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Editorial

Uterus transplantation: Where do we stand in 2018?



The first birth of a healthy child in 2014 to a woman who had undergone uterus transplantation (UTx) under the care of Mats Brännström's team in Sweden [1] astounded the medical world and the general public. This birth provided proof of concept for UTx, after over a decade of scepticism in the medical community. UTx opens up a new field of gynaecology and brings this surgical specialty into the domain of transplantation surgery, with a whole new culture to learn in terms of surgical technique, graft monitoring, the need to coordinate a large multidisciplinary team around the patient (a surgeon with UTx expertise, an obstetrician, a fertility specialist, etc.), follow-up of the patient's immunosuppressive therapy, and so on.

After this first birth, numerous heated debates have raged in the medical community, the media and the general population. In the medical community, UTx has attracted fierce detractors who have criticized surgeons' excessive zeal for new and challenging techniques and the unnecessary risk to the mother and child. Some of these detractors previously denounced gestational surrogacy (GS), only to defend it after the first exceptional results of the Swedish team were published. At the same time, patients with congenital uterine agenesis, and therefore absolute uterine factor infertility, and patient advocacy groups for these women began to dream of the possibility of motherhood.

In theory, three paths to parenthood exist for women with acquired or congenital absolute uterine factor infertility: adoption, GS, and UTx. These three pathways are actually very different life choices for women, none of which could replace the others. While the legalization of GS has been broached regularly in various reviews of France's bioethics legislation, there has been little or no discussion on UTx.

Meanwhile, on the sidelines of the debates on these societal choices, several teams around the world embarked on their own UTx programmes in the wake of the first birth reported in 2014 by the Swedish team. And less than 5 years later, at least 38 uterus transplants had been performed and 12 healthy children had been born through this technology (Table 1) [2].

The first uterus transplant was actually performed in 2000 by Fageeh et al. [3]. The feasibility of this surgery was proved by the return of menstruation, but 99 days after transplantation the uterus was found to be necrotic, probably due to prolapse of the transplanted organ and consequent torsion of the pedicles. In 2011, a Turkish team published the first pregnancy obtained after UTx, which unfortunately ended at 7 weeks' gestation [4,5]. In 2014, after over 10 years of research and the development of several animal models, Prof. Brännström's Swedish team achieved the

ultimate goal of UTx: the birth of a healthy child [1,2]. In its first clinical trial, the Swedish team performed 9 uterus transplants (using living donors) that resulted in 2 explantations and 7 viable grafts with resumption of menstruation [6–8]. Eight live healthy children were born by caesarean section to the 7 women with a functional transplanted uterus.

Since then, several other teams around the world have launched UTx programmes: in 2015, the Chinese team led by Wei et al. published its first successful transplant of a uterus retrieved from a living donor via a laparoscopic robot-assisted approach [9]. Next, teams from Dallas and Cleveland in the US published their own experiences. In Dallas, 5 uterus transplants from living donors were performed; 2 were successful, while the first 3 resulted in explantation [10]. The patients with a functional transplanted uterus produced 2 live healthy children. The Cleveland team transplanted a uterus from a brain-dead donor, but it had to be removed soon after due to septicaemia [11]. More recently, a German team successfully performed 2 uterus transplants. A third graft was retrieved but not transplanted due to atherosclerosis of the uterine arteries [12]. A Czech team reported having performed 2 living donor and 2 brain-dead donor uterus transplants but did not report the graft outcomes or their surgical technique [13]. Teams often only present results of their UTx programmes through the media rather than in the scientific literature. For example, there were reports in 2018 of the first birth of a child after transplantation of a uterus from a brain-dead donor in Brazil, but no details are available. In 2017, in India, a series of 3 living donor uterus transplants was reported in the media. Similarly, in Serbia, a uterus was transplanted from a living donor to her monozygotic twin sister, obviating the need for immunosuppressive therapy for the recipient. She gave birth to a healthy child (unpublished data). To our knowledge, no data were published about women follow-up after UTx or pregnancy.

Other UTx programmes in development can be identified among the clinical trials listed on the website clinicaltrials.gov [14]. A Belgian team in Ghent is currently recruiting patients for an UTx trial using brain-dead donors. A US team in Philadelphia is also recruiting for an UTx programme using living donors. Other teams, notably at Al-Dakahlia, Egypt, and in England, are due to begin recruitment. After several years of research and the development of an animal model, a trial of UTx using brain-dead donors by France's pioneering Limoges team opened for enrolment in 2015. Enrolment began, but the programme was temporarily suspended for administrative and organizational reasons. Two other French teams (in Paris and Rennes) are developing animal models (ovine and porcine) before embarking on an UTx

Table 1

Summary of the uterine transplants carried out, the donor type, any complications, and outcomes.

