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COMMENTARY
Facial transplantation: from the early trials to ethical and clinical guidelines

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Abstract
Facial transplantation is a complex technique that involves a number of risks. However, although it is not a lifesaving transplant, for individuals in dramatic conditions due to severe facial disfigurements, it constitutes the only possibility of recovering an acceptable quality of life. For this reason, even from an ethical point of view, it is considered an important therapeutic resource, provided it is conducted in rigorously-controlled conditions.

Key words
- ethics
- organ
- transplantation
- risk

Organ transplantation is one of the most important medical developments to have taken place in recent decades. The number of individuals who benefit from this therapeutic resource every year continues to rise.

For a number of years now, in addition to organ transplants, multi-tissue transplants have also been possible. In these procedures, a number of tissues are harvested from a donor cadaver and used to reconstruct parts of the recipient's body. Although multi-tissue transplants are not life-saving procedures, they can allow huge improvements in the recipient's quality of life.

The first multi-tissue transplant was performed on 23 September 1998 when, at the Édouard-Herriot Hospital in Lyon, a team led by Jean-Michel Dubernard transplanted the right hand (harvested from a deceased forty-one-year-old man) on to forty-eight-year-old New Zealander Clint Hallam, who had undergone an amputation.

Dozens of hand, upper limb and even lower limb transplants have been performed since.

Of the various types of multi-tissue transplants, facial transplants are particularly complex from a technical standpoint and, above all, raise important ethical questions [1].

Those who are eligible for face transplants are carefully-selected individuals who have severe facial disfigurations for various reasons and for whom there are no longer any alternative conventional plastic surgery or reconstruction options [2]. These individuals have severe limitations when expressing themselves, in their interpersonal relationships and when breathing and eating. So far, a few dozen face transplants have been conducted around the world. In most cases, the transplant regards a limited part of the face below the eyes, including the cheeks down to the chin. All those cases approved for facial transplantation had extremely serious lesions, for which there were no reconstruction options.

The first face transplant was performed in France at Amiens university hospital on 27 November 2005 by two teams (led by surgeons Jean-Michel Dubernard and Bernard Devauchelle). The patient (Isabelle Dinoire, a 38-year-old mother-of-two whose face had been mauled by her Labrador) was transplanted the tip of a nose, lips and chin [3, 4].

The second face transplant was performed on 14 April 2006 at Xijing military hospital in the city of Xian, in northern China, on a thirty-year-old patient, Li Guoxing, who had been attacked by a bear in 2004 [5]. This case was more complex than the previous transplant performed in France: two-thirds of the patient's face were completely disfigured and the transplant involved a cheek, upper lip, nose and one eyebrow. The patient was discharged on 30 July 2006.

Although the techniques used have improved over time, facial transplantation is still a highly complex procedure. Suffice to think that for the first facial transplant performed in Canada (in spring 2018 by surgeon Daniel Borsuk on a patient who had lost his nose and upper jaw in a hunting accident), it took 12 hours to harvest the tissues from the donor, 16 hours to prepare the recipient and 18 hours for the transplant.

From a clinical standpoint, the issues connected with a highly complex procedure are obvious: "Facial allografts could fail in the short or the long term. Technical failure, immunological problems, and poor selection of patients are significant risks" [6].

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Given the limited number of transplants performed to date, few follow-up data are available. Some of the data available highlight the numerous risks. For example, a group of French researchers followed the results of seven patients who received transplants between 2000 and 2009. Four of them had suffered firearm injuries to the face, one had suffered burns and two had had facial tumours. Over an average of six years' follow-up, two patients died (one due to failure of the transplant and infections and another committed suicide just over three years after the transplant). All the patients experienced episodes of rejection and the surviving patients continued taking high doses of steroids for years after the surgical procedure [7].

Face transplants also raise serious ethical issues, especially as regards self-identification, interpersonal relationships and social involvement [8, 9].

Further important issues regard the donor, the consent expressed while he/she was alive and the family's assent.

