



ARC

ACCADEMIA ROMANA DI CHIRURGIA

Tecnologica – Oncologica – Specialistica

Surgical treatment of intermediate/advanced hepatocellular carcinoma on cirrhosis

Antonino Cavallari

Accademico Corrispondente

Roma, 2 aprile 2004



130 liver resection for HCC on cirrhosis (1996-2003)

Early vs intermediate/advanced HCC

Early HCC (Milano criteria): 88 pts (68%)

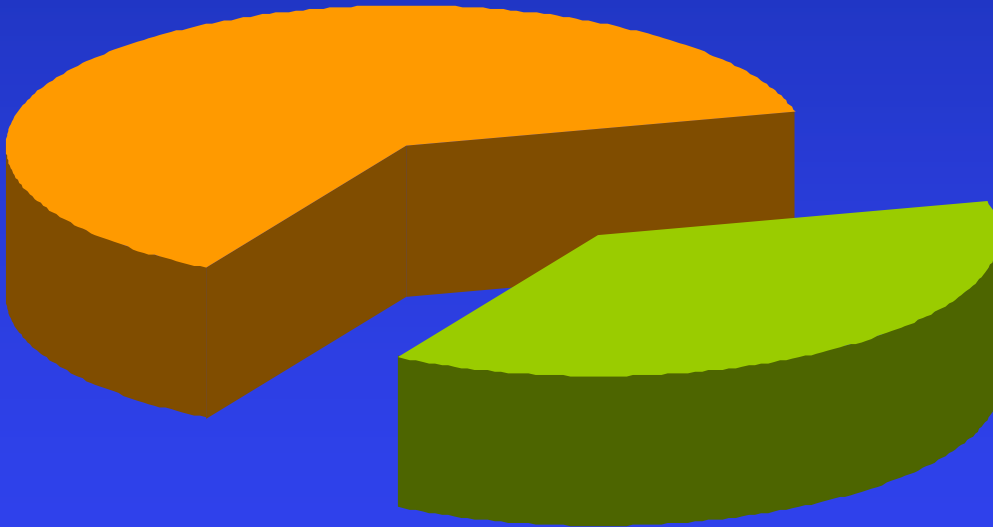
Intermediate/advanced HCC: 52 pts (32%)

M:F = 35:17

**Age = 66 ± 8 yrs.
(range 46-81)**

Child's class A

**P.o. mortality = 1 pt
(1,9%)**



130 liver resection for HCC on cirrhosis (1996-2003)

Intermediate/advanced HCC:

Features of the tumor

1 nodule	32 pts (61%) [5,2-13 cm]
2 nodules*	11 pts (21%) [2,7-22 cm]
≥ 3 nodules	5 pts (10%) [1,8-5 cm]
Thrombosis of a main portal branch	2 pts (4%)
Invasion of the biliary tree	2 pts (4%)

***1 pt underwent resection + RF thermal ablation**



130 liver resection for HCC on cirrhosis (1996-2003)

Intermediate/advanced HCC: results

	<i>Early (Milano criteria)</i>	<i>Intermediate/advanced</i>
Recurrent HCC	43%	55%
No recurrence	57%	45%
Alive	74%	66%
Dead	26%	34%
Survival mean + SD (range)	32 $\pm$ 22 mos. (2-81 mos.)	21 $\pm$ 16 mos. (3-77 mos.)



130 liver resection for HCC on cirrhosis (1996-2003)

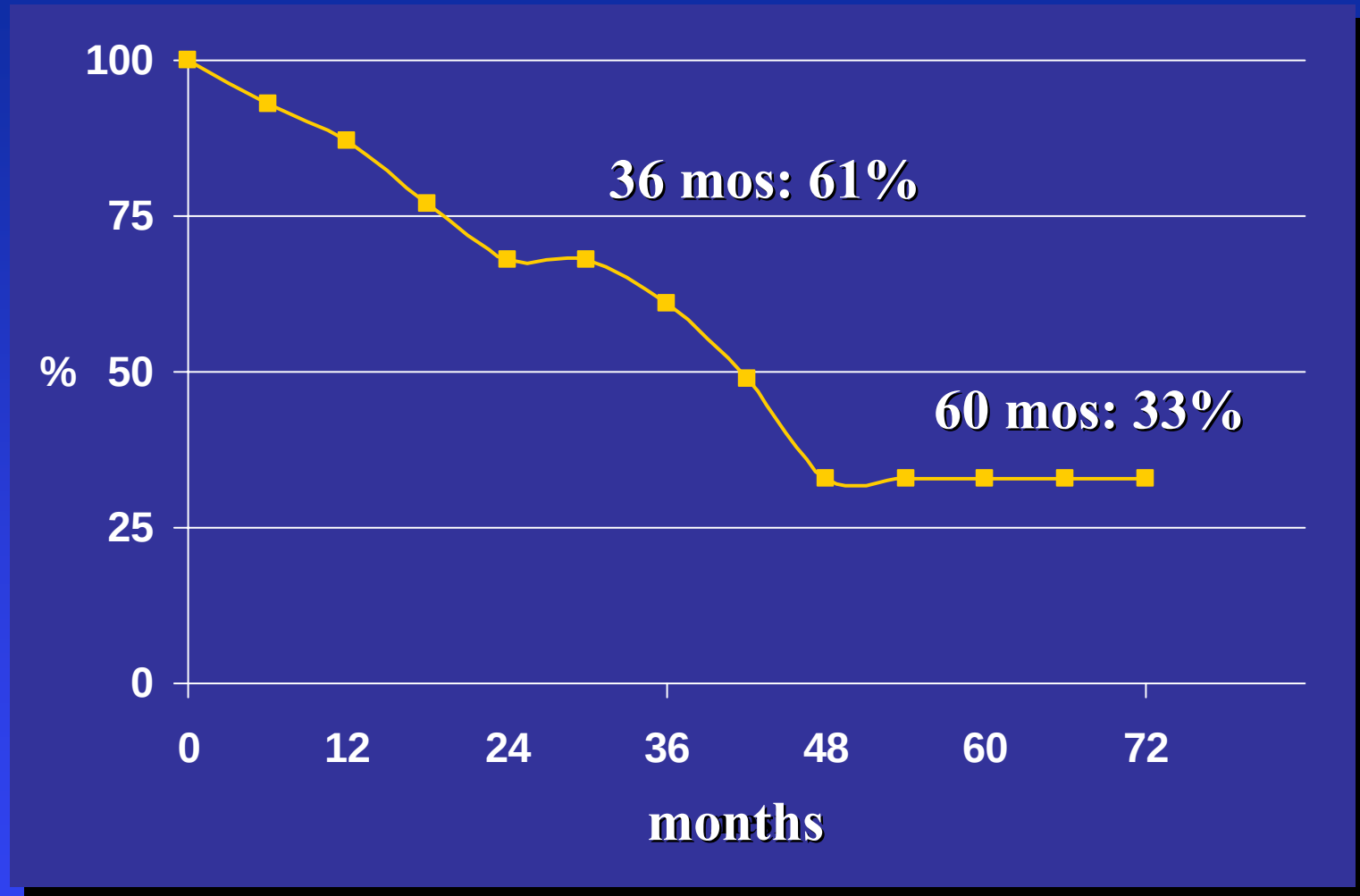
Intermediate/advanced HCC: survival with and without recurrence

	<i>Recurrent HCC</i>	<i>No recurrence</i>
51 pts with i/a HCC	55%	45%
Survival mean + SD (range)	24 $\pm$ 17 mesi (3-77 mesi)	25 $\pm$ 17 mos. (24-67 mos.)

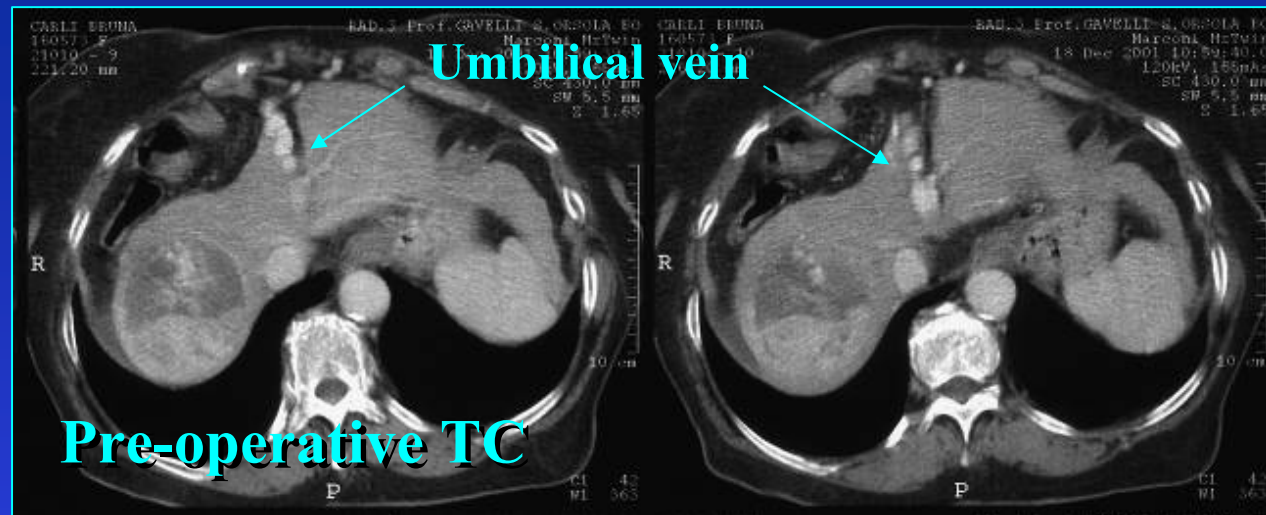


130 liver resection for HCC on cirrhosis (1996-2003)

Intermediate/advanced HCC: actuarial survival

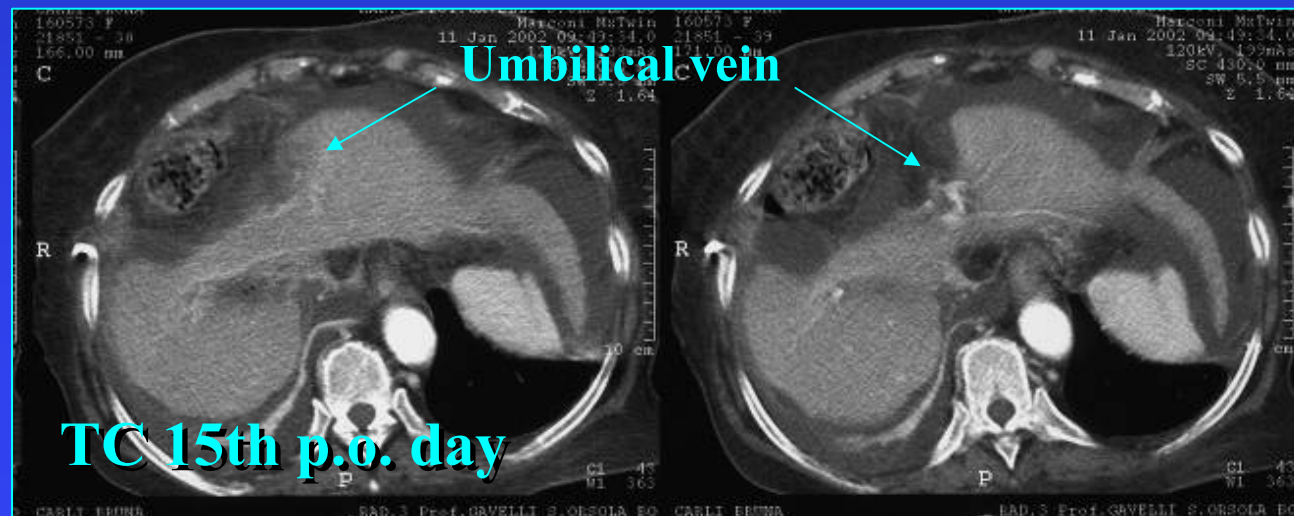


Liver resection for HCC on cirrhosis ≥ 5 cm

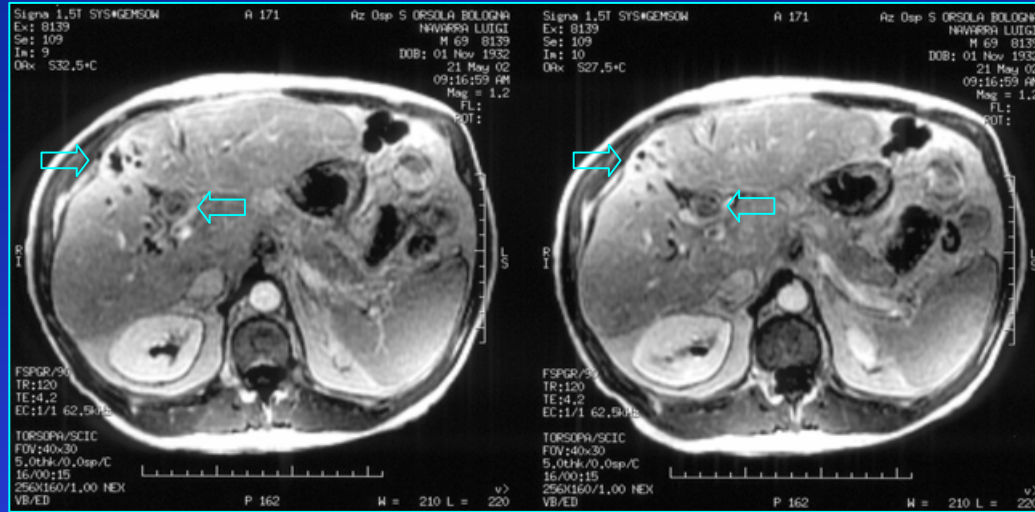


B. C., 82 yrs

- July 2001: diagnosis of HCC on cirrhosis, Child A6
- August 2001: surgical exploration (elsewhere)
- December 2001: surgical resection
- April 2002: no evidence of recurrence



Liver resection for HCC on cirrhosis invading the biliary tree

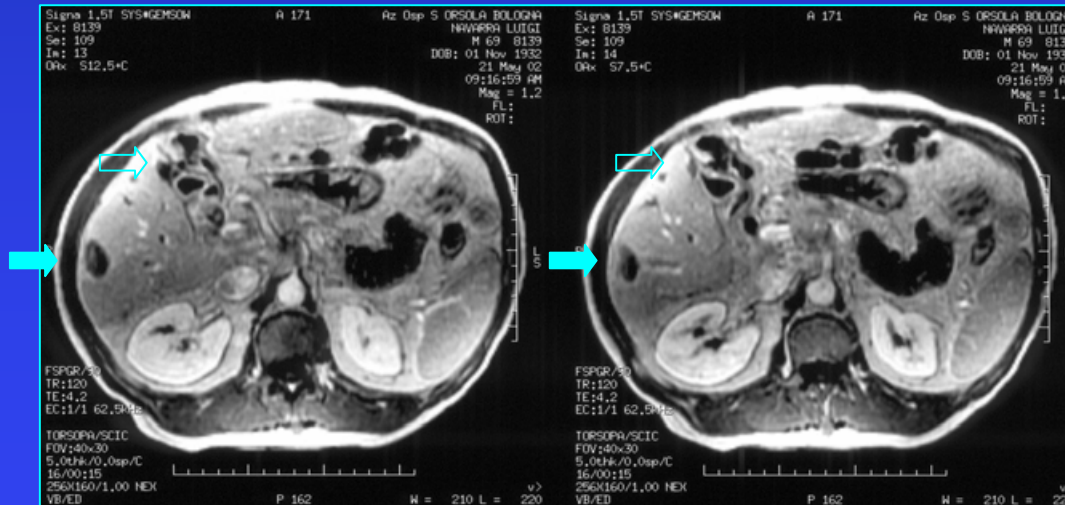


N. L. 69 yrs

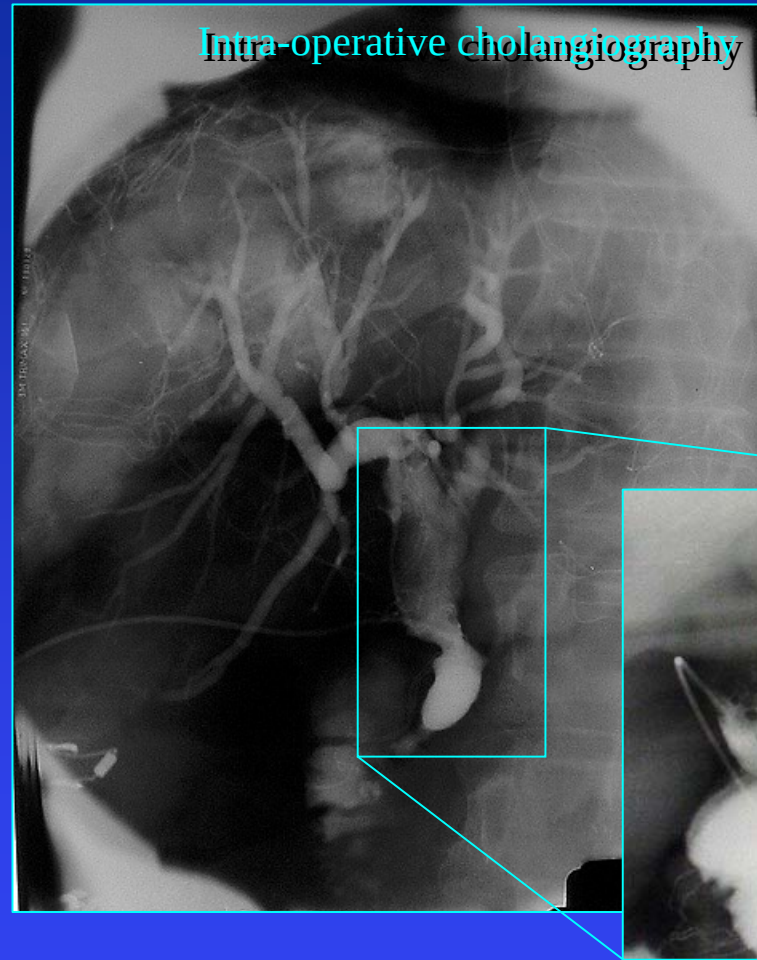
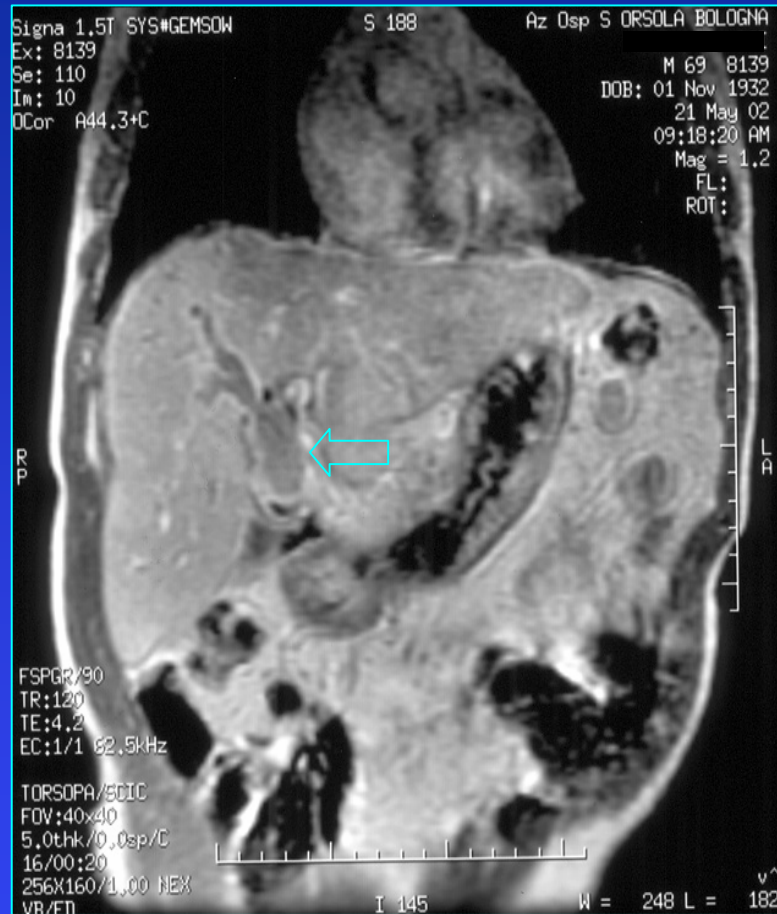
- October 2001: diagnosis of multinodular HCC, seg VI (8 mm) and seg VIII (30 mm) with invasion of the segmental biliary branch

