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Surgical, ethical, and psychosocial considerations in head transplantation

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Surgical, Ethical, and Psychosocial Considerations in Head Transplantation

INTRODUCTION

Transplanting a head and brain is perhaps the final frontier of organ transplantation. The goal of body-to-head transplantation (BHT) is to sustain the life of individuals who suffer from terminal disease, but whose head and brain are healthy. Ideally BHT could provide a life-saving treatment for several conditions where none currently exists.

BHT is no ordinary experiment, to transfer a head to another body involves extraordinarily complex medical challenges as well as ethical and existential dilemmas that were previously confined to the imagination of writers of fiction. The possibility of replacing an incurably ill body with a healthy one tests not only our surgical limits, but also the social and psychological boundaries of physical life and alters what we recognize life to be.

The purpose of this target article, the complementary manuscript focused on immunological issues in BHT, and the accompanying Commentaries by scholars and practitioners in medicine, immunology, and bioethics is to review major surgical and psychosocial-ethical and immunological considerations surrounding body-to-head transplantation. We hope that together these ideas will provide readers with a comprehensive overview of the possibilities and challenges associated with BHT and initiate professional discussion and debate through which this new frontier in medicine is considered and approached.

HISTORY

Head transplantation and the controversy it stirs are not new. In 1908, as an application of his research on blood vessel surgery, American physiologist Charles Guthrie unsuccessfully transplanted the head of a donor dog onto the neck of a recipient dog [1]. In this research, Guthrie collaborated with French surgeon, Alexis Carrel, who in 1912 received a Nobel Prize for this work. Others later argued that the credit for this vascular research should have gone to Guthrie, but the controversy surrounding Guthrie's head transplant experiments likely influenced the Nobel committee's decision to exclude him from the award [2].

In the 1940s and 50s, Russian scientist and organ transplant pioneer Vladimir Demikhov developed several surgical techniques for transplanting heart, lung-heart, limbs, and a head in dogs [3]. Demikhov's innovations focused primarily on developing surgical techniques to transplant these organs/tissues and not on immunological or ethical barriers associated with performing these surgeries.

In the early 1970s, neurosurgeon Robert White led a team in the US that performed head transplants in monkeys [4]. Benefitting from newly developed immunosuppression medications, White reported the procedure as successful with postoperative restoration of smell, taste, hearing, and motor function of the face in the transplanted heads. The high dose of immunosuppression required to prevent the head from rejecting, however, caused the monkeys to die 9 days post-transplant [5]. In spite of this remarkable neurosurgical achievement, White's head transplant research received extensive criticism, particularly from animal rights activists, being called "barbaric" and "epitomiz(ing) the crude". White himself was called "Dr. Butcher" [6]. The effect this had on White is captured in his own words, "it is now possible to consider adapting the head-transplant technique to humans. Whether such dramatic procedures will ever be justified in the human area must wait not only upon the continued advance of medical science but more appropriately the moral and

social justification of such undertakings..." [4, pps 602-4].

Since White's experiments few animal studies have been conducted, and generally these were not intended to test the feasibility of head transplants. For example, Hirabayashi et al. [7] and Sugawara et al. [8] transplanted infant rat heads in order to study the regulation of craniofacial bone growth, and Niu et al. [9], transplanted rat heads to study brain function following long periods of ischemia. Finally Ren, et al. described the development of a mouse model to develop surgical approaches for head transplantation [10].

SURGICAL CONSIDERATIONS

Surgical or technical considerations in BHT consist of identifying a young brain-dead donor with all healthy organs and then, removing the head and body from their respective recipient and donor, and transplanting the head onto the healthy donor body.

As was the case in solid organ and vascularized composite allografts, in BHT the surgical challenges were the first to be studied (see history above) prior to addressing immunological, ethical, and psychosocial barriers. Many of the surgical and technical challenges associated with head transplantation have already been solved by early pioneers in animal experiments, by present-day head and neck and trauma surgeons who routinely treat disease and injuries in the region, and by transplant and reconstructive surgeons who routinely perform solid organ and vascularized composite allografts. In fact the surgical techniques used today to reconstruct tissues in the head and neck region, after trauma or removal of cancerous tumors may be technically more challenging than those that would be used to transplant a healthy recipient head onto a healthy donor body. However, since transplanting the head would include the brain, there are important surgical and technical considerations unique to BHT that have yet to be addressed in animal research prior to clinical application. Below we discuss a few of these considerations.

