



## WELCOME TO THE INTERNATIONAL REGISTRY ON HAND COMPOSITE TISSUE TRANSPLANTATION

The International Registry on Hand and Composite Tissue Transplantation collects detailed information on a voluntary basis from any case of composite tissue allotransplantation.

[> What is the  
IRHCTT?](#)

A joint venture  
between the



International Hand  
and Composite Tissue  
Allotransplantation  
Society



The  
**Transplantation**  
Society

### INFORMATION ABOUT THE REGISTRY

The International Registry on Hand and Composite Tissue Transplantation (IRHCTT) was founded in May 2002. The primary purpose of the Registry is to collect information from each case of composite tissue allotransplantation (CTA), as it allows us to know what it is happening in this new field of transplantation. Presently it includes cases of upper extremity and face allotransplantation performed all over the world.

### PRIVACY POLICY

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

### CURRENT UPDATE ON THE WORLD WIDE EXPERIENCE

Current update on the world wide experience



### NEXT MEETINGS

12/06/2012  
**XXIV TTS Congress**  
July 15-19, 2012 Berlin (Germany)

12/06/2012  
**Eleventh Meeting of the  
International Hand and  
Composite Tissue  
Allotransplantation  
Society**  
August 29-31, 2013 Wrocław

**REGISTRY**

[> LOGIN](#)

**[www.handregistry.com](http://www.handregistry.com)**



# IRHCTT

- 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  
Ningbo, China  
Munich, Germany  
Pittsburgh, USA

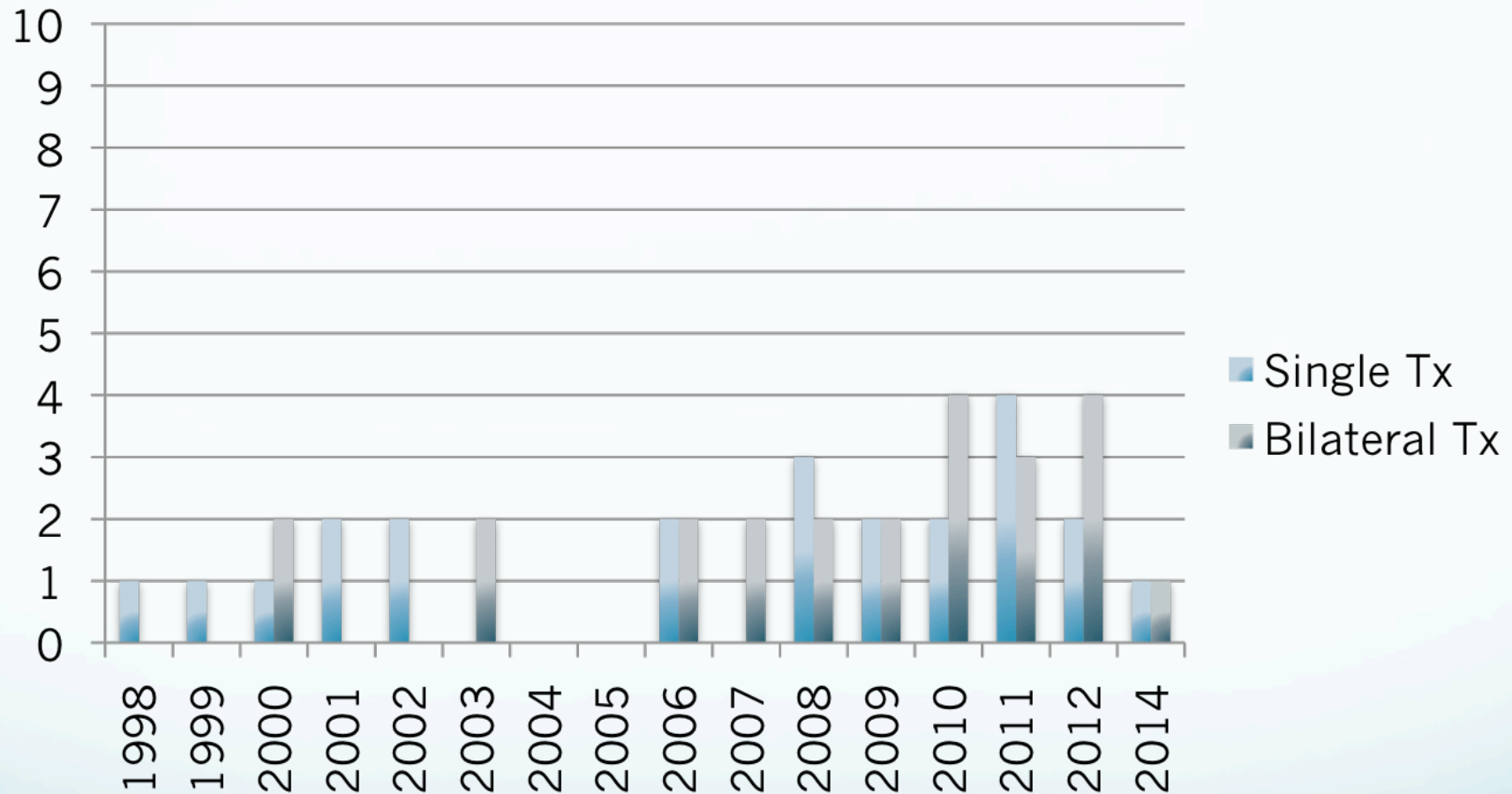


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# IRHCTT-Upper extremity

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

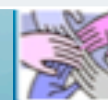


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# HAND RECIPIENT CHARACTERISTICS

Recipients											
Sex	38M/9F										
Race	white										
Age at transplant	37.44 yrs (17-65)										
Time since amputation	2 months to 34 years										
Side of hand loss	24 both			18 right				5 left			
Level of amputation (forearm)	Palmar 13		Wrist 18	Distal forearm 11			Mid forearm 9		Proximal forearm 13		
Level of amputation (arm)	Elbow 1			Mid-arm 2		Proximal arm 2		Distal arm 1			
Type of amputation 19 working injuries	Clean cut 8	Crush 9		Explosion 12		Electric 6		Burn 4	Sepsis 3	Other 3	
R/D CMV status	-/- 17			+/- 11			-/+ 8			+/- 9	
R/D EBV status	-/- 15			+/- 17			-/+ 1			+/- 6	



