

Surgical Management of Colorectal Cancer Liver Metastases

Marilyn Ng, MD

Dept. of Surgery M&M Conference

Downstate Medical Center

Jan 3, 2013



Case Presentation

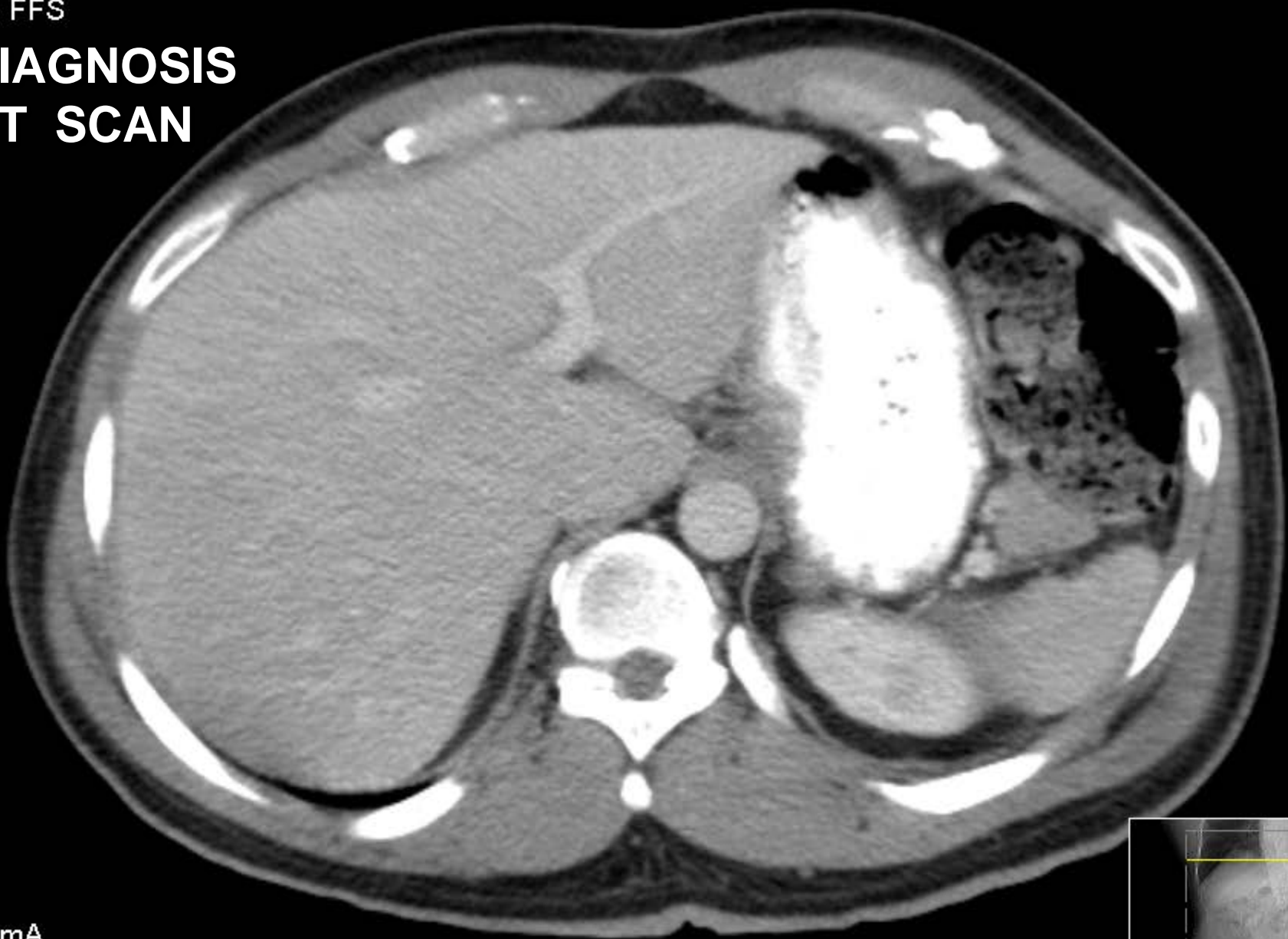
- **53 yo man with Stage IIB (uT4aN0Mx) rectal cancer (dx 4/2012)**
- **s/p neoadjuvant 5-FU chemotherapy & 5040 Gy EBRT (5/21/12 - 6/28/12)**
- **s/p laparoscopic proctectomy, colo-anal anastomosis & loop ileostomy (pT2N0Mx; 13 LN negative)**

