



HAL
open science

Hypothermic Machine Perfusion Preservation: a Proof of Concept for Uterus Transplantation

Ludivine Dion, Carla Sousa, Karim Boudjema, David Val-Laillet, Sylvie Jaillard, Nathalie Rioux-Leclercq, Erwan Flécher, Vincent Lavoué

► To cite this version:

Ludivine Dion, Carla Sousa, Karim Boudjema, David Val-Laillet, Sylvie Jaillard, et al.. Hypothermic Machine Perfusion Preservation: a Proof of Concept for Uterus Transplantation. *Fertility and Sterility*, 2023, 120 (6), pp.1259-1261. 10.1016/j.fertnstert.2023.08.020 . hal-04227901

HAL Id: hal-04227901

<https://hal.science/hal-04227901>

Submitted on 30 Oct 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Hypothermic Machine Perfusion Preservation: a Proof of Concept for Uterus Transplantation.

Hypothermic Machine Perfusion for Uterus Transplantation

Ludivine DION MD^{1,2*} ; Carla SOUSA¹ ; Karim BOUDJEMA MD, PhD³ ; David VAL-LAILLET⁴ ; Sylvie JAILLARD MD, PhD^{2,5} ; Nathalie RIOUX-LECLERCQ MD, PhD^{2,6} ; Erwan FLECHER MD, PhD⁷ ; Vincent LAVOUE* MD, PhD^{1,2}

¹ Rennes University Hospital, Department of Gynecology, Hôpital Sud, France.

² Irset - Inserm UMR_S 1085, Rennes

³ Rennes University Hospital, Department of Hepatobiliary Surgery and Liver Transplantation, Pontchaillou, France.

⁴ Nutrition Metabolisms and Cancer (NuMeCan), INRAE, INSERM, Univ Rennes, St Gilles, France. david.val-laillet@inrae.fr.

⁵ Rennes University Hospital, Department of Cytogenetics and Cell Biology, Pontchaillou, France.

⁶ Rennes University Hospital, Department of Pathology, Pontchaillou, France.

⁷ Rennes University Hospital, Department of Thoracic and Cardiovascular Surgery, Pontchaillou, France, signal and Image Treatment Laboratory (LTSI), Inserm U1099, Rennes, France.

* Correspondence: Corresponding author : Ludivine DION, M.D., Service de Gynécologie, CHU de Rennes, Hôpital Sud, 16 Bd de Bulgarie, 35,203 Rennes Cedex 2, France ; ludivine.dion@chu-rennes.fr; ORCID : 0000-0001-8914-5756

Acknowledgments :
BioMedicin Agency for financial support

Abstract

Objective : To describe the feasibility of Hypothermic Machine Perfusion (HMP) in Uterus Transplantation (UT) to potentially improve the preservation of the uterus to enhance graft preservation in the DBD context.

UT is a new surgical approach to treat absolute uterus infertility, it can be performed after living donation (LD) or after Donation after Brainstem Death (DBD). In DBD context, uterus is typically the last organ removed after other vital organs with the exception of the Baylor team, which removes the uterus first. This key aspect imposes an unavoidable mild temperature ischemia for more than one hour for the uterus during the removal of the vital abdominal and chest organs. In renal transplantation, the perfusion machine reduces the risk of Delayed Graft Function, thus we hypothesize that machine perfusion could result in a reduction of uterus graft dysfunction. The uterus graft dysfunction could be expressed by a low embryo implantation rate, pregnancy loss or vascular pregnancy diseases such as preeclampsia or fetal growth restriction". To date, static cold storage (SCS) of the uterus is the only standard method for preservation prior to transplantation. HMP is an emerging method that could potentially improve the preservation of the uterus to enhance graft preservation in the DBD context.

Design : This video article shows all the technical details of using the HMP for uterine transplantation.

Subjects : porcine model

Intervention : Porcine uterus was retrieved from a DBD domestic animal model and flushed with KPS MP (Bridge To Life[®]) at 4°C. After vascular preparation on the back table, the uterus was perfused by KPS MP through a cannula in the aorta using the Vitasmart device (Bridge To Life[®]) for 18 hours. Then, the uterus was transplanted to the porcine recipient.

Main Outcome Measures : The macroscopic appearance of the uterus at the end of HMP and the assessment of the uterus vascularization after transplantation in the recipient compared to native uterus.

Results : This video shows the cannulation of the iliac vessels, cooling and removal of uterus on a porcine model, uterus preservation using HMP during 18 hours and then uterus transplantation in a new recipient pig with the reperfusion of the transplanted uterus next to the native, intact uterus of the recipient. The macroscopic appearance of the uterus at the end of HMP appeared viable and was perfectly flushed. The assessment of the uterus vascularization after transplantation in the recipient was similar to native uterus.

