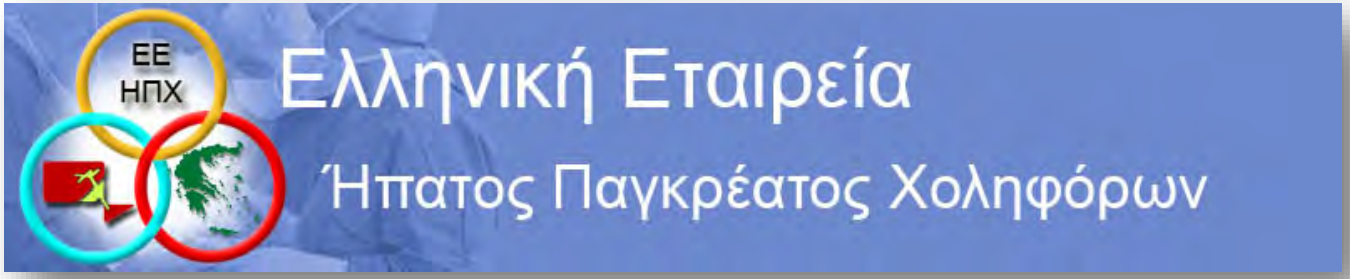
HBP Surgery- mCRC



Χειρουργικές Παθήσεις του Ήπατος

Νεότερα δεδομένα

ΕΣ Φελέκουρας.

Αν. Καθ Χειρουργικής, ΕΚΠΑ

Liver resection for mCRC: Late results

Natural History of mCRC

- If No Tx median survival is 9 ms.
- 5- year survival is rare.

mCRC: Current Tx

- **Liver resection (LRx)**
- Systemic Chemotrerapy: All forms

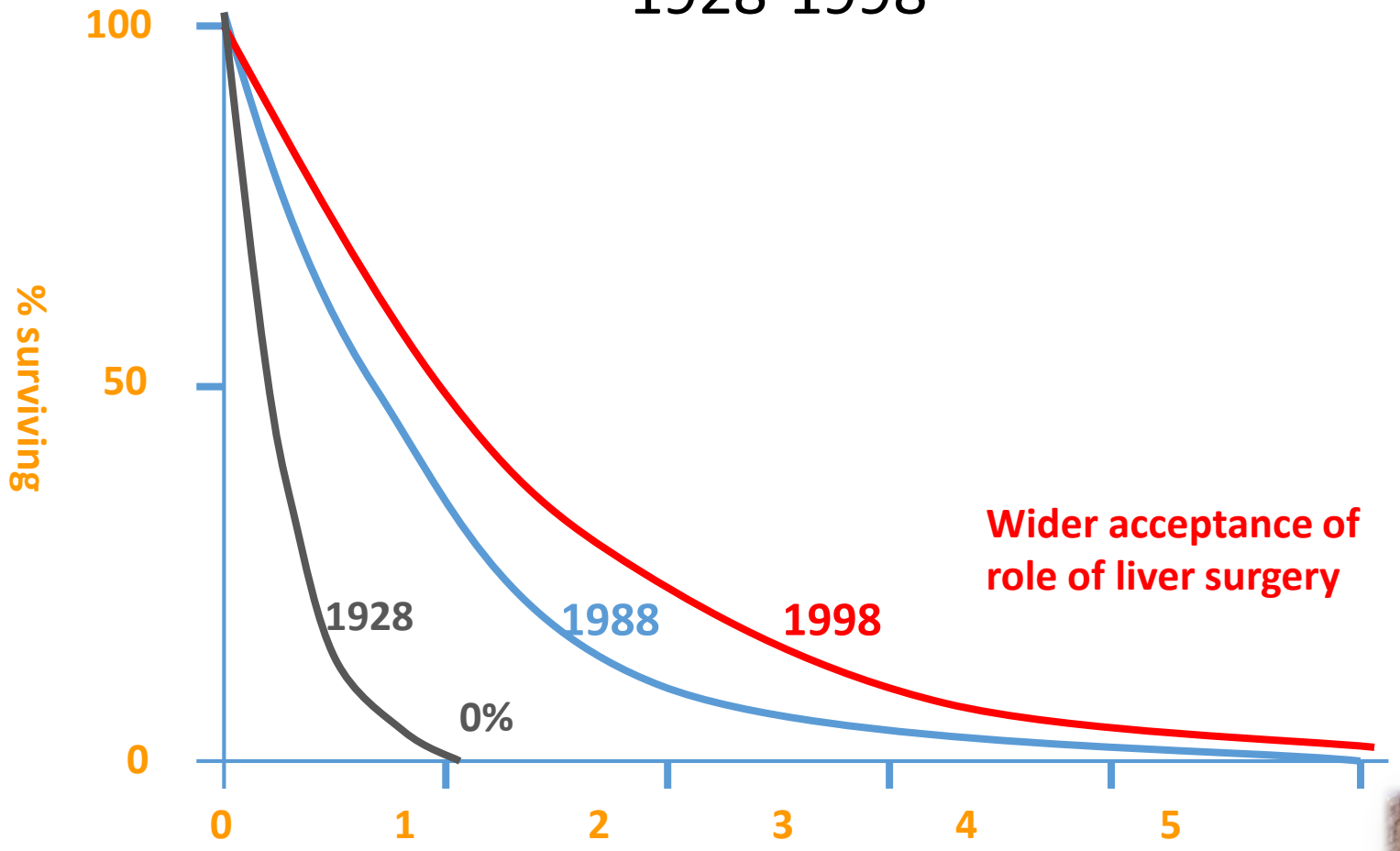
- Radiofrequency ablation
- MWA
- Hepatic artery infusion
- Various

- Combination

- Especially with sChemo

HBP Surgery- mCRC

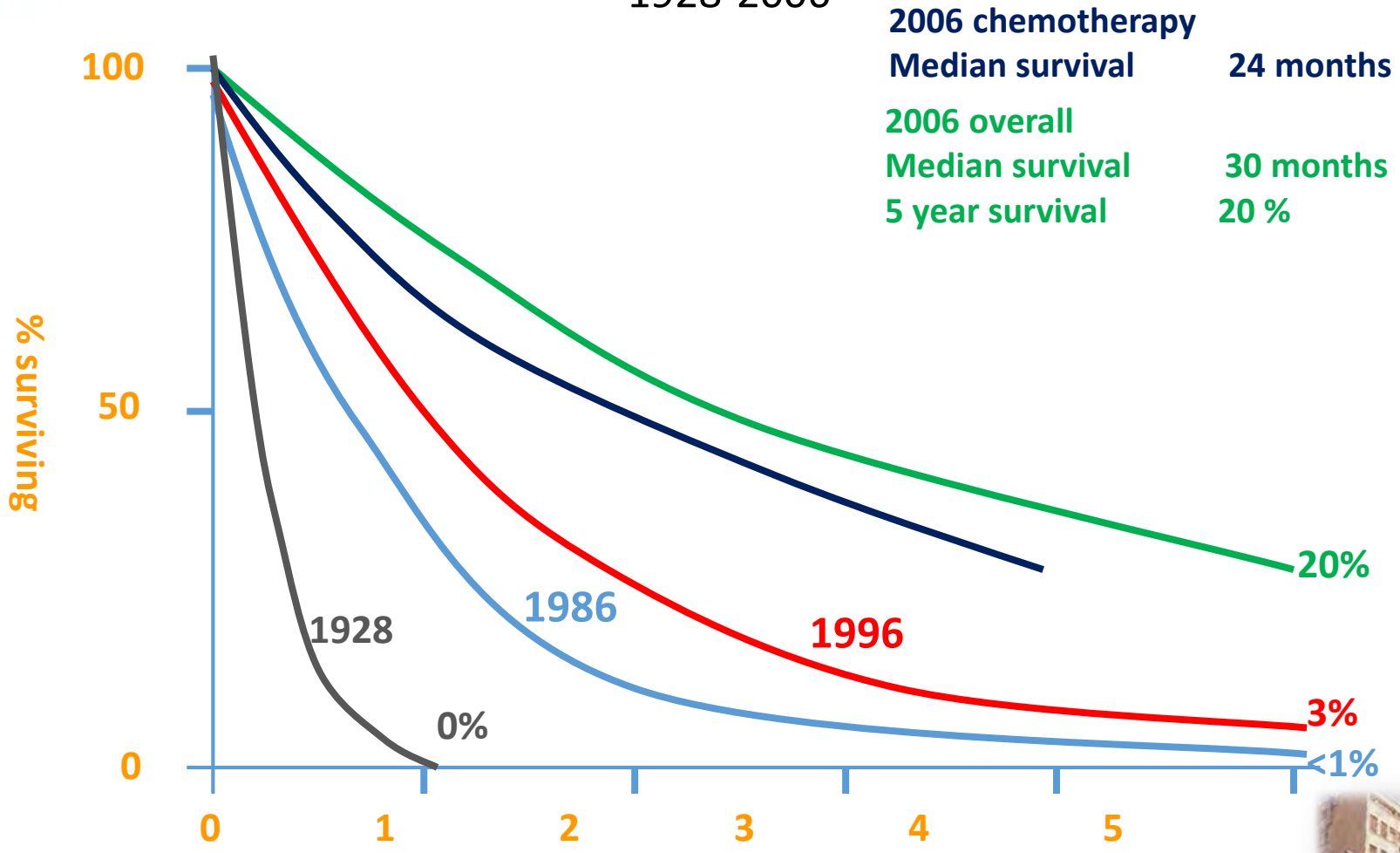
Overall survival in advanced colorectal cancer
1928-1998



Rougier P et al. Brit J Surg 1995

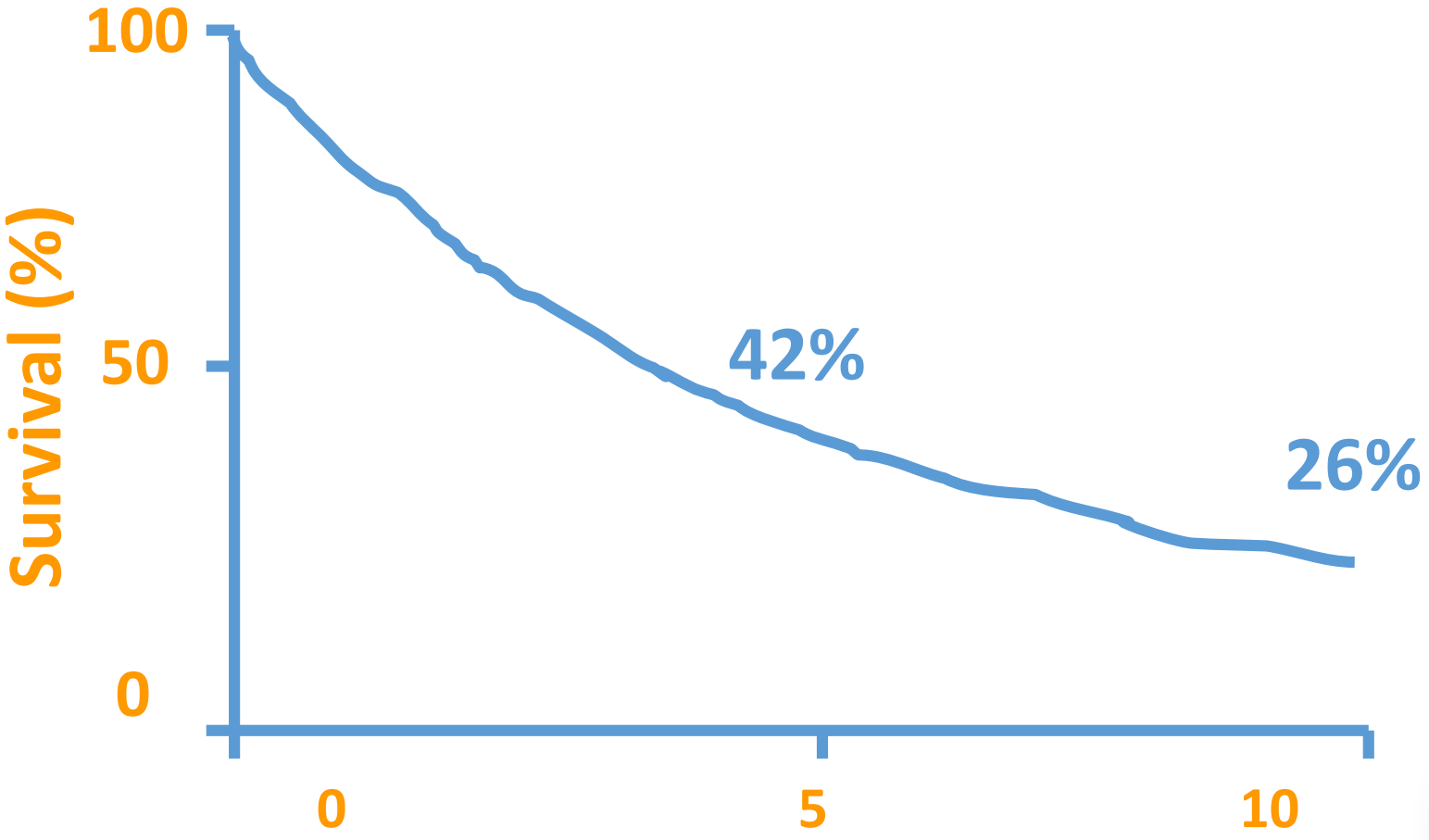
HBP Surgery- mCRC

Overall survival in advanced colorectal cancer
1928-2006



HBP Surgery- mCRC

LiverMetsurvey.org
4100 resections 1974-2006



Adam et al. HPB 2006; 8(S2): 52

Facts

Level of evidence: category 2a

- Complete hepatectomy Rx (R0) is the proper Tx for Liver mCRC
  - The primary tumor must have an R0 Rx *
  - There should be no UnRx extrahepatic sites of disease
- Synchronous Tx: feasible
- Re-Resection: is feasible
- In UnRx pts reevaluation should be considered in 2 months intervals post Chemotherapy

Management of Colorectal Metastases Summary

Meticulous surveillance	+	Aggressive multimodality therapy	=	Potential ↑ survival

The 5-year overall survival following resection of CRC liver metastases today is up to

58%

HBP Surgery- mCRC

Assessment of Resectability.

Patient selection.

- How much is the future liver remnant (FLR).

- In 2006 the AHPBA, SSO, SSAT put the

  Indications for hepatectomy for mCRC.

  – Ability to obtain margin-negative resection (R0)
  – while leaving a FLR consisting of at least two contiguous hepatic sectors, adequate inflow, outflow, biliary drainage, and
  – a greater than 20% FLR of liver volume in a healthy liver..

HBP Surgery- mCRC

General Prognostic factors

1. Preoperative CEA level
2. LN status of primary tumor
3. Disease free interval
4. Extrahepatic disease
5. Resection margin

Clinical risk score(CRS)

Five clinical parameters were selected, as criteria for long-term outcome prediction.

1. primary nodal status,
2. disease-free interval from the primary to liver metastases <12 months
3. number of hepatic tumors > 1
4. pre-operative CEA level > 200 ng/ml,
5. size of the largest hepatic tumor > 5 cm,

The 5-year survival for patients with zero points was 60%, whereas that for those with five points was 14%

Not included the margin status and the presence of extrahepatic lesions, because they thought that these two are if positive contraindications for liver resection

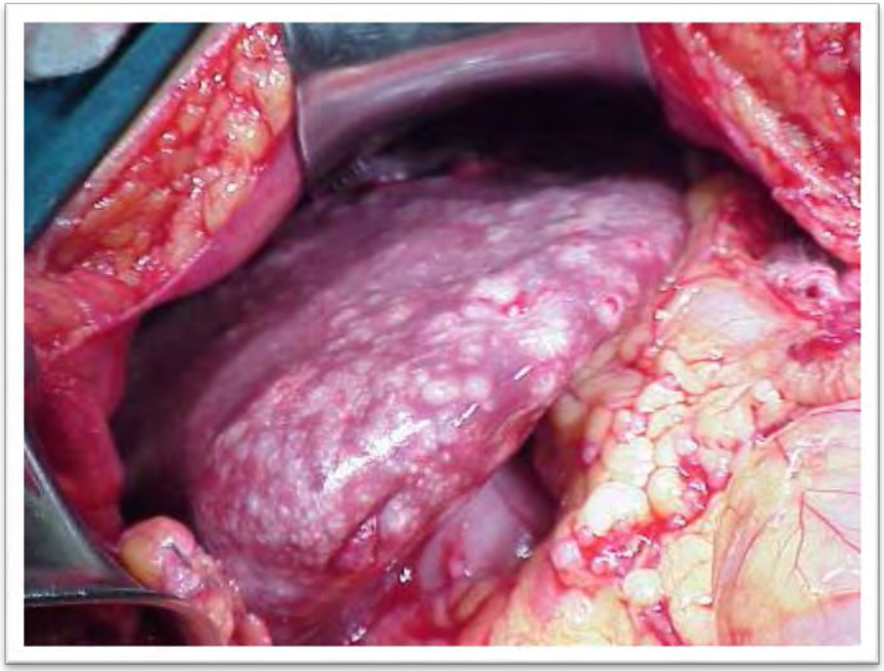
Fong et al Ann Surg. 1999 Sep;230(3):309-18;

HBP Surgery- mCRC

Contraindications for Hepatectomy today

- non-treatable primary tumor
- locoregional recurrence
- widespread pulmonary disease
- peritoneal disease
- extensive nodal disease, such as retroperitoneal, mediastinal or portal nodes
- bone or CNS metastases.

(Category of evidence II; strength of recommendation B)



Garden OJ et al Gut. 2006 Aug;55 Suppl 3:iii1-8

HBP Surgery- mCRC

mCRC: Hepatectomy

Assessment of Resectability.

- **Extrahepatic Disease.**

Table 1. Five-year Overall Survival of patients with EHD undergoing hepatic resection for CLM.

