The primary purpose of the IRHCTT is to collect information on voluntary basis.

It allows to know what happens in this new field of transplantation, which is considered experimental with uncertain results and short follow-up.

Data are only presented in aggregate form. International privacy and data security have been provided to ensure patient data and centre confidentiality.

At present the IRHCTT includes cases of upper extremity and face allotransplantations performed all over the world.
IRHCCT: Hand

Antalya, Turkey
Atlanta, USA
Boston, USA
Brussels, Belgium
Innsbruck, Austria
Leeds, UK
Los Angeles, USA
Louisville, USA
Lyon, France
Melbourne, Australia
Mexico City, Mexico
Monza, Italy
Paris, France
Philadelphia, USA
San Antonio, USA
Valencia, Spain
Wroclaw, Poland
Guangzhou, China
Harbin, China
Nullguangxi, China
Munich, Germany
Pittsburgh, USA
IRHCTT - Upper extremity
Follow-up: 4 months - 16 years

IRHCCT
47 Recipients
23 single upper extremity Tx
24 bilateral upper extremity Tx

Recipients from China: 12
8 unilateral upper extremity Tx
3 bilateral upper extremity Tx
1 palm
1 thumb
# HAND RECIPIENT CHARACTERISTICS

<table>
<thead>
<tr>
<th>Recipients</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td>38M/9F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td>white</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age at transplant</strong></td>
<td>37.44 yrs (17-65)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Time since amputation</strong></td>
<td>2 months to 34 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Side of hand loss</strong></td>
<td>24 both</td>
<td>18 right</td>
<td>5 left</td>
<td></td>
</tr>
<tr>
<td><strong>Level of amputation (forearm)</strong></td>
<td>Palmar 13</td>
<td>Wrist 18</td>
<td>Distal forearm 11</td>
<td>Mid forearm 9</td>
</tr>
<tr>
<td><strong>Level of amputation (arm)</strong></td>
<td>Elbow 1</td>
<td>Mid-arm 2</td>
<td>Proximal arm 2</td>
<td>Distal arm 1</td>
</tr>
<tr>
<td><strong>Type of amputation</strong></td>
<td>Clean cut 8</td>
<td>Crush 9</td>
<td>Explosion 12</td>
<td>Electric 6</td>
</tr>
<tr>
<td>19 working injuries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>R/D CMV status</strong></td>
<td>-/- 17</td>
<td>+/+ 11</td>
<td>-/+ 8</td>
<td>+/- 9</td>
</tr>
<tr>
<td><strong>R/D EBV status</strong></td>
<td>-/- 15</td>
<td>+/+ 17</td>
<td>-/+ 1</td>
<td>+/- 6</td>
</tr>
<tr>
<td>Hand Donor Characteristics</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>--------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>35 M/12F</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31 (15-62)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HLA mismatch</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6, 11, 5, 7, 4, 3, 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cold preservation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>41</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Perfusion solution</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UW: 34, IGL-1: 4, HTK: 3, Custodiol: 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cold Ischaemia time (hours)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 (30 minutes-12:30)</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
HAND

DONOR/RECIPIENT

- Cross match negative in all cases
- Gender match: 5 cases of unmatched gender
- Skin colour match: good in 35 cases and fair in 10 cases
- Limb size match: good in 39 cases and fair in 6 cases
SURGICAL PROCEDURE

- B, A, V, FT, ET, N: 15 hands
- B, A, V, ET, FT, N: 3 hands
- B, A, V, N, ET, FT: 6 hands
- B, A, V, N, FT, ET: 12 hands
- B, A, V, FT, N, ET: 3 hands
- B, A, V, ET, N, FT: 1 hand
- B, A, N, FT, ET, V: 2 hands
- B, ET, FT, A, N, V: 3 hands
- B, ET, FT, N, V, A: 3 hands
- B, FT, ET, N, V, A: 5 hand
- B, FT, ET, V, N, A: 2 hands

B, A, V: 74% of hands

Duration of procedure: 2-21.38 hours (12 hours)

B = Bone  
A = Artery  
V = Vein  
FT = Flexor tendons  
ET = Extensor tendons  
M= muscles  
N = Nerves

BMNAV: 2 arms
BMNVA: 2 arms
BAVMN: 2 arms
INDUCTION THERAPY

**TAC:** 37 recipients (10-20 ng/ml)
**MMF:** 37 recipients (2000 mg)

**STEROID:** 42 recipients
- *intraoper.:* 500-1000 mg (50-1000)
- *POD 1:* 250-500 mg (20-500)
- *POD 7:* 50 mg (10-250)
- *POD 14:* 20-50 mg (5-200)
- *POD 30:* 5-20 mg (5-100)

