USE OF A HEAT EXCHANGER TO CONTROL THE TEMPERATURE OF CRYOPROTECTANT ENTERING THE BODY

BACKGROUND

The Cryonics UK (CUK) call-out manual includes a procedure for cooling the cryoprotectant before it enters the body via the carotid artery during perfusion. The arrangement was based on much earlier advice but there have been concerns about its effectiveness; that it could heat up the cryoprotectant fluid rather than cool it. This is reflected in warnings in the call-out manual. As a consequence, the heat exchanger system has not normally been used during perfusion.

To check these concerns, tests were carried out in April 2019, just prior to a CUK training meeting. Testing was intended to give an indication of the effectiveness of the method and to provide sufficient information to allow improved methods to be adopted. It was not intended to provide data on exact rates of cooling for different conditions.

TESTING CARRIED OUT

The test conditions used were:

- Water was used to simulate 10% and 30% VM1 perfusate. Part of the time it was used at ambient temperature (about 8°C) and at other times it was cooled with ice (to about 4 to 5°C) to simulate perfusate stored in a refrigerator.
- The cooling fluid used in the heat exchanger circuit was an ethylene glycol-based antifreeze as used for car engines.
- Ice cubes and freezer blocks from a domestic freezer were used (in separate tests) to cool the cooling fluid.
- The rate of flow of "cryoprotectant" (i.e. the water used in the tests to simulate cryoprotectant) was adjusted to be similar to the rates expected during a typical perfusion. Adjustment was based on visual inspection of outflows and a flow indicator. From observed level changes in the fluid reservoirs, a "moderate" flow, used to simulate initial rates expected in most cases, was about 0.5L/min. A "slow" rate of around 0.1L/min was also used to simulate cases where there is poor patient uptake.

EXISTING EQUIPMENT SET-UP

The heat exchanger set-up was assembled and run using the submersible pump arrangement given in the CUK manual and shown in Figures 1 and 2. In addition, temperature probes were introduced to check the temperature of the "cryoprotectant" before and after passing through the heat exchanger and of the antifreeze coolant .

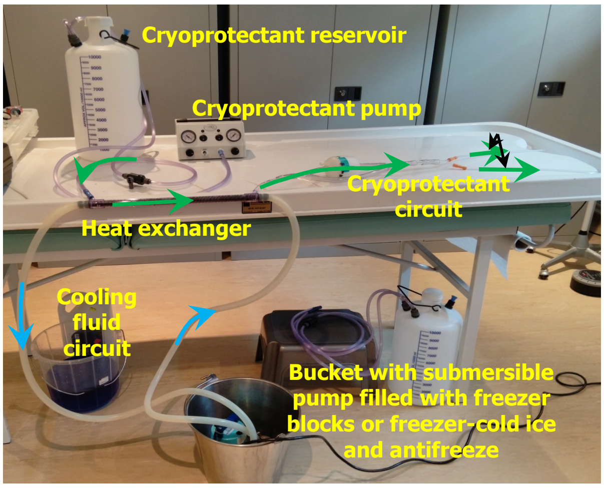

Figure 1 Old procedure: equipment

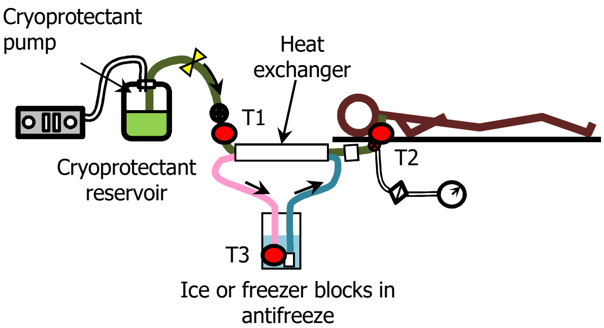

Figure 2 Old procedure: schematic

Temperature readings at points T1 and T2 (Figure 2) showed that, for both freezer blocks and ice cubes, the "cryoprotectant" was heating up by about 2°C as it passed through the heat exchanger. The antifreeze in the bucket was also found to be heating up, despite flowing through the cold freezer blocks or ice cubes.

