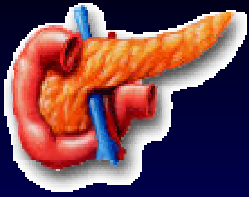


# **SPK and IAK - initial results in Budapest**



**Robert Langer M.D., Ph.D., FACS**

**Department of Transplantation and Surgery  
Semmelweis University, Budapest, Hungary**



# Diabetes – Financial Aspects

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- **UK – 9% of the NHS**

→ Currie CJ et al: *Diabet Med* (1997) 14: 686-92

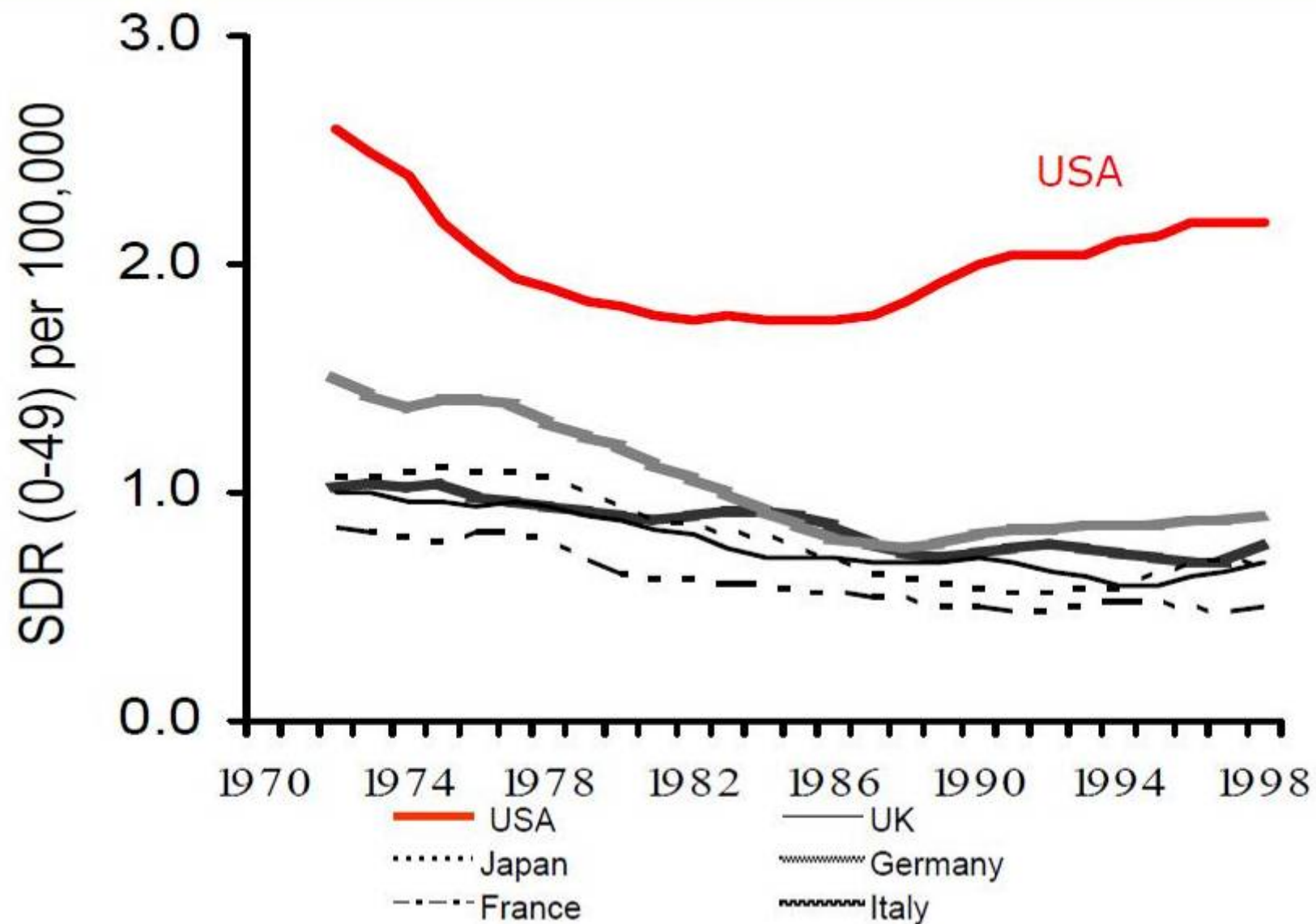
- **USA - 14,6% (4,5%DM) ~ \$100 billion/year**