- October 2001-January 2002: repeated sessions of RF thermal ablation and alcoholization

- May 2002: neoplastic invasion of the right and the common bile duct



Liver resection for HCC on cirrhosis invading the biliary tree



N. L. 69 yrs
- **May 2002:**
segmentectomy
VIII, clearance of
the common bile
duct and biliary
drainage.



Liver resection for HCC on cirrhosis invading the biliary tree



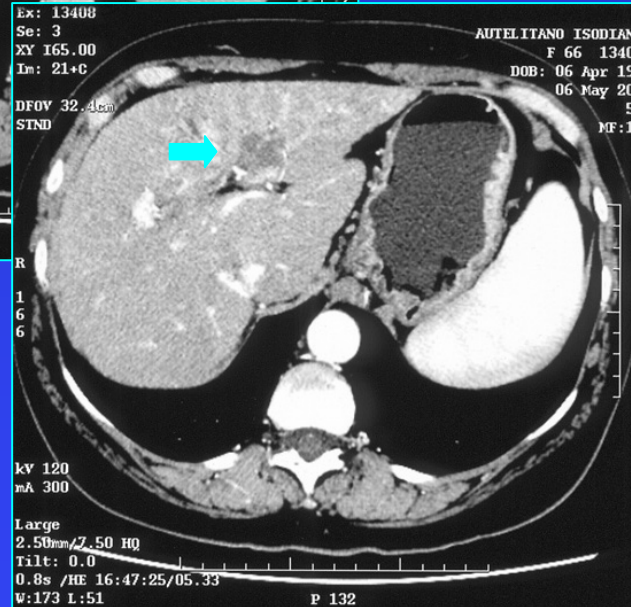
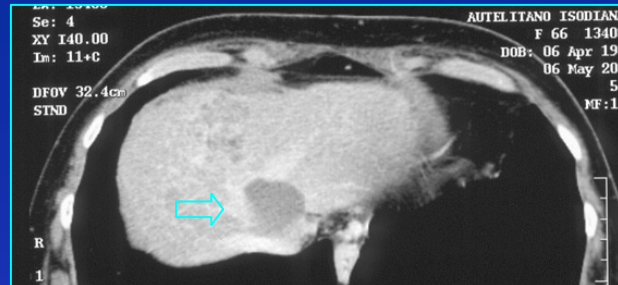
N. L. 69 yrs

**- July 2002: post-operative
cholangiography: no
evidence of recurrence**



**Clinica Chirurgica 2
Università di Bologna**

Liver resection for HCC on cirrhosis invading the left portal branch



A. I., 66 yrs (I)

- HCV-related chronic hepatitis
- Child's class A5

May 2002:

- multinodular HCC of the left liver lobe
- thrombosis of the left portal branch
- paracaval biliary cyst
- alpha-fetoprotein level: 738 ng/ml



Clinica Chirurgica II
Università di Bologna

Liver resection for HCC on cirrhosis invading the left portal branch



A. I., 66 anni (II)

May 2002:

- left hepatectomy

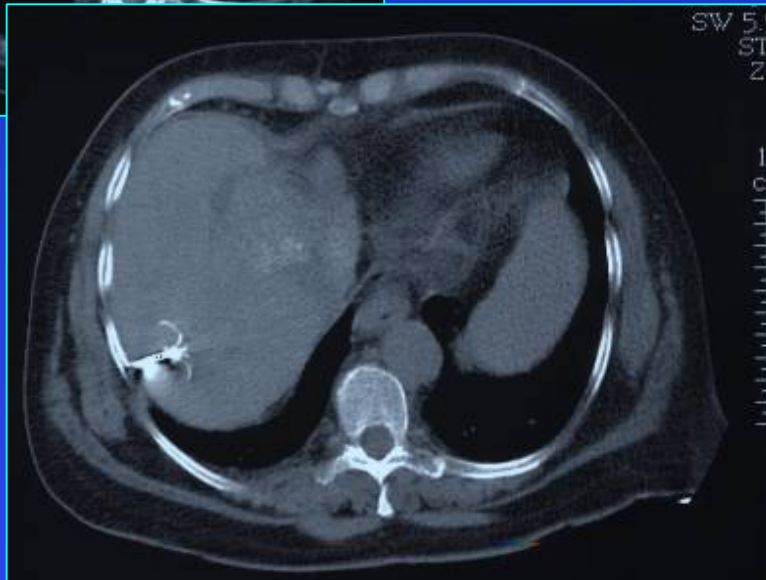
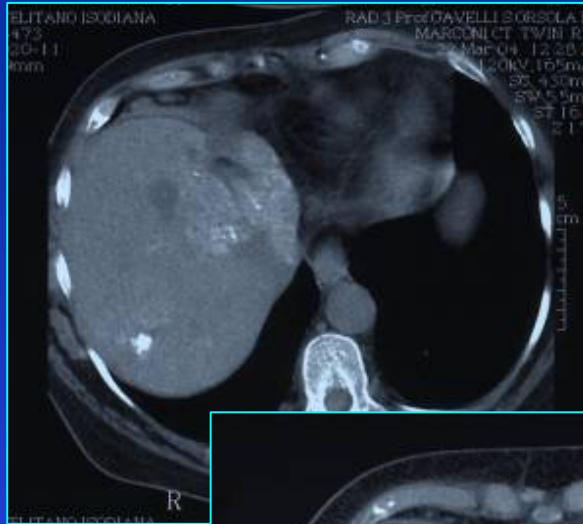
November 2002:

- alfa-fetoprotein level: 7 ng/ml

- no evidence of recurrent disease



Liver resection for HCC on cirrhosis invading the left portal branch



A. I., 66 anni (III)

March 2004:

- Nodule of recurrent HCC in seg VII**
- TACE**
- RF TC-guided thermal ablation of the nodule**



CONCLUSIONS

Liver resection for intermediate/advanced HCC on cirrhosis should be proposed in:

- Child's class A patients**
 - Without evidence of extra-hepatic metastasis**
 - Without tumour thrombus in the main portal vein or in the inferior vena cava**
-
- In case of recurrent disease, multimodal treatments, either surgical or percutaneous, may significantly prolong survival**
 - Intermediate/advanced HCC are usually observed in aged patients (≥ 65 yrs). Liver surgery is still the treatment of choice after accurate selection.**





Insufficienza epatica acuta: attualità e prospettive

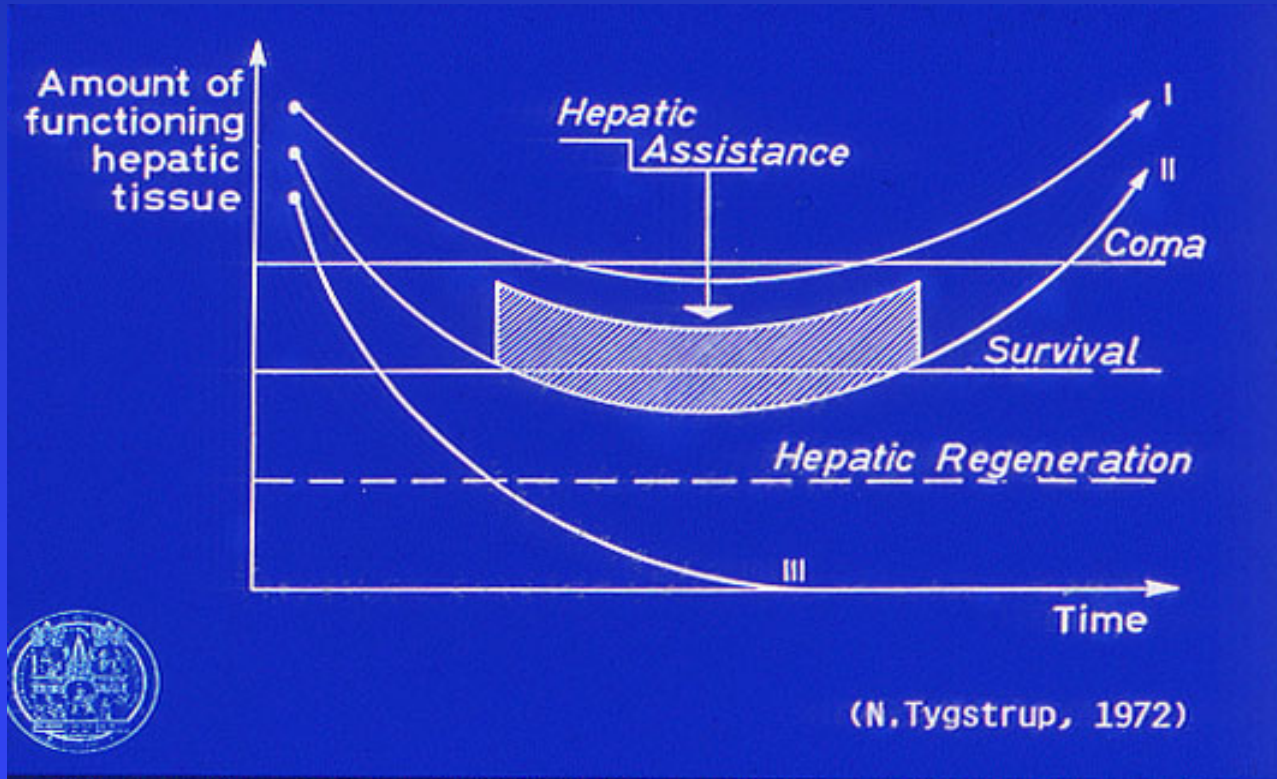
Antonino Cavallari

*Dipartimento di Discipline Chirurgiche, Rianimatorie e dei Trapianti
U.O. Chirurgia Generale; Programma Trapianto di Fegato (Dir. Prof. A. Cavallari)
Centro di Ricerca Biomedica applicata (CRBa)
Università degli Studi di Bologna*



PREMESSA

Il “goal” principale nel trattamento dei pazienti con insufficienza epatica acuta è di ottimizzare le condizioni per favorire la rigenerazione del fegato nativo in necrosi



INTERNATIONAL SYMPOSIUM ON



ARTIFICIAL SUPPORT SYSTEMS
FOR ACUTE HEPATIC FAILURE

*The Directors of Smith and Nephew
Associated Companies Ltd.*

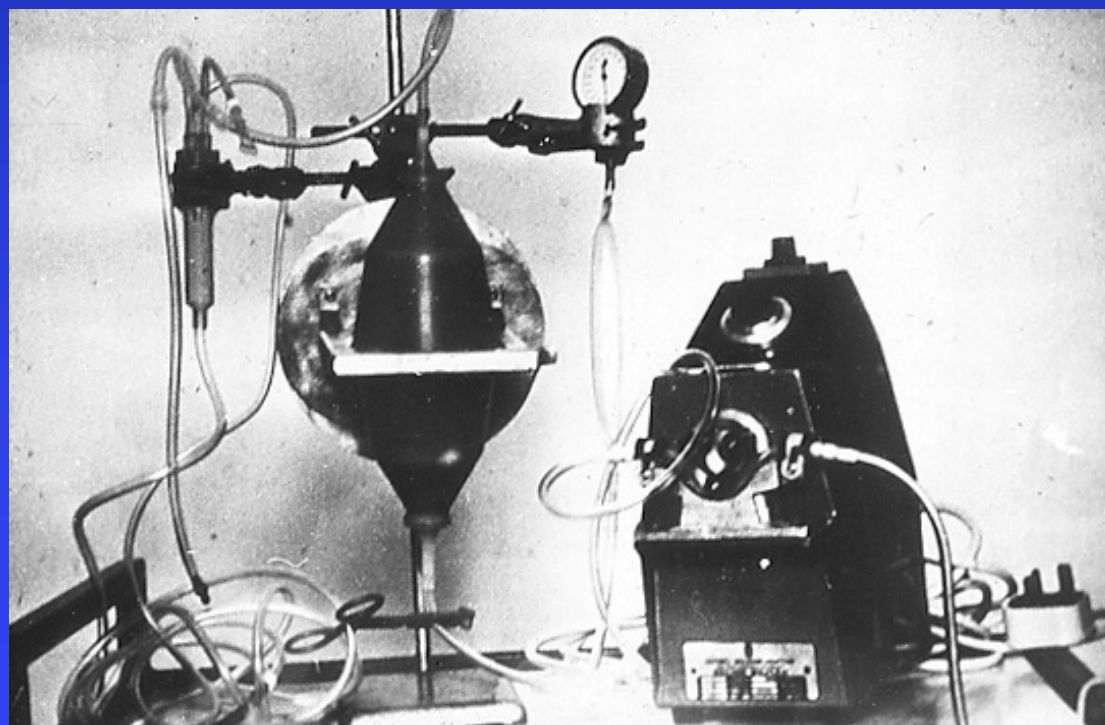
have much pleasure in inviting
DR A. CAVANARI

LONDON - SEPTEMBER 1974



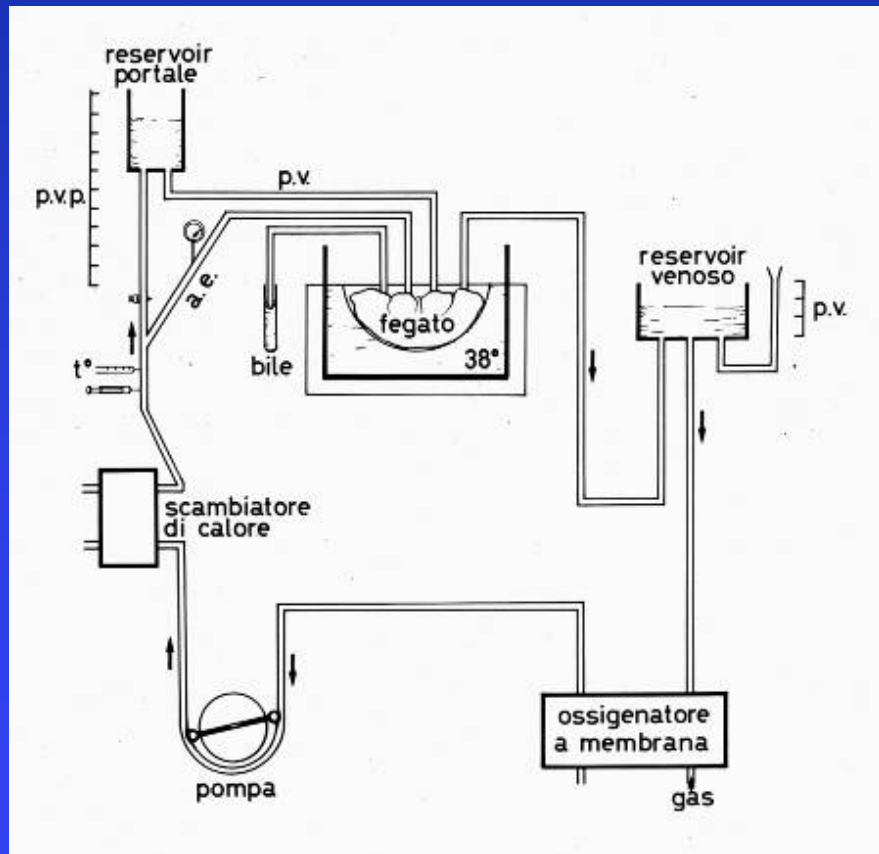
International symposium
on artificial support systems
for acute hepatic failure