# HAND DONOR CHARACTERISTICS

Sex	35 M/12F				
Age (years)	31 (15-62)				
HLA mismatch	6 11	5 7	4 7	3 7	2 1
Cold preservation	41				
Perfusion solution	UW: 34	IGL-1: 4	HTK: 3	Custodiol: 2	
Cold Ischaemia time (hours)	5 (30 minutes-12:30)				



# 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**

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

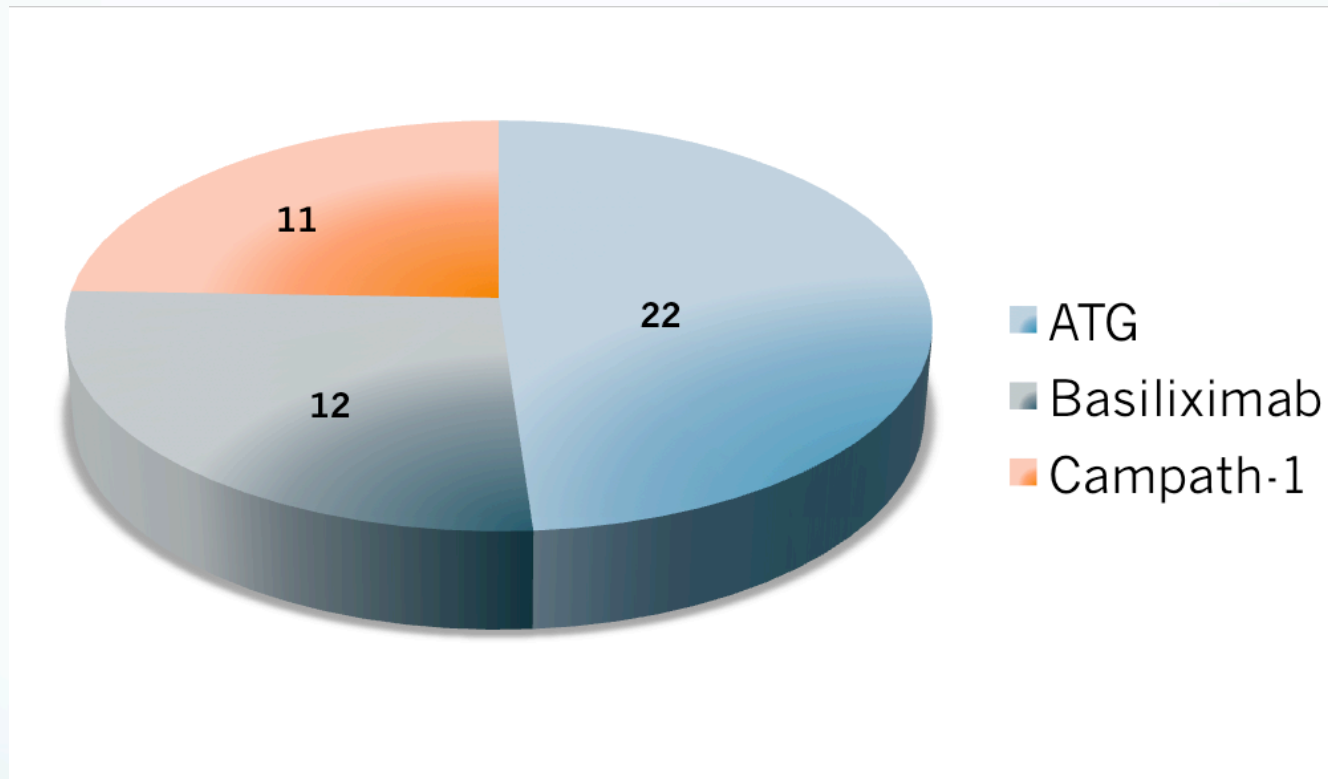
Duration of procedure: 2-21.38 hours (12 hours)



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# 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)

