The American Journal of Bioethics

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/uajb20

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Available online: 17 Aug 2010


To link to this article: http://dx.doi.org/10.1080/15265160490496507

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On the Ethics of Facial Transplantation Research

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Transplantation continues to push the frontiers of medicine into domains that summon forth troublesome ethical questions. Looming on the frontier today is human facial transplantation. We develop criteria that, we maintain, must be satisfied in order to ethically undertake this as-yet-untried transplant procedure. We draw on the criteria advanced by Dr. Francis Moore in the late 1980s for introducing innovative procedures in transplant surgery. In addition to these we also insist that human face transplantation must meet all the ethical requirements usually applied to health care research. We summarize the achievements of transplant surgery to date, focusing in particular on the safety and efficacy of immunosuppressive medications. We also emphasize the importance of risk/benefit assessments that take into account the physical, aesthetic, psychological, and social dimensions of facial disfiguration, reconstruction, and transplantation. Finally, we maintain that the time has come to move facial transplantation research into the clinical phase.

Introduction: Advances in Transplant Surgery and Ethical Criteria

The field of transplantation surgery has always pushed the boundaries of medicine forward. In doing so it has repeatedly raised unprecedented ethical questions. Today, as teams around the world consider performing a human facial transplantation, the frontiers of medical ethics are again being tested. Not long ago the pressing ethical issues in transplantation concerned the scarcity of donated organs and the deaths of potential recipients that resulted from this lamentable scarcity (Veatch 2000). With the relatively recent advent of human hand transplantation, however, ethical reflection has shifted to the need to weigh the risks the patient assumes for the sake of receiving a donated organ that, unlike a heart or liver, is not necessary for his or her survival.

The aim of this essay is to address these ethical issues when they arise for human facial transplantation research. When considering facial transplantation research, the ethical concerns must be based on the scientific, surgical, psychological, and social dimensions of the procedure and its aftermath. Therefore, this article devotes considerable space to discussing these dimensions in so far as they have implications for ethics. The ethical questions that arise here are complex and, as we have indicated, unprecedented. Issues of the psychological hopes, anxieties, and stability of transplant recipients have always caused ethical concerns, but with facial transplantation the psychological and social dimensions loom much larger: what is at stake is a person’s self-image, social acceptability, and sense of normalcy as he or she subjectively experiences them. To formulate these broad concerns in the language of medical research ethics, many of the “risks” and “benefits” of the surgery seem unpredictable.
As one of the teams preparing to perform human facial transplantation, a key part of our program at the University of Louisville consists of soliciting and incorporating professional discussion into our protocol. The purpose of this essay is to present our reflections on human facial transplantation research to the biomedical ethics community in order to solicit their responses. We view this essay as a component of the “open display and public and professional discussion” required for proceeding in an ethical manner toward the performance of an innovative surgical procedure. As the reader will see below, this is one of the four ethical criteria that Dr. Francis Moore stipulated for undertaking such procedures (Moore 1988, 1989). Our team adopted these criteria and is adhering to them as part our program’s ethical guidelines. Throughout this essay we shall refer to the steps our team at the University of Louisville has taken to meet both Moore’s criteria and the ethical standards applicable to all health care research.

In part I of this article, we sketch the surgical procedures that are presently utilized in treating facial disfigurements.

In part II, we presuppose the guidelines and regulations formulated by The Nuremberg Code, the Declaration of Helsinki, The Belmont Report, and various official documents that form the basis for the ethical evaluation of all health care research performed today, and we examine facial transplantation from this point of view. We accordingly address the permissibility of facial transplantation research in terms of risk/benefit assessment, informed consent, and privacy and confidentiality.

In part III, we address the criteria enunciated by Francis Moore for judging the acceptability of innovative surgery (Moore 1988, 1989; Siegler 1998). Since we believe that Moore’s criteria prompt us to focus on issues not routinely included in the ethics of research, we also deem it important to examine facial transplantation in the light of these requirements.