Donor body procurement:

The system for procuring the donor body is well established and used routinely in solid organ and vascularized composite allografts. As was the case in hand and face transplantation the first cases will be experimental and receive a great deal of media attention; therefore, safeguards will have to be activated and emphasized to protect the donor family's right to privacy (Discussed in detail in: Wiggins et al. 2004 [11]).

Head and body operations on the respective recipient and donor:

The surgery would be conducted like a standard head and neck procedure. To prepare the donor body, the skin would be incised circumferentially, starting from the anterior aspect of the neck. All major structures would first be identified, tagged, and then severed following an order with muscles, major vessels, airway, esophagus, pharynx, and nerves, finalizing with the posterior cervical muscles, vertebral vessels, and the spine. Ideally, the bone would be detached through an intervertebral disc, thus permitting an arthrodesis when the recipient head is reattached. As a final step, the spinal cord would be severed.

To prepare the recipient head the operation would follow the same order as the body harvest, beginning with the skin incision, followed by identifying, tagging, and detaching each major structure at the same level of neck as in the donor and leaving the thyroid, parathyroids, and the thymus attached.

Ischemia time:

As surgical reattachment of the recipient head to the donor body will take many hours, the first priority will be to maintain blood flow to the recipient head and donor body to minimize tissue ischemia. Interruption of blood flow to the brain for more than a few minutes results in irreversible brain damage [12]; therefore, it will be essential that measures be taken to minimize ischemia time. This can be achieved through the use of existing extracorporeal oxygenated circulation and hypothermia techniques that temporarily take over the function of the heart and lungs during open-heart (heart-lung bypass machine) surgeries or during extracorporeal membrane oxygenation (ECMO). The recipient and donor respectively, would be connected to these pumps that would maintain blood perfusion in the head and body prior to their removal until the surgical team has reattached the blood vessels between the recipient head and the donor body. At this time the body would be weaned off the pumps first, and the heart in the donor body would take over perfusion of the newly reconnected recipient head before it is disconnected from ECMO. Hypothermia might also be used, depending on experimental findings, to maintain tissues at low temperatures slowing metabolism and protecting against ischemic injury.

Head - body reattachment:

The operation to reattach the recipient head to the donor body would follow a similar stepwise order as in replantation surgery. First the spinal cord would be reattached by peripheral nerve coaptation techniques (see below) and the cervical spine joined using rigid plate fixation to provide stability to the neck. Next the carotid and vertebral arteries (if not bypassed), and then the internal jugular vein would be anastomosed on one side of the neck. A temporary bypass would be continued in the contralateral carotid artery, until that artery and the accompanying vein are anastomosed and the circulation to the head and brain is restored. Following full revascularization induction immunosuppression would be administered sequentially (see accompanying paper focused on immunological considerations)

Once the principal blood vessels between the recipient head and the donor body are reattached and the blood supply is restored to all the organs and the brain, the remainder of the reconstruction would follow standard head and neck reconstruction techniques. The alimentary tract and tracheal continuity would be reestablished; all cervical nerves nearest their target organs or muscles (vagus, phrenic, laryngeal nerves etc.) coapted, and the muscles would be reconstructed and reattached. The incisional fascia and skin would be reapproximated with placement of closed suction drains.

Spinal cord reattachment:

Reattachment of severed spinal cord remains a major hurdle to BHT since existing attempts have been unable to successfully restore function. Several promising technologies to restore function after spinal cord injury are presently being investigated and can be broadly categorized into three approaches: 1) delivery of neural-derived cells into the site of injury or bypassing the injury using peripheral nerve grafts, 2) modification of the CNS environment, and 3) electrical stimulation [13]. An example, in the first category, consists of using stem cells harvested from the olfactory bulb (olfactory ensheathing cells), which when implanted into the site of non-scarred injury have been shown to act as a bridge for the distal and proximal ends of the injured spinal cord through the transected tissue enabling axons to regenerate and reconnect [14]. A recent clinical case-report using this approach described partial restoration of ambulation in a patient who was confined to a wheelchair following complete cord transection [15].

Another approach used in several different animal models and a few clinical cases consists of using peripheral nerves to bypass the spinal cord injury. This method has been shown to incompletely restore motor and sensory function [16].

Finally, electrical stimulation has been shown to promote axonal regrowth following spinal cord injury in both animal models [17-18] and clinically [19]. Recently, electrical current and training were applied to the spinal cords of several patients with complete lower extremity motor paralysis after which they were able to achieve voluntary movement in their lower extremities. From this the authors concluded that their treatment with electrical stimulation resulted in "...re-establishment of functional connectivity among neural networks between the brain and the spinal cord" [20].