Study	Year	# of Patients	Patients with EHD(% of total)	5 year Overall Survival of patients with EHD(%)
Scheele et al.[11]	1995	469	47(10)	26
Fong et al.[13]	1999	1001	43(4)	18
Minagawa et al.[97]	2000	235	17(7)	21
Elias et al.[18]	2003	376	111(29)	20
Elias et al.[19]	2005	308	84(27)	28
Carpizo et al.[21]	2009	1369	127(9.3)	26

Six large studies in the past two decades that examined the significance of EHD and the overall 5-year survivals in patients with CLM that underwent hepatic resection.

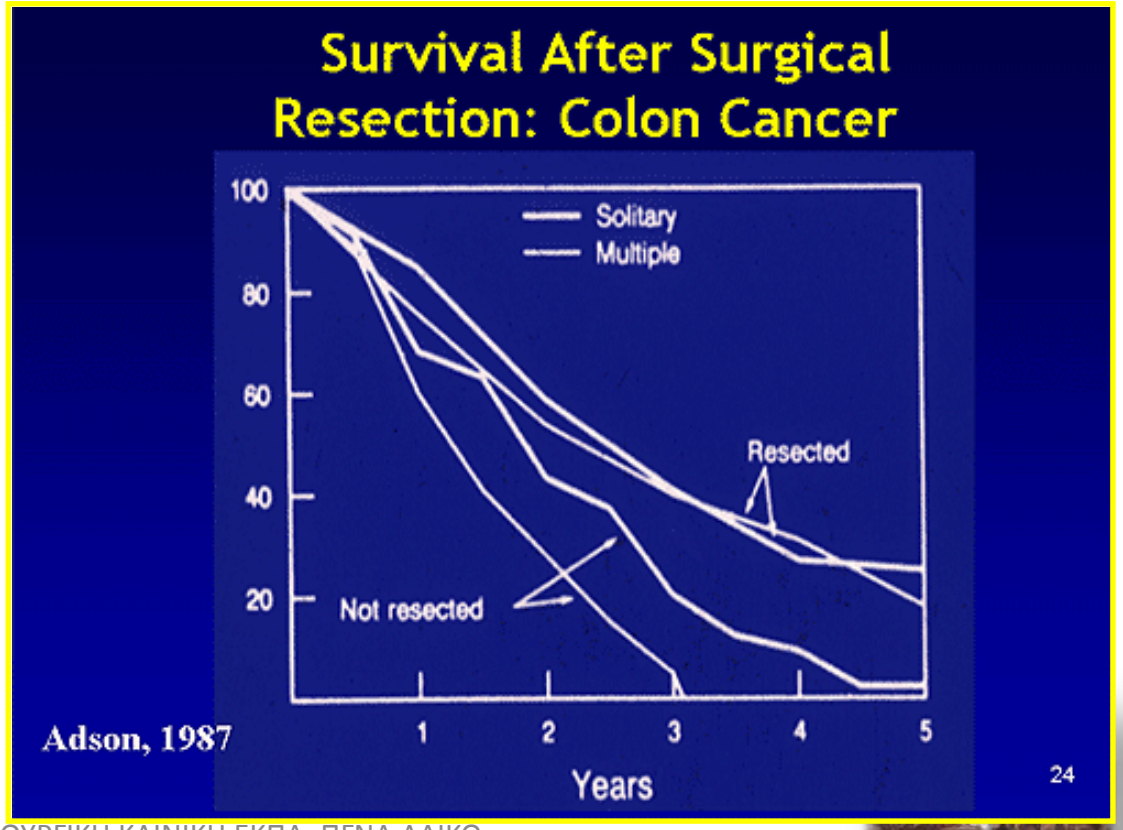
HBP Surgery- mCRC

mCRC: Hepatectomy

- **Assessment of Resectability.**
  - **Multifocal Disease.**
  - **Bilobar Disease.**

R0 hepatectomy 5-year Survival better than R1

25,8 months vs 17 months

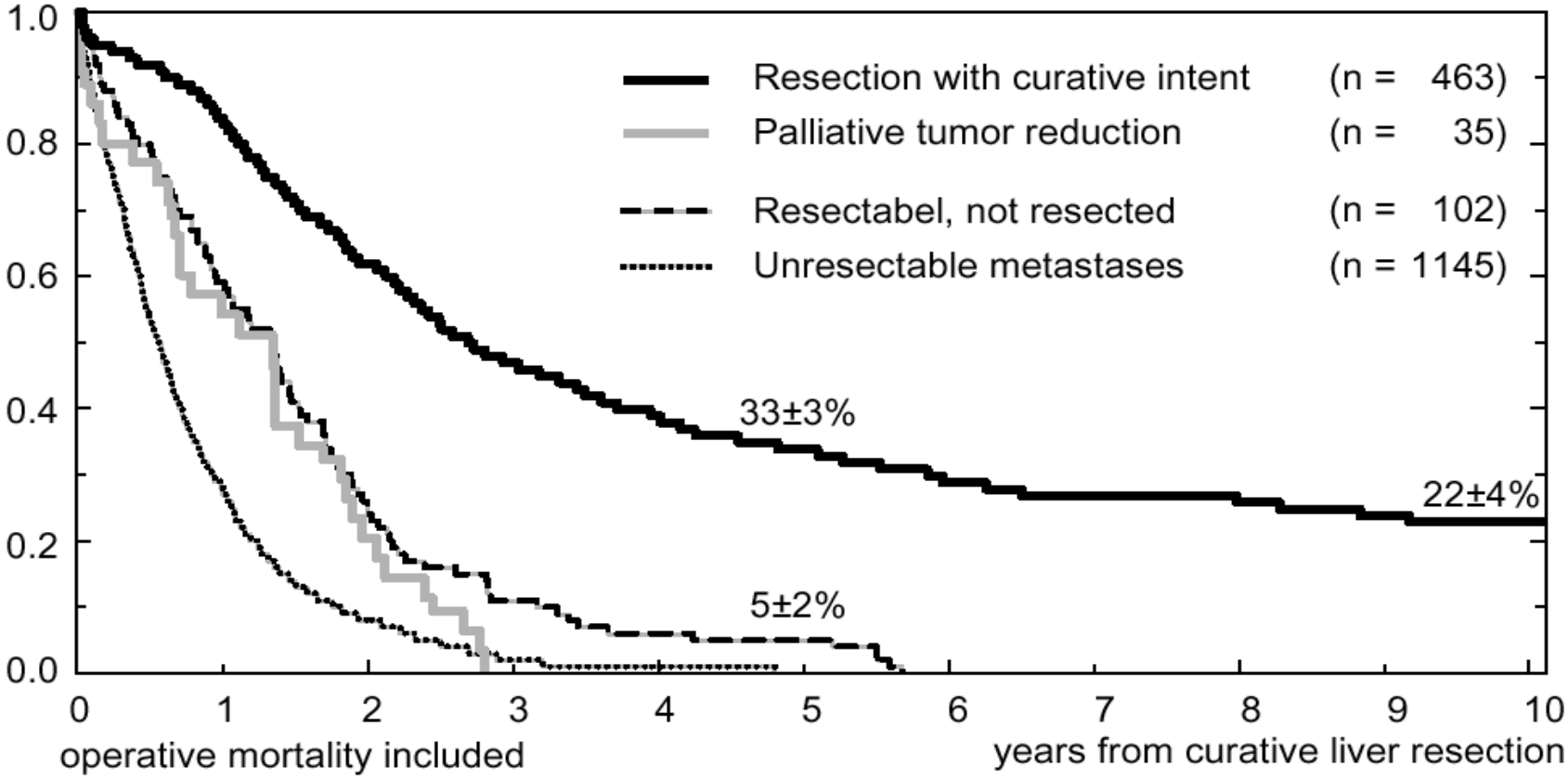


Background-CRM

Adson MA. World J Surg. 1987 Aug;11(4):511-20

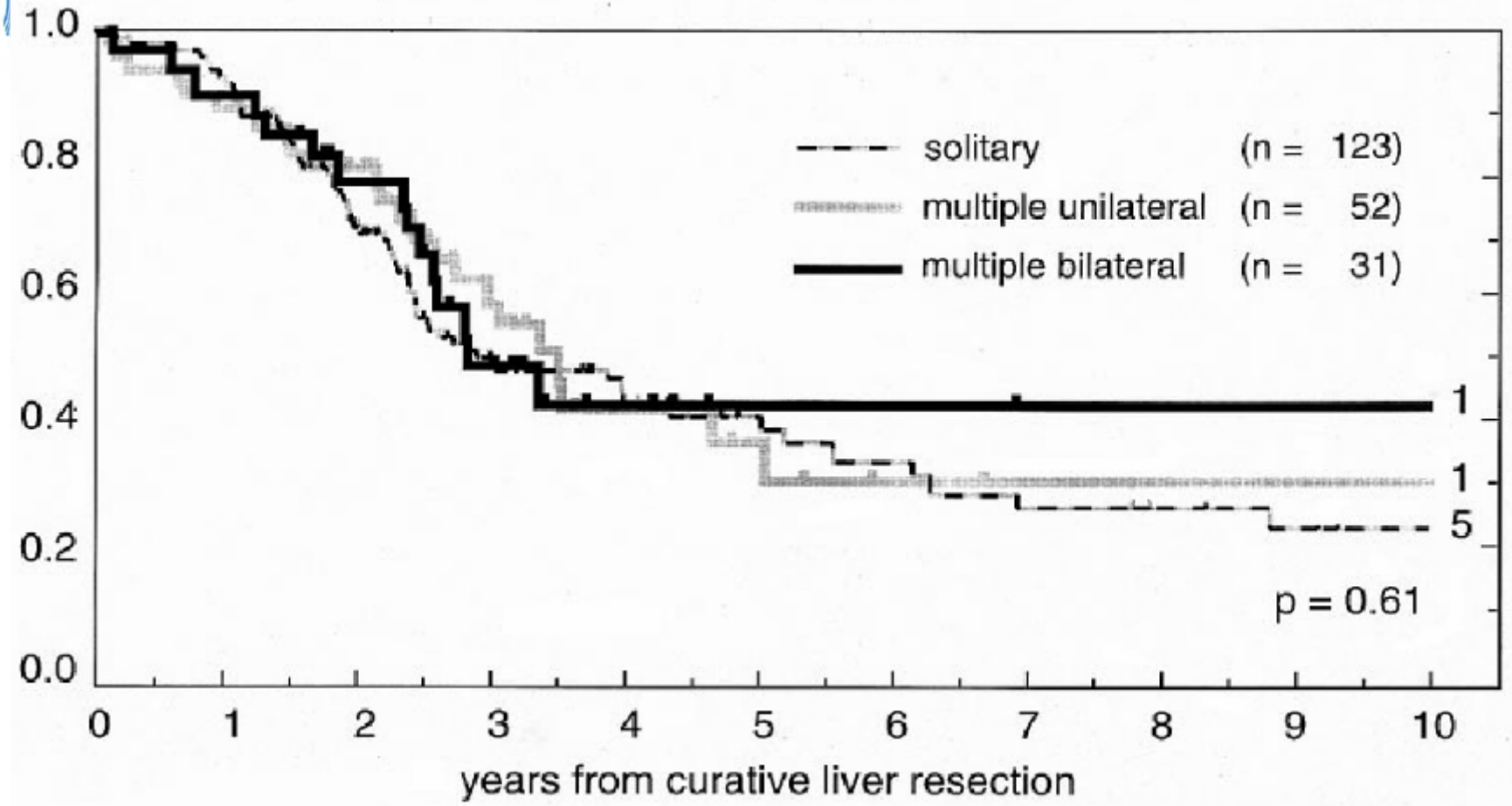
HBP Surgery- mCRC

1,745 consecutive patients with colorectal liver metastases, 1961-1993; Germany



Scheele J, Altendorf-Hofmann. *Langenbeck's Arch Surg* 1999

HBP Surgery- mCRC

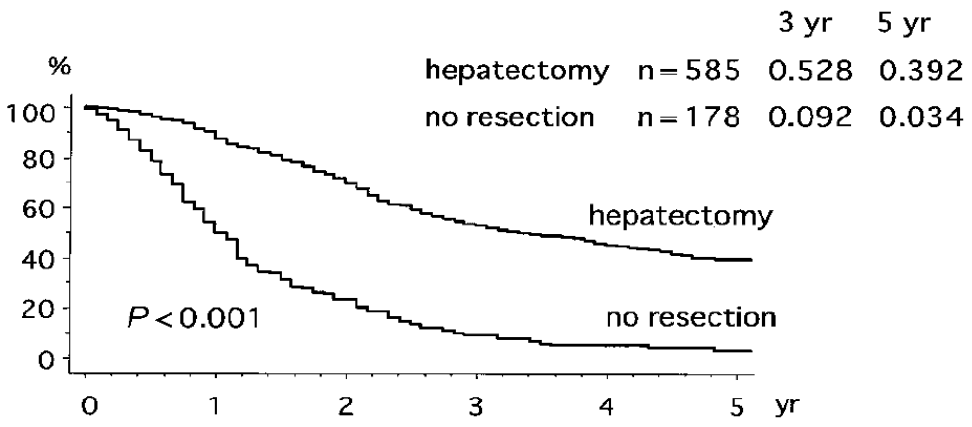


Ο αριθμός και η ανατομική θέση των ηπατικών μεταστάσεων στο Ήπαρ δεν έχουν προγνωστική άξια όταν γίνεται εκτομη R_0

Schnele and Altendorf-Hofmann. ***Langenbeck's Arch Surg*** **1999**

HBP Surgery- mCRC

Kato, Tomoyuki M.D. et al, Diseases of the Colon & Rectum 2003.



- 763 hepatic metastases
- 585 hepatectomy pt
- 5 year survival 39.2% (vs. 3.4%)

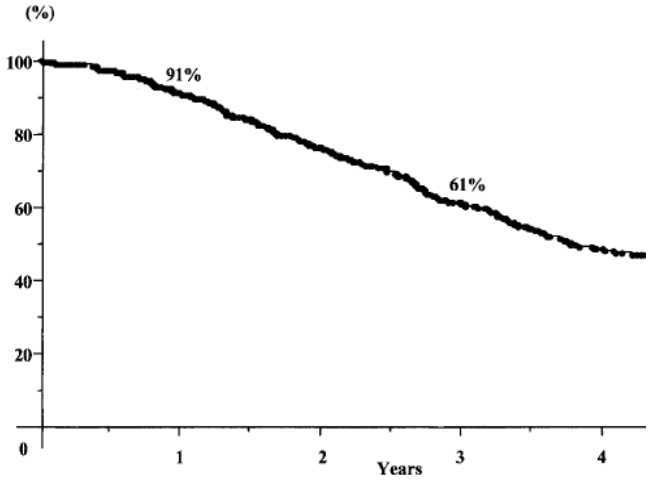
- Recurrence after hepatectomy : Remnant liver (41.4%), Lung (19.2%)

(*Ann Surg* 2003;238: 871–884)

Liver Resection for Colorectal Metastases

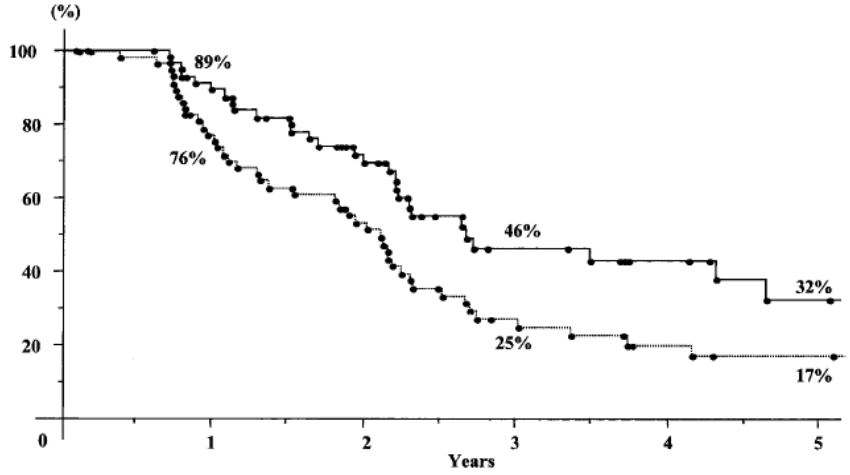
The Third Hepatectomy

René Adam MD, PhD, Gérard Pascal, MD, Daniel Azoulay, MD, PhD, Kuniya Tanaka, MD, Denis Castaing, MD, and Henri Bismuth, MD, FACS Hon



Patients at risk	No	1 year	2 years	3 years	4 years
Overall survival	615	476	324	228	163

FIGURE 2. Cumulative survival after first hepatectomy for colorectal metastases.



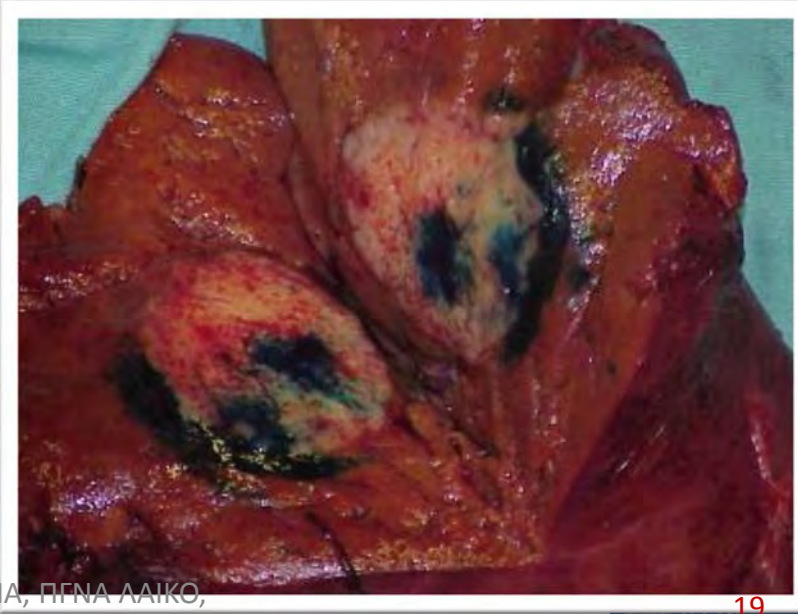
Patients at risk	N	1 year	2 years	3 years	4 years	5 years
Overall survival	60	48	29	15	9	6
Disease-free survival	60	42	26	11	7	5

FIGURE 3. Cumulate overall (—) and disease-free survival (—) after third hepatic resection for colorectal metastases.