September 2nd & 3rd 1974
— London



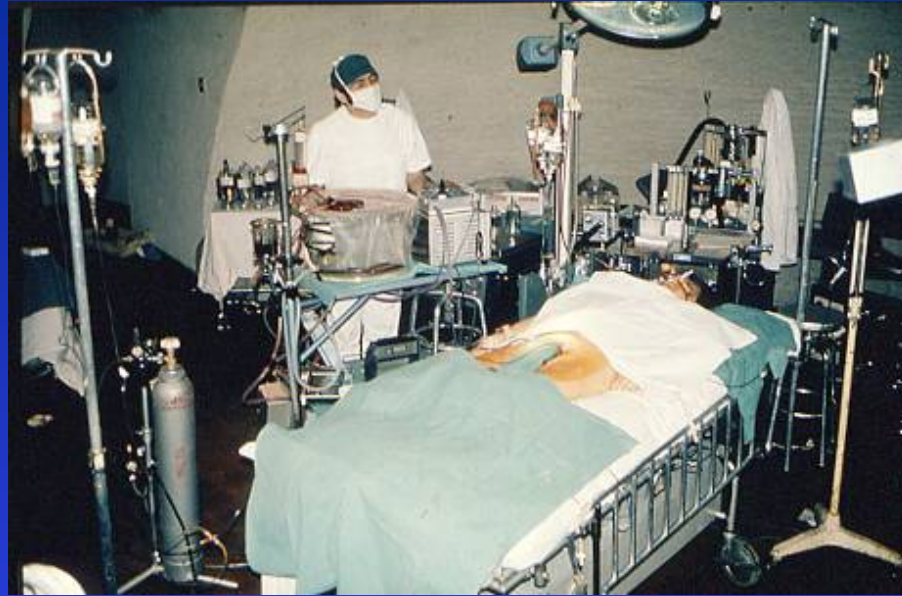
Assistenza epatica sperimentale

Perfusione di fegato eterologo isolato in circuito

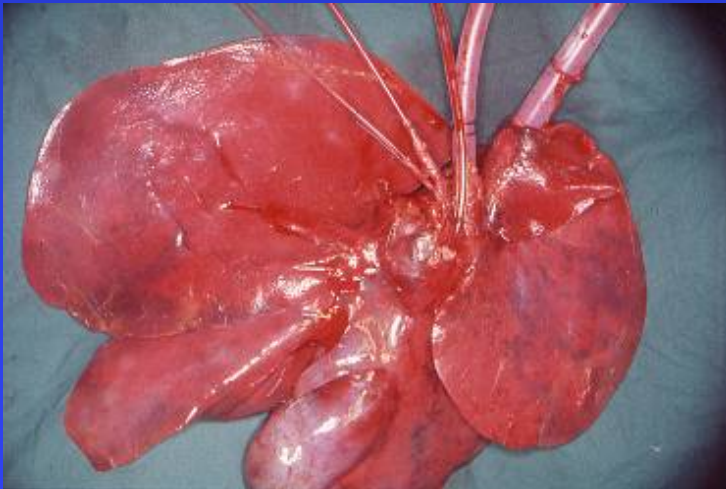




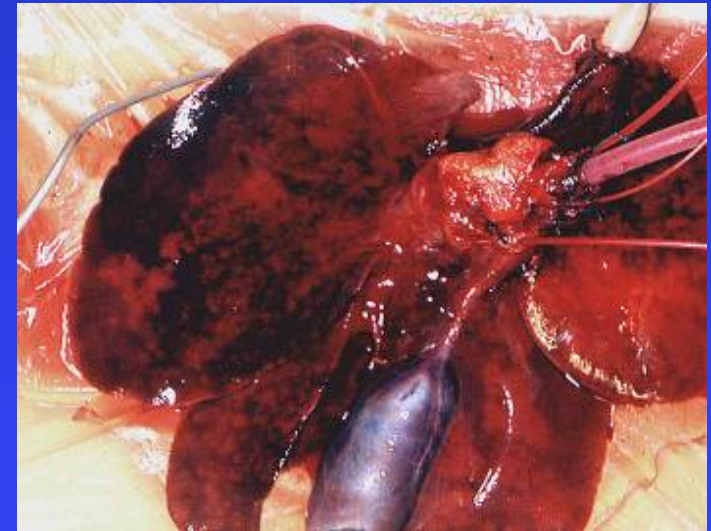
Esperienza clinica di assistenza epatica con perfusione di fegato eterologo



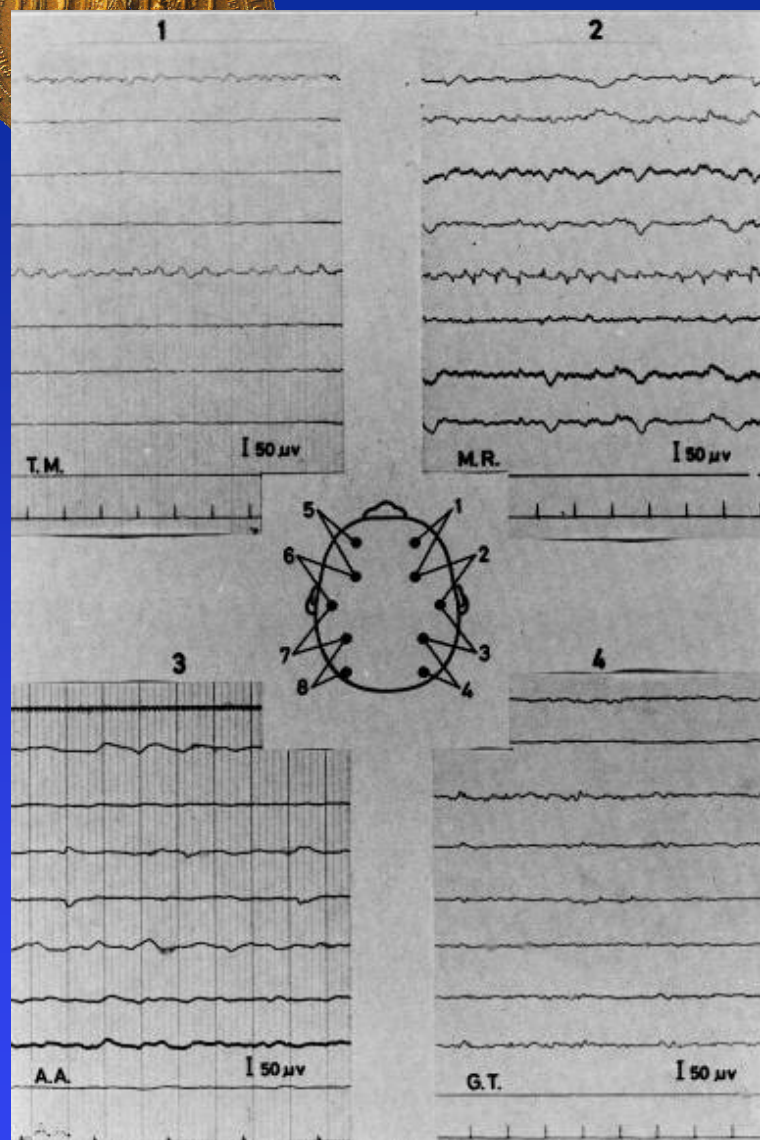
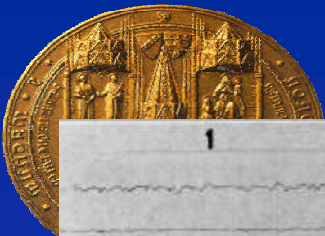
Bologna 1974



Inizio perfusione



Fine perfusione

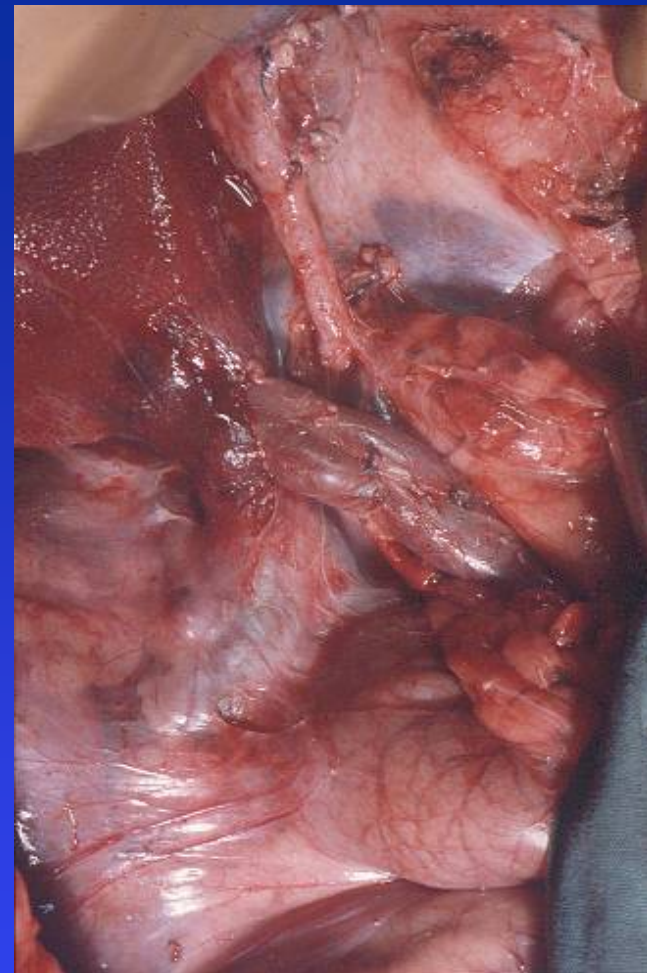
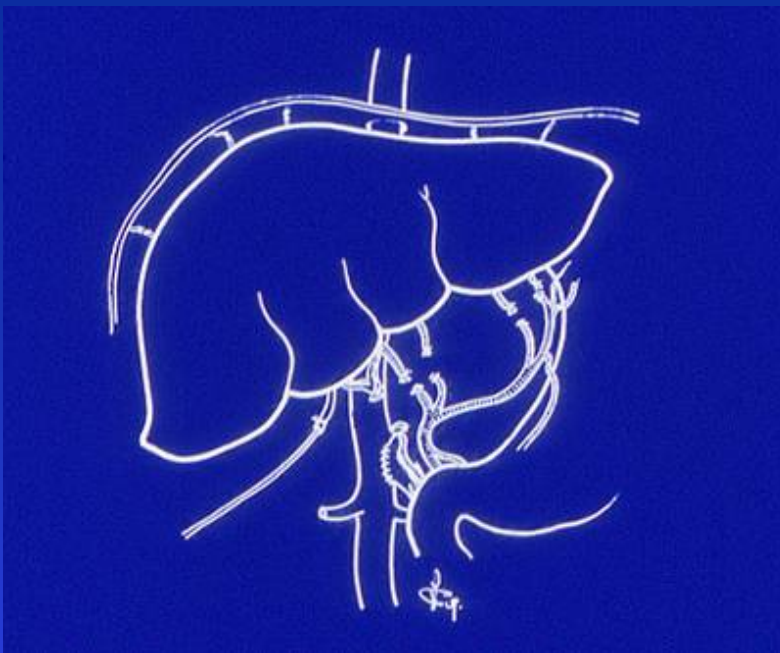


	PAZIENTE	PERFUSIONE		GRADO DI COMA I - V	AMMONIEMIA µg /100 ml		BILIRUBINA mg/100 ml		ATT. PROTR. %		FIBRINOGEN. mg/100 ml		PIASTRINE x 10 ³		STATO NEUROLOG.
		n°	durata ore		p	d	p	d	p	d	p	d			
MAIALE	T.M.	1	4	V	175	100	28	12	12	28	140	100	50	11	invariato
MAIALE		2	4	V	180	150	19	17	40	34	140	100	100	14	invariato
BABBUINO	M.R.	3	5	IV	200	150	15	4	28	40	180	180	500	100	invariato
BABBUINO	A.A.	4	11	V	320	100	16	7	10	40	0	90	170	41	migliorato
BABBUINO	G.T.	5	8	V	400	100	9	3	11	40	140	110	280	100	migliorato

Contributo sperimentale alla terapia
della insufficienza epatica acuta
Atti. Soc. It. Chir. 76° Congr. 1974



Devascularizzazione epatica nel maiale



Anastomosi Porto-Cava

Bologna, 1979



Epatectomia totale nel maiale

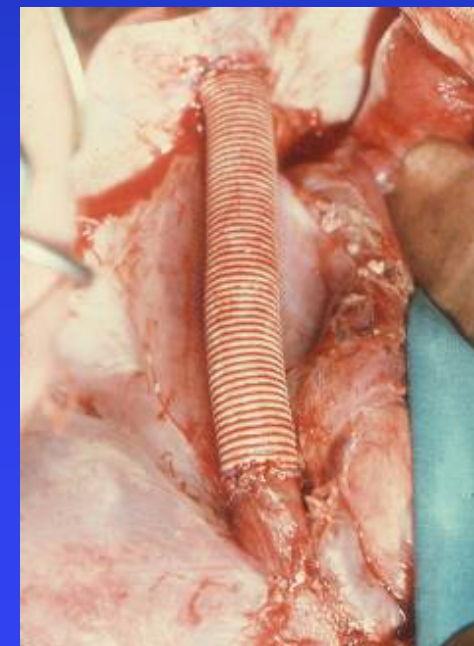
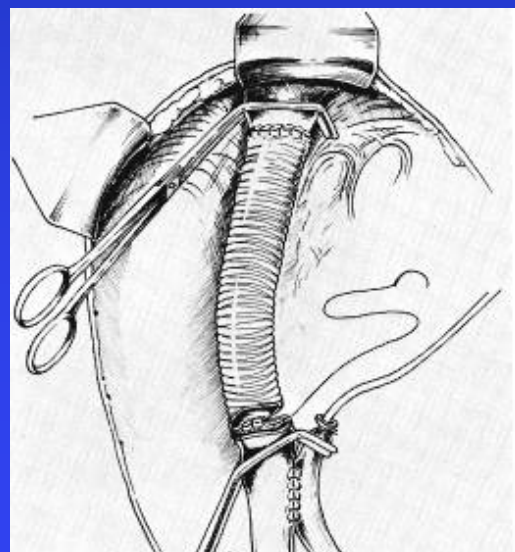
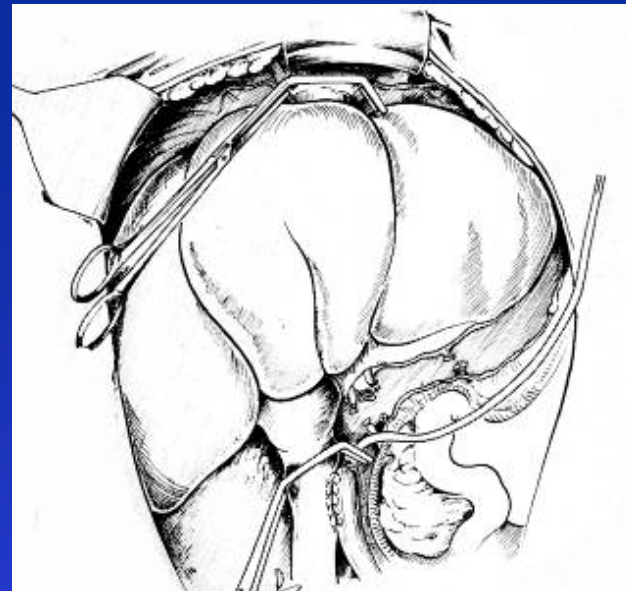
Atti del VI Congresso della Società di Ricerche in Chirurgia
(Bari, novembre 1980)

L'epatectomia totale nel maiale

A MAZZIOTTI - L. ANTONINI - R. BELLUSCI - E. CAROLI
V. PAPA - P. RICCIO - L. SOLAINI - A. CAVALLARI

Estratto da:
IL POLICLINICO - Sez. Chirurgica
vol. 88 - N. 1-2 - 1981

EDIZIONI LUIGI POZZI S.r.l. - ROMA





Rigenerazione epatica

- Tecnica della ipotermia epatica *in situ*
- Resezioni epatiche estese

Pubblicazioni:

Ipotermia epatica in situ nel maiale: contributo sperimentale.
Atti. Soc. It. Chir. 77° Congr. 1975

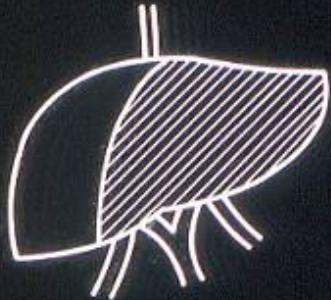
- Hepato-portal circulatory changes in the regenerating pig liver. *Ital J Surg Sci 1981.*

IPOTERMIA EPATICA



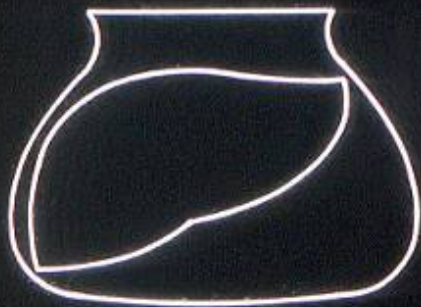
Perfusione di fegato
extracorporeo nella
terapia dell'insufficienza
epatica acuta

Ischemia: 30'



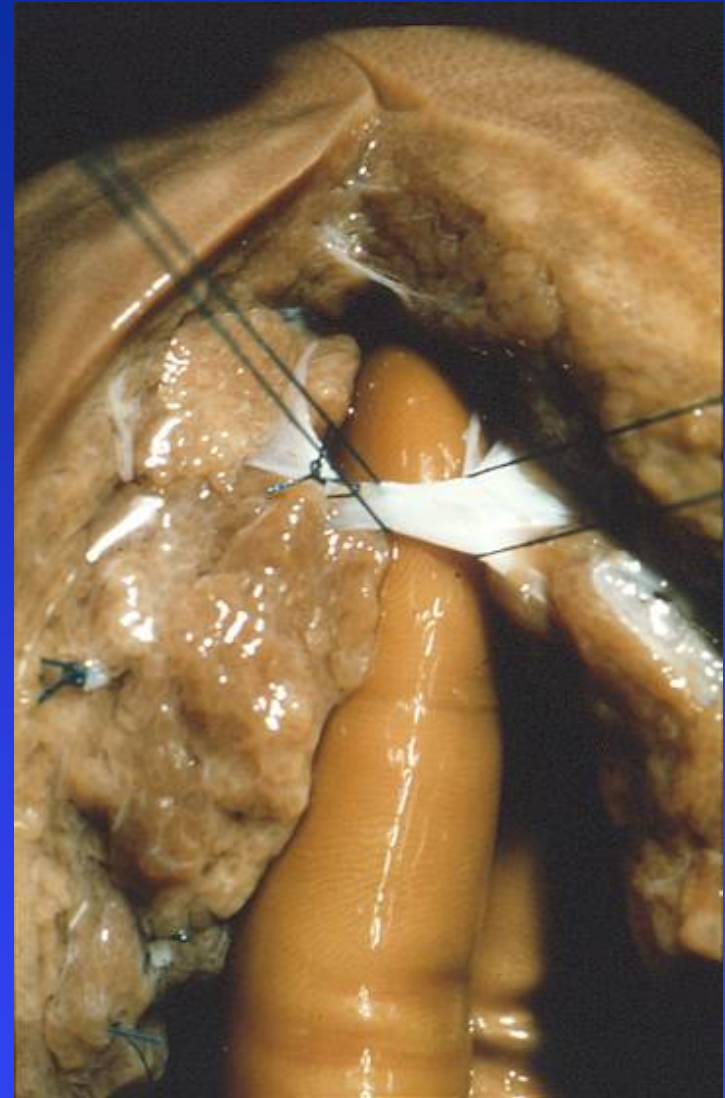
Resezione epatica
estesa in ipotermia
selettiva