In another approach using electrical stimulation scientists have developed a device implanted in the motor cortex of the brain that records brain activity associated with locomotion. This activity is transmitted to a computer that interprets, reconfigures, and wirelessly transmits the signals to a second device that stimulates nerves in the lower spinal cord, distal to the injury, that in turn stimulate muscles in the limbs responsible for locomotion. Using this technology the researchers have restored almost normal walking in previously paralyzed primates (21).

Once these approaches for repairing, reattaching, or bypassing spinal cord lesions are demonstrated to be effective treating spinal cord injuries in some of the 250,000 to 500,000 new cases that occur each year worldwide [22] they could be used in BHT. As outlined in the accompanying article on immunological consideration, use of selected immunosuppressive drugs, such as Tacrolimus and Sirolimus, may significantly accelerate nerve growth once they are coapted.

Exit Strategy:

If the transplant fails due to technical complications or due to uncontrolled rejection, the head/brain could not be sustained on life support for sufficiently long periods to identify another donor body. This would imply certain death for the patient with no satisfactory exit strategy.

Post transplant support:

Post-operatively the patient will be maintained in the intensive care unit under strict isolation (as in bone marrow transplantation) and will remain on ventilator support and full circulatory support as necessary, including intraaortic balloon. Enteral feeding would be started through a jejunostomy tube when feasible. Intensive general rehabilitation treatment for quadriplegia will be started as soon as the patient recovers from neurogenic shock characterized by bradycardia, hypotension, and hypothermia due to alteration of the sympathetic nerves and liberation of the vagus. Other signs and symptoms that would need to be addressed include paralytic ileus and neurogenic bladder which both may need pacemakers. Long-term ventilatory support may be necessary until diaphragmatic muscle function returns with phrenic nerve pacing. Initially all musculature would be hypotonic, evolving to a spastic state as time passes. Treatment of spasticity and passive physiotherapy would be started as soon as possible after transplantation. After the initial phase of neurogenic shock is resolved and the patient has recovered from the operation, he/she would be transferred to a Spinal Cord Trauma Unit where a full acute spinal cord injury rehabilitation protocol would be initiated [23].

ETHICAL CONSIDERATIONS and PUBLIC SENTIMENTS

Technology and knowledge push the limits of both medicine and society's ability to process it. In the contemporary world, change comes rapidly, and although technology and culture advance together in a series of mutually informing leaps, individuals and social groups who are more distant from innovations are often left to their own devices and to numerous communication media to make sense of those changes.

This social dynamic is clear in transplantation medicine. The public reaction to the first kidney transplant in 1954 is widely known. Many demonized Joseph Murray as "playing God" and violating the rules of both nature and the divine. A similarly negative reaction occurred after the first heart transplant and 50 years later in discussions leading to the first human hand and face transplants.

Early critics saw hand and face transplants as a morally reprehensible remedy of severe disfigurement and minimized the value of these transplants, claiming that (1) hand and face transplantation was life enhancing, and not life saving, and therefore not worth the risk of surgery and immunosuppression, or (2) society should change to become more accepting of severely disfigured appearance [24-32].

There was also a high "yuck" factor regarding the prospect of hand and face transplants, which indicated that individuals had difficulty grasping the idea of having another person's face or hands, perhaps the body's most intimate and socially significant parts, grafted onto their own bodies.

But what of head transplantation? Early public reaction has been largely horror or cool to the idea. While the scholarly and public reaction to the possibility of head/brain transplantation has included the "yuck factor" and worries about identity and appearance, many have stated that this experiment is "across the line" and question whether it will work or should be done.

One way to measure public reaction, albeit non-scientific, is to assess responses to media stories about BHT. Three Internet sites [33-35] have issued stories about BHT and solicited public responses, 73 of which made a statement of support or non-support of BHT. The responses were about equally divided: 36 stated that BHT is worthwhile and beneficial and 37 stated that the surgery was wrong and misguided and should not be attempted. Non-supporters listed 49 reasons against BHT such as doubts about technical feasibility, psychosocial consequences, economic feasibility, and social justice (e.g. the surgery would favor the rich at the expense of the poor). People who reply to Internet entries are self-selecting, making these data unconvincing; however, these responses offer a slight hint as to the public's thinking on BHT.

