Intestinal Transplantation (Itx)

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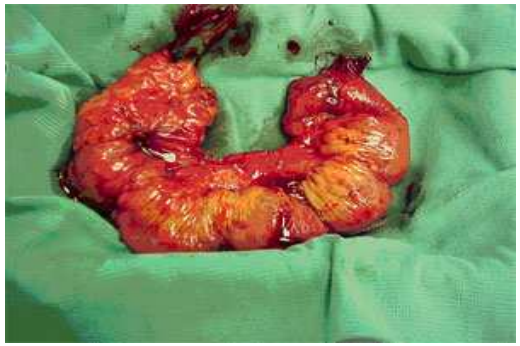
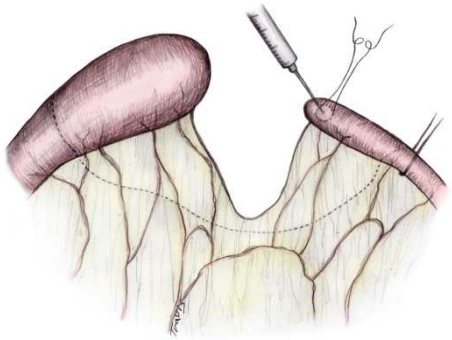
29/10/2009





- short bowel syndrome

Total parenteral nutrition (TPN) = First line treatment of short bowel syndrome

Irreversible Short Bowel Syndrome

And

Severe TPN and/or SBS-related complications:

Consider Intestinal Transplantation

Transplanting the bowel = overcoming adversity

- Naturally **infected** organ
- Particularly sensitive to **rejection**
- **Chronically sick** patients
- **Complex** surgery
- **Immunosuppression**

Intestinal Transplantation (Itx)

- *History*
- *International Registry*
- *UZ Leuven Experience*

Alexis Carrel: First experimental intestinal transplantation early 1920-30

History of clinical ITx

- Pre-Cyclosporine era (60’s 70’s)
- Cyclosporine era (80’ early 90’s)
- Post Cyclosporine (Tacrolimus) era (late 90’s 2000)

Pre CsA era (60's 70's)

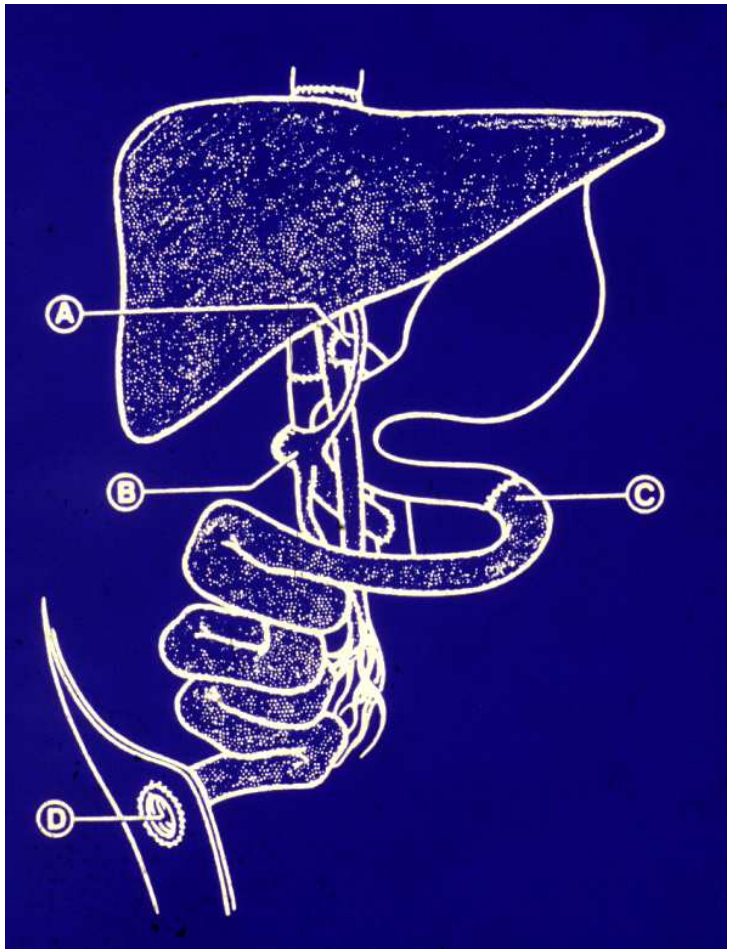
- Kidney Tx successful
- First attempt at ITx Richard Lillehei Minneapolis (1967)
- 8 attempts: all failed
  - Technical
  - Rejection
  - Infection
  - Suspicion of GVHD?
- Poor results
- Decreased interest
- Development of TPN

Cyclosporine A era (80’s early 90’s)

- Liver, heart Tx became clinical reality
- New interest in ITx but:

- Deceiving results - poor graft and recipient survival (rejection - infection)
- Many centers abandon ITx programmes

Combined Liver Transplantation



Grant

Lancet 1990

Why is it difficult to transplant the intestine?

Successful intestinal Tx between syngeneic rats

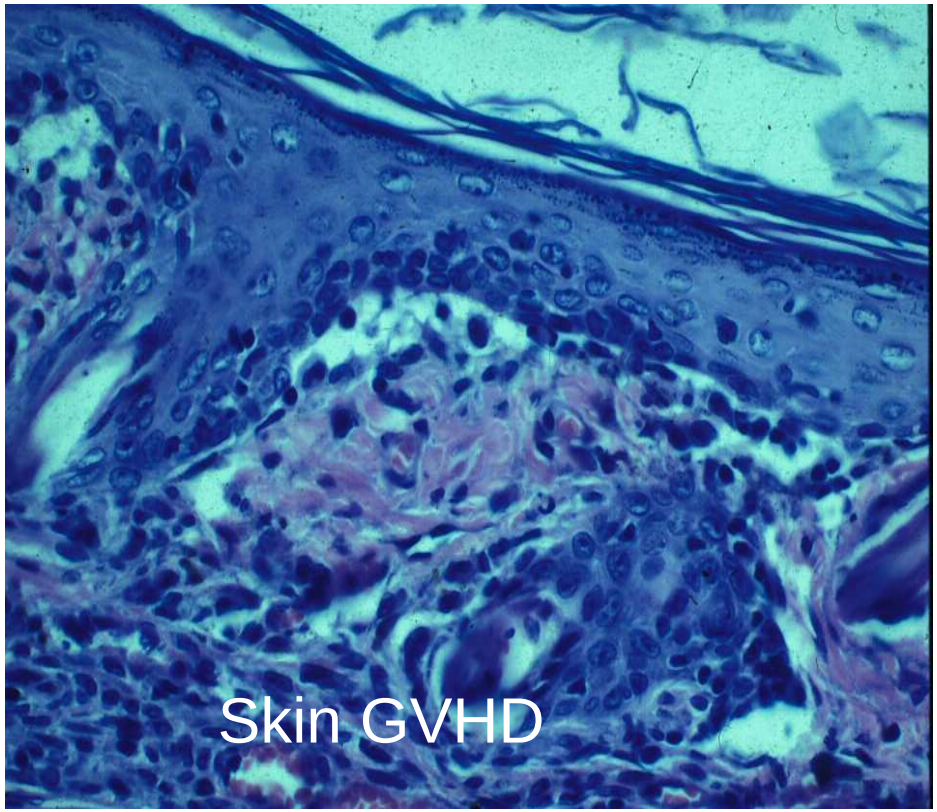
Successful intestinal Tx between identical twins

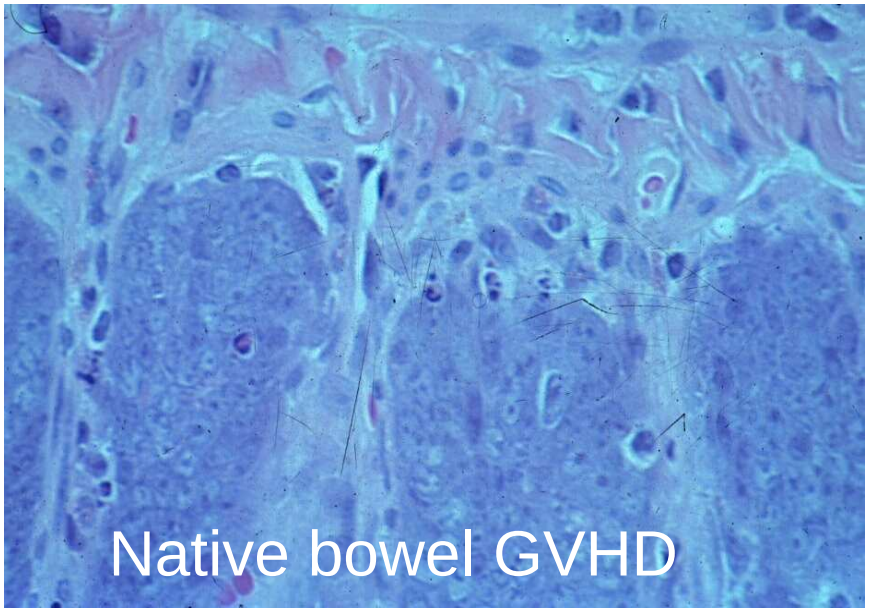
Geneva, Stanford, Chicago 80's 90's

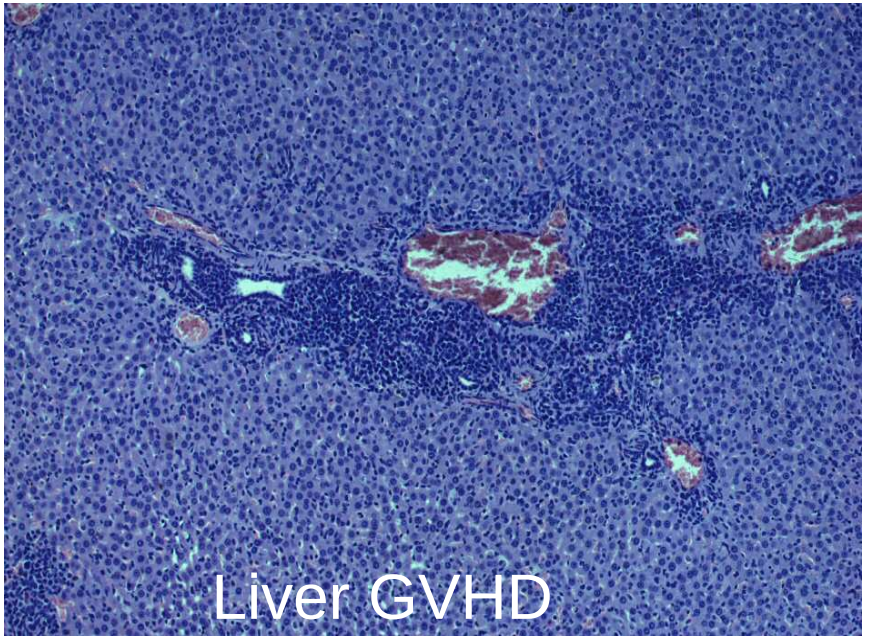
The obstacle to transplantation of the intestine is not physiological but immunological

GVHD

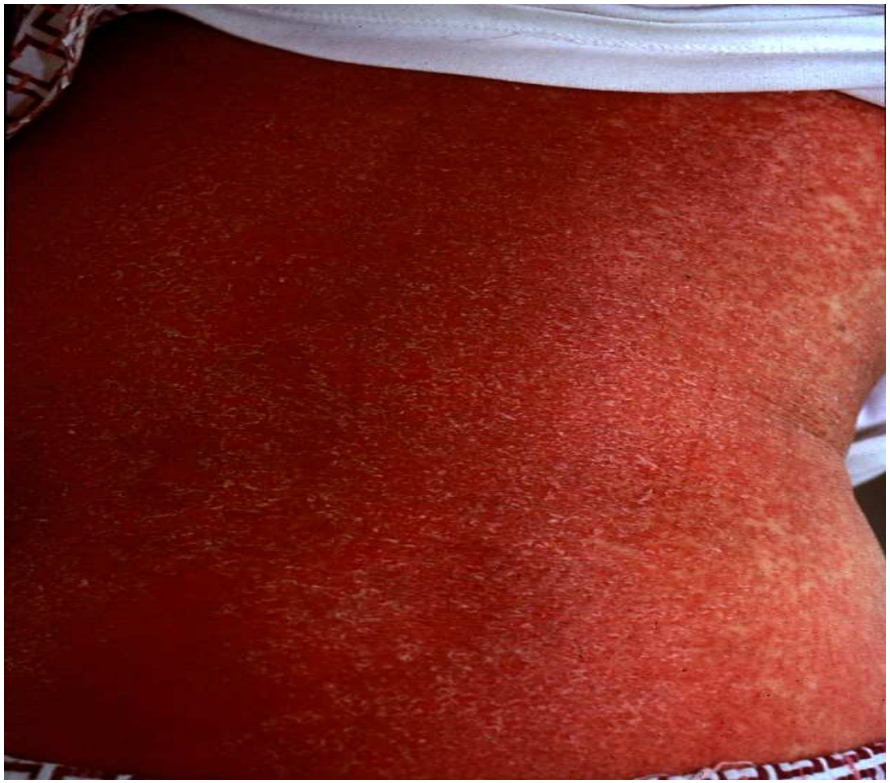
(like after bone marrow Tx)