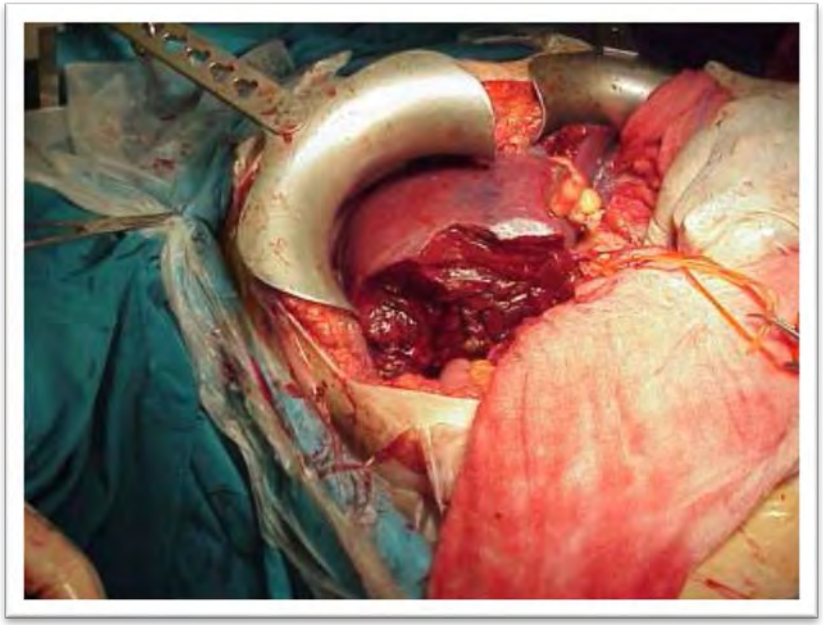
HBP Surgery- mCRC

mCRC: Hepatectomy

- **Technical Considerations.**
  - Synchronous Disease.
  - Portal Vein Embolization
  - Two-Stage Hepatectomy.



Synchronous liver resection (and Liver first approach)



(*Ann Surg* 2004;240: 1037–1051)

A Two-Stage Hepatectomy Procedure Combined With Portal Vein Embolization to Achieve Curative Resection for Initially Unresectable Multiple and Bilobar Colorectal Liver Metastases

Daniel Jaeck, MD, PhD, FRCS, Elie Oussoultzoglou, MD,* Edoardo Rosso, MD,* Michel Greget, MD,† Jean-Christophe Weber, MD, PhD,* and Philippe Bachellier, MD**

- **Conclusions:** In selected patients with initially unresectable MBCLM, a TSHP combined with PVE can be achieved safely with long-term survival similar to that observed in patients with initially resectable liver metastases.

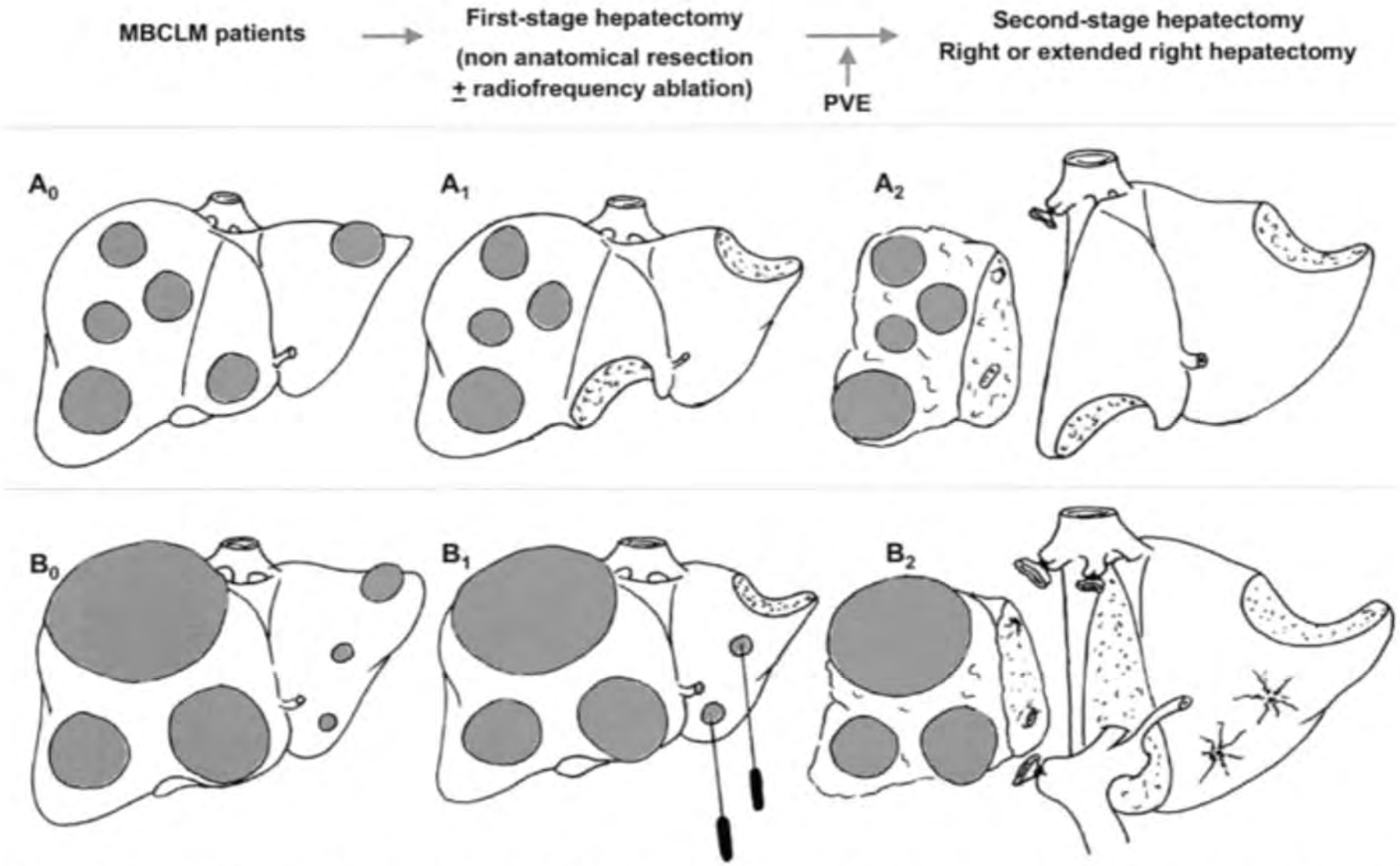
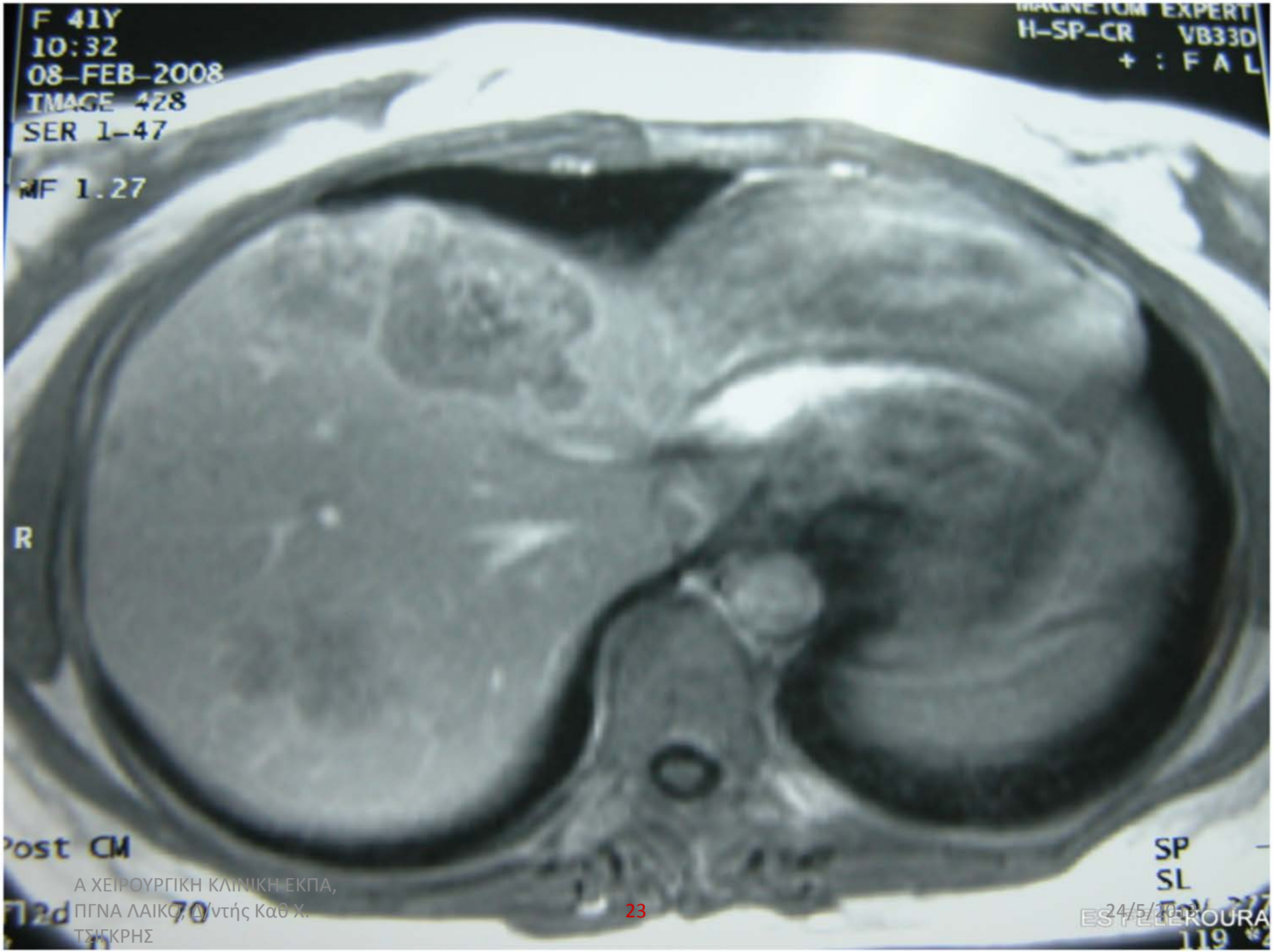
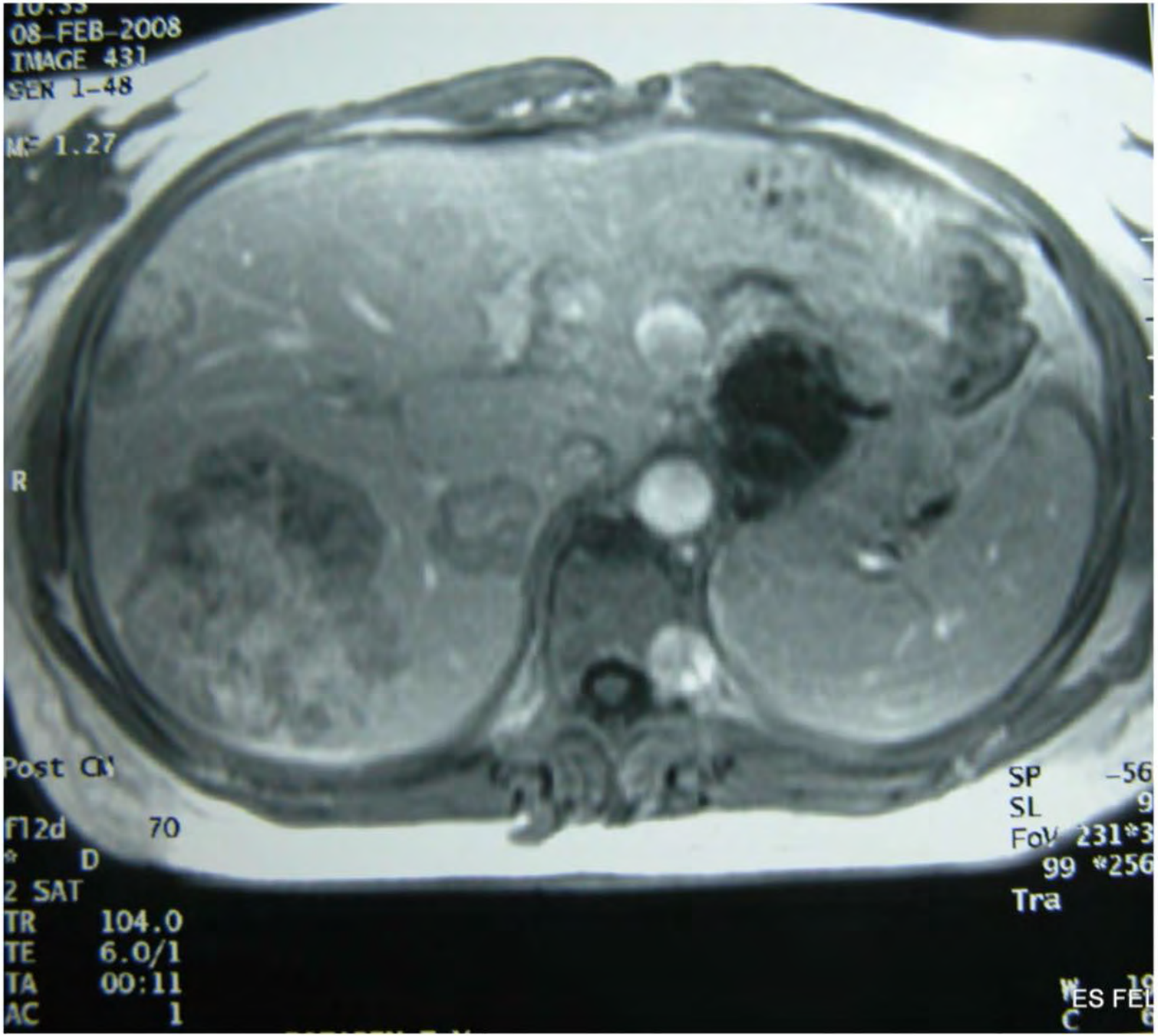
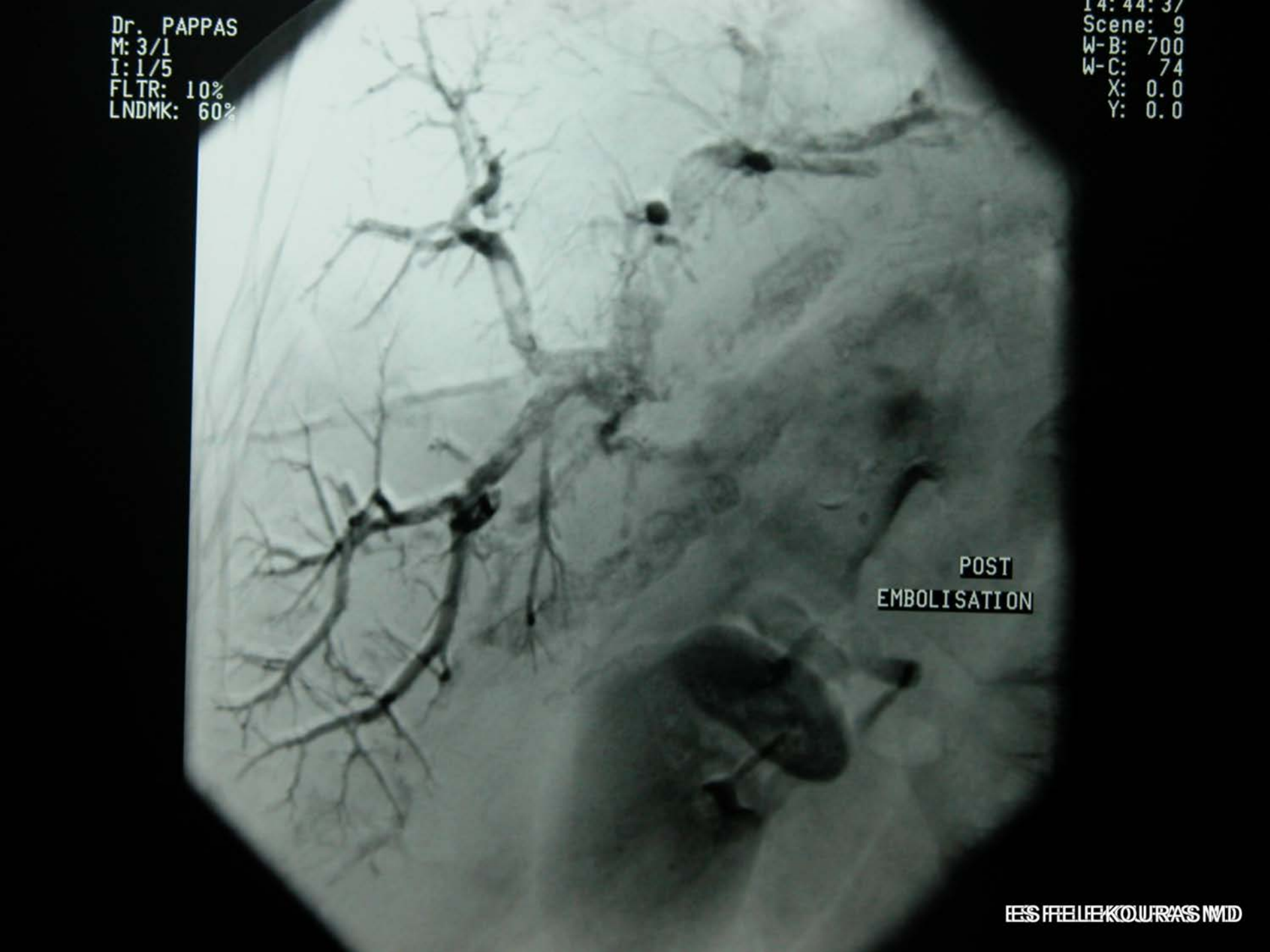