Ischemia: 90'



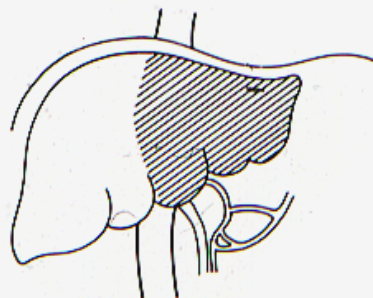
Conservazione di
fegato per trapianto

Ischemia: 4-16 ore

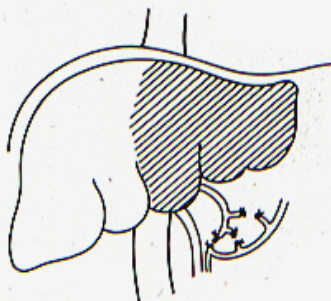


RIGENERAZIONE EPATICA DOPO RESEZIONE IN VARIE CONDIZIONI SPERIMENTALI

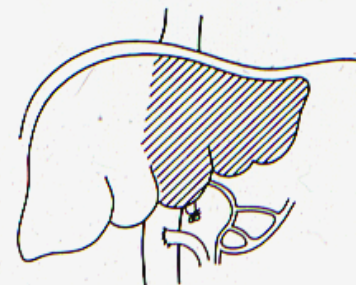
A - normale vascolarizzazione



B - esclusione del circolo arterioso



C - esclusione del circolo portale



INSTITUTE of CLINICAL SURGERY
UNIVERSITY of BOLOGNA
(Dir. prof. L. Possati)

EXPERIMENTAL LIVER REGENERATION

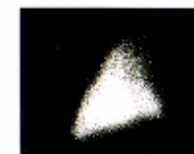
LIVER SCAN (lateral view)

1st group: intact blood supply

4th DAY



PRE OPERATIVE



21st DAY



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UNIVERSITY of BOLOGNA
(Dir. prof. L. Possati)

EXPERIMENTAL LIVER REGENERATION

LIVER SCAN (lateral view)

2nd group: hepatic artery ligation

4th DAY



PRE OPERATIVE



21st DAY



INSTITUTE of CLINICAL SURGERY
UNIVERSITY of BOLOGNA
(Dir. prof. L. Possati)

EXPERIMENTAL LIVER REGENERATION

LIVER SCAN (lateral view)

3rd group: porta-caval shunt

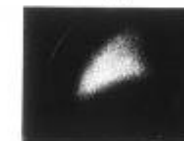
4th DAY



PRE OPERATIVE



21st DAY





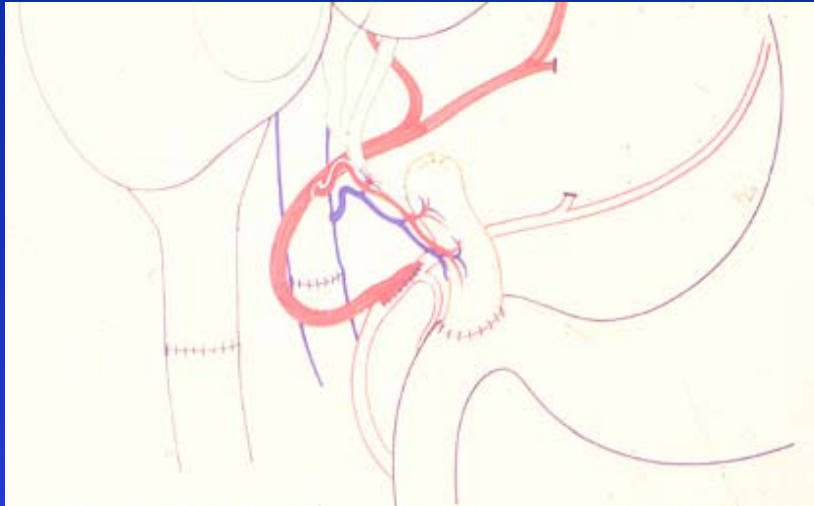
Trapianto di fegato sperimentale

- Tecnica chirurgica
- Conservazione ipotermica del fegato
- Studio dello sludge biliare

Publicazioni:

- Trapianto ortotopico di fegato nel maiale: tecnica chirurgica.
Bullettino Sci. Med, 1971.
- Studio sperimentale sulla conservazione di fegato.
Il Policlinico, Sez. Chir., 1976

Trapianto ortotopico di fegato nel maiale



Implant of the whole biliary tree with duodenal segment in liver transplantation in the pig.

Technical note.

16th Congress ESSR, 1981.

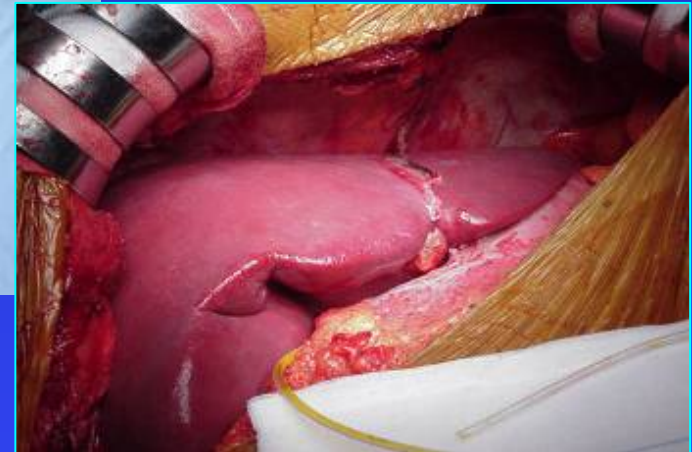
“Napoleone”





Pittsburgh, 1985

Liver transplantation for fulminant hepatic failure



Thomas E. Starzl, 1985



Primo trapianto di fegato per epatite fulminante a Bologna



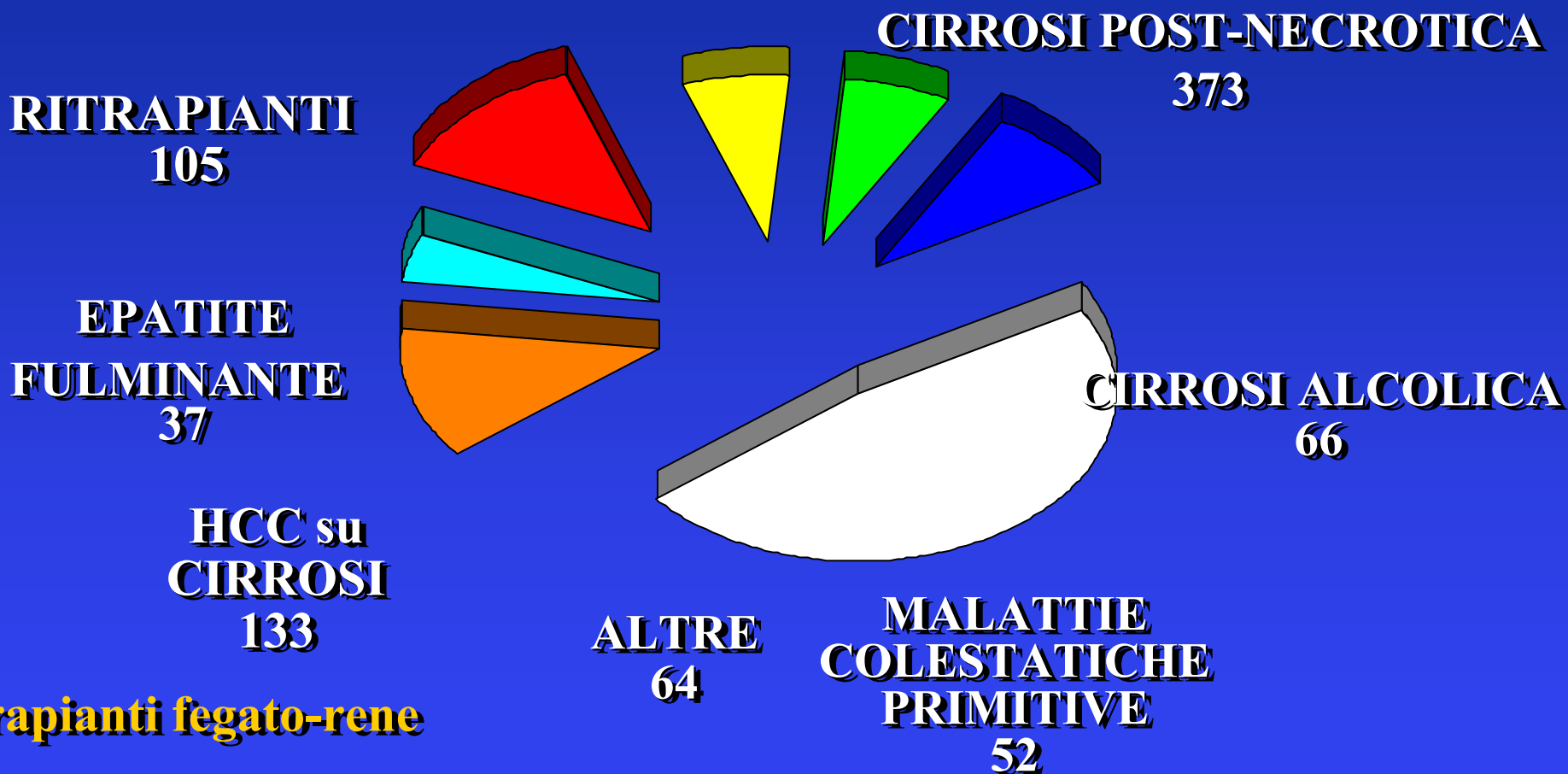
Gennaio 1988



Clinica Chirurgica II - Università di Bologna

830 Trapianti di Fegato

Aprile 1986 – Ottobre 2003

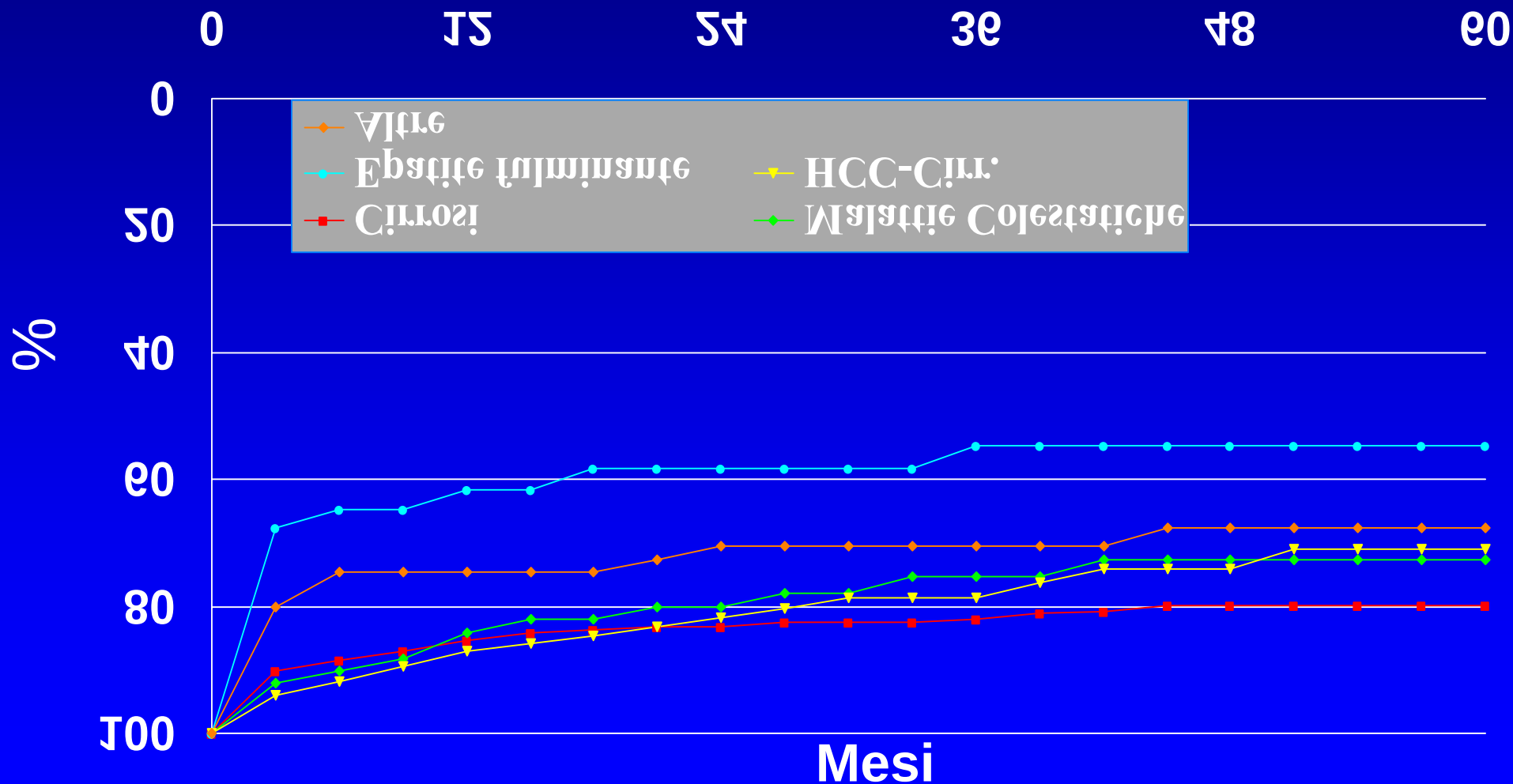


- 6 trapianti fegato-rene
- 5 trapianti fegato-cuore



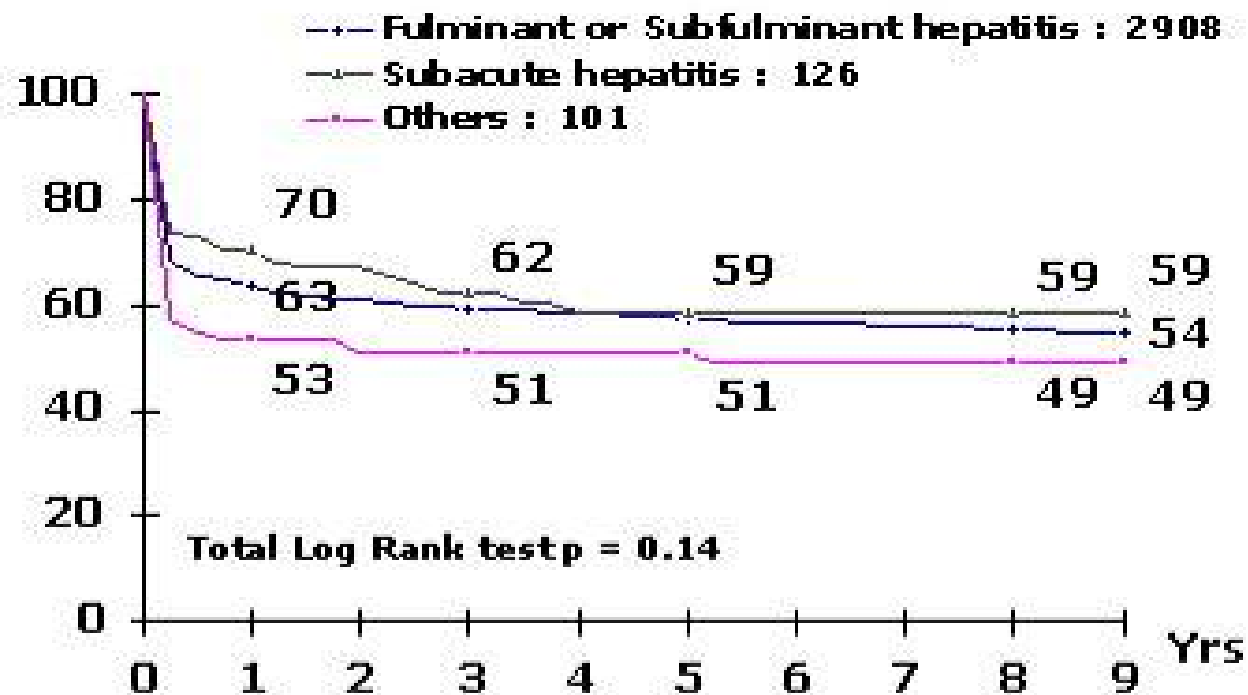
Trapianto di Fegato a Bologna

Sopravvivenza per Indicazione





Survival of Patients with Acute Hepatic Failure as the First Indication of Liver Transplantation 01/1988 - 06/2000



Situazione attività di donazione



Centro
Nazionale
Trapianti

Donatori effettivi in Europa – 2000

per milione di popolazione

16,5

SPAGNA	33,9
BELGIO	25,6
AUSTRIA	24,3
FINLANDIA	19,9
PORTOGALLO	19,5
NORVEGIA	17,6
FRANCIA	16,9
ITALIA	15,3
SVIZZERA	14,0

Donatori per zona geografica – Anno 2000



NORD

D. Effettivi	n. 591 (pmp 23,0)
D. Utilizzati	n. 562 (pmp 21,9)



CENTRO

D. Effettivi	n. 156 (pmp 14,1)
D. Utilizzati	n. 134 (pmp 12,1)



SUD e ISOLE

D. Effettivi	n. 133 (pmp 6,4)
D. Utilizzati	n. 125 (pmp 6,0)

D. Effettivi n. 880
(pmp 15,3)

D. Utilizzati n. 821
(pmp 14,2)

Donatori per Regione (p.m.p)

- **Emilia Romagna** 30.1
- **Friuli** 26.0
- **Piemonte/V.d'Aosta** 23.3
- **Liguria** 23.2
- **Veneto** 23.2



ANNALS OF SURGERY
Vol. 234, No. 6, 723-731
© 2001 Lippincott Williams & Wilkins, Inc.

