**Title**

Controlled administration and hperoxygenation of cold preservation solution in controlled DCD donors undergoing abdominal-normothermic regional perfusion

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**Introduction**

The organs of donors undergoing circulatory determination of death (DCDDs) usually experience a period of static cold storage. SCS precedes further evaluation and reconditioning through ex-situ machine perfusion, or direct transplantation. This hypothermic preservation period, aimed at reducing metabolic demands, is initiated in-situ, through both topic and intravascular cooling. The latter is induced through the administration of a high volume of cold preservation solution (CPS) by gravity. CPS displaces the blood from the splanchnic circulation, and provides a perfusate decreasing the potential damages of ischemia and cooling.

In DCDDs, in the setting of abdominal normothermic regional perfusion (A-NRP), the extracorporeal circuit and cannulae may be employed to infuse and oxygenate CPS, ensuring a controlled flow and increasing dissolved oxygen ($O_2$) in the blood-free perfusate.

**Methods**

We aimed to assess feasibility, safety and effectiveness of a controlled administration of CPS through the NRP circuit and through the arterial cannula, and of its oxygenation through the membrane lung (ML) in DCDDs undergoing A-NRP.

Immediately after NRP, CPS was actively administered through the circuit accompanied by a flow of $O_2$ to the ML. The CPS flow was set at 400 ml/min if body surface area ≤1.7 and 500 if >1.7, with 1:1 CPS to sweep gas flow ratio. The drainage cannula was used to vent the venous system. The perfusion strategy is described in figure 1 A-D.

We measured the CPS partial pressure of $O_2$ ($P_{CPS}O_2$) at the beginning and at the end of its administration. The circuit was strictly monitored to assess for potential procedure related complications.

**Results**

We implemented this approach in 29 DCDDs undergoing A-NRP. In 13 donors oxygen was added to the CPS (table), achieving a median $P_{CPS}O_2$ of 648.5 mm Hg (IQR 76.5). Hyperoxygenation was stable throughout CPS administration (5-8 L).

Mean and median $P_{CPS}O_2$ were consistently above 600 mm Hg for all Celsior® and IGL-1® solutions samples. Mean $P_{CPS}O_2$ was 500 mmHg with Belzer UW®, administered once. Anyway, this is still compliant with hyperoxygenation definition. Mean/median $P_{CPS}O_2$ were consistently above 600 mmHg for all the circuits, independently from these integrating polypropylene (PP) or polymethylpentene (PMP) MLs.

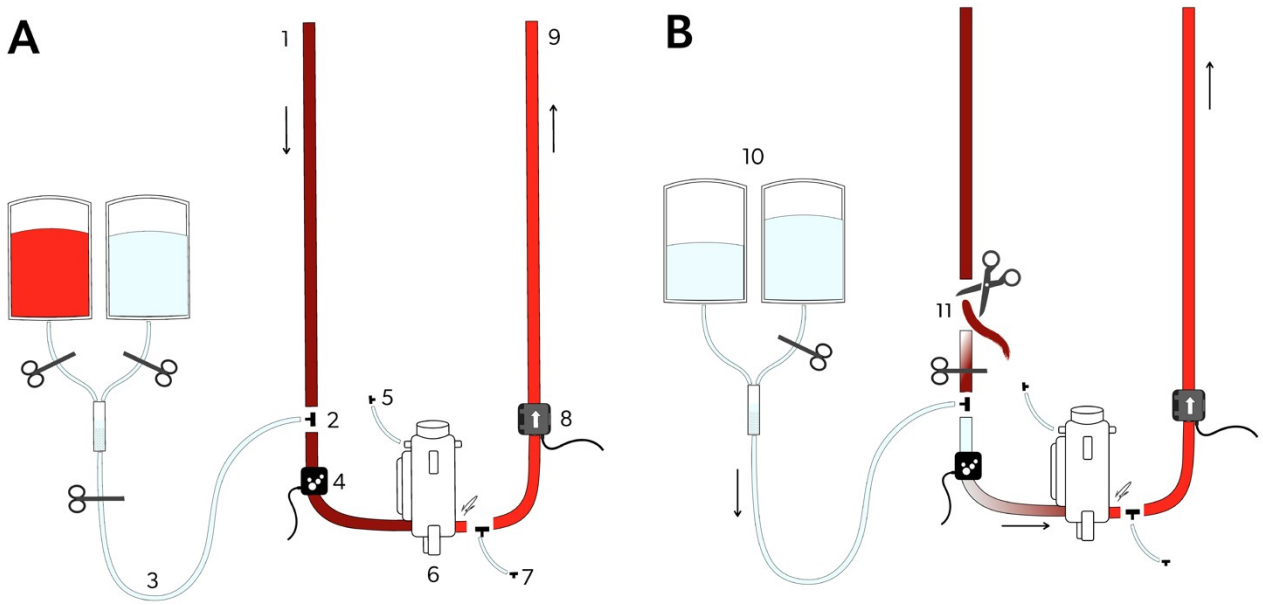
$P_{CPS}O_2$ in control samples from bags before administration was below 100 mm Hg. Median $P_{CPS}O_2$ in samples from controls infused through the circuit without gas flow (but passing through the ML fibers) was 187 mmHg (IQR 45).