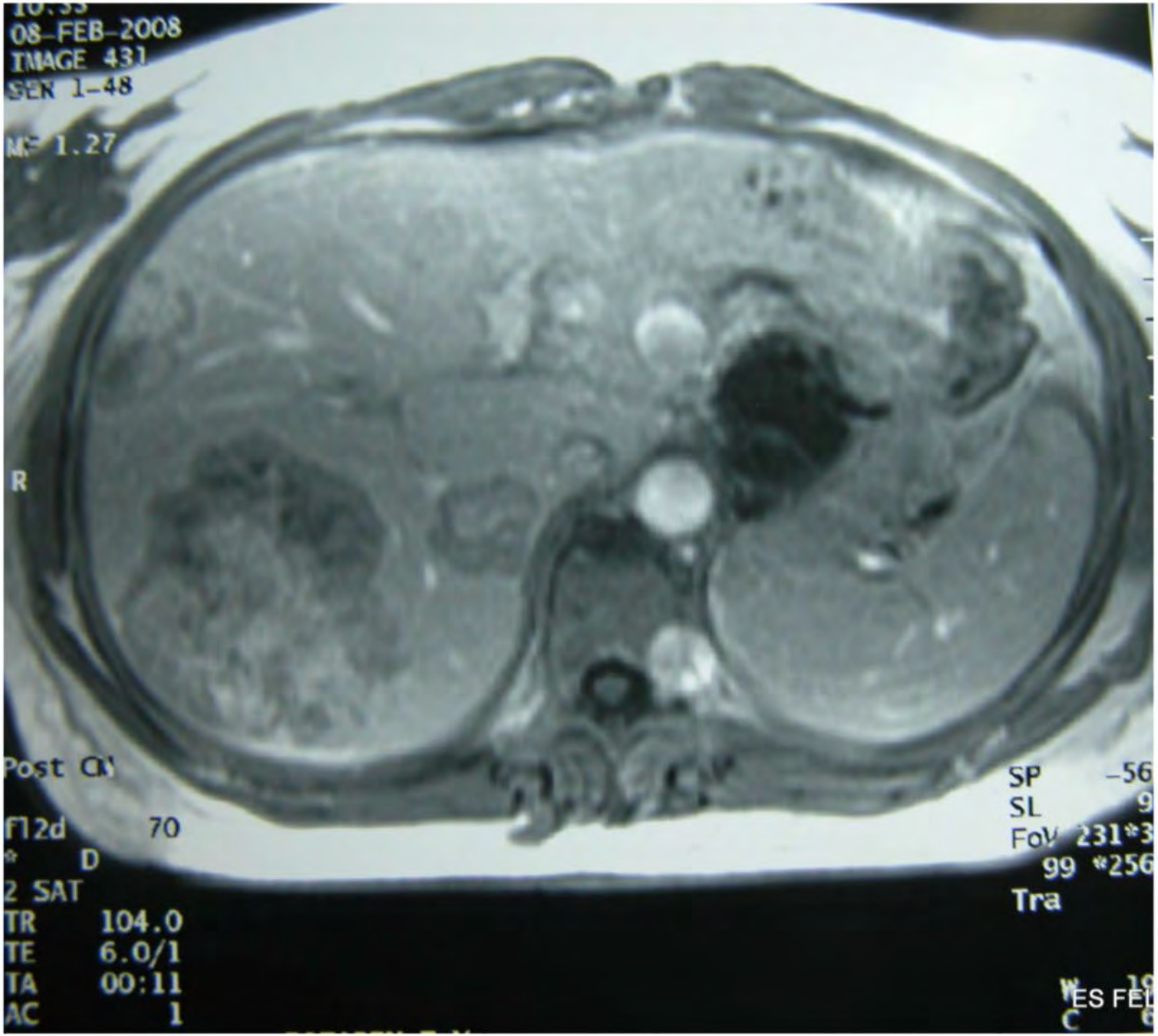
FIGURE 1. Patients with MBCLM (●) undergoing a TSHP. A_0, Patient with 2 metastases in the left hemiliver. A_1, First-stage: nonanatomic resection clearing the left liver of all metastases. A_2, Second-stage (right hepatectomy) after PVE (not shown): atrophy of the right and hypertrophy of the left liver. B_0, Patient with 4 metastases in the left hemiliver. B_1, First-stage: Radiofrequency destruction (●) and nonanatomic resection were associated to clear the left liver of all metastases. B_2, Second-stage (right hepatectomy) after PVE (not shown).

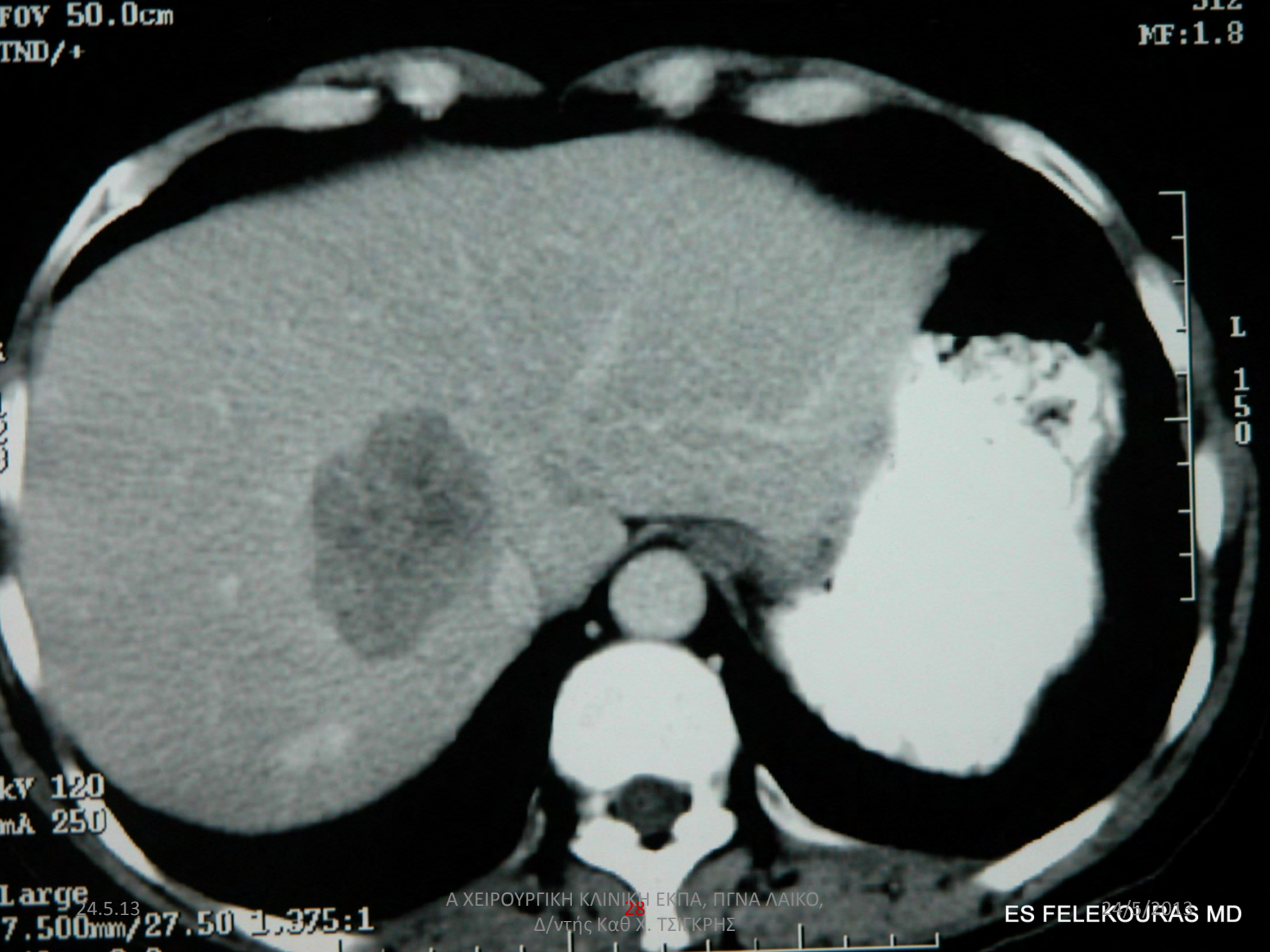

F 41Y
10:32
08-FEB-2008
IMAGE 428
SER 1-47
MF 1.27
H-SP-CR
VB33D
+ : F A L
R
Post CM
SP
SL


08-FEB-2008
IMAGE 431
SER 1-48
1.27
R
Post C
F12d 70
D
2 SAT
TR 104.0
TE 6.0/1
TA 00:11
AC 1
SP -56
SL 9
FoV 231*3
99 *256
Tra

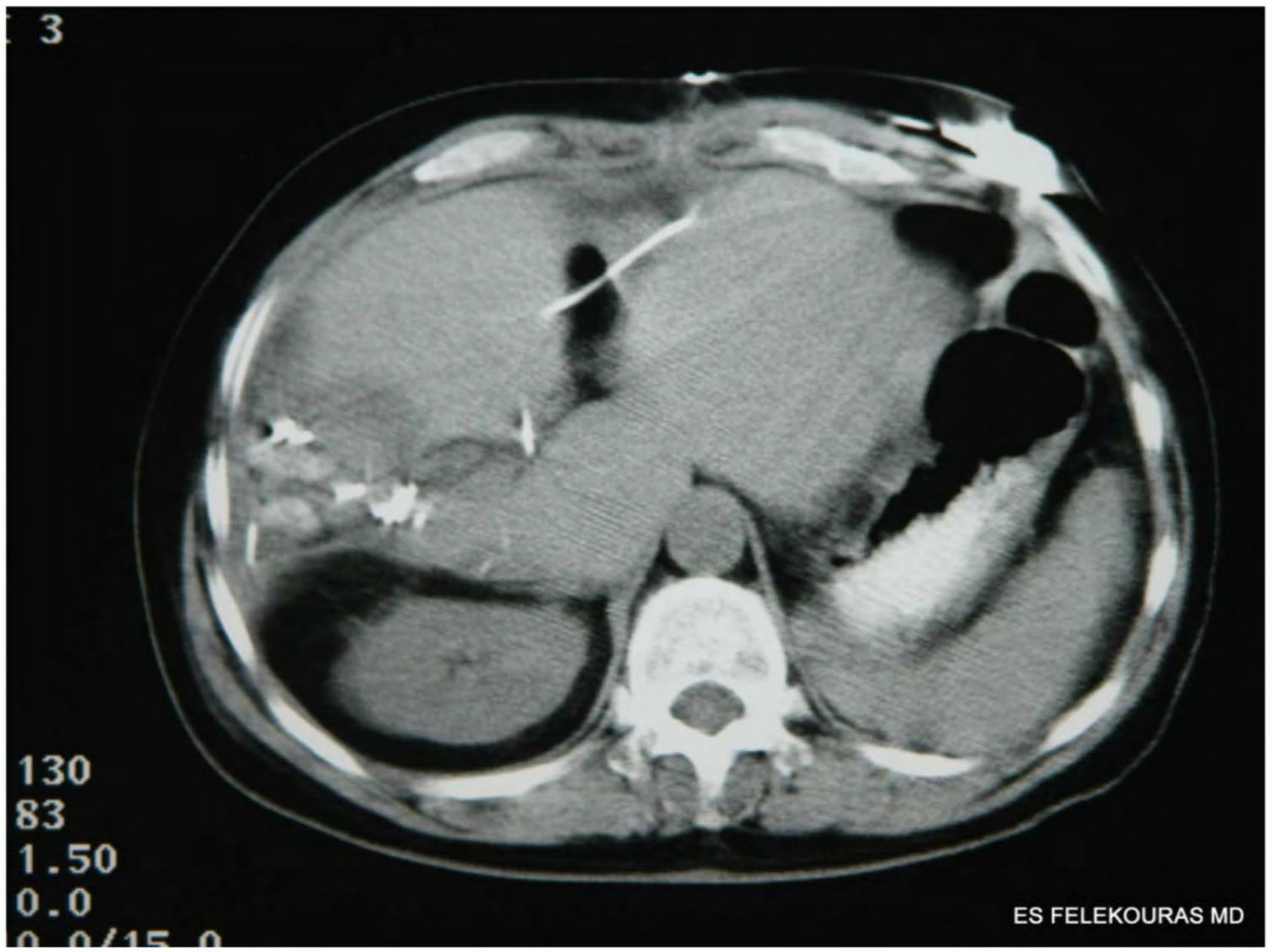

GLIATI ANNA/AX
P.G.N.A. "LAIKO"
7332
Dr. PAPPAS
M: 3/1
I: 17/20
FLTR: 10%
ABDOMEN SEL.
02-Sep-08
14:36:38
Scene: 8
W-B: 700
W-C: 50
X: 0.0
Y: 0.0
IES FTELLEKOURAS MD


Dr. PAPPAS
M: 3/1
I: 1/5
FLTR: 10%
LNDMK: 60%
14:44:37
Scene: 9
W-B: 700
W-C: 74
X: 0.0
Y: 0.0
POST
EMBOLISATION


08-FEB-2008
IMAGE 431
SER 1-48
1.27
R
Post Cx
F12d 70
D
2 SAT
TR 104.0
TE 6.0/1
TA 00:11
AC 1
SP -56
SL 9
FoV 231*3
99 *256
Tra


FOV 50.0cm
TND/+
MF:1.8
L
150
kV 120
mA 250
Large
7.500mm/27.50 1.375:1


XY S420.00
In: 56+C
DFOV 50.0cm
STND/+/
DOB: 01 Jan 1957
12 Mar 2007
512
MF:1.7
R
kV 120
mA 250
Large
7.500mm/27.50 1.375:1
Tilt: 0.0
0.8s /HE+ 17:46:40/12.00
ES FELEKOURAS MD


3
130
83
1.50
0.0
ES FELEKOURAS MD

HBP Surgery- mCRC

Predicting poorer outcome after resection of colorectal liver metastases

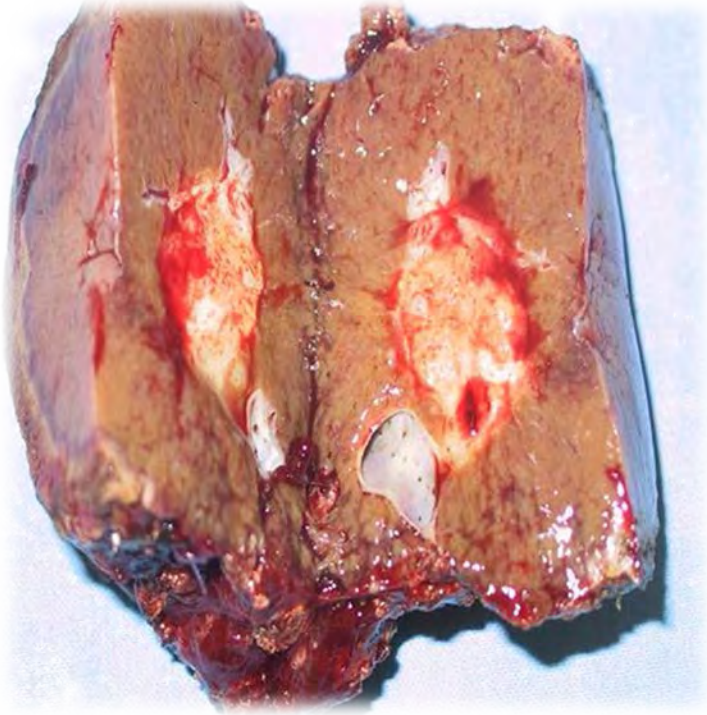
- **Positive resection margin**
- Extrahepatic disease
- Node positive (stage 3) primary colorectal cancer
- Disease free interval from primary tumour <1 year
- Largest metastasis >5 cm
- Number of metastases >1
- CEA >200 ng/ml
- Age of patient

Nordlinger et al. Cancer 1996; 77: 1254-62
Fong et al. Annals of Surgery 1999; 230: 309-15

Assessment of Resectability

Impact of Margin Status

- It should be at least 10 mm (Classic)



HBP Surgery- mCRC

Impact of resection margin on 5-year survival after hepatic resection

Resection margin	Hughes 1989 (n=800) [2]	Ohlsson 1998 (n=111) [5]	Fong 1999 (n=1001) [1]	Iwatsuki 1999 (n=305) [3]	Minagawa 2000 (n=235) [4]
Positive	**18%**	**0**	**20%**	**8%**	**-**
< 1 cm	**26%**	**22%**	**-**	**31%**	**45%**
> 1 cm	**44%**	**31%**	**-**	**38%**	**24%**

[1]Fong Y, et al. Ann Surg 1999;230:309–18

[2]Hughes KS, et al. Surgery 1988;103:278–88

[3]Iwatsuki S, et al. J Am Coll Surg 1999;189:291–9

[4]Minagawa M, et al. Ann Surg 2000;231:487–99

[5]Ohlsson B, et al. World J Surg 1998;22:268–76

HBP Surgery- mCRC

- Even in the patients with microscopically positive margins, (R1) the 5-year survival could be as high as 17.1%

- involvement of hepatic pedicle lymph node (HPLN)
  - The survival rate in patients with positive HP-LN was significantly lower than in the negative group (3-year survival 19 vs 62%, P< .0001),
  - however, those with the involvement of lymph nodes limited to the hepatoduodenal ligament and retropancreatic portion demonstrated a much superior prognosis to those that the lymph nodes around the common hepatic artery and celiac axis were involved after the R0 resections (3-year survival 38 vs 0%, P< .001).