→ Rubin RJ et al: *J Clin Endocrinol Metab* (1994) 78: 809A-F

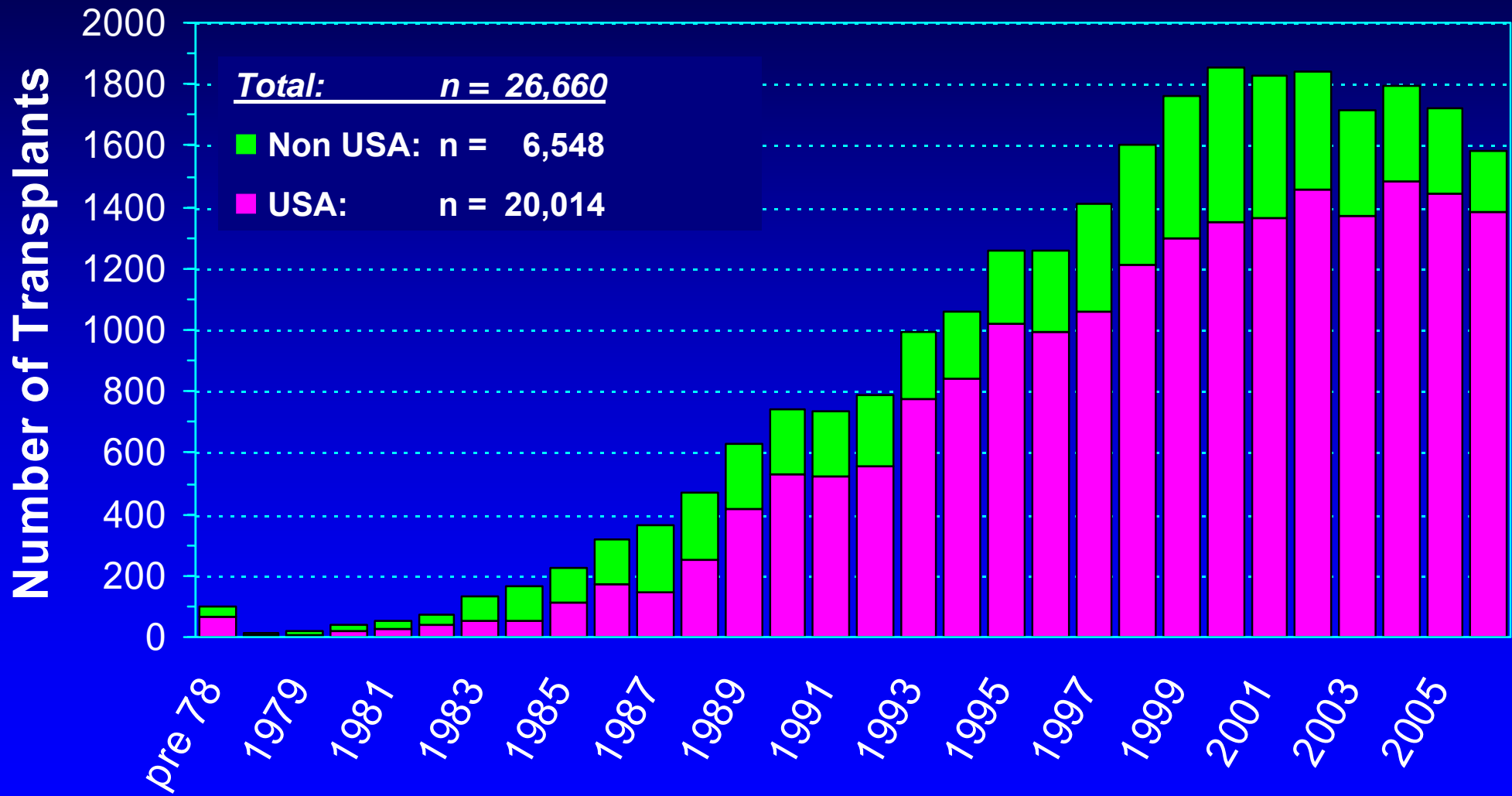
- **Age 7-40: costs - \$52 000**

→ Songer TJ: *Diabet Metab Res* (1992) 8: 389-404

## Mortality from diabetes among under 50s



# Pancreas Transplants Worldwide



# Pancreas Transplants Worldwide

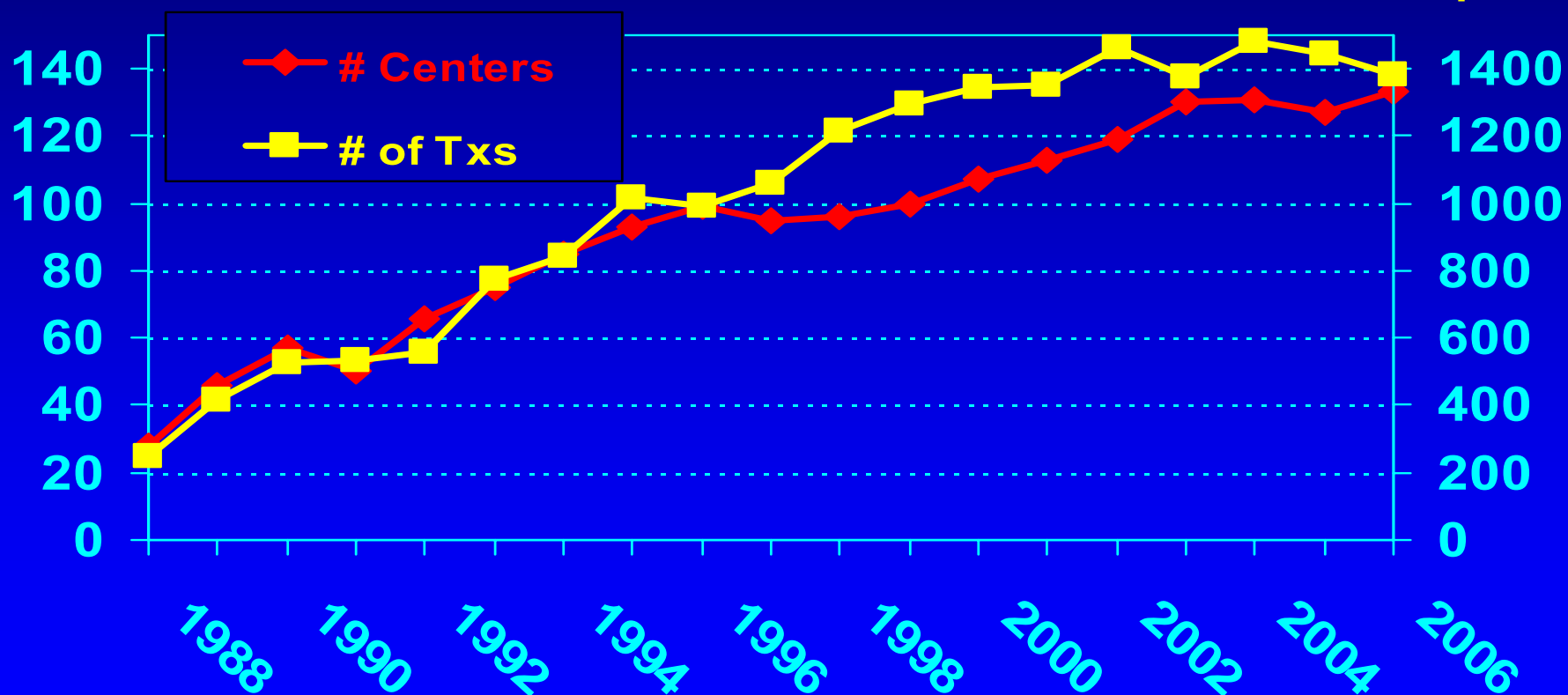


# Number of Tx Centers and Number of Tx's

USA Pancreas Transplants 1/1/1988 - 12/31/2006

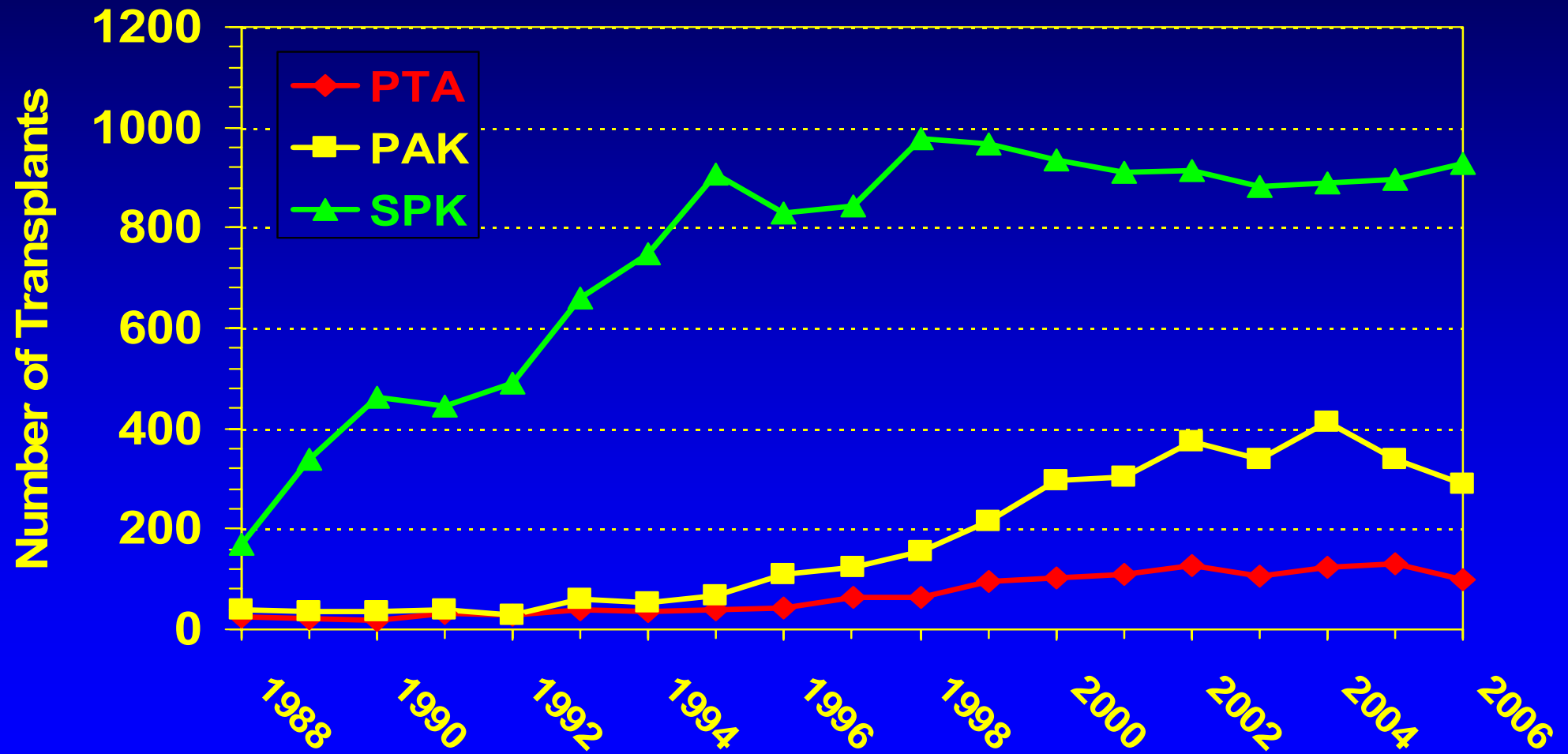
Centers

Transplants

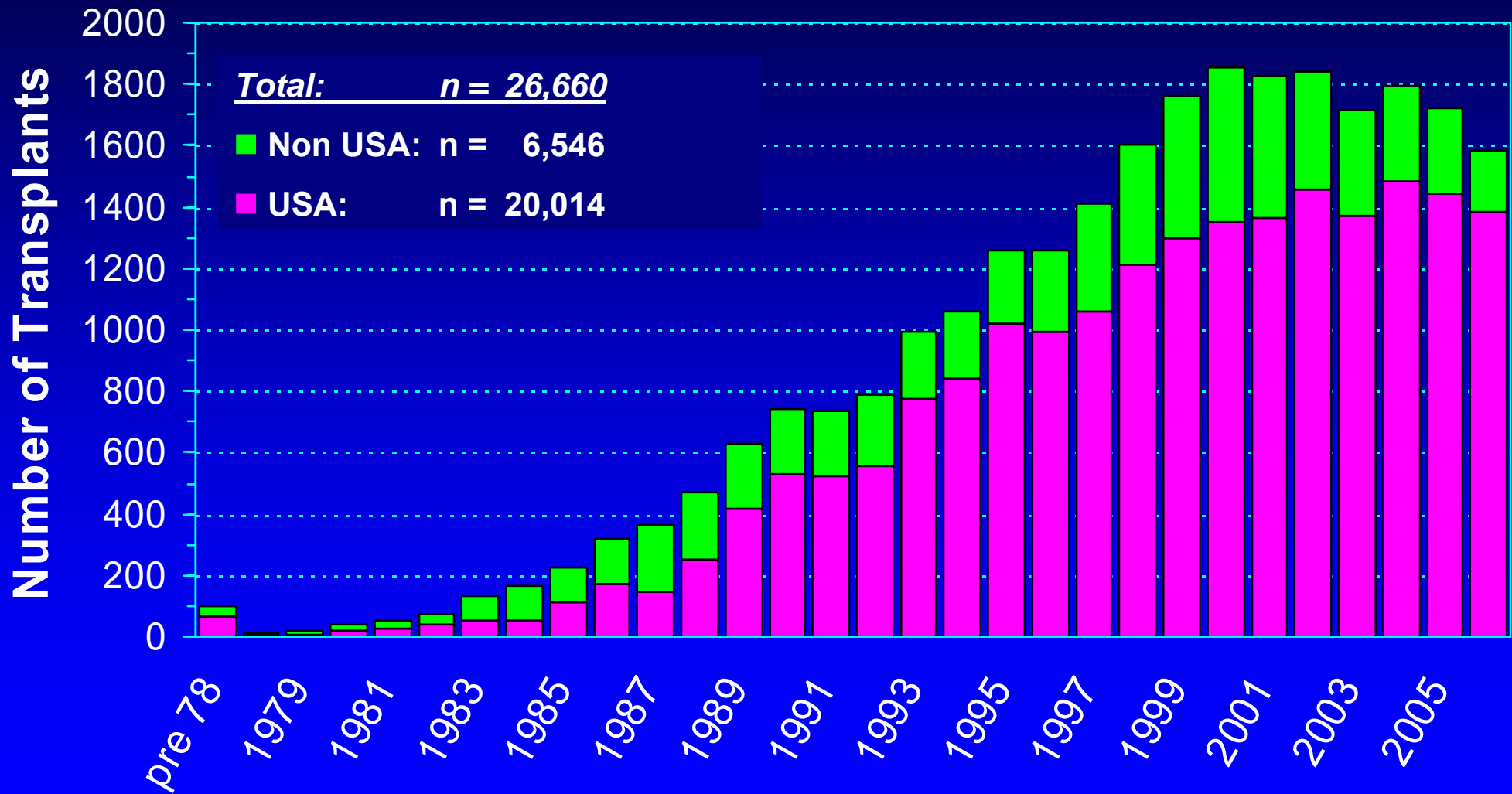


# Pancreas Transplant Categories

USA SPK, PAK and PTA Transplants

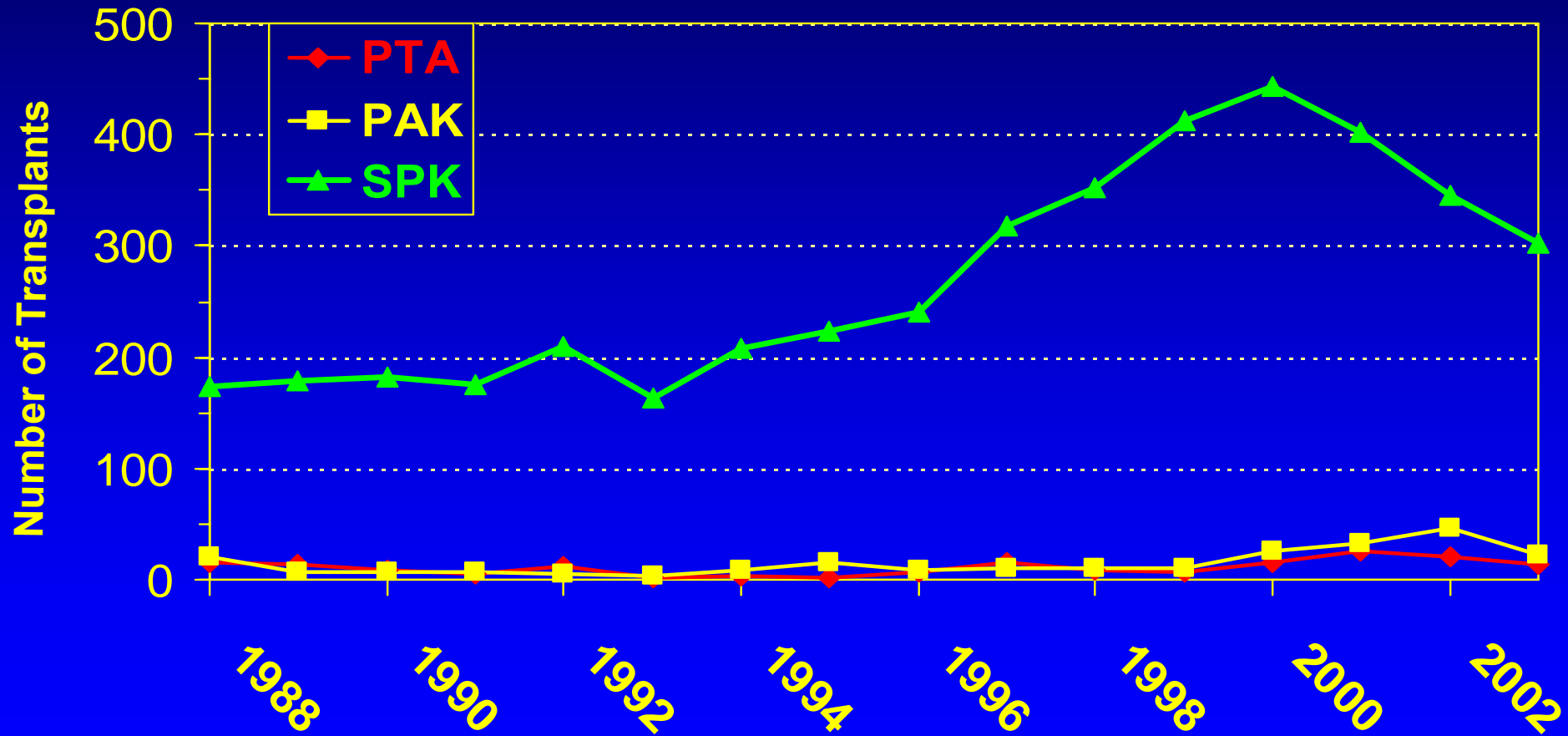


# Pancreas Transplants Worldwide



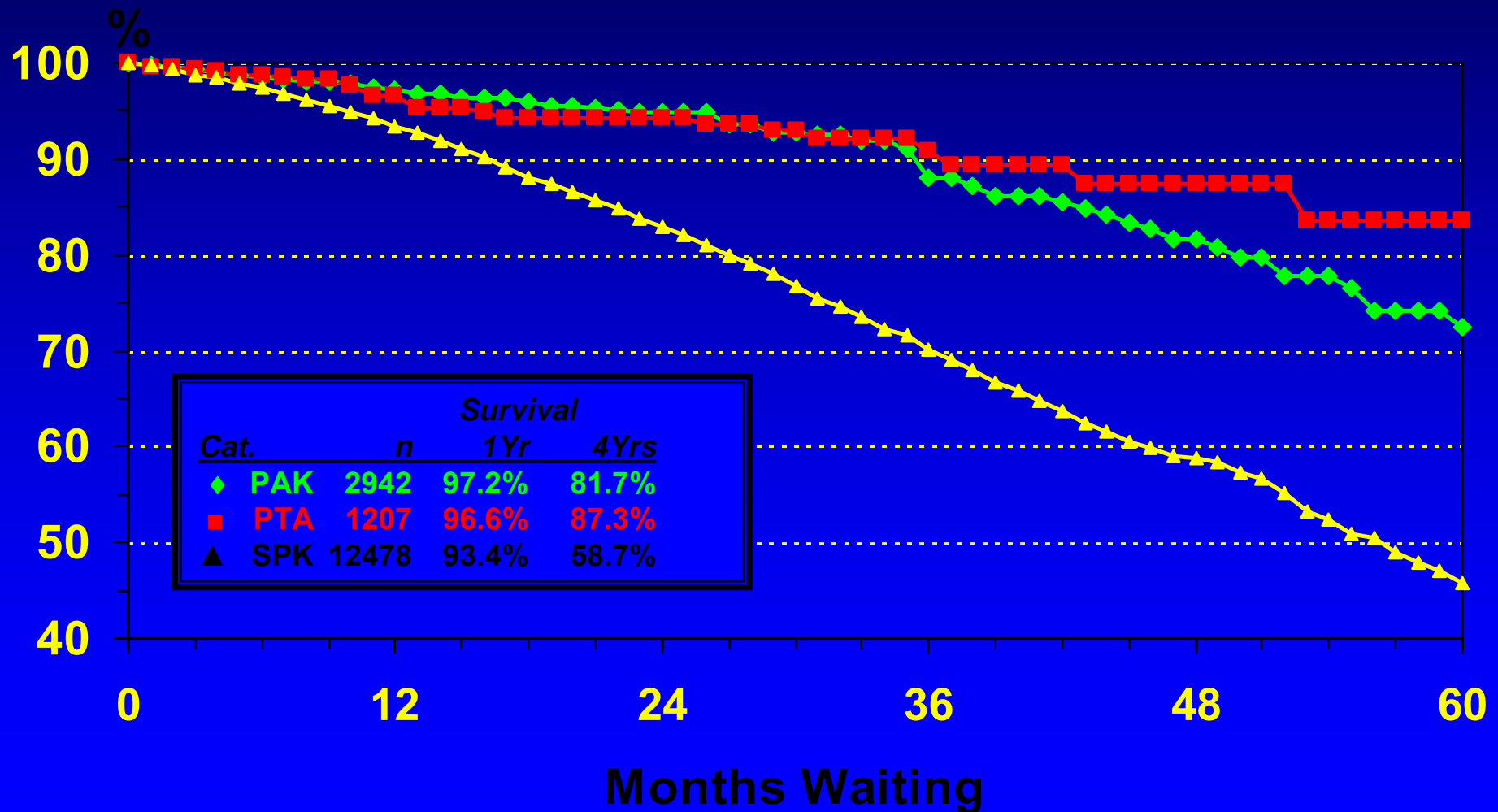
# Pancreas Transplant Categories

Non-US SPK, PAK and PTA Transplants 1/1/1988 - 12/31/2003



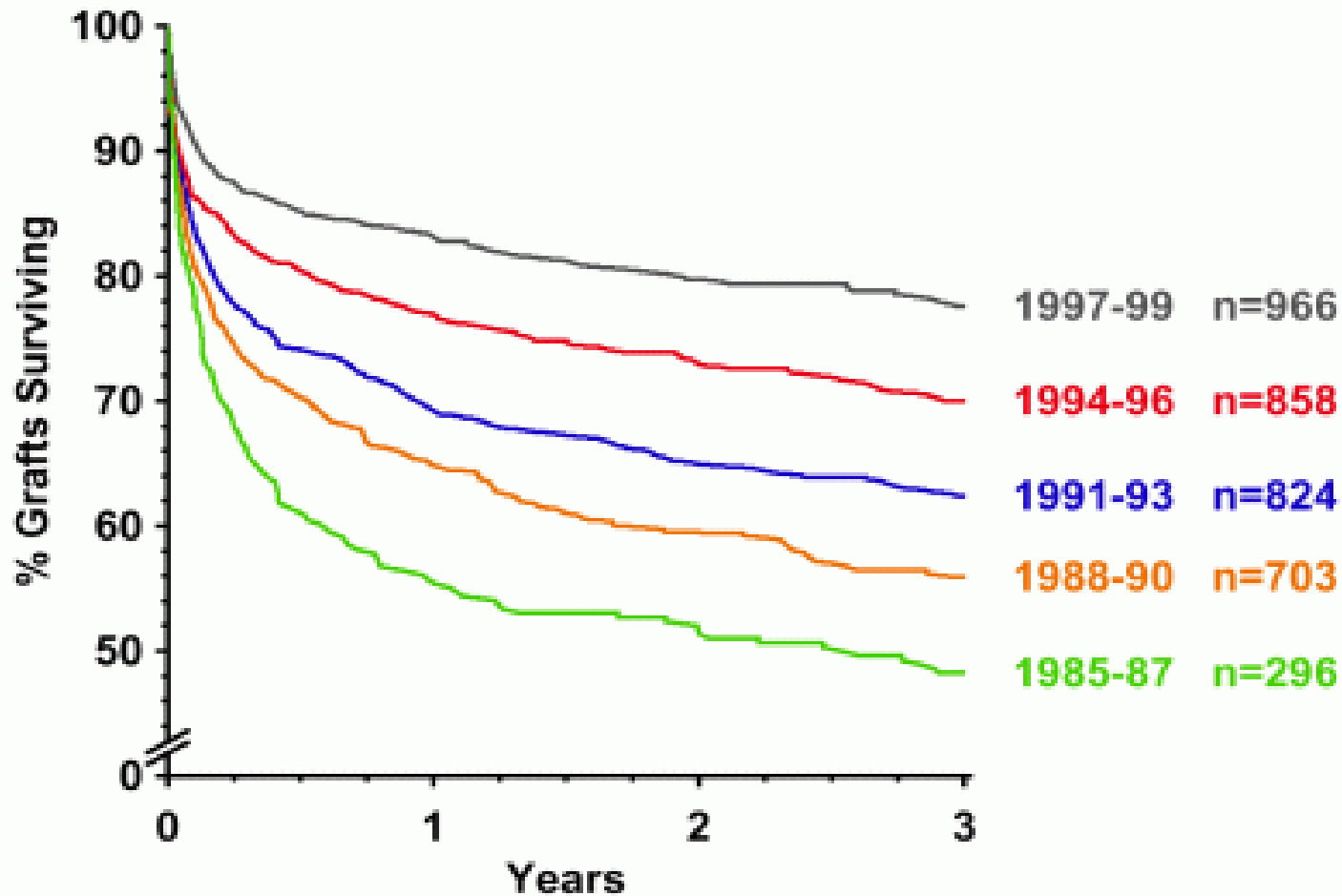
# Patient Survival while Waiting

UNOS Pancreas Waiting List 1/1/1995 – 5/31/2003