Medical & Surgical History

- **Refused adjuvant chemotherapy**
- **Bilobar hepatic metastases on CT scan for rectal abscess (7 months post-op)**
- **Elective right hepatectomy and metastasectomies for metachronous hepatic metastases**

Slice: 5 mm
Couch: 78.2
Pos: FFS

DIAGNOSIS CT SCAN



F: B
496 mA
120 kV
Image no: 12
Image 12 of 99



Slice: 5 mm
Couch: 143.4
Pos: FFS

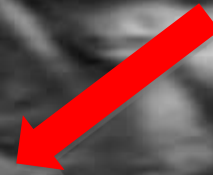
DISCHARGE CT SCAN



F: B
188 mA
120 kV
Image no: 20



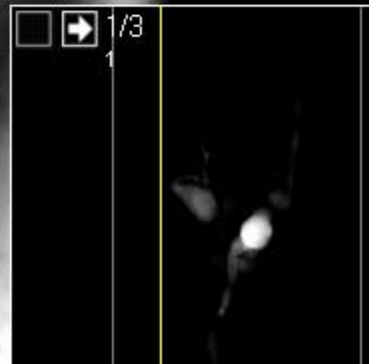
MRI

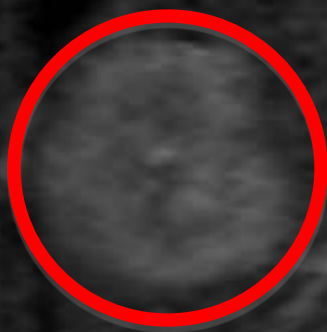


Pos: FFS
FoV: 335 mm
Series: 301
Image 7 of 32
11/21/2012 2:42:39 PM

F

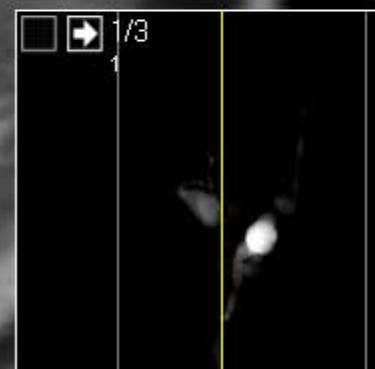
Side 1





Pos: FFS
FoV: 335 mm
Series: 301
Image 14 of 32
11/21/2012 2:42:39 PM

Side
1



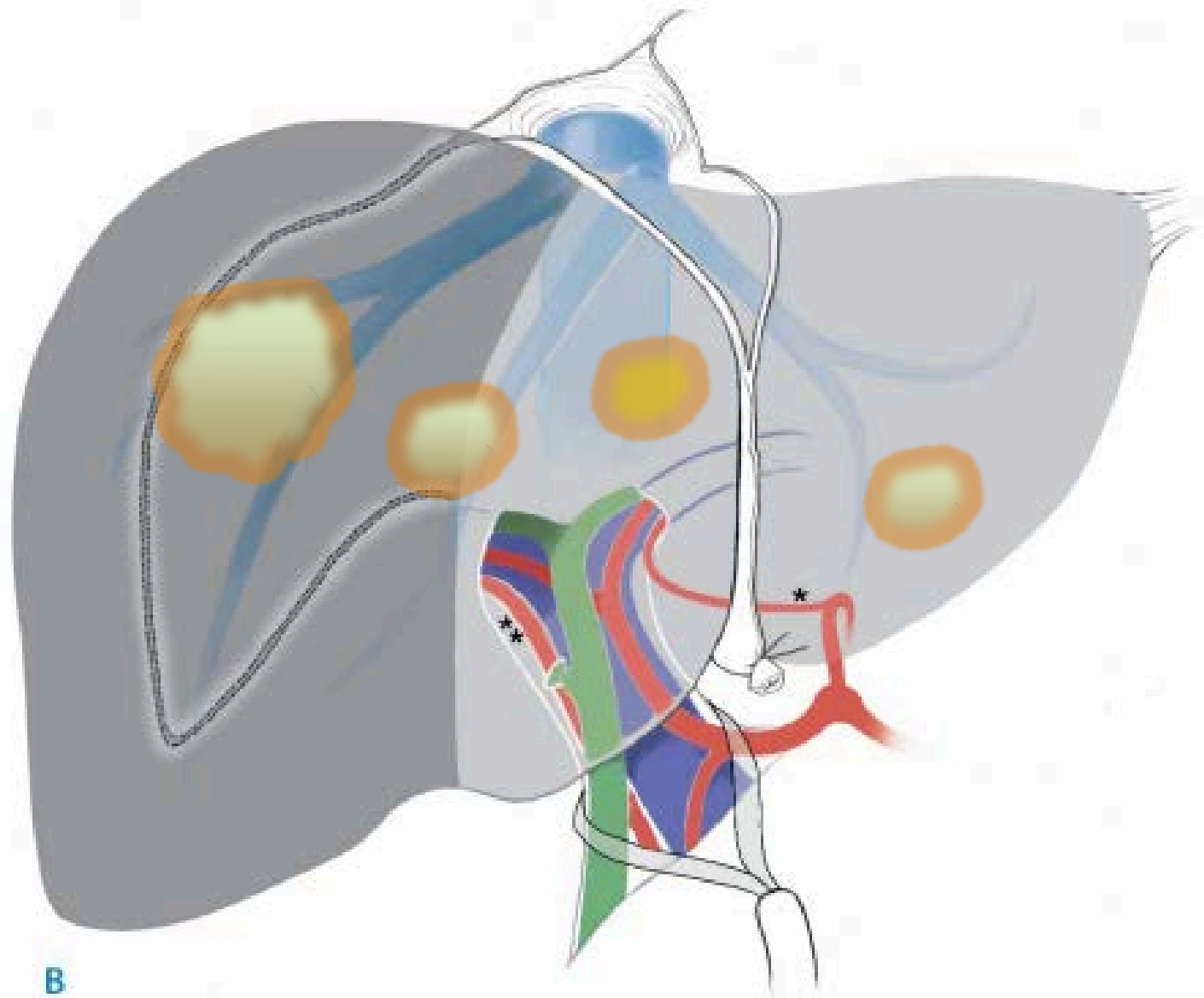
F

PET SCAN



On Physical Exam

- **Tm 99.2 BP 106/60 HR 78**
- **Abd: soft, ND, NT, loop ileostomy,
no palpable masses or hernias**
- **CEA: 3.03 (3/12) → 17.7 (11/12)**



B



Right Hepatectomy & Metastasectomy

- Cholecystectomy
- Right hepatic artery transected & porta hepatis encircled
- Right portal, short hepatic & right hepatic vein transected
- Right hepatectomy & segment IV & II metastasectomies



Pathology Results

- **Right hemi-liver:**
 - **Metastatic adenocarcinoma, moderately differentiated**
 - **Adenocarcinoma present on the liver capsule**
 - **Resection margin: negative**
- **Liver, segment IV: negative for carcinoma**
- **Liver, segment II: metastatic adenocarcinoma, moderately differentiated**
- **Gallbladder & PV LN: negative for carcinoma**

Post – Op Course

- **POD#1: Advanced to diet**
- **POD#4: D/C left JP drain**
- **POD#6: D/C right JP drain**
- **POD#8: Discharged home**
- **Oncology to start FOLFOX**





Management of Hepatic Metastatic Colon Cancer

- **History & Epidemiology**
- **Regional Treatment**
- **Neoadjuvant Chemotherapy (CTx)**
- **Timing of Hepatectomy**
- **Post-resection Therapy**

www.downstatesurgery.org

History of Hepatic Metastatectomy

- **1886 – Dr. Langebeck**
- **1891 – Dr. Lucke excised
1st malignant liver lesion**
- **1943 – Dr. Cattell performs
1st colorectal hepatic
metastasectomy**



Colorectal Cancer (CRC)