Eur J Surg Oncol. 2006 Jun;32(5):473-83. Epub 2006 Mar 31. Review

HBP Surgery- mCRC

- Even though 1-cm resection margin was traditionally considered necessary to minimize hepatic recurrence and overall survival
- more recent publications have advocated that a < 1 cm resection margin should not preclude resection of liver secondaries provided that a nonpositive resection margin can be obtained

- Several reasons may explain these conflicting data:

The emerging role of

RFA Energy

(does it add any benefit in LRx for mCRC?)

HBP Surgery- mCRC

Meta-analysis

Conclusion: ……

…….No enough evidence to prove RFA safety or efficacy in the treatment of mCRC.

Sutherland LM et al Radiofrequency ablation of liver tumors: a systematic review.

Arch Surg. 2006 Feb;141(2):181-90.

HBP Surgery- mCRC

Background: Surgical resection is the gold standard in the treatment of resectable colorectal liver metastases (CRLM). In several centers, resection is being replaced by radiofrequency ablation (RFA), even though there is no evidence yet from randomized trials to support this. The aim of this study was to critically review the oncological evidence for and against the use of RFA for resectable CRLM.

Methods: An exhaustive review of RFA of colorectal metastases was carried out.

Results: Five-year survival data after RFA for resectable CRLM are not available. Percutaneous RFA is associated with worse local control, worse staging, and a small risk of electrode track seeding when compared with resection (level V evidence). For tumors ≤3 cm, local control after surgical RFA is equivalent to resection, especially if applied by experienced physicians to nonperivascular tumors (level V evidence). There is indirect evidence for profoundly different biological effects of RFA and resection.

Conclusions: A subgroup of patients has been identified for whom local control after RFA might be equivalent to resection. Whether this is true, and whether this translates into equivalent survival, remains to be proven. The time has come for a randomized trial.

Key Words: Colorectal liver metastases—Radiofrequency—Resection—Review—Randomized trial.

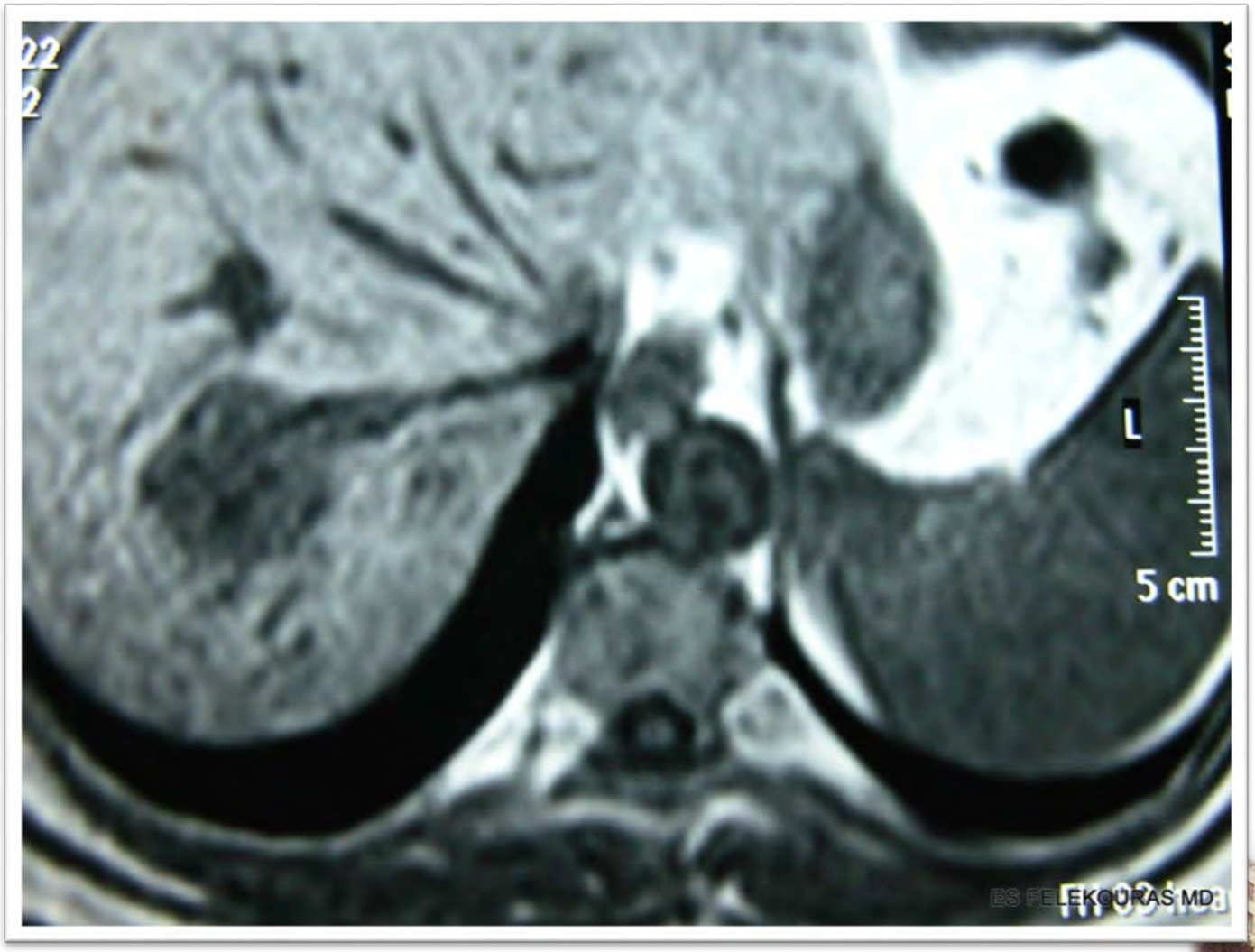
Ann Surg Oncol. 2008 Jan;15(1):144-57. Epub 2007 Sep 29.

TABLE 4. *Oncological for and against RFA for resectable CRLM*

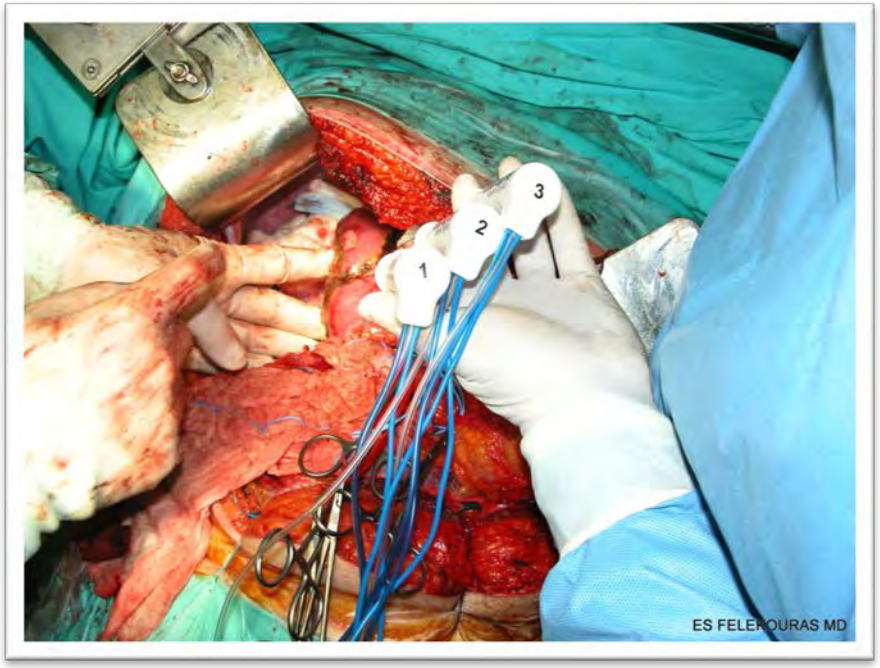
	Level of evidence[a]	Type of evidence
Arguments with direct evidence		
In favor of resection		
Better local control (except for tumors ≤3 cm using RFA via a surgical approach)	V	Meta-analysis of case series
Better staging: resection allows better intraoperative staging and hence an optimized treatment strategy in 40% of patients (vs. percutaneous RFA; not vs. surgical RFA)	V	Case series
No electrode track seeding (0%–1.4% risk after percutaneous RFA)	V	Case series
In favor of RFA		
No arguments with direct evidence found		
Arguments with indirect evidence		
In favor of resection		
Risk of post-RFA intrahepatic seeding	VII	Level V evidence for increased seeding after RFA in HCC
Risk of increased local and distant spread through increased matrix metalloproteinase (MMP) activity	VII	Level II evidence for increased MMP activity after RFA; level V evidence for worse prognosis in patients with increased MMP activity
In favor of RFA		
(Resection) techniques with more parenchymal sparing allow a higher reintervention rate for new metastases and a better survival	VII	Level V evidence for resection
Less immune suppression through less blood loss after RFA vs. after resection	VII	Level V evidence for less blood loss after RFA; level V evidence for relation between perioperative transfusion and survival
Stronger stimulation of cellular immunity after RFA vs. after resection	VII	Level II evidence from animal RCT
Balance between resection and RFA unknown		
Stimulation of growth of residual tumour cells after RFA vs. after resection	VII	Level II evidence from animal RCT for increased stimulation in one study and decreased stimulation in a second study
Risk of hematogenous metastases through increased presence of tumour cells in peripheral blood, both after RFA and after resection	VII	Level V evidence for increased presence of tumour cells in peripheral blood both after RFA and post-resection; relation to hematogenous metastases unknown
Post-RFA increased heat shock protein expression (HSP), with both beneficial and detrimental effects	VII	Level II evidence for increased HSP expression after RFA; level II evidence for beneficial effects of increased HSP expression; level V evidence of detrimental effects of increased HSP expression

RFA, radiofrequency ablation; CRLM, colorectal liver metastases; HCC, hepatocellular carcinoma; RCT, randomized controlled trial; HSP, heat shock protein.