The problem was traced to the submersible pump which is quite powerful, at 750W, which is transferred to the coolant solution as heat. This more than negates the cooling effect of the ice cubes or freezer blocks, and results in the antifreeze warming to about 20°C. This validates the concerns that the procedure would be counter-productive, and CUK's earlier reluctance to use it. Any arrangement must have a pump whose motor is outside the coolant circuit and that is cooled externally of the coolant circuit.

NEW ARRANGEMENT

The problem of the submersible pump was solved by using a roller pump that had previously been used to deliver cryoprotectant during perfusion of patients (now replaced by a pressure system). This is a much more complicated and costly piece of equipment than is really needed but was used since CUK has two of these pumps that are no longer used for perfusion.

The circuit is essentially the same as that shown in Figure 2 but, unlike the submersible pump, the roller pump requires the coolant circuit to be initially free of air with the coolant reservoir above the level of the pump. The change of that part of the circuit is shown in Figure 3, and the equipment is shown in Figure 4. The antifreeze was initially at ambient temperature (8°C)

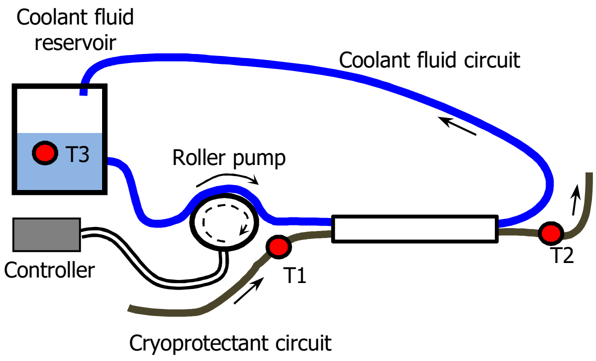

Figure 3 New pump circuit

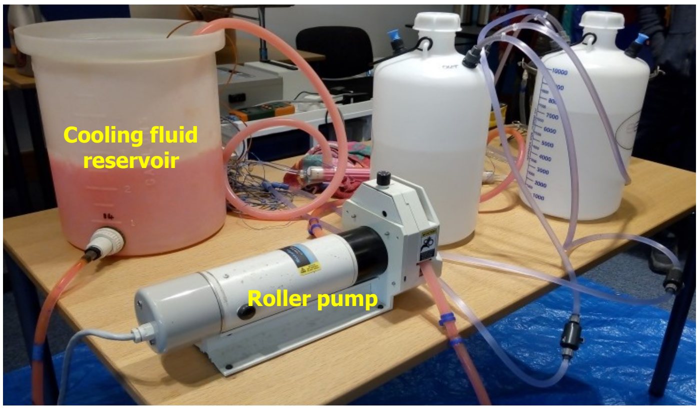

Figure 4 Equipment for new circuit

The main findings of the tests were:

- Freezer blocks gave little cooling of the "cryoprotectant"; typically only 1 to 2°C for "cryoprotectant initially at about 5°C.
- Ice cubes cooled the "cryoprotectant" from 5°C to 1°C for a "moderate" flow rate; a 4°C cooling. "Cryoprotectant" at 8°C was cooled to 4°C; also a 4°C cooling. Tests at "low" flow cooled "cryotectant" from 8°C to 1-2°C; a 6-7°C cooling. For very low flow, the "cryoprotectant", being actually water in the test, froze in the heat exchanger.
- With ice cubes in the coolant reservoir, the temperature of the antifreeze cooling fluid hovered at about -11 to -10°C throughout most of the testing, rising to about -9°C after 30 minutes of continuous pumping, indicating that the ice cubes were continuing to cool the fluid effectively but that fresh ice would probably be needed after about 45 minutes.
- Demonstrations of the procedure during the weekend training session, using ice cubes that had been kept in an electric cool box for some hours, gave similar amounts of cooling of the "cryoprotectant" even though the ice cubes had become slightly warmer, giving an antifreeze coolant temperature of about -9 to -8°C.