- **ATG:**
- **Basiliximab:**
- **Campath-1:**

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*IRHCTT* 
**INTERNATIONAL REGISTRY ON HAND AND COMPOSITE TISSUE TRANSPLANTATION**
MAINTENANCE THERAPY
3 months

- **Steroids**: 37 recipients
  POD 90: 10 mg/d (5-50 mg)

- **Tacrolimus**: 43 recipients

- **Mycophenolate mofetil**: 41 recipients (500-2000 mg/d)

- **Sirolimus**: 3 recipients
MAINTENANCE THERAPY

In the follow-up

- Tacrolimus, mycophenolate mofetil, steroids: 14 patients
- Switch from tacrolimus to sirolimus: 8 patients
- Switch from Tacrolimus to Belatacept: 1 patient
- Switch from MMF to Sirolimus: 3 patients
- Steroid-free treatment: 9 patients
- MMF-free treatment: 11 patients
- Everolimus: 1 patient
- Sirolimus: 1 patient
- Low dose Tacrolimus, Sirolimus, MMF, steroid: 3 patients
Episodes of acute rejection

In the first year after the transplantation 85% of the recipients developed AR episodes.
Therapy of AR episodes

- IV Steroids: 65%
- ATG: 2.7%
- Campath-1: 4%
- Rituximab: 1.3%
- Increase in steroid oral dose: 45%
- Topical immunosuppressants: 95%
- Extracorporeal photochemotherapy: 2.7%
Chronic rejection

- Four teams declared “chronic” rejection:
  - 1. Chronic rejection and patient decision of amputation (771 days after Tx): amputation
  - 2. Chronic rejection after ongoing AR episodes and no compliance (12 years after Tx): amputation
  - 3. Chronic rejection due to no reported AR episodes and self-medication (13 years after Tx)
  - 4. Graft vasculopathy (11 years after Tx): amputation of one finger
- Intimal thickening, acute ischemia of the grafted hand: amputation
**COMPLICATIONS/SIDE-EFFECTS**

**Opportunistic infections**
- CMV infections or reactivations: 5
- Herpes virus: 2
- Herpes zoster: 1
- Clostridium difficile infection: 2
- Cutaneous mycosis: 3
- Bacterial infection: 11
  - 1 osteitis
  - 1 pneumonia with sepsis

**Metabolic complications:**
- Hyperglycemia: 21 (resolution in 13 cases in the first post-operative period)
- Increased creatinine values: 9
- Arterial hypertension: 5
- Leukopenia: 2

**Other:**
- Deep venous thrombosis: 1
- Arterial thrombosis: 2
- Pulmonary edema and congestive heart failure: 1

**Prophylaxis**
- Antibiotics: 38 patients 10 days (1d-180d)
- Gancyclovir: 32 patients 180 days (5d-540d)
- Candida: 30 patients 180 days (7d-365d)
- Pnumocystis carinii: 30 patients 180 days (10d-365d)
- Trimsulfatan Nystatin: 22 patients (8d-6 mo)
COMPLICATIONS/SIDE-EFFECTS

**Opportunistic infections**
- CMV reactivation: 4
- Herpes virus: 2
- Herpes zoster: 1
- EBV infection: 1
- Condylome: 2
- Cutaneous mycosis: 3
- Bacterial infection: 14
  - 3 infections of graft connective tissues

**Malignancies:**
- Basal cell carcinoma of nose: 1
- Post-transplant lymphoproliferative disease: 1

**Metabolic complications:**
- PTDM: 4
- Increased creatinine values: 5
- End-stage renal disease (haemodialysis): 1
- Arterial hypertension: 5
- Avascular necrosis of the hip: 2
- Hyperparathyroidism: 1
- Pulmonary embolism: 1
Functional recovery
Single hand transplantation

years

HTSS
DASH score

years
Functional recovery
Bilateral hand transplantation

Graph showing the recovery over years with HTSS, Right hand, Left hand, and DASH score.
Graft survival
UPPER EXTREMITY

- **GRAFTS REMOVED in Western countries:**

- A hand graft due to bacterial infection and bleeding (45 days after Tx) in a simultaneous face and bilateral hand Tx

- Bilateral hand transplantation due to sepsis and necrosis (5 days after Tx) in a simultaneous face and bilateral hand Tx

- Bilateral hand transplantation due to necrosis of distal phalanges (15 days after Tx)

- A hand graft due to poor vascularisation (3 days after Tx)

- A hand graft due to the non compliance of the patient (29 months after Tx)

- A hand graft due to intimal hyperplasia (275 days after Tx)

- A hand graft due to chronic rejection and patient decision of amputation (771 days after Tx)

- A hand graft due to patient non compliance, ongoing rejection episodes, and patient decision of amputation (12 years after transplantation)

- Seven hands were removed in China for “progressive” rejection
Patients Survival