In part IV, we raise the question, Is it time to perform a facial transplant? Based on parts II and III we summarize eight criteria that, we think, must be satisfied in order to answer this question in the affirmative. We then consider that we have satisfied these criteria at the University of Louisville and that therefore it is justifiable to move forward with performing an experimental facial transplant.

I. Present-Day Procedures for Treating Facial Disfigurements

Facial disfigurement can result from trauma, extirpation of tumors, major burns, severe infections, or congenital birth defects. Patients with such disfigurements number in the thousands (Lee and Mathes 1999). The most advanced treatments available today consist of reconstructing these defects by surgically reattaching the original tissues (Buncke 1996; Thomas et al. 1998), transferring autologous tissues from another part of the body (Angrigiani and Grilli 1997; Priabaz and Fine 2001), and/or using prosthetic materials to replace the missing tissues (Beumer, Roumanas, and Nishimura 1995). By far the best outcomes are achieved with the first alternative, when the original tissues can be salvaged and used to reconstruct the defect. Unfortunately, in most cases the original tissue cannot be salvaged, either because the trauma or disease causing the loss destroyed it beyond use or because the original tissues never existed in the first place (as in congenital birth defects).

When, as in most cases, the original tissues are not available, autologous tissue and/or prosthetic materials are used to reconstruct large tissue defects of the face. In these situations, complications caused by prosthetic materials (e.g., infection or rejection) are common, donor site morbidity (at the location from which the autologous tissues are taken) is almost always present, and multiple “revision” operations and prolonged rehabilitation are usually required. Moreover, functional and aesthetic recovery is usually poor, and the resulting deformity almost always leads to major psychosocial morbidity. The latter in turn often prompts these patients to retire to a secluded environment, becoming social recluses (Lefebvre and Barclay 1982; MacGregor 1990).

A possible solution to the above scenario is to reconstruct these severe facial deformities with identical tissues transplanted from brain-dead human donors (Composite Tissue Allotransplantation), as is done in solid organ transplantation. Composite Tissue Allotransplantation (CTA) in the form of human hand transplantation has recently received a great deal of attention in scientific circles and in the lay media. In the more than twenty hand transplants performed to date, the fact that the tissues used (human hands from brain-dead donors) were identical in both form and function to those originally lost has resulted in excellent early (five years) functional and aesthetic outcomes.

If facial transplantation were available for clinical application in the above-cited example, one could envision a single operation to replace the burned facial tissues with healthy donor tissues identical to the tissues destroyed in the accident. Following surgery, there would be a few revision
operations giving the patient a normal appearance and nearly normal function, allowing him or her to return to a normal life in a relatively short time.

In spite of these advantages that facial transplantation has over current reconstructive methods, the main disadvantage is that patients receiving facial tissues from a donor would, like solid organ recipients, have to take potentially toxic immunosuppressive drugs for life in order to prevent rejection. The risks posed by these drugs raises the central question concerning facial transplantation: Do the benefits of facial transplantation justify the risks posed by the immunosuppressive drugs?

II. Official Ethical Codes for Research on Human Subjects

Here we shall address three of the main requirements of the ethics of research using human subjects: (1) risk/benefit assessments, (2) informed consent, and (3) privacy and confidentiality.

Risk/benefit assessments

Ethical codes governing medical and surgical research require careful risk/benefit analyses.

The Declaration of Helsinki states:

Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interest of science and society. (Jonsen, Veatch, and Walters 1998)

The Belmont Report clarifies the extent of risks and benefits that need to be considered:

Many kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological, physical, legal, social and economic harm and the corresponding benefits. (Jonsen, Veatch, and Walters 1998)

The extent of risks and benefits may go beyond the individual subject, according to The Belmont Report: “Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society)” (Jonsen, Veatch, and Walters 1998).