# 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**



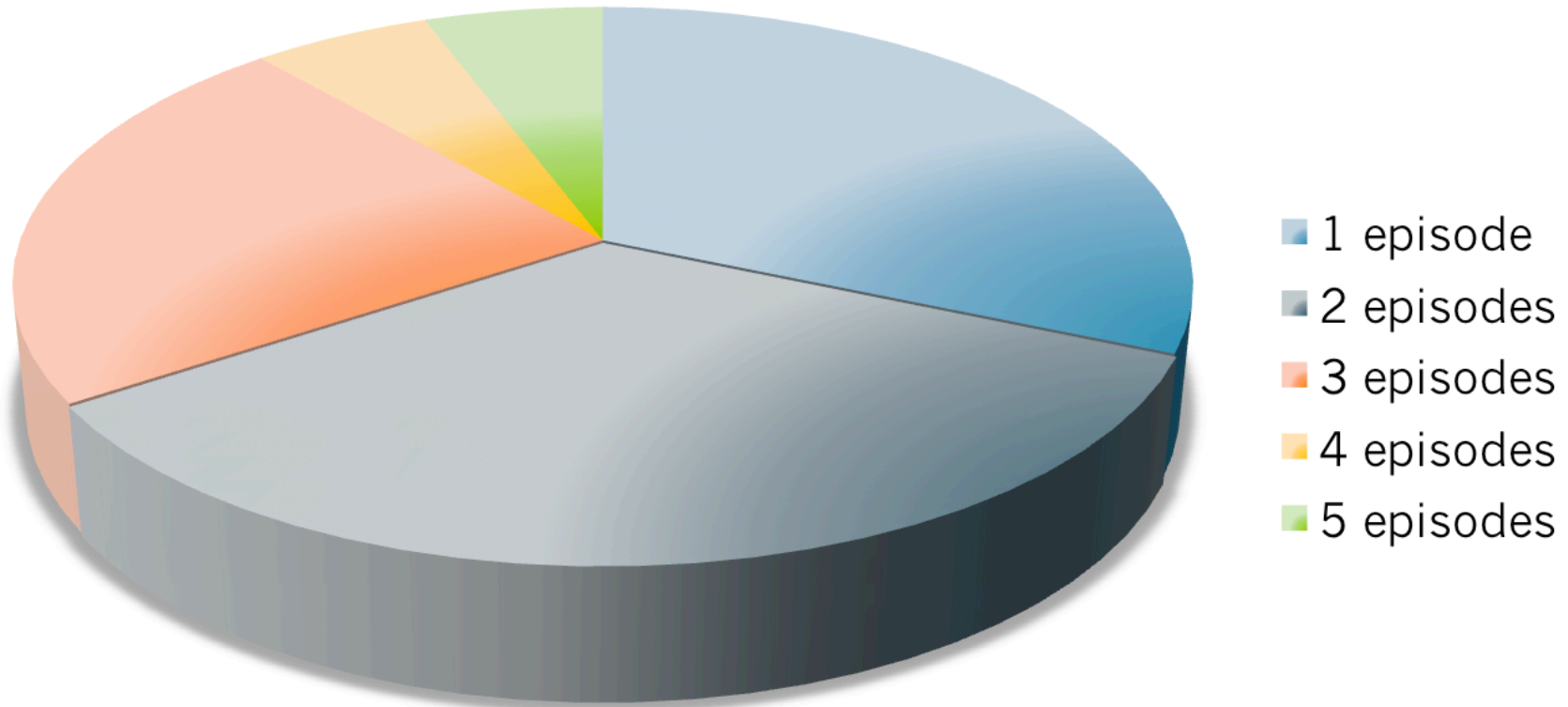
# MAINTENANCE THERAPY

## 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

## Prophylaxis

Antibiotics: 38 patients 10 days (1d-180d)

Gancyclovir: 32 patients 180 days (5d-540d)

Candida: 30 patients 180 days (7d-365d)

Pneumocystis carinii: 30 patients 180 days (10d-365d)

Trim sulfatan Nystatin: 22 patients (8d-6 mo)

## *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



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# 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