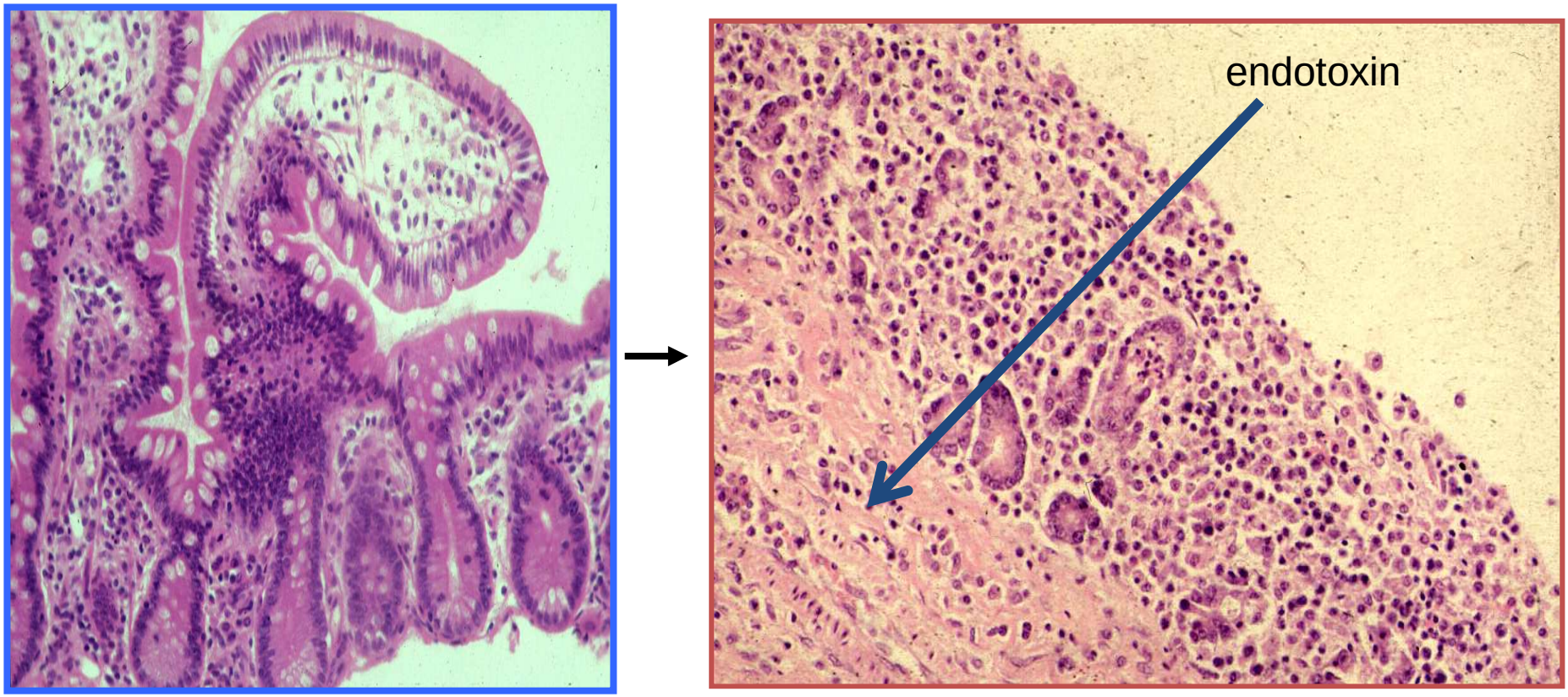


Graft versus Host Disease



Rejection +++

Disappearance of normal mucosal architecture



Hierarchy in susceptibility to rejection

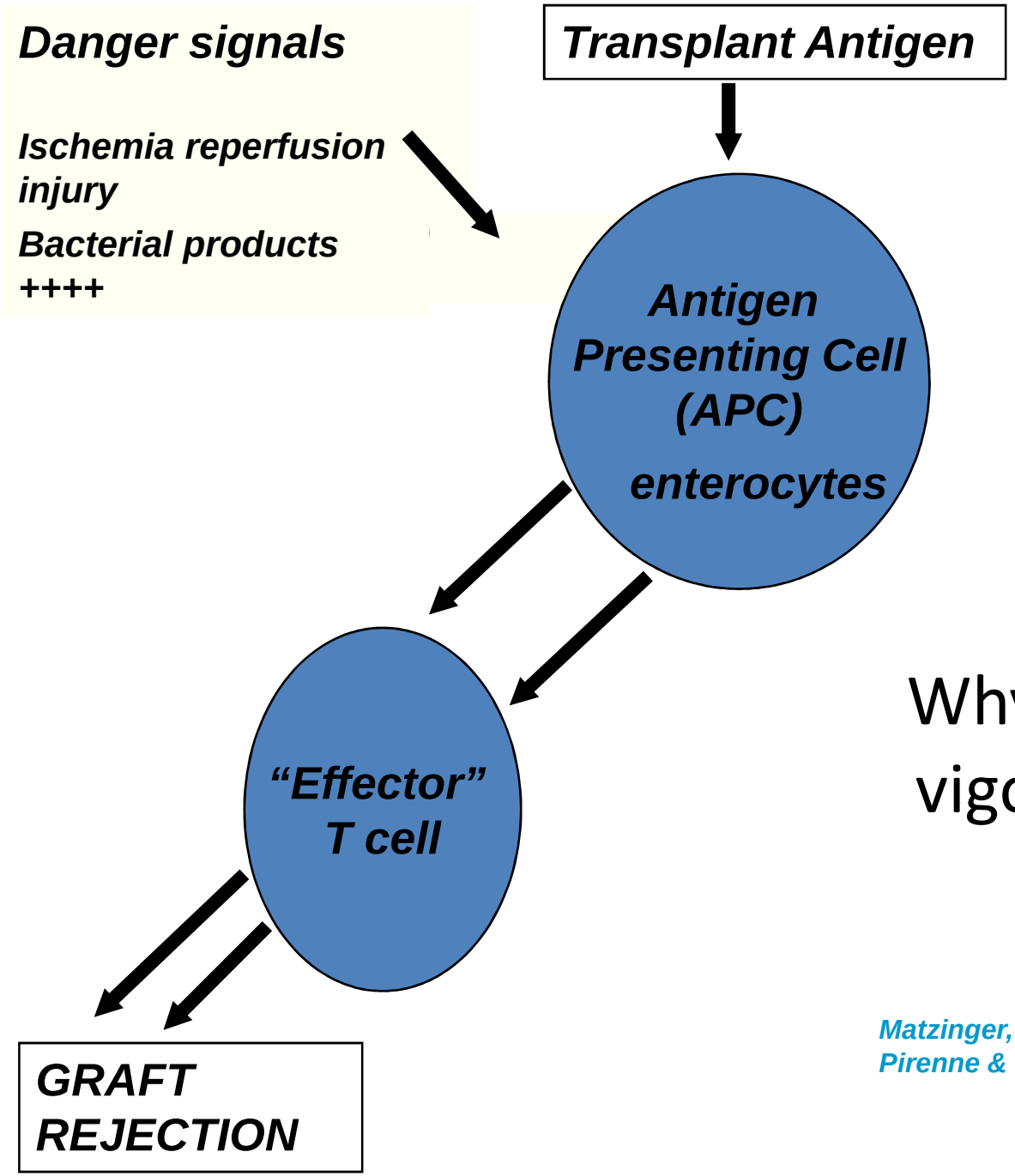
Liver

Kidney

Pancreas

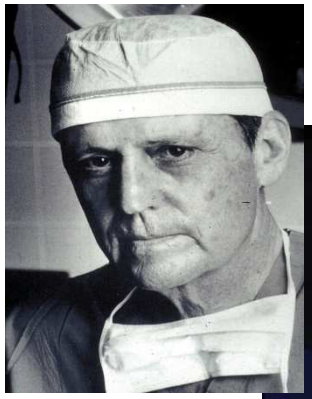
Bowel

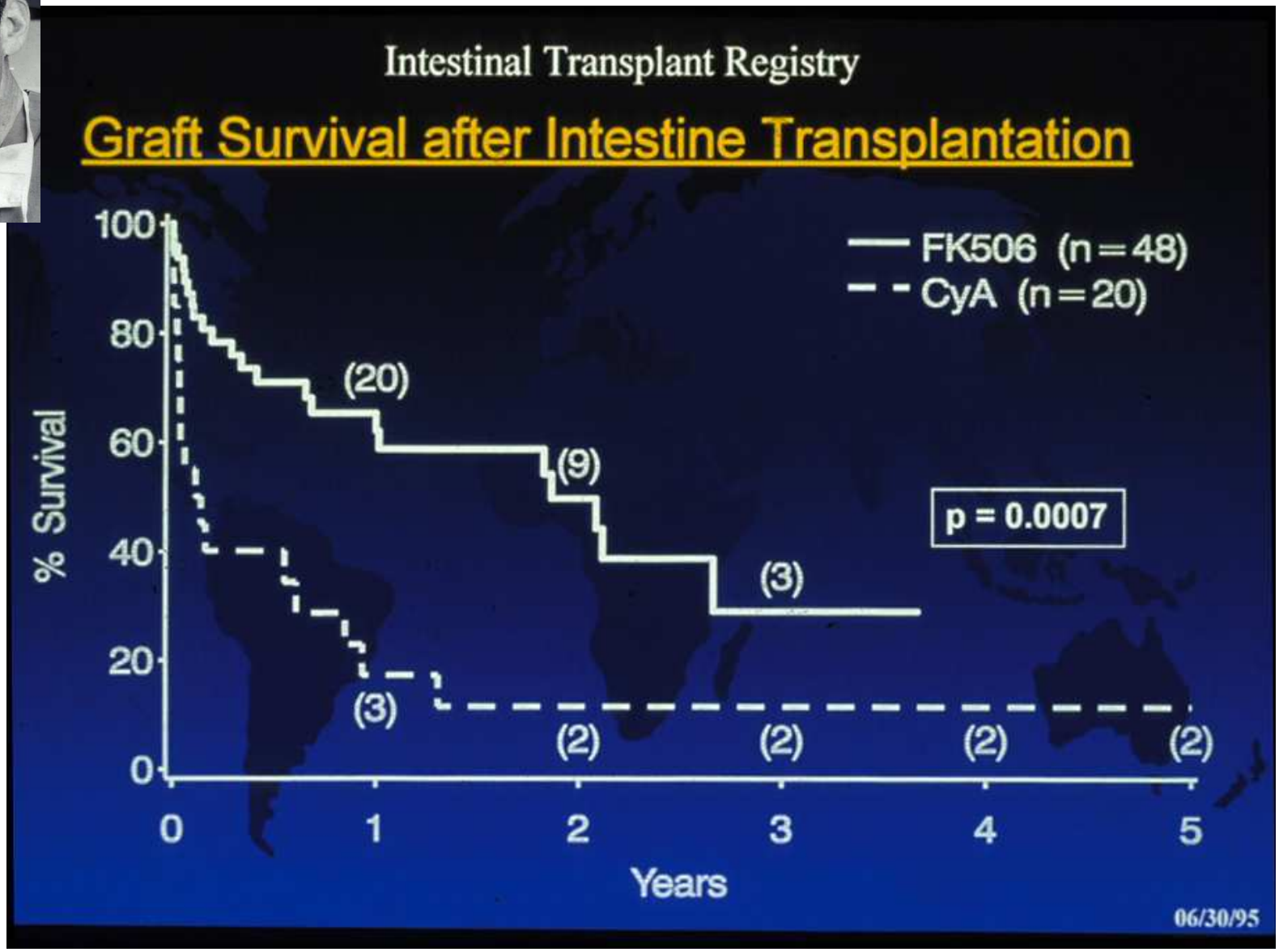
Ileum > jejunum > large bowel / stomach



Why is rejection so vigorous after ITx?

Matzinger, Ann N Y Acad Sci 2002
Pirenne & Kawai, Transplant Immunology 2005




Intestinal Transplant Registry
Graft Survival after Intestine Transplantation
FK506 (n=48)
CyA (n=20)
% Survival
100
80
60
40
20
0
(20)
(9)
(3)
(3)
(2)
(2)
(2)
(2)
p = 0.0007
0
1
2
3
4
5
Years
06/30/95

Indications for Intestinal Transplantation

Irreversible Short Bowel Syndrome

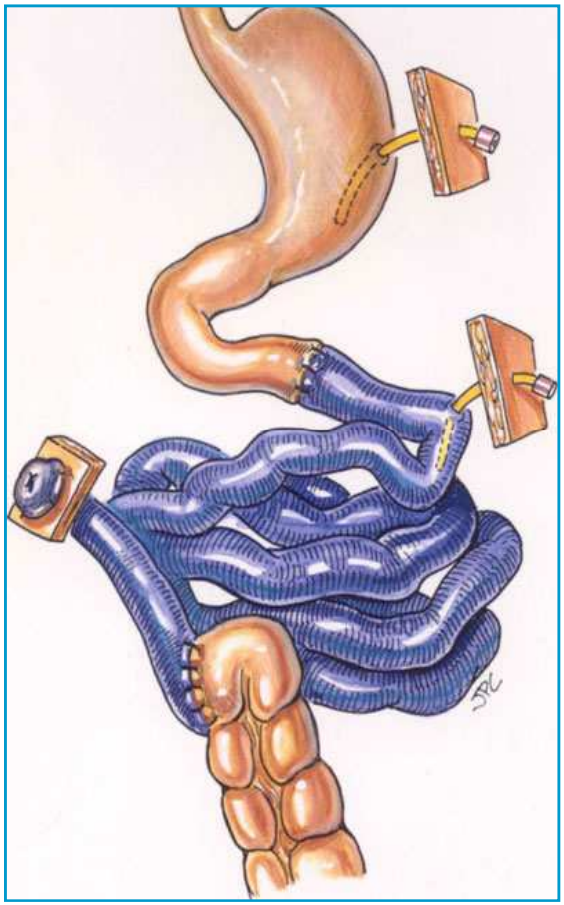
And

Severe TPN and/or SBS-related complications:

- *Liver failure*
- *Shortage venous access*
- *Infection venous access*
- *Major electrolyte disturbances*

Patients in whom the prognosis is better with ITx than TPN

3 types of ITx



Isolated ITx

Liver & Intestinal Tx

Multivisceral Tx

ITx Registry Database Description Intestine transplants April 1985 – May 2007

Number of Centers	73
Number of Transplants	1720
◆ SBT	746
◆ SB/Liv	594
◆ MVT	380
Number of Patients	1608
Current Survivors	909

ITx Participating Countries

Birmingham
Boston (2)
Charleston
Chicago *(4)*
Dallas
Houston
Indianapolis
Iowa City
Kansas City
Los Angeles (2)
Madison
Miami
Minneapolis
New Orleans
New York (2)
Oklahoma City
Omaha
Pittsburgh
Rochester
Seattle
St. Louis
Stanford
Washington, DC

London
Toronto (2)
Edmonton

Torreon

Sao Paulo

Buenos Aires(2)