	Country	Brain-dead (BD)/ living donor	Surgical approach	Donor complications	Mean operative time Donor Recipient	Cold ischaemia	Warm ischaemia	Viable graft (menstruation)	Graft survival	Pregnancy birth
2000	Saudi Arabia	Living	Laparotomy	Ureteral injury (double-J stent)	Unk. Unk.	Unk.	Unk.	Yes	Necrosis Explantation D99	No No
2011	Turkey	BD	Laparotomy	NA	Unk. Unk.	Unk.	Unk.	Yes	Yes	Yes No, vacuum aspiration
2012 2013	Sweden Series of 9 grafts	Living	Laparotomy	Ureterovaginal fistula (pyelostomy, ureteral reimplantation)	11 h 37 min 4 h 46 min	1 h 18 min	1 h 23 min	Yes, 7	2 explantations: 1 for uterine artery thrombosis 1 for pelvic abscess	Yes, 8 Yes, 8
2015	China (Xi'an)	Living	Robot-assisted (donor) Laparotomy (recipient)	No	6 h 8 h 50 min	3 h 33 min	1 h 29 min	Yes	Yes	Unk.
2015	United States (Dallas) Series of 5	Living	Laparotomy	Suture dehiscence Defecation disorder	8 h 12 min 5 h 18 min	3 h 30 min	1 h 02 min	Yes, 2	3 explantations: 2 for uterine artery thrombosis	2 2*
2016	United States (Cleveland)	BD	Laparotomy	NA	Unk.	Unk.	Unk.	No	No Fungal infection	0
2016	Czech Republic (9)	BD 4 Living 5	Laparotomy	Plaie de l'uretère	5 h 56 min 4 h 06 min	5 h 08 min	Unk.	Yes, 6	3: 2 thrombosis, 1 HSV infection	0
2016	Brazil	BD	Unk.	Unk.	Unk.	6 h 20 min	1 h 30 min	Yes, 1	Yes	1 1
2017	Germany Series of 3	Living	Laparotomy	0	10 h 35 min 5 h 14 min	Unk.	Unk.	Yes, 2	1 uterus not transplanted (atherosclerosis discovered intraoperatively)	No
2017	Serbia (1)*	Living	Laparotomy	Unk.	Unk.	Unk.	Unk.	Unk.	Yes	1 1
2017	India (3)*	Living	Laparoscopy (failed) Laparotomy	Unk.	Unk.	Unk.	Unk.	Unk.	Yes	Unk.
2017	Sweden (2)	Living	Robotic (donor)	Unk.	Unk.	Unk.	Unk.	Unk.	Yes	Unk.
	China (Guangzhou)	Living	Laparoscopy (failed)	Unk.	Unk.	Unk.	Unk.	Unk.	Unk.	Unk.

Unk.: unknown; *: unpublished data.

programme. The team at Hôpital Foch is currently recruiting patients for living-donor UTX.

UTx surgery is complex and ambitious, and although the world's first success was reported just 5 years ago, technical simplifications have already been proposed. Uterus retrieval surgery has been modified to reduce the risks of morbidity to living donors. Wei's team in China performed radical hysterectomy using a robot-assisted laparoscopic approach [9], resulting in a much shorter operation: 6 h, versus 11 h for the Swedish team with an open abdominal approach. Wei's team [9] is the first to have successfully used ovarian veins for bilateral venous drainage, obviating the need to dissect the deep uterine veins. A clinical trial of robot-assisted laparoscopic uterus retrieval from live donors is underway in Sweden, with plans to recruit 10 donor/recipient pairs [2]. This minimally invasive approach should improve the postoperative recovery of living donors and will potentially enable more precise dissection of the uterine pedicles and ureter. Similarly, to avoid the need for complex dissection of the uterine vein pedicles and the associated risk of ureteral injury, some teams have suggested "sacrificing" the uterine veins and using the ovarian veins instead for the venous drainage of the graft. However, this option is dependent on the quality of the donor's utero-ovarian veins, which can be variable, with varices being a common occurrence. The Dallas team also used the utero-ovarian veins for bilateral venous drainage and demonstrated that this provides sufficient venous outflow for graft survival [10].

UTx is therefore a rapidly developing field, in terms of both new programmes and technical refinements. In under 5 years, at least 10 countries have carried out at least one uterus transplant and in at least 4 countries it has resulted in delivery of a healthy child. While a period of ethical and societal reflection on UTX is more than justified, the French authorities may now be justified in authorizing and fostering the development of UTX in France, in view of the global advances made. Obviously, a team's authorization will have to be dependent on the stringent preparation of their UTX programme. Health authorities, in partnership with scientific societies, could draw up the specifications for an UTX programme, indicating the conditions that must be met before it can start. These prerequisites could be the development of an animal model, a research programme, evaluation, and education and training to enable the experience acquired to be shared at national level. The facilities required at the centre where the UTX programme is based will also need to be specified. These must include a centre for surgical transplantation and the follow-up of transplant recipients, an assisted reproduction centre, and a maternity unit with facilities for high-risk pregnancies.

Declarations of interest

None.

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