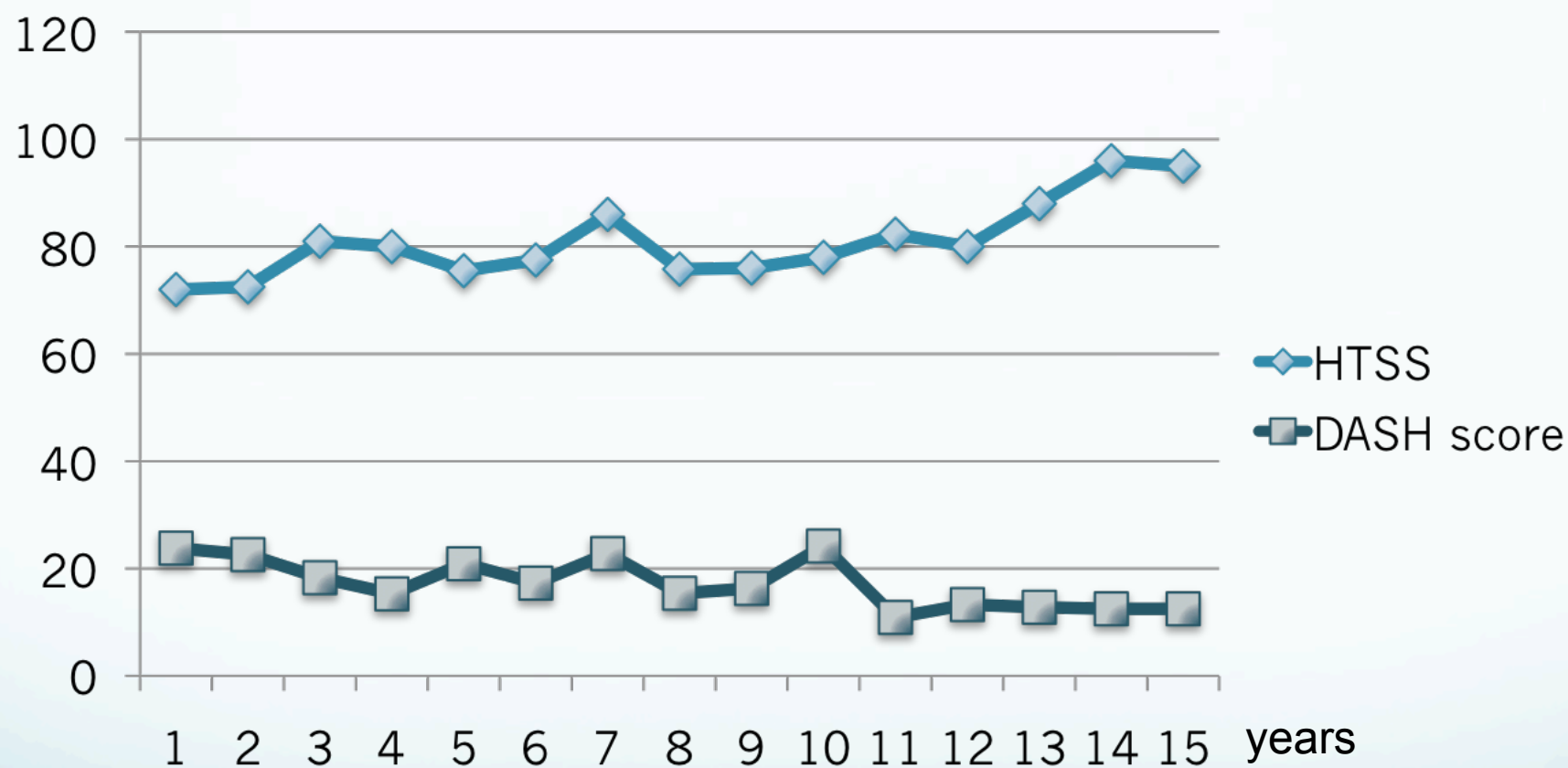
## *Metabolic complications:*

- 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



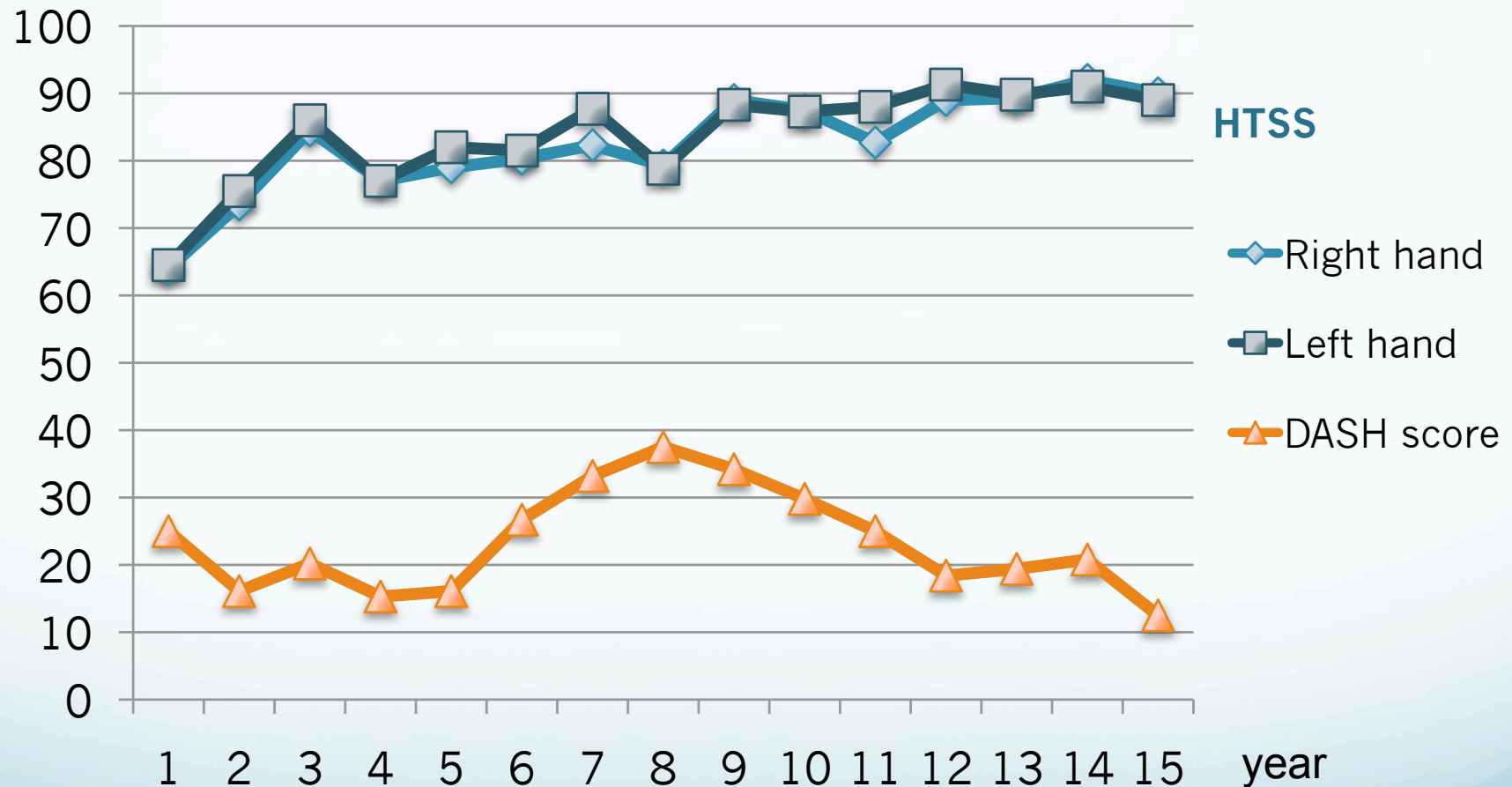
# Functional recovery

## Single hand transplantation

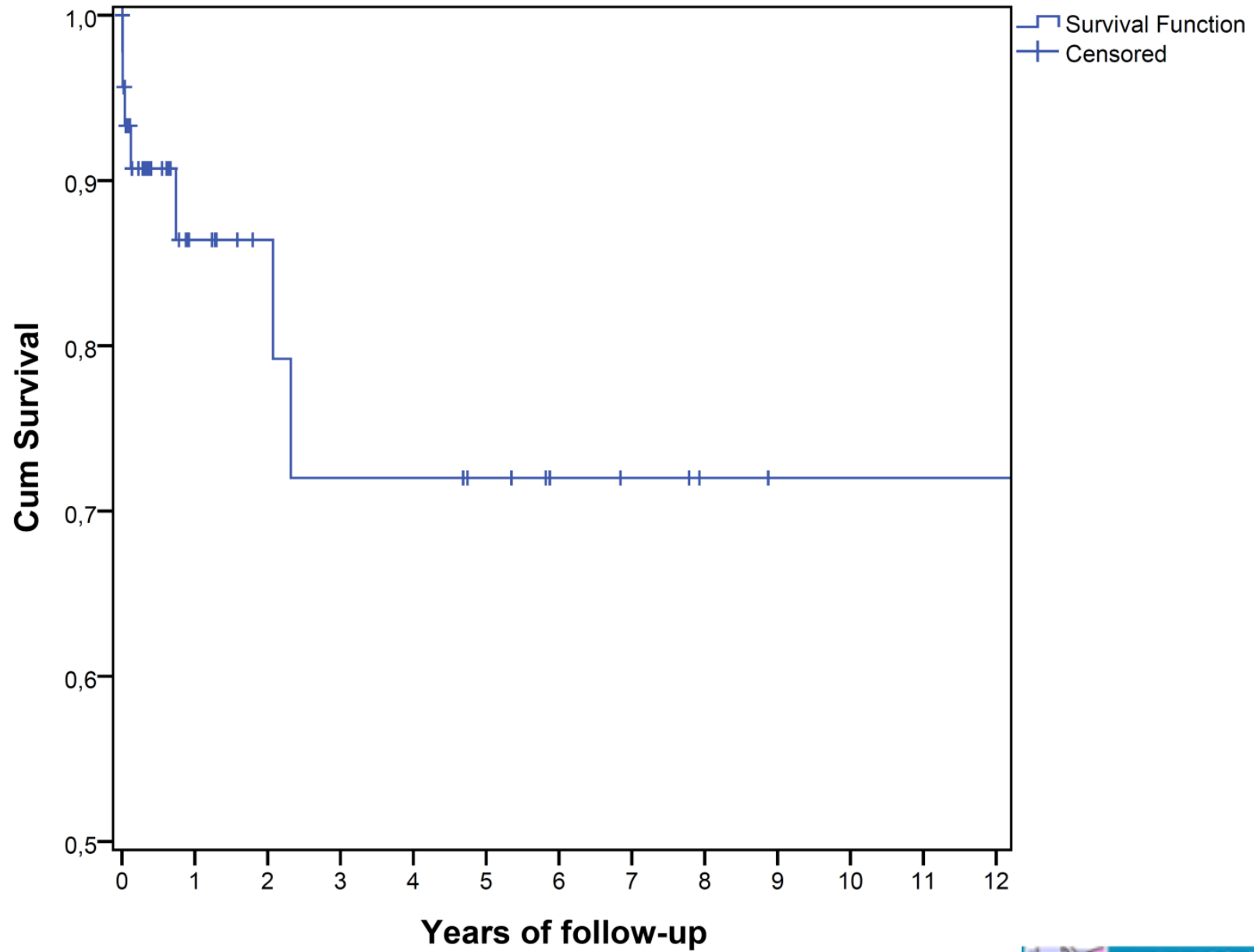


# Functional recovery

## Bilateral hand transplantation



## Graft Survival



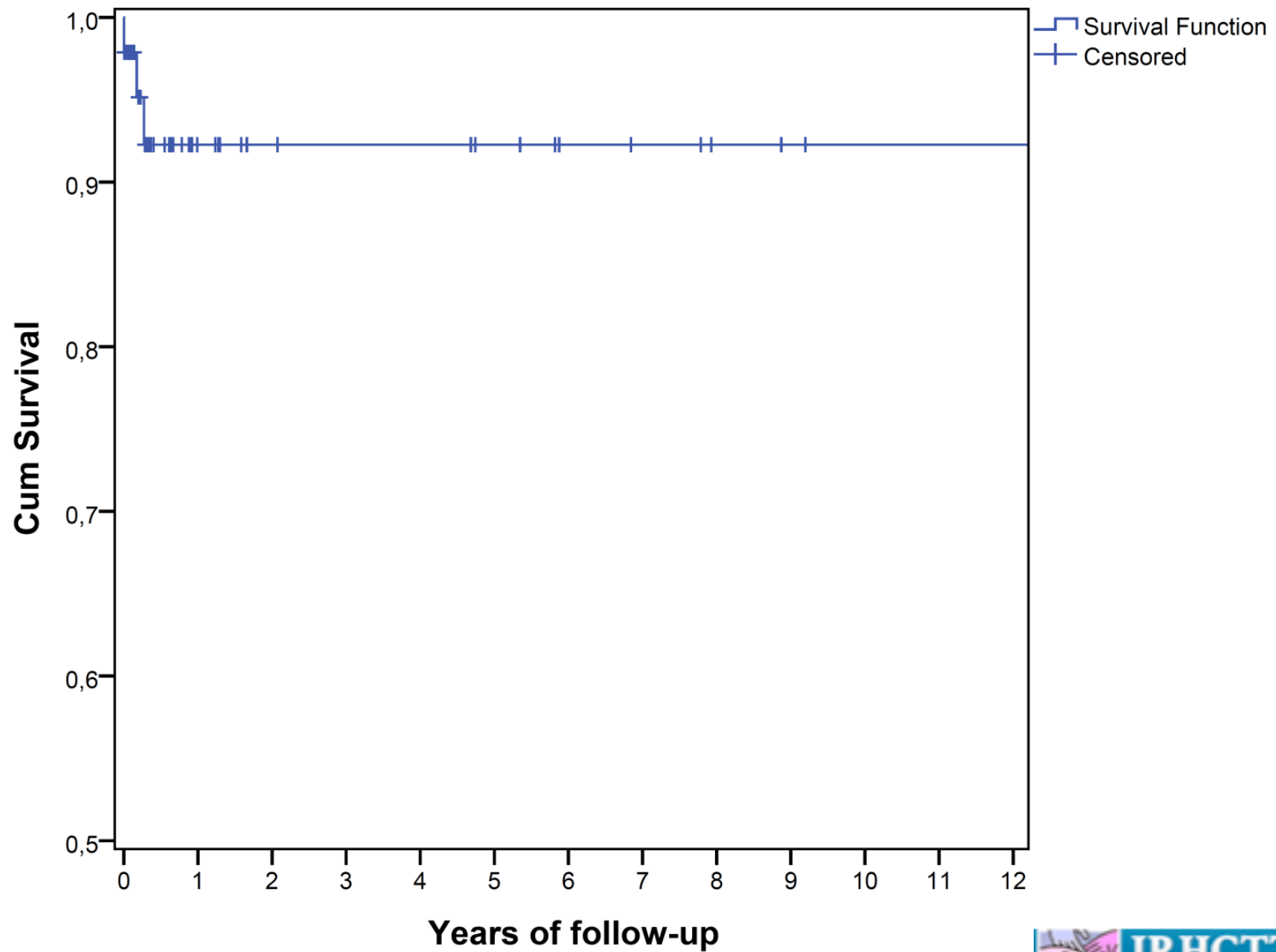
# Graft survival

## 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



# 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

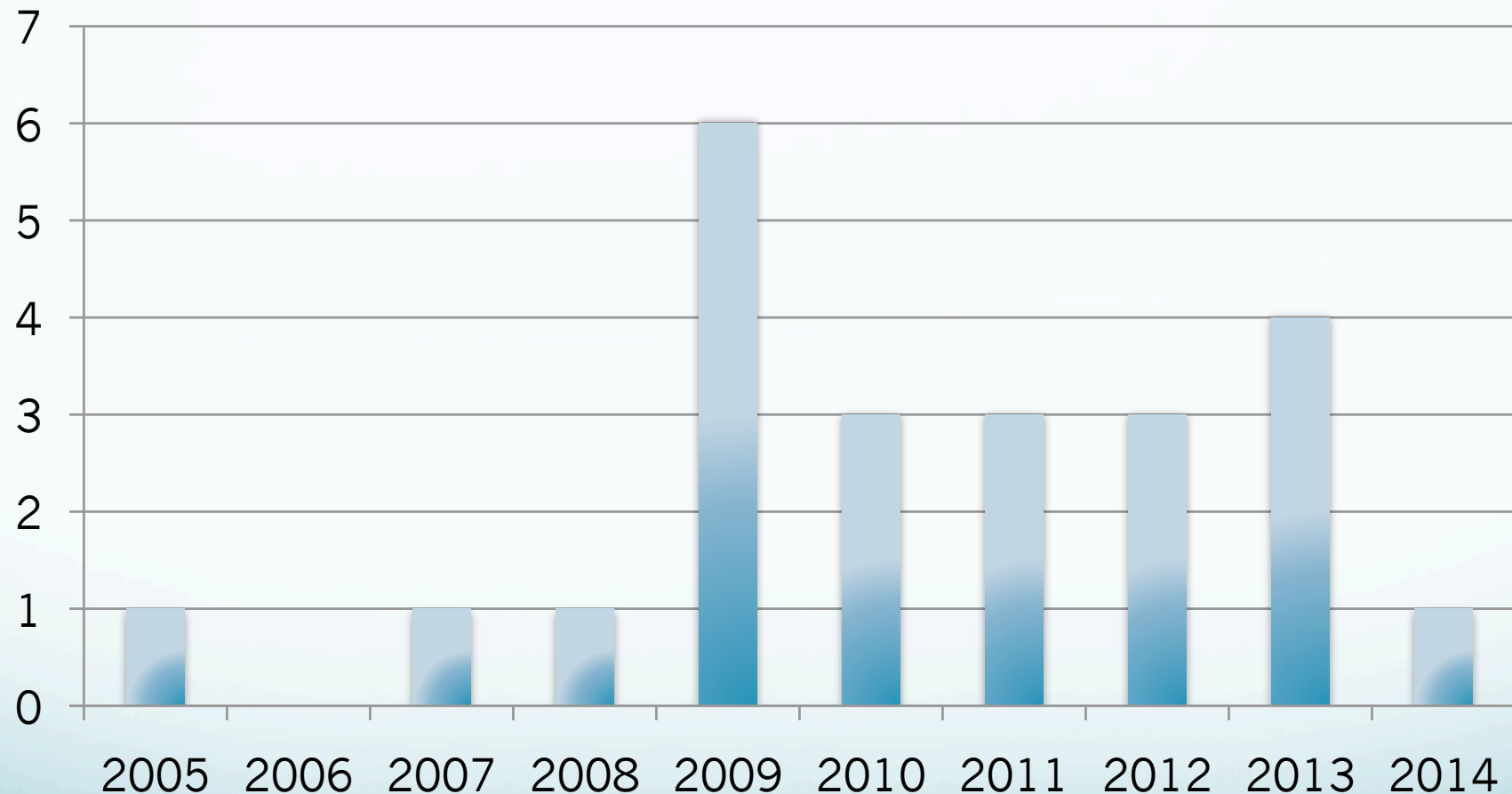


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# IRHCTT-Face

## Follow-up: 4 months-8 years



23 partial or total face allotransplantations



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# RECIPIENT CHARACTERISTICS

## Face

Age (years)	35 (19-59)			
Sex	18 M/5 F			
Race	22 White/1 Black			
Surgery before Tx (n°)	19 patients (3-23)			
Cause of disfiguration	Trauma 12	Congenital 2	Tumor/malformation 2	Burning 7
Time since disfiguration	(4 months-35 years)			
HIV +	1			
HBV +	1			
HCV +	2			



# DONOR CHARACTERISTICS

## Face

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



# DEFICIT

Aesthetic units	Bilateral	Single side	Central
Forehead	10	1	
Brow	19	-	
Perioral	17	2	
Cheek	17	1	
Ear	2	1	
Nose			16
Upper lip			18
Lower lip			17
Chin			17
Tongue			4

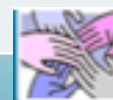


# Functional deficit

Blindness	3
Swallowing	Yes: 3
	Impaired: 8
	No: 6
Eating	Oral: 7
	Feeding tube: 4
	Enteral tube: 6
Speeching	Normal: 2
	Slurred: 11
	Unintelligible: 7
Tracheostomy	16