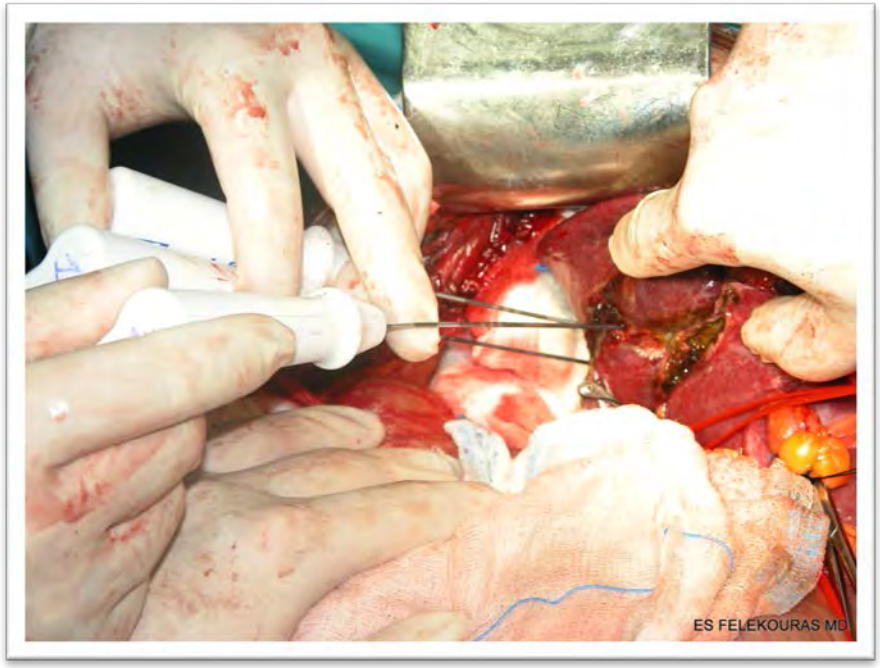
HBP Surgery- mCRC



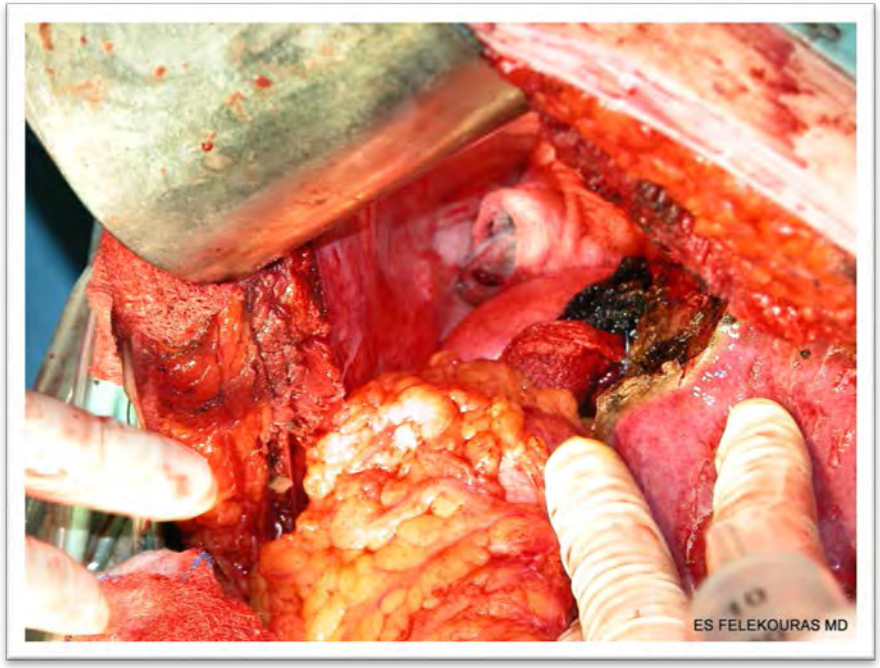
HBP Surgery- mCRC

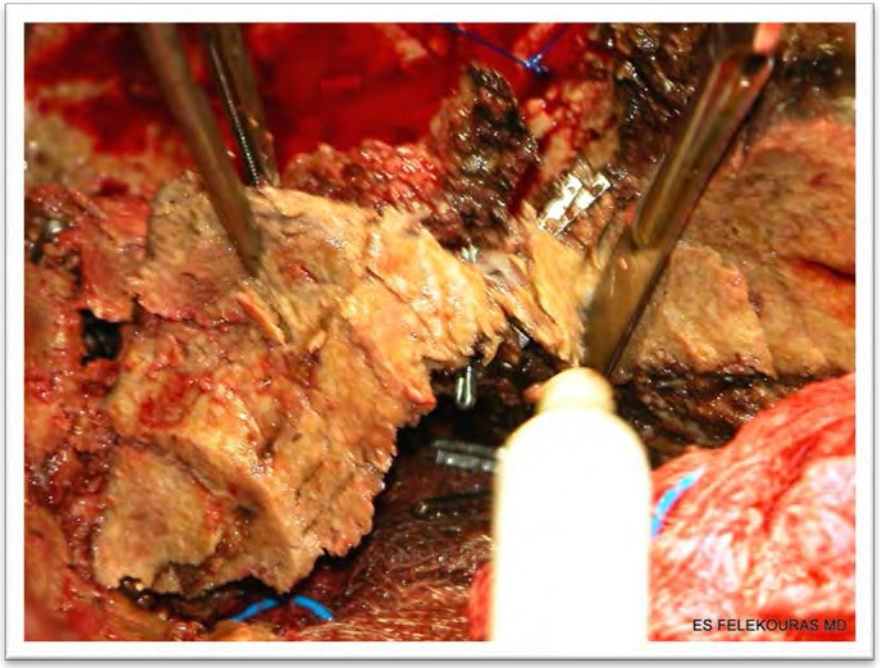


HBP Surgery- mCRC



HBP Surgery- mCRC

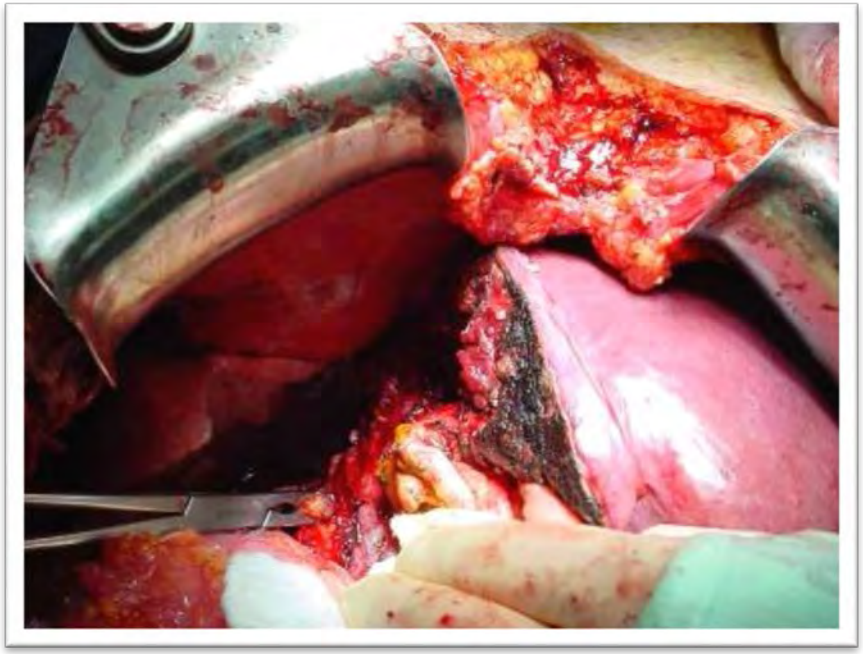




HBP Surgery- mCRC

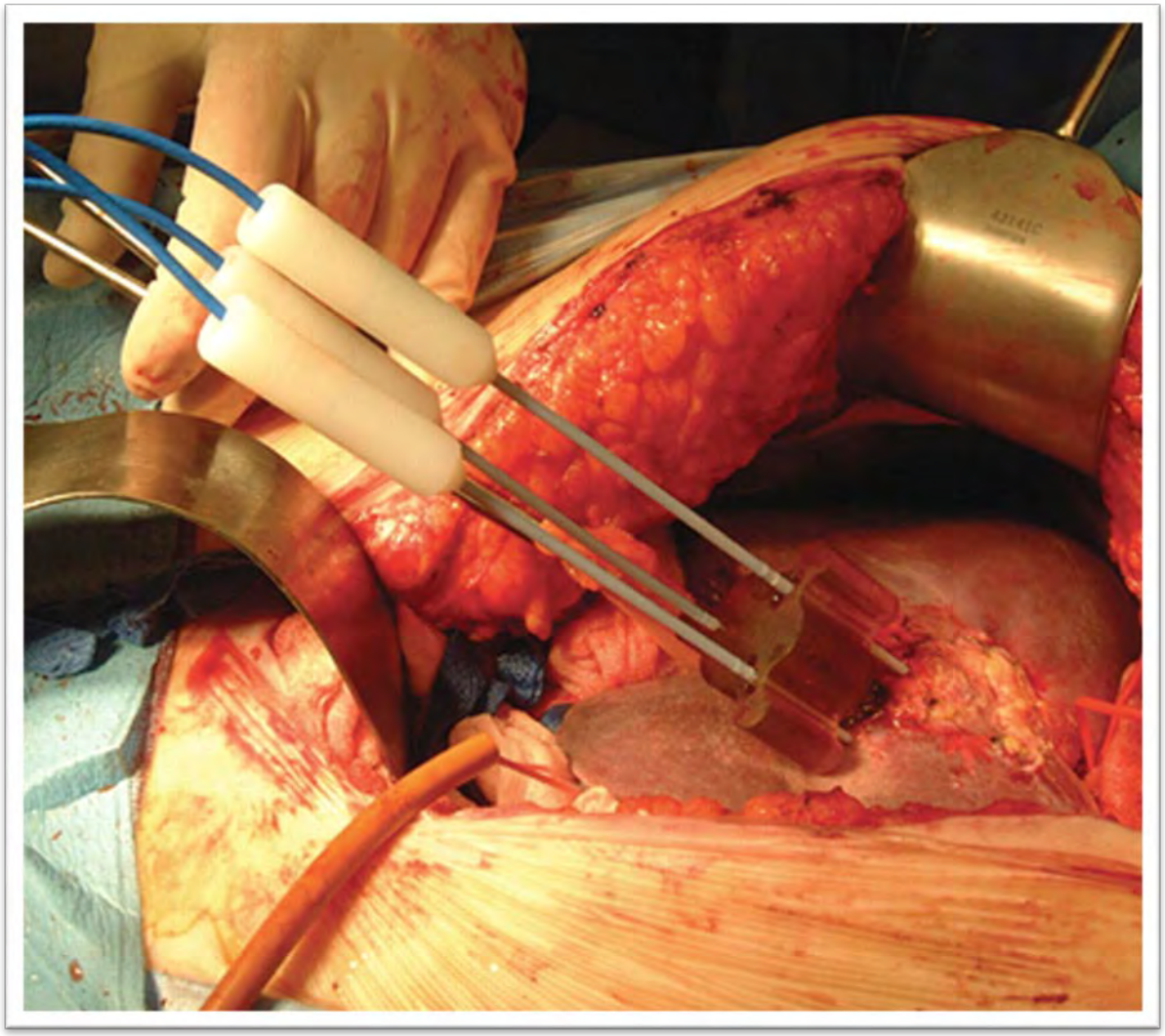
HBP Surgery- mCRC

Difficulties



HBP Surgery- mCRC

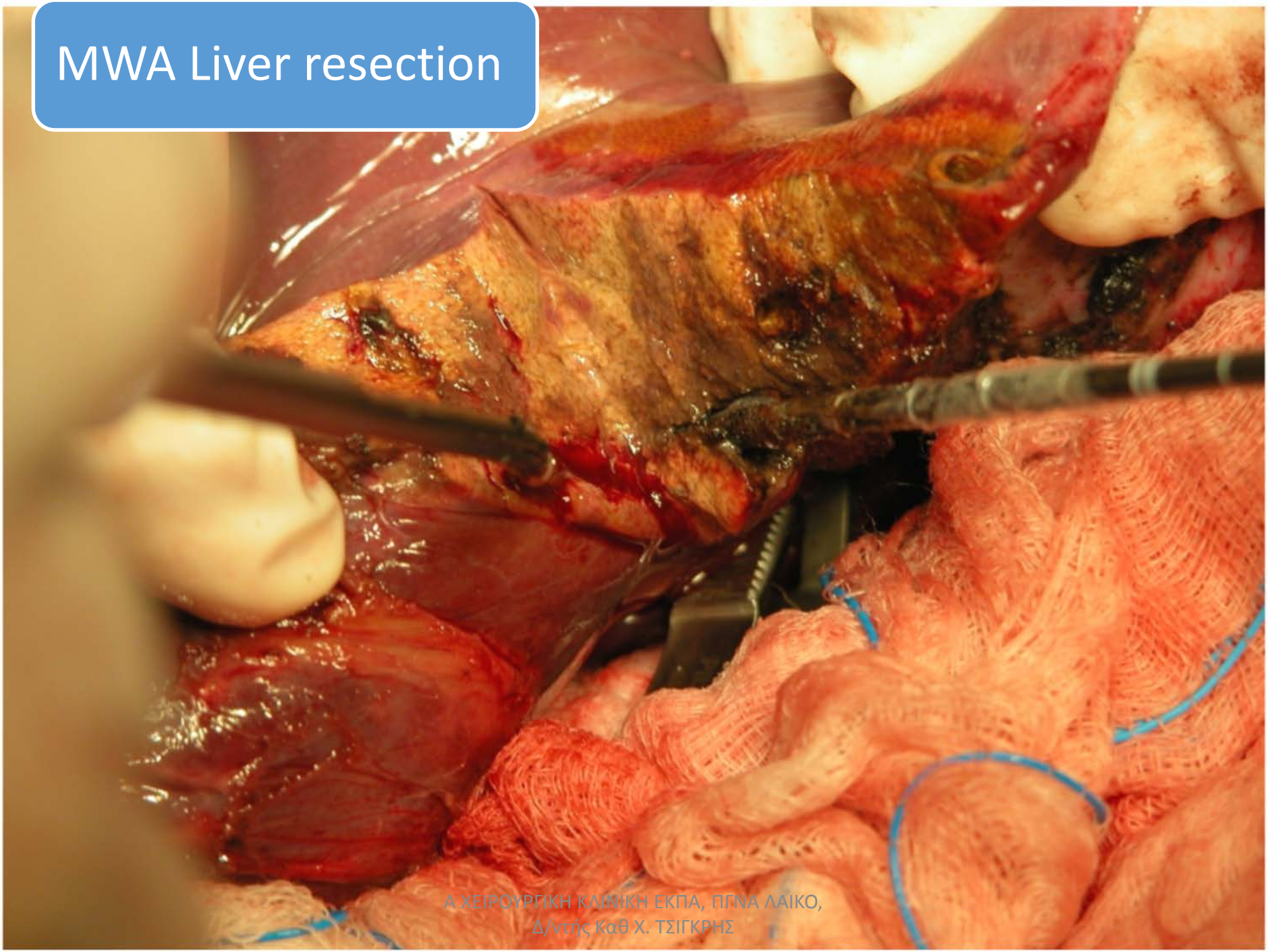
MWA

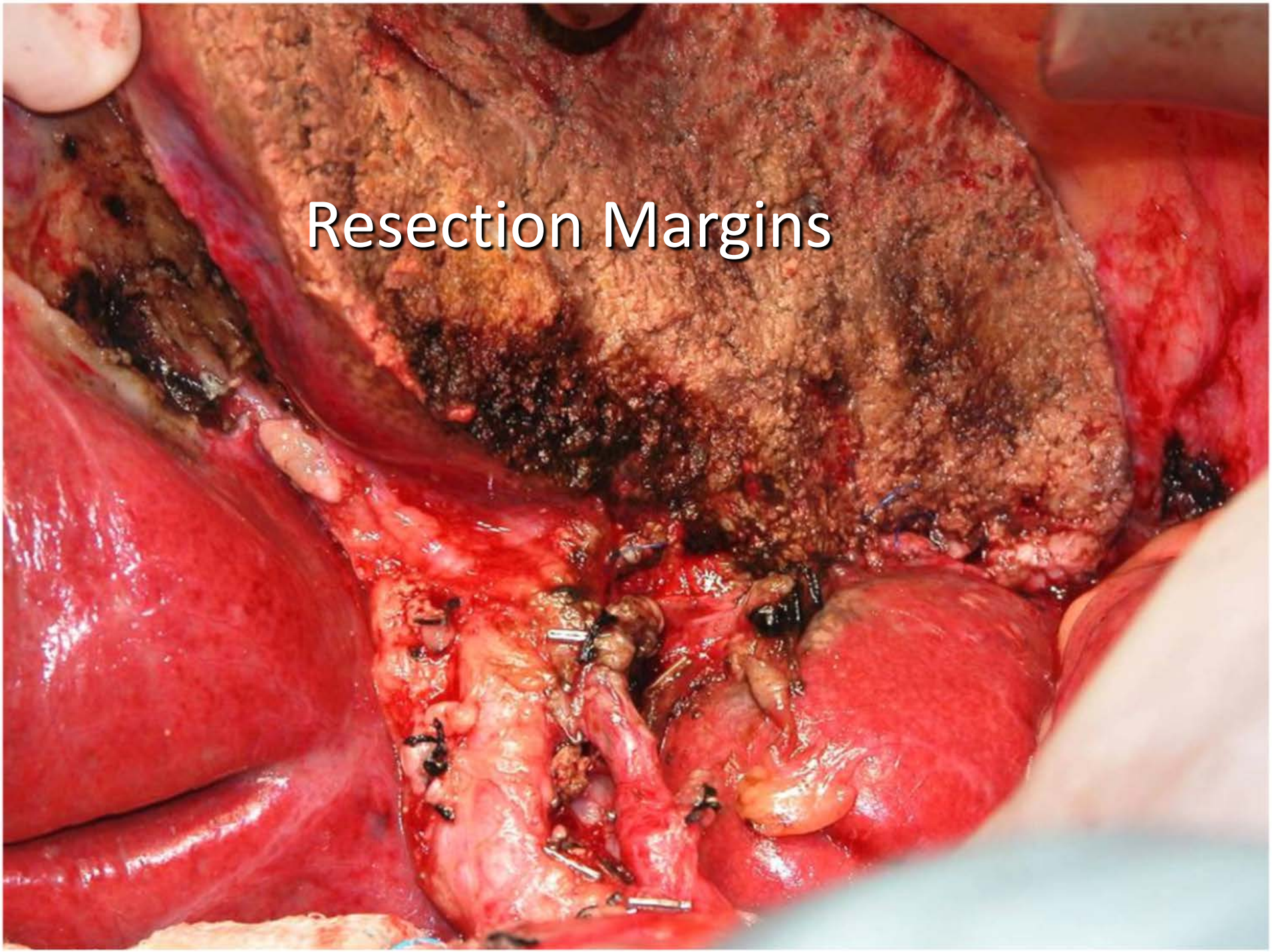


Simon, C. J. et al. Am. J. Roentgenol. 2006;187:W333-W340

48-year-old woman with colorectal carcinoma metastases

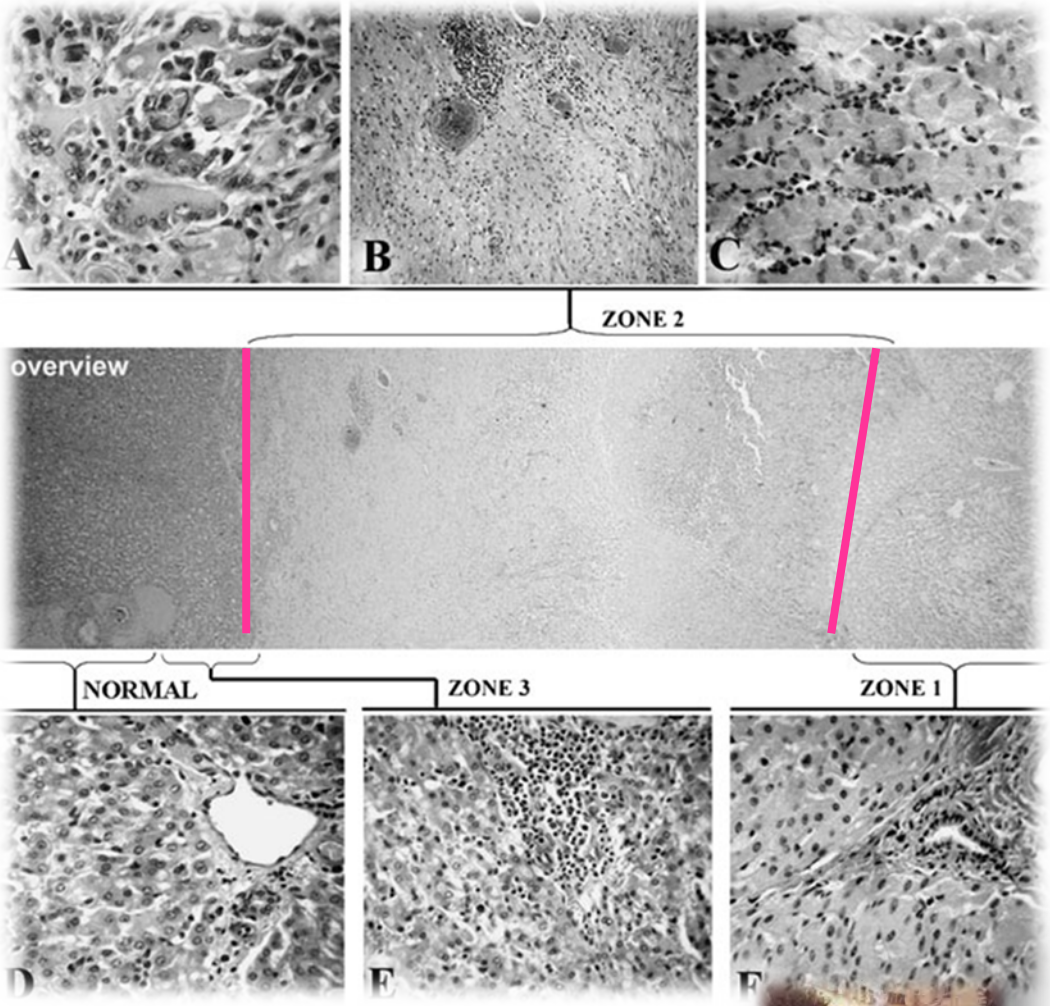
MWA Liver resection




Resection Margins

RFA Assisted LRx: 2001-2004 (3)
Resection Margins

- 50 LRxs
- Positive 7/50 (14%)
- The 1 cm ablated zone we leave behind is additional security



Felekouras et al. Surg Endosc (2005) 19: 1237–1242

RFA Assisted LRx for mCRC: 2004-2009 (1)

- Pts (No) **(Group B)** 32
  - **Rxs (No)** **63**
- Age 59 (43-78)
  - Men 18
  - Women 14
- Major LRx 4
  - RLRx 3
  - LLRx 1
- Minor LRx 59
  - Segmentectomies 13
  - Wedge 46
- RFA time 30 (10-140) median
- Transection time 34 (11-145) median
- R status
  - R0 23
  - R1 3
  - R2 6

RFA Assisted LRx for mCRC : 2004-2009 (1)

• **Pringle**	**1**
• **Pts Transfused**	**4**
– PRBS (No)	1,4 (0 – 5)
• Complications	4
– MI	0
– Biloma	0
– Abscess	3
– Bile Fistula	0
– GI bleeding	0
– DVT	0
– Small for size liver	0
– Pleural effusion	1
• **Mortality 30 day**	**0**

HBP Surgery- mCRC

mCRC

Results:…..On final pathology …..