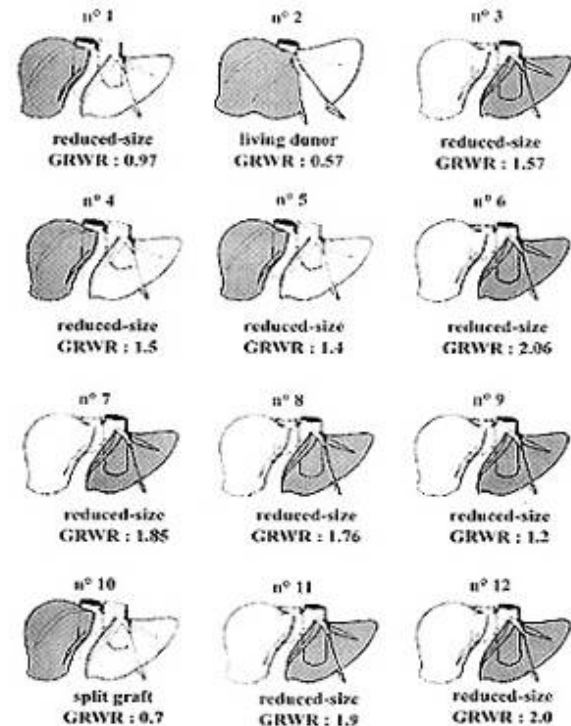
Auxiliary Partial Orthotopic Versus Standard Orthotopic Whole Liver Transplantation for Acute Liver Failure

A Reappraisal From a Single Center by a Case-Control Study

Daniel Azoulay, MD, PhD, Didier Samuel, MD, PhD, Philippe Ichaï, MD, Denis Castaing, MD, Faouzi Saliba, MD, René Adam, MD, PhD, Eric Savier, MD, Monzer Danaoui, MD, Alaoua Smail, MD, Valérie Delvart, MS, Vincent Karam, MD, PhD, and Henri Bismuth, MD, FACS (Hon)

From the Hepatobiliary Surgery and Liver Transplant Unit, UPRES 1596, IFR 89.9, Hôpital Paul Brousse, Université Paris Sud, Villejuif, France

Schematic representation of the surgical procedure in 12 cases of APOLT (graft in white, remaining native liver in grey)

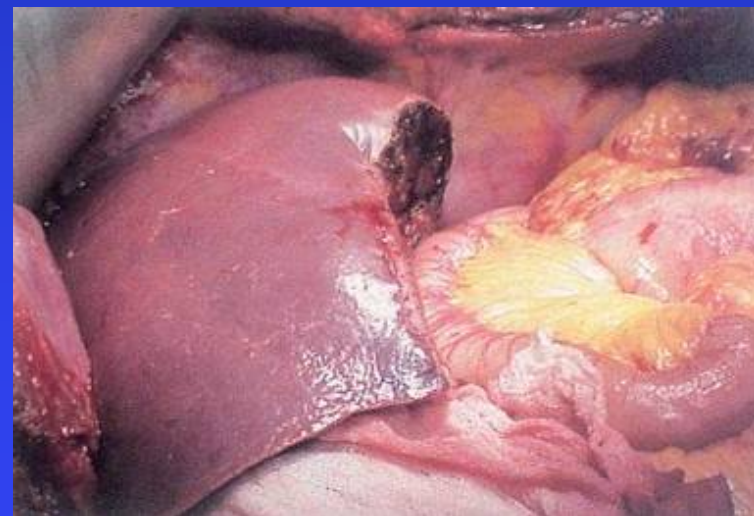
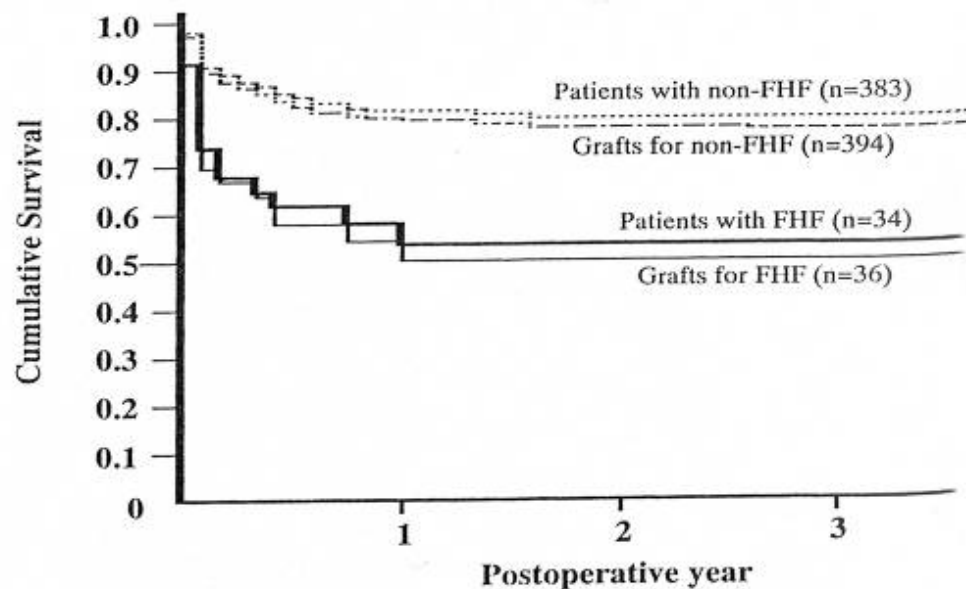




LIVING DONOR LIVER TRANSPLANTATION FOR FULMINANT HEPATIC FAILURE¹

SHINJI UEMOTO,^{2,3} YUKIHIRO INOMATA,⁴ TAKAKI SAKURAI,⁵ HIROTO EGAWA,⁴ SHIRO FUJITA,⁴
TETSUYA KIUCHI,⁴ MICHIIHIRO HAYASHI,⁴ MOTOHIKO YASUTOMI,⁴ HIROHIKO YAMABE,⁵ AND
KOICHI TANAKA^{2,4}

*Organ Transplantation Unit, Department of Transplantation Surgery, and Laboratory of Anatomic Pathology,
Kyoto University Hospital, 54 Kawara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan*





American Journal of Transplantation 2003; 4: 286–289
Blackwell Munksgaard

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doi: 10.1046/j.1600-6143.2003.00310.x

Case Report

First Report of Cryopreserved Human Hepatocytes Based Bioartificial Liver Successfully Used as a Bridge to Liver Transplantation

Umberto Baccarani^{a,*}, Annibale Donini^b, Andrea Sanna^b, Andrea Risaliti^a, Alessio Cariani^b, Bruno Nardo^c, Antonino Cavallari^c, Gerardo Martinelli^d, Lorenza Ridolfi^e, Gianni Bellini^f, Mario Scalamogna^g and Fabrizio Bresadola^a

^aDepartment of Surgery & Transplantation University of Udine, Udine, Italy

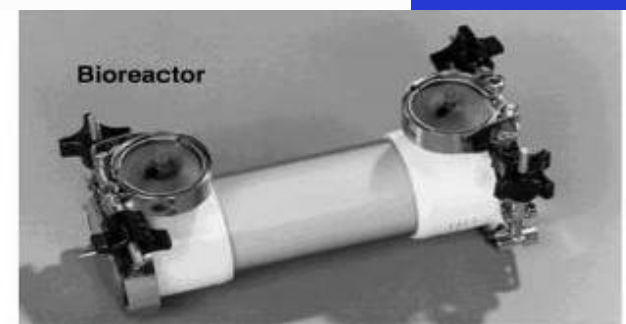
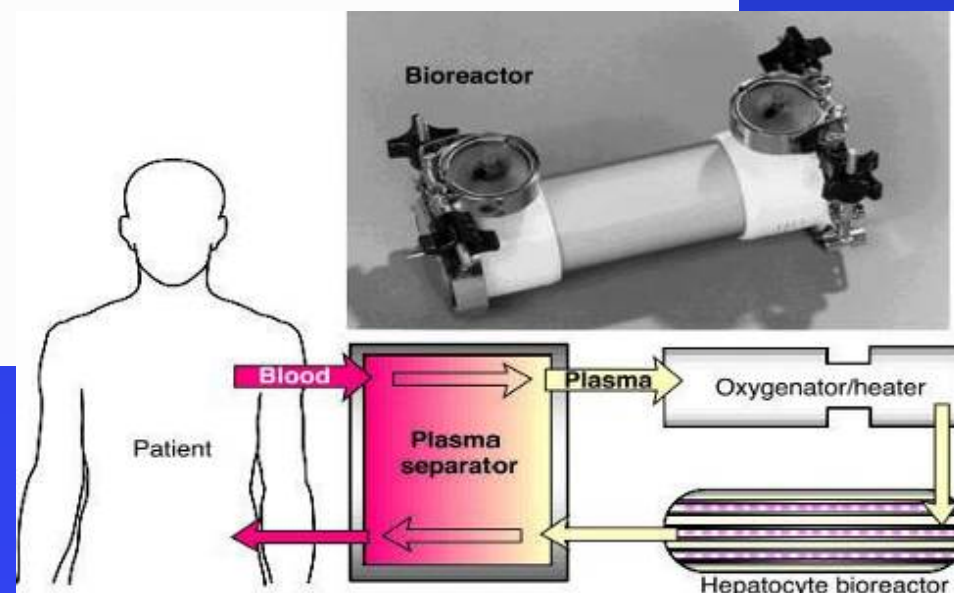
^bDepartment of Surgery, University of Ferrara, Ferrara, Italy

^cDepartment of Surgery & Transplantation and

^dIntensive Care Unit University of Bologna, Bologna, Italy

^eAIRT Emilia Romagna, Bologna, Italy, ^fRanD S.r.l, Medolla (MO), Italy ^gNord Italia Transplant program Milano, Italy

*Corresponding author: Umberto Baccarani, umberto.baccarani@uniud.it





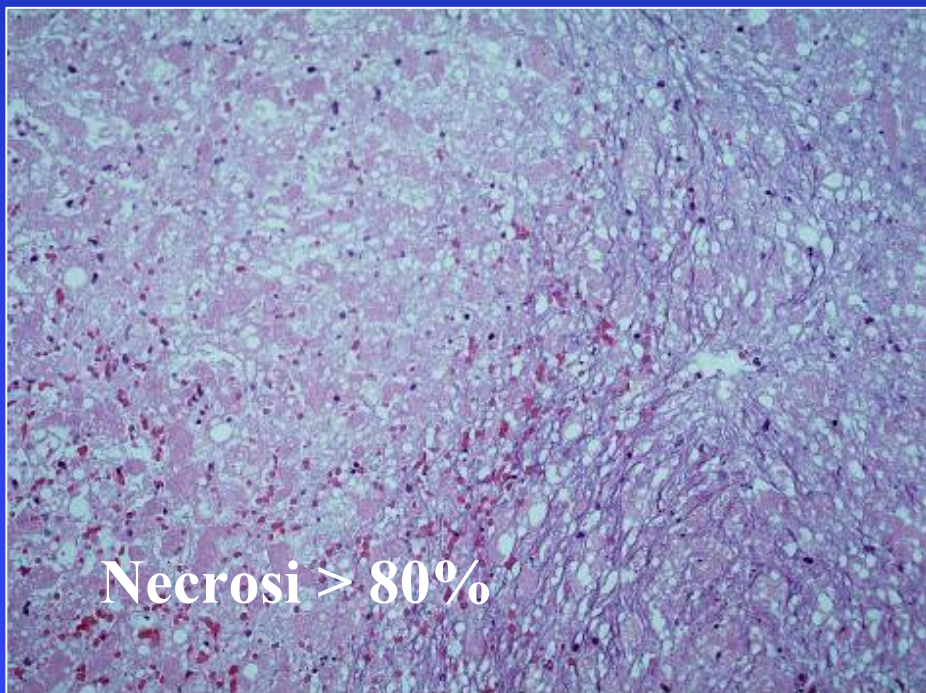
Arterializzazione della vena porta

Background clinico

Case report

♂ 38 anni, OLT per cirrosi post-necrotica (HBV, HDV, HCV)

Dopo 10 gg: trombosi a. epatica



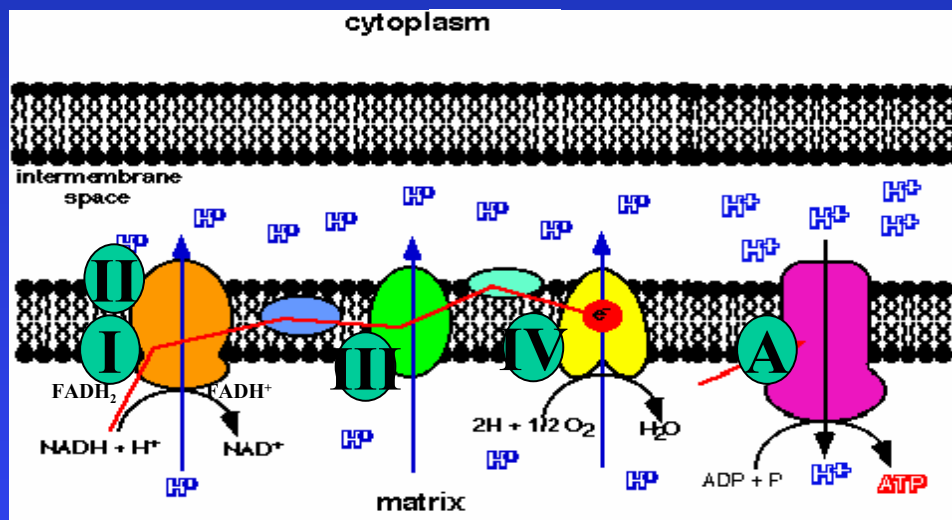
Arterializzazione Vena Porta





OBIETTIVI

- ✓ Incrementare l'apporto di ossigeno al fegato attraverso il flusso portale
- ✓ Favorire il processo di fosforilazione ossidativa

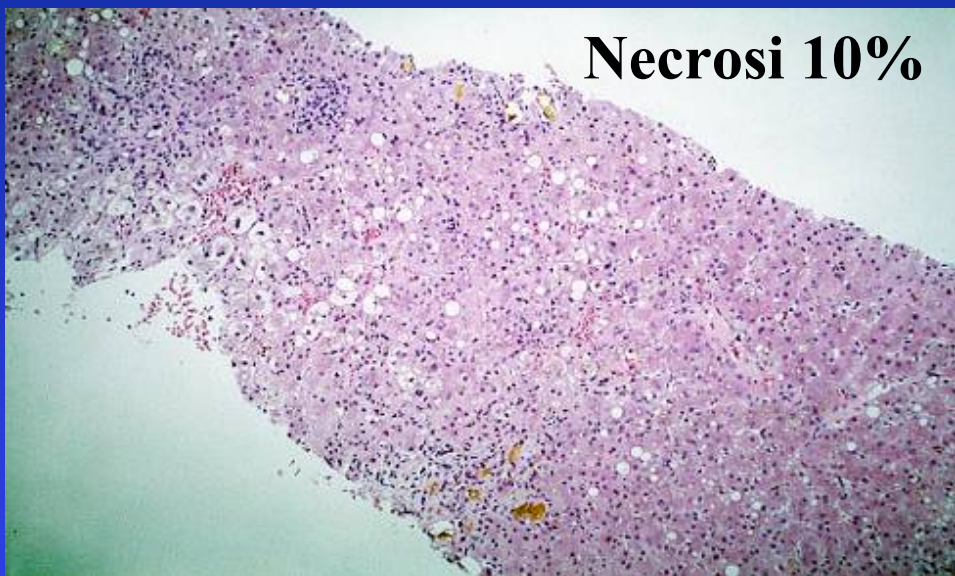


- ✓ Favorire la rigenerazione epatica



BACKGROUND

Case report



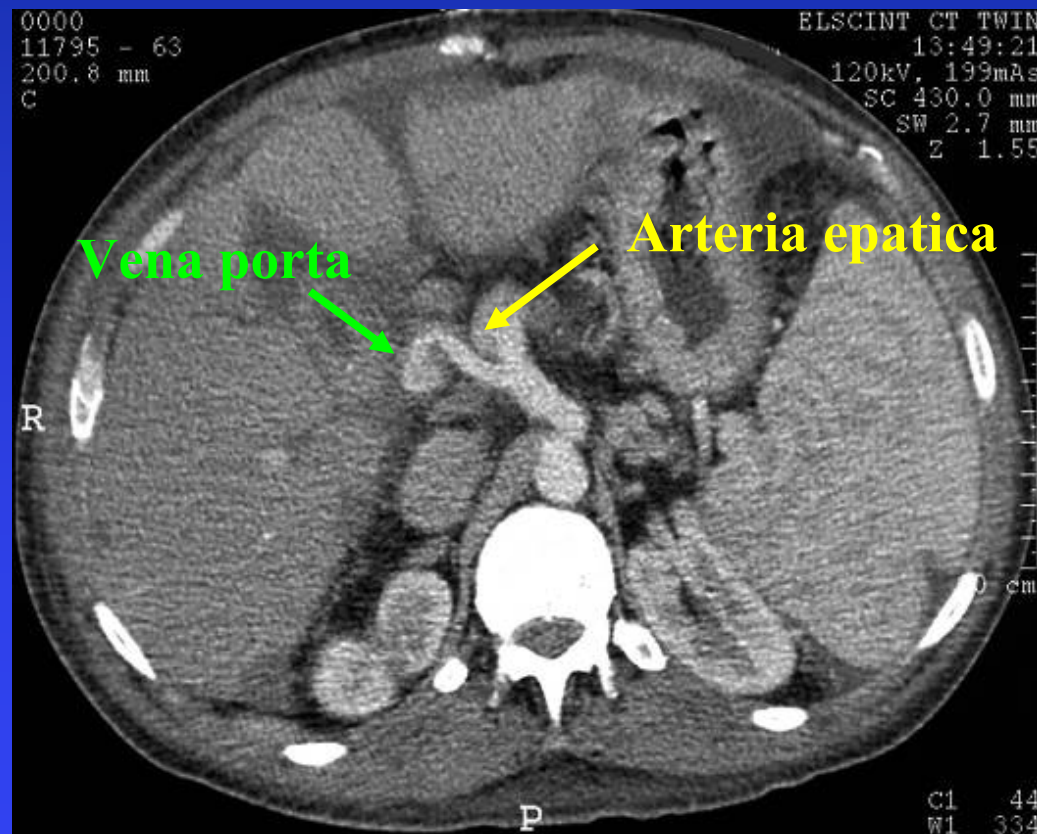
Biopsia a 24 giorni dopo AVP

“Arterialization of the Portal Vein in a Patient with a Dearterialized Liver Graft and Massive Necrosis”