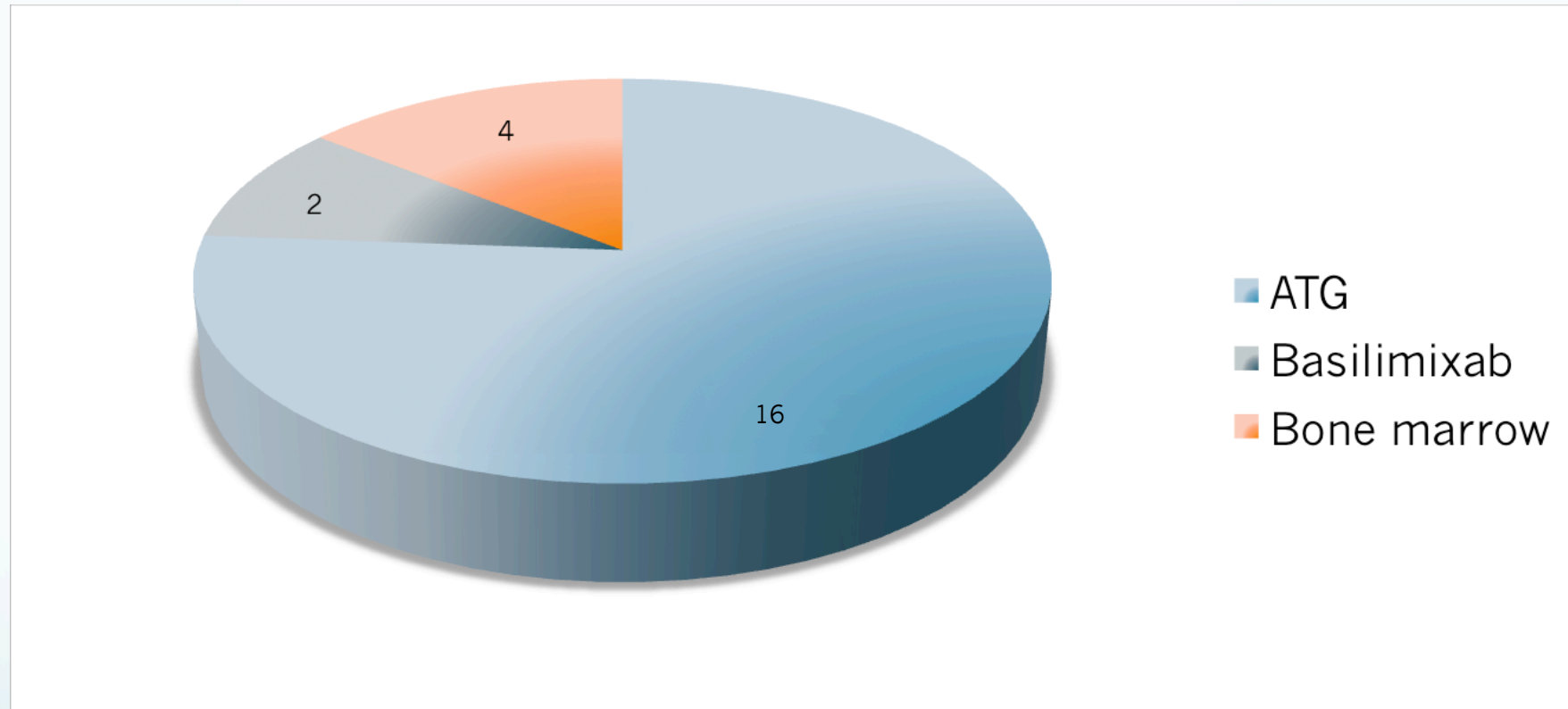


GRAFTED UNITS	
Scalp	6
Forehead	9
Ear	3
Upper eyelid	8
Lower eyelid	9
Lacrimal glands	3
Nose	15
Cheeks	18
Upper lip	17
Lower lip	16
Tongue	2
Chin	16
Neck	13
Salivary glands	10
Other Simultaneous face and bilateral upper extremity Tx in 2 cases	Facial bones in 13 cases; Pharynx, infraorbital floor, hard palate, toothed mandible





# 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)



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# FACE MAINTENANCE THERAPY

At 3 months

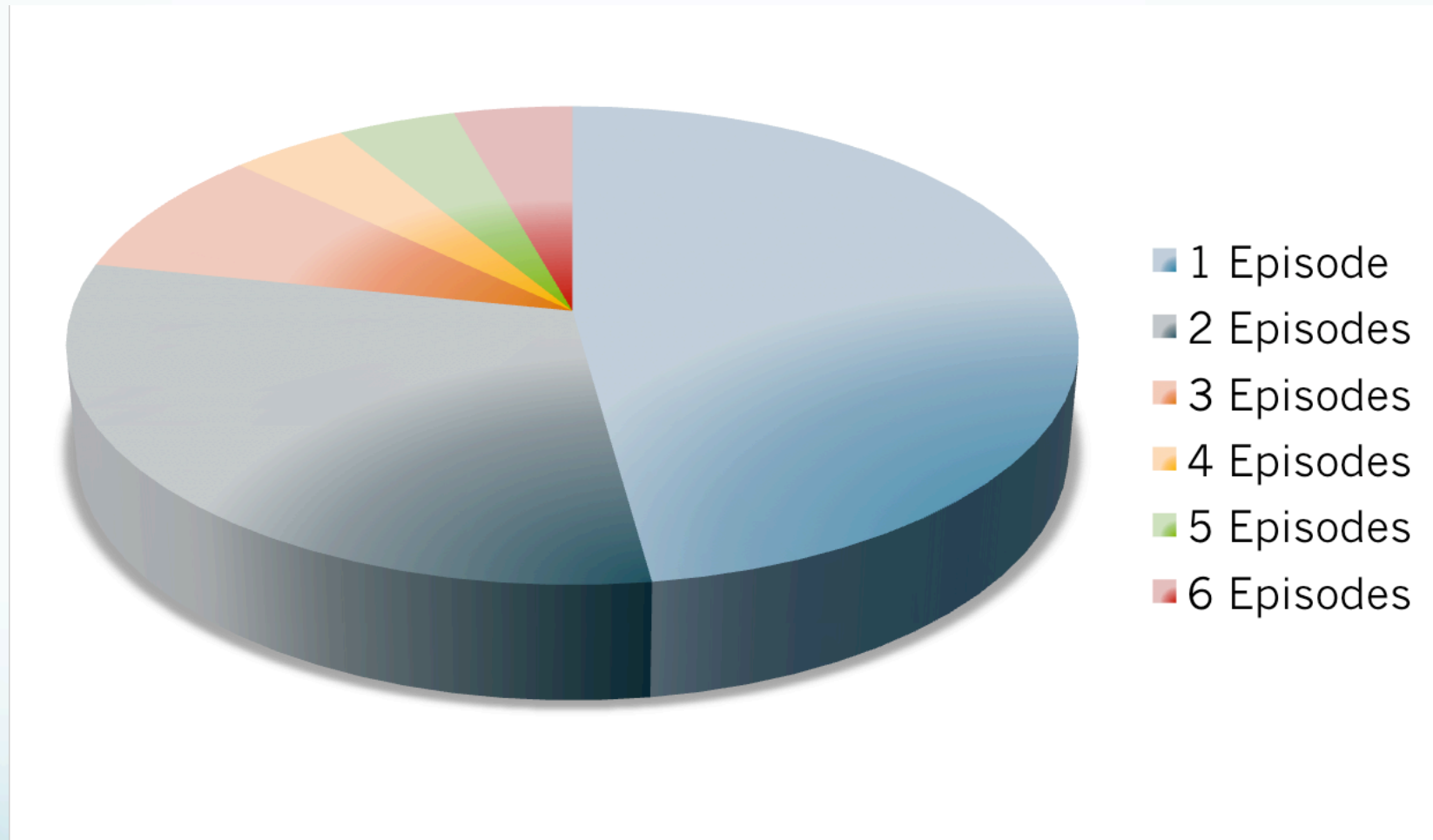
- Steroids: all patients but one
- Tacrolimus: all patients
- Mycophenolate mofetil: all patients but one