- Group A: 20 pts with RFA assisted resection (2001-2004)
- Group B: 32 pts with RFA assisted resection (2004-2009)
- Group C: 45 ασθενείς **NON RFA** assisted resection (1995-2001)

HBP Surgery- mCRC

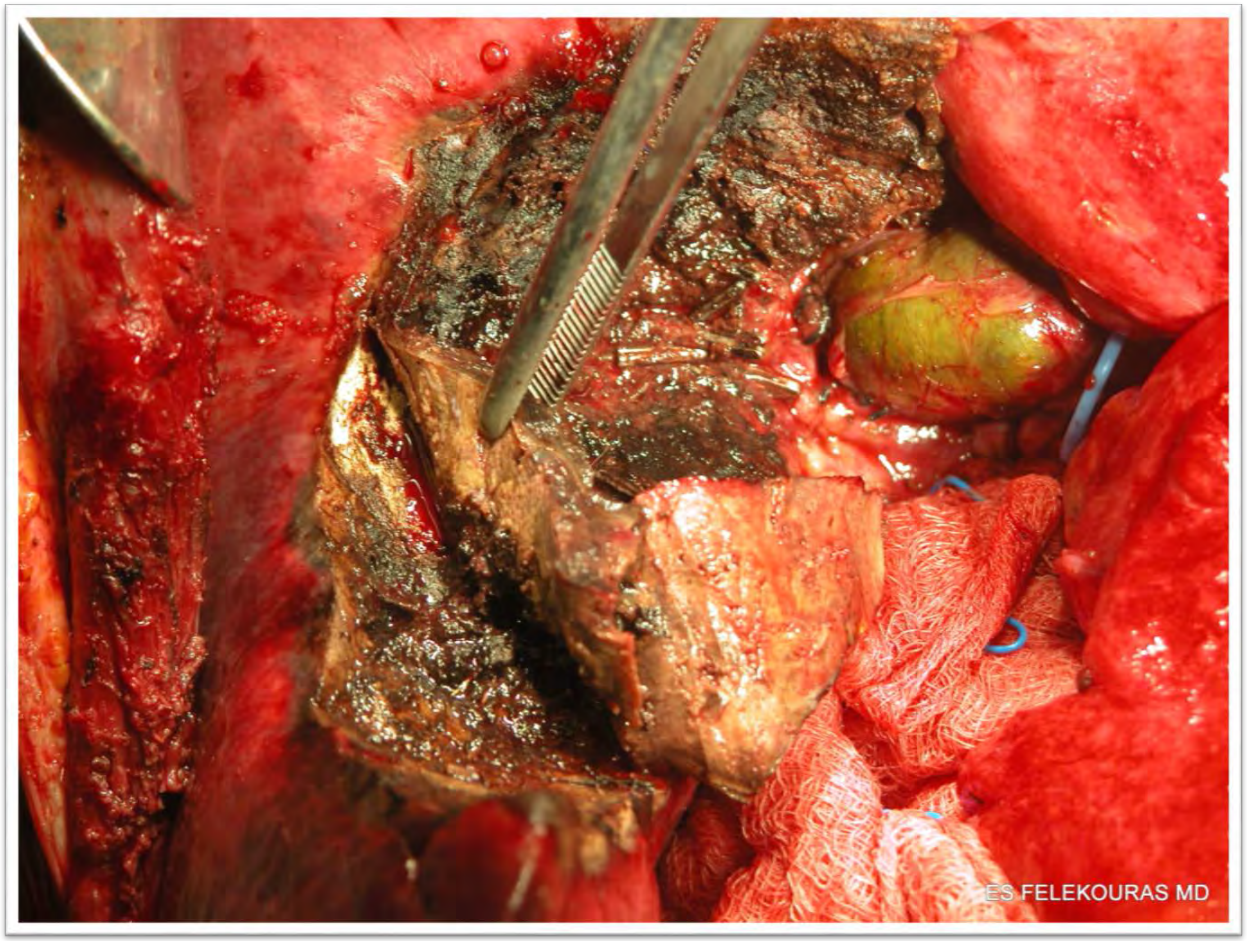
- Comparing the group A with group C, the negative margins are as seen on histology
  - 17/20 (85%) in group A
  - 25/32 (81,25%) in group B
  - 33/45 (73,33%) in group C,

SS (X^2 test, $P < 0,05$)

- Ablated rim negative in group Ba
  - 94,11% (1/17 pts)
  - 92,59 % (2/27 Rxs)

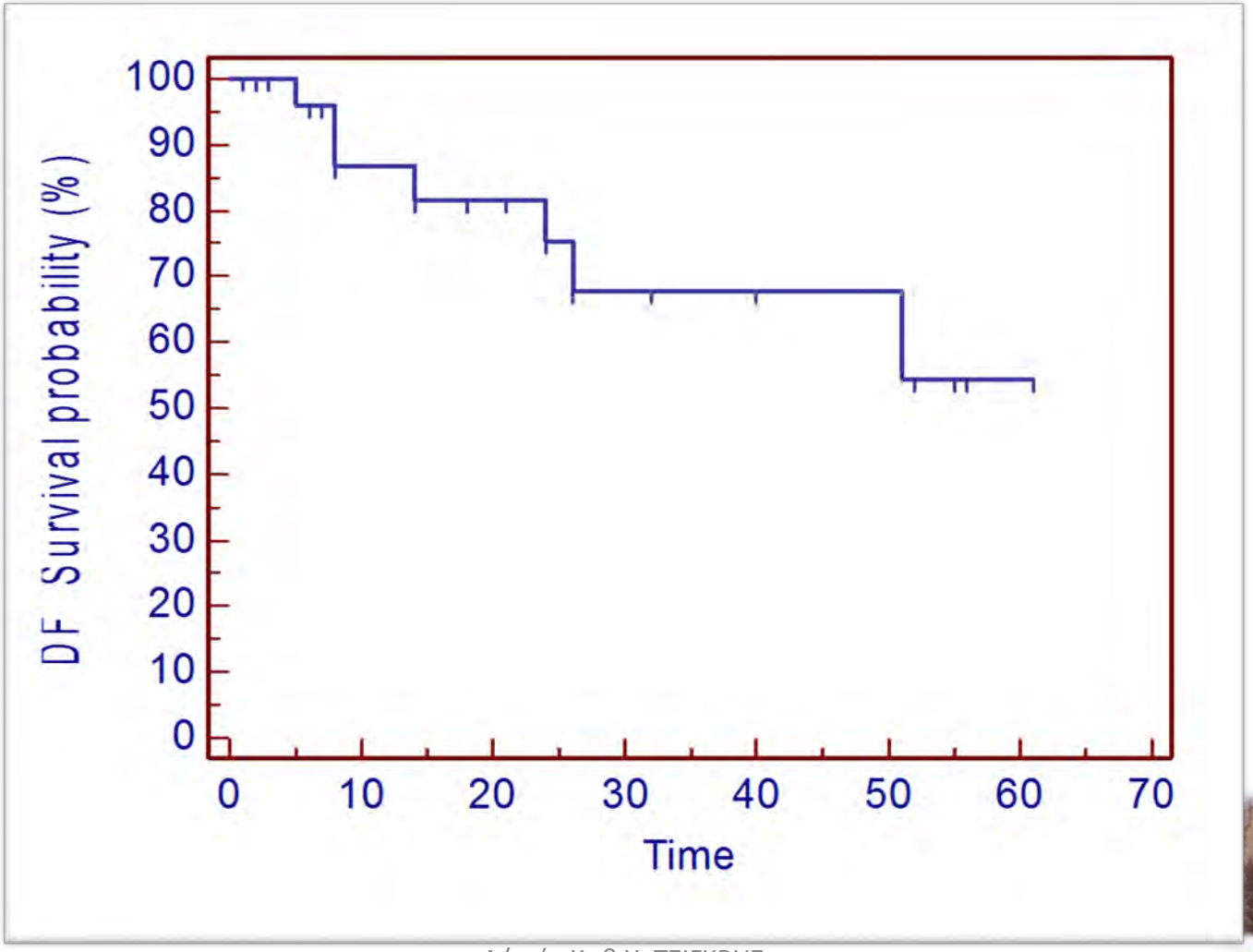
- Towards a real R0 LRx

HBP Surgery- mCRC



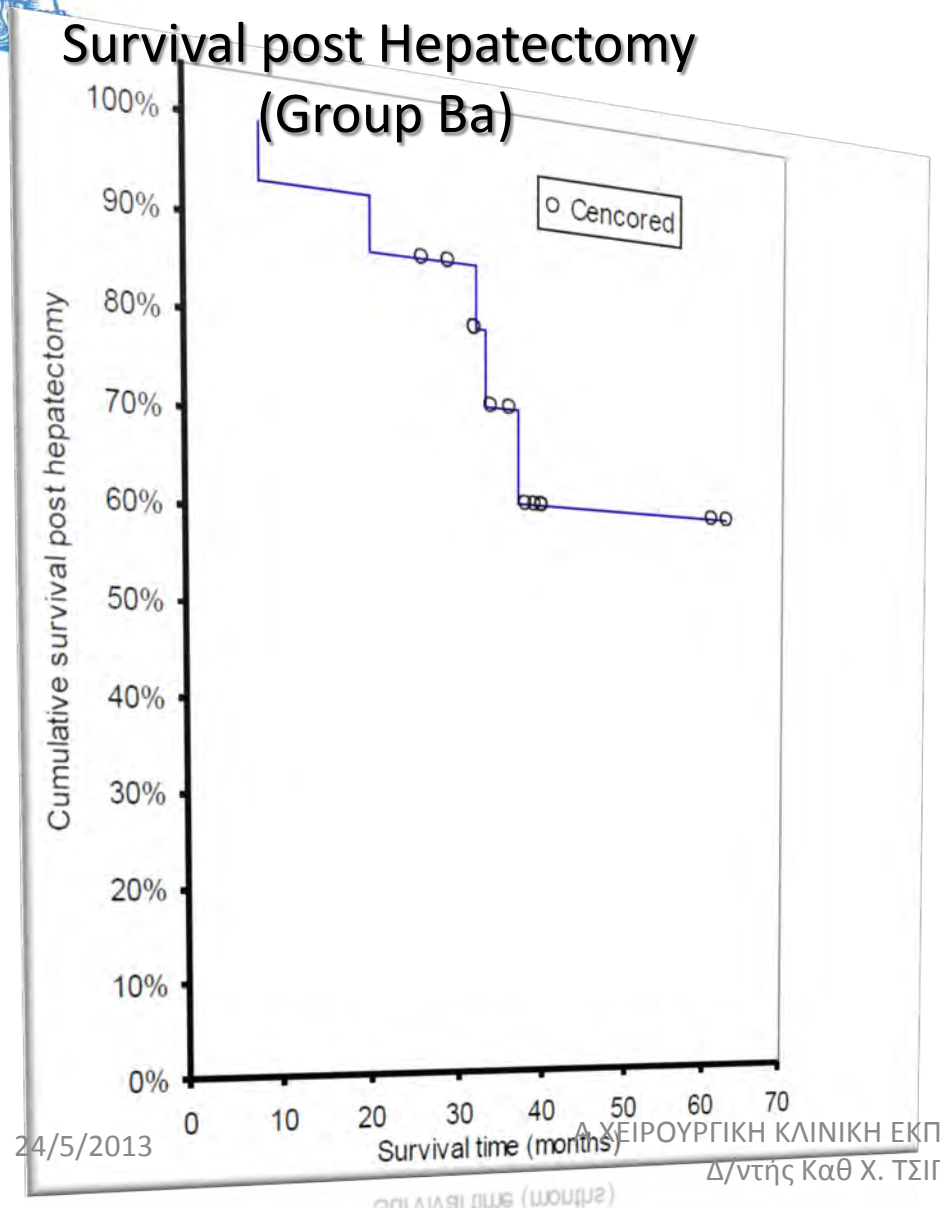
HBP Surgery- mCRC

DF Survival

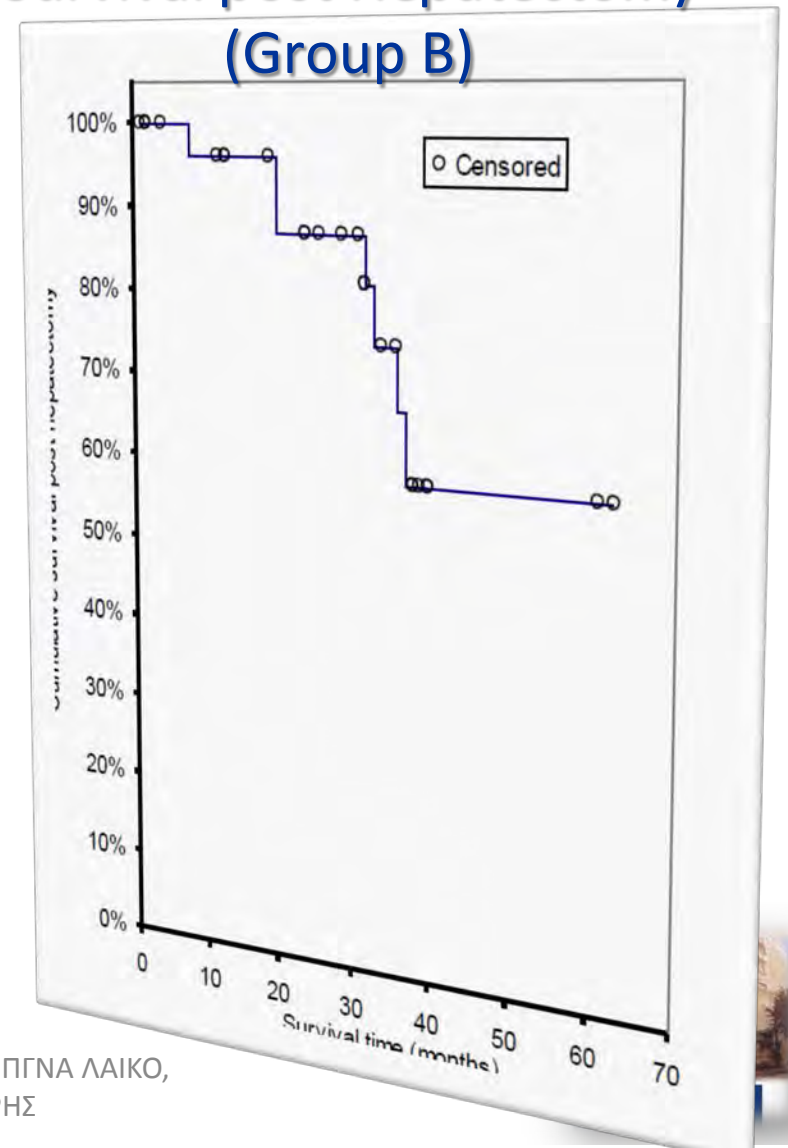


HBP Surgery- mCRC

Survival post Hepatectomy (Group Ba)

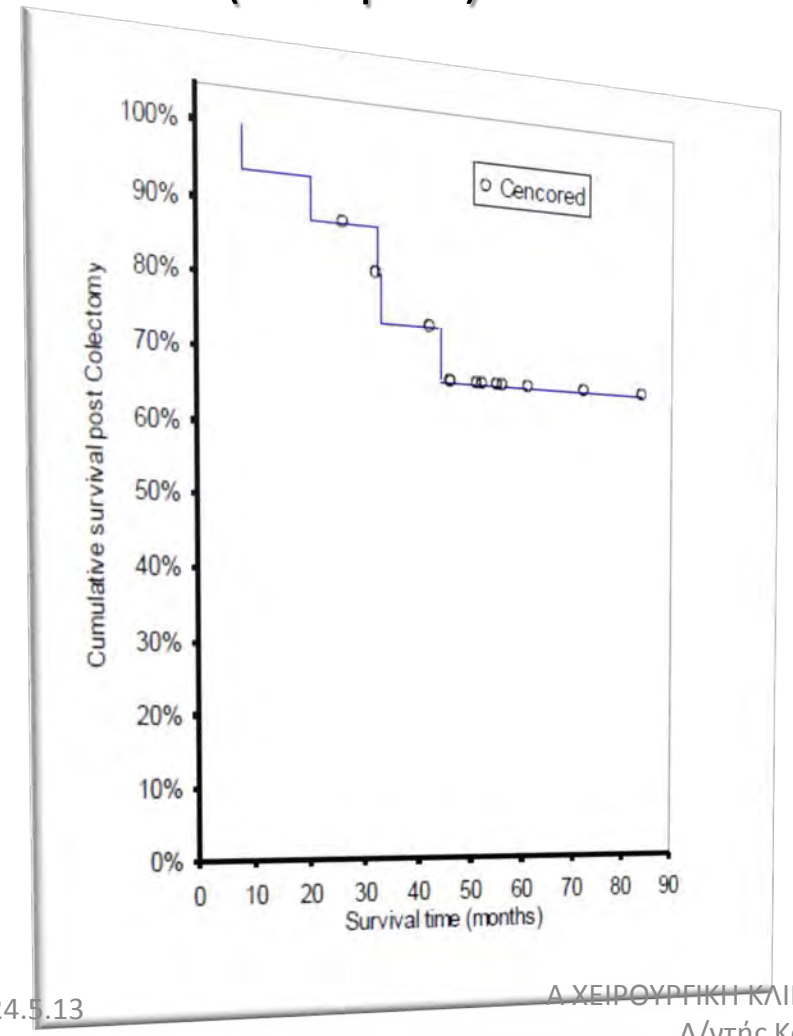


Survival post Hepatectomy (Group B)

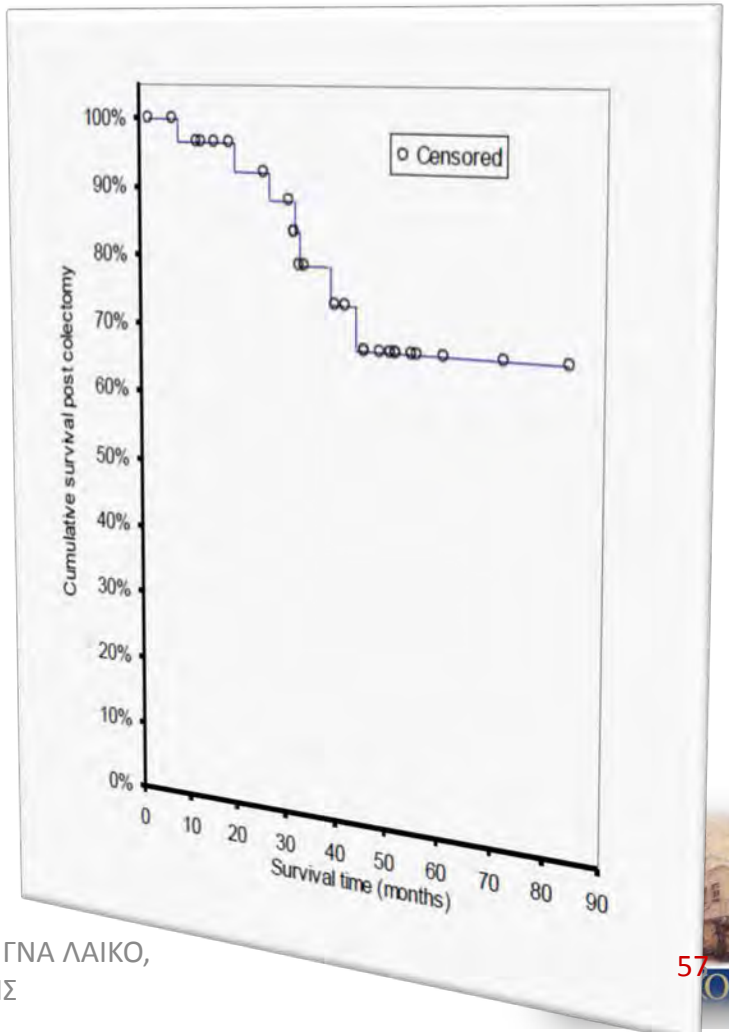


HBP Surgery- mCRC

Survival post Colectomy (Group Ba)

