The Technical, Immunological and Ethical Feasibility of Face Transplantation
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Introduction
The human face and facial transplantation has long captured the interest and imagination of scientists, the media and the lay public. The surprising similarity of our faces are unique parts of our anatomy that like no other we associate with special qualities that make us uniquely human. Our face is more than the anatomical location where our sensory, auditory and visual organs are situated. We use facial expressions to communicate with the world around us and our face is the window through which we convey feelings and emotions. We communicate these feelings in our spoken language with terms like “let’s do it”, “face to face”, “man’s face” and “face value”. This is a great importance we attach to our face that makes facial disfigurement such a devastating condition. All of the physical changes, none is more socially devastating than facial disfigurement. In a large number of cases facial disfigurement leads to depression, social isolation, and even the risk of suicide. Facial pain, if not explained or alleviated by an amputated limb, a clamp, or a wheelchair, facial disfigurement elicits anxiety, fear and a wish to remove it from one’s sight. In the words of a patient suffering with facial disfigurement: “I’ve spent fifteen years being treated for nothing other than looking different from everyone else. It was the pain from that, from feeling ugly, that I’d always viewed as the great tragedy in my life. The fact that I had cancer seemed minor in comparison.”

Facial transplantation could provide an excellent alternative to current treatments for facial disfigurement caused by burns, trauma, extirpation or congenital birth defects. As the introduction of solid organ transplantation provided an effective and established treatment for patients suffering from end-stage organ failure, we envisaged that revolutionizing the field of transplant immunology could in the future also revolutionize the field of reconstructive surgery for severe facial disfigurement. The introduction of organ transplantation into the clinical arena brought with it many technical, immunological and ethical issues surrounding facial transplantation and elicited professional discussion from the surgical community.

Technical Issues
Current methods of treating facial disfigurement consist of repairing or reattaching the original tissues, transferring autogenous tissues from the body, using prosthetic materials to restore facial appearance and function. By far the best outcomes are achieved when the original tissues can be salvaged and used to reconstruct the defect. In cases when this is not possible either because of the trauma or disease causing the loss the tissue beyond (major crush injuries, severe burns, tumor invasion) or because the original tissues never existed in the first place (congenital birth defects) reconstructive surgeons must resort to autologous tissue transfers or prosthetic materials. In the former instance, skin grafts are used for simple wound coverage while skin and composite tissue flaps are used to reconstruct complex tissue defects. In the latter instance prosthetic materials are specially designed to camouflage the defect.

Over the past 20 years current treatment options have experienced many advances. Plastic surgeons have refined new grafting methods and new techniques used to care for the skin once it is transplanted. Techniques that enable the use of bioengineered skin products have greatly improved wound care and improved outcomes. Skin and composite tissue flaps transfer techniques have revolutionized the field of reconstructive facial surgery. By enabling surgeons to reconstruct very small blood vessels and nerves, advances in microsurgical techniques and instrumentation have made it possible to transfer live tissues from any part of the body to reconstruct complex facial tissue defects. Prosthetic materials are devices made of a variety of different synthetic materials. New materials have improved these devices with improved match (color and texture) to the tissues adjacent to the defect they cover.

In spite of these advances, current treatments for severe facial disfigurement are still far from ideal. While the methods that use autologous tissue do a good job of “filling in” the defect, the absence of facial tissues results in little to no functional recovery, the aesthetic outcome is poor at best and the donor site from where the tissues are taken often present major problems. In some severely injured patients more than 100 procedures over periods of 10 to 20 years have been required. In these complex cases this extended series of reconstructions are fraught with complications, frequently fail to achieve the intended result, and often worsen the deformity. Treatments using prosthetic materials are excellent for giving the patient a normal static aesthetic appearance but they provide no functional or dynamic return, robbing the patient of his or her ability to communicate with facial expressions.