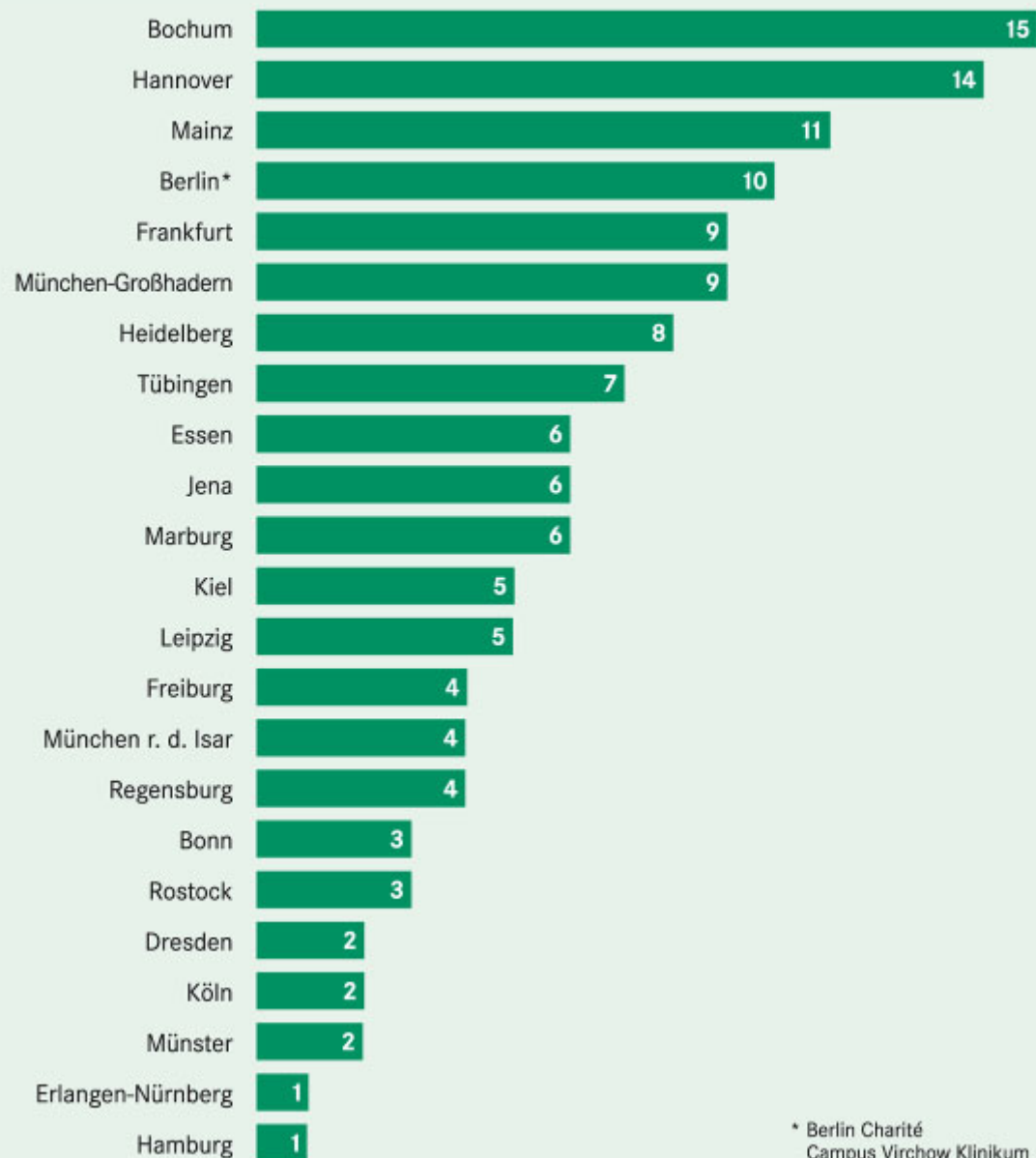
# Transplant Year

## First Combined Kidney/Pancreas Transplants Pancreas Graft Survival



# Pankreas- und kombinierte Pankreas-Nieren-Transplantationen

ANZAHL NACH TRANSPLANTATIONSZENTREN

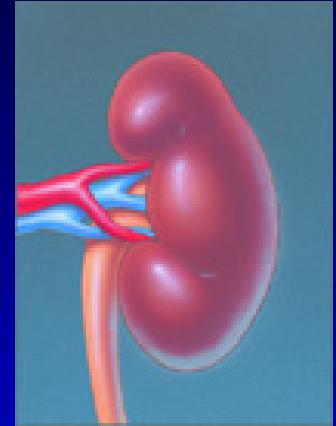


\* Berlin Charité  
Campus Virchow Klinikum

# Diabetes and transplantation in Hungary

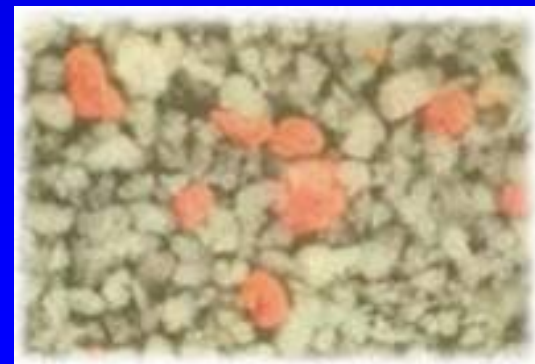
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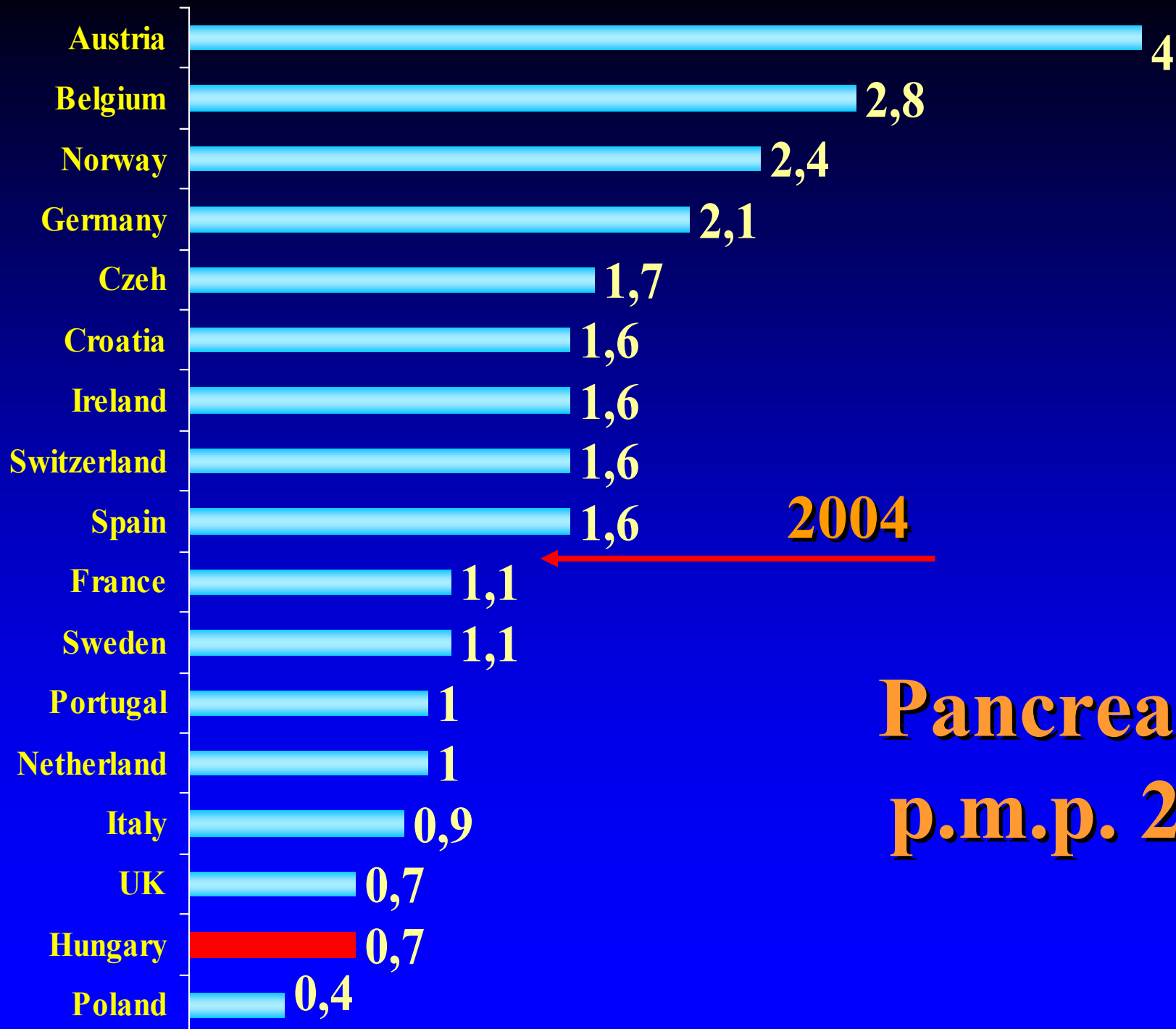
- 1980 first KTX for diabetes



- 1998 Pécs,  
2004 Budapest - SPK

- 2003 Budapest - IAK





**2004**

**Pancreas tx  
p.m.p. 2003**

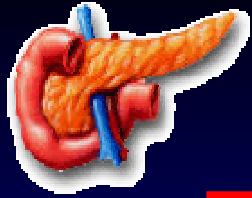


# INDICATION FOR SPK

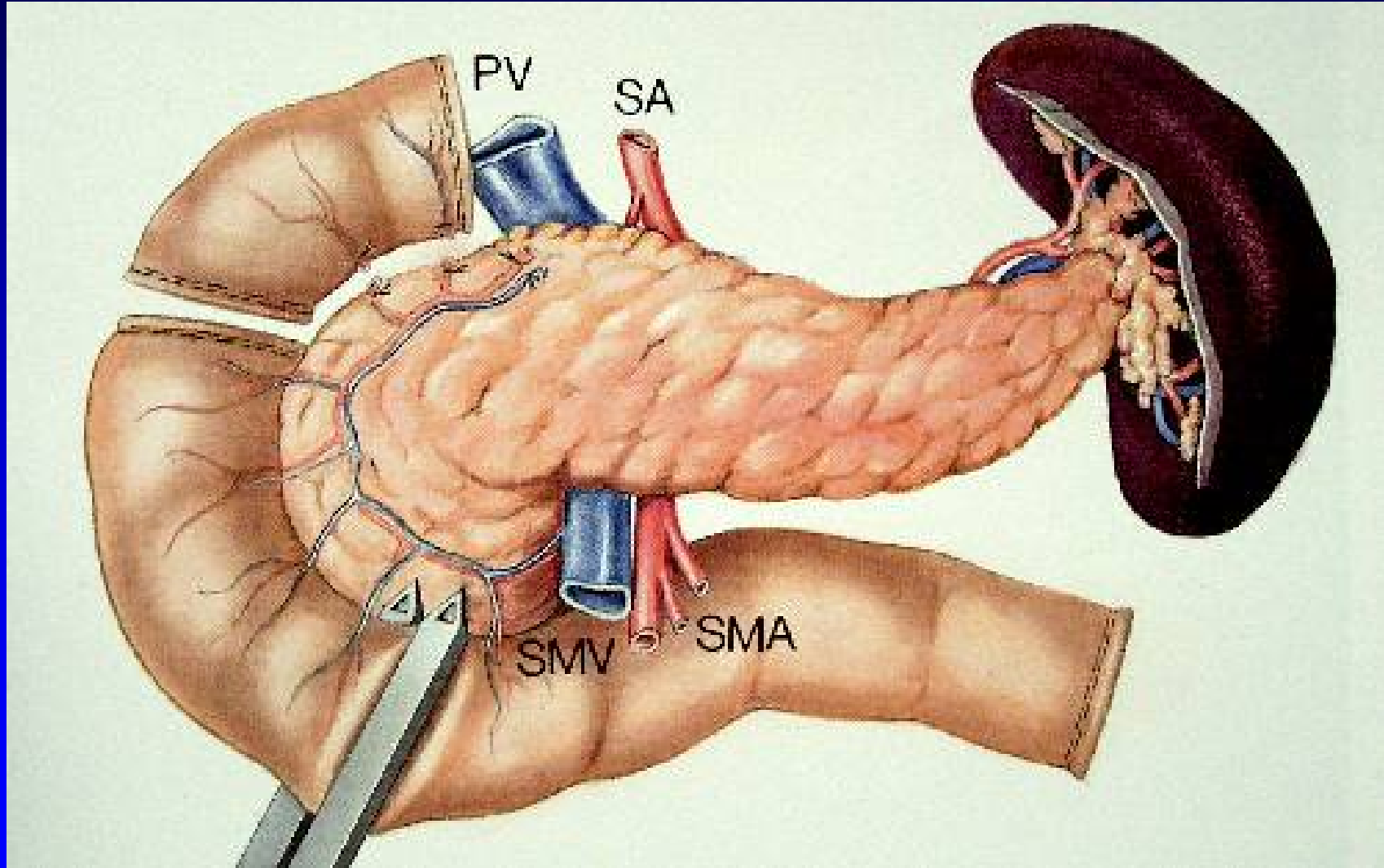


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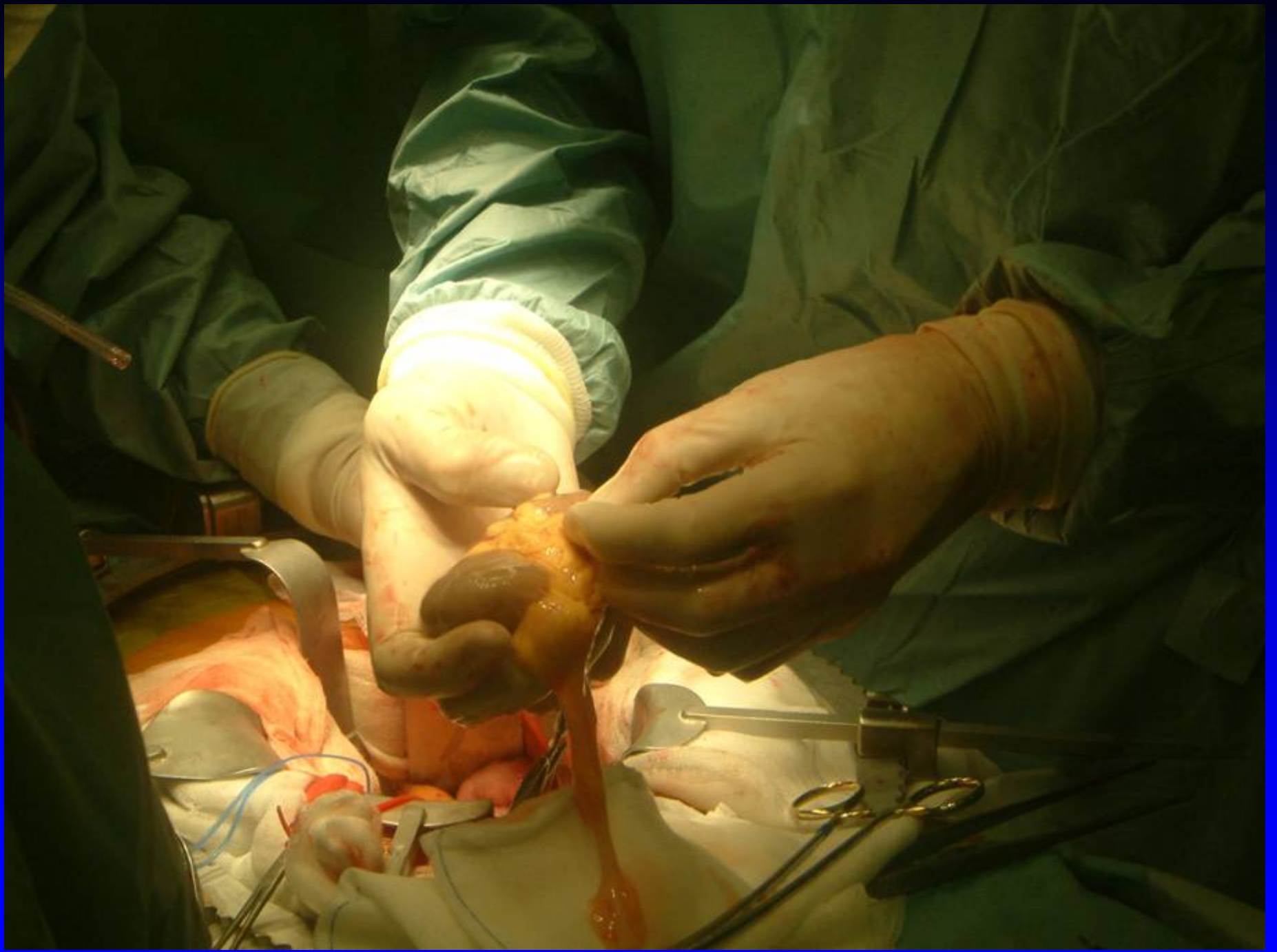
- **Type 1 diabetes with uremia**
- **Type 2 is less than 5% -  
routinely NOT accepted**