Despite comparable criticisms, three general but important ethical differences exist between hand and face transplants, in the years before the initial operations and the contemplated BHT at one year before the scientifically or experimentally unsupported targeted date of 2017 proposed by Canavera [36-37].

First, head transplantation, when performed in patients with terminal conditions but intact brain function such as multiple organ failure in ALS, unlike hand and face transplants, would be life saving. Many opponents of hand and face transplants based their criticisms on the likely consequences of immunosuppression for a non-life-saving operation. Risks

associated with the immunosuppression protocol could therefore be justified for BHT. Although the immunosuppression protocol has yet to be specified for BHT (see accompanying “immunological considerations” article), lowering the risk of rejection by suppressing the immune system, assuming that it is tolerable, is ethically on par with transplantation of vital organs.

Second, the recent experience of hand and face transplantation provided the language and framework for analyzing the ethical determinants of these types of procedures. Prior to the first face transplant, scholars and physicians engaged in a lengthy and rich dialogue on the surgical, ethical, and psychosocial aspects of the procedures in scientific [38-39] and public [40] debate forums, as well as in scientific peer reviewed publications [41-49]. Kiwanuka [32] found 45 articles on ethics of face transplantation in a search of article databases between 2002 and 2005, the year of the first operation. These publications constituted a mature discourse on the ethical merits of face transplantation, covering various surgical, immunological, and ethical topics. Fifteen core ethical themes, e.g. identity, appearance, informed consent, and risk-benefit, especially concerning immunosuppression were discussed [32].

In the cases of early organ (especially kidney and heart) and hand and face transplantation, public criticism abated after the patient outcomes proved successful. Research addressing the ethics of face transplantation, after the first procedure was performed in 2005, changed its tenor, shifting from tentativeness and doubt to general approval and ethical tolerability [32]. It concluded that face transplantation became accepted as a reasonable and necessary option for the most severe cases of facial disfigurement.

Given the often-poor quality of life of severely disfigured individuals and the research findings that showed that potential candidates were willing to accept the risks of immunosuppression to remedy that poor quality of life [41, 49-50], hand and face transplantation procedures were initiated in 1998 and 2005, respectively. The bioethical debate preceding hand and face transplantation influenced how the introduction of this new treatment was accepted by the public. Now more than 130 hand and 33 face transplants have been performed worldwide. Current research on hand and face transplantation ethics focuses on improving ethical practices by addressing practical matters that arise from experience [32, 51-52].

The ethics of BHT, however, have not been widely articulated and have not reached the level of sophistication that preceded the first face transplants. The absence of significant debate may be a result of the lack of developmental research in the field. Prior to the first face transplant, many scholarly articles describing animal and cadaver studies of face transplants, breakthroughs in immunosuppression, development of novel and applicable microsurgery techniques, and profound discussions of the bioethics appeared in the literature. The momentum of that research made it clear that a face transplant was imminent.

Conversely, relatively little scientific work has been undertaken or published about BHT, and scant data exists on which to base and predict the likelihood of success or even what may define or constitute success. For example, an October, 2016, search of PubMed using the terms “ethics,” “head transplantation,” and “opinion”, replicating Kiwanuka’s [32] analysis of manuscripts published about the ethics of face transplantation, found only two publications focused on the ethics of BHT – one was a 670-word letter to the editor [53] and

the other was an editorial [54]. Until now minimal animal research on BHT has been conducted (cf 10, 55) and only one theoretical approach has been published [56]. The dearth of full peer-reviewed research on this subject suggests that declarations of intent to experiment on human subjects [36-37, 53, 56, 58] are preceding the scientific and ethical debate.

Consequently, informed consent will be impossible to achieve. Without established protocols based on convincing experimental data, patients are unable to recognize the risks of BHT; therefore, prospective patients, IRBs, and society-at-large cannot conduct a conventional risk/benefit analysis.

Since patients who would be eligible for BHT suffer from conditions that have no known cures, they may feel desperate to save their lives and to pin unrealistic expectations on an untried intervention. Desperation may expose individuals to the unethical unexplored risks of BHT based on little previous experimental or clinical data.

Third, from an economic perspective, BHT could be considered an inefficient expenditure of resources. Where one body could save one life per BHT, the same donor body could save and enhance 10 to 15 lives through multiple organ (pancreas, lung, intestines, liver, heart, kidney, hands, and face) and tissues (cornea, bone, tendons, heart valves, veins, and skin) donations. On these grounds, BHT could be accused of failing to address current medical needs, given the large number of patients on organ and tissue waiting lists.