Medellin

Birmingham
Cambridge
Leeds
London

Brussels
Leuven

Coimbra

Madrid

Göteborg
Stockholm
Uppsala

Paris
Villejuif

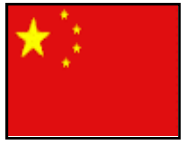
Bergamo
Milano
Rome
Bologna

Neumünster
Tübingen
Berlin, Keil
Cologne

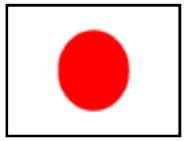
Innsbruck

Geneva

Groningen



Nanjing
Tianjin
Wuhan
Xi'an

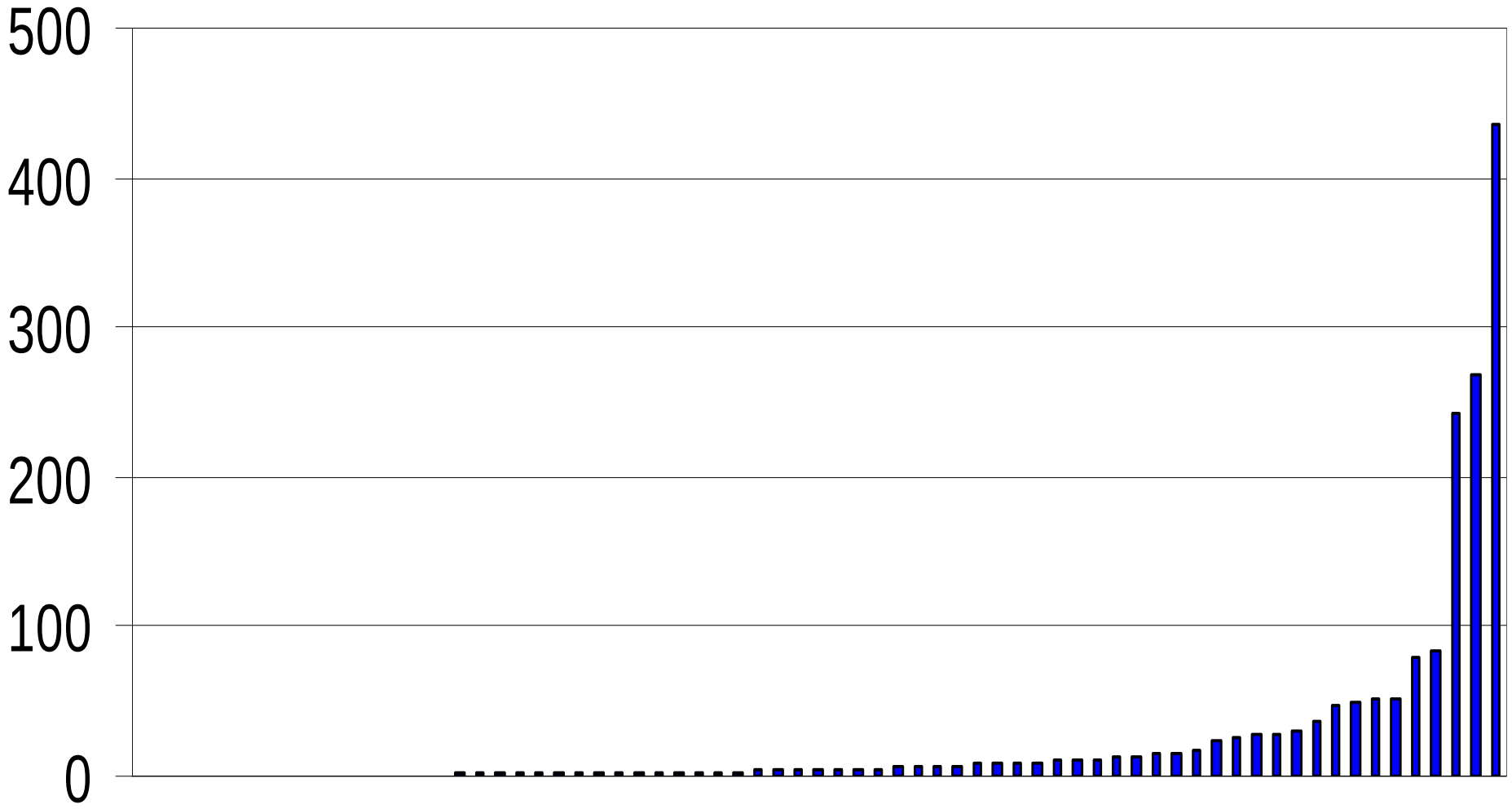


Kyoto
Osaka
Sendai

Santiago

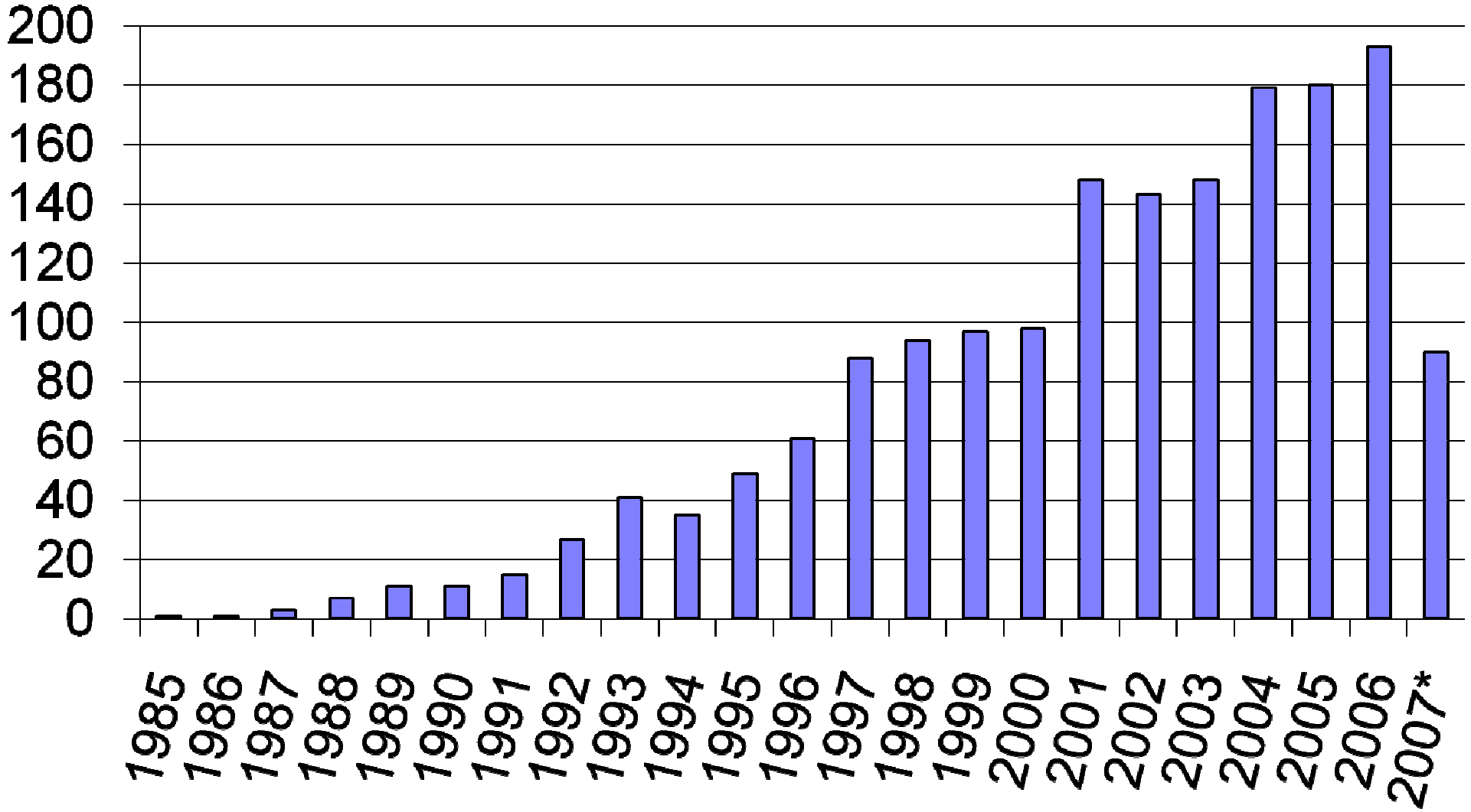
Tehran

69 Participating Programs Ordered by Case Volume



Complete Data Set

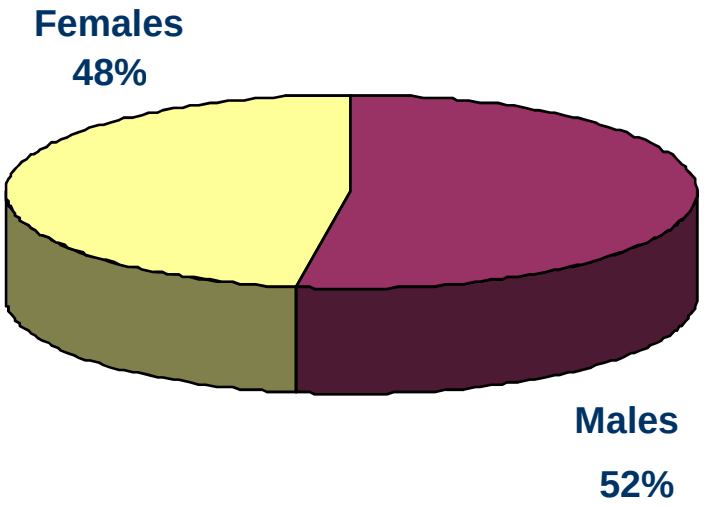
Intestinal Transplants by Year



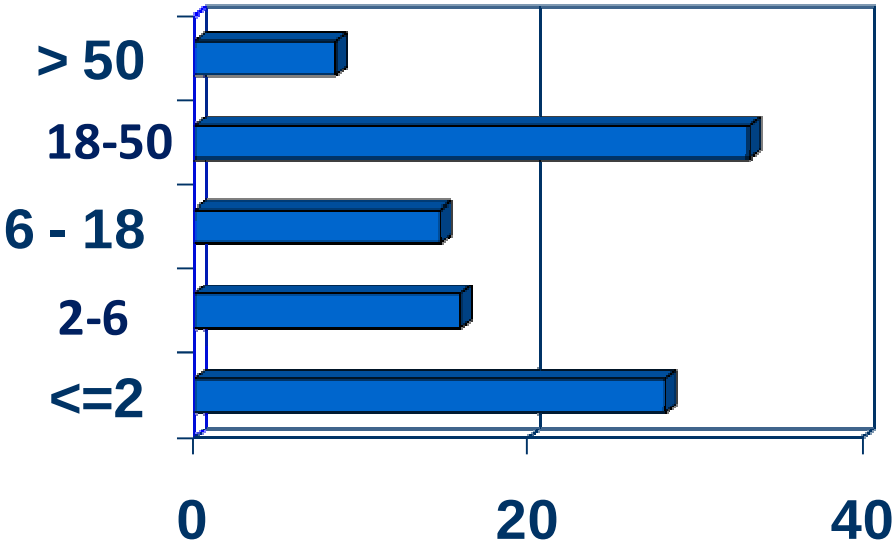
* -Jan 1 to May 31

ITx Demographics

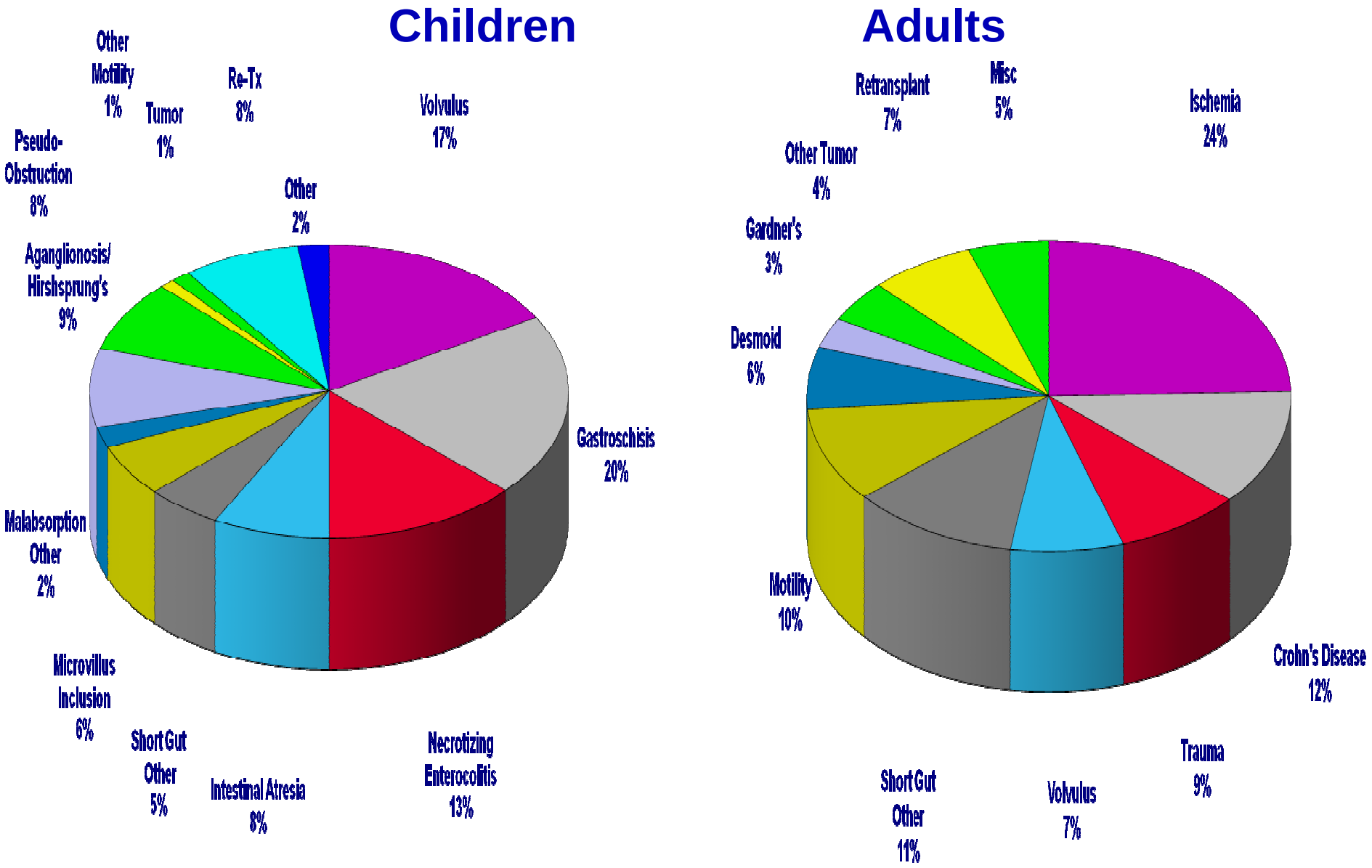
Gender Distribution



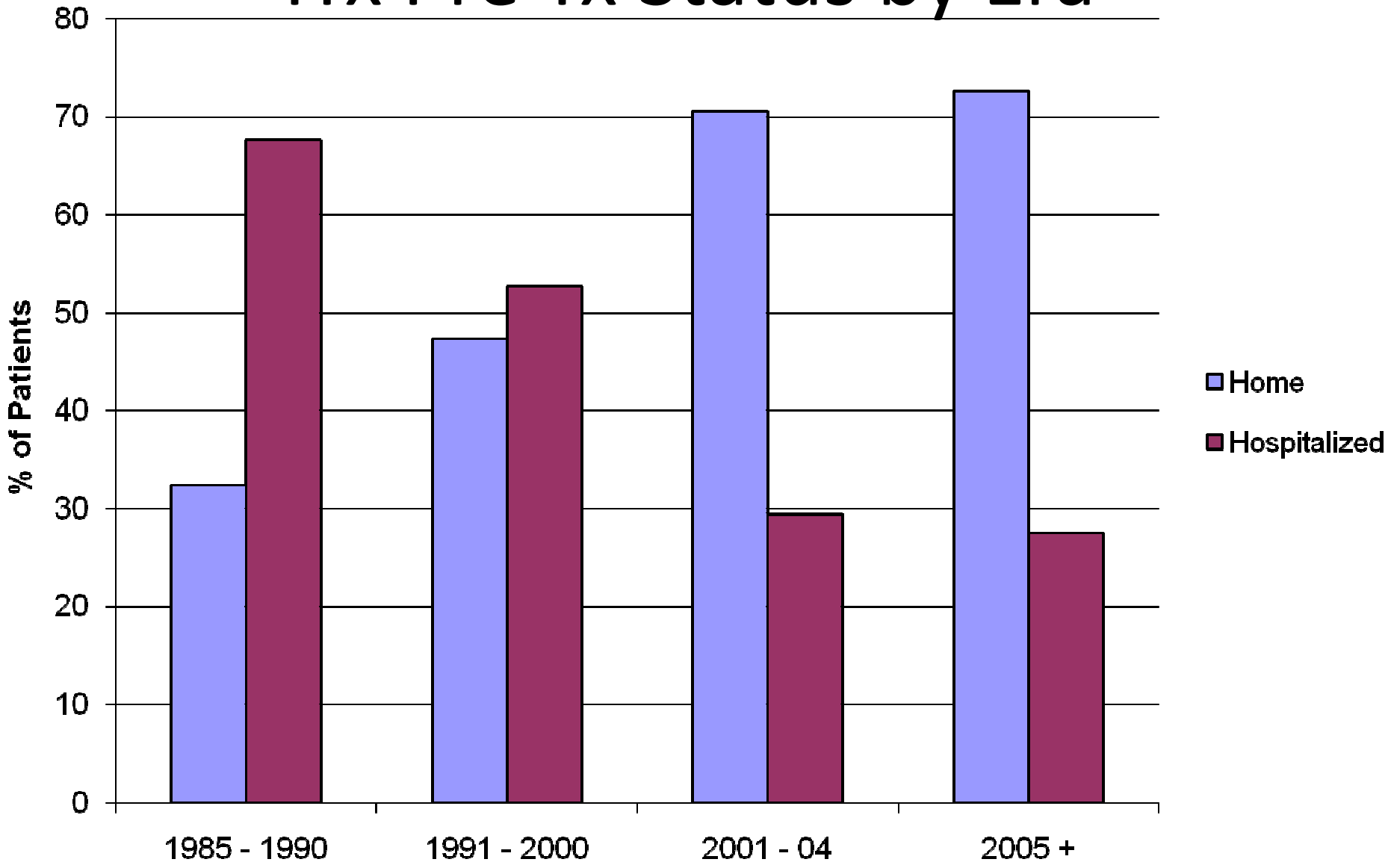
Age at Transplant



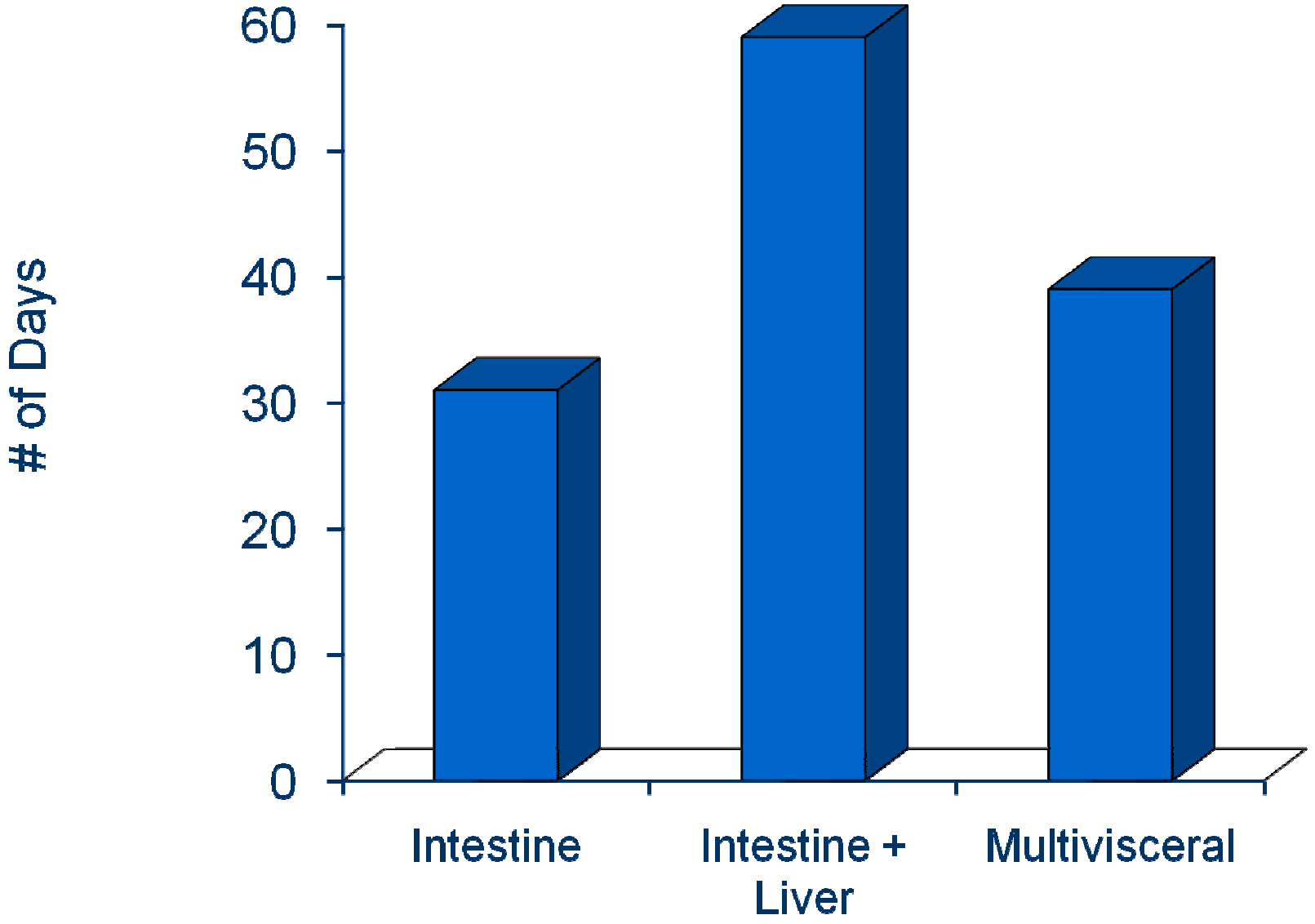
Causes of short bowel syndrome leading to ITx