Risk/benefit assessments must be carried out by three different parties. The individual subjects themselves must make such comparisons. The investigative team must make them. And the Institutional Review Board (IRB) reviewing the research proposal must perform them. Regarding the IRB’s duties, the U.S. Department of Health, Education and Welfare’s Institutional Guide, On the Protection of Human Subjects, states:

The committee should carefully weigh the known or foreseeable risks to be encountered by subjects, the probable benefits that may accrue to them, and the probable benefits to humanity that may result from the subject’s participation in the project or activity. If it seems probable that participation will confer substantial benefits on the subjects, the committee may be justified in permitting them to accept commensurate or lesser risks. (Jonsen, Veatch, and Walters 1998)

Risk/benefit assessment in facial transplantation

In the light of these codes we must seek to develop a clear understanding of the risks to which a patient treated with a facial transplant would be exposed in comparison with the possible benefits. The main risks are those related to the surgical transplant procedure and the lifelong immunosuppression medications that patients would have to take in order to prevent the transplanted tissue from being rejected. The expected benefits primarily would be improvements in quality of life in the form of restored function and aesthetic appearance and the concomitant improvement in the recipient’s body image and sense of self. These benefits would probably also increase the recipient’s ease and ability in social interactions with other people. While using transplanted tissues to reconstruct facial deformities would significantly improve a patient’s quality of life, in most cases these procedures would not be life-saving in the strict sense of the word. This situation stands in contrast to life-saving treatments, like heart and liver transplants, in which the risk/benefit ratio is more readily conceptualized.

Below we discuss the risks and the benefits of facial transplantation and apply them to the “risk and benefit” lessons learned in solid organ transplants and the recent hand transplants.

General Risks of Organ Transplantation Compared to Face Transplantation

Risks Related to Surgery. While facial transplantation is a complex procedure, it does not pose more risks than conventional reconstructive procedures in which the patient’s own tissue is used to repair defects. In a 1998 multicenter study, Dupont et al. (1998) estimated this mortality to be no higher than 0.0567%, which was a figure far higher than that reported in most studies. In addition, compared to
conventional reconstructive procedures, facial transplant procedures would utilize tissues taken from a donor rather than from the patient’s own body and would thus obviate the complications associated with donor site morbidity. Also, conventional reconstructive methods can require over 100 revision surgeries over many years whereas, if successful, facial transplantation would require only a few surgeries. Since each surgical procedure carries with it inherent risks, it could be argued that conventional reconstructive methods are associated with more risks than facial transplants.

Risks related to immunosuppression

The immunosuppression-related risks in facial transplantation are also expected to be the same as those experienced by the solid organ and hand transplant recipients, who receive the same drug regimens. The most common complications associated with the use of immunosuppressants include increased incidence of: (1) infections, (2) malignancies, and (3) end-organ toxicity. In rare instances malignancies associated with immunosuppressive therapy can result in death. The incidences of these complications, in the particular case of tacrolimus and mycophenolate mofetil/prednisone combination therapy (the drug regimen that would most likely be used in facial transplants), are as follows:

Infections: The incidence of opportunistic infections (bacterial, fungal, and viral, including CMV) reported in kidney transplant recipients using tacrolimus and mycophenolate mofetil (MMF) range from 8.4% to 31% (Daoud et al. 1998; Stratta 1997). When this complication occurs, the initial treatment usually consists of the appropriate antibiotic, antifungal, or antiviral agent. In rare cases it is necessary to lower the level of immunosuppression, or even to halt immunosuppressive drugs altogether.

Malignancies: In transplant recipients, there exists a 1.2% incidence of posttransplant lymphoproliferative disease (PTLD) and an 11.1% incidence of nonmelanoma skin carcinoma (reported over a three-year period of follow-up) (Mathew 1998). When malignancies occur in heart, lung, or liver transplant patients, immunosuppression must be continued because of the life-saving nature of the transplanted organ. However, in facial transplantation, as in kidney transplantation, immunosuppression could be halted so that the patient’s immune responsive-
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regimen and its side-effects, and a sense of personal responsibility for the success of the procedure (Zdichavsky et al. 1999).