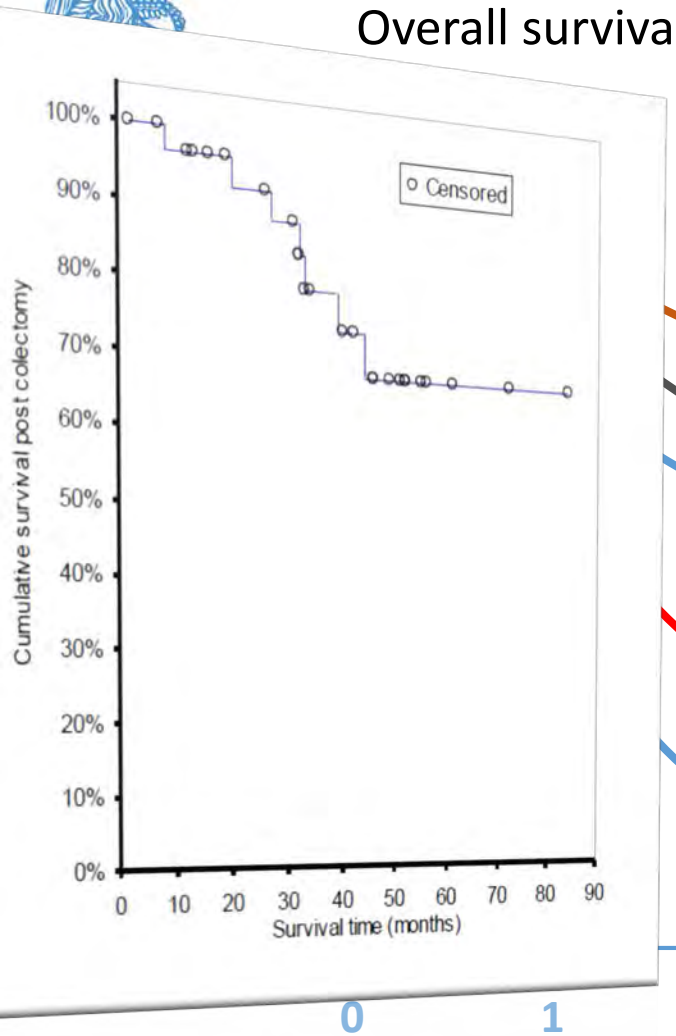


Survival post Colectomy (Group B)



HBP Surgery- mCRC

Overall survival in advanced colorectal cancer in 2016?



2006 chemotherapy
Median survival 24 months

2006 overall
Median survival 30 months
5 year survival 20 %

2016?
5 year survival 50 % ?

50% ?

20%

1996

3%

<1%

0 1 2 3 4 5

Years after diagnosis of colorectal metastases

Go home message

HBP Surgery- mCRC

RFA Assisted LRx

might be a solution for better outcome

in pts with mCRC

HBP Surgery- mCRC

NE metastatic to the liver

HBP Surgery- mCRC

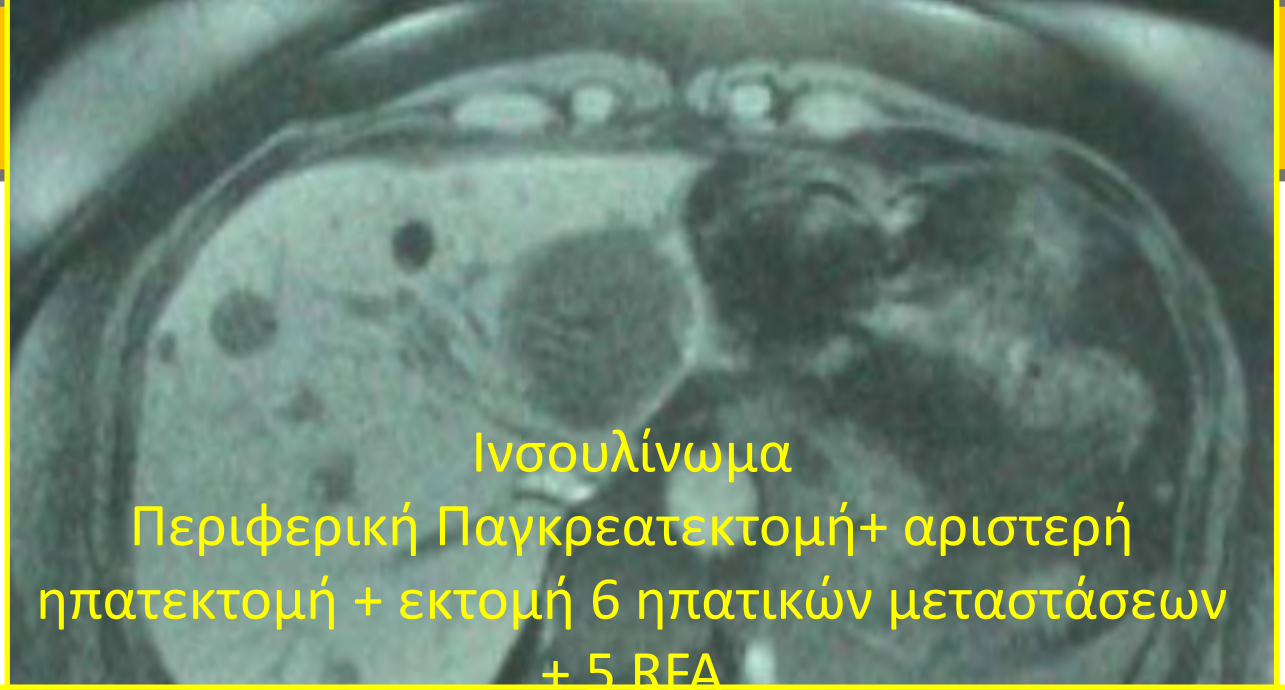
Neuroendocrine Hepatic Metastases

Does Aggressive Management Improve Survival?

(*Ann Surg* 2005;241: 776–785)

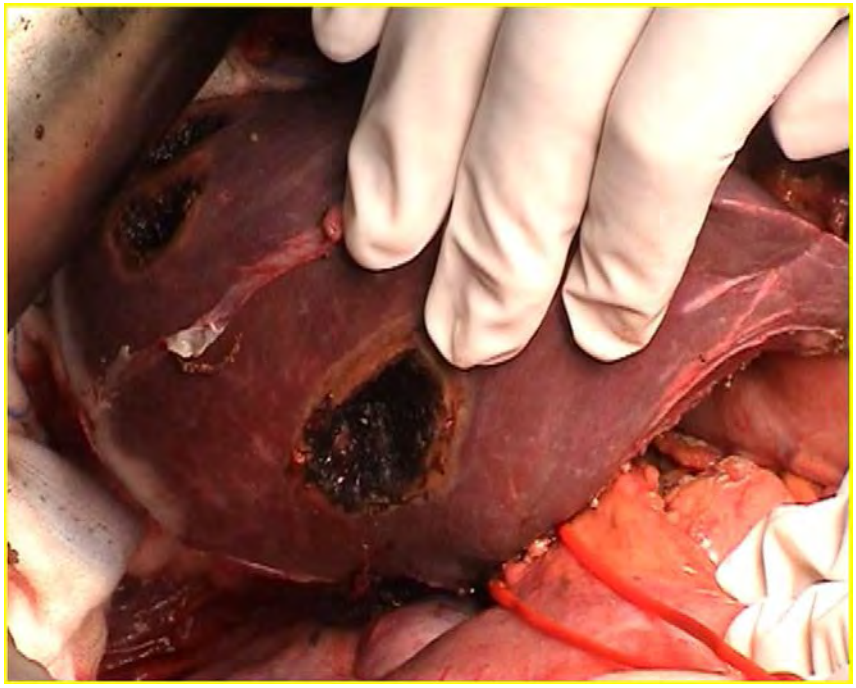
John G. Touzios, MD, James M. Kiely, MD,* Susan C. Pitt, BA,* William S. Rilling, MD,† Edward J. Quebbeman, MD, PhD,* Stuart D. Wilson, MD,* and Henry A. Pitt, MD**

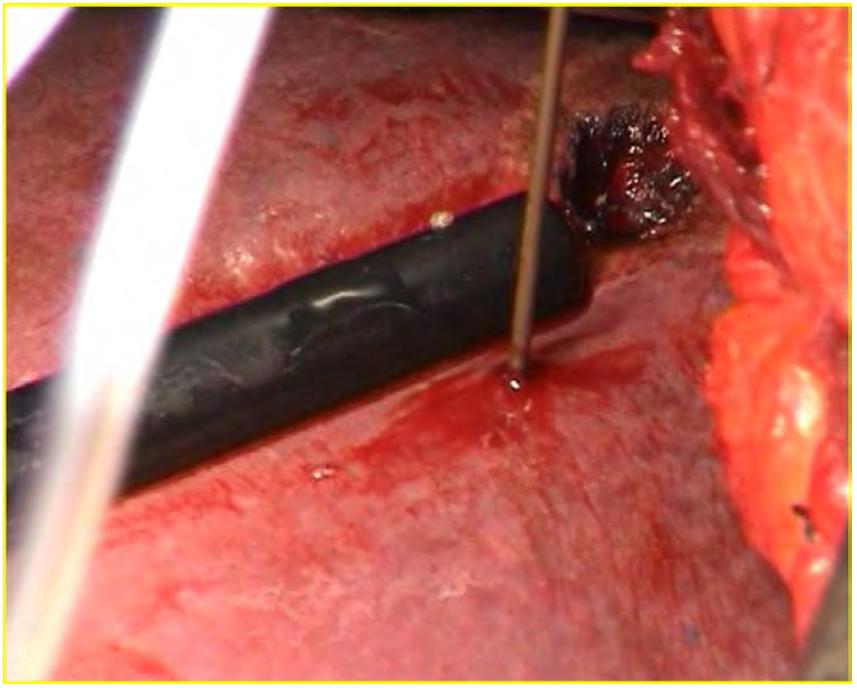
- **Conclusions:**
- These data suggest that aggressive management of neuroendocrine hepatic metastases does improve survival, that chemoembolization increases the patient population eligible for this strategy,
- and that patients with more than 50% liver involvement may not benefit from an aggressive approach.



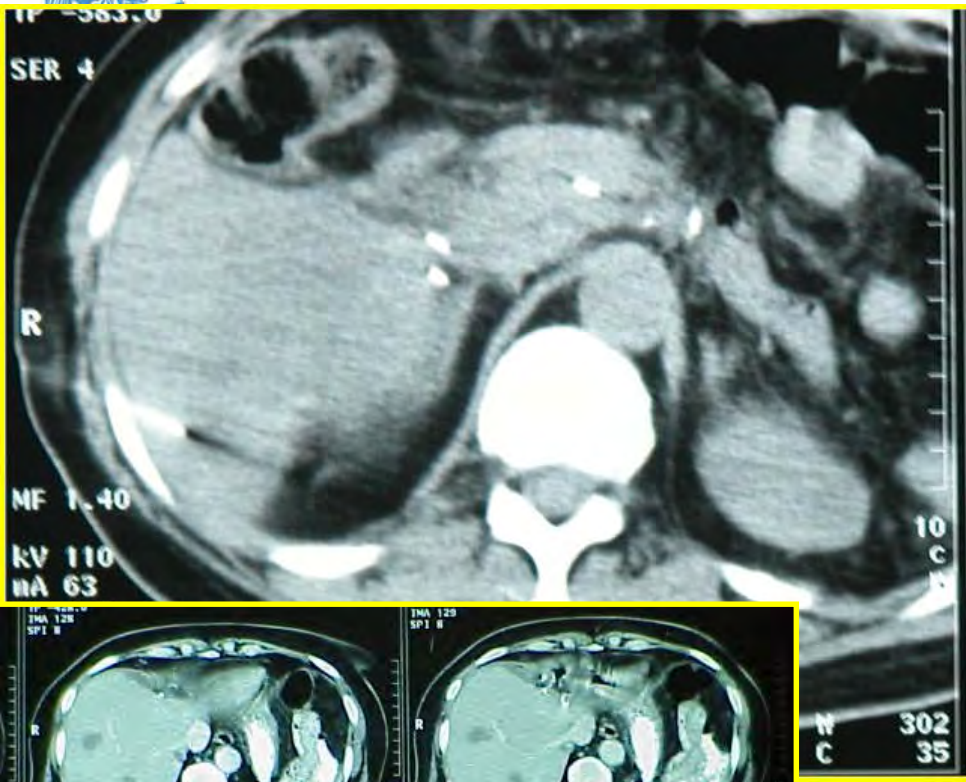
Ινσουλίνωμα
Περιφερική Παγκρεατεκτομή+ αριστερή ηπατεκτομή + εκτομή 6 ηπατικών μεταστάσεων + 5 RFA

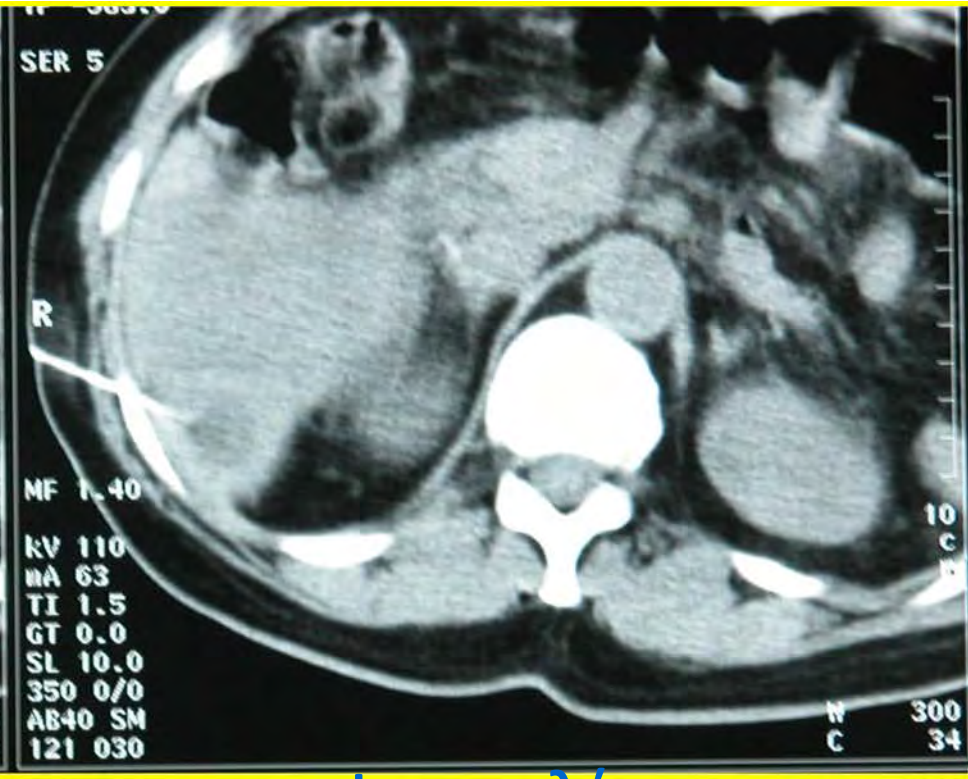
HBP Surgery- mCRC

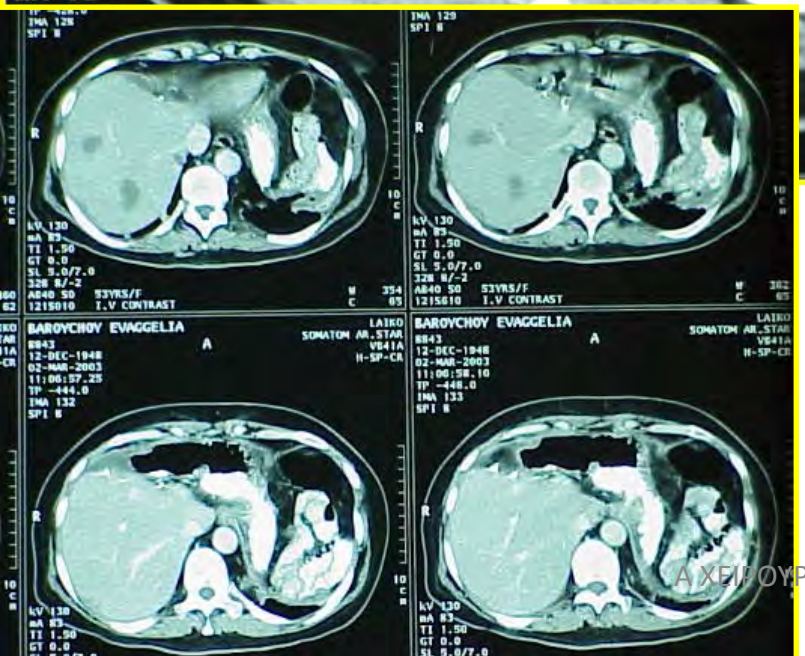




HBP Surgery- mCRC







Ινσουλίνωμα

1 RFA

(μετά 1 έτος)

Εν ζωή 3 έτη


Q & A