The scientific preparation for BHT has not yet been achieved, and this is a necessary and critical first step for surgical innovations [57]. Parenthetically, traditional development of innovative surgery may be difficult to accomplish in the present regulatory environment because animal welfare boards may not approve head/brain transplant experiments in which suffering and death to animals are likely [53]. Consent by a dying person to a surgical experiment that has not followed the standard protocols of research development could be interpreted by IRBs as coercive and is forbidden by several Conventions (The Nuremberg Code, the Declaration of Helsinki, and The Belmont Report).

Lastly, BHT may have legal implications as well. Offspring of a transplanted body may pose questions as to inheritance, and question its parentage, custody, and relation to the donor's parents - all this may require unraveling. There is no certainty that the donor's parents will see offspring of their brain-dead child as a godsend, as has been posited [58].

PSYCHOSOCIAL CONSIDERATIONS

Head/brain transplantation, with current technology, is unproven and carries many undeterminable risks; three outcomes are possible. First, if the operation is successful and full function is restored (unlikely), patients will require long-term extensive rehabilitation and psychological interventions, including a coordinated program of occupational and physical therapy to accelerate sensory and fine motor control. Social services should coordinate and manage an extended period of unemployment, secure housing during the long recovery, and provide mental health assistance to the patient and family.

Relatedly, Cartolovni and Spagnolo [53] predict that BHT recipients will experience mind and body dissonance of such magnitude that insanity and death are possible. The body, they argue, represents the corporeality of existence, and individuals will fail to adjust to a new and dramatically different physical presence.

Transplantation literature, however, does not predict such an outcome. Transplant recipients typically adjust their identities to incorporate the donor into their own sense of selfhood. Recipients frequently perceive transplanted organs and tissues as “gifts of life”. In studies on face transplantation outcomes, identity confusion or disruptions in self-identity have yet to be reported. For some, the opposite has been noted: self-esteem, social integration, and overall mental health have improved after transplantation [59-62]. Face transplantation appears to enable psychological health by allowing patients to approach a normal appearance and correct some of the physical limitations that often accompany severe disfigurement.

Nonetheless, BHT may create confusion about the relationship between body and identity in ways unlike other transplants. First, the percentage of the body that is now from “another” creates a scale of adaptation not previously encountered. Consequently, patients may think differently about receiving a full body than patients getting individual body parts. For example, previous actions by “the body,” such as having committed a crime or terminated a pregnancy, or getting body art, may lead to questions concerning the level of responsibility and ownership a person may feel for the actions of a body that previously was not their own [63].

Second, given that so far life expectancies in animal BHTs were measured in minutes/hours/days, it is reasonable to assume that the probability of death due to catastrophic failure is high. Patients and their family will require psychological preparation for the possibility of not surviving the surgery.

Third, surviving recipients without successful spinal cord reconnection will face a number of comprehensive quality of life and psychological well-being problems. It is likely that initial candidates will already be more than quadriplegic. Given that the successful connection of completely severed ends of spinal cords has yet to be accomplished, the best of today’s technology predicts that quadriplegia will continue for uncertain duration. Patients who survive will express relief that their life-threatening illness has ended; however, in time they may experience the psychosocial consequences, such as low quality of life and depression, that quadriplegia poses [64].

CONCLUSION

Head/brain transplantation is a complex medical/surgical/immunologic/and ethical undertaking is ripe with technical and immunologic concerns and challenges the professional responsibility of the medical community to society-at-large. While several of the remaining questions can be addressed in well-planned experimental protocols in appropriate animal and cadaveric models, many issues and problems remain unknown. To ensure that productive research advances science and avoids destructive and unnecessary controversy and sensationalism that stifles progress, it is important to engage in open dialogue and debate with professional peers [11, 39, 65], potential patients, and the general public, through open forums [66], websites, print, and broadcast media. These conversations are difficult because of the different languages and agendas each community and individual brings to the table. Despite this, the effort is necessary as the final result is a wider and deeper understanding of the questions, concerns, and ultimate benefits of disciplined research and the new treatments they generate.