Moreover, the recipient of a new face must deal with a new appearance, but to some extent this resembles the risk of receiving a new hand, which also reshapes one’s sense of one’s appearance. What is unique to facial transplantation, however, is that facial appearance is intimately and profoundly associated with one’s sense of personal and social identity. Therefore, the recipient of a face must adapt to his or her own responses to this new “identity” as well as to other people’s responses to it. It is expected that such adaptations will not occur once and for all; rather, they will repeatedly occur and undergo modifications over time. Moreover, it will be impossible for the recipient of a transplanted face to escape a bright public spotlight, and such publicity will be invasive and long-term. Such risks might be mitigated by careful patient selection, ongoing monitoring, and psychiatric intervention, as indicated.

Social Risks. As in cases of solid organ and hand transplantation, the family of the recipient of a face will be responsible for care-giving and social and psychological support. The recipient and his or her family will also be subjected inevitably to intrusive publicity and media coverage. In addition to these risks to the family of the recipient, there are other risks that we might imagine affecting the larger society. For example, a successful facial transplant might be interpreted as conveying the message that a good quality of life cannot be achieved by people with disfiguring conditions. There also exists the possibility that the public may develop unrealistic expectations for the outcomes of such surgery, perhaps to the point of creating an inappropriate demand for its use in less worthy cases, such as cosmetic enhancement for the aging rich or for criminal identity concealment. The facial transplant research team cannot prevent these or other misconceptions. What the team can do is provide accurate information in order, it is hoped, to shape public opinions in a responsible manner.

General Benefits of Organ Transplantation Compared to Face Transplantation

Benefits associated with facial transplantation can be separated into three categories: functional benefits, aesthetic/psychological benefits, and social benefits. The relative value of these three types of benefits is important when assessing the risk/benefit equation for a transplant candidate and developing a triage strategy. For example, a hand transplant provides predominantly functional and, to a lesser degree, aesthetic benefits. The combination of these two benefits contributes to the psychological benefit derived from this procedure. A transplanted hand takes the place of the lost/missing hand in the spatial resolution of the patient. This has important psychological implications and is a great benefit of this procedure. This was clear in the repeated statements by Louisville’s first hand transplant recipient, in which he asserted that his transplanted hand gave him a sense of being “whole” and “complete” (Klapheke 1999).

Functional Benefits. Functional recovery of the facial tissues offers several important benefits. Depending on the extent of the original deformity, the anticipated benefits include restoration of blinking for eye protection, improved oral continence, and restoration of facial expression and sensory function.

Aesthetic and Psychological Benefits. The human face is unquestionably the most important aesthetic anatomical feature of the human body. Much of how other people react to us depends upon our aesthetic appearance. Moreover, the appearance of our face is the predominant anatomical feature by which we identify and differentiate ourselves from others. In a large number of cases facial disfigurement leads to depression, social isolation, and even the risk of suicide (Robinson, Rumsey, and Partridge 1996; Ye 1998). By replacing the disfigured face with a “normal” appearing/functioning face, facial transplantation would provide important psychological benefits.

Social Benefits. Closely related to functional, aesthetic, and psychological benefits is the enhanced social capacity of the subject. Although a period of adaptation will be required for both the subject and others involved, the subject’s willingness and ease in engaging in social interactions should improve. Restoring the abilities to make facial expressions, enjoy an aesthetically acceptable appearance, and interact comfortably with others lends significant weight to the benefit side of the risk/benefit equation.

Informed consent

Ever since The Nuremberg Code (Jonsen, Veatch, and Walters 1998), informed consent has been fundamental to any research performed with human subjects. The Belmont Report grounds this requirement in the basic ethical principle of respect for persons.
The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject’s physical and mental integrity and on the personality of the subject. (Jonsen, Veatch, and Walters 1998)

In the case of transplantation research, there are two groups of persons whose privacy and confidentiality should be respected. The first is the donor and his or her family, and the second is the recipient and his or her family.

Facial Tissue Donor

The privacy and confidentiality of the donor and his or her family ought to be respected to the extent permitted by law. All reasonable efforts should be made to protect the donor’s anonymity. Identifying information ought not to be publicly revealed. The donor’s family must be informed, however, that the research team cannot prevent someone (e.g., a member or friend of the donor’s family) who knows about the case from publicizing information on his or her own.