Conclusion

To our knowledge, we describe here for the first time the UT procedure in DBD context on an animal model, and the use of HMP for uterus preservation in UT programs. HMP could allow the duration of cold ischemia to be prolonged without altering the uterine graft, thus increasing the number of uterus grafts available for a greater number of women recipients. Nevertheless, this assertion has to be validated in human context.

Suggested Reading :

1. Brännström M, Belfort MA, Ayoubi JM. Uterus transplantation worldwide: clinical activities and outcomes. *Curr Opin Organ Transplant*. 2021.
2. Brannstrom M, Johannesson L, Dahm-Kahler P, Enskog A, Molne J, Kvarnstrom N, et al. First clinical uterus transplantation trial: a six-month report. *Fertil Steril*. 2014;101(5):1228-36.
3. Fageeh W, Raffa H, Jabbar H, Marzouki A. Transplantation of the human uterus. *Int J Gynaecol Obstet*. 2002;76(3):245-51.
4. Wei L, Xue T, Tao KS, Zhang G, Zhao GY, Yu SQ, et al. Modified human uterus transplantation using ovarian veins for venous drainage: the first report of surgically successful robotic-assisted uterus procurement and follow-up for 12 months. *Fertil Steril*. 2017;108(2):346-56.e1.
5. Brucker SY, Brannstrom M, Taran FA, Nadalin S, Konigsrainer A, Rall K, et al. Selecting living donors for uterus transplantation: lessons learned from two transplantations resulting in menstrual functionality and another attempt, aborted after organ retrieval. *Arch Gynecol Obstet*. 2018;297(3):675-84.
6. Puntambekar S, Telang M, Kulkarni P, Puntambekar S, Jadhav S, Panse M, et al. Laparoscopic-Assisted Uterus Retrieval From Live Organ Donors for Uterine Transplant: Our Experience of Two Patients. *J Minim Invasive Gynecol*. 2018;25(4):622-31.
7. Ozkan O, Akar ME, Ozkan O, Erdogan O, Hadimioglu N, Yilmaz M, et al. Preliminary results of the first human uterus transplantation from a multiorgan donor. *Fertil Steril*. 2013;99(2):470-6.
8. Flyckt R, Kotlyar A, Arian S, Eghtesad B, Falcone T, Tzakis A. Deceased donor uterine transplantation. *Fertil Steril*. 2017;107(3):e13.
9. Ejzenberg D, Andraus W, Baratelli Carelli Mendes LR, Ducatti L, Song A, Tanigawa R, et al. Livebirth after uterus transplantation from a deceased donor in a recipient with uterine infertility. *Lancet*. 2019;392(10165):2697-704.
10. Chmel R, Novackova M, Janousek L, Matecha J, Pastor Z, Maluskova J, et al. Reevaluation and lessons learned from the first 9 cases of a Czech uterus transplantation trial: Four deceased donor and 5 living donor uterus transplantations. *Am J Transplant*. 2019;19(3):855-64.
11. Jones BP, Saso S, Bracewell-Milnes T, Thum MY, Nicopoullou J, Diaz-Garcia C, et al. Human uterine transplantation: a review of outcomes from the first 45 cases. *Bjog*. 2019;126(11):1310-9.
12. Testa G, Anthony T, McKenna GJ, Koon EC, Wallis K, Klintmalm GB, et al. Deceased donor uterus retrieval: A novel technique and workflow. *Am J Transplant*. 2018;18(3):679-83.
13. Tardieu A, Dion L, Lavoue V, Chazelas P, Marquet P, Piver P, et al. The Key Role of Warm and Cold Ischemia in Uterus Transplantation: A Review. *J Clin Med*. 2019;8(6).
14. Tingle SJ, Figueiredo RS, Moir JA, Goodfellow M, Talbot D, Wilson CH. Machine perfusion preservation versus static cold storage for deceased donor kidney transplantation. *Cochrane Database Syst Rev*. 2019;3(3):Cd011671.
15. Kisu I, Kato Y, Obara H, Matsubara K, Matoba Y, Banno K, et al. Emerging problems in uterus transplantation. *Bjog*. 2018;125(11):1352-6.
16. Putman JM, Zhang L, Gregg AR, Testa G, Johannesson L. Clinical pregnancy rates and experience with in vitro fertilization after uterus transplantation: Dallas Uterus Transplant Study. *Am J Obstet Gynecol*. 2021.

17. Fronek J, Kristek J, Chlupac J, Janousek L, Olausson M. Human Uterus Transplantation from Living and Deceased Donors: The Interim Results of the First 10 Cases of the Czech Trial. *J Clin Med.* 2021;10(4).
18. Dion L, Santin G, Nyangoh Timoh K, Boudjema K, Jacquot Thierry L, Gauthier T, et al. Procurement of Uterus in a Deceased Donor Multi-Organ Donation National Program in France: A Scarce Resource for Uterus Transplantation? *J Clin Med.* 2022;11(3).

Journal Pre-proof



Journal Pre-proof