Uterus transplantation: current state and future perspectives
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The last frontier to conquer in female infertility is absolute uterine factor infertility (AUFI), affecting around 200,000 women in Europe. Our research group initiated a step-by-step developmental animal-based research approach on uterus transplantation (UTx) in 1999 and have optimized all aspects of the procedure in several animal species. Today 13 human UTx attempts have been performed, with 9 of them by our team. The other have been single attempts taking place in Saudi Arabia (2000), Turkey (2011), China (2015) and USA (2016).

In early 2013 our team completed the surgeries of a series of totally 9 human UTx, with live uterus donors. Eight recipients were MRKH patients and one had been hysterectomized because of cervical cancer. The mean age of the recipients was 31.5 +/- 3.9 years. Five donors were mothers and this included the donor of the cervical cancer patient. Other donors were close relatives and in one case family friend. The mean age of the donors was 53.0 +/- 7.0 years. IVF treatments were done before transplantation. The donor surgery involved uterine isolation with pedicles of the uterine arteries and veins and including large parts of the internal iliacs. The duration of these surgeries were between 10h 17min and 13h 8min. No donor needed perioperative blood transfusion and the hospital stay was 6 days. One complication occurred, with a uretero-vaginal fistula in donor #2 two weeks after surgery and repaired 3 months later.

In the recipient a midline incision was used and the external iliac artery and vein were mobilized bilaterally. Bilateral end-to-side anastomosis was accomplished between the uterine artery and one major uterine vein on each side, using 7-0 and 8-0 sutures on arteries and veins, respectively. After commencement of uterine perfusion the vaginal-vaginal anastomosis was accomplished. The graft was fixed to the round, cardinal and sacrouterine ligaments and an extensive leaf of bladder peritoneum of the graft was sutured on top of the bladder for extra structural support. The duration of recipient surgery operations varied between 4h 10min and 5h 56min. None needed perioperative blood transfusion and the hospital stay varied between 3 and 9 days. The recipients received two ATG treatments perioperatively and corticosteroids for 4 days. They were then only on double immunosuppression with tacrolimus and MMF/azathioprine.

Two patients were hysterectomized during the initial months due to uterine complications (thrombosis, uterine abscess). The other 7 patients experienced regular menses from 2 months after UTx and embryo transfers were initiated 12-16 months after transplantation. So far 5 out of the 7 patients have delivered healthy babies (71% take-home baby rate). Two out of these women got pregnant at their first single-ET and the other three at ET 5-7. The babies were delivered by c-sections in week 31+5 (no. 1; preeclampsia) and in week 34-36 (no. 3-5). The babies had normal weights for gestational age at birth and have developed normal, with three children now more than one-year old. A sixth recipient was pregnant but miscarried at week 14 and only one woman has so far (4 ETs) not been pregnant. This gives a total clinical pregnancy rate of 86% in this cohort of 7 UTx patients that have undergone IVF and ET. No other UTx attempts have resulted in live births and early pregnancy (with miscarriage) has only been reported in one case (Turkey case).

We are now planning to develop the method of live-donor UTx further by performing the surgery of the donor as primarily a robotic-assisted laparoscopic procedure. We think will shorten the complex uterus procurement from the donor.

In conclusion, UTx has proved to be a successful treatment for the previously untreatable AUFI condition. The technique should be developed further within clinical trials until it is established as a clinical treatment with high patient safety and efficiency.