Facial Tissue Recipient

In the case of an innovative therapeutic procedure like facial transplantation, there are two reasons for concern about the confidentiality and privacy of the recipient and his or her family:

1. The full scientific reporting and discussion of this procedure and its results may be restricted too greatly by efforts to maintain the privacy of the subject. For example, in the publication of the outcomes of the operation it may be highly desirable, from a scientific point of view, to provide unaltered photographs of the face of the recipient. Also, in conference presentations it might be very helpful, again from a scientific point of view, to hear the recipient him- or herself speak about his or her experience and to respond to questions. Hence the mandate to respect privacy and confidentiality may conflict with scientific requirements.

2. The prospect of a facial transplant has already attracted significant media attention, and as the likelihood—and then the reality—of such a phenomenon develops, the interest of the media in it will inevitably become greater. It is difficult to
imagine, then, how the media can be kept from discovering the identity and much other information about the recipient and his or her family. Indeed, for the recipient, “privacy” may not be possible.

In a recent article entitled “High-Profile Research and the Media: The Case of the AbioCor Artificial Heart,” E.H. Morreim carefully examined the issue of disclosure of information to the public (Morreim 2004). She pointed out that, from a scientific point of view, the ideal way to provide information to the public is through publications in refereed professional journals. Peer-reviewed publications are better able to provide accurate scientific information than are press releases that occur as the research project progresses. Nonetheless, she noted that high-profile research cannot enjoy such luxury in a society that prides itself on its “freedom of the press.” She sought, then, to sort out the competing obligations to disclose information to the public, to maintain the research subject’s privacy and confidentiality, and to publish the procedures and results of medical/surgical research in professional journals.

Morreim (2004) pointed out that in our society we must recognize “the right of free press” and the public’s “desire to know” about health care innovations. Freedom of the press, she asserted, “does not mean that anyone is required, in the first place, to provide a reporter with whatever information he wants” (Morreim 2004). Similarly with the public’s “desire to know” some kind of information: it does not entail that anyone has the duty to produce the information (Morreim 2004).

Nevertheless, in keeping with our established policy of “open display and professional and public discussion and evaluation,” we believe we are obligated to release to the press basic clinical and surgical information about facial transplants. This obligation, however, must be balanced against the research subject’s right to privacy and confidentiality. Morreim (2004) seems to have concluded that “materially significant trends in the progress of the trial” should be disclosed to the public, and “Patients should not be permitted to veto the disclosure of such information” (Morreim 2004). Affirming the patient’s right to privacy, however, she added,

Patients should be able to control some kinds of information. Clearly, purely personal details such as marital status, education, occupation, and the like should be governed by the patient (Morreim 2004).

And, she continued,

Additionally, patients and families should have the opportunity to review press releases in advance to correct errors, delete unsuitable personal information, and influence the tone of the report. (Morreim 2004)

These suggestions will guide our approach to press releases and to protecting the subject’s privacy and confidentiality. Accordingly, we shall inform the subject and his or her family that we shall need to publish in professional journals some identifying information about the subject. We shall seek, however, to restrict such information to solely what is necessary for scientific purposes. In addition, we shall inform the subject at the outset that we shall provide press releases. As press releases are prepared, the general nature of the information that will be released will be disclosed to the subject and the subject’s family, and they will be given the opportunity to review the information and offer suggestions. We shall also inform the subject that extensive media attention is likely to be forthcoming and that we cannot guarantee that their identities and other personal information will not be discovered and published by the media. As the press releases are prepared, we shall provide subjects and their families the opportunity to review them in advance and offer suggestions. Subjects and their families will remain at liberty to control personal information in so far as this can be done in the light of the intense media spotlight.

III. Francis Moore’s Criteria for Innovative Surgical Procedures

In our facial transplantation program at the University of Louisville, in addition to the above ethical requirements, we have also adopted and are following criteria recommended by Dr. Francis Moore (1988, 1989). In 1988 article, Moore offered four criteria for determining whether it is ethically acceptable to employ an innovative surgical technique. His criteria were: (1) the scientific background of the innovation, (2) the skill and experience of the team (“field strength”), (3) the ethical climate of the institution, and (4) open display and public and professional discussion and evaluation (Moore 1988).