The recipient's mental health makes a crucial contribution to the success or failure of a face transplant. For this reason, subjects have to be chosen very carefully. Indeed, the multidisciplinary transplant teams involved always include psychologists and social workers.

When face transplants were in their early days, a number of authoritative institutions had expressed their opinion against face transplants.

For example, in Great Britain, face transplantation was first proposed on 25 November 2002 by surgeon Peter Butler, of the Royal Free Hospital in London, for a twenty-three year-old woman, called Elizabeth, who had a very serious road traffic accident on 21 September 2001. An opinion was sought of the Royal College of Surgeons, which published its opinion in November 2003 (the opinion was subsequently updated in November 2006) [10]. The report identified a number of issues that were particularly serious from a technical and scientific, psychological and ethical point of view. The Royal College came to the following conclusions: "The working party believes that until there is further research and the prospect of better control of these complications it would be unwise to proceed with human facial transplantation. Equally this conclusion does not underestimate the suffering of those patients who might be tempted by the prospect of facial transplantation. This conclusion is not adverse to facial transplantation. Indeed, it acknowledges the need to recognise it as a possible future treatment. It simply means that the work should take a much more incremental approach than some of the current hype surrounding it has suggested" [11].

On 19 February 2002, the French Comité Consultatif National d'Éthique (CCNE) was consulted regarding the topic by Laurent Lantieri, a plastic surgeon employed at the Henri Monor Hospital in Crétil, who proposed a protocol for facial transplantation. On 6 February 2004, the CCNE published its opinion, which highlighted the related issues [12] and whose conclusions were largely negative: "(T)here are ambiguities for both donors and recipients. Facial transplantations are not the same as organ transplantation and are far indeed from the graft of limbs. That is why they should not be practised before further and complimentary research have made it possible to evaluate with precision the risks inherent to this type of intervention, and to validate the results" [13].

Although the practice should still be considered experimental, over a decade after these positions were adopted, the results obtained are encouraging. For example, according to the data published in the American Journal of Transplantation in January 2015, olfactory and eating abilities were restored in 100% of cases, whereas the ability to breathe, talk, and control facial expressions improved in 93%, 71% and 76% of cases, respectively [14].

The utmost caution is required. However, the encouraging results and the fact that the transplant is the only possible way to recover certain functions and to restore the possibility of social relationships for individuals with severe facial disfigurements, lead us to consider facial transplantation an important therapeutic resource and one for which there are no alternative options.

The technique is also becoming a reality in Italy. Indeed, on 21 May 2015, the National Transplant Centre (Centro Nazionale Trapianti) submitted its project "Partial or complete facial allograft for the treatment of complex disfigurements secondary to burns, traumas, malformations and tumours" to the Ethics Committee of the Italian National Institute of Health (Istituto Superiore di Sanità) for assessment. Italian regulations (at the time an agreement dated 14 February 2002 [15], which was subsequently renewed in 2018 [16]), indeed, require that for experimental transplants the National Transplant Centre must acquire the opinion of the Ethics Committee and consult the Italian National Health Council (Consiglio Superiore di Sanità). The Italian National Institute of Health Ethics Committee approved the protocol on 4 August 2015. Despite being aware that the technique is still in the experimental stage, that there are considerable risks and that it is not a lifesaving transplant, the Committee attached special importance to the fact that this kind of transplant may constitute the only possibility for restoring an acceptable quality of life for those in dramatic conditions [17]. Subsequently, on 10 November 2015, the Italian National Health Council also expressed its favourable opinion, expressing a need for "the inclusion, in the consent form, of the possibility of performing subsequent fine-tuning procedures, in order to obtain the best possible result" [18].

This new transplantation frontier constitutes, for a very limited number of people with very severe disfigurements, the only possibility of improving their quality of life. The selection of candidates for transplantation, as well as the donors, must be particularly stringent. The use of this technique must therefore remain a rare event.

Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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