Facial transplantation would make it possible to use healthy facial tissues (identical to the recipient’s original tissues) to reconstruct the defect and thus provide better outcomes and

Grainger’s early musical education was also influenced by Dr Henry O’Hara, a surgical colleague and friend of Hamilton Russell, who introduced the 10 year-old Grainger to Louis Pabst, regarded as the outstanding piano teacher in Melbourne. O’Hara had qualified in medicine at the Royal City of Dublin Hospital and had also served with the Dublin opera company while still a student. In 1878 he began a career in Melbourne as a general practitioner and, later, as a general surgeon. For a time he lived opposite the Grainger family and in 1882 he delivered their son Percy.

O’Hara had a wide circle of medical friends with whom he gave frequent musical parties in aid of charities, which included the Alfred hospital to which he was appointed as surgeon in 1878. His friends included Nellie Melba, whose father, David Mitchell, was one of his patients and also an architect colleague of Percy’s father. John Grainger failed to pringle to O’Hara that in view of his fine baritone voice he should pursue a career in singing.

The young Percy Grainger therefore grew up in the close company of Graingers who were at the centre of the Melbourne musical world and who had a major influence on his musical development. Grainger’s early career centered on the recognition of his brilliance as a virtuoso pianist, particularly during his stay in London between 1901 and 1914. His abiding interest, however, lay in composition and the study of folk song. Compositions such as ‘Molly on the Shore’ and ‘Country Gardens’ brought him early fame and have never lost their immense popularity. Percy and his friend of Grieg and a lifelong champion of his work, especially his interest in folk music.

They also visited Hamilton Russell’s home and birthplace in Farnhaming, Kent. In a letter to his niece, Vera Chapman, in February 1926, Russell wrote, “...there is going to be a Leslie Centenary celebration in Edinburgh next year, and I felt that whatsoever happens must be there. That and various other things may well be a party of Percy Grainger’s coming here on a concert tour in June, and your going home next year, and one or two other things several years hence...”. Russell wrote to Grainger on 20th November 1925 that Grainger coming to Farnhaming with his mother in 1907? You were a very little girl then”.

Grainger stayed with Hamilton Russell at his home at Cliveden Mansions, East Melbourne, in 1924 during a recital and lecture tour and with his then travelled to San Francisco, on the SS Maunganui.

Russell was to receive a prestigious Fellowship from the American College of Surgeons, which was awarded for his 20 years work on the origins and treatment of inguinal hernia. An example of the closeness of the relationship between the two men was given by Bird who noted that during this journey the two men discussed their shared interests ofFlagellism (Grainger) and homosexuality (Russell). Bird’s theory was that the first time these topics had been discussed between the two friends David Pear, co-editor with Malcolm Gillies, “The all-round man or letters of Percy Grainger”, 1914-1961” has summarized the following, unpublished, entry from the diary entries in the “Alldridge-Grainger-Ström Saga”.

“PG discusses on page DR’s ‘Sexual-unsanity’. He used to tell his mother telling him of a time when Amy Black, (a Melbourne acquaintance), who PG describes as a ‘cheeky, unseenly, shameless scoundrel’, said to DR Russell that he was ‘lacking in masculinity’. Rose Grainger, (PG’s mother), said that this caused Dr Russell to blush uncontrollably. PG writes that he later understood the meaning behind this blank when Russell confessed to PG in 1908 that he was a ‘same-sex-lover (homosexual)’.”

PG writes further that Dr Russell told him he developed a profound can early influence on the development of an American musical genius. Grainger died of metastatic cancer of the prostate on February 20th 1961.

Acknowledgements
I am indebted to the following people for their generous help with this paper: Susan Carden FRACS, Ann T Daymond (great-niece of Robert Hamilton Russell), Rosemary Florrimell (Curator of the Grainger Museum, University of Melbourne), Malcolm Goldsworthy (Farnhaming). Amanda Roberton FRACS, and Colin Smith (Archivist, Royal Australasian College of Surgeons). I should also like to acknowledge my indebtedness to Mr John Bird’s superb biography of Grainger that stimulated this little study of the relationship between two great men.

Conflicting Interests
No declared references.