A. Cavallari, B. Nardo, P. Caraceni

N Engl J Med, Vol. 345, No. 18 - November 1, 2001 - 1352-1353

TC dopo 24 gg dopo AVP



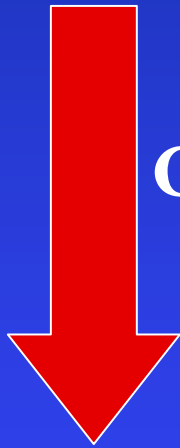


METODI

MODELLO SPERIMENTALE

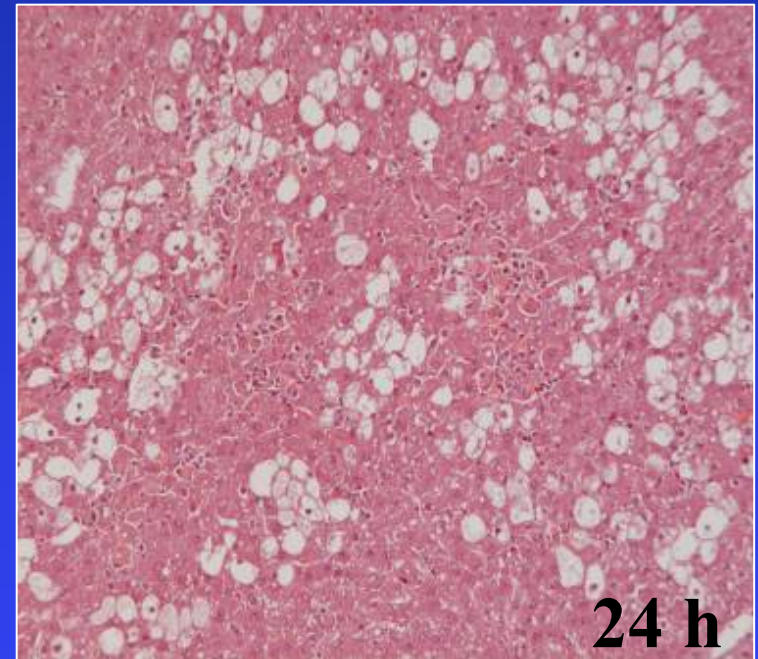


SPRAGUE-DAWLEY



CCl_4 5 ml/kg i.p.

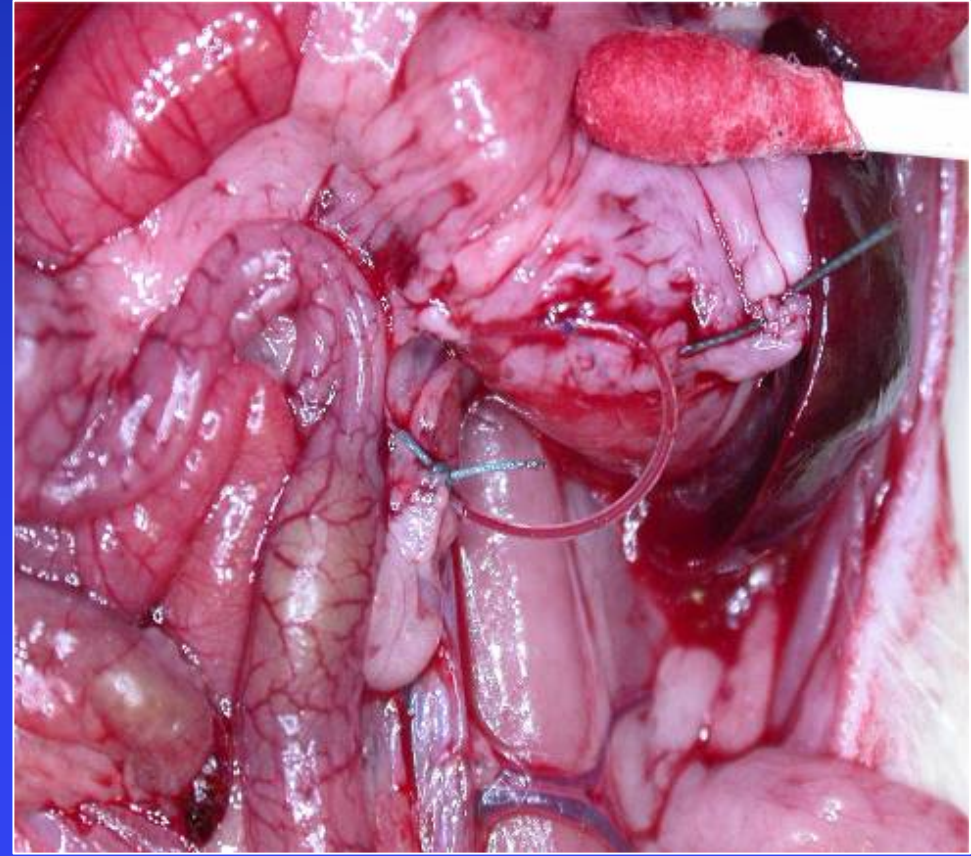
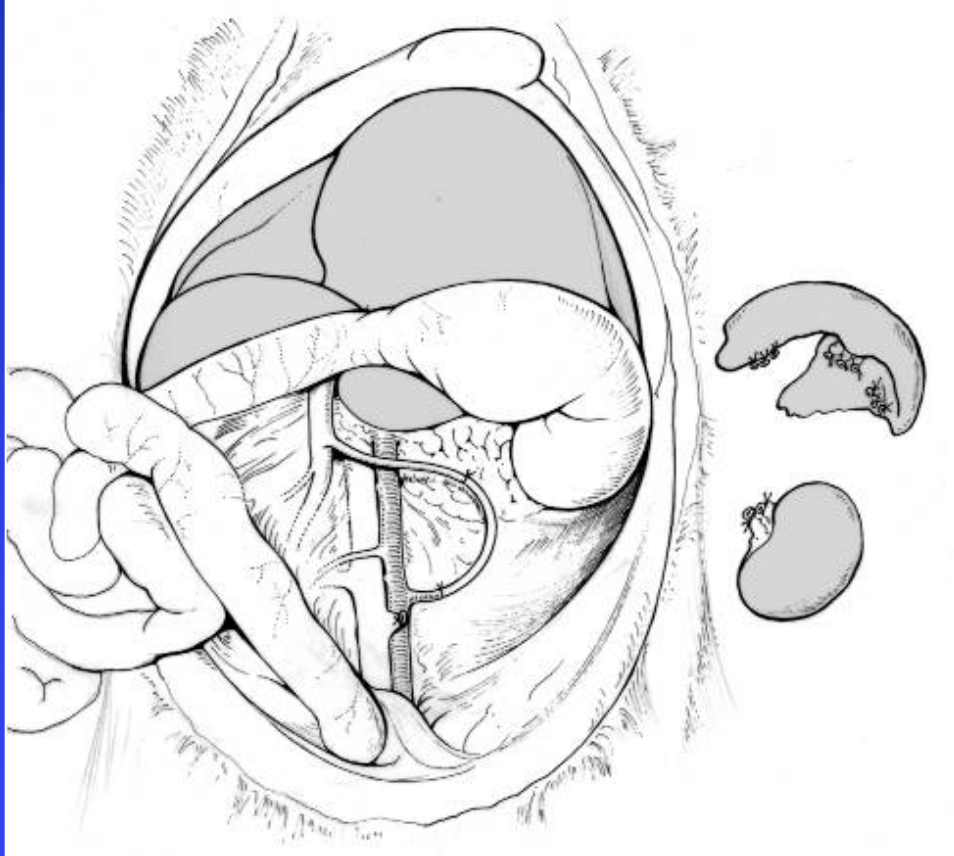
NECROSI EPATICA MASSIVA





METODI PROCEDURA CHIRURGICA

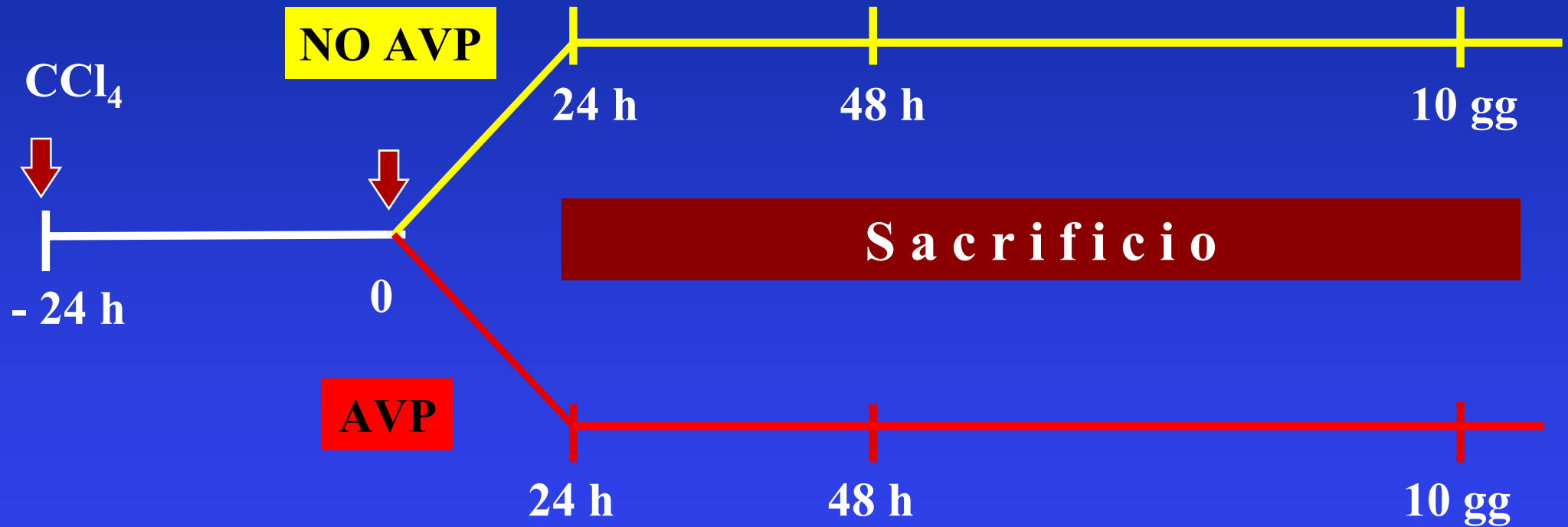
ARTERIALIZZAZIONE DELLA VENA PORTA





METODI

PROTOCOLLO SPERIMENTALE



☒ **Prelievi ematici:** ALT, AST, creatinina ed emogasanalisi (vena porta)

☒ **Prelievi tissutali:** fegato (lobo destro e mediano)

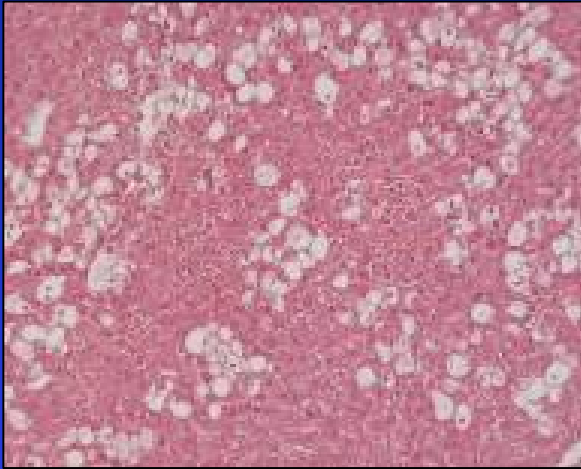


RISULTATI

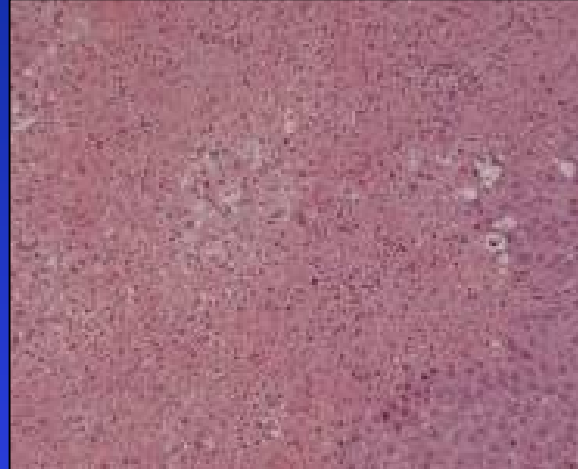


ISTOLOGIA EPATICA

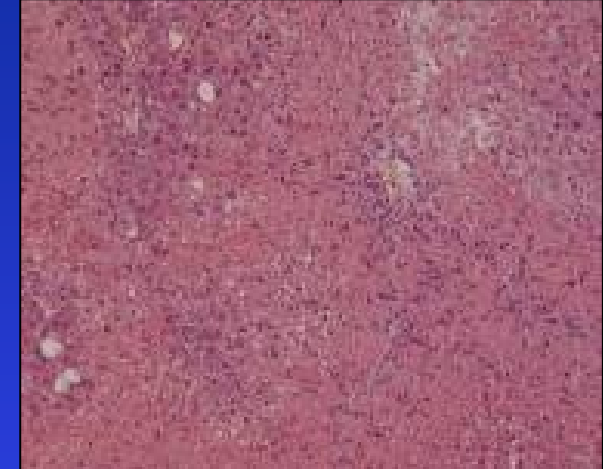
CCl_4



24 h

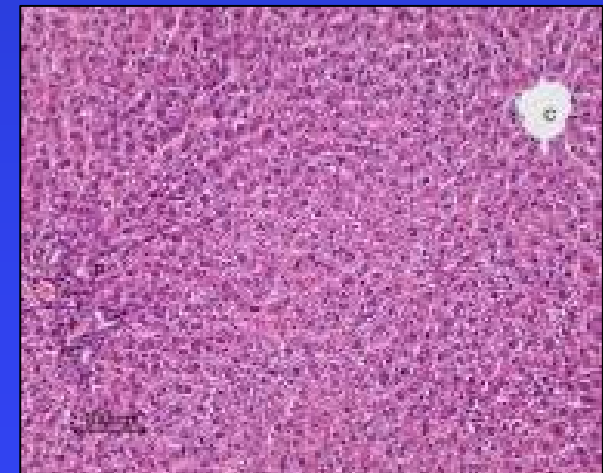
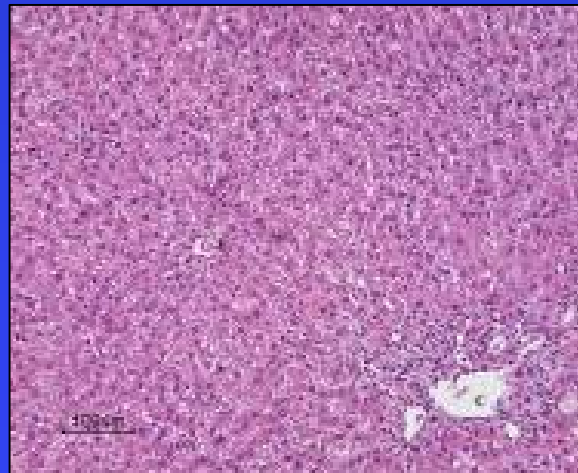
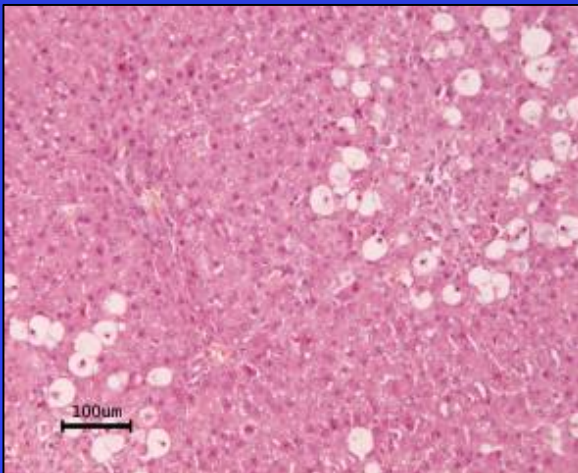