REFERENCES:

- [1] C. Guthrie Charles, *Blood-Vessel Surgery and its Applications*, International Medical Monographs, Edward Arnold, London, Longmans, Green & Co., New York, 2012.
- [2] HE Stephenson, Jr., RS Kimpton, GM Masters GM, *American's First Nobel Prize in Medicine or Physiology: The Story of Guthrie and Carrel*, Midwestern Vascular Surgery Society, Boston, MA, 2000.
- [3] IE Konstantinov, *At the cutting edge of the impossible: A tribute to Vladimir P. Demikhov*, *Tex. Heart Inst. J.* 36(2009): 453-458. PCID:PMC2763473.
- [4] RJ White, et al. *Primate cephalic transplantation: Neurogenic separation, vascular association*, *Transpl. Proc.* 3 (1971) 602-4.
- [5] J McCrone, *Monkey business*, *Lancet Neurology.* 2 (2003) 772.
- [6] C Bennett, *Letter to the editor: Cruel and unneeded*. *New York Times* <http://nytimes.com/1995/08/26/opinion/1-cruel-and-unneeded-324295.html> August 26, 1995 (accessed 15.06.09).
- [7] S Hirabayashi, K Harii, A Sakurai, EK Takaki, O Fukuda, *An experimental study of craniofacial growth in a heterotopic rat head transplant*, *Plast. and Reconstructive Surg.* 82 (1988) 236-243.
- [8] Y Sugawara, S Hirabayashi, K Harii, *Craniofacial growth in a whole rat head transplant: How does a non-functional head grow?* *J. of Craniofacial Genetics and Developmental Biol.* 19 (1999) 102-108.
- [9] A Niu, K Shimazaki, Y Sugawara, K Nobufumi, *Heterotopic graft of infant rat brain as an ischemic model for prolonged whole-brain ischemia*, *Neuroscience Letters.* 325 (2002) 37-41.
- [10] XP X Ren, YJ Ye, PW Li, ZL Shen, KC Han, Y Song, *Head transplantation in mouse model*, *CNS Neurosci & Therapeutics.* 21 (2015) 615-618. Doi 10.1111/cns.12422.
- [11] OP Wiggins, JH Barker, S Martinez, M Vossen, C Maldonado, F Grossi, C Francois, M Cunningham, G Perez-Abadia, M Kon, JC Banis, *On the ethics of facial transplantation research*, *Am. J. of Bioeth.* 4 (2004) 1-12.
- [12] ME Raichle, *The pathophysiology of brain ischemia*, *Annals of Neurology.* 13 (1983) 2-10.
- [13] S Hamid, R Hayek, *Role of electrical stimulation for rehabilitation and regeneration after spinal cord injury: an overview*, *Eur. Spine J.* 17 (2008) 1256-69.
- [14] N Keyvan-Fouladi, G Raisman, Y Li, *Functional repair of the corticospinal tract by delayed transplantation of olfactory ensheathing cells in adult rats*, *The J. of Neuroscience.* 23 (2003) 9428-9434.

- [15] P Tabakow, G Raisman, et al., Functional regeneration of supraspinal connections in a patient with transected spinal cord following transplantation of bulbar olfactory ensheathing cells with peripheral nerve bridging, *Cell Transplant.* 23 (2014) 1631-55.
- [16] JS Oppenheim, DE Spitzer, CJ Winfree, Spinal Cord bypass surgery using peripheral nerve transfers: Review of translational studies and a case report on its use following complete spinal cord injury in a human, *Neurosurg. Focus.* 26 (2009) E6.
- [17] RB Borgens, AR Blight, ME McGinnis, Functional recovery after spinal cord hemisection in guinea pigs: The effects of applied electric fields, *J. Comp. Neurol.* 296 (1990) 634-653.
- [18] RB Borgens, JP Toombs, AR Blight et al, Effects of applied electric fields on clinical cases of complete paraplegia in dogs. *J. Restor. Neurol. Neurosci.* 5 (1993) 305-322.
- [19] R Brissot, P Gallien, MP Le Bot, et al., Clinical experience with functional electrical stimulation-assisted gait with parastep in spinal cord injured patients, *Spine.* 25 (2000) 501-508.
- [20] YP Gerasimenko, DC Lu, et al., Noninvasive reactivation of motor descending control after paralysis. *J. of Neurotrauma.* 32 (2015) 1968-1980.
- [21] Marco Capogrosso, et al., A brain-spine interface alleviating gait deficits after spinal cord injury in primates. *Nature*, (Nov 2016) 539:284-288. doi:10.1038/nature20118)
- [22] World Health Organization 2013. Spinal Cord Injury. <http://www.who.int/mediacentre/factsheets/fs384/en/> (accessed October 4, 2015).
- [23] HN Hadley, BC Walters, Guidelines for the management of acute cervical spine and spinal cord injuries, *Neurosurg.* 72 (2013) 1-259.
- [24] S Hettiaratchy, PEM Butler, WPA Lee, Lessons from hand transplantations, *Lancet.* 357 (2001) 494.
- [25] NF Jones, Concerns about human hand transplantation in the 21st Century, *The J. of Hand Surg.* 27A (2002) 5.
- [26] A Caplan, D Katz 2003. About face, *Hastings Center Report.* 33 (2003) 8.
- [27] X Bosch, Surgeon denied ethics approval for face transplantation, *Lancet.* 363 (2004) 871.
- [28] KJ Maschke, E Trump, Facial transplantation research: A need for additional deliberation. *Am. J. of Bioeth.* 4 (2004) 33-35.
- [29] PJ Morris, JA Bradley, L Doyal, M Early, P Hagen, M Milling, N. Rumsey, Facial transplantation: A working party report from the Royal College of Surgeons of England. *Transplant.* 77 (2004) 330-338.
- [30] C Strong, Should we be putting a good face on facial transplantation? *Am. J. of Bioeth.* 4