5. Grainger PA. Percy Grainger: A Saga, Grainger Museum, Special Collections and Archives.
applied for the position of Medical Superintendent of the Horsham hospital in Victoria. His application failed and one of the selection committee members, Dr O Hara, was left with the impression that there must be something “crook” with a gentleman who had such high qualifications and such splendid testimonials from England but who was applying for a position in an up-country hospital in Victoria.6

Meeting with the Grainger family
John Bird has written a detailed description of the life of the Grainger family in Melbourne in the 1880’s and 1890’s.7 He records that John and Percy’s parents, moved to New Street, North Brighton, soon after their marriage. And it was here that their son, named George Percy Grainger, was born on July 8th 1882 under the care of Dr Henry Michael O’Hara. Dr O’Hara also counselled and supported Rose in her later maternal problems which concerned her husband’s drinking and infidelity.8

The Graingers, who were both musical, moved to Glenferrie in 1887 and John Grainger, who was an architect and engineer, worked with David Mitchell whose daughter Nellie was later to develop an international career.9 The Graingers also met the young Percy Grainger and his mother and he appreciated a wide range of music, particularly that of Bach, and it was here that their son, named George Percy Grainger, was born on July 8th 1882 under the care of Dr Henry Michael O’Hara. Dr O’Hara also counselled and supported Rose in her later maternal problems which concerned her husband’s drinking and infidelity.8

Hamilton Russell met the Graingers in Glenferrie in his role as general practitioner and soon became an intimate friend of the family. He treated John Grainger, without much success, for alcohol-related problems but his patient left Melbourne to visit his parents in England and Hamilton Russell helped him pack and embark. Percy Grainger quotes Hamilton Russell as saying to his son, “ you’ll be all right”. This proved to be unduly pessimistic and John returned to Adelaide a few months later. However, he never again lived with his father and son. In 1892, Rose and Percy moved to the suburb of Auburn and in 1893 to South Yarra, closer to the centre of Melbourne. Hamilton Russell moved to the suburb of Auburn and then to Plover Street, East Melbourne in 1910. Here he was joined by one of his sisters, Ellen Maude, who stayed with him for 4 years, and after her return to England he had a relationship with a Presbyterian nurse, which, by coincidence, had been reconstructed by Grainger’s father on a site that is now occupied by a Hilton hotel.8

Hamilton Russell returned to a surgical career in 1892 with his appointment as an honorary surgeon at the Melbourne Hospital for Sick Children, and here he developed a life-long interest in the cause and treatment of congenital heart disease in adults and children. These studies, which defined the role and importance of congenital pericardial sacs in the aetiology and treatment of her- nias, were to bring him fame in the surgical world, and were accompanied by publications on a wide range of subjects, which included urology, orthopaedics, cancer and liver disease:

General and paediatric surgery -
- inguinal and femoral hernia
- colic intussusception
- hydrocele
- childhood pyopecty
- sacs-pelvis hernia

Urology -
- hypropusias
- enuresis
- antural trauma

Orthopaedic -
- joint dislocations fractures
- bone infections
- tuberculosis and pyogenic infection of the bone joint

Neurosurgery -
- head injury

Thoracic surgery- pediatric thoracotomy

Miscellaneous -
- cleft palate, breast cancer, choriocarcinoma

These papers described major surgical innovations in hypoplasias repair, and the correction of urethral structures. It is not generally known that Lord Lister was present at the first of these operations as a spectator of the surgery performed by the urethra and made the original observation that a strip of urethral mucosa will refashion into a tube without structure formation. He published drawings of this in a new technique in the Journal of Surgery in 1892.10 He also published a method of treating limb fractures which was widely adopted and used, and which even now is referred to as ‘Hamilton Russell traction’.

An appointment to the Alfred hospital in 1901 marked a significant advance in his surgical career and increased opportunities for medical writing and for teaching the antiseptic technique of surgery learned from Lord Lister. He soon became recognised as an innovative and skilful surgeon and was appointed as the first dean of the medical school in 1919. In 1927 he became a foundation council member and director general of the new Australasian College of Surgeons, where his portrait now hangs.11 He remained at the Alfred hospital where he stayed on the staff for 20 years.