The scientific background of the innovation

This criterion requires that the scientific preparation for proceeding to carry out an innovative surgical procedure must have been carefully and fully developed. The scientific preparation for facial
transplantation is derived primarily from solid organ and hand transplantation research. In addition, unique to hand and facial transplantation, the risk vs. benefit equation in these non-life-saving procedures is being studied (Cunningham et al. 2004).

The vast majority of solid organ transplantation research that bears relevance to facial transplantation has focused on identifying and developing new immunosuppressive drugs and drug combinations that effectively suppress rejection while also causing minimal side effects. The relevant literature is full of basic science and clinical research describing the development and evaluation of these drugs (Gorantla et al. 2000). In 1997, experiments conducted in our laboratory in a large animal model (Ren et al. 2000) demonstrated that one of these new drug combinations (tacrolimus/MMF/prednisone) successfully prevented rejection of transplanted skin, muscle, bone, and other tissues making up the hand while causing minimal systemic toxicity (Jones et al. 1999; Shirbacheh et al. 1998). Based on these experiments, teams in Lyon (France), Louisville (USA), and Guangzhou (China) performed in 1998 and 1999 the first four human hand transplants using this same drug regimen (Dubernard et al. 1999; Francois et al. 2000; Jones et al. 2000).

From an immunological standpoint, since the face contains mostly the same tissues as the hand, it is reasonable to assume that the same immunosuppressive drug regimen found to be effective in the animal research that preceded human hand transplants and in the human hand transplants that followed should also be effective in facial transplantation.

In addition to this animal research, the scientific preparation for facial transplantation must include empirical studies that address the critical ethical questions that such procedures pose. We are therefore in the process of carrying out several studies that aim to answer the central question, “Do the benefits of facial transplantation justify the risks posed by the immunosuppressive drugs required to prevent rejection?” While the risks of immunosuppression are generally accepted for “life-saving” organ transplantation procedures, these same risks are questioned when it comes to “non-life-saving” or “quality-of-life improving” procedures like facial transplantation. To address this issue we designed a questionnaire-based study (Cunningham et al. 2004) to assess the amount of risk individuals are willing to accept to receive the benefits of facial transplantation. Our initial findings from over 250 individuals in four populations questioned (healthy normal subjects, upper extremity amputees, organ transplant recipients, and individuals with facial disfigurements) indicate that they would accept significantly more risk to receive a facial transplant than a single hand, double hand, larynx, foot, or even a kidney transplant (Banis et al. 2002). The last point is intriguing since kidney transplantation is a universally accepted treatment for which the risk vs. benefit ratio goes largely unquestioned.

Siegler (1998) has claimed that central to the ethical concerns with respect to these procedures is the question of whether “the equipoise consideration has been satisfied.” He defined equipoise as “a situation of uncertainty in which the clinical investigator regards the potential outcome of an experiment or clinical trial as truly balanced between its potential for benefiting the patient or for causing unintended harms” (Siegler 1998). The key term here is “uncertainty.” At stake is an uncertainty that remains at the point at which we have gained as much knowledge as we can through scientific studies; and therefore, additional knowledge can be attained only by actually performing the experimental procedure and following the outcome. We believe that facial transplantation has reached a position of equipoise because we are destined to remain uncertain about whether the benefits will outweigh the harms (or vice versa) until we perform the procedure and observe the actual results.