Cum Survival

Years of follow-up

Survival Function
Censored
Patient survival

UPPER EXTREMITY

- One patient died (simultaneous face and bilateral hand transplantation) for cerebral anoxia on day 65
- One patient died (bilateral arm transplantation) for pulmonary edema and congestive heart failure on day 1
- One patient died for sepsis on day 101
IRHCCT: Face

Amiens-Lyon, France
Antalya, Turkey
Barcelona, Spain
Boston, USA
Cleveland, USA
Paris, France
Seville, Spain
Valencia, Spain

Baltimore, USA
Belgium
Poland
Xi’an, China
IRHCTT-Face
Follow-up: 4 months–8 years

23 partial or total face allotransplantations
## RECIPIENT CHARACTERISTICS

**Face**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35 (19-59)</td>
</tr>
<tr>
<td>Sex</td>
<td>18 M/5 F</td>
</tr>
<tr>
<td>Race</td>
<td>22 White/1 Black</td>
</tr>
<tr>
<td>Surgery before Tx (n°)</td>
<td>19 patients (3-23)</td>
</tr>
<tr>
<td>Cause of disfiguration</td>
<td>Trauma: 12, Congenital: 2, Tumor/malformation: 2, Burning: 7</td>
</tr>
<tr>
<td>Time since disfiguration</td>
<td>(4 months-35 years)</td>
</tr>
<tr>
<td>HIV +</td>
<td>1</td>
</tr>
<tr>
<td>HBV +</td>
<td>1</td>
</tr>
<tr>
<td>HCV +</td>
<td>2</td>
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</table>
# DONOR CHARACTERISTICS

## Face

<table>
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<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46 (17-65)</td>
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<tr>
<td>Sex</td>
<td>18 M/5 F</td>
</tr>
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<td>Cold preservation</td>
<td>16</td>
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<tr>
<td>Perfusion solution</td>
<td>UW: 13</td>
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<tr>
<td></td>
<td>Celsior: 1</td>
</tr>
<tr>
<td></td>
<td>IGL-1: 2</td>
</tr>
<tr>
<td></td>
<td>Scott: 2</td>
</tr>
<tr>
<td>Cold ischaemia time (hours)</td>
<td>2 (0-6)</td>
</tr>
<tr>
<td>R/D CMV status</td>
<td>-/- 7</td>
</tr>
<tr>
<td></td>
<td>+/- 7</td>
</tr>
<tr>
<td></td>
<td>+/-1</td>
</tr>
<tr>
<td></td>
<td>+/-3</td>
</tr>
<tr>
<td>R/D EBV status</td>
<td>+/-2</td>
</tr>
<tr>
<td></td>
<td>+/-10</td>
</tr>
<tr>
<td></td>
<td>-/-4</td>
</tr>
<tr>
<td></td>
<td>+/-2</td>
</tr>
<tr>
<td>Skin match</td>
<td>Good 17</td>
</tr>
<tr>
<td></td>
<td>Fair 4</td>
</tr>
<tr>
<td>HLA mismatches (n°:pt)</td>
<td>0:1</td>
</tr>
<tr>
<td></td>
<td>1:1</td>
</tr>
<tr>
<td></td>
<td>3:3</td>
</tr>
<tr>
<td></td>
<td>4:6</td>
</tr>
<tr>
<td></td>
<td>5:8</td>
</tr>
<tr>
<td></td>
<td>6:1</td>
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</tbody>
</table>
## DEFICIT

<table>
<thead>
<tr>
<th>Aesthetic units</th>
<th>Bilateral</th>
<th>Single side</th>
<th>Central</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forehead</td>
<td>10</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Brow</td>
<td>19</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Perioral</td>
<td>17</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Cheek</td>
<td>17</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Ear</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Nose</td>
<td></td>
<td></td>
<td>16</td>
</tr>
<tr>
<td>Upper lip</td>
<td></td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>Lower lip</td>
<td></td>
<td></td>
<td>17</td>
</tr>
<tr>
<td>Chin</td>
<td></td>
<td></td>
<td>17</td>
</tr>
<tr>
<td>Tongue</td>
<td></td>
<td></td>
<td>4</td>
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</tbody>
</table>
## Functional deficit