(2004) 13-14.

[31] PA Clark, Face transplantation: Part II – An ethical perspective. *Med. Sci. Monit.* 11 (2005) RA41-47.

[32] H Kiwanuka, EM Bueno, JR Diaz-Siso, GC Sisk, LS Lehmann, B Pomahac, 2013. Evolution of ethical debate on face transplantation. *Plast. and Reconstructive Surg.* 132 (2004) 1558-68. doi: 10.1097/PRS.0b013e3182a97e2b.

[33] National Geographic.

<http://phenomena.nationalgeographic.com/2015/06/12/surgeon-reveals-head-transplant-plan-but-patient-steals-the-show/>, 2015 (accessed 16.06.07).

[34] National Geographic. 2015.

<http://phenomena.nationalgeographic.com/2015/05/05/human-head-transplant-proposed-how-did-we-get-here/>, 2015 (accessed 16.06.07).

[35] 9gag.com. I really hope this works but I'm really afraid of the results...Frankenstein syndrome or pure genius? <http://9gag.com/gag/aW6wBBZ?ref=9g.m.mw>, (accessed 16.06.08).

[36] T Lamont, "I'll do the first head transplant." Italian surgeon Sergio Canavero says he will change medical history as soon as 2017 – he even has a volunteer. Can it be done? *The Guardian*, <https://www.theguardian.com/science/2015/oct/03/will-first-human-head-transplant-happen-in-2017>, 2015 (accessed 16.06.08).

[37] H Thomas, First human head transplant could happen in two years, *New Scientist*, 25 February, 2015.

[38] K Black and C Hewitt, tissue transplantation workshop. Washington, DC: Department of Veterans Affairs, Rehabilitation Research and Development Service. 1991.

[39] JH Barker, JW Jones, et al. 1998. Composite tissue transplantation: A clinical reality? *Transplant. Proc.* 30 (1998) 2686-2787.

[40] JH Barker, Naked Science – Face of the future, public debate on the feasibility of face transplantation. In: *Public Debate on the Feasibility of Face Transplantation*, London Science Museum, Dana Center. London, UK, November 19, 2003.

[41] S McCabe, et al. 1998. Using decision analysis to aid in the introduction of upper extremity transplantation, *Transplant. Proc.* 30 (1998) 2783-2786.

[42] M Siegler, 1998. Ethical issues in innovative surgery: Should we attempt a cadaveric hand transplantation in a human subject? *Transplant. Proc.* 30 (1998) 2779-2782.

[43] D Dickenson, G Widdershoven, Ethical issues in limb transplants, *Bioethic.* 15 (2001) 110-124.

[44] JH Barker, et al. 2004. The technical, immunological and ethical feasibility of face transplantation, *International J. of Surg.* 2 (2004) 8-12.