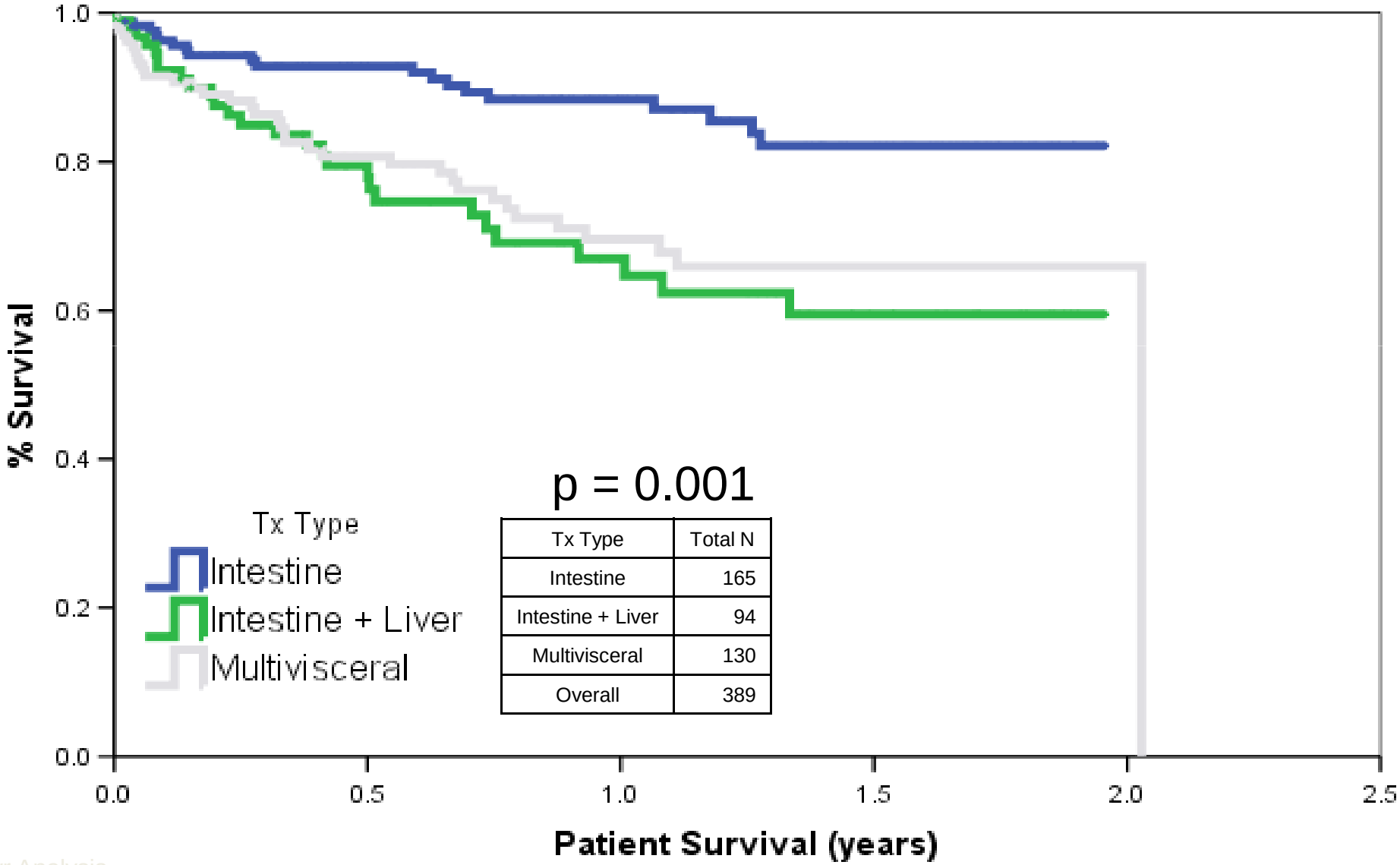
ITx Pre Tx Status by Era



Median Hospital Stay 2005 – 2007



2005-07 Patient Survival - Transplant Type

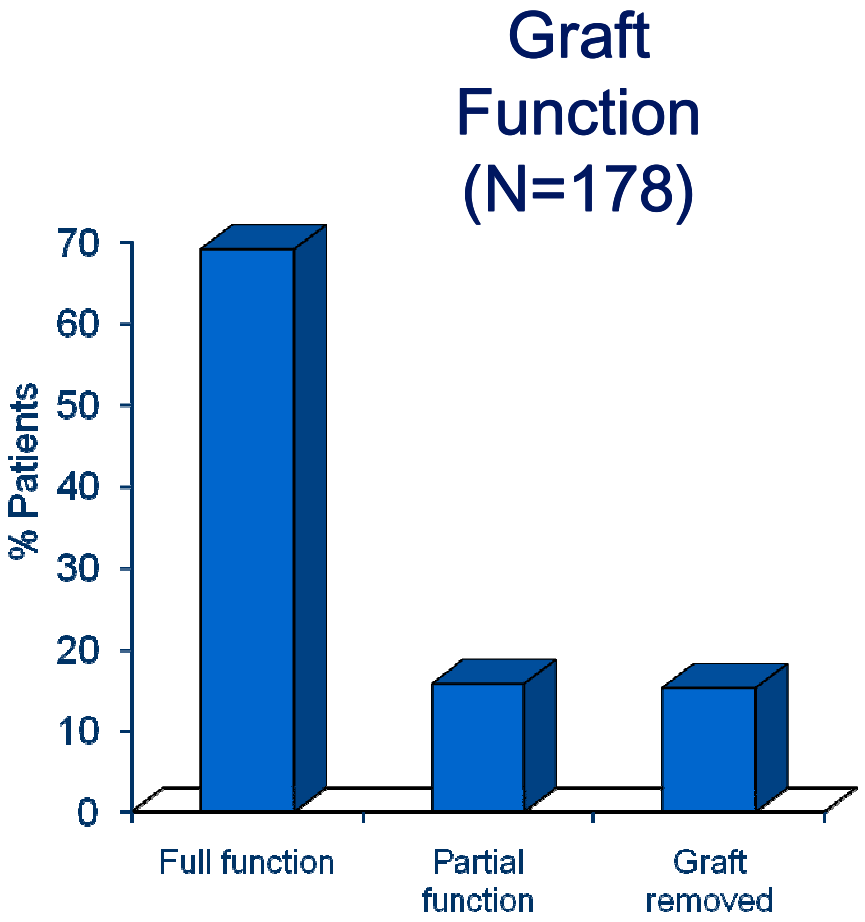


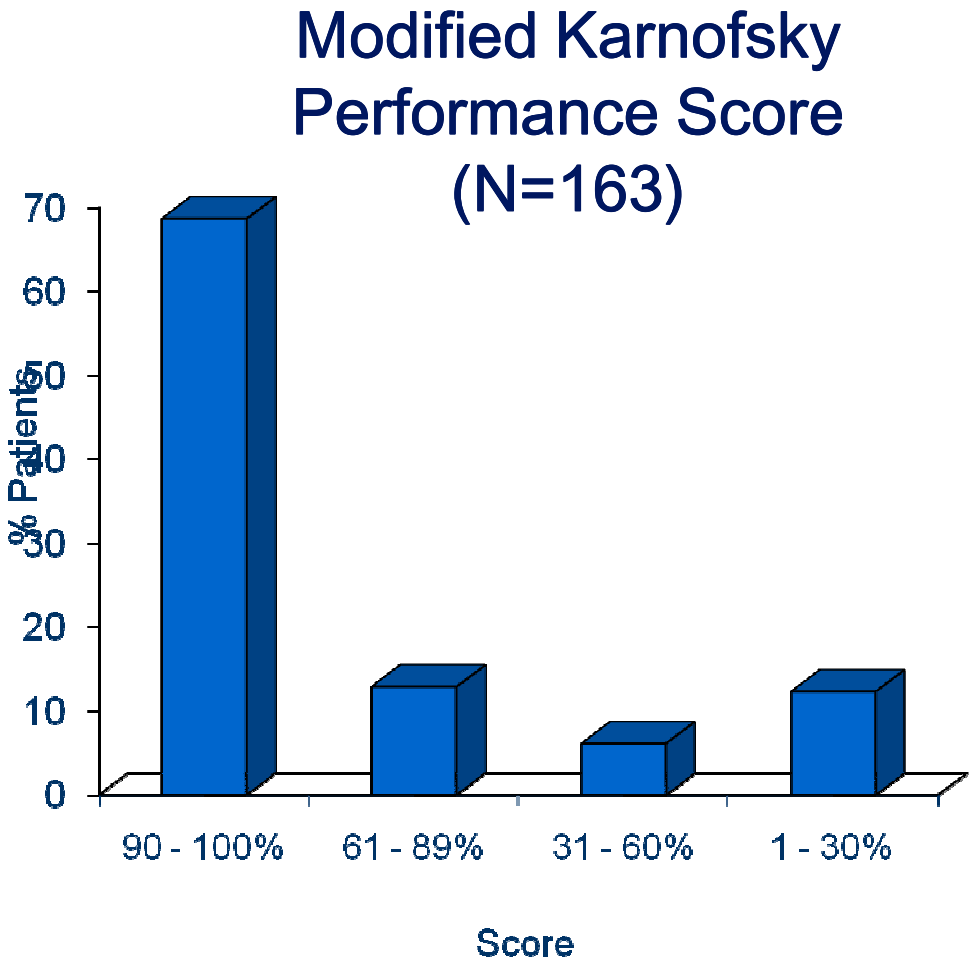
Tx Type	Total N
Intestine	165
Intestine + Liver	94
Multivisceral	130
Overall	389

2 yr Analysis

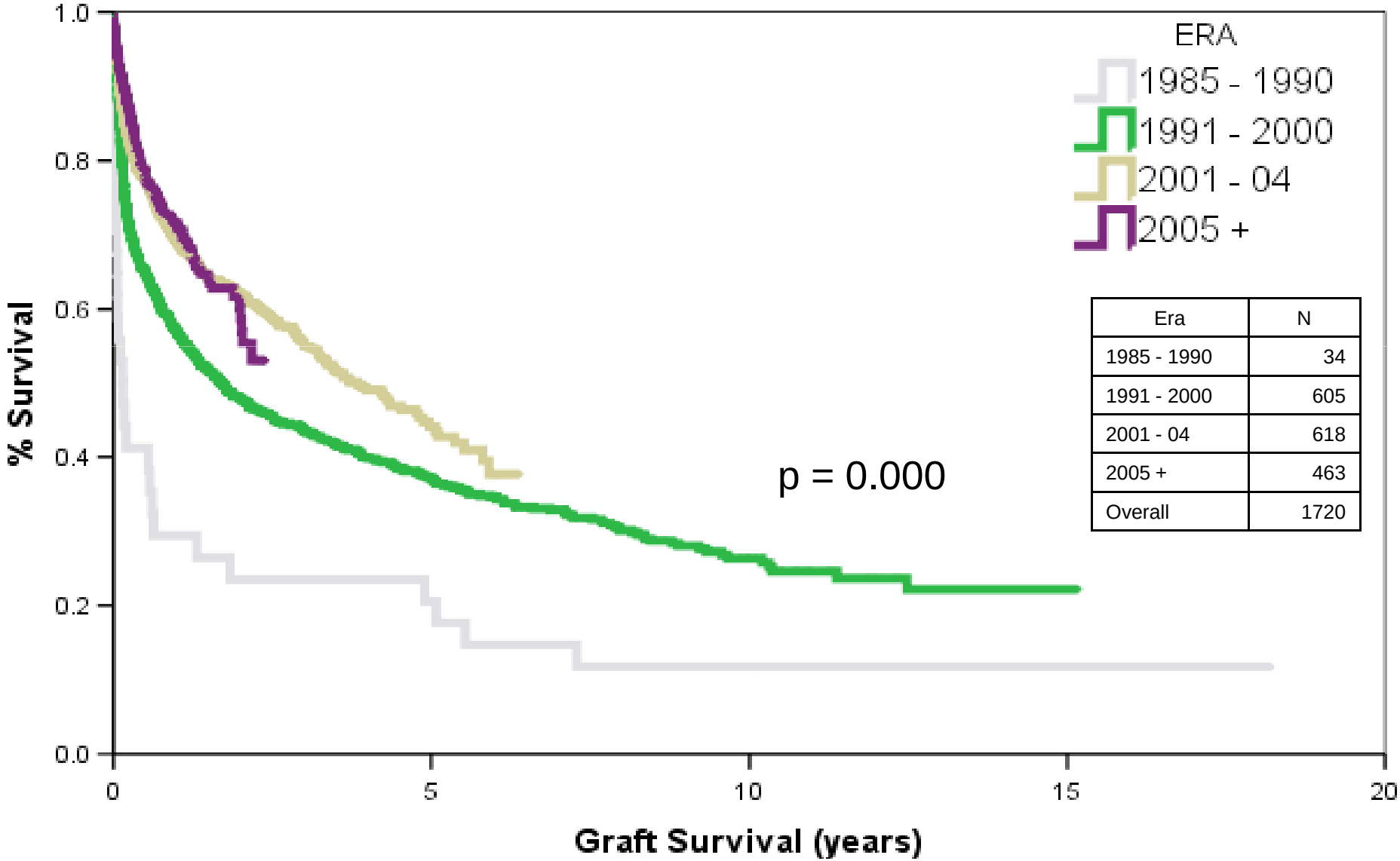
Intestinal Transplant Registry March 31, 2005

Alive Patient Status > 6 Months Post Tx 2005 - 2007





ITx Graft Survival - Transplant Era

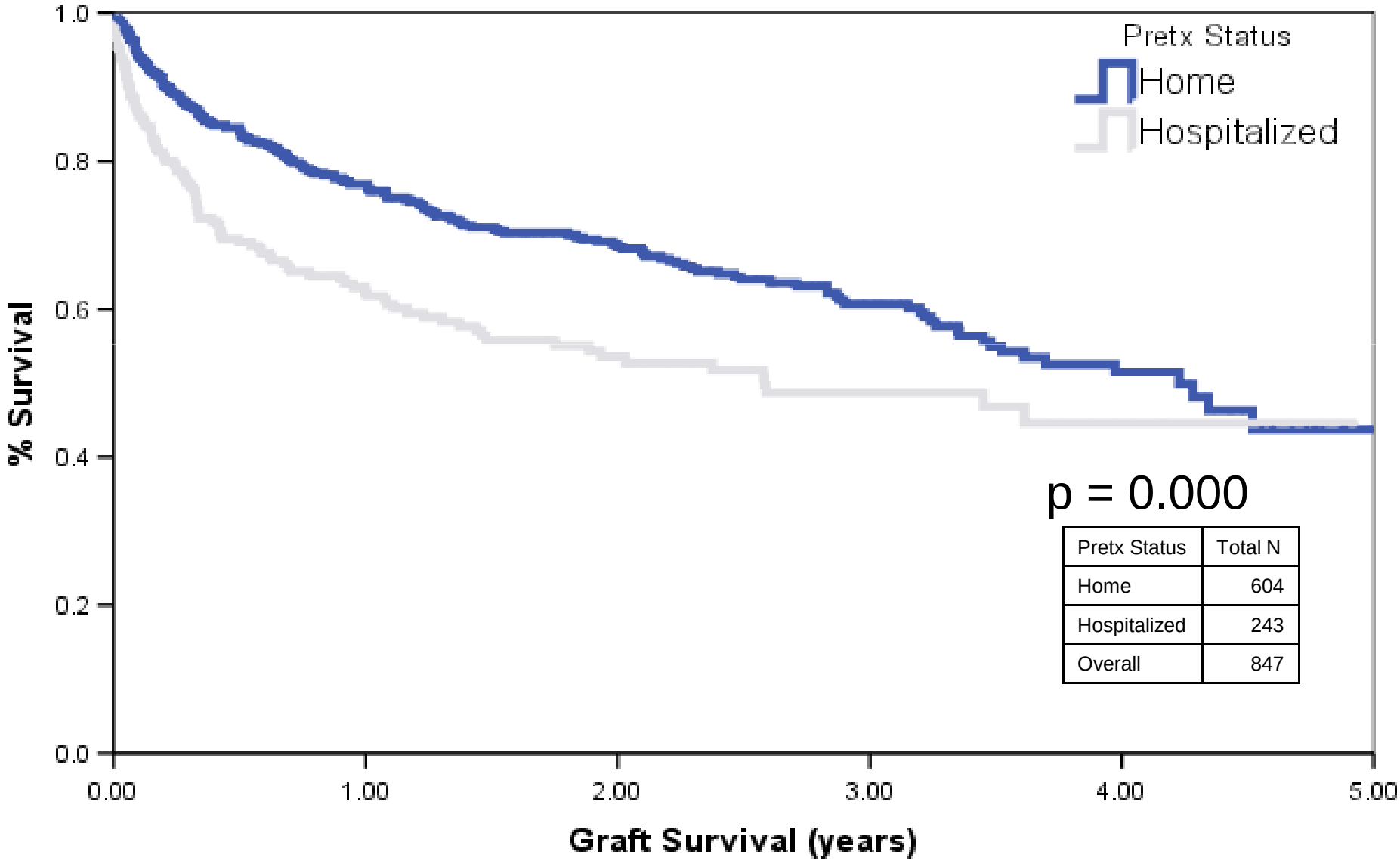


Era	N
1985 - 1990	34
1991 - 2000	605
2001 - 04	618
2005 +	463
Overall	1720

Graft Survival 2002-07
(Univariate Analysis)

Variable	Signficance
Pre-Tx status home or in hospital	0.00
Rejection within 3 months	0.024
Centre Case Volume	0.003