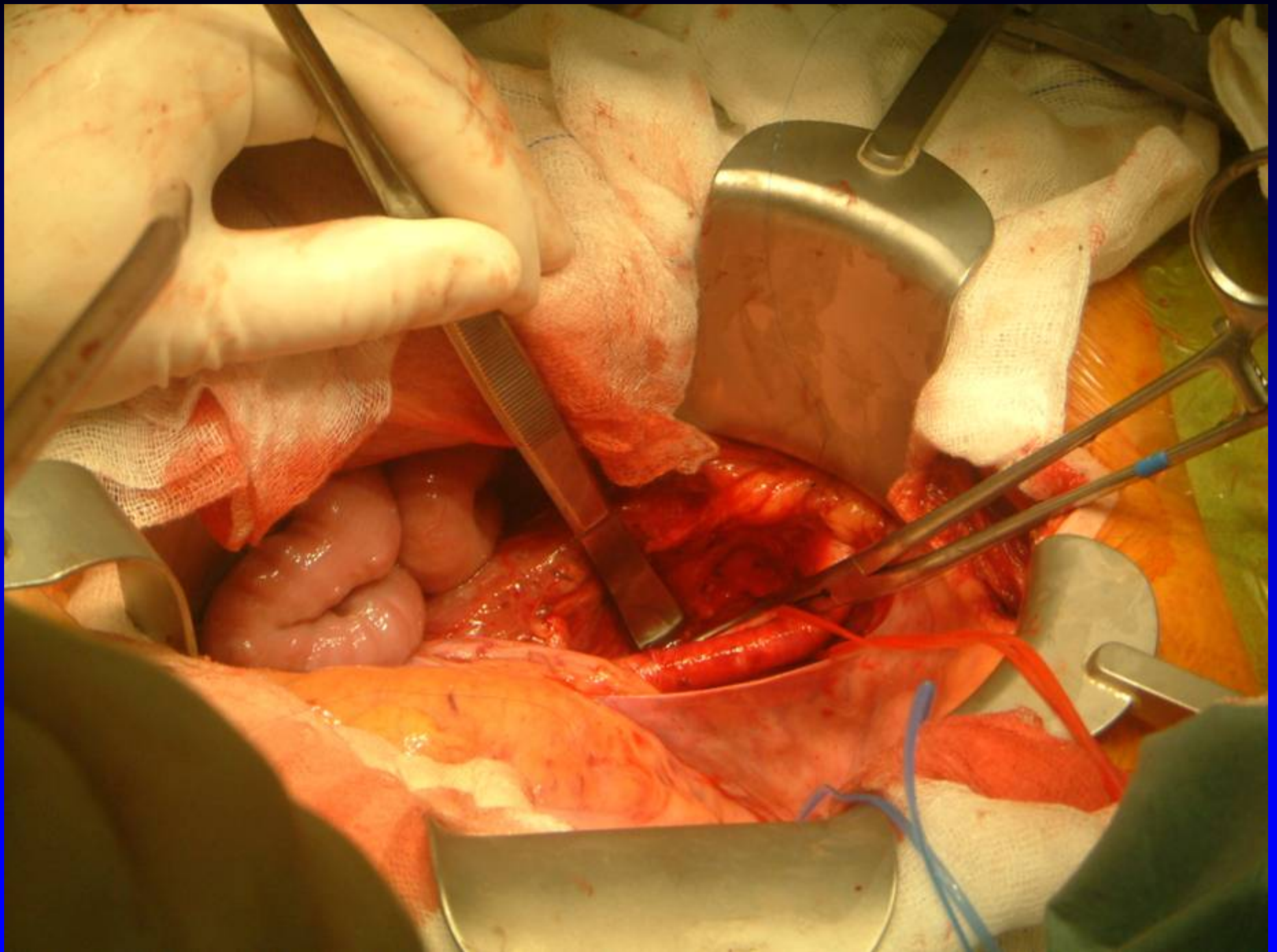


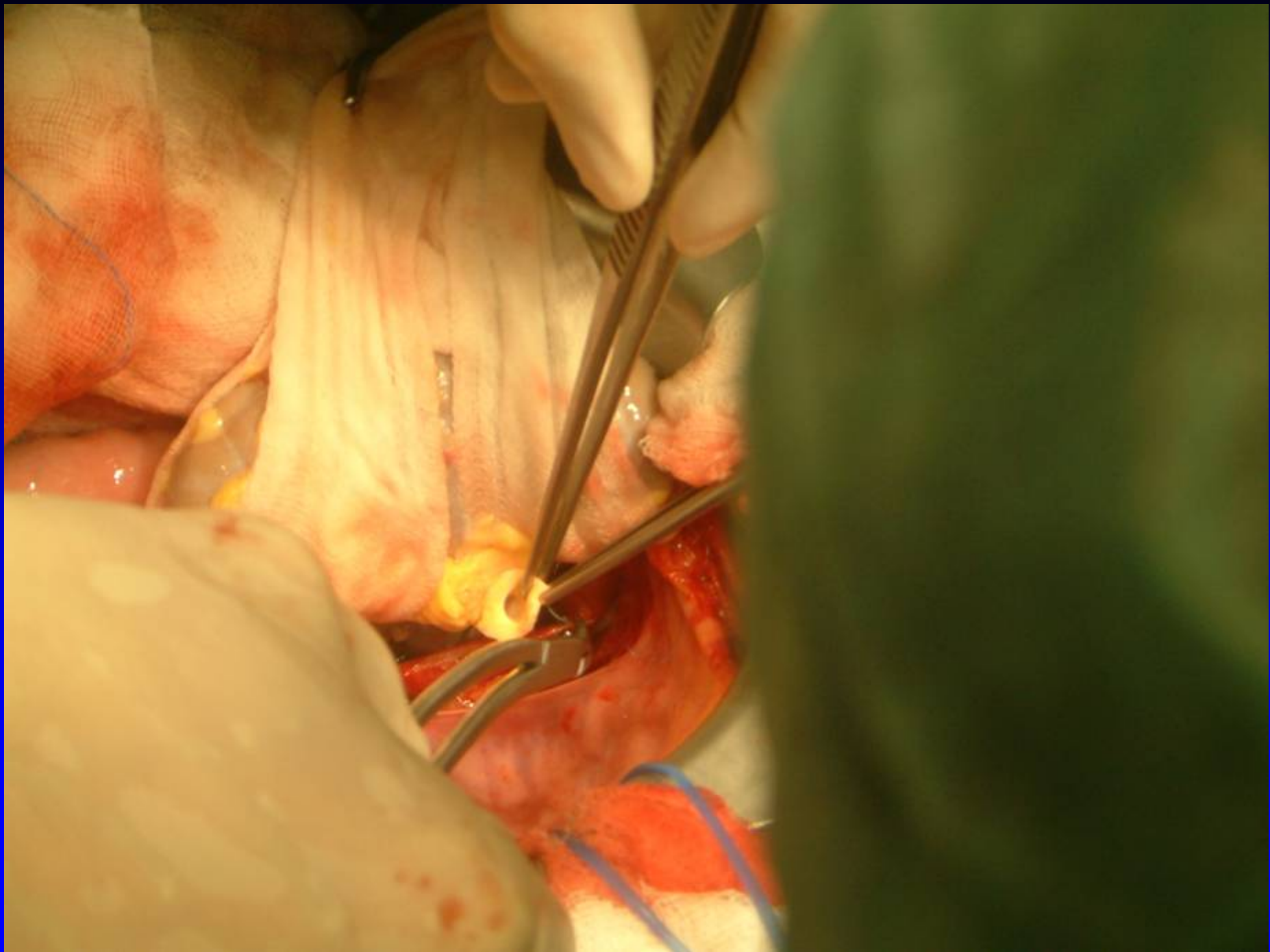
# Pancreas Explantation

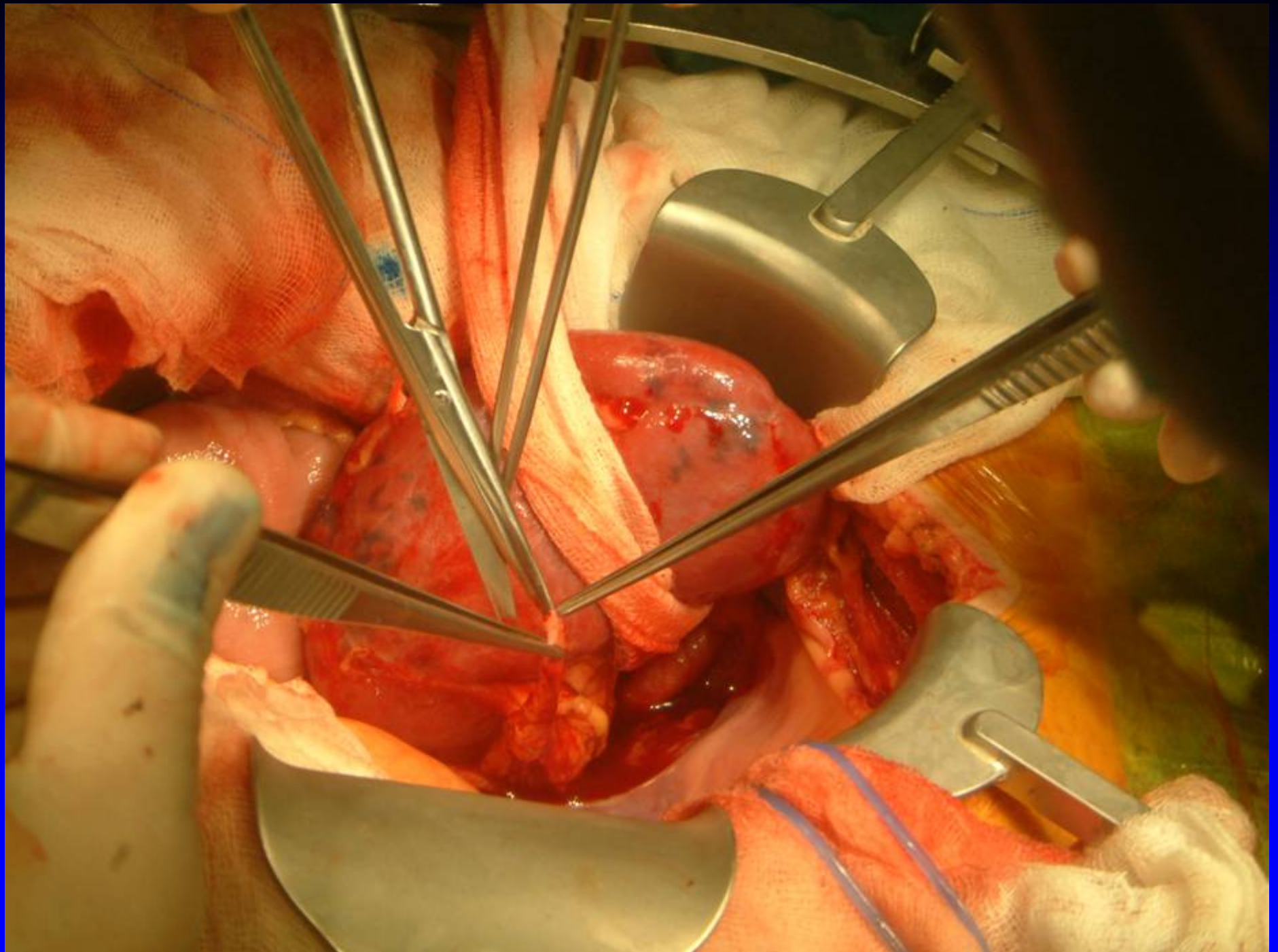


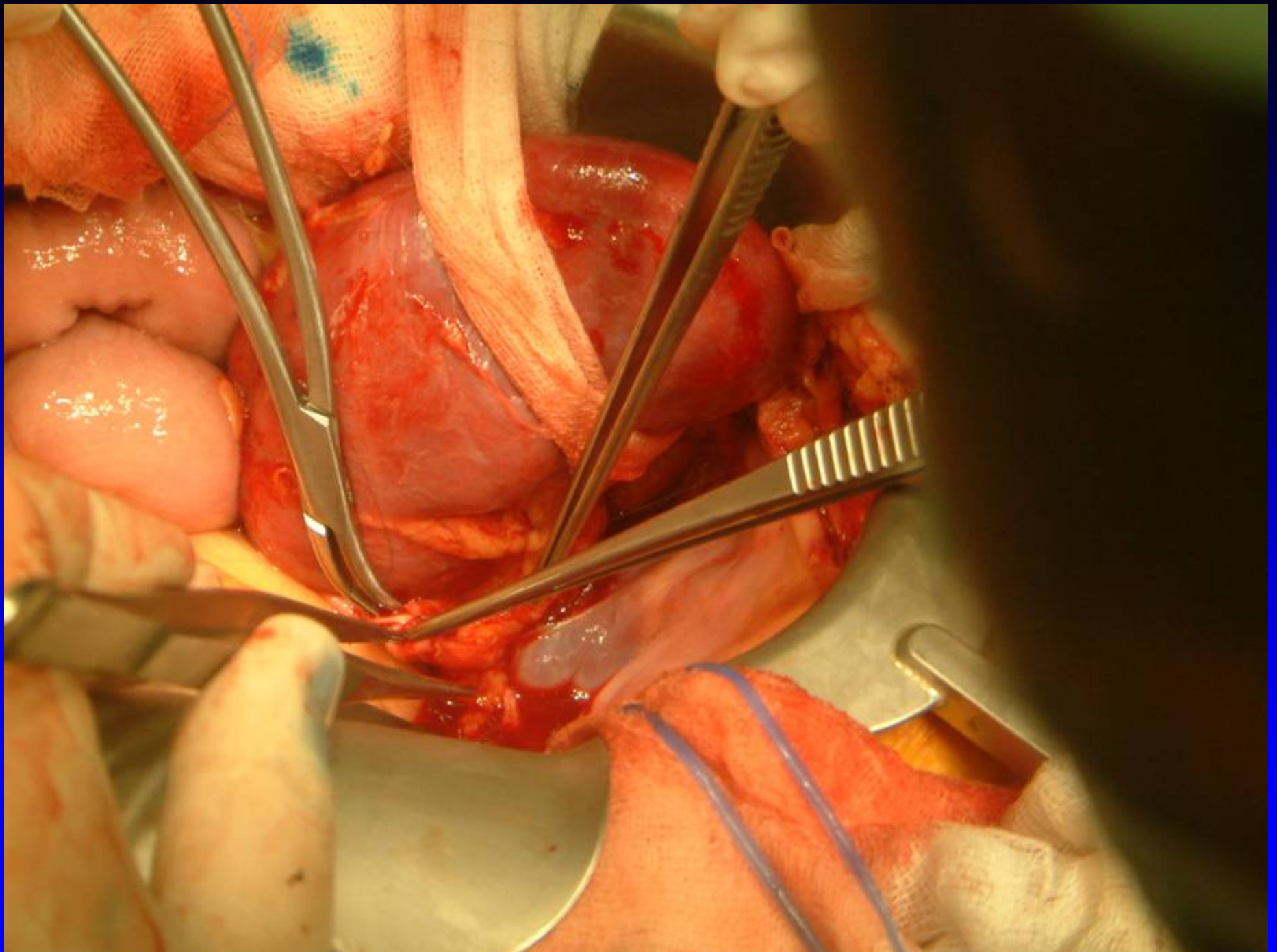


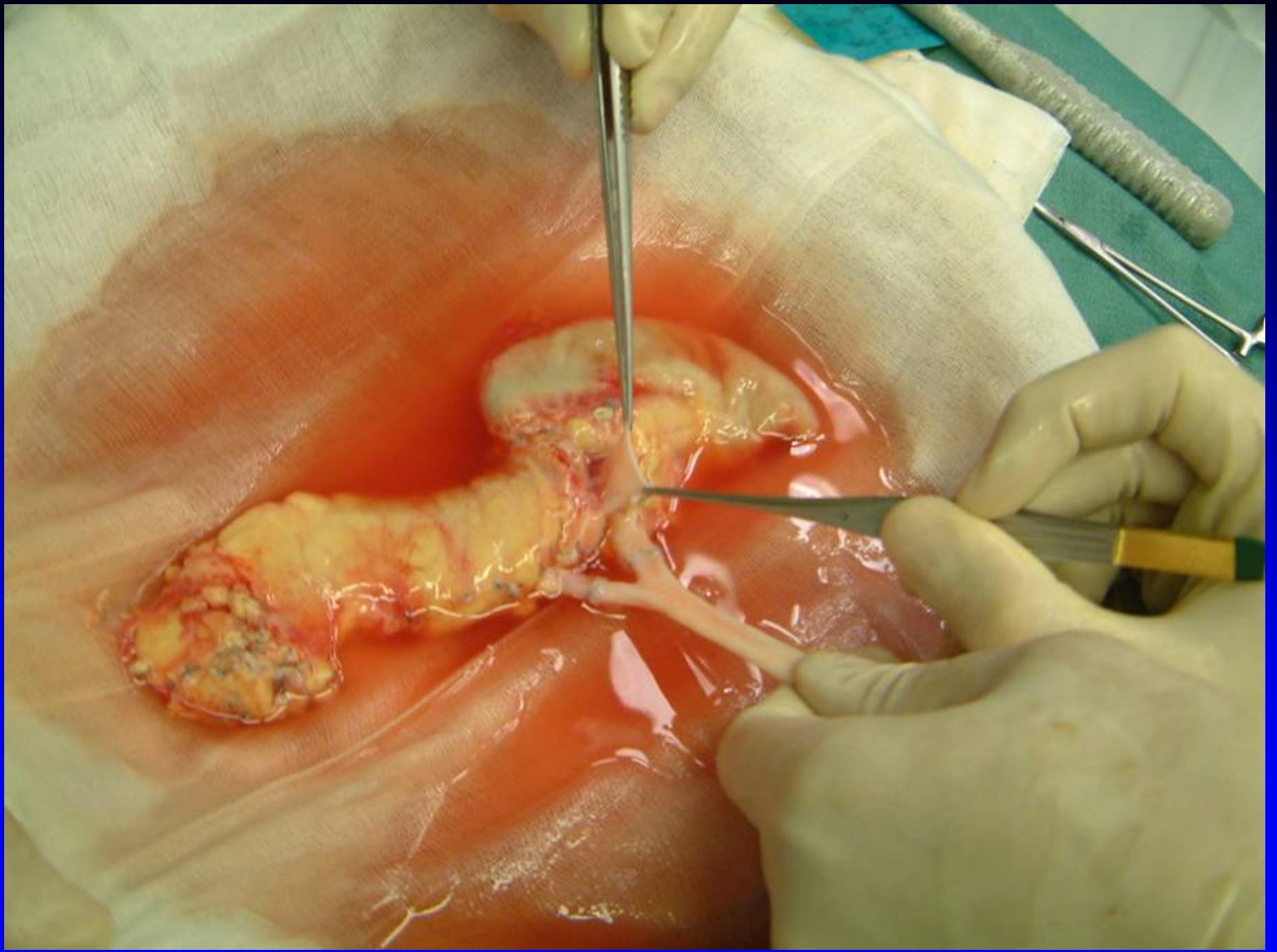


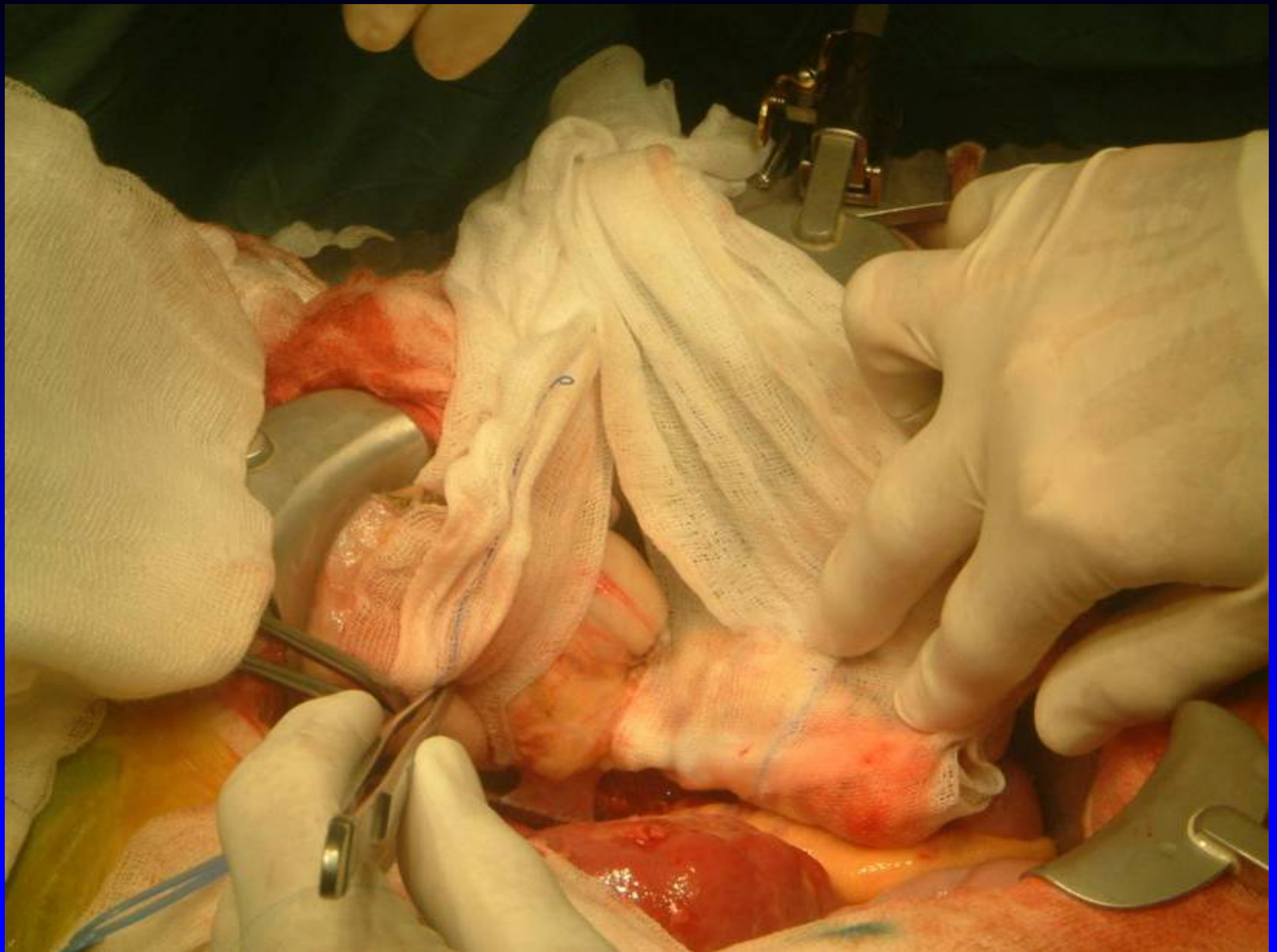


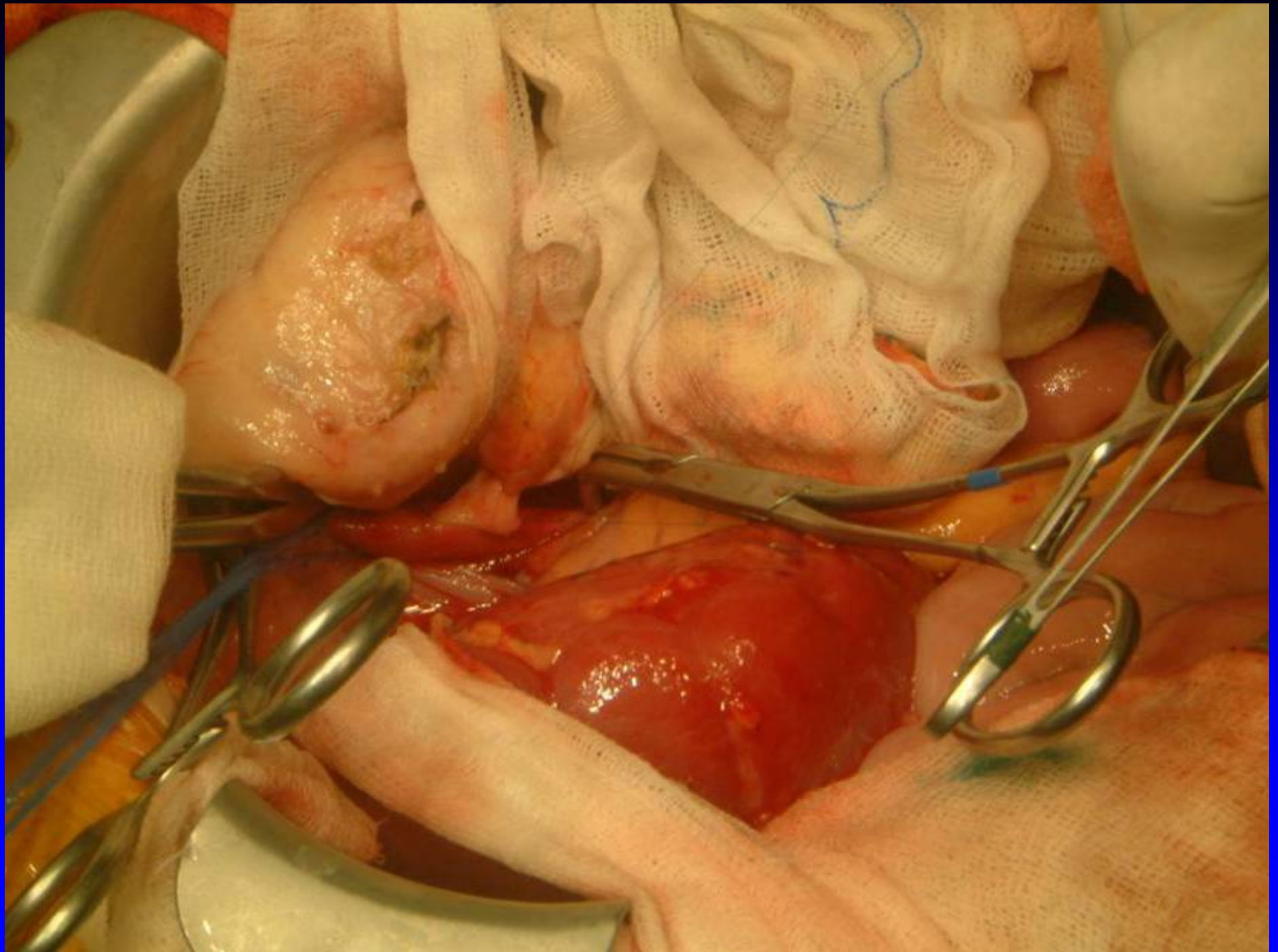




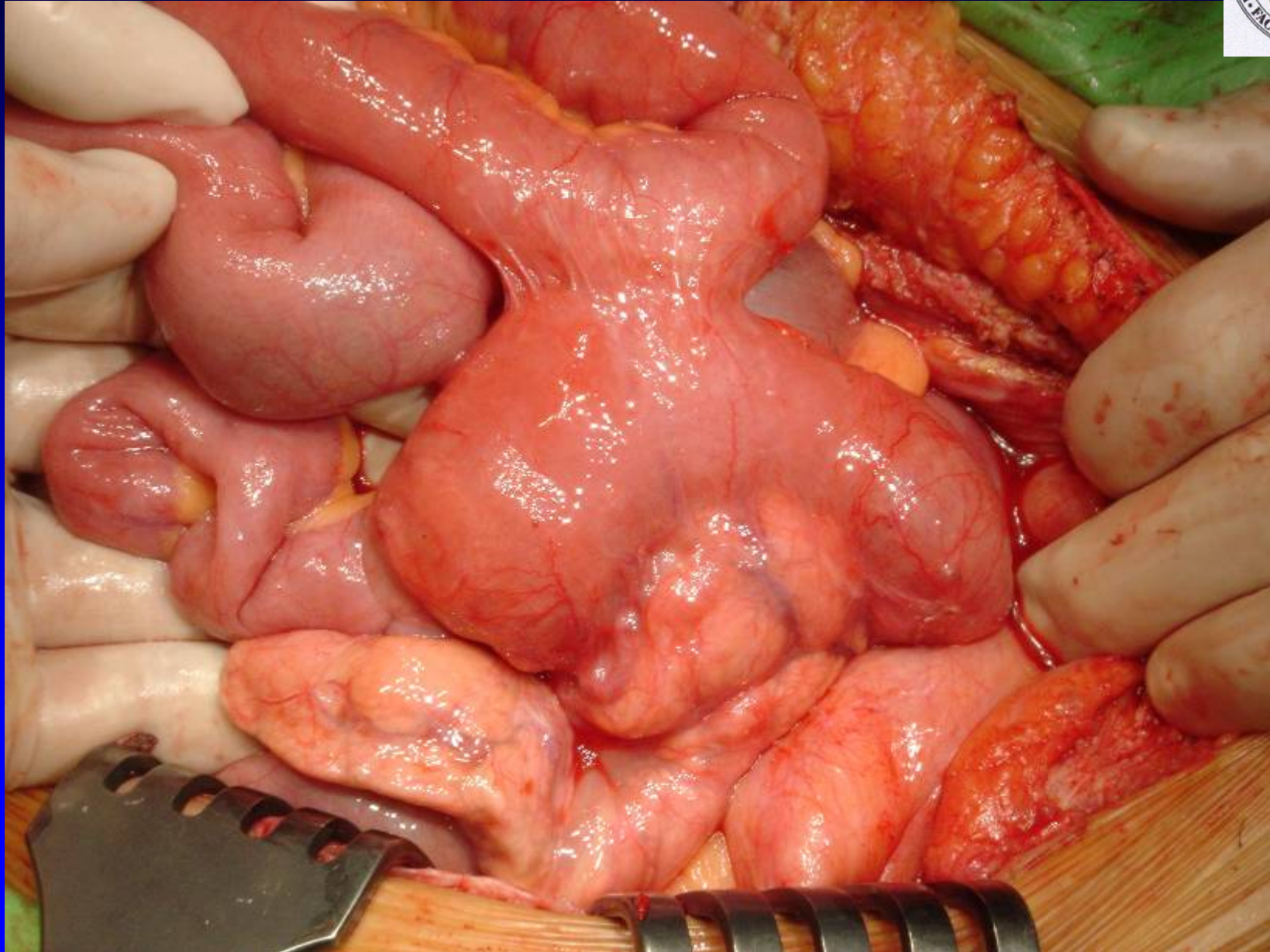


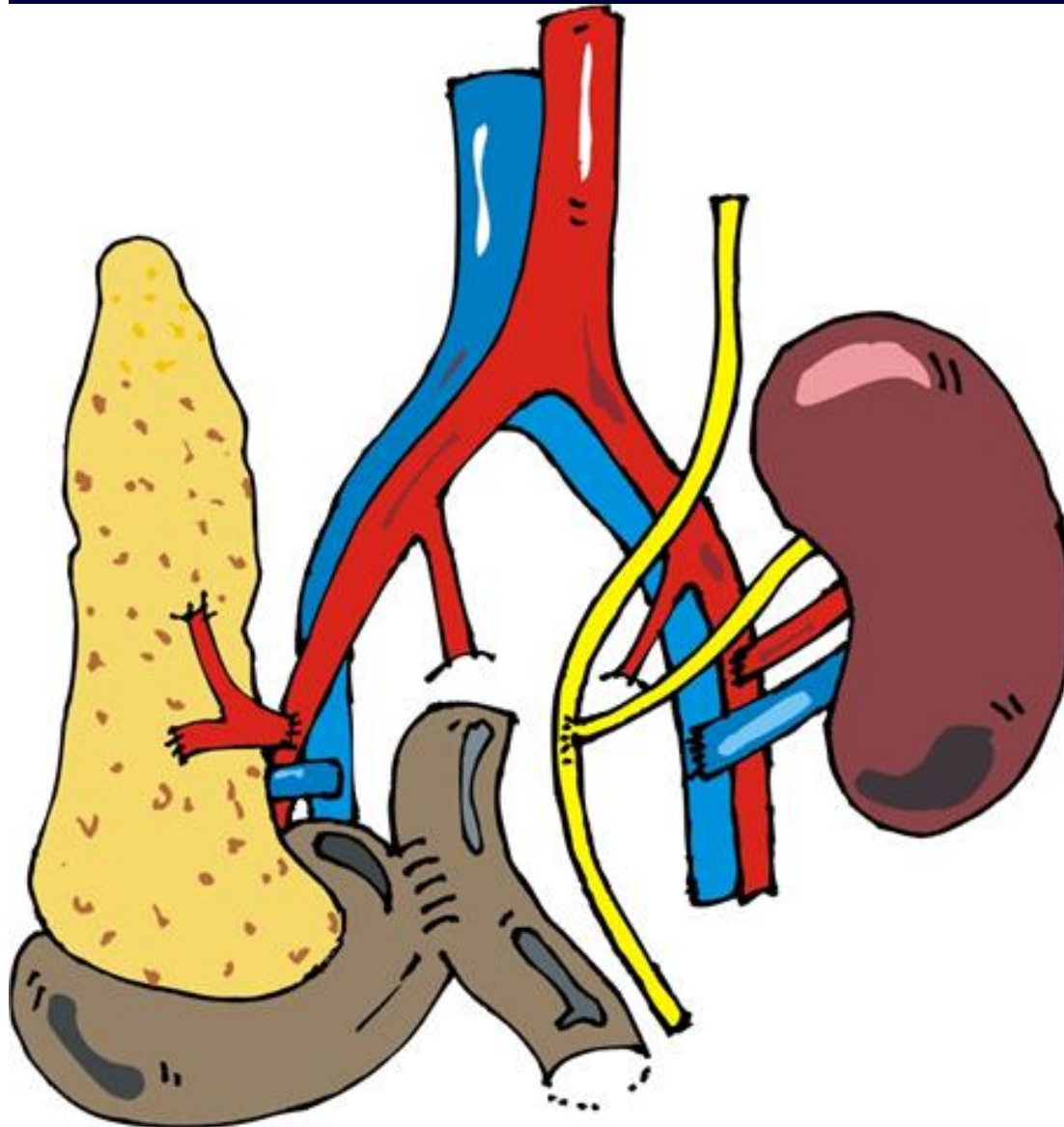






# SPK





3D  
Ex: 22519  
Se: 5 +c  
Volume Rendering No cut

SE TRANSZPLANTACIOS KLINIKA  
GULRICH PEETER  
M 46 1 58/03/16  
Dec 27 2004



No VOI  
kv 120  
mA 200  
1.0  
3.0 mm/1.0sp  
Tilt: 0.0  
11:04:01 AM  
W = 395 L = 396

IAL



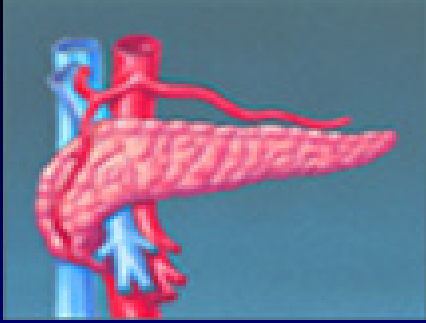


# IMMUNOSUPPRESSION



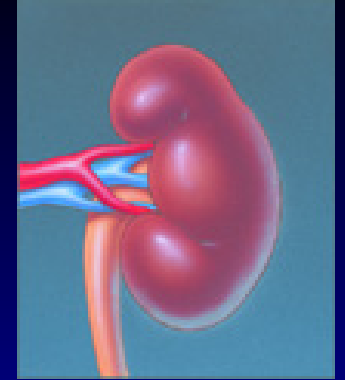
