



# The long road to penile allotransplantation in South Africa

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In the collective imagination, transplantation is the epitome of surgery, including the concepts of sacrifice, gift and life. Since 1950, the year in which Joseph Murray performed the first successful kidney transplant in the history of medicine in Boston. The evolution of medical sciences and technology has led to the interplay of millions of lives of recipients, donors and surgeons (1-4).

Urologists have always been widely involved in transplantation, especially kidney transplantation, which currently represents one of most explanted and transplanted organs in the world (5).

While the kidneys, heart, liver, lungs and corneas are historically the most explanted and transplanted organs, in recent years we have witnessed a race pushing the limits of ethics and technology with the proposal and execution of new types of transplants, such as hand, face, penis and even head transplants (1-5).

In the wake of these developments, the first penile transplant attempt was carried out in Beijing in 2006, which failed due to an early psychological rejection in the early post-operative days (6). However, the Chinese team demonstrated the technical feasibility of the surgery, opening the doors to what in 2014 was the first successful operation of its kind by the Department of Urology of Tygerberg Hospital and Stellenbosch University (7).

To date, out of five attempts made worldwide, four interventions have been successful: two carried out at the aforementioned South African center (in 2014 and 2017) and two others (one of the surgeries included a simultaneous scrotal transplantation) carried out respectively at the Massachusetts General Hospital in Boston and John Hopkins University Hospital in Baltimore in 2016 and 2018 (8).

The aim of this paper is to provide a global vision on penile transplantation, including possible indications and future prospects, as well as ethical and donor procurement issues.

## Is there a need for penile transplantation?

Penile loss and injury can have various causes. In South Africa in particular, a significant number of healthy young men are rendered aphallic each year due to complications resulting from ritual circumcisions which are widely practiced. In fact, ritual circumcisions are a deeply rooted practice in South African culture, especially among the Xhosa-speaking people of the Eastern Cape (7,9,10).

Circumcision is an integral part of a larger initiation ritual, which is generally an eagerly awaited event in a young person's life, symbolizing his transition to manhood and failure to do so results in social stigmatization (9,10). During the ritual process, the circumcisionist removes the foreskin with an assegai (traditional spear). A hemostatic bandage of a strip of buckskin or cloth and herb leaves are wrapped tightly around the penis. The initiates are then confined to a hut for the next eight days, during which the consumption of certain foods and drink is limited (7,9,10).

Current ritual circumcision practices in South Africa have raised serious health problems. The complications of the procedure can lead to severe penile mutilation which often results in amputations of various degrees for about 250 young people a year. Moreover, among the young people who are hospitalized in the days following the procedure, due to complications of the same, there is a mortality of almost 9% (7,9,10).

In fact, given the secrecy and confidentiality of the tribes about these practices, the true incidence of post-procedural complications is difficult to establish. In fact, a “complaint” of complications can often be seen as an act of weakness or even be punished (9).

Ritual circumcision is typically performed in a non-clinical setting by a traditional surgeon with little, if any, clinical training. In addition to the surgical risks, if the hemostatic bandage is applied too tightly, it may happen that the penile skin or the entire organ undergo necrosis. Also, initiates are discouraged from drinking fluids in the days following circumcision, in an attempt to reduce urine output to prevent acute urinary retention. As a result, dehydration initiates predisposition to thrombosis of the blood vessels in the penis, increasing the risk of penile necrosis. Poor sterility and hygiene contribute to the exacerbation of the problem. In fact, about a hundred deaths a year are due to septicemia (9,10).

However, ritual circumcisions are not the only cause of penile amputation. South Africa is one of the countries with the highest incidence of penile cancers, also due to the high prevalence of HIV and sexually transmitted diseases. Currently, this incidence is estimated to be in the order of 6 patients per 100,000 inhabitants, which translates into more than 3000 diagnoses per year of penile carcinomas requiring surgical therapy. Furthermore, diagnostic delays of the penile tumors themselves, requiring subsequent radical surgery adds to the morbidity (7).