The Skill and Experience of the Team (“Field Strength”)

Moore (1998, 1999) emphasized that the skill and experience of the team undertaking the innovative procedure is crucial. Obviously, such a procedure can be truly “tested” for its safety and efficacy only if the skills and experience of the team performing the procedure are unlikely to be the cause of failure. Moreover, the “field strength” of the team must be assured in order to protect the subjects from harm. The Nuremberg Code enunciates this ethical concern for beneficence:

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment. (Jonsen, Veatch, and Walters 1998)

The team at the University of Louisville is composed of experts who have extensive experience in the scientific, clinical, surgical, and psychological areas pertinent to facial transplantation. This
includes specialists in reconstructive surgery, head and neck surgery, transplant surgery, immunology, psychology, psychiatry, ethics, Institutional Review Board participation, and organ procurement. The reconstructive and head and neck surgeons on our team are familiar with and regularly employ the latest techniques described above to remove, transfer, and reconfigure autologous tissues to reconstruct facial deformities. Indeed, members of the team have pioneered many of the techniques used today for reconstructing complex facial deformities (Banis and Acland 1984). In addition, the team has acquired relevant skills and experience through having established a program for and performed successful human hand transplants. It is such “field strength,” we think, that is necessary in order to take the next step of performing a human facial transplantation.

**Ethical climate of the institution**

What is at stake here is ultimately the motivation for undertaking the innovative procedure. Moore was concerned that the innovation not be performed mainly for the purposes of institutional or professional self-aggrandizement. He thought that it should rather be carried out primarily for its potential contributions to those people who are in need of the procedure. As he expressed it:

> When the epiphenomena of medical care, such as capital gain, investor profit, institutional representation, surgeon ego, municipal pride, and chauvinism, become the true objective of the procedure, then the ethical climate of the institution is no longer acceptable for therapeutic innovation (Moore 1988; Siegler 1998).

Adherence to this ethical requirement is essential but difficult to verify. How can we determine what a person’s or an institution’s motivations are? Usually people and institutions engage in sizable projects with a variety of motives for doing so.

> We suggest that the ethical issues here pertain to possible conflicts of interest. If desires for enhanced reputation, financial reward, professional vanity, and so on motivate those involved to compromise the scientific, medical, surgical, or ethical aspects of the procedure, “then the ethical climate of the institution is no longer acceptable for therapeutic innovation.” An institution may seek an enhanced reputation and even financial profit from being “the first” to advance therapeutic techniques. Indeed, numerous health care institutions highly prize their public reputations for being “first” with innovative procedures, and this usually does not lead people to suspect unethical conduct. The desire to be first becomes unethical only when it motivates the institution to undertake the innovation in a manner that fails to follow strict scientific, medical, surgical, and ethical demands. The key question then becomes this: Have the institutions and professionals involved adhered as much as can reasonably be expected to scientific, medical, surgical, and ethical requirements in performing this new procedure? If these requirements have been met, then it matters little what other motivations may be operative. And this would seem to be the case especially in view of the fact that such motivations can usually not be detected or proven.

**Open display and public and professional discussion and evaluation**

Moore (1998) recognized that it is crucial that innovative surgical procedures be openly displayed before the broad community of professionals in the field as well as before the general public. In order to ensure that the issues surrounding facial transplantation would be submitted to public and professional discussion, evaluation, and criticism, we at the University of Louisville have organized and participated in several conferences addressing these manifold issues. Moreover, we have published the proceedings from these conferences in trade journals to make them accessible to as wide a professional audience as possible. Feedback we have received from public and professional discussion has allowed us to rethink and revise various components of our program. In fact, although our institutional review board proposal has been virtually complete for over three years, we have postponed submitting it for approval and have rather repeatedly fine-tuned it based on criticisms we have received from professional and public discussions.

> Below we list the main examples of efforts we have made to meet Moore’s recommendation of open display and public and professional discussion and evaluation.

In November 1997, we hosted the first International Symposium on Composite Tissue Allotransplantation in Louisville, Kentucky. The workshop brought together international experts in immunology, transplant, plastic, and hand surgery, research, and ethics to evaluate the scientific, ethical, and clinical barriers standing in the way of performing the first human hand transplants. After two days of discussion the consensus was reached that sufficient animal research had been done and that it was time...
to move on to the clinical phase of this research (Barker et al. 1998).