We report one case of minor air entrance, managed without interrupting perfusion.

**Conclusions**

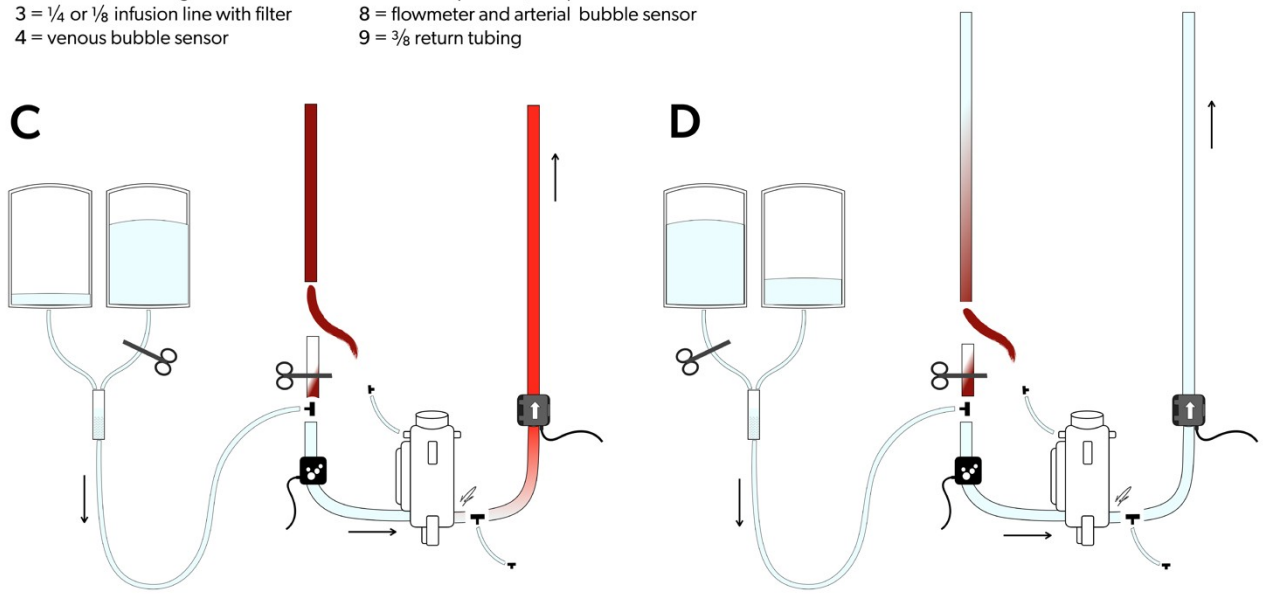
The infusion of an oxygenated CPS through the NRP circuit could be feasible and effective in ensuring a consistent and controlled CPS flow, inducing a fast SCS initiation. Moreover, the provision of a flow of $O_2$ through the ML during CPS infusion may consistently and significantly enhance the amount of dissolved oxygen. The oxygenation of the cold blood-free perfusate may improve tissue oxygenation, potentially providing a substrate for the organs during cold ischemia. This approach requires the same equipment used for NRP, with no increase in procedure related costs.