Conventional reconstructive techniques, with the use of grafts and flaps, lead to functionally and aesthetically imperfect results of replacing the normal penile organ. In addition, they are burdened with frequent complications, which include flap atrophy or necrosis, urethral stricture, and extrusion of the prostheses (11,12).

The use of a bundle cutaneous flap of the radial forearm, which is currently the most used in common practice, can also compromise functional capacity in patients who depend on manual labor to earn a living. The use of prostheses associated with free-flap reconstructive techniques are burdened by high costs, often not sustainable by the patient, as well as by a high rate of complications such as the extrusion of the prosthesis itself.

For these reasons, penile transplantation could represent a valid answer to the problem as well as an effective option to the reconstructive surgical treatments currently available (11,12).

## Ethical issues

The possible social value of penis transplantation in South Africa is justified by the relatively large number of young adults undergoing partial or total penectomies following ritual circumcisions and traumatic injuries (7,9). The ethical issues surrounding penile transplantation are complex and are in part similar to those involving face transplantation, especially regarding self-acceptance of body image (9,13-24).

Although it is not strictly speaking a “life-saving” intervention, it can bring about a significant improvement in quality of life, especially for some of these patients who are still very young. Therefore, penile loss can not only lead to possible complications from the point of view of voiding, but also a complete renunciation of sexuality and paternity (7,9).

Often, such patients fall into a profound depressive crisis, exacerbated by the unacceptable further stigma and marginalization to which they are subjected by their own family and relational entourage. This depression results in a high suicide rate for these individuals.

As part of the project aimed at developing penile allograft surgery, the correct identification of candidates is first of all important in order to minimize the risk-benefit ratio (7,13-24).

In addition to the physical risks of long-term immunosuppression after transplantation, these patients face potential risks of ostracism and psychological harm.

In fact, the environment surrounding the possible candidate is also fundamental. The post-operative period should be managed with extreme sensitivity and respect for privacy, in order to prevent stigma or discrimination (9).

Another important consideration is adherence to immunosuppressive treatment and proper compliance with follow-up. The age category between 18 and 25 years is the one that presents the greatest risk for non-adherence to immunosuppression in kidney transplant recipients (9).

Furthermore, the psychological effect of penis transplantation cannot be underestimated and could induce psychosis or non-acceptance of the organ, which happened, for example, in the case of the first patient operated on in China in 2006 (6). In this case, in the early postoperative period, the patients developed a psychological rejection of the transplanted penis and therefore asked the surgeons to remove the organ.

For all these reasons Penile transplantation should be performed only in patients with severe damage to the penis, in appropriate institutions under the protocols approved by institutional review boards. Appropriate selection criteria should be established, and the risk/benefit ratio must be considered for each individual patient.

### **Project development and team training**

It is essential, for all transplants, but in particular for an experimental procedure such as penis transplantation, to have an ideal setting and a well-trained and well-supported team. The renal transplant team of the University of Stellenbosch - Tygerberg Hospital (tertiary hospital) is the one that took overall charge of the project, i.e., educating, choosing and coordinating the team, organizing training, the donor list, the choice of candidates, cadaveric organ harvesting, operating room and post-operative care, guaranteeing privacy and providing assistance.

The kidney transplant unit is served by a mixed team of urologists and nephrologists: urologists take care of organ harvesting and transplantation as well as any vascular access, while nephrologists are responsible for post-operative care, and in particular for immunosuppression.

The first phase of the project involved the approval of the project as the recommendations of Idea, Development, Exploration, Assessment and Long term study (IDEAL) at the local ethics committee (25),

The training phase of the team, including the background knowledge of years of kidney transplant surgery, with the addition of surgeons from the Department of Plastic Surgery, consisted of theoretical planning of the operation, training on a cadaver to become familiar with the tissues, anatomy, vascular and nerve micro-anastomoses, and testing the coordination of the team. The third phase concerned the enrolment of potential recipients on the waiting list.