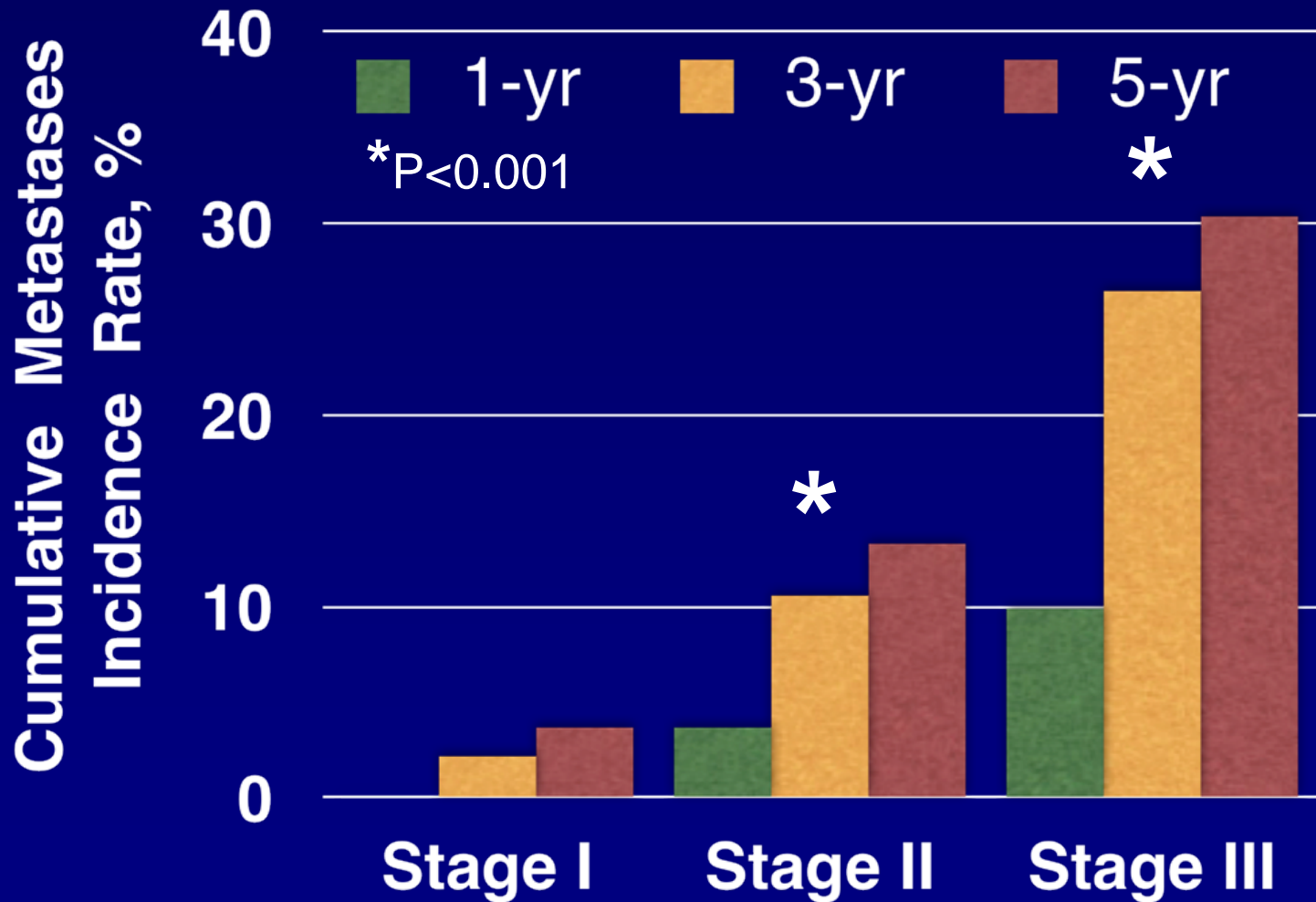
- **Lifetime risk for CRC: 4.96%**
- **Incidence: ~ 144,000 Americans / year**
- **Mortalities: ~ 52,000 / year**
- **Liver is dominant metastatic site**
- **Isolated liver metastases treatable**

5-Year Survival by AJCC Stage

- **Colorectal liver metastases (CLM) will develop in 35 – 55%**
- **15-25% synchronous LM**
- **20-25% will develop metachronous LM**