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- **ATG 5 days**
- **Sirolimus (8-12 ng/ml)**
- **Cyclosporine (150-100 ng/ml)**
- **Prednisolone (500-125-20 mg)**



## SPK Results (n=20)

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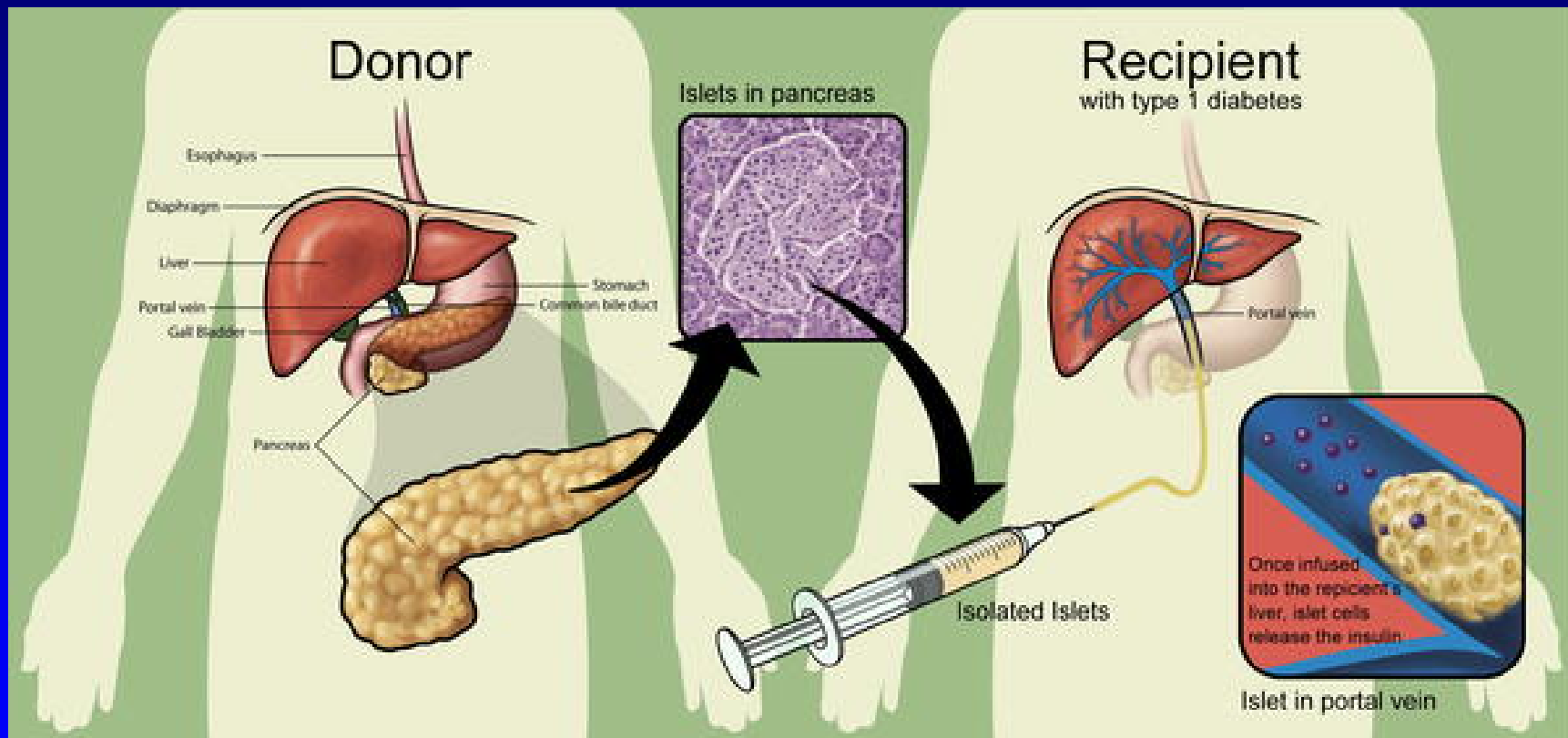


- Donor age: 28.9 J      BMI: 22.1
- Recipient age: 37.1 J      BMI: 21.7
- CIT kidney: 9:56 h
- CIT pancreas: 10:58 h
- Operation time: 3:18 h
- Complications: 7x bleeding, 3x abscess, 1 CMV
- HD: 0, (1 PNF) insulin 0, rejection 0, (thr.1)

A microscopic image showing a dense field of islet cells, which are clusters of endocrine cells. The cells are stained, showing a mix of reddish-brown and purple hues. The overall appearance is a textured, granular surface.