48 h



10 giorni

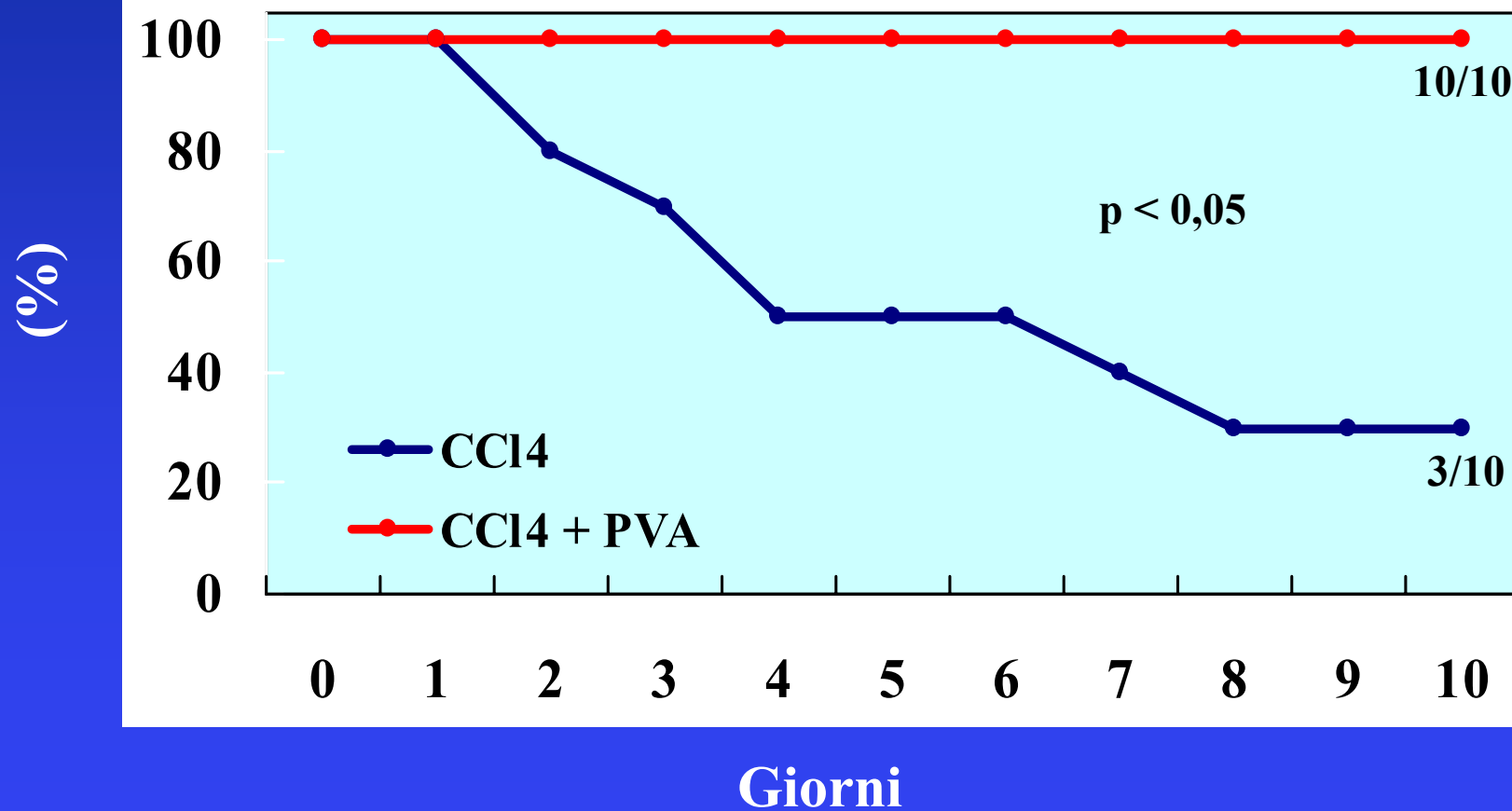
CCl_4
+
AVP





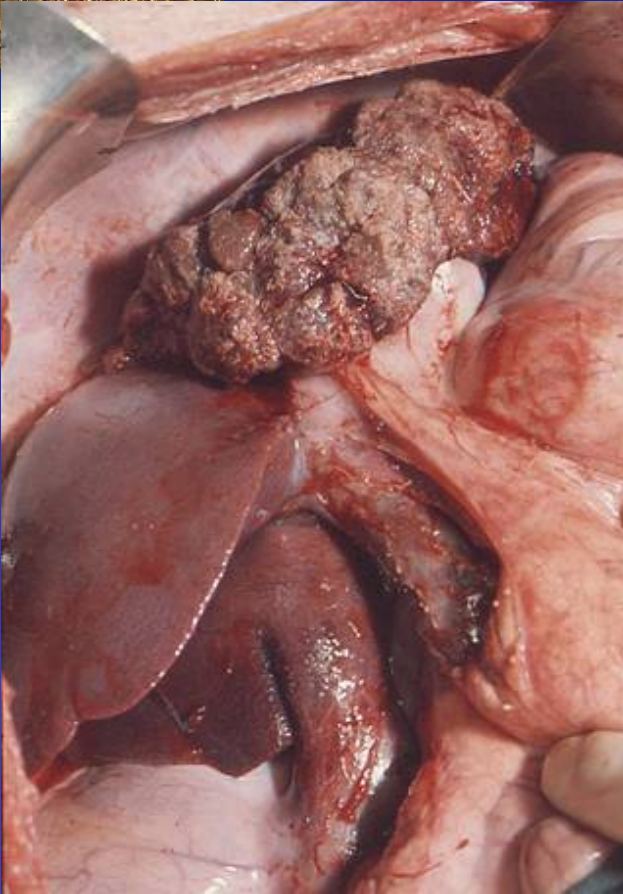
RISULTATI

SOPRAVVIVENZA





Rigenerazione epatica nel maiale



Hepatic artery sustained liver regeneration after resection and portocaval shunt.
Atti 13th Congress European Society for Surgical Research, 1978



1980



2003



Insufficienza epatica acuta

CASO CLINICO

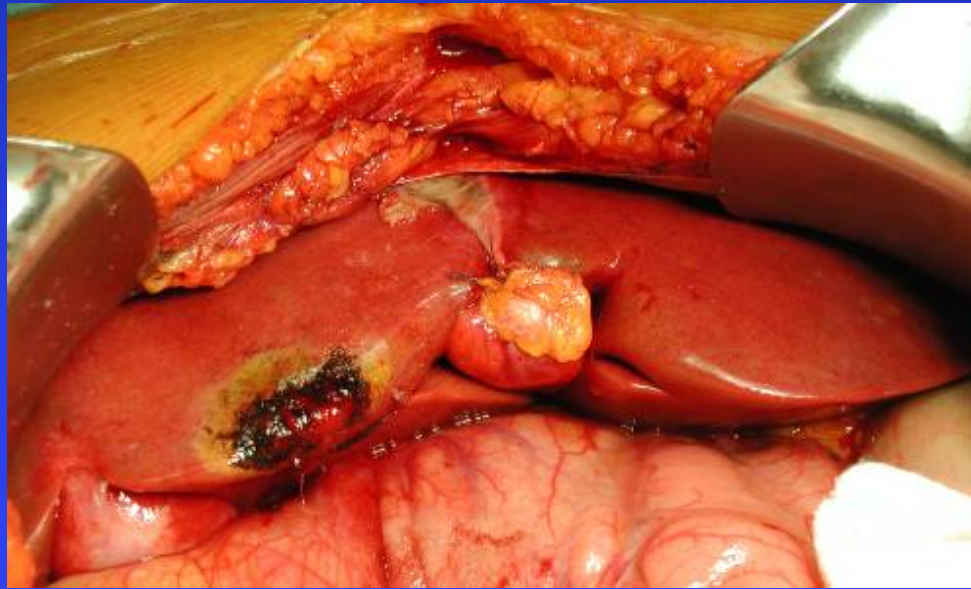
- Donna di 25 anni
- *11 ottobre 2003 (Rianimazione):*
 - Insufficienza epatica acuta da sospetta reazione idiosincrasica a farmaci
 - Richiesta urgente per trapianto di fegato
- *11 e 12 ottobre 2003*
 - Fegato Bioartificiale con epatociti umani (BAL)



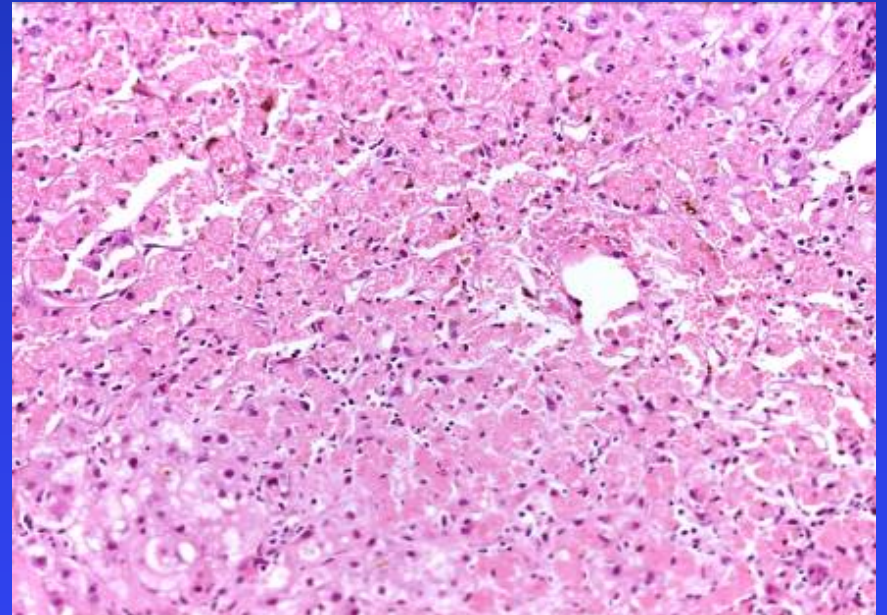
Necrosi epatica massiva nell'uomo

Donna di 25 anni, in coma per IEA da reazione idiosincrasica a farmaci

aspetto macroscopico



esame istologico

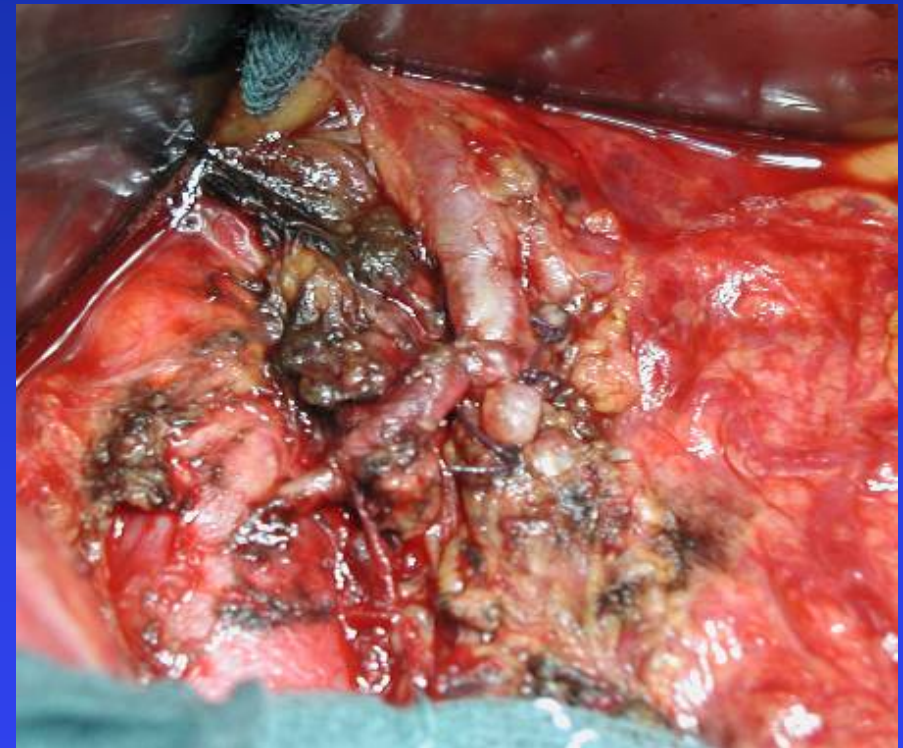
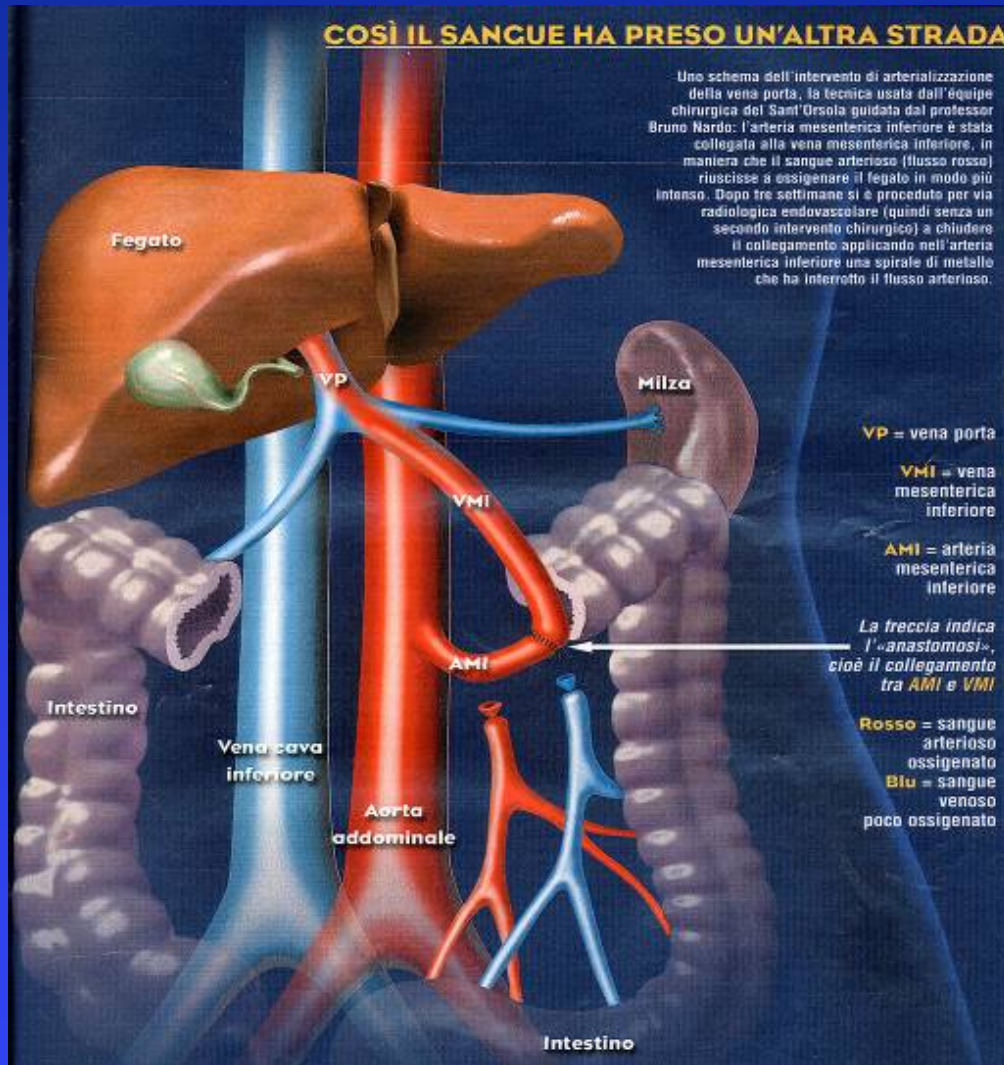


13.10.2003



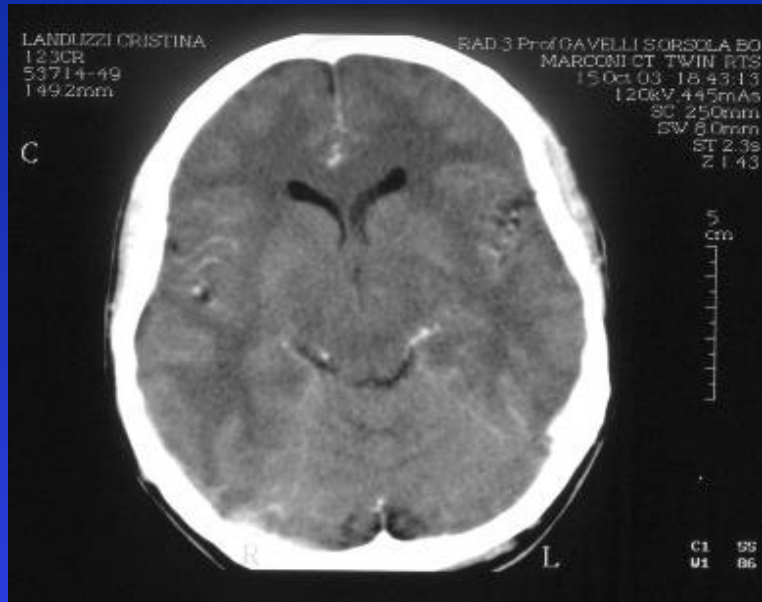
Arterializzazione della Vena Porta nell'uomo

