Face and Upper Extremity Transplantation

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Disclaimer

• I have no proprietary or financial interest in any of the disorders, products, or devices mentioned

• The information presented is used with permission of the patient(s) in accordance with HIPAA

Thank You
Presentation Overview

- A background of transplantation
- Upper extremity transplantation
- Donor selection
- Recipient selection
- Psychosocial aspects
- Face transplantation
- Case review
  - The operation
  - Results
- Complications and the future
- Conclusions
- Questions

Background

A history of transplantation

- Attempts at limb transplantation are documented as early as the Third Century
- Technology
  - Allowing vascular anastomoses
  - Xenograft kidney transplants were attempted in 1906 (Jaboulay)
- Scientific advances
  - Azathioprine and prednisolone allowed transplants between genetically non-identical individuals in 1960s (Medewar, Elion, Calne)
- Determination
  - Kidney transplantation in identical twins in 1954 (Murray)
  - First kidney allograft in 1959 (Murray)
VCA: The first limb ‘transplant’

Saint Cosmas and Damien
• Patron Saints of surgeons, physicians, orphanages, dentists, and against the plague
• Provided free medical service
• Accused of being Christians
• Sentenced to death by torture
• Decapitated September 26, 287

A history of VCA


• First ‘modern’ hand transplant performed in 1964 in Ecuador; bilateral procedure failed due to rejection (no immunosuppression)
• First ‘successful’ single hand transplant performed in 1998 in Lyon, France; failed due to patient non-compliance (Dubernard)
• First long-term successful hand transplant performed in 1999 in Louisville, KY (Breidenbach)
• First bilateral hand transplantation performed in 2000 in Lyon, France with good success
• First face transplant (partial) performed in 2005 in France (Dubernard, Duvauchelle)
• Approximately 70 hand transplantations have subsequently been performed in 10 countries worldwide
• Approximately 30 face transplants have been performed, 8 in the USA
• United States centers for VCA include Louisville, KY, Pittsburgh, PA, Johns Hopkins, MD, San Antonio, TX, Atlanta, GA, Duke, NC, Mayo Clinic, MN, UCLA, and Boston, MA

The International Registry
Upper extremity transplantation

Significance of the hand

- Function
  - Motor
  - Sensory
- Expression
  - Gestures
  - Interpersonal contact
  - Emotion
  - Symbolism
- Cosmesis
  - 'Point of contact'
  - Noticeable
- Sense of 'wholeness'

Indications for hand transplant

- Congenital
- Acquired
  - Tumor
    - Vascular malformation
    - Cancer
  - Trauma
    - Crush/explosion (69%)
    - Burn (9%)
    - Industrial/laceration (9%)
    - Electrical (5%)
    - Gunshot wound
    - Animal attacks
  - Infection
    - Sepsis (6%)
- Loss of bilateral upper extremities
- Loss of a dominant upper extremity
Statistics

- Approximately 6,000-10,000 upper extremity amputations are performed in the US annually.
- Traumatic amputations are most common in 15-45 age bracket and comprise 70% of all upper extremity amputations.
- Incidence has been declining over past 20 years, likely due to improved industrial safety standards.
- Males at significantly higher risk than females.
- Approximately 1,224 extremity amputations have been reported related to U.S. war-related activities.
- Ratio of soldiers surviving with limb amputations now higher than in past, likely due to improved body armor (1:28 vs. 1:70-90).
- Significant associated personal and societal impact.

Traditional options for amputees

Prosthetic options

<table>
<thead>
<tr>
<th>Active</th>
<th>Passive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body-powered</td>
<td>Cosmetic</td>
</tr>
<tr>
<td>(cable)</td>
<td></td>
</tr>
<tr>
<td>Externally</td>
<td></td>
</tr>
<tr>
<td>powered</td>
<td></td>
</tr>
<tr>
<td>(myoelectric)</td>
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</tbody>
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1. Variable appearance
2. Targeted functionality
3. Insensate
Reconstructive options

Krukenberg Procedure

- Surgical procedure first described over 80 years ago
- Conversion of forearm stump into pincer via separation of radius and ulna
- Powered by pronator teres muscle
- Preserves sensation and proprioception