Hamilton Russell’s ability as a pianist was well recognised by his friends, particularly for his interpretation of the music of Bach and Schumann. Bird quotes from Grainger’s own writing in a “Sketch for the above article: English pianism and Harold Bauer” (1945), in which Grainger compares Hamilton Russell’s pianism favourably with that of the internationally acclaimed musician Sir Charles Halle.12

Hamilton Russell continued to have a close professional and social relationship with the young Percy Grainger and his mother and he clearly had a great influence on Grainger’s musical development by introducing him to recitals and orchestral concerts as well as to the musicians themselves. The boy met concert pianists such as the Australian Ernest Hitcheson, from whom he learned to appreciate a wide range of music, particularly that of Bach, and it is clear that Hamilton Russell helped to mould Grainger’s early musical tastes.13 Bird concludes that “There is no doubt that Russell was a lifelong friend, a musical touch-tone and without his influence, music could have withered and died”.13

Hamilton Russell was a long-standing and respected member of the Grainger family, as both a mentor and, perhaps, father figure to the young Grainger; eliminate many of the problems associated with current treatments. Facial transplantation would consist of removing facial tissue from a brain dead donor (solid organ donor) and transplanting it to a recipient to reconstruct the facial defect. The severely scarred and fibrotic tissue on the recipient’s face would be removed and replaced with anatomically and functionally normal tissues, which over a period of 1-2 years would be expected to regain significant facial nerve function and animation.

Donor tissue procurement: When the donor is located and confirmed to meet the pre-established inclusion criteria the recipient will be notified, brought to the hospital and prepared for surgery. At the same time the members of the surgical team will accompany the solid organ procurement team to retrieve the donor tissue. The technical details of retrieving the donor facial tissues are challenging and technique dependent. It is expected that in most cases all of the soft tissue down to the bone will be needed to reconstruct a severely disfigured face. At its most basic, the donor facial tissue will be matched to and patterned from the defect defined by the recipient’s deformity. This segment of tissue will include skin, subcutaneous tissue, muscle, and the arteries, veins and nerves necessary to satisfactorily perfuse and innervate the facial musculature of the transplanted facial tissue.

Facial tissue implantation: While surgical implantation will take many hours, the first surgical priority will be to revascularize the facial tissue retrieved from the donor so as to minimize the ischemia time. It is important to note that the tissues that will be transplanted in this procedure (skin, subcutaneous tissue, muscle) can withstand relatively long periods of ischemia; therefore it is not anticipated that this will present a problem. If the defect reaches the bone, then transfer will involve more microsurgical techniques. Arteries and veins will be reattached and as many as twenty facial motor nerve branches and major sensory nerves could be repaired.

In the event the full face is not required to reconstruct the defect, proportionately fewer artery, vein and nerve repairs will be necessary. While revascularizing the donor facial tissue is the best case scenario, and will most likely be possible in facial transplantation procedures, it is well known that, due to its rich blood supply, skin grafts can survive on only one good perfusing vessel.17 Once the vessels are reattached and the blood supply is restored to the transplanted tissue, the remainder of the reconstruction – reattachment of many delicate structures and nerves can be carried out in a methodical and unhurried fashion and could take as long as 8 to 16 hours to complete.

If it becomes necessary to remove the transplanted facial tissue, due to technical complications, the patient’s treatment protocol would revert to conventional reconstructive methods (grafts, flaps, etc.) depending on the cause of failure.

In many respects current methods that repair and reattach damaged tissues via stents and reconstructive autologous tissues to reconstruct facial deformities are more technically challenging than transplanting healthy facial tissues from a donor. The technical expertise and techniques needed to transplant human facial tissue are common practice and are performed daily in most centers where complex facial reconstructive procedures are performed. These methods have been developed and improved over the years and are the basis for current facial reconstructive and aesthetic techniques.