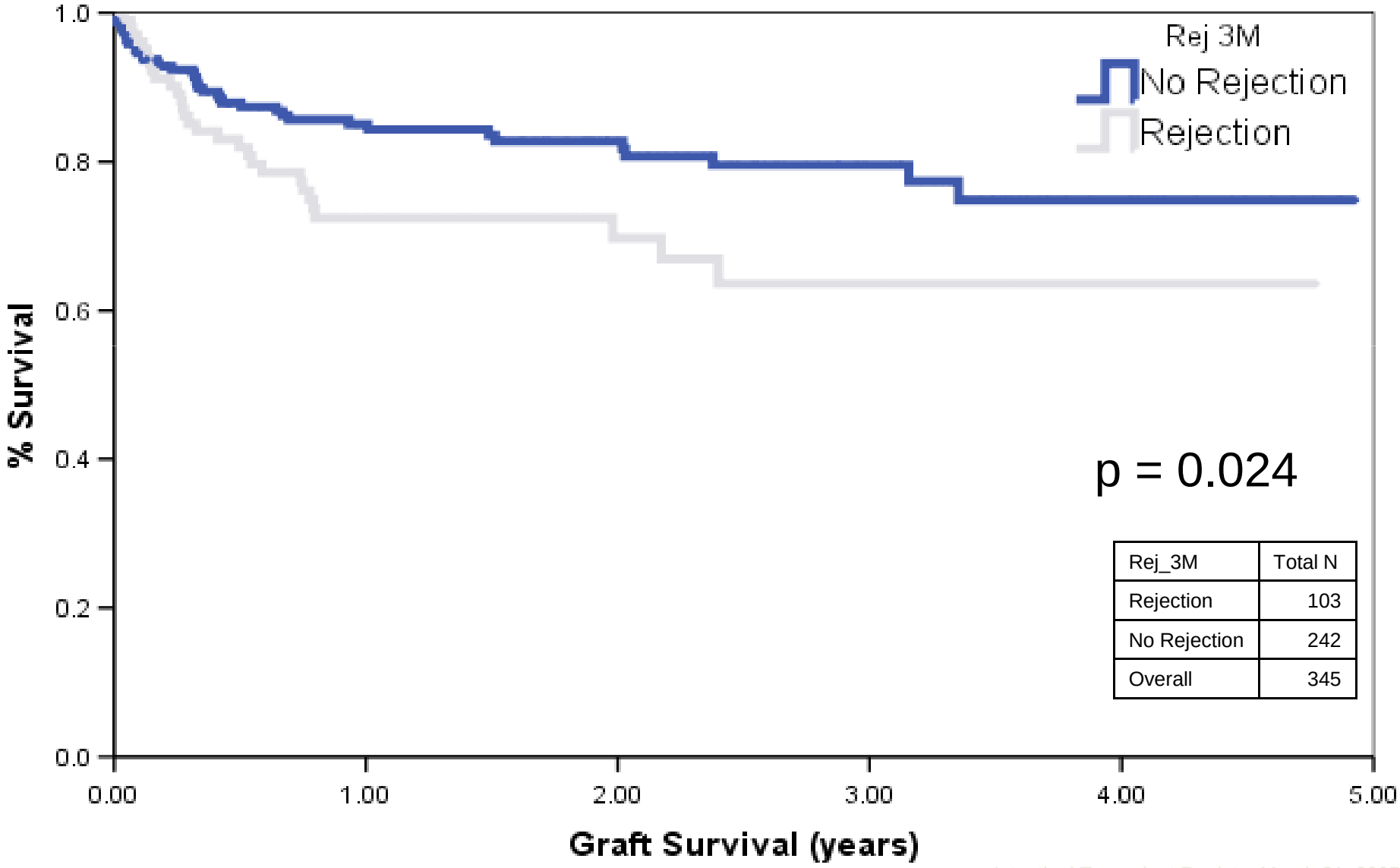
Pre Tx Status



p = 0.000

Pretx Status	Total N
Home	604
Hospitalized	243
Overall	847

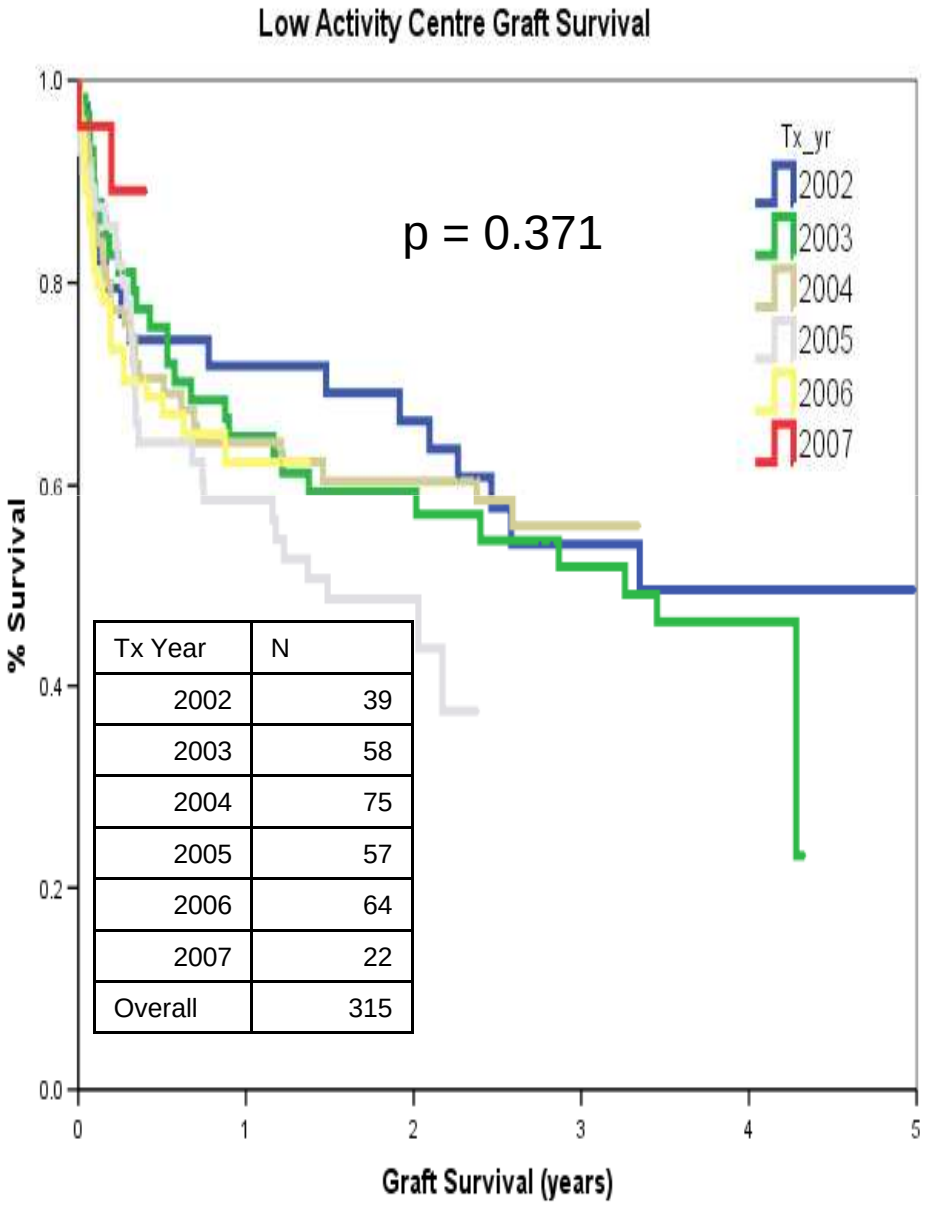
Rejection @ 3 months



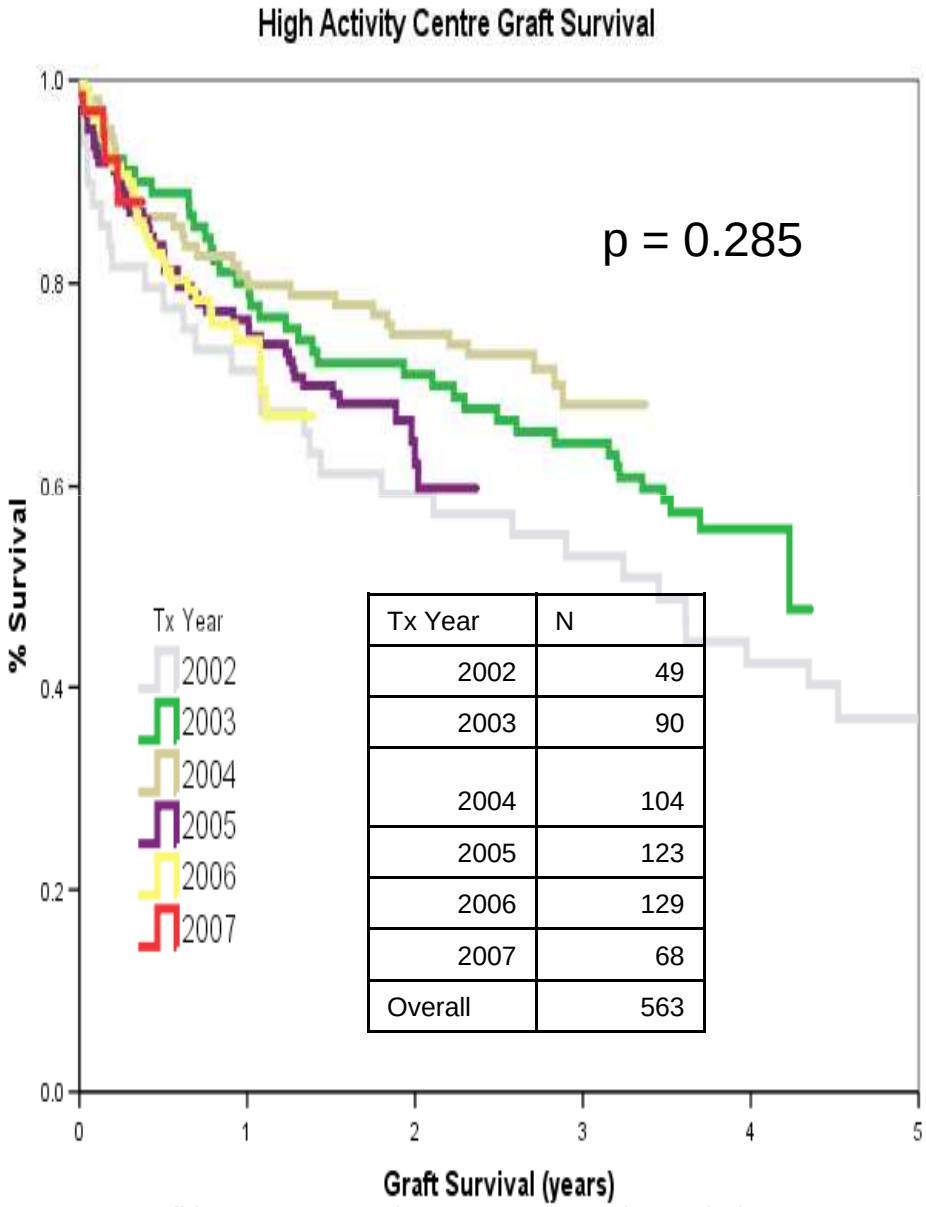
Rej_3M	Total N
Rejection	103
No Rejection	242
Overall	345

Intestinal Transplant Registry March 31, 2005

Graft Survival by Year (2002-07)

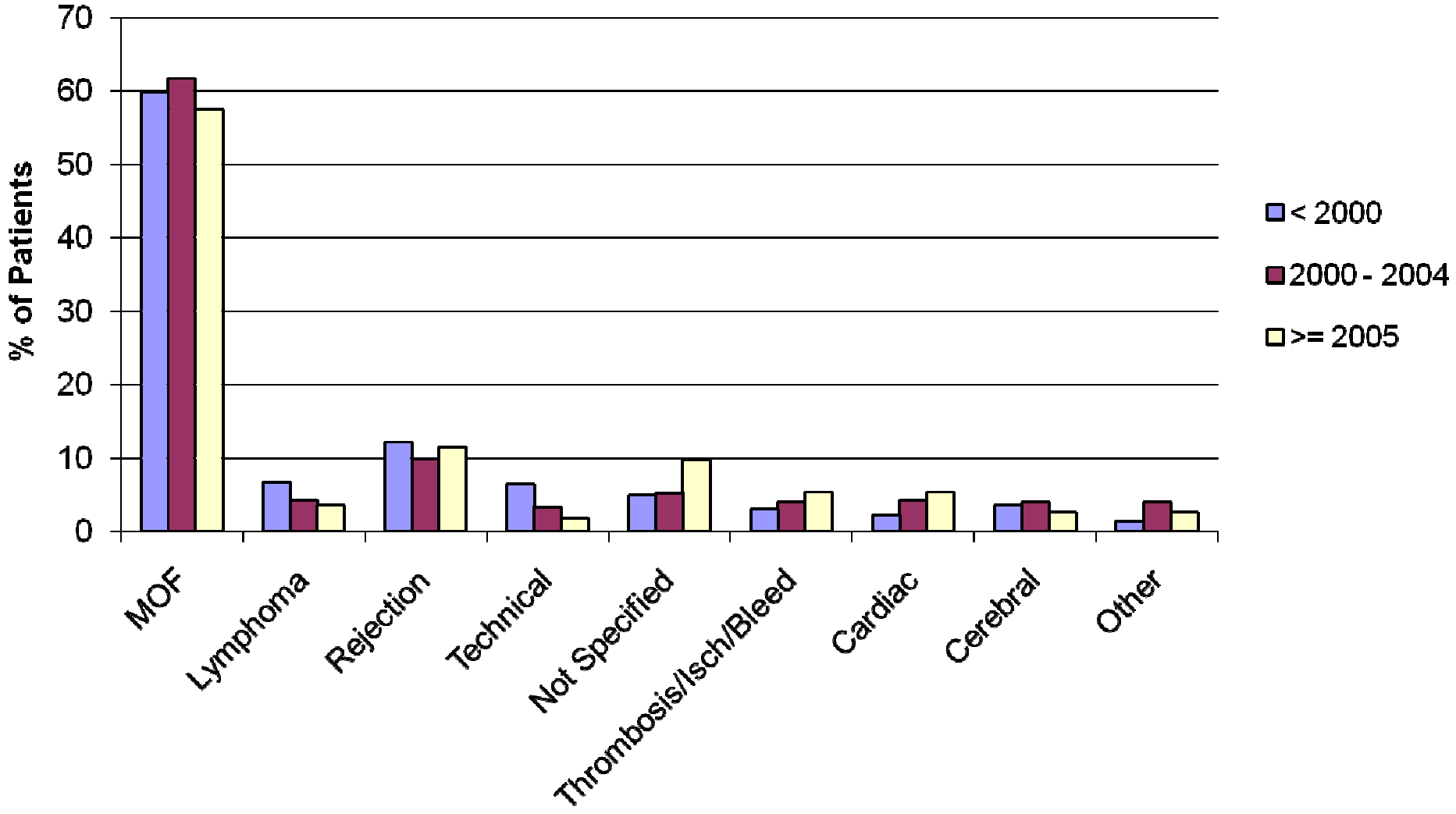


Tx Year	N
2002	39
2003	58
2004	75
2005	57
2006	64
2007	22
Overall	315



Tx Year	N
2002	49
2003	90
2004	104
2005	123
2006	129
2007	68
Overall	563

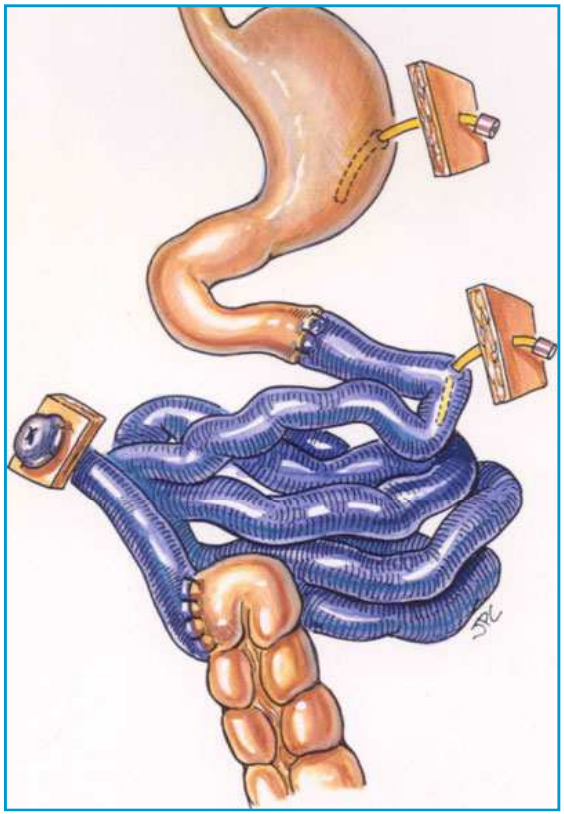
Causes of Death - % Distribution



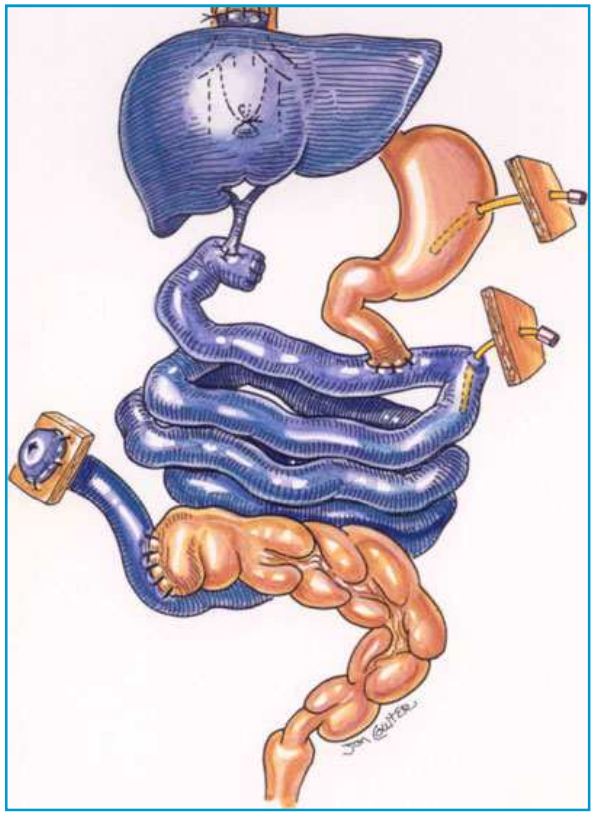
Immunosuppression

- Induction: Thymoglobulines, Anti-IL2 receptor blockade
- Tacrolimus > cyclosporine

Intestinal Tx Leuven 2000-2009: n=9



4 Isolated ITx

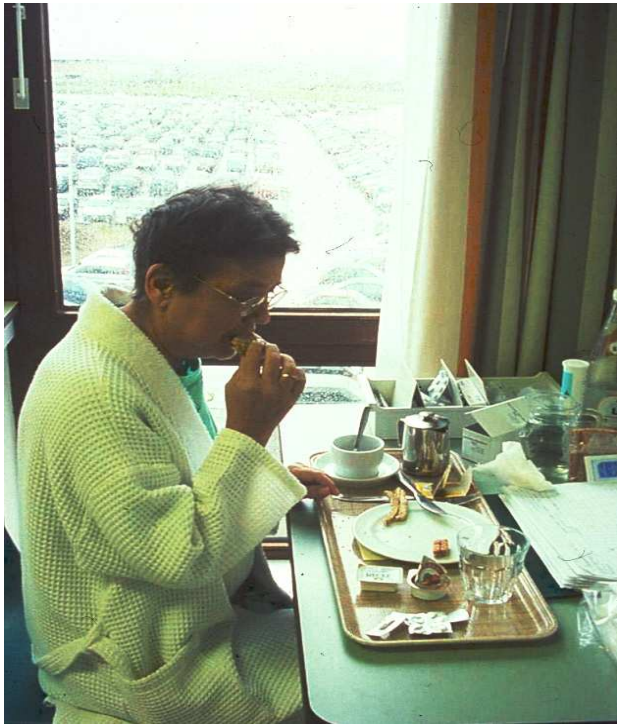


4 Liver & Intestinal Tx

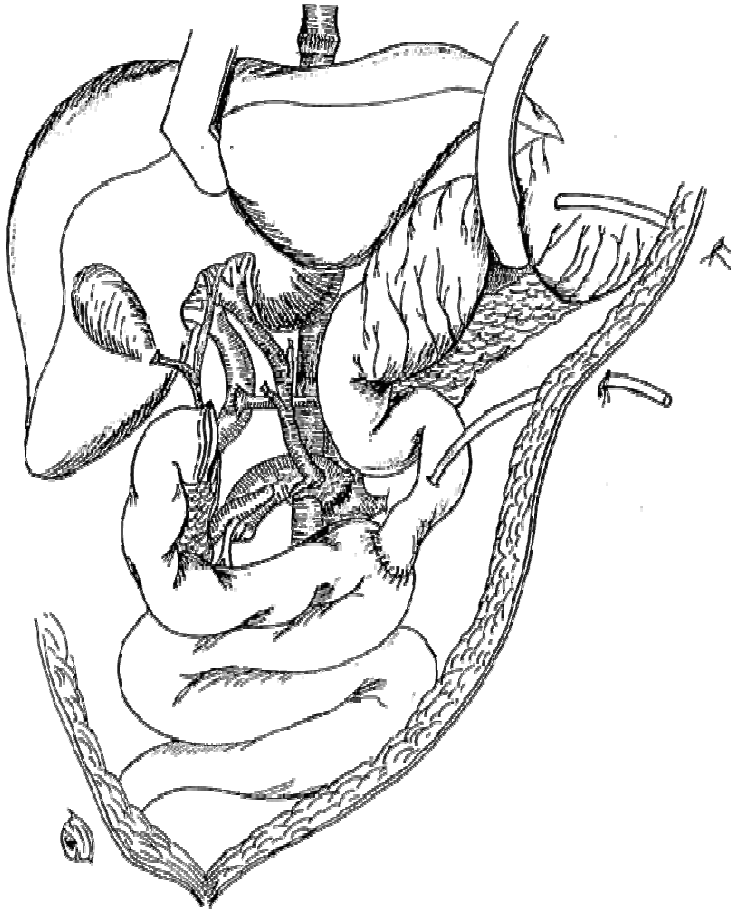
1 Multivisceral Tx

Intestinal Tx case 1

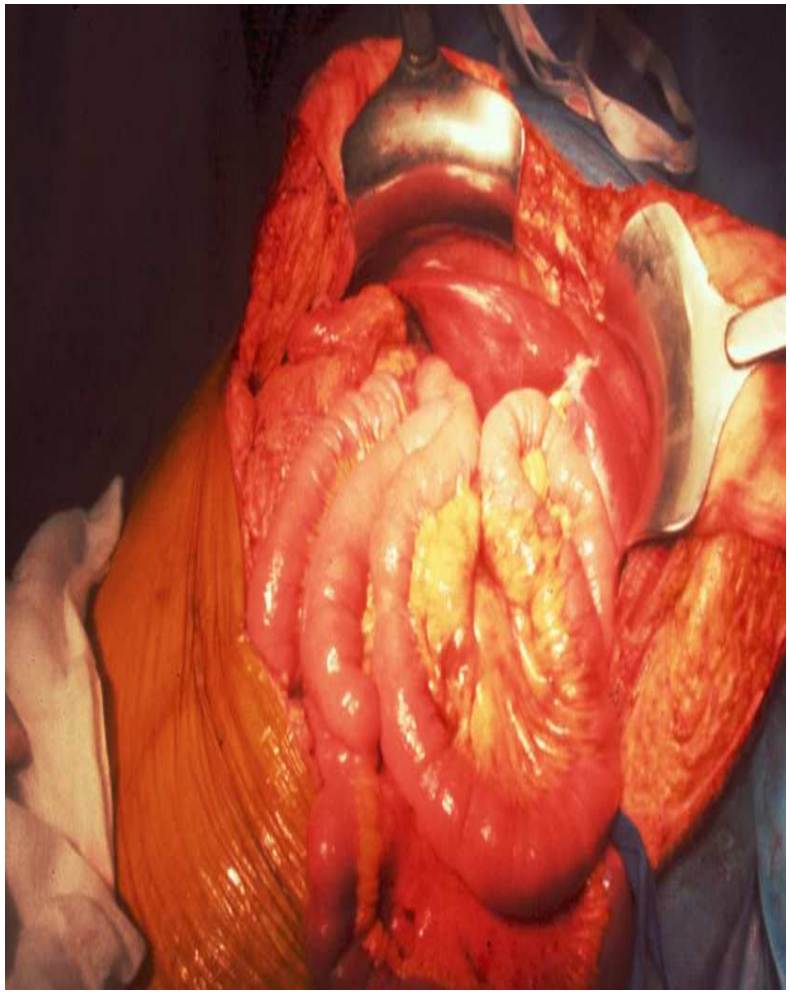
- **55 yo female**
- **Small bowel resection** (infarct)
- **Progressive TPN-induced liver failure**
- **Combined liver and bowel Tx**
- **Revisions for pancreatitis, wound absess**
- **9 years postTx well**