Tecnica chirurgica

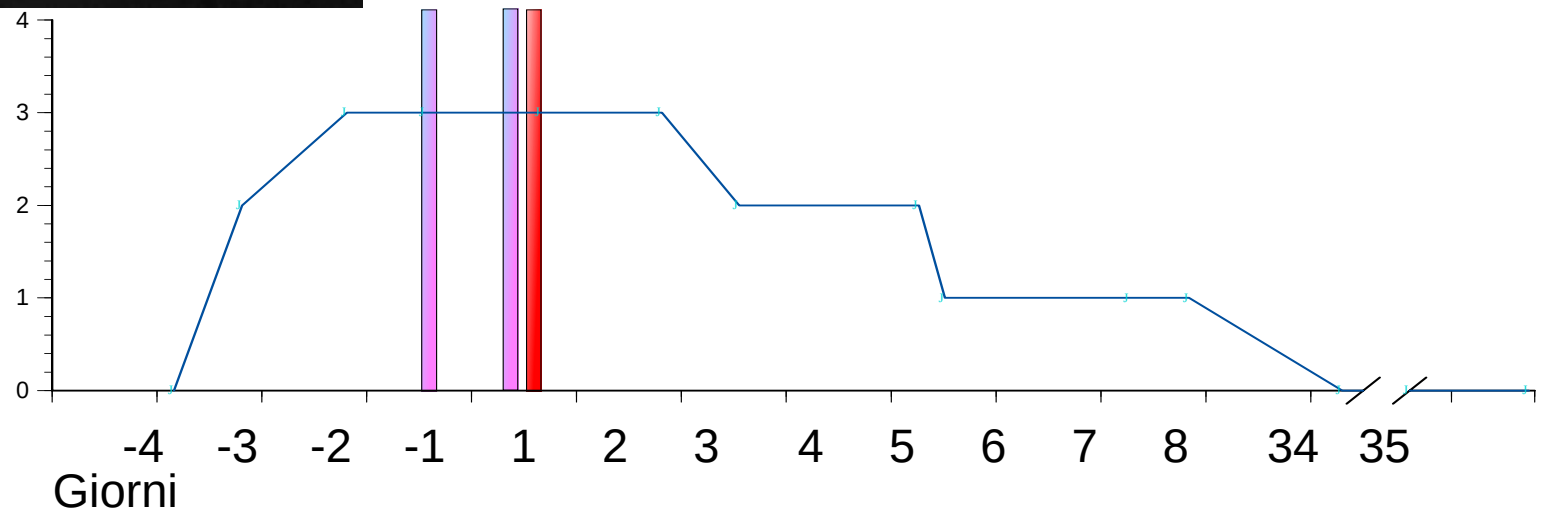




Arterializzazione della Vena Porta nell'uomo



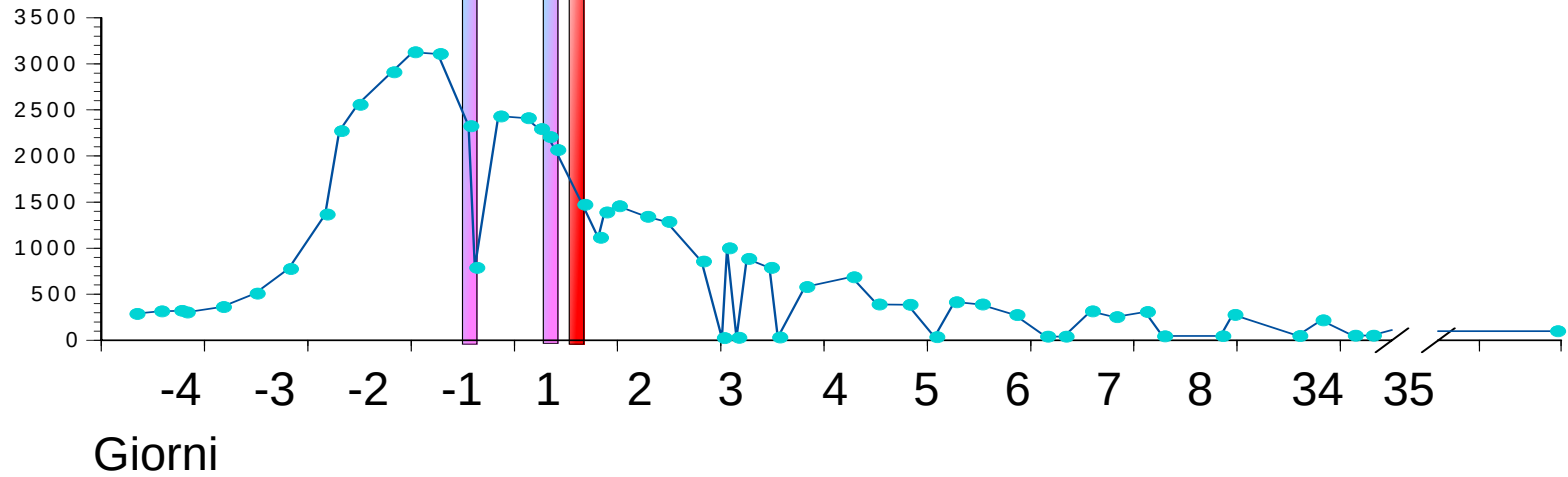
Stato neurologico



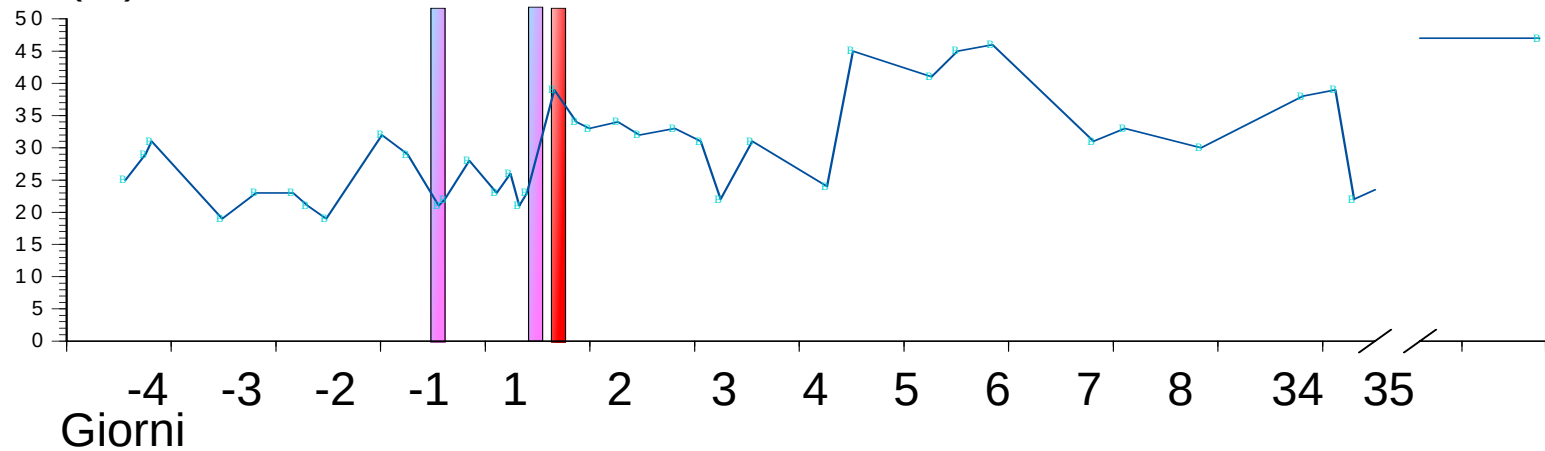


Arterializzazione della Vena Porta nell'uomo

GPT (U/L)



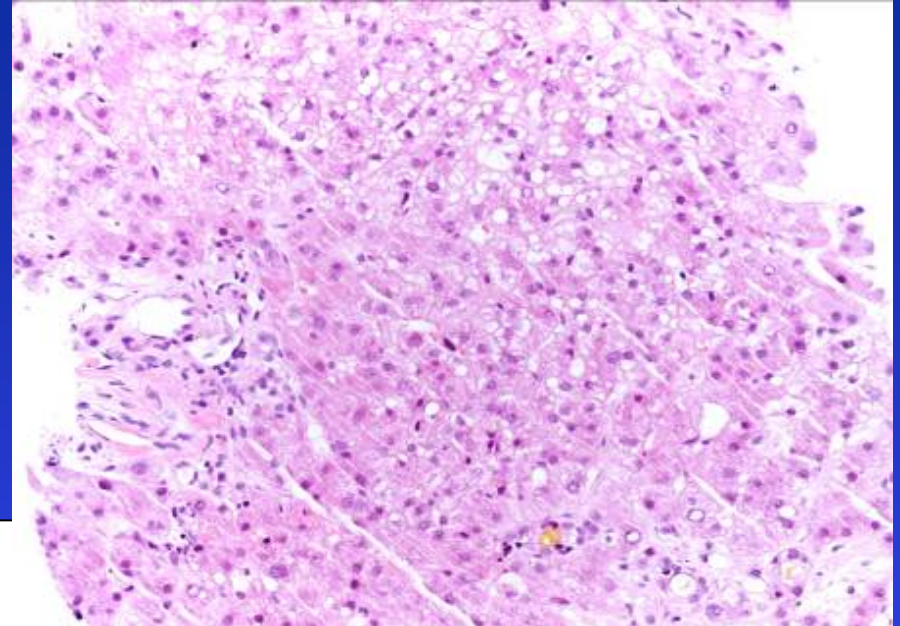
PT (%)



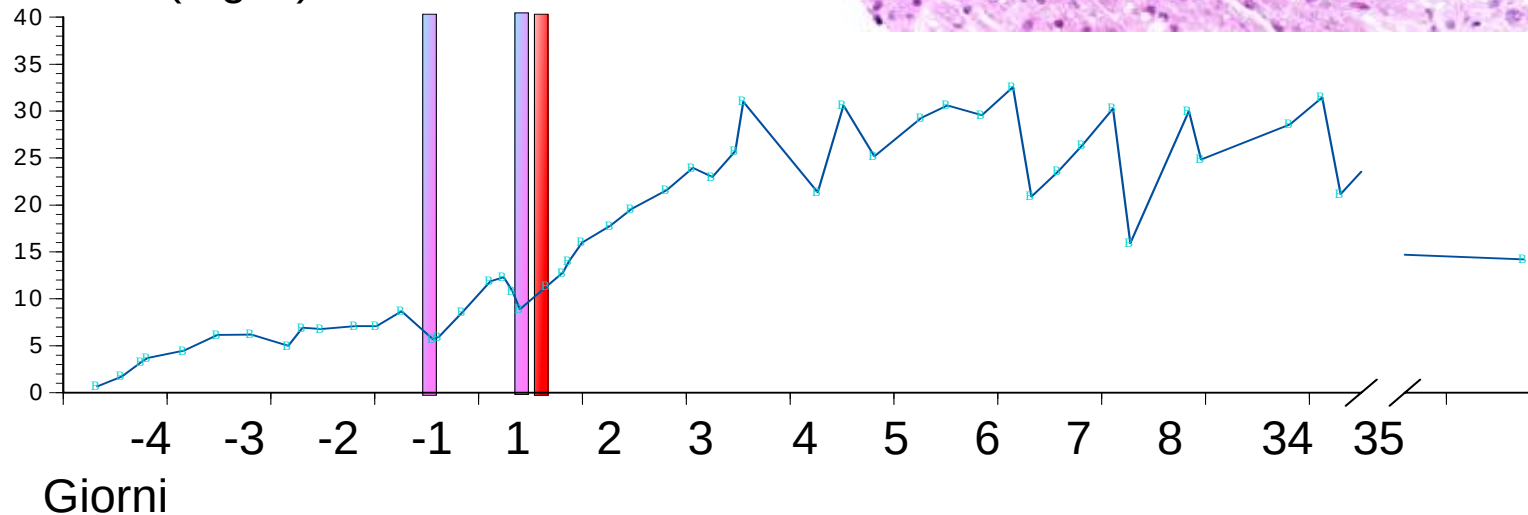


Arterializzazione della Vena Porta nell'uomo

Biopsia di controllo
(3.11.2003)



Bilirubina (mg/dl)





Arterializzazione della Vena Porta nell'uomo

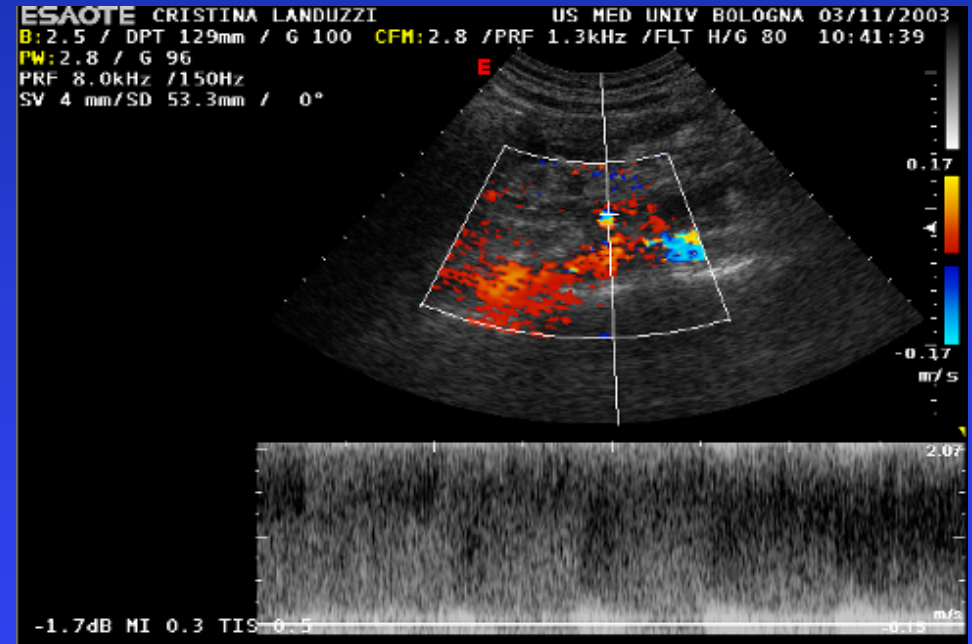
Controllo shunt chirurgico

Arteriografia



22.10.2003

Eco-Doppler



3.11.2003



Arterializzazione della Vena Porta nell'uomo

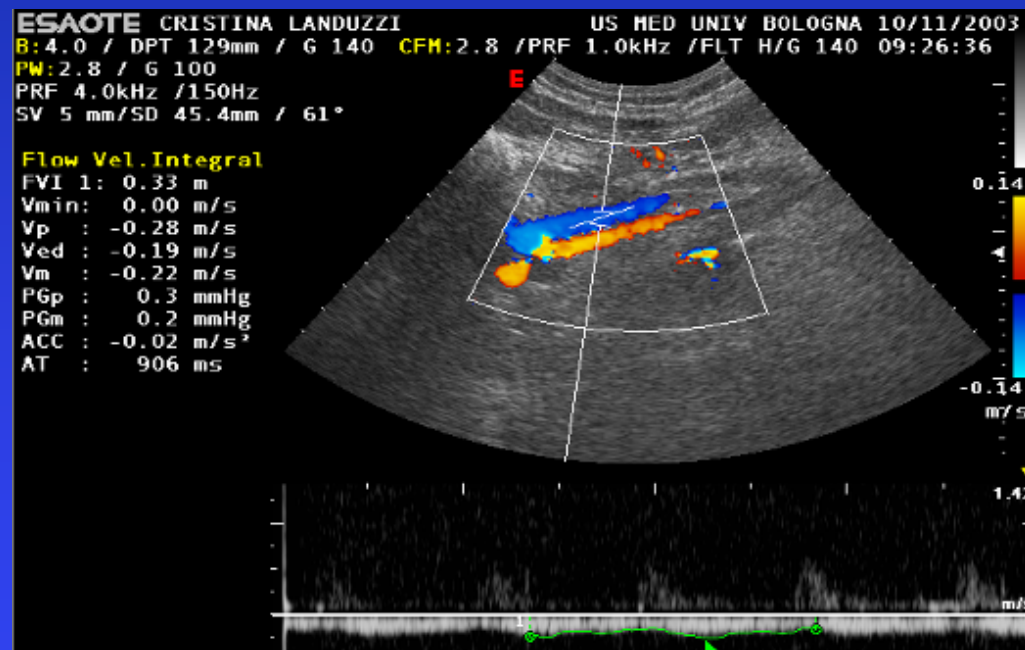
Chiusura radiologica dello shunt chirurgico

Arteriografia



5.11.2003

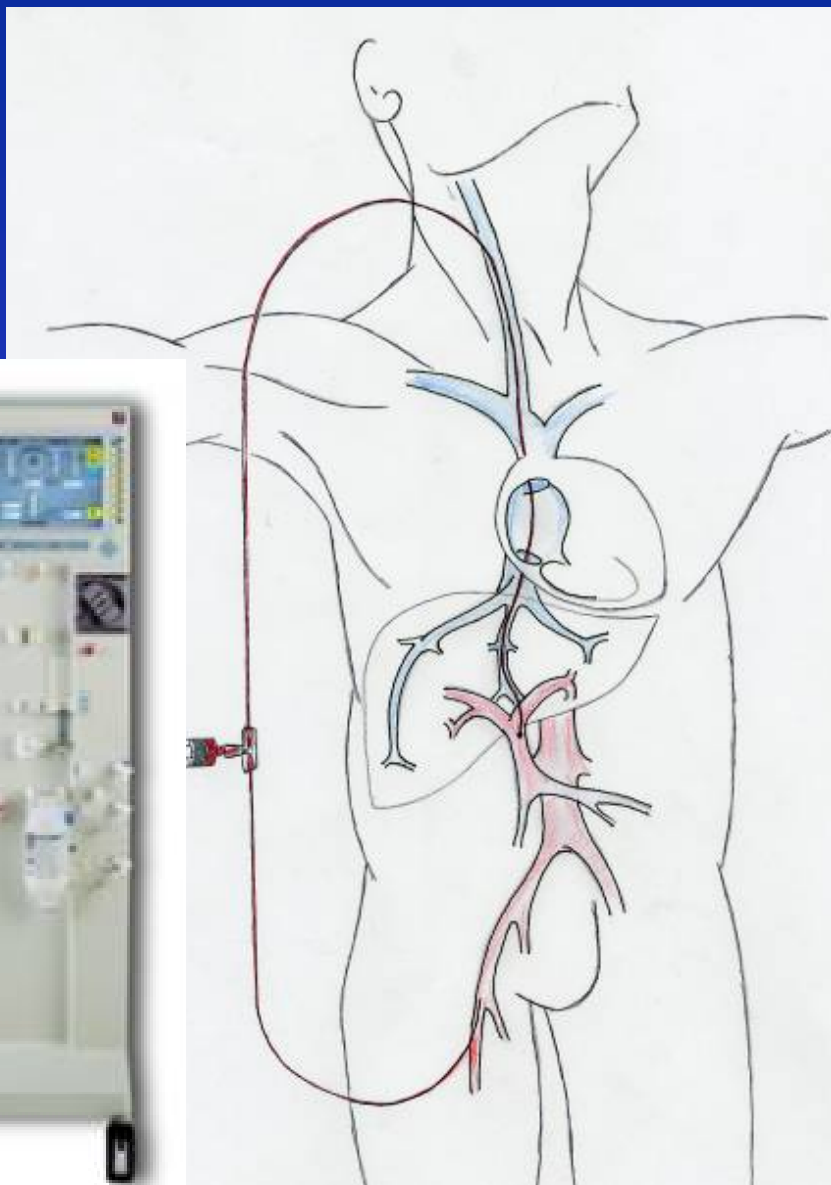
Eco-Doppler



10.11.2003



Dicembre 2003



Dispositivo per la AVP percutanea

PCT, IB, aprile 2003



Arterializzazione della Vena Porta nell'uomo

Conclusioni

Sulla base dei dati preclinici e clinici fin qui acquisiti, sarebbe opportuno includere tale intervento nell'ambito del trattamento multidisciplinare dei pazienti affetti da insufficienza epatica acuta in attesa del trapianto di fegato