Immunological Issues

Facial transplantation is a relatively rare concept, since the face and the hand contain mostly the same tissues it is reasonable to assume that the same immunosuppressive regimen found to be effective in human hand transplants should also be used in face transplantation. In 1997 experiments in a large animal model18 demonstrated that a new immunosuppressive drug regimen widely used in organ transplantation, tacrolimus and mycophenolate mofetil (MMF) in a prevascularized composite tissue allotgraft rejection, while causing minimal systemic toxicity.19, 20 Based on these experiments in 1998 and 1999 teams in Lyon (France), Louisville (USA) and Guangzhou (China) performed the first 4 human hand transplants using this same drug regimen.19, 20

In case of complications common complications associated with the use of immunosuppressants include increased incidence of infections, malignancies, and end-organ toxicity. In the case of macrolide/monoclonal antibodies (e.g. Atgam) accidental contact with tourist drug regimens that would most likely be used in face transplantation, the incidence of these complications are as follows.

Infections: The incidence of opportunistic infections, including CMV, HSV, and fungal and bacterial infections, is increased, which may be associated with the use of immunosuppressants. A marked decrease in the incidence of infections, malignancies, and end-organ toxicity. In the case of macrolide/monoclonal antibodies (e.g. Atgam) accidental contact with tourist drug regimens that would most likely be used in face transplantation, the incidence of these complications are as follows.

Immunosuppressive: In kidney transplant recipients (receiving similar doses of MMF at 2g/day as would facial transplant recipients) there exists a 1.2% incidence of post transplant lymphoproliferative disease (PTLD) and 11.1% incidence of non-melanoma skin carcinomas.21 In order to prevent rejection and consequent death. In the case of kidney transplantation, however, in addition to the appropriate oncologic treatment, immunosuppression is usually tailored to the patient’s immune responsiveness against the tumor. This would also be possible for facial transplantation, where the
Robert Hamilton Russell,

Since everyone.
The question.

While the risks of immunosuppression are generally accepted for

This success in animal research followed by the success of over

Functional and aesthetic recovery, for as long as 5 years

produced by the Royal College of Surgeons; Facial Transplantation; ethical issues the reader is directed to the recent publication pro-

"organ transplantation procedures, these same risks
do the benefits

The Journal of Surgery

The Fenners

A paragraph in the will of Hamilton Russell, (1931) states "To my brother George Russell, who was my only brother and my only remaining relative, I leave the sum of one hundred and thirty-five pounds, payable into the hands of the Maryland Insurance Company of America (sic) in the City of Baltimore."

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Robert Hamilton Russell, surgeon, and Percy Grainger: an intimate relationship

Robert Hamilton Russell was born on 2nd September 1860 into a long-established family of farmers in the village of Farningham, and benefits. As with all innovative medical advances ultimately professional and public discussion and with this inform the patient about a new treatment from research, clinical experience, clinical scientists is to gather as much knowledge as possible is important that teams proposing to perform this procedure presenting. To assure that facial transplantation moves into the clinical arena performing an innovative procedure of this type will always be destined to remain uncertain about whether the benefits will outweigh the harms (or vice versa) until we actually perform the procedure in humans and follow the outcomes.

In summary, we believe that for a select population of severely disfigured patients, this research and further research, despite its recognized risks, could provide a better treatment option than current methods. The actual surgical techniques necessary to perform the face transplant are commonly performed and are readily available today. From an immunological standpoint since face and hand contain mostly different tissues to assume that the same immunosuppressive regimen found to be effective in human hand transplantation should also work in face transplantation. While there are risks associated with these immunosuppressive drugs these risks have been extensively studied in large populations of solid organ recipients: one year results of a multi-center, randomized dose ranging trial. 2000; 18: 407-414.