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Count</th>
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<tbody>
<tr>
<td>Blindness</td>
<td></td>
<td>3</td>
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<tr>
<td>Swallowing</td>
<td>Yes: 3</td>
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</tr>
<tr>
<td></td>
<td>Impaired: 8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No: 6</td>
<td></td>
</tr>
<tr>
<td>Eating</td>
<td>Oral: 7</td>
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</tr>
<tr>
<td></td>
<td>Feeding tube: 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Enteral tube: 6</td>
<td></td>
</tr>
<tr>
<td>Speeching</td>
<td>Normal: 2</td>
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<tr>
<td></td>
<td>Slurred: 11</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unintelligible: 7</td>
<td></td>
</tr>
<tr>
<td>Tracheostomy</td>
<td></td>
<td>16</td>
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<tr>
<td>GRAFTED UNITS</td>
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<tr>
<td>------------------------------------</td>
<td>-----</td>
<td></td>
</tr>
<tr>
<td>Scalp</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Forehead</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Ear</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Upper eyelid</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Lower eyelid</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Lacrimal glands</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Nose</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Cheeks</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Upper lip</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Lower lip</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Tongue</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Chin</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Neck</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Salivary glands</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simultaneous face and bilateral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>upper extremity Tx in 2 cases</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Facial bones in 13 cases; Pharynx,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>infraorbital floor, hard palate,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>toothed mandible</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FACE
INDUCTION THERAPY

TACROLIMUS: 11
MMF: 13
TOPICAL TAC: 3
TOPICAL STEROID: 1

STEROID (intraoper.): 100 mg
STEROID (7 d): 50 mg (20-70)
STEROID (14 d): 20 mg (10-40)
STEROID (30 d): 10 mg (10-50)
FACE MAINTENANCE THERAPY

At 3 months

- Steroids: all patients but one
- Tacrolimus: all patients
- Mycophenolate mofetil: all patients but one

In the follow-up:

- Switch from tacrolimus to sirolimus: 3 patients
- Steroid-free treatment: 6 patients
- MMF withdrawal and sirolimus + tacrolimus: 1 patient
- MMF withdrawal: 3 patients
EPISODES OF ACUTE REJECTION

face

Banff score 2-3
Therapy of AR episodes

- IV Steroids
- ATG
- Campath 1H
- Topical immunosuppressants
- Increase in immunosuppressant oral dose
- Extracorporeal photochemotherapy
SIDE-EFFECTS

Face

Opportunistic infections

- CMV reactivation: 2
- Herpes virus: 6
- EBV infection: 1
- Mycosis: 2
- Bacterial infection: 10
  - 2 facial cellulitis
  - 1 pneumopathy
  - 1 pneumonia with sepsis (acute ischaemia of grafted hands)
- 1 sepsis
- Clostridium difficileis colitis

Metabolic complications:

- Hyperglycemia: 3 (requiring insuline)
- Increased creatinine values: 4

Other:

- Deep venous thrombosis: 1

Prophylaxis

Antibiotics: 16 patients (7d-60 mo)
Gancyclovir: 14 patients (1 week-12 mo)
Candida: 11 patients (1-6 mo)
Pnumocystis carinii: 15 patients (3-12 mo)
Trimsulfatan Nystatin: 11 patients (1-6 mo)
SIDE-EFFECTS (Face) in the follow-up

**Opportunistic infections**
- Herpes virus: 6
- CMV infection: 2
- EBV: 1 infection
- Pox virus infection: 2
- Bacterial infection: 10  
  - 1 facial cellulitis
  - 1 pneumopathy
  - 1 sepsis

**Metabolic complications:**
- Hypertension: 2
- Increased creatinine values: 6
- Increase in γ-GT values: 1
- Increase in transaminase: 1
- Neutropenia: 1
- PTDM: 2

**Malignancies:**
- PTLD, leyomyosarcoma: 1
- Basal cell carcinoma of recipient face: 1
- Uterus carcinoma: 1
- Pharyngo-laryngeal neoplasia: 1
## FACE
### Daily Activities

<table>
<thead>
<tr>
<th>Activity</th>
<th>2</th>
<th>1</th>
<th>0</th>
<th>-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open and close eyelid R/L</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Nose function</td>
<td>9</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chew</td>
<td>8</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Swallow</td>
<td>10</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Drink</td>
<td>9</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Eat</td>
<td>8</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Speak</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Smile</td>
<td>5</td>
<td>6</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Kiss</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Blow</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

2: No difficulty; 1: mild difficulty; 0: severe difficulty; -1: unable;
FACE
Patient survival

- One patient died (simultaneous face and bilateral hand transplantation) for cerebral anoxia on day 65.
- One patient died for pharyngo-laryngeal neoplasia 3 years after transplantation.
- One patient from China died 2 years after transplantation.
Conclusions

- An immunosuppressive treatment similar to that used in solid organ transplantation allows CTA survival and function;

- We do not know to what extent we can taper the immunosuppressive load in the long-term: can IS decrease induce AR episodes??

- The high rate of AR episodes - if promptly treated - does not seem to adversely influence graft survival. Can the insufficient or absent AR treatment induce ongoing episodes and finally chronic rejection?

- Can several additional surgical procedures favour DSA production and AR episodes??

- Incidence and features of chronic rejection;

- Careful recipient selection and severe follow-up are imperative