# Islet cell transplantation

# ISLET CELL TRANSPLANTATION



# PRODUCTION OF COLLAGENASE

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# PITFALLS OF ISLET TX

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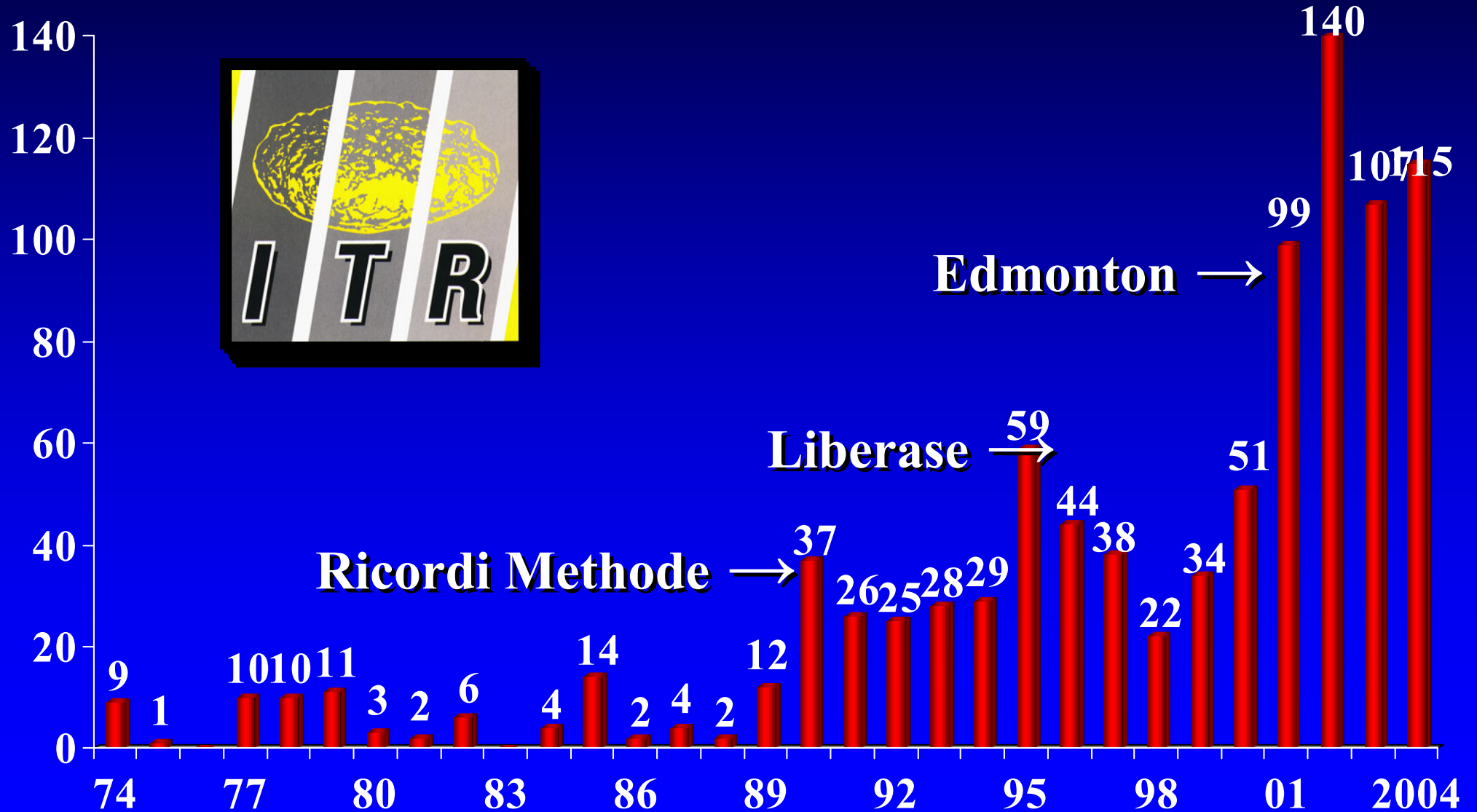
- Theoretically easy, but...
- 80% isolation success, but 15% remains
- 1,5 million Langerhans islet = 1 ml!!!
- Just 20% will be transplanted!
- Only parts around 150 $\mu$ m
- Variability of the donor and the recipient

# SEPARATION

COBE 2991

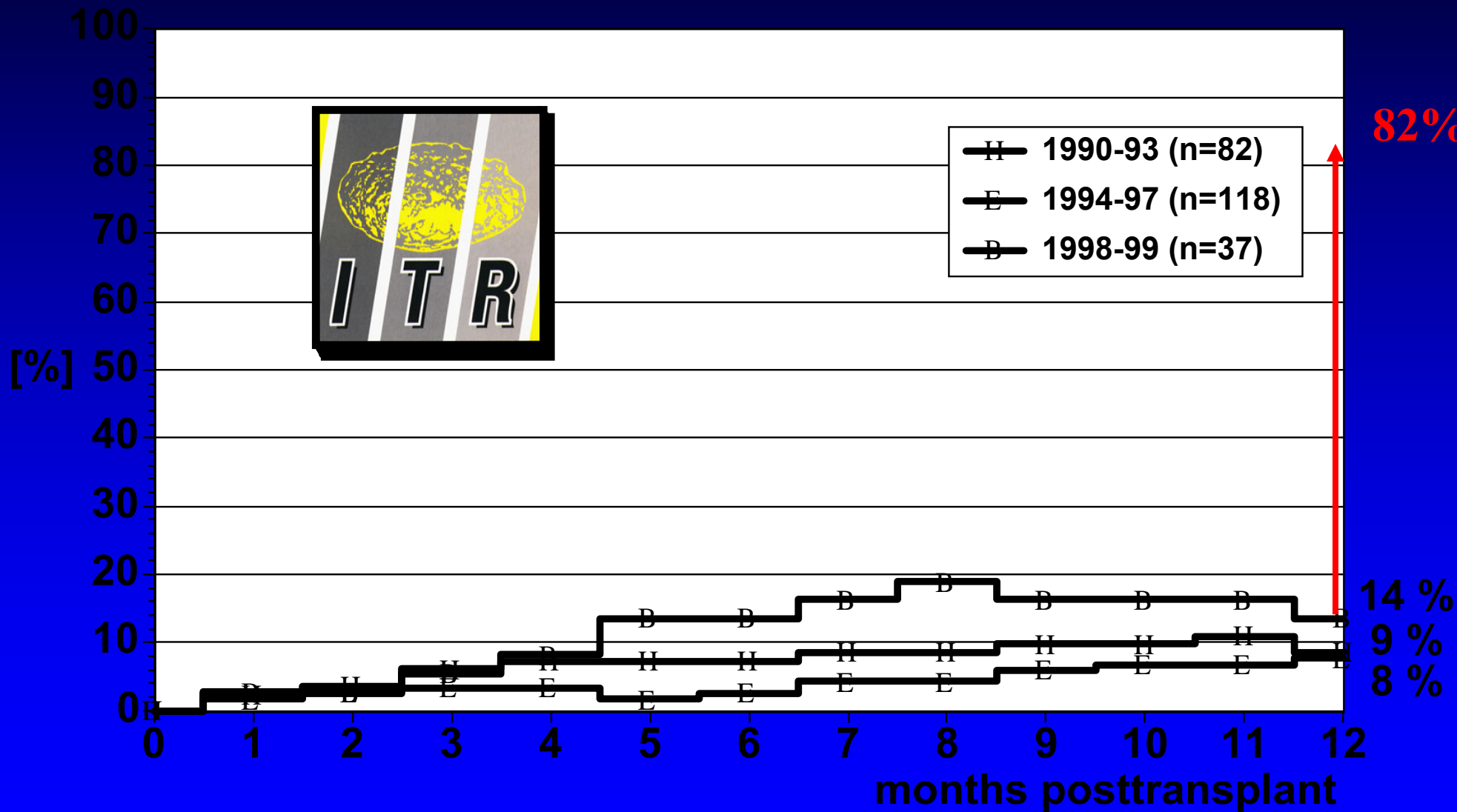


# ISLET CELL ALLOGRAFTS 1974-2003



# One-Year Insulin Independence by ERA

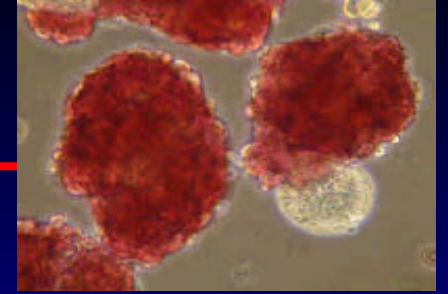
C-Peptide Negative Type-1 Diabetic Recipients; 1990-1999; n=237\*