Stage	Survival, %
I	93.2
IIa	84.7
IIb	72.2
IIIa	83.4
IIIb	64.1
IIIc	44.3
IV	8.1

Metachronous CLM Rate



Potential for Cure

- 5-year survival 10% after chemotherapy
- 5-year survival 24–58% after resection
- Only 20% have resectable isolated-

CLM TABLE Relative Survival of Synchronous and Metachronous Metastases

	Synchronous Liver Metastases			Metachronous Liver Metastases		
	1 Year (%)	5 Years (%)	<i>P</i>	1 Year (%)	5 Years (%)	<i>P</i>
All patients	34.8	3.3		37.6	6.1	
Treatment			<0.001			<0.001
Resection for cure	78.5	10.8		79.1	29.0	
Palliative resection	42.7	3.8		49.3	1.2	
Palliative chemotherapy	55.1	2.9		55.7	3.1	
Symptomatic treatment	21.2	2.5		20.6	0.7	

NS indicates not significant.

Treatment Modalities

- **Ablation techniques**
- **Regional / systemic chemotherapy**
- **Radiation therapy**
- **Surgical resection** - only treatment to be associated with survival plateau

Traditional Resectability Factors

Metachronous lesion

Resectable
extrahepatic disease

Unilobar metastases

4 or less metastases

Largest lesion < 5 cm

Achieve > 1 cm
resection margin

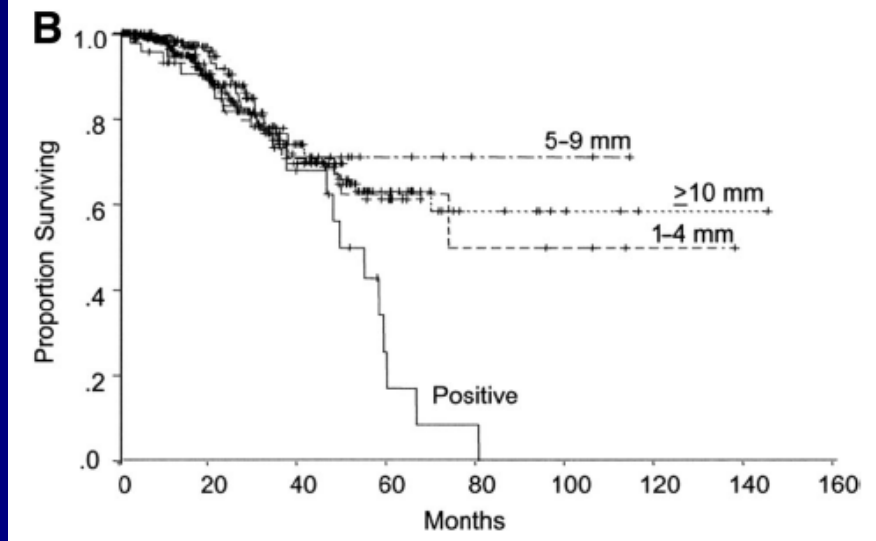
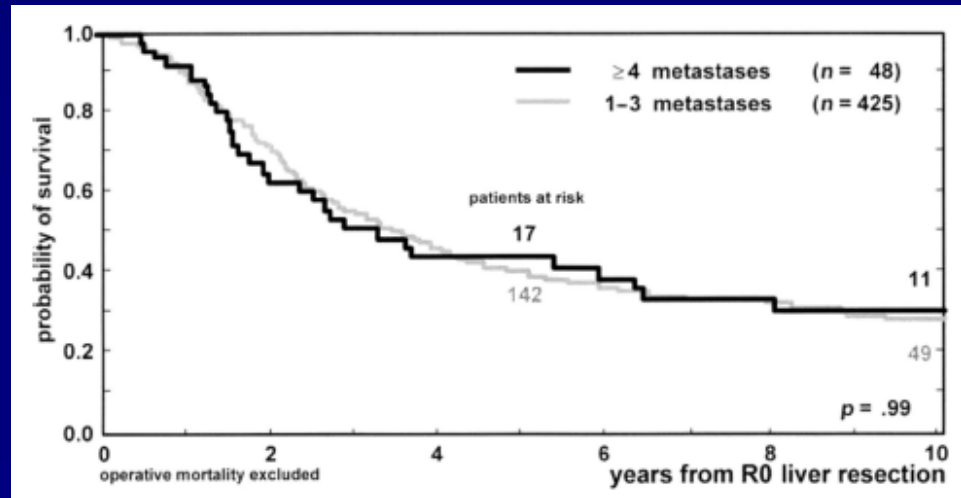
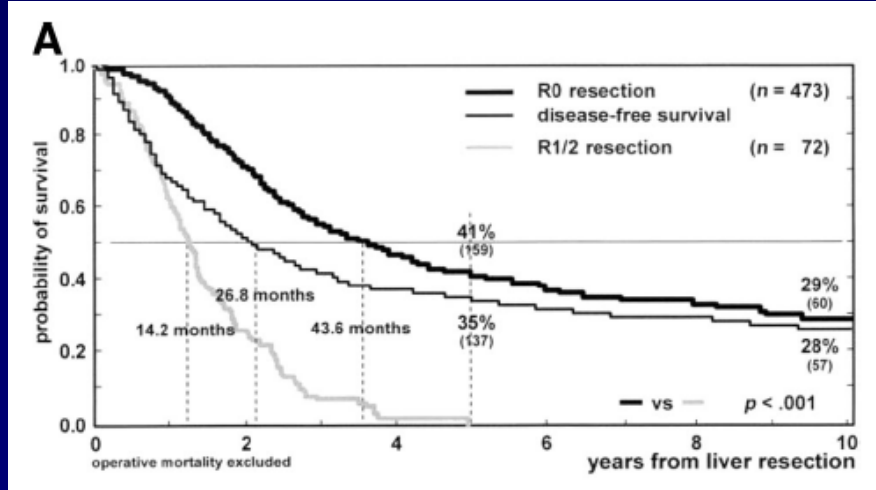
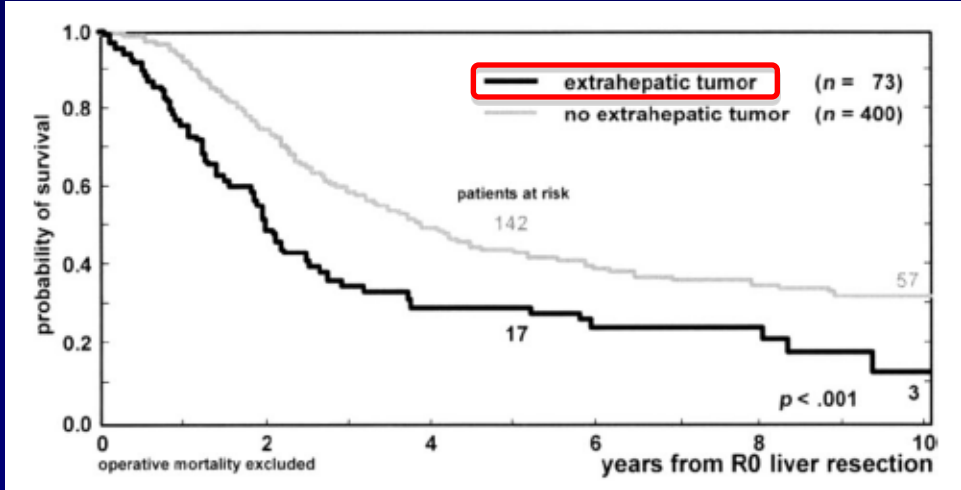
➤ Only < 10%
eligible for
resection