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**



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# 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 difficile 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)

Pneumocystis carinii: 15 patients (3-12 mo)

Trim sulfatan 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  $\gamma$ -GT values: 1
- Increase in transaminase: 1
- Neutropenia: 1
- PTDM: 2

## *Malignancies:*

- PTLD, leiomyosarcoma: 1
- Basal cell carcinoma of recipient face: 1
- Uterus carcinoma: 1
- pharyngo-laryngeal neoplasia: 1

# FACE

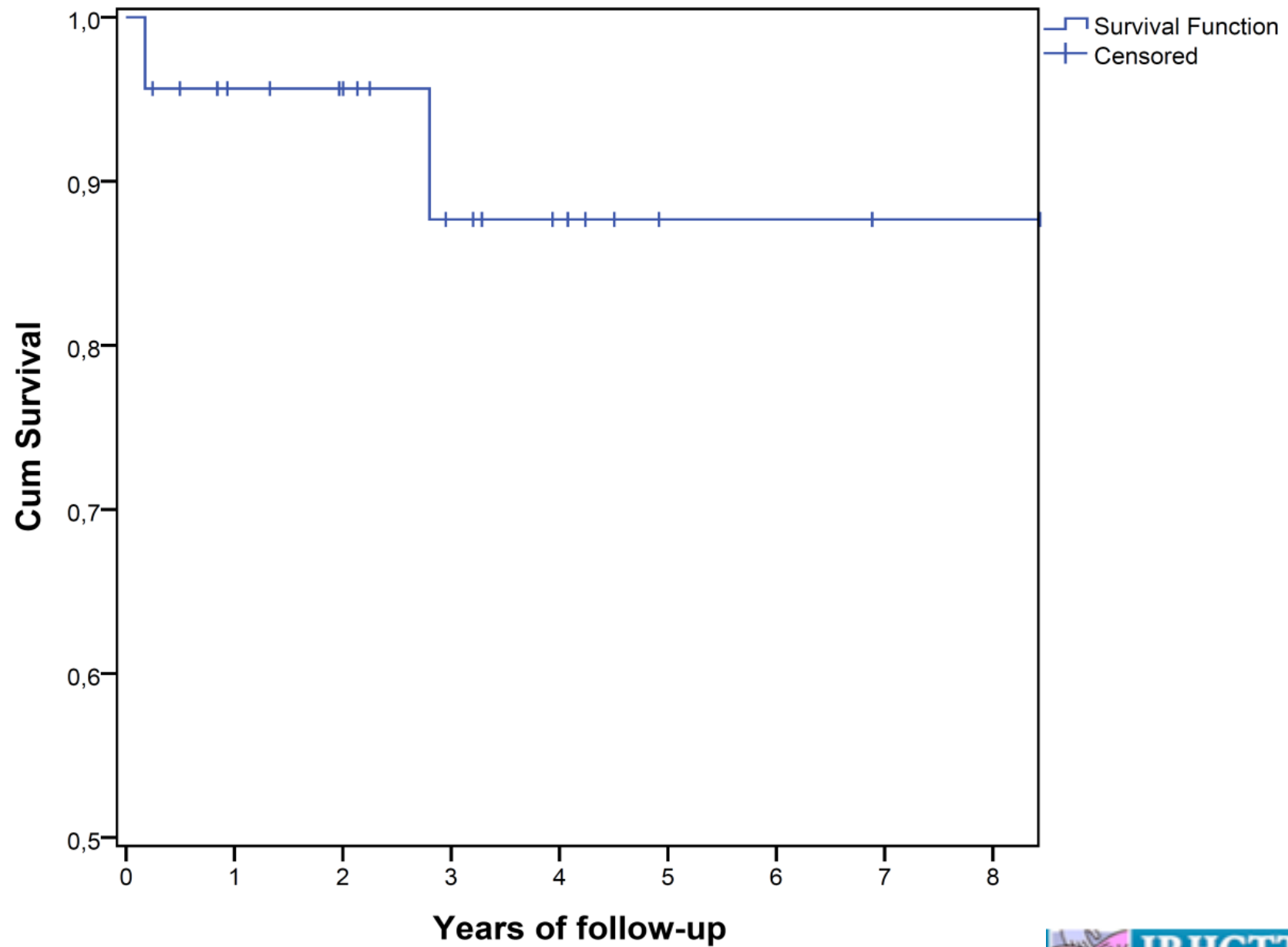
## Daily Activities

	2	1	0	-1
Open and close eyelid R/L	6	3	1	2
Nose function	9	3	0	0
Chew	8	4	1	1
Swallow	10	2	1	1
Drink	9	3	1	1
Eat	8	2	1	1
Speak	3	6	2	2
Smile	5	6	2	2
Kiss	3	4	4	2
Blow	3	4	4	3

2: No difficulty; 1: mild difficulty; 0: severe difficulty; -1: unable;



## Patients Survival



# 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