\* Only well documented cases



# Why IAK ?



- **Less than an operation**
- **Immunosuppression already existent**
- **Easy to repeat**
- **4-y PAK better than KTA!!**



**Teamwork!**

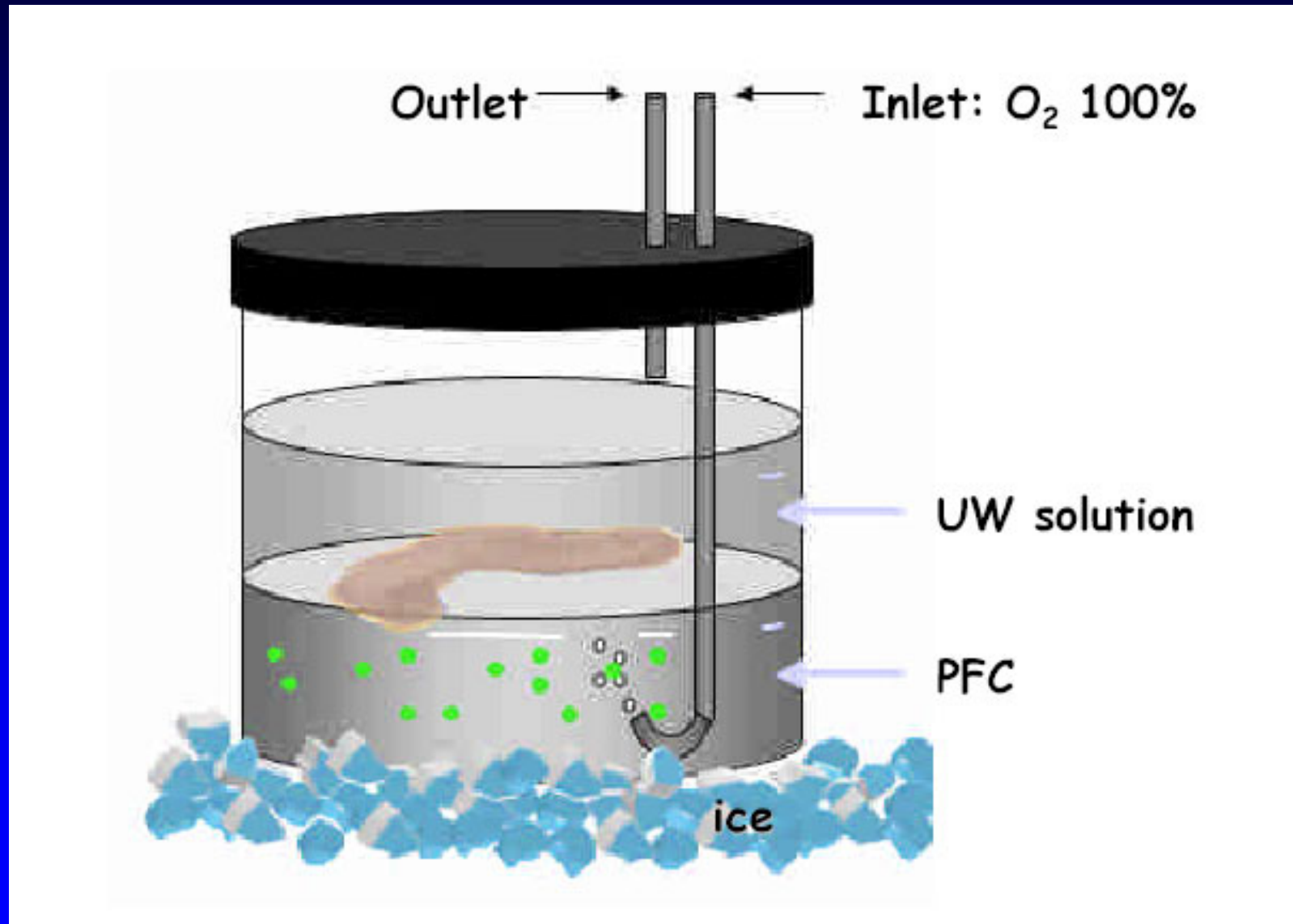
→ Langer RM, Máthé Z et al: *Transpl Proc* 36: 3113-15. (2004)

# Why Geneva?



- **Experimental phase, let us choose (one of) the best**
- **One of the 10 biggest centers**
- **No „learning curve”**
- **Cost efficient**
  - **Labor building: ~ \$ 2 million**
  - **One isolation: ~ \$ 10 000 – 20 000**

# Two-layer method



→ Kuroda Y et al: *Transplantation* 1988



# In the Geneva lab...

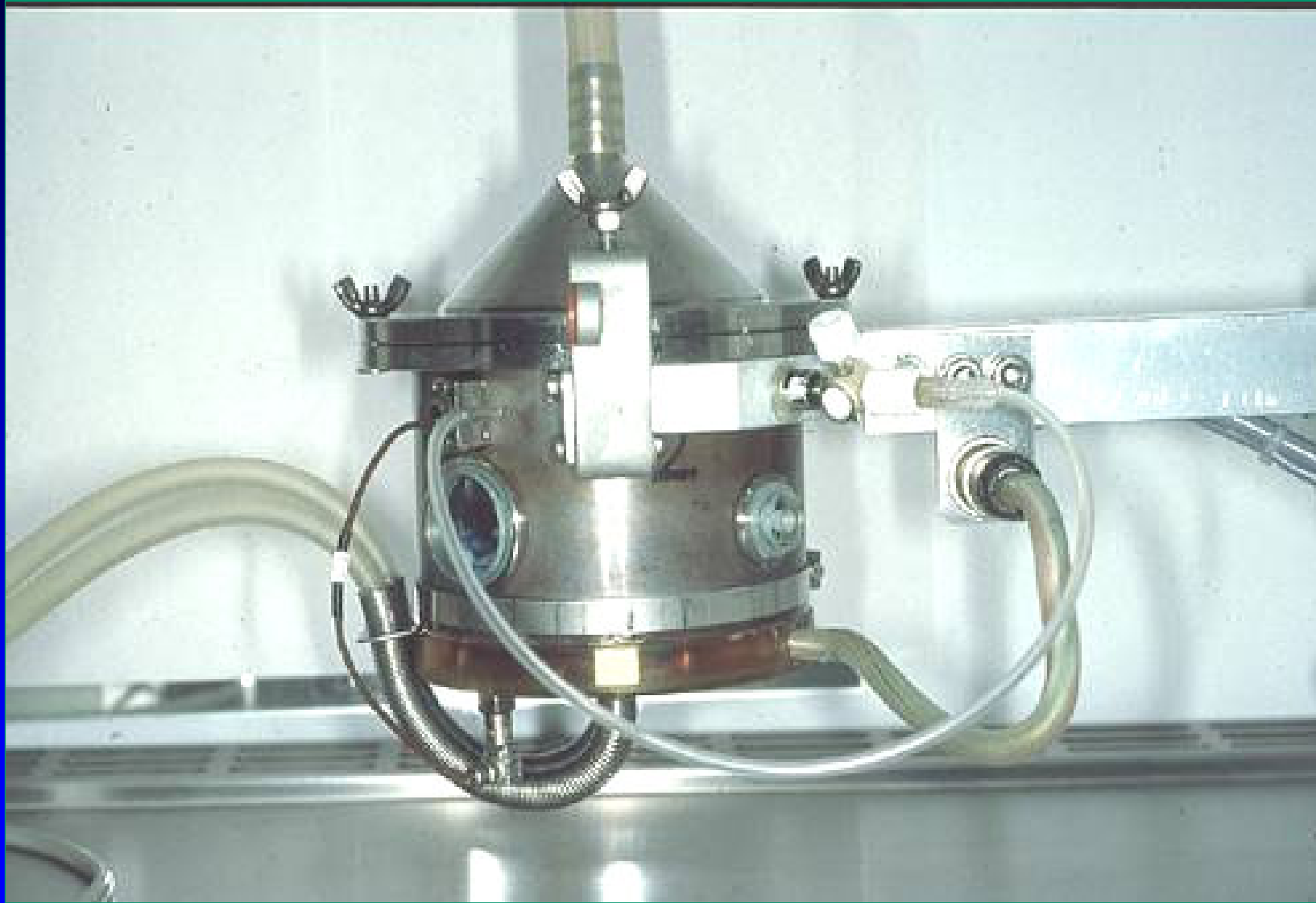
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**CIT: 6:52 (5:10-8:20)**

# The Ricordi Method

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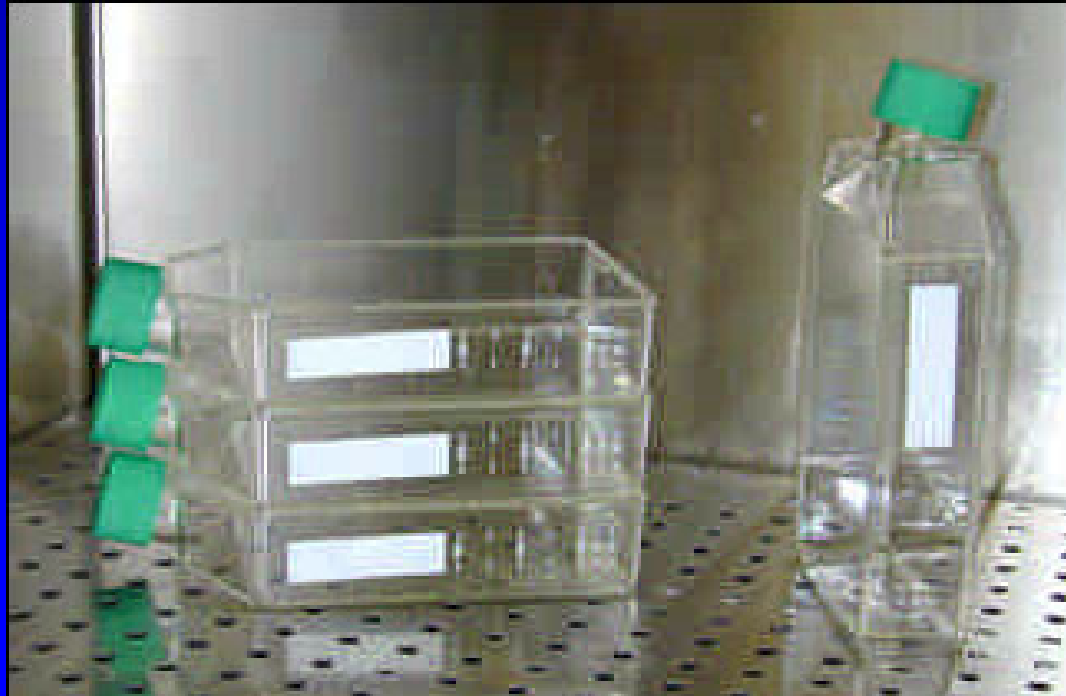


→ Ricordi C et al.: Diabetes 1988; 37; 413-20

# Overnight culture

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- Possible to remove the damaged cells
- Cell regeneration
- Time to gain to make the suspension



# Islet suspension

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Scale 1 : 19,500,000  
Lambert Conformal Conic Projection,