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Solid Organ and Composite Organ Transplantation - the dynamic equilibrium of rejection and immunosuppression

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Abstract  
Transplantation remains one of the most discussed surgical specialties within the media, both from a scientific and ethical point of view. In a lifetime transplantation has moved from a speculative experiment to a relatively commonplace lifesaving set of procedures. Within medicine, transplantation offers interaction between some of the sickest patients and the crafts of surgeons, clinical immunologists, transplant specialists, and bioengineers, as well as being the subject of huge quantities of clinical and basic scientific research. The many high profile advances in transplantation in recent years have been made possible by some very significant developments in the armamentarium of immunosuppressive drugs available for combating the rejection process. In this article, we will briefly discuss the rejection process and the drugs which are used to counter it.

The Rejection Process  
Rejection of solid organ transplants revolves around the CD4+ T lymphocyte; the helper T cell. This cell is activated by the presentation to it of fragments of allografts by antigen-presenting cells (APCs) on their MHC class II molecules.1,2 This interaction of the T cell’s receptor with the MHC class II/antigen complex leads to internal signalling within the T cell, which then increases the production of the cytokine, interleukin 2 (IL-2). IL-2 is responsible for on-going activation of T cells. This activation leads to the effector arm of the immune response being recruited to perform the task of destroying the transplanted graft. The effectors include cytotoxic T lymphocytes, which act to kill the graft directly, antibodies produced by B-lymphocytes, or antigen non-specific macrophages, which cause a local ‘delayed type hypersensitivity’1,2 Since the helper T cell is key to the generation of such immune responses all current immunosuppressive drugs are designed to prevent this T cell activation, in addition to any other roles they may play.

Methods of Preventing Transplant Rejection.  
Aside from the miraculous but apocryphal (St Cosmos and St Damian) method of transferring the supposed organs of these saints to people in need, the technique for joining the limbs to the trunk that in its own way was a technological tour de force to assay the gold and interpret the legends of lost civilisations are beautiful but their reality might exceed the expectations of many sceptics.

Discoveries.  
Approximately three years ago, a shaft was being dug to provide foundation pits for aenheim protective cover over the archaeological excavations at Akrotiri, a site at the southern tip of the crescent shaped island of Thira (Santorini) in the Cyclades. Amongst the rubble, a woman wearing a perfectly preserved wooden box that was thought to serve some late bronze age domestic role. On opening the box, the archaeologists were both surprised and delighted to discover a most beautifully crafted and perfectly preserved Golden Ibex about the size of a new born kitten (figure 3). Closer inspection revealed that it was well preserved and in the original position with the trunk. The local experts assumed it was fabricated by using the lost wax technique but the technique for welding the limbs onto the trunk was a mystery; as was its role within this lost Civilisation.

Figure 2. The island of Santorini (Thira) near Greece blew its top. In the most cataclysmic volcanic eruption in the recorded history of our planet, 300km2 of magma in the form of pumice and volcanic ash buried the Island and its civilisation.

Figure 3. The Golden Ibex.  
As an object, this sublimely proportioned artefact can be looked upon in many ways. Firstly, as an object revered for its beauty and for all we know, venerated in its time as a household God, a pocket size adumbration of the Golden Calf worshipped by the children of Israel a few years after the exodus from Egypt. Secondly, it could be looked upon as an archaeological curiosity, capable of throwing light on the bronze age civilisations of the Cycladic islands and their trading links with Egypt and the South and the biblical Kingdoms to the East. Finally it was a technological tour de force to assay the gold and interpret the techniques for joining the limbs to the trunk that in its own way would shed light on its archaeological provenance.

Old and New Civilisations Collide  
In the last week of June 2001, a group of us as assembled on the Island of Santorini as guests of Mr Peter Nomikos, the founder of Photoelectron Corporation for a scientific advisory Board meeting. I had been working with Photoelectron Corporation for

The Golden Ibex of Santorini - A Convergence of Cultures & Technologies

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Background  
3600 years ago the Island of Santorini (Thira) near Greece blew its top. In the most cataclysmic volcanic eruption in the recorded history of our planet, 300km2 of magma in the form of pumice and volcanic ash buried the Island and its civilisation.

Art & History  
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