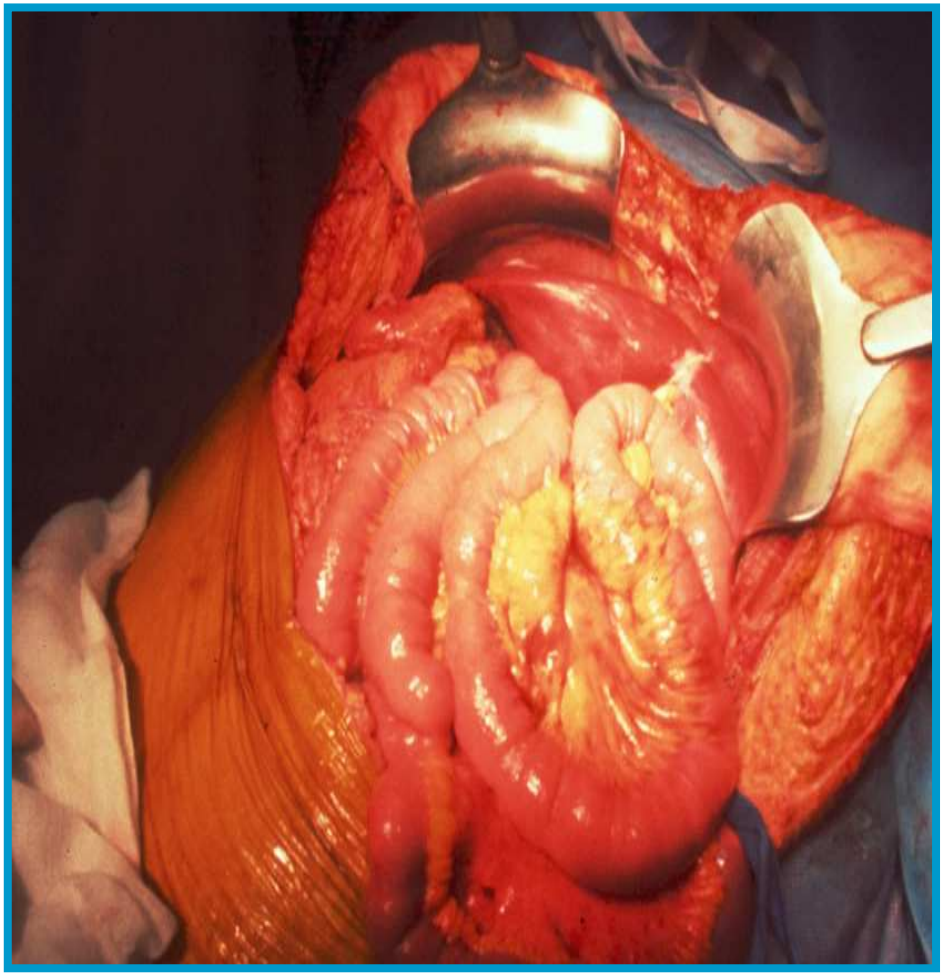
Surgical technique used
Combined liver/pancreatic head/small bowel Tx



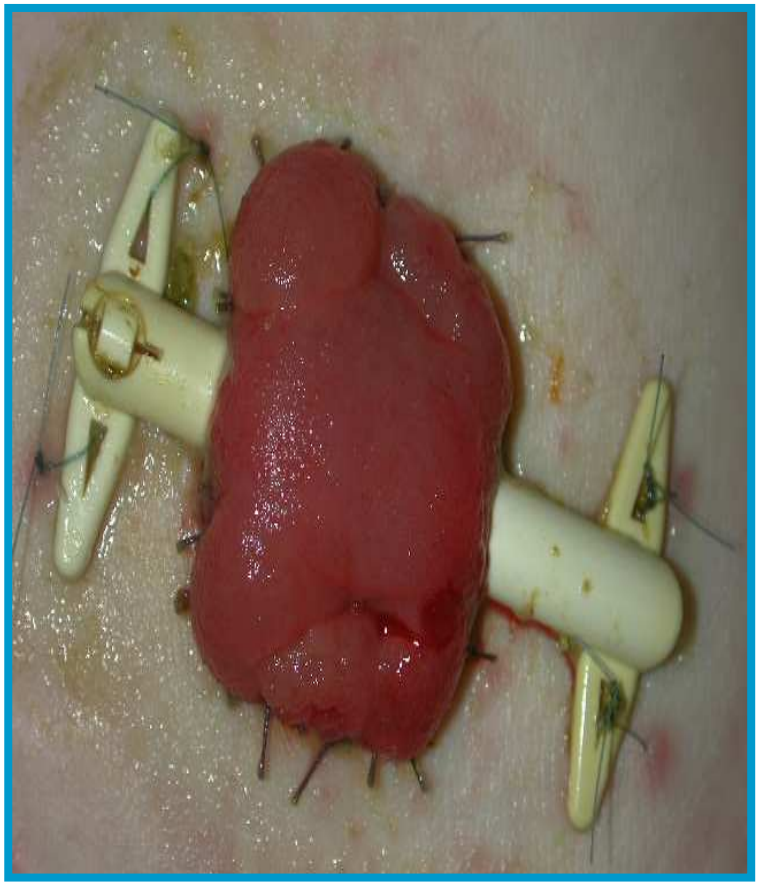
Sudan et al. A new technique for intestinal transplantation. Transplantation, 2001, 72: 1846