➤ Of which a third
will have a
chance for cure

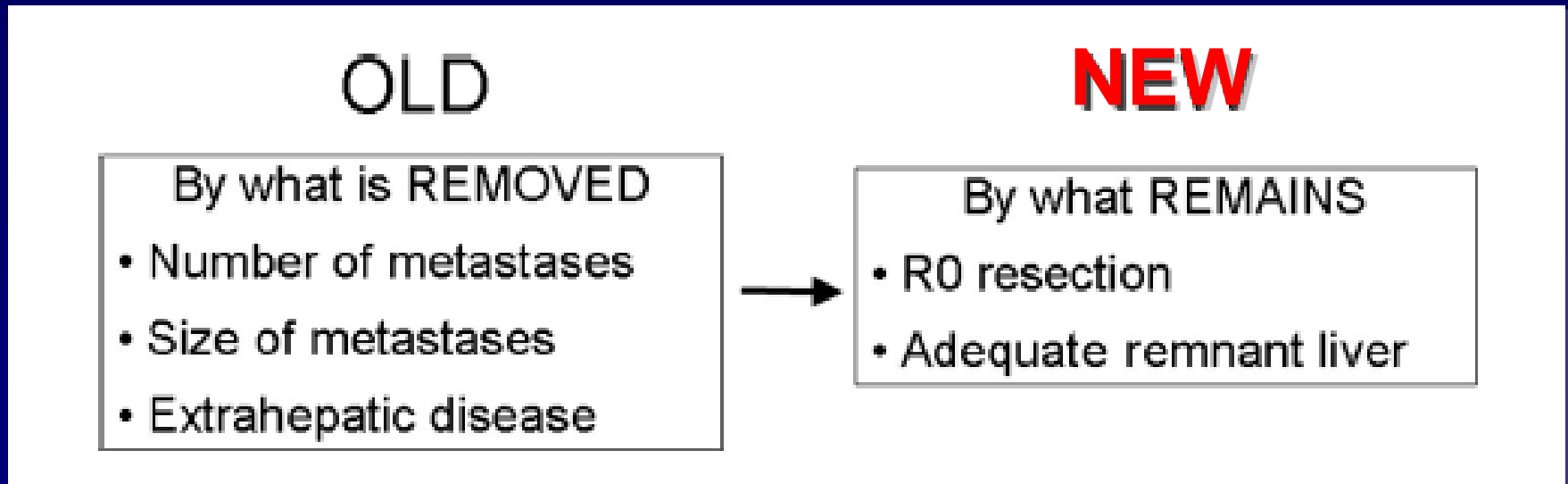
Expanding Criteria for Resectability of Colorectal Liver Metastases

TIMOTHY M. PAWLIK, RICHARD D. SCHULICK, MICHAEL A. CHOTI

Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA



New Paradigm of Resectability



Proceed with liver resection when potentially curative irrespective of prognostic factors

New Resectability Criteria

- **Disease needs to be completely resected (R0 resection)**
- **At least two adjacent liver segments need to be spared**
- **Preserve vascular inflow & outflow, as well as biliary drainage**

New Resectability Criteria

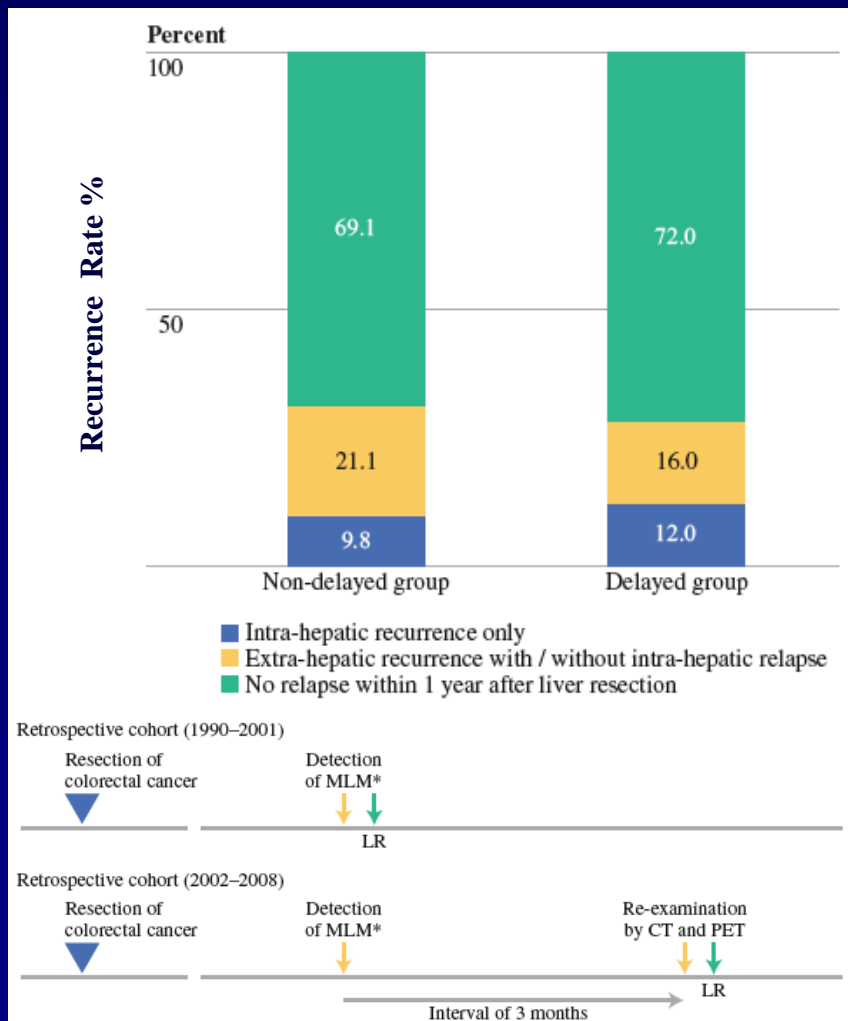
- **Volume of the future liver remnant must be adequate**
 - **At least 20% of the total estimated liver volume for normal parenchyma**
 - **30-60% volume, if liver is injured by chemotherapy-steatosis or hepatitis**
 - **40-70% volume in the presence of cirrhosis**