1. Poor appearance
2. Basic functionality
3. Sensate

Challenges in limb transplantation

<table>
<thead>
<tr>
<th>TECHNICAL</th>
<th>IMMUNOLOGICAL</th>
<th>ETHICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective bony fixation</td>
<td>Rejection delay or prevention</td>
<td>Immune suppression for non-lifesaving organ</td>
</tr>
<tr>
<td>Microsurgical technology</td>
<td>Tolerance</td>
<td>Allocation of finite resources</td>
</tr>
<tr>
<td>Nerve regeneration</td>
<td>Minimize or eliminate</td>
<td>Selection of patients</td>
</tr>
<tr>
<td>Reliable into remodeling</td>
<td>Realization-related morbidity</td>
<td>Informed consent (experimental procedure)</td>
</tr>
<tr>
<td>Coordination</td>
<td></td>
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<tr>
<td>Rehabilitation</td>
<td></td>
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Hand transplantation overview

<table>
<thead>
<tr>
<th>CRITERION</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range of Motion</td>
<td>Mildly diminished active/passive range in wrist</td>
</tr>
<tr>
<td></td>
<td>Digital range of motion variable</td>
</tr>
<tr>
<td>Gross Motor</td>
<td>Extrinsic flexor and extensor function noted within days of procedure</td>
</tr>
<tr>
<td>Fine Motor</td>
<td>Intrinsic function variable, with return over course of 3-5 years</td>
</tr>
<tr>
<td>Sensibility</td>
<td>Recovery of at least protective sensibility in nearly all patients</td>
</tr>
<tr>
<td></td>
<td>Variable fine touch discrimination</td>
</tr>
<tr>
<td>Aesthetics</td>
<td>Generally good to excellent</td>
</tr>
</tbody>
</table>
Hand transplantation results

- 85% have had episode of acute rejection within 1st year, all resolved with immunosuppressive boost therapy
- 96% of transplants have survived; failures due almost exclusively to medical noncompliance
- Early post-transplant infection risk reported to be 11% (primarily hospital acquired organisms) which have typically been treatable
- Time window not yet sufficient to comment on downstream malignancies attributable to immunotherapy
- Only mild long-term endocrine derangement

The risk-benefit balance

<table>
<thead>
<tr>
<th>BENEFITS</th>
<th>RISKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>True anatomic restoration</td>
<td>Potential for rejection</td>
</tr>
<tr>
<td>Potential sensibility</td>
<td>Increased risk of malignancy and infection</td>
</tr>
<tr>
<td>Functional capacity at least equivalent to prosthesis</td>
<td>Possibility of microsurgical failure</td>
</tr>
<tr>
<td>Superior cosmetic appearance</td>
<td>Potential for renal and/or endocrine impairment</td>
</tr>
</tbody>
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Face transplantation
A history of facial reconstruction

- World War I
- The Guinea Pig Club

Facial reconstruction now

Restoration (not reconstruction)

Full Facial Transplant Procedure

Brigham and Women's Hospital
Plastic Surgery Transplantation Program
Boston Massachusetts
**Indications for face transplant**

- **Congenital**
- **Acquired**
  - Tumor
  - Neurofibromatosis
  - Vascular malformation
  - Cancer
- **Trauma**
  - Gunshot wound
  - Explosion
  - Burn
  - Animal attacks
  - Industrial

- **Oral incompetence**
- **Oronasal fistulae**
- **Motor dysfunction**
- **Sensory dysfunction**
- **Severe malformation**

**International face experience**

**Transplants by country**

- Belgium: 2
- China: 3
- France: 3
- Spain: 6
- Turkey: 1
- USA: 1

**Mechanism of injury**

- Animal attack: 8
- Burns: 3
- Cancer: 3
- Electrical burns: 4
- Explosion: 3
- Gunshot wound: 1

**BWH face transplant experience**

- Jim
- Dallas
- Mitch
- Chalia
- Carmen
BWH face transplant experience

- A new paradigm in reconstruction
- The beginning of restorative surgery

Pre-operative

Post-operative

Animating

Face transplant outcomes

- Technical
- Medical
  - Rejection
  - Metabolic
- Functional
  - Airway
  - Swallowing and mastication
  - Speech
  - Sensory recovery
  - Facial expression
- Cosmetic
- Social