In May 2000, we convened the 2nd International Symposium on Composite Tissue Allotransplantation in Louisville, Kentucky to share the early results of the first human hand transplants and invited teams who had performed other types of composite tissue allotransplantation procedures (namely, larynx, bone, tendon, and nerve). Three hand transplant teams reported encouraging early immunological and functional findings. They reported that the immunosuppressive drug regimen [tacrolimus/MMF/Prednisone] they were using effectively prevented hand rejection, allowed for good recovery of hand function, and caused minimal toxic side-effects in their first patients (Barker, Vossen, and Banis 2004; Barker et al. 2002; Gorantla et al. 2001).

We have also published discussions of the present and future state of composite tissue allotransplantation in professional trade journals (Barker, Vossen, and Banis 2004; Barker et al. 2002; Gorantla et al. 2001).

On November 19, 2003, our team participated in a public discussion at the Dana Center of the London Science Museum. At this gathering four professionals from various fields related to facial transplantation explained their work and their respective positions on the question of whether the time had come to perform human facial transplants. This two-hour event specifically focused on the public’s participation and their opinions (Morris and Monaco 2004). Following this meeting the proceedings were posted on the Dana Center’s website, and the public was invited to post its views. Finally, in addition to these public forums for discussion, we have also openly made our program available to the public in several sources of print, radio, and television media.

IV. Is It Time to Perform a Facial Transplant?

In light of the above discussion we would like to put forward a set of criteria for determining whether the point has been reached, in the preparation and development of this innovative surgical procedure, at which it is justified to perform an experimental facial transplant. The criteria we propose are these:

1. Moore’s criterion of “scientific background of the innovation.” The preparatory scientific groundwork has been laid through laboratory and clinical investigations of the pertinent medications, technology, procedures, and ethical issues. This preparatory work has significantly reduced the risks of the proposed procedure.

2. Moore’s criterion of “skill and experience of the team (‘field strength’).” The surgeons and clinicians involved in the research project possess the knowledge, experience, skills, and technical abilities needed for it.

3. Moore’s criterion of “open display and public and professional discussion and evaluation.” Items (1) and (2) above have been publicized so that professional and lay persons who have so wished have had sufficient opportunity to discuss and criticize the performance of the procedure. Moreover, these responses and criticisms have been seriously considered by the research team and have, when appropriate, influenced the revision of the research proposal.

4. Moore’s critique of the “ethical climate of the institution.” The innovation is not being performed for purposes of institutional prestige or professional recognition. It is rather the criteria enumerated here that are the truly governing ones.

5. The remaining uncertainties regarding facial transplantation and its consequences can be resolved either by proceeding to actually performing the procedure on human subjects or by postponing it and waiting for further developments. Undoubtedly, postponing the procedure would allow for the development of medical innovations. An analogy can be imagined in the manned mission to the moon. This venture would have been aided by the development of the microcomputer, digital camera, and other innovations produced during the past three decades. Such innovations, however, were not essential for a successful moon mission. We submit that, in an analogous way, future medical developments will provide only minimal knowledge compared to that which will be gained from performing the procedure. An example of this is in the knowledge gained from performing human hand transplants. Despite the arguments made against them as too precipitous and uncertain, over twenty hand transplants have been performed. As a result, the field has gained a wealth of knowledge based on direct evidence that would not have been possible if we had not dared to perform the procedure in the face of the uncertainties.

6. There exist informed subjects who, deeming the procedure beneficial, want to undergo it and who will not be able to undergo it if it is postponed in order to wait for further developments.
7. There exist indefinitely many other potential subjects who could in the future benefit from this procedure if it proves to be successful.

8. The procedure has been subjected to the established regulatory scrutiny and reviews, including approval by the relevant IRB.

If these eight criteria are satisfied, we submit that it would be justified to actually perform the experimental procedure on qualified, voluntary, and informed human subjects. Furthermore, we maintain that at the University of Louisville these criteria have been satisfied for the procedure of human facial transplantation. There arrives a point in time when the procedure should simply be done. We submit that that time is now.

Received 9 March 2004; accepted 1 April 2004; revision received 4 April 2004; posted for commentary 5 April 2004.

Competing Interests Statement
The authors declare that they have no competing financial interests.

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