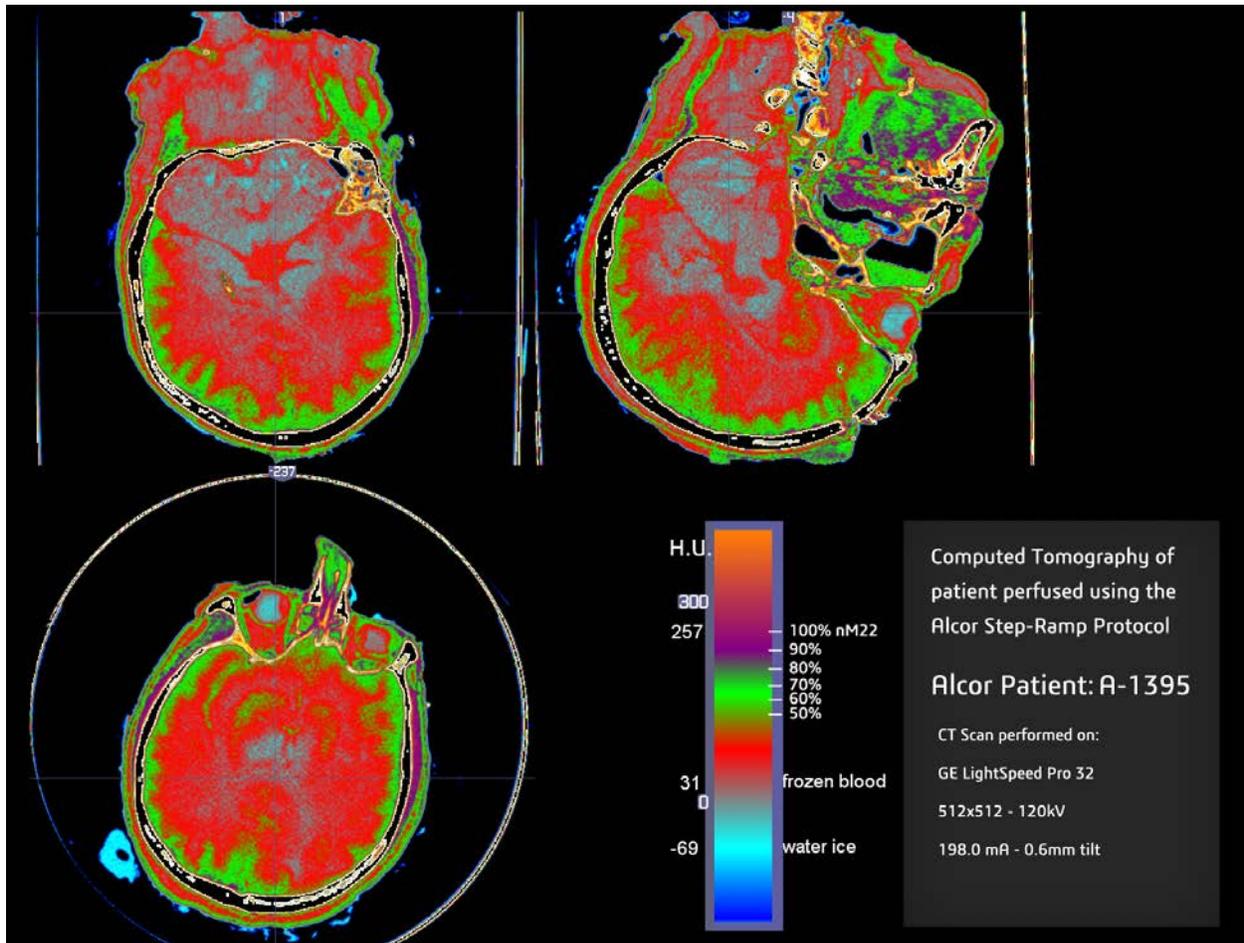
11. Graphs and CT Scans







Cryoprotectant Distribution



Note: These CT scans were made at liquid nitrogen temperature (-196°C) on June 30, 2018.