- 1 death reported in the literature
- 2 additional deaths
- Rejection
  - 1-3 acute episodes between 18 days and 17 months
  - No chronic rejection seen
- Improvement in mastication and speech by 6 months
- Sensory recovery beginning at 3 months
- Improved olfaction
- Recovery of facial expression variable by 18 months

A new paradigm

- 21 years old former soldier
- MVA – high voltage injury
- Conventional reconstruction

- 31 years old
  - Cannot close eyes
  - No nose
  - No sensation
  - Oral incompetence
  - Stared at in public

- 32 years old
  - Can fully close eyes
  - Functional nose
  - Sensation in face
  - Can fully close lips
  - Barely noticeable

$184,000

$337,000
Medical breakthroughs

• 200-year Anniversary of the New England Journal of Medicine

• Greatest medical breakthroughs

Case review
Complications, the future, and conclusions

Risks and complications

- **Operative**
  - Loss of transplant
  - Secondary reconstruction

- **Immune suppression**
  - Rejection
    - 85% within 1 year
  - Metabolic
    - Renal
    - Hepatic
    - Endocrine
    - Malignancy

- **Function**

- **Psychosocial**
  - Informed consent
  - Dependence concerns
  - Coping
  - Independence

Ongoing questions…

- **Patient selection and eligibility**
  - Acceptable risk-to-benefit ratio?
  - Not a life-saving procedure
  - Incommensurate benefit to risks related to enhanced body image versus improved functionality

- **Requirement for lifelong immunosuppression**
  - Malignancy
  - Renal/liver complications
  - Endocrine complications
  - Infection
  - Shortened life expectancy?

- **Short follow-up and numbers**
  - Inadequate data

- **Questionable ability for informed consent**
  - Can patients even give truly informed consent in these situations?
  - Skin color, gender, etc.
  - Pediatric – can parents make an informed choice?

- **Financial**
  - QALY for prosthetics exceed transplantation in unilateral
  - Different health systems and payer circumstances may alter options and eligibility
Ongoing questions…

- Risk of loss of other (life-saving) organs in a donor
  - Is this ethically justifiable?
- Competing motivations
  - Financial, media, altruism, etc may provide conflicting motivations
- Multiple extremity, hand/face concurrently
  - Poor track record of success with anything greater than two limbs at a time
  - In patients with prior solid organs is the risk of VCA acceptable as it may compromise the life-saving kidney
- Protecting patient confidentiality
  - May be difficult to ensure confidentiality of the recipient and/or donor – most relevant in smaller geographic regions
- Congenital
  - What’s the potential benefit? Can a child with a congenital absence get cortical reintegration?
- Team dynamics and disagreement
  - Team-level issues about resolving moral distress that may be present and/or developing procedures for reaching consensus
- Issues surrounding organ procurement
  - Need to educate organ procurement coordinators and potentially provide options for individuals who perceive hand transplantation as morally objectionable
- Justice across programs
  - Disparities in availability
- Congenital
  - What is the potential benefit? Can a child with a congenital absence get cortical reintegration?
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The future

- Immunosuppression
  - Lower doses based on serologic markers
  - Less toxic agents
  - Fewer drugs
  - Tolerance (the ‘Holy Grail’)
- Nerve regeneration
  - The ‘Achilles heel’ of transplantation (limits level)
  - Traditional approaches (such as nerve transfer) do not work in these patients
  - Accelerating nerve growth or maintaining motor end plates during nerve recovery
- Prosthetics
  - Improved function
  - Improved durability
  - Sensation
  - Bionic integration (the ‘Six Million Dollar Man’)
  - The ‘cell phone’ analogy
- The right operation for the right patient

The ‘team’
Conclusions

- Traditional approaches for managing upper extremity amputations and facial injuries are limited in their capacity to meet functional and aesthetic reconstructive goals
- Transplantation offers a promising alternative to these traditional options based on world experience to date
- Organ donation and partner hospitals are critical to success
- Patient selection and teamwork are absolutely critical

Questions?

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