Transplantation

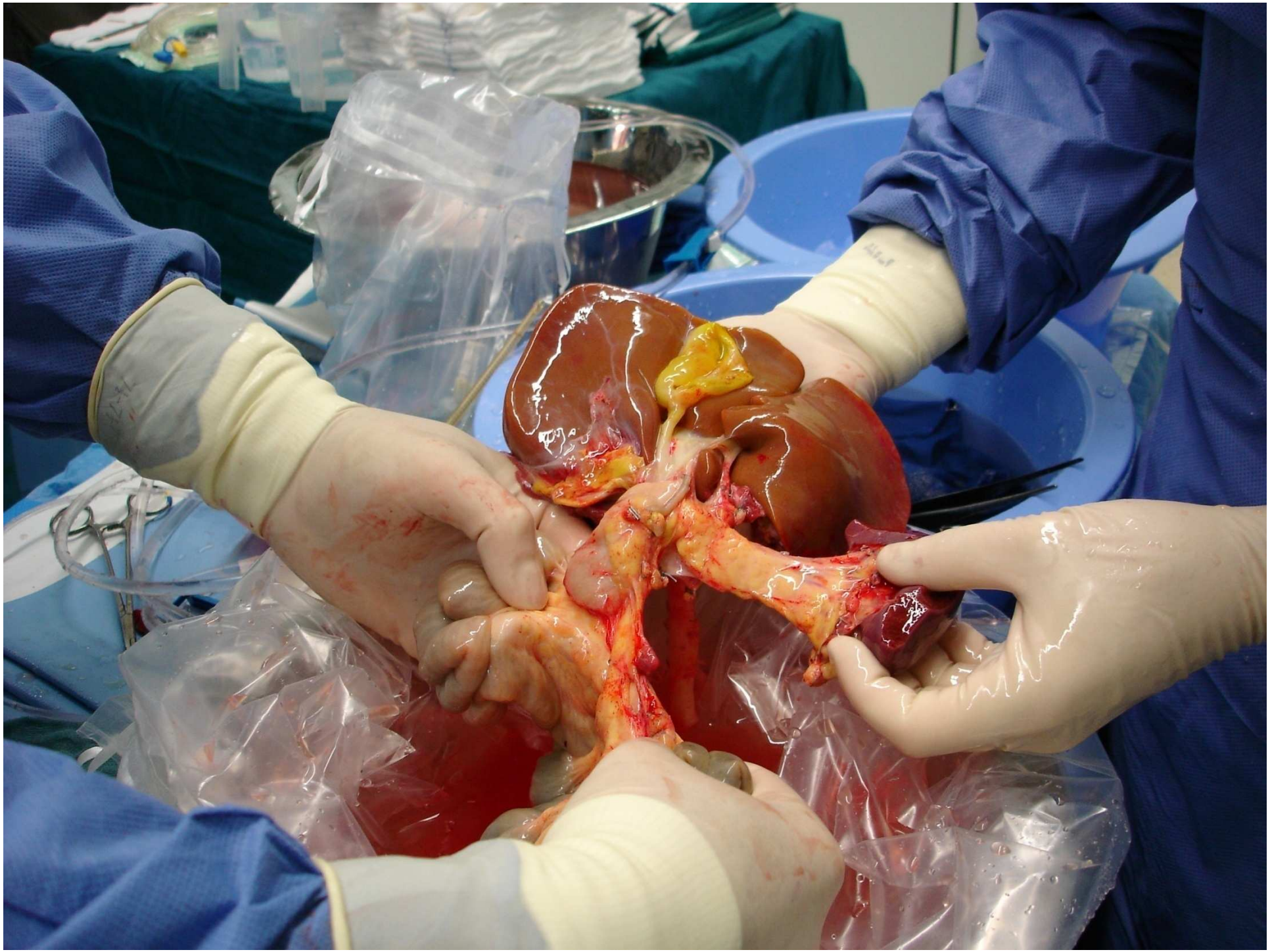


Stomy

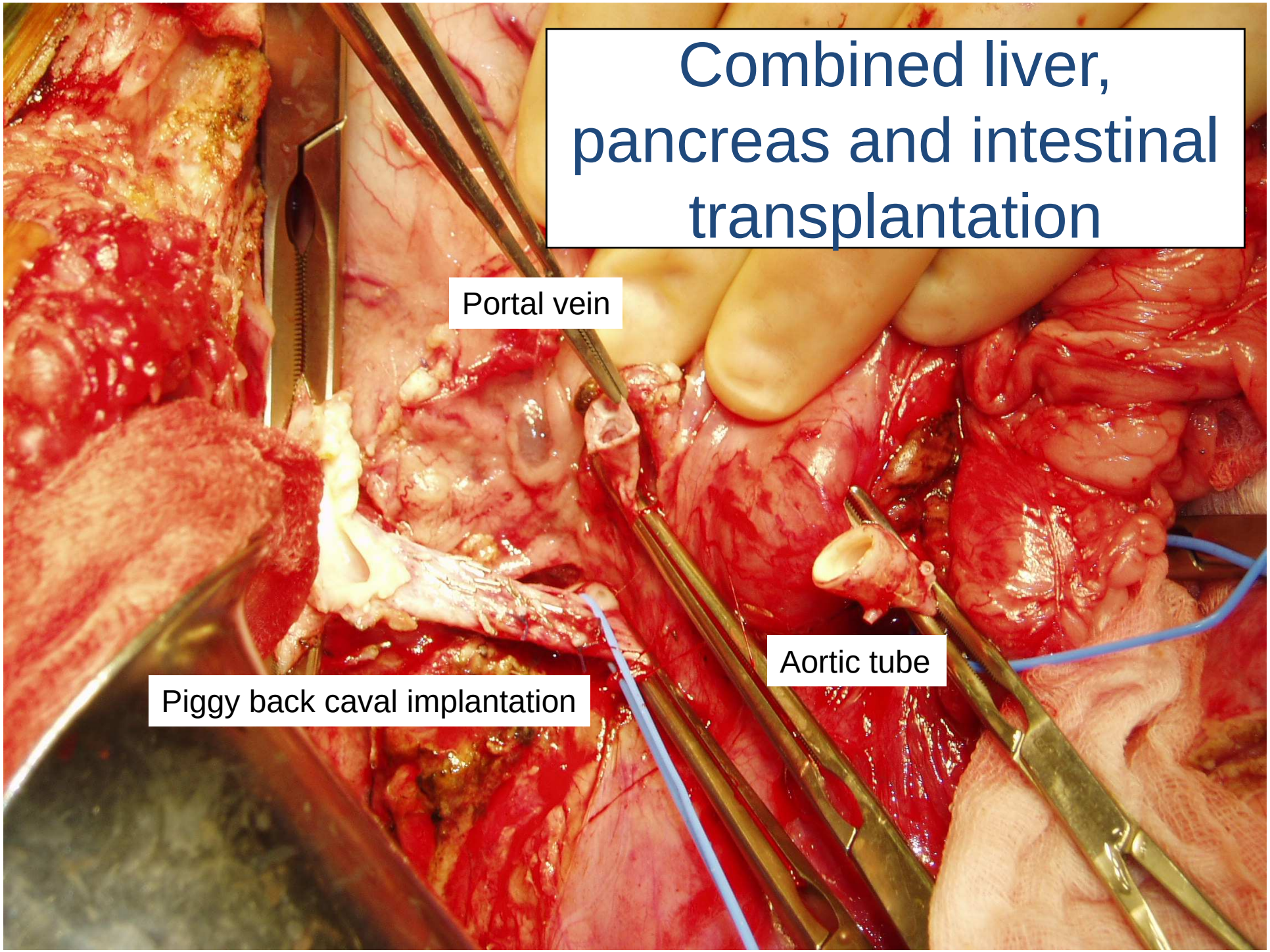


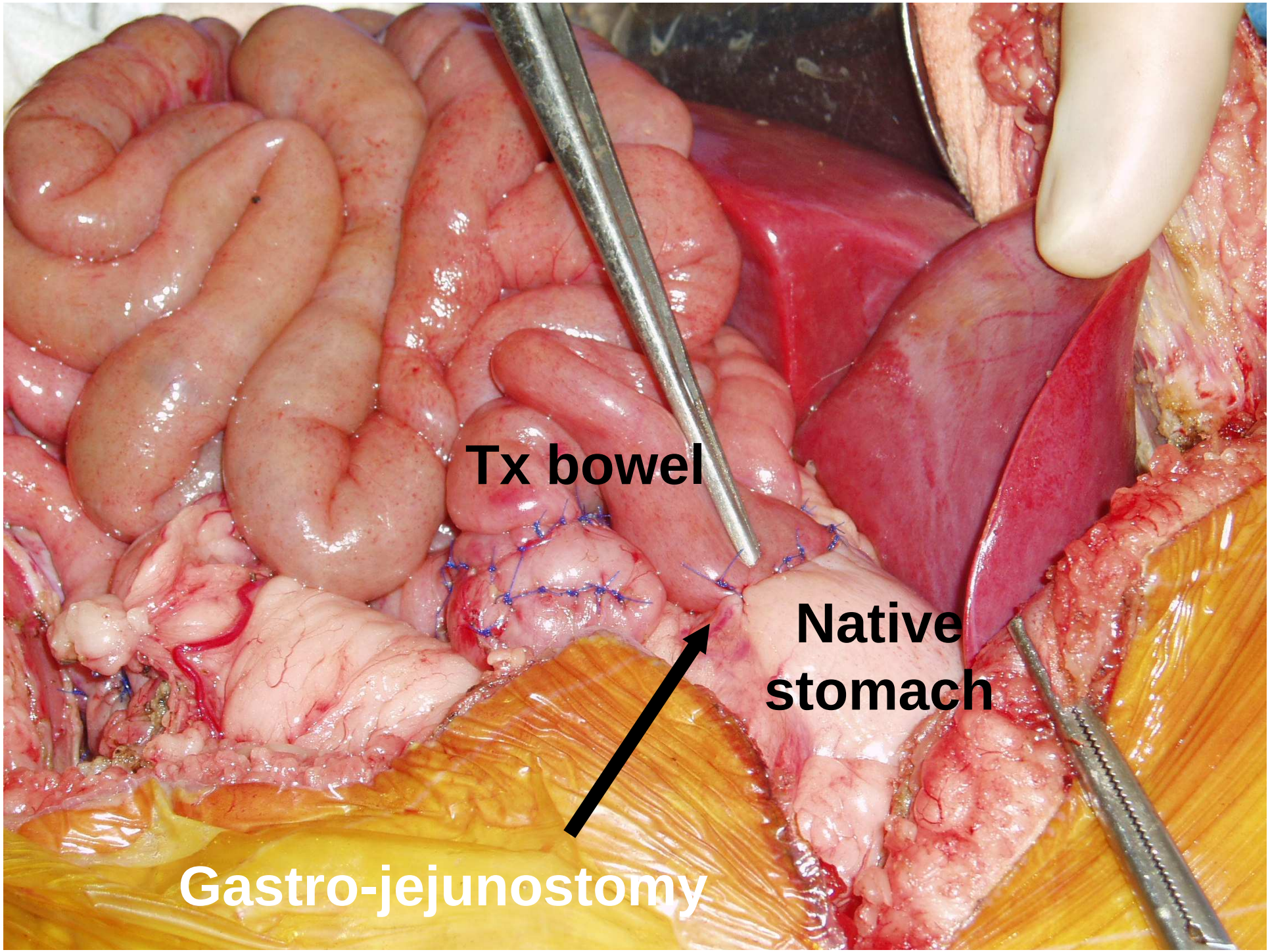
Intestinal Tx case

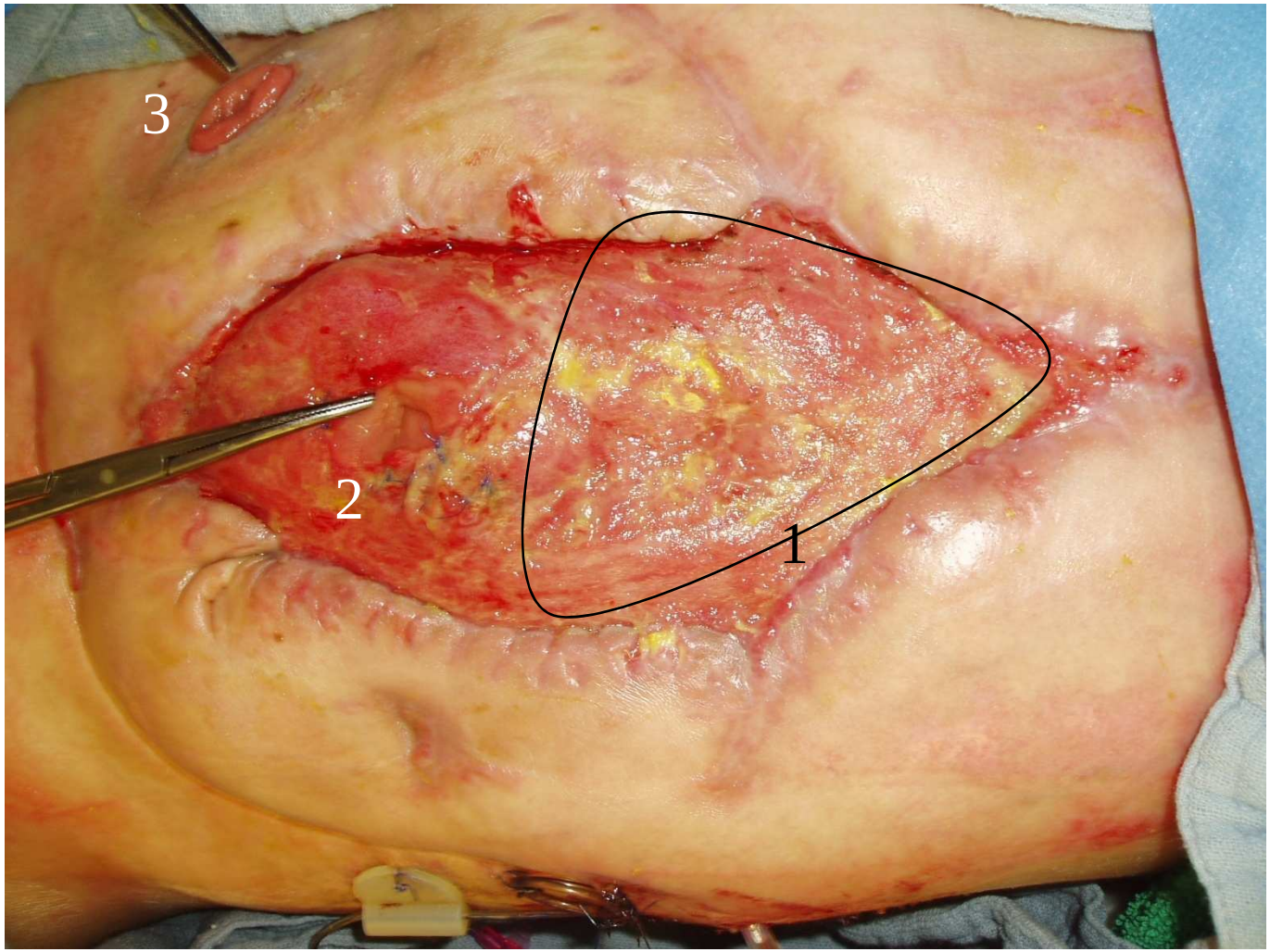
- **2 yo boy**
- **Small bowel resection** (volvulus)
- **Progressive TPN-induced liver failure**
- **Combined liver and bowel Tx**
- **Wound problems +++**
- **4 years postTx well**



Combined liver, pancreas and intestinal transplantation




Tx bowel
Native stomach
Gastro-jejunostomy



Open abdomen (15 x 7 cm) with granulating tissue (1)

Tear in small bowel (2), proximal of initial ileostomy (3)

Vac system

Wound manager

Repeated surgery

Skin graft

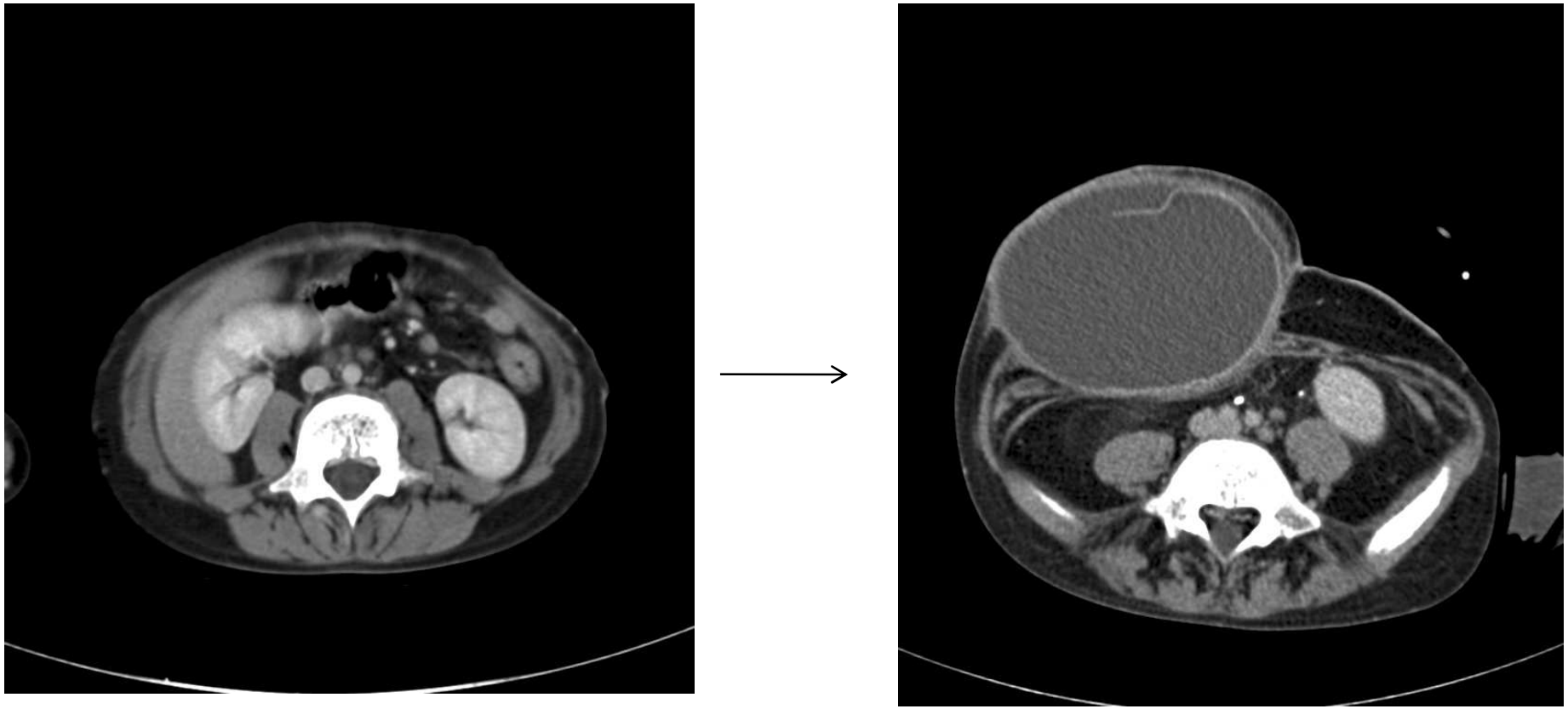
Intestinal Tx case

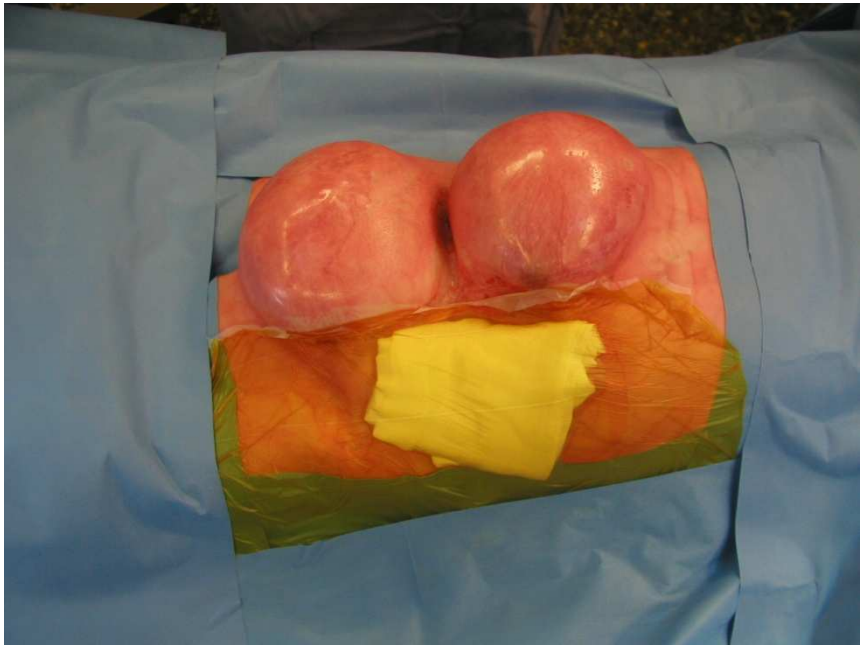
- **9 yo girl**
- **Premature - bowel resection**
- **Liver cirrhosis**
- **Combined liver, duodenum, pancreas, small, large bowel Tx**
- **To avoid problems encountered in previous case, expansion prosthesis were placed**
- **1 year postTx; doing well**