During the third phase of the project, young men who have had total penile amputations resulting from ritual circumcisions were identified. Most of the patients included on the waiting list had been sent from other hospitals, following complications resulting from circumcisions. Candidates aged >18 years were placed on a waiting list similar to that for kidney transplants, after signing informed consent. All candidates underwent an evaluation and complete physical, hematological, immunological and psychological analysis, before being declared suitable and definitively approved for their

placing on the waiting list. The participant selected to receive the transplant was informed about the potential risks and benefits of the procedure.

The patients excluded from the waiting list after evaluation were those patients who possessed a residual phallus such as to be able to perform all functions of the organ in at least an acceptable manner, making the risk/benefit ratio of the procedure unfavorable and/or too risky. These patients were referred to a recovery program run by psychologists and plastic surgeons.

Patients placed on the waiting list were screened for HBV, HIV, tissue typing and ABO blood group. Patients with HIV, HBV or any other chronic or acute pathologies (active tuberculosis, psychiatric pathologies, cancer) or who abused substances, would possibly be excluded from the program.

The urological criteria for exclusion were the possession of a penis capable of guaranteeing penetration and urination while standing.

From the waiting list, the candidates were chosen on the basis of the classical criteria of immunological compatibility and priority placing on the list itself.

Candidates were asked to complete the Medical Outcomes Study Questionnaire Short Form 36 Health Survey (SF-36) for the assessment of the overall perceived health status. This questionnaire would subsequently be completed also at 6, 12 and 24 months post-operative. The International Index for Erectile Function (IIEF-5) would be administered at 24 months.

### **Outcomes of the first operated case at Tygerberg Hospital**

During the early postoperative period, the first operated patient developed a urethrocutaneous fistula that failed to close spontaneously and required surgical repair at 3 months (7). Penile rehabilitation consisted of maintenance tadalafil for 3 months after surgery and erections were first reported by the recipient 3 weeks after surgery. The patient was carefully monitored and the immunosuppressive medication was well tolerated throughout, with no clinical signs of rejection. Two years after the operation, the patient reported regular satisfactory sexual intercourse in a stable relationship with normal ejaculation and orgasm. He accepted the penis as his own, despite a small tuft of donor pubic hair growing at the dorsal base of the graft. At 24 months, the maximum urine flow rate (Q<sub>max</sub>) was 16.3 mL/s from a volume voided of 109 mL, with a normal

flow-time curve. At a visit 18 months after the transplant, the recipient declared to be finally satisfied of his life (7).

Outcomes regarding the second operated patient will be soon published in detail. However, as already presented in some congresses and meetings, he is doing well, with good functional (urinary and sexual) outcomes and good tolerance to the immunosuppressive medication.

### Future perspectives

Like any new surgical technique, the demonstration of its feasibility does not only lead to making it a possible solution or procedure in response to a clinical problem, but it also paves the way for further possible scenarios, indications and applications.

As mentioned, penile transplantation has seen the light in South Africa, mostly due to the important social problem caused by a large number of young adults who, every year, are made aphallic following complications resulting from ritual circumcision.

However, there are many other possible indications for this intervention, even in Western populations where young men are not exempt from being emasculated following the development of penile neoplasms or traumatic causes (7).

With this in mind, it would be useful for Western countries to launch feasibility studies that examine the possible demand and the cost/benefit of the eventual establishment of one or more penile transplant departments.

### Conclusions

Penile transplantation, of which currently only four cases have been successfully performed in the world, is an experimental method that can be perfected. Despite the fact that it is not easy to organize and perform, it has been proven to be a safe, feasible and effective procedure.

Penile allograft may represent a new way forward to improve the sexual and urinary function of amputee patients, although we are aware that, before expressing oneself definitively, it is necessary to have data from a large case series and with long term follow-up.

Despite this, we are also aware of what we have seen with our own eyes: the lives of young boys changed radically for the better and who have literally been “reborn” thanks to this incredible intervention.

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