- [45] F Baylis, A face is not just like a hand: Pace Barker, *Am. J. of Bioeth.* 4 (2004) 30-32.
- [46] M Cunningham, R Majzoub, P Brouha, et al., Risk acceptance in composite tissue allotransplantation reconstructive procedures – instrument, design and validation, *Eur. J. of Trauma.* 30(2004) 12-16.
- [47] EH Morreim, About face: Downplaying the role of the press in facial transplantation, *Am. J. of Bioeth.* 4 (2004) 27-9.
- [48] PE Butler, A Clarke, RE Ashcroft, 2004. Face transplantation: When and for whom? *Am. J. of Bioeth.* 4 (2004) 16-17.
- [49] K Ramsey, RK Majzoub, et al. 2006. Investigation of risk acceptance in hand transplantation, *J. of Hand Surg.* 31A (2006) 295-302.
- [50] JH Barker, LA Furr, M Cunningham, et al, Investigation of risk acceptance in facial transplantation, *Plast. Reconstruction Surg.* 118 (2006) 663-670.
- [51] JT Shores, Composite tissue allotransplantation: Hand transplantation and beyond, *J. of the Am. Academy of Orthop. Surg.* 18 (2010) 127-131.
- [52] SE Jensen, Z Butt, A Bill, et al., Quality of life considerations in upper limb transplantation: Review and future directions, *J. of Hand Surg. Am.* 37(2012) 2126-2135.
- [53] A Cartolovni, AG Spagnolo, 2015. Ethical considerations regarding head transplantation, *Surg. Neuro. Int.* 6 (2015)103. doi: [10.4103/2152-7806.158785](https://doi.org/10.4103/2152-7806.158785)
- [54] JH Barker, JM Frank, L Leppik, 2015. Head transplantation: editorial commentary. *CNS Neurosci. Ther.* 21(2015) 613-4. doi: [10.1111/cns.12434](https://doi.org/10.1111/cns.12434).
- [55] XP Ren, Y Song, YJ Ye, PW Li, KC Han, ZL Shen, JG Shan, K Luther, BF Yang, Allogeneic head and body reconstruction: mouse model, *CNS Neurosci. Ther.* 20 (2014): 1056-1060. doi:[10.1111/cns.12341](https://doi.org/10.1111/cns.12341).
- [56] S Canavero 2013. HEAVEN: the head anastomosis venture project outline for the first human head transplantation with spinal linkage (GEMINI), *Surg. Neurol. Int.* 13 (2013): S335-42. doi: [10.4103/2152-7806.113444](https://doi.org/10.4103/2152-7806.113444).
- [57] FD Moore, Three ethical revolutions: Ancient assumptions remodeled under pressure of transplantation, *Transplant. Proc.* 20 (1988) 1061-1067.
- [58] S Canavero, Commentary, *Surg. Neuro. Int.* 6 (2015)103. doi: [10.4103/2152-7806.158785](https://doi.org/10.4103/2152-7806.158785)
- [59] G Chang, B Pomahac, Psychosocial changes 6 months after face transplantation, *Psychosomatics.* 54 (2013) 367-371.
- [60] KL Coffman, MZ Siemionow, Face transplantation: Psychological outcomes at three-year follow-up, *Psychosomatics.* 54 (2013) 372-378.

- [61] S Fischer, M Kueckelhaus, R Pauzenberger, EM Bueno EM, B Pomahac, Functional outcomes of face transplantation, *Am. J. of Transplant.* 15 (2015) 220-233.
- [62] R Smeets, C Rendenbach, M Birkelbach, A al-Dam, A Grobe, H Hanken, M Heiland, Face transplantation: On the verge of becoming clinical routine? *BioMed Res. International*, [dx.doi.org/10.1155/2014/907272](https://doi.org/10.1155/2014/907272) (2014) (accessed 16.11.02).
- [63] BS Turner, *Regulating Bodies: Essays in Medical Sociology*, Routledge, London, 1992.
- [64] MC Rousseau, S Pietra, M Nadji, T Billette de Villemeur, 2013. Evaluation of quality of life in complete locked-in syndrome patients. *J. of Palliat. Med.* 16 (2013) 1455-1458.
- [65] JC Banis, JH Barker, et al. Responses to selected commentaries on the AJOB target article "On the ethics of Facial transplantation research". *Am J. of Bioeth.* 4 (2004) W23-W31.
- [66] *Naked Science – Face of the future, public debate on the feasibility of face transplantation.* London Science Museum, Dana Center. London, UK. November 19, 2003.

Target Article - Surgical, Ethical, and Psychosocial Considerations in Head Transplantation

Highlights

- Body-to-head transplantation (BHT) is perhaps the final frontier of organ transplantation.
- The goal of BHT would be to sustain the life of individuals who suffer from terminal disease, but whose head and brain are healthy.
- Surgical, ethical, psychosocial, and immunologic hurdles associated with BHT are enormous.
- Here we discuss the surgical, ethical, psychosocial considerations associated with BHT.
- The goal is to give readers a comprehensive overview of the possibilities and challenges associated with BHT.