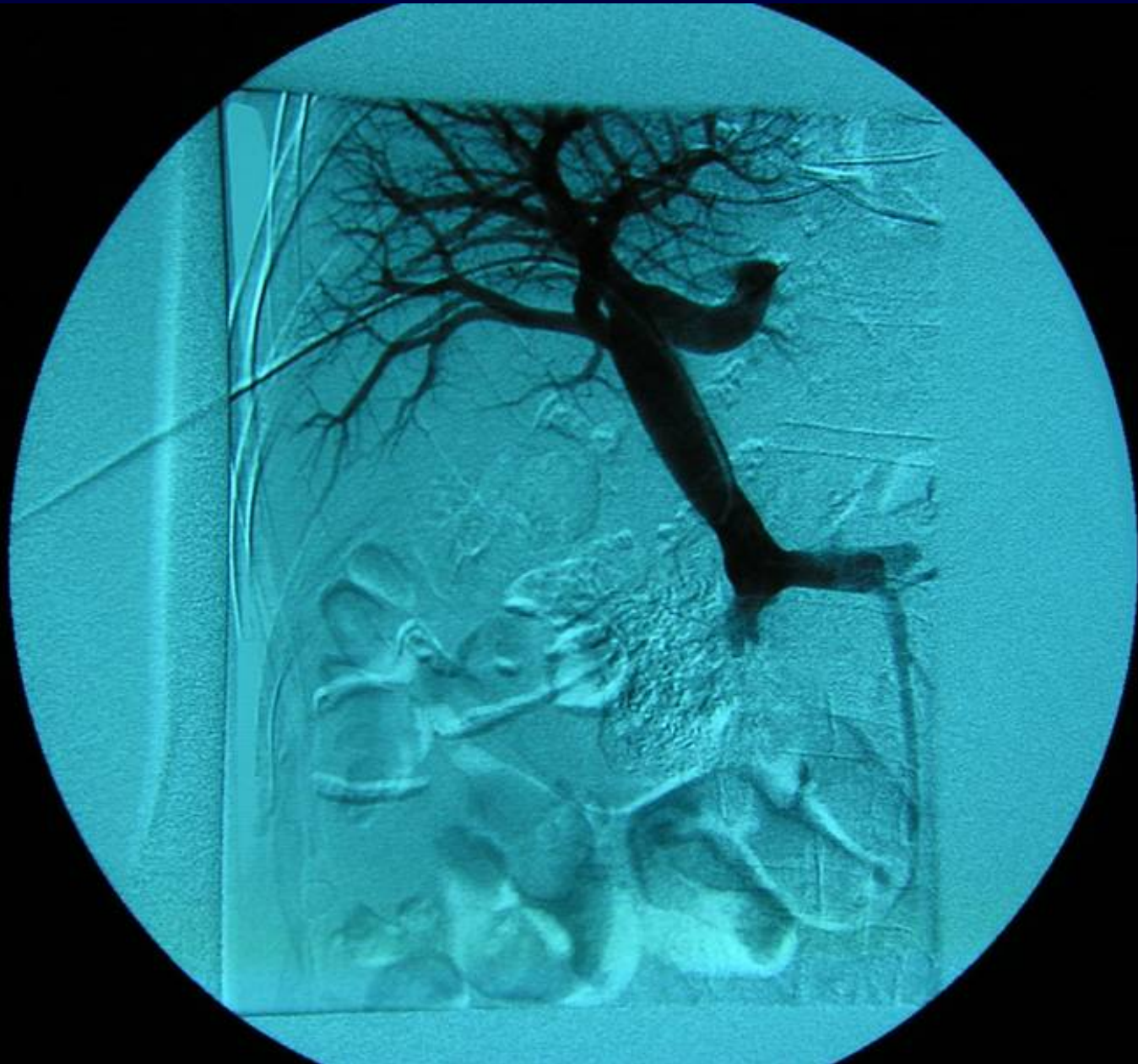


# Islet cell transplantation



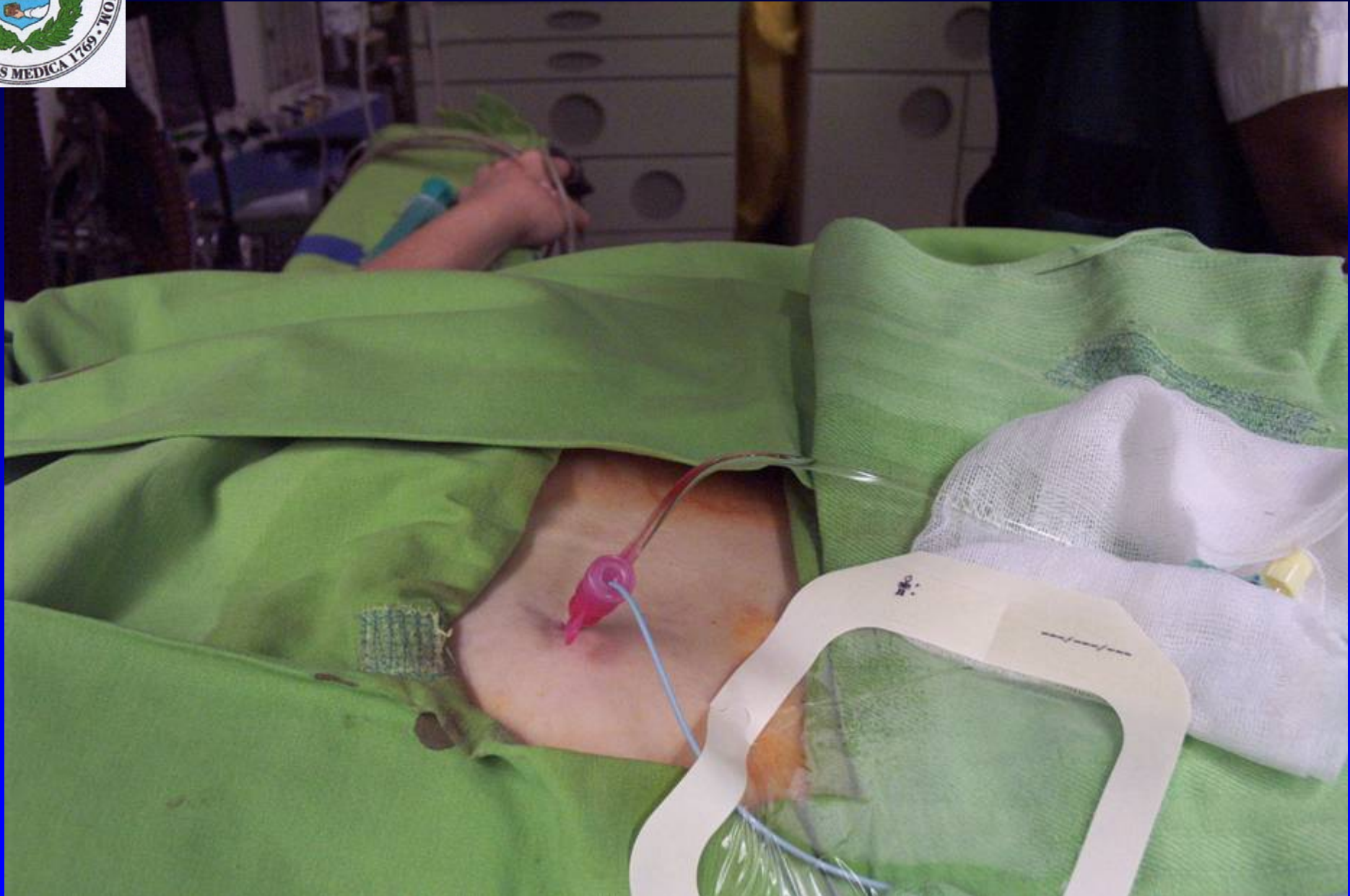


# Islet cell transplantation





# Islet cell transplantation



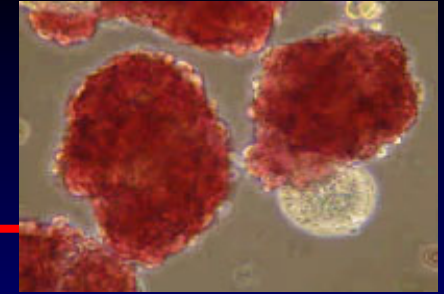


# The „hand-bag” method





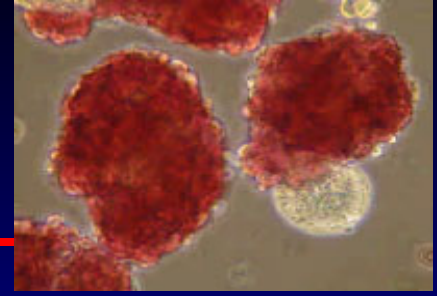
# IAK results



- Donor age: 42.5 years, (35-57) BMI: 28.0 (22.9-34.6)
- Isolation success: 61.5% (8/13)
- Recipient age: 42 years; since 6.6 y tx, 33.9 y DM
- Waiting time: 7.3 months
- Median follow up: 27.4 (3.5-41.6) months
- Complications: 1 bleeding,  
the portal pressure remained constant in all cases
- All became metabolically stable!

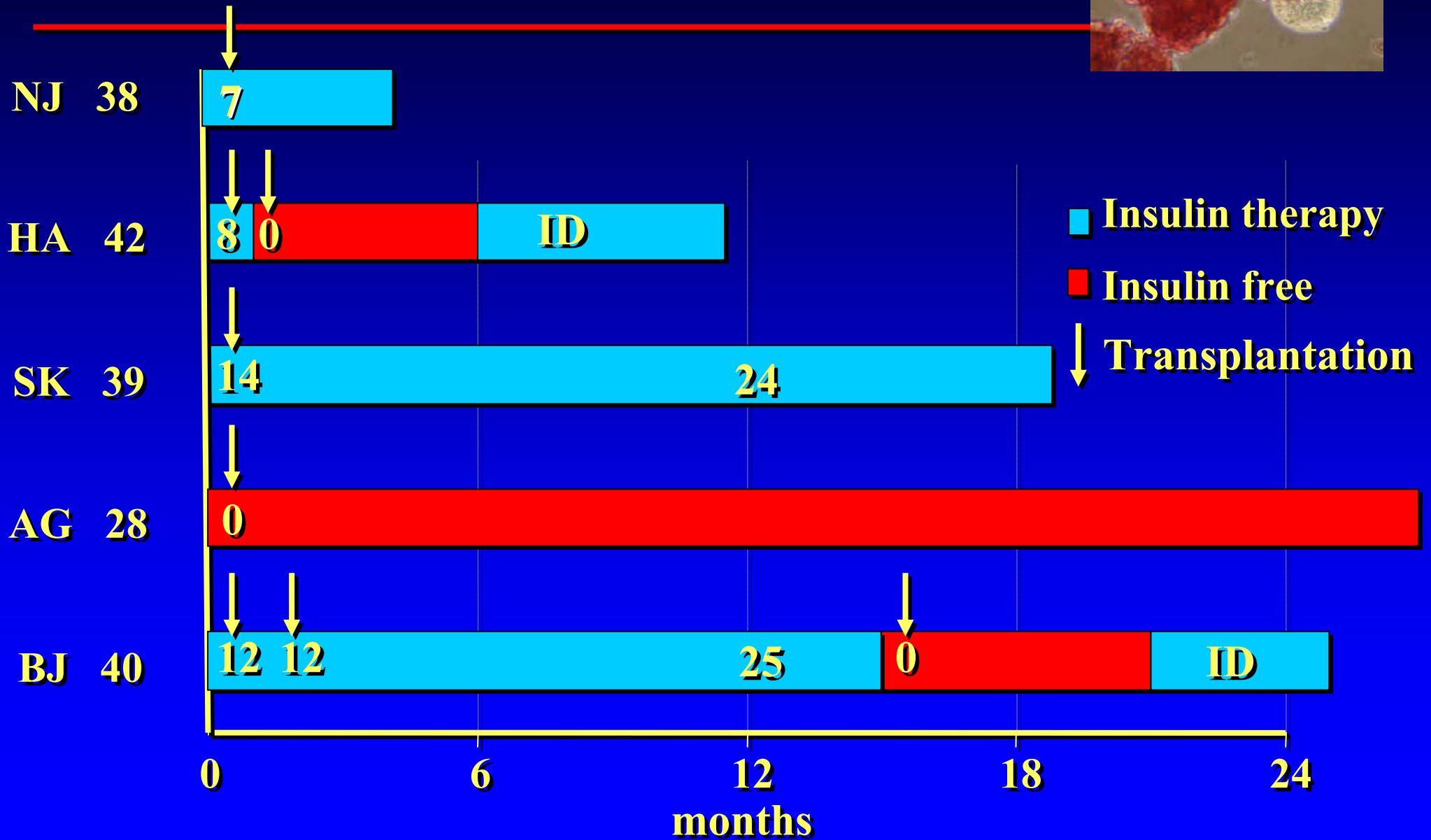
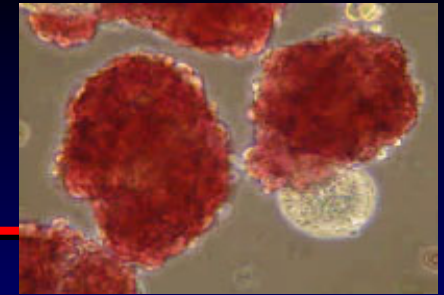


# IMMUNOSUPPRESSION



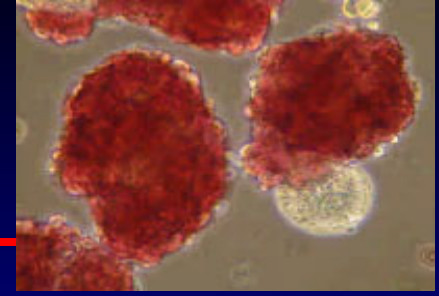
- **Sirolimus 8-12 ng/ml**
- **Low-dose tacrolimus 4-6 ng/ml**
- **Daclizumab 1 mg/kg  
5x q fortnight**

# IAK results (n=5)

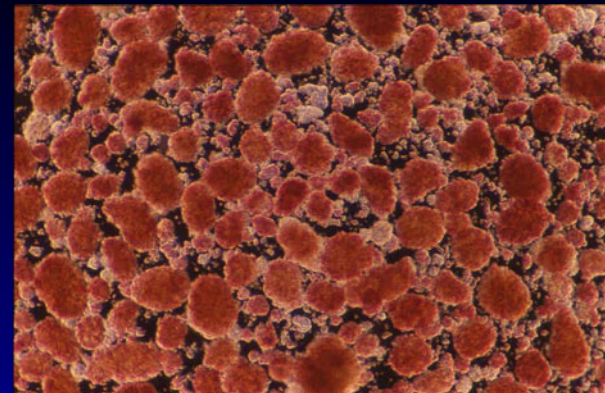
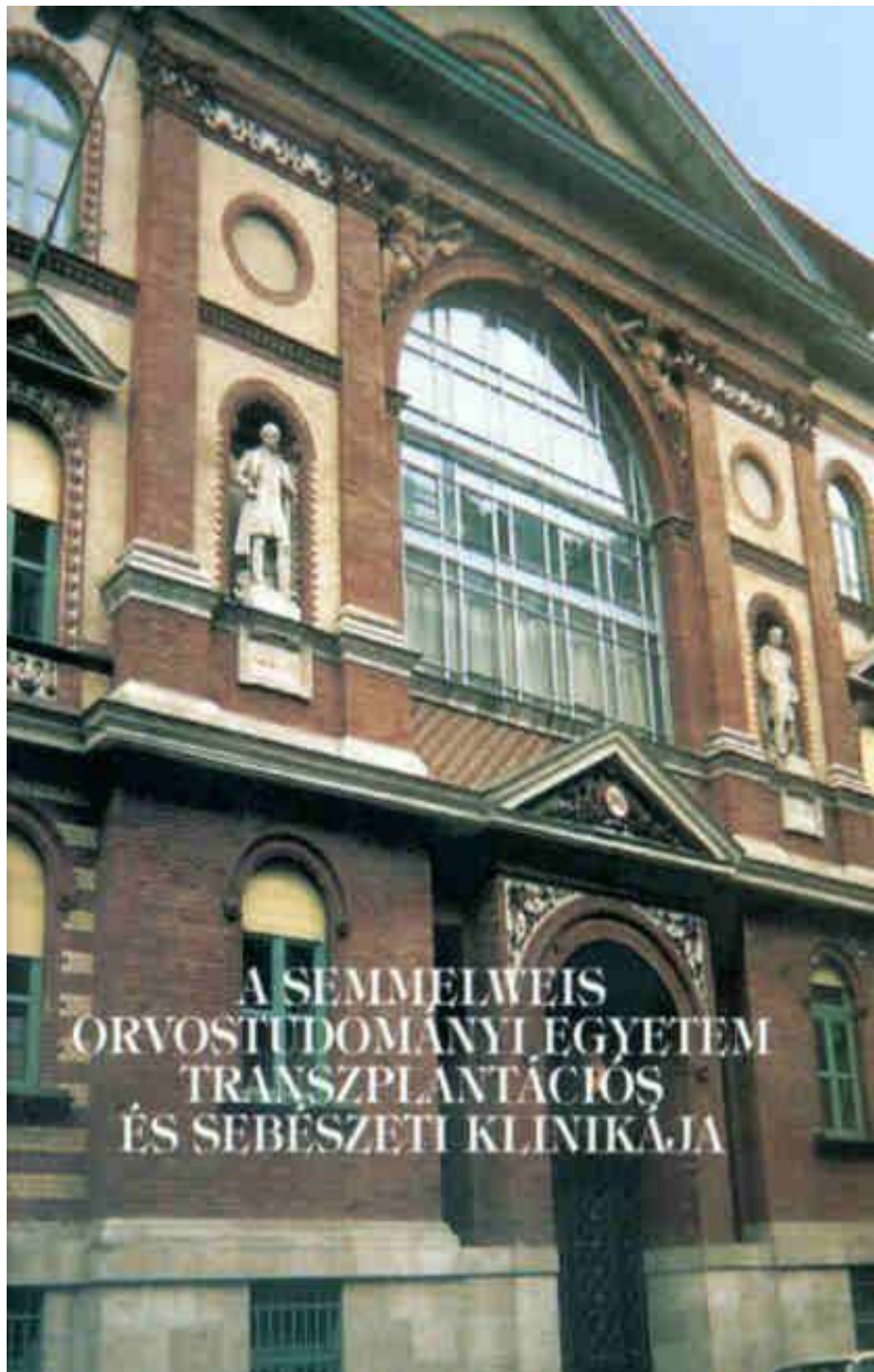




# CONCLUSION



- **The results are not comparable with the solid organ results**
- **Patients will be immunized (100% PRA)**
- **Cost effectiveness? – still in the experimental phase**



**Thank you for  
your attention!**