ADDITIONAL TESTING

Further testing was carrited out during the week following the meeting to check actual fridge and freezer temperatures and to assess the advantages of pre-cooling the antifreeze. The use of car screen-wash was also assessed. The findings were:

- Most domestic freezers are usually set to -18°C but checks on two fridge/freezers showed variations over time, with actual temperatures ranging from -18°C to -12°C. However, since ice that had been kept in a cool box for several hours worked almost as well (see above), these variations do not seem to significantly affect the efficacy of the procedure.

- Checks using concentrated car screen wash, stated to give protection to -20°C, confirmed that it remained liquid in a freezer, so could be pre-cooled in a freezer to improve cooling. Screenwash diluted to give protection to -10°C turned into a soft slush but did not freeze solid. This means that it could be used to augment the ice for cooling, taking advantage of its lower melting point. These improvements could enable the method to be used to cool concentrated cryoprotectant below 0°C if it had not been pre-cooled in a freezer.

WHAT HAS BEEN LEARNED

The lessons to be learned from the testing are:

- A submersible pump is unsuitable because the heat generated by the pump is transferred to the cooling fluid, resulting in the cryoprotectant being warmed, not cooled.
- Ice from a freezer will cool the antifreeze coolant to about -11°C during perfusion, allowing cryoprotectant at about 4°C to 8°C to be cooled by about 4°C for moderate flows and by about 6°C to 8°C for low flows. This gives sufficient temperature control to ensure that dilute cryoprotectant fluid can be delivered at optimum temperature.
- Freezer blocks, which potentially offer better performance than ice cubes because of their lower melting point, do not perform well because of their lower surface area and poor heat transmission through their plastic sides. However, freezer-cooled screen wash or antifreeze diluted to give protection to -10°C produces a slush that should be more effective than ice.
- Antifreeze or screen wash that gives protection to at least -20C can be pre-cooled in a freezer prior to use without freezing.
- To ensure good temperature control, it is essential to monitr the temperature at point T2 (just before entering the patient). Temperatures at points T1 and T3 should also be monitored if at all possible during a perfusion. This monitoring can be achieved using CUK's existing temperature probes and data logger which can monitor 4 probes simultaneously, allowing an additional probe to monitor patient temperature in the usual way.
- The method is suitable for cooling dilute cryoprotectant solutions (e.g. Cryonics Institute's 10% and 30% VM1 solutions) which are stored in a refrigerator at about 4°C but is not suitable the concentrated solution (e.g. Cryonics Institute's 70% VM1) that has been stored in a freezer at about -18°C prior to use. It could, however, be used in an emergency to cool concentrated perfusate that had not been kept in a freezer.
- It should be possible to increase the amount of cooling by using screenwash/antifreeze slush as described above, in combination with pre-cooled cooling fluid. This would be useful at all stages but would be particularly advantageous for concentrated cryoprotectant in a case where it had not been possible to pre-cool it in a freezer. However, further tests on this will be carried out before recommending this procedure in the CUK manual.

CONSEQUENCES FOR CUK PERFUSION METHODS

- The temperature of cryoprotectant entering the patient should be monitored and, for low concentration cryoprotectant, a decision made as to whether it should be cooled using the heat exchanger. This will depend on its initial temperature.
- If cooling is used, the new method using our roller pump (or other non-subersible pump) should be used. A submersible pump should not be used.
- Insulating covers should be used over the cryoprotectant reservoir bottles to keep the cryoprotectant as cool as possible during perfusion. This is particularly important for higher concentration cryoprotectant which is normally delivered too cold to be further cooled by this method, and which often has low flow rates.
- The cooling fluid should be pre-cooled in a freezer where possible. Pre-cooling antifreeze or screen wash diluted to give a nominal -10°C protection solution would further improve performance. This could be kept in plastic boxes (e.g. 1-litre sandwich or ice cream boxes) so that it can be tipped into the coolant reservoir.
- These changes in procedure should take place with immediate effect and will be incorporated in the next update of the CUK call-out manual.