Resectable Synchronous CLM: One-Stage

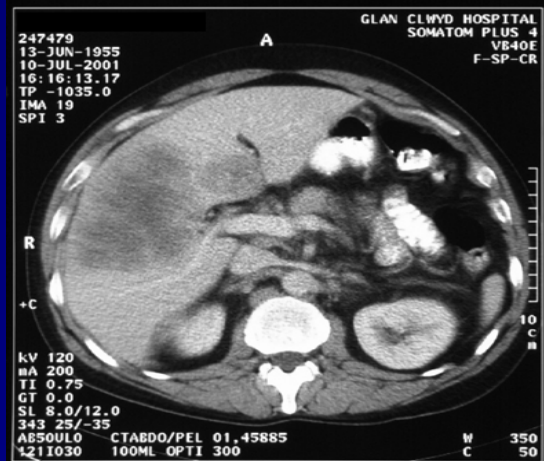
- **Best for right-side colon lesion with:**
 - **CLM left lateral segments or**
 - **CLM superficial right lobe**
- **Better than systemic therapy**
- **Highly selected patients**

Timing of MLM Resection: Immediate or Delayed

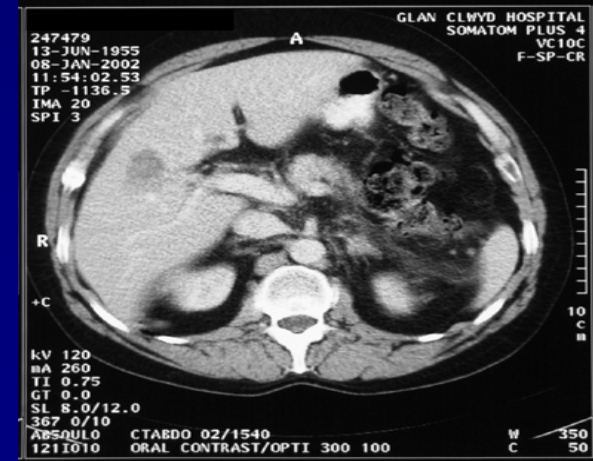
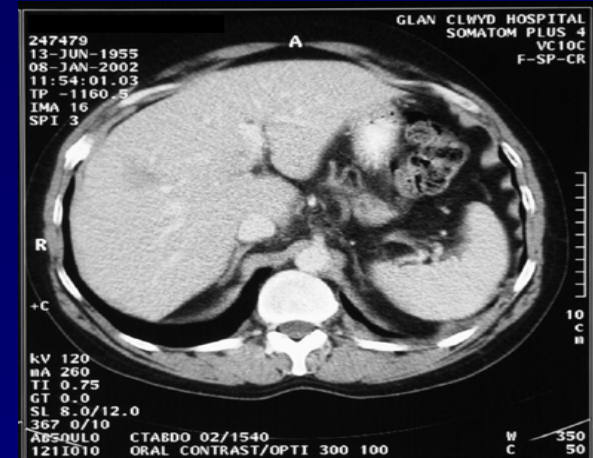


- No difference in recurrences or survival
- Delayed resection offered no clinical benefit

Pre-Op Chemotherapy



**FOLFIRI
(5 months)**