As the manipulation of the drainage limb of the circuit increases the risk for disruption and air entrance, extreme caution should be exerted to prevent, promptly recognize and manage this complication. If a small venous cannula is used for NRP, parallel venting through the right atrium should be considered, to avoid venous congestion with fast CPS infusion.




**Legend**

1 = ⅜ drainage tubing
2 = ⅜ - ⅜ - luer straight connector
3 = ¼ or ⅛ infusion line with filter
4 = venous bubble sensor
5 = venous (pre-ML) sample site
6 = centrifugal pump/membrane lung block
7 = arterial (post-ML) sample site
8 = flowmeter and arterial bubble sensor
9 = ⅜ return tubing
10 = CPS bags
11 = site of venous venting



| CPS administration through NRP circuit | | | | | | | | | | Portal Vein Infusion (by gravity) volume (L) | Organs considered for Procurement/ Transplantation | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Circuit Type | ML | CPS type | $P_{CPS}O_2$ mm Hg Initial | $P_{CPS}O_2$ mm Hg Final | volume (L) | flow (LPM) | SGF (LPM) | $FsO_2$ | Mechanical Complications | | Liver | Kidney |
| BE-MECC | PP | Celsior® | 479 | 649 | 6 | 0,4 | 0.4 | 1 | NO | 2 | P/T | P/T |
| BE-MECC | PP | IGL-1® | 747 | 583 | 7 | 0.5 | 0.5 | 1 | NO | - | P/T | P/T |
| BE-MECC | PP | IGL-1® | 648 | 658 | 7 | 0.4 | 0.4 | 1 | NO | 2 | P/T | - |
| BE-MECC | PP | IGL-1® | 714 | 671 | 7 | 0.5 | 0.5 | 1 | NO | 1 | P/T | P/- |
| BE-MECC | PP | Celsior® | 765 | 723 | 8 | 0.5 | 0.5 | 1 | NO | - | - | P/T |
| HLS 7050 | PMP | IGL-1® | 587 | 644 | 6 | 0.5 | 0.5 | 1 | minor air entrance | 2 | P/T | P/T |
| BE-MECC | PP | Celsior® | 618 | 641 | 7 | 0.5 | 0.5 | 1 | NO | 2 | P/T | P/T |
| HLS 7050 | PMP | IGL-1® | 547 | 619 | 6 | 0.5 | 0.5 | 1 | NO | 2 | P/T | P/- |
| Euroset AMG PP1 | PP | Belzer UW ® | 454 | 547 | 7 | 0.5 | 0.5 | 1 | NO | 2 | P/T | P/T |
| HLS 7050 | PMP | IGL-1® | 602 | 660 | 5 | 0.5 | 0.5 | 1 | NO | 2 | P/T | P/T |
| HLS 7050 | PMP | Celsior® | 683 | 681 | 7 | 0.5 | 0.5 | 1 | NO | 2 | P/T | P/- |
| HLS 7050 | PMP | IGL-1® | 710 | 729 | 5 | 0.5 | 0.5 | 1 | NO | 2 | P/T | P/T |
| HLS 7050 | PMP | IGL-1® | 621 | 654 | 5 | 0.5-0.7 | 0.5-0.7 | 1 | NO | 2 | P/T | P/T |

| | Overall n = 22 | Initial n = 11 | Final n = 11 | Celsior® n = 4 | IGL-1® n = 6 | Belzer UW® n = 1 | PP ML n = 7 | PMP ML n = 4 |
|---|---|---|---|---|---|---|---|---|
| $P_{CPS}O_2$ mm Hg mean (SD) | 639.8 (±76) | 628.85 (±96.6) | 650.69 (±49.4) | 654.9 (±85.2) | 649.6 (±56.1 | 500.5* | 635.5 (±93.4) | 644.7 (±52.6) |
| $P_{CPS}O_2$ mm Hg median (IQR) | 648.5 (76.5) | 621 (123) | 654 (30) | 665 (57.75) | 651 (64.5) | - | 648.5 (111.5) | 649 (67) |

CPS, cold preservation solution; IQR, interquartile range; LPM, later per minute; ML, membrane lung; NRP, normothermic regional perfusion; $P_{CPS}O_2$, partial pressure of oxygen in the CPS; P, procured; PP, polypropylene; SD, standard deviation; T, transplanted. * Only administered once during the study period.