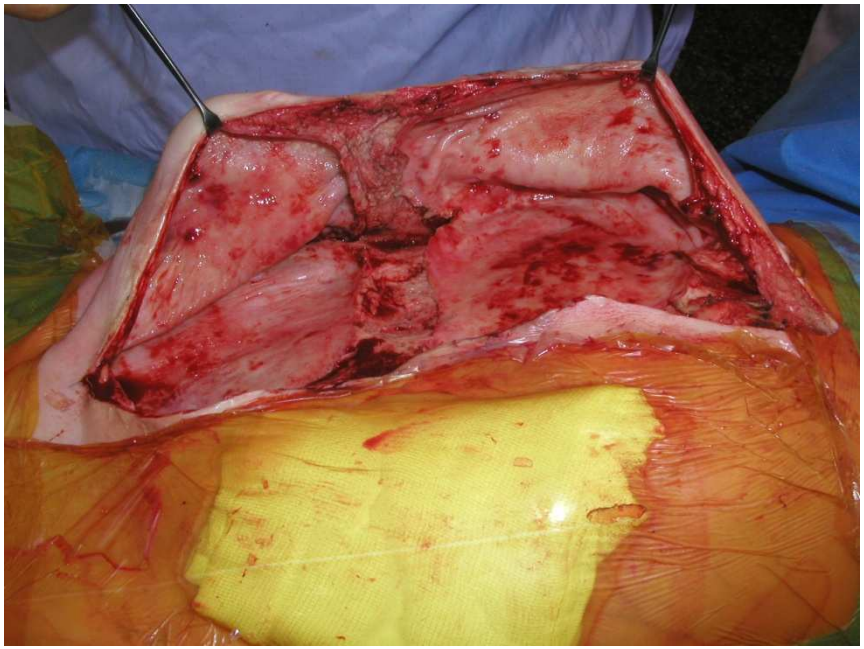
*Subcutaneous Expansion Prothesis**

R Hierner, plastic surgery*

Skin expansion preTx to make 1ary closure at time of Tx possible





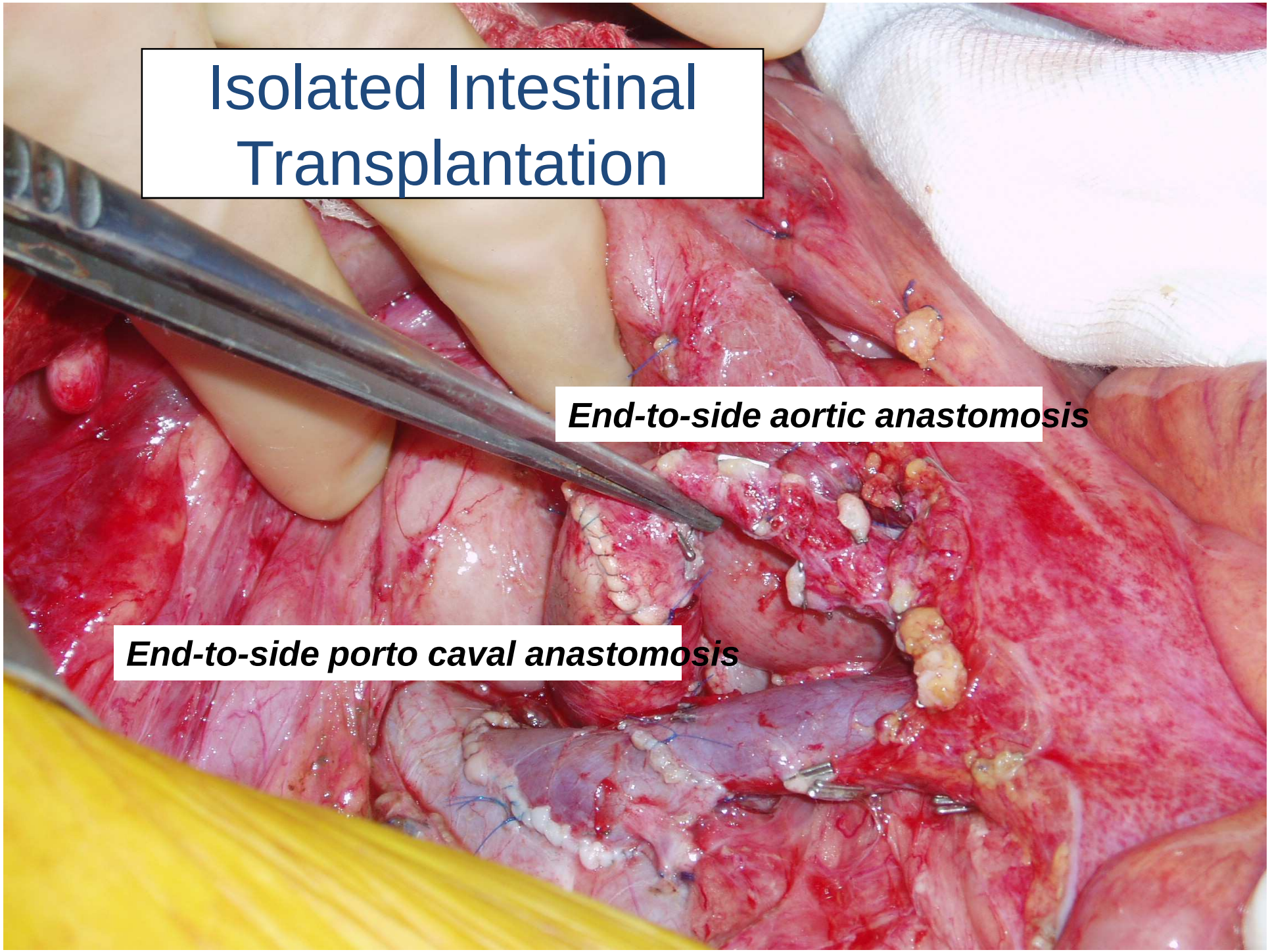


Intestinal Tx

Chronic pseudoobstruction

No problem of space because native intestine distended and still present

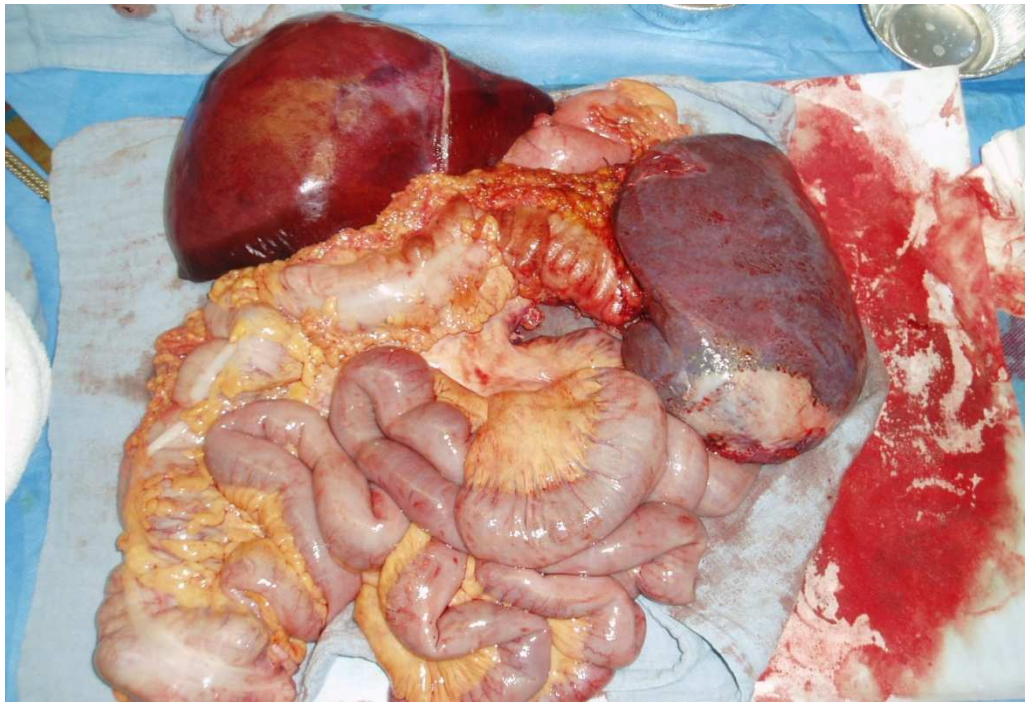
Isolated Intestinal Transplantation



Trekking in the swiss alps
18 months after Intestinal Transplantation

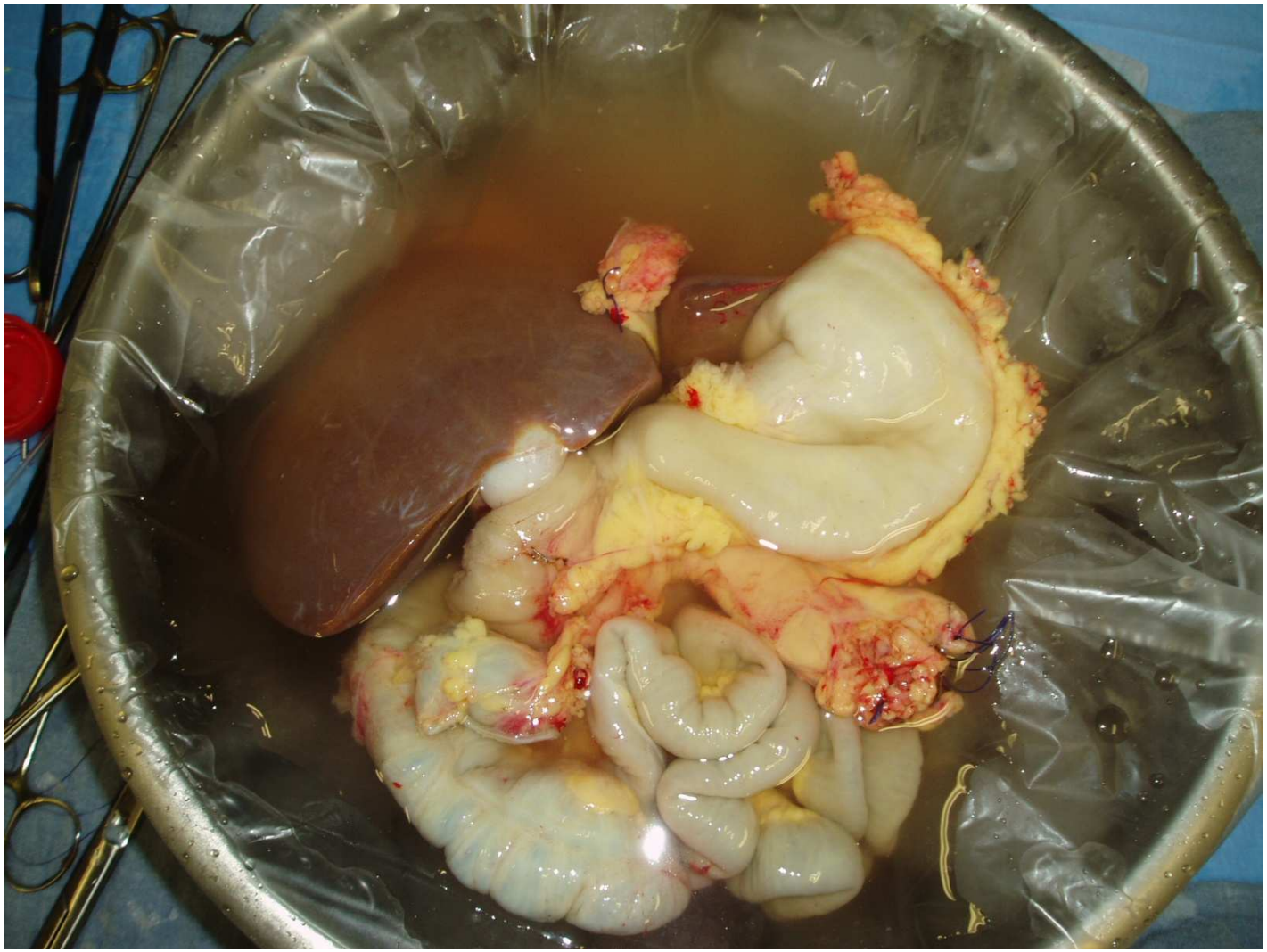
Multivisceral Transplantation

Complete splanchnic thrombosis (Antiphospholipid syndrome) and uncontrollable bleeding: ICU Bound
En bloc resection of abdominal viscera

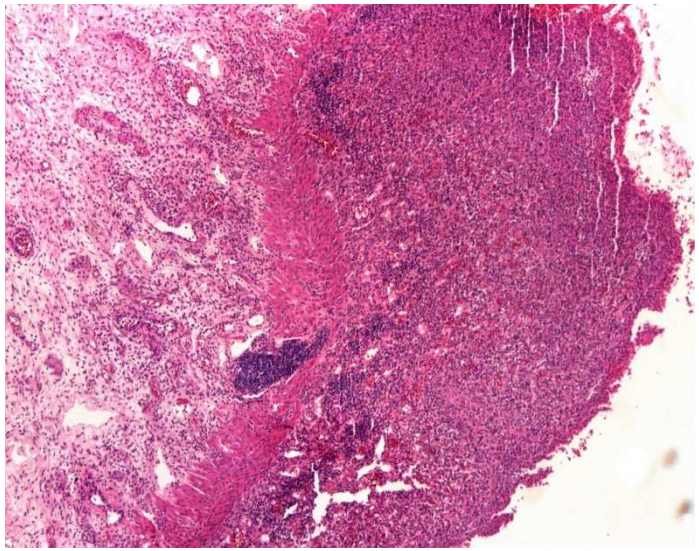


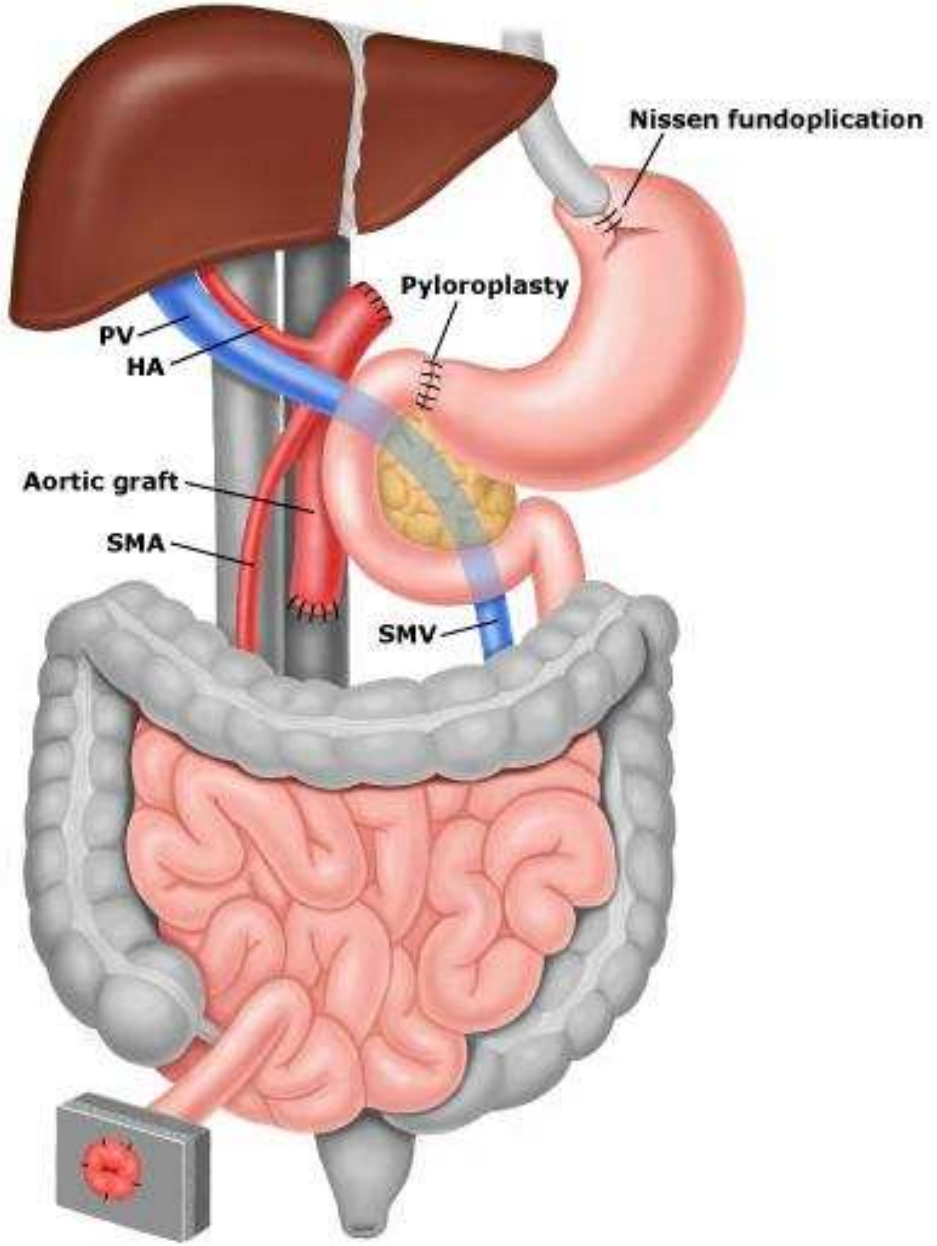
Donor graft:

en bloc liver/duodenum/pancreas/
spleen/stomach/ small bowel and colon



Multivisceral Transplantation





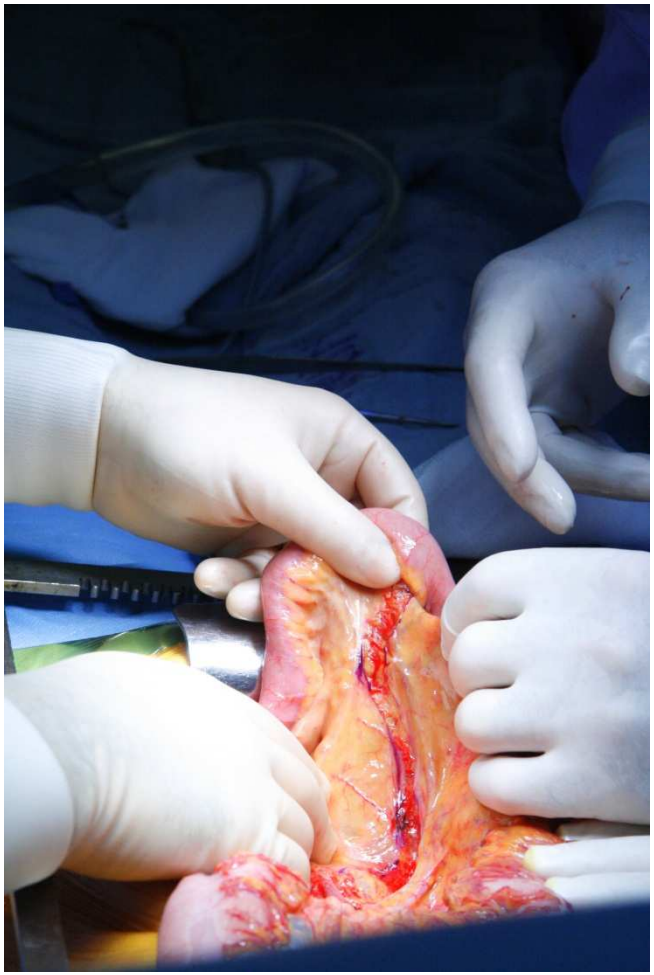
Live donation ITx

- **30 yo female**
- **Churg strauss syndrome (tumors in the mesentery)**
- **Ultra short bowel No abdominal domain**
- **Bowel Tx (2 m distal ileum) from live donor (mother)**

Subcutaneous prostheis

- Small abdominal capacity

Bowel Tx (2m distal ileum) from living donor



In cooperation with Dr E. Benedetti, U of Illinois Chicago

Overall results Leuven ITx group

Follow up: 1 year to 8 years

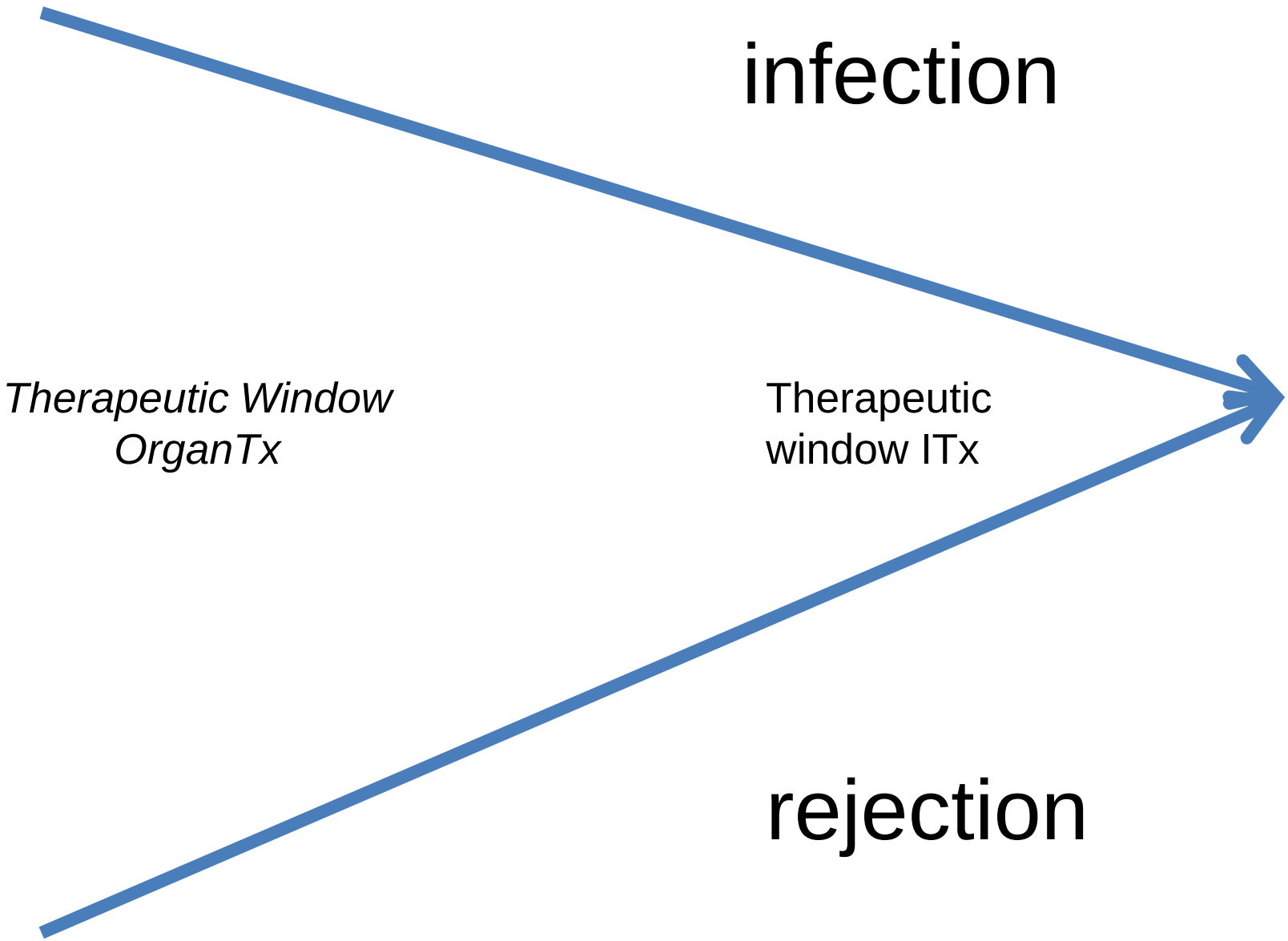
- **Patient Survival: 7/9 (77.7%) (~50% Itx registry)**
  - *1 cerebral bleeding 4 mths post MVTx*
  - *1 aspergillosis 5 mths post isolated ITx*

- **No “technical” death**

- **No “technical” graft loss**

Itx = most challenging form of organ Tx for ICU team

Poor nutrition
Complex surgery
Infected milieu
Immunosuppression
permanent alert for rejection & infection
Long ICU stay


infection
Therapeutic Window
OrganTx
Therapeutic
window ITx
rejection

Intestinal Transplantation conclusions (1)

- Intestine has always been « behind » in comparison with other organ tx
- ITx has matured into a clinical reality for patients with severe complications from short bowel & TPN
- In this patient group, prognosis is better with a transplant than under TPN

Intestinal Transplantation conclusions (2)

- Factors associated with *better outcome*: absence of rejection first 3 months, preTx home status, center experience, children, (liver)
- Since 2000, survival has not improved. Thus, new approaches are required to take ITx to the next level

Medics & paramedics team

- ***ICU P Ferdinande, D Vlasselaers, L Desmet, G Van den Berghe et al***
- ***Nurses E662, E341, E441, E449, E443, ICU, OR***
- Abdominal Tx surgery: *W Coosemans, R Aerts, D Monbaliu, J Pirenne*
- Transplant coordination: *J de Roey, B Desschans*
- Transplant Pediatrics: *R Lombaerts et al*
- Gastroenterology: *M Hiele, G Van Assche et al*
- Gastroenterology Pediatry: *I Hoffman et al*
- Anesthesiology: *M Verhaegen, M Van de Velde, E Vandermeersch et al*
- Hepatology: *F Nevens et al*
- Urology: *G Bogaert et al*
- Abdominal Surgery: *M Miserez, F Penninckx et al*
- Plastic en Reconstructive Surgery: *R Hierner et al*
- Radiology: *D Vanbeckevoort et al*
- Pathology*: K Geboes, N Ectors, et al*
- HLA labo: *MP Emonds et al*
- Stoma nurse, Logopedist, Occupational therapy, Social worker, Dietist, Kinesitherapist, Psychology

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S *Louis, S Brouard, JP Soulillou et al*

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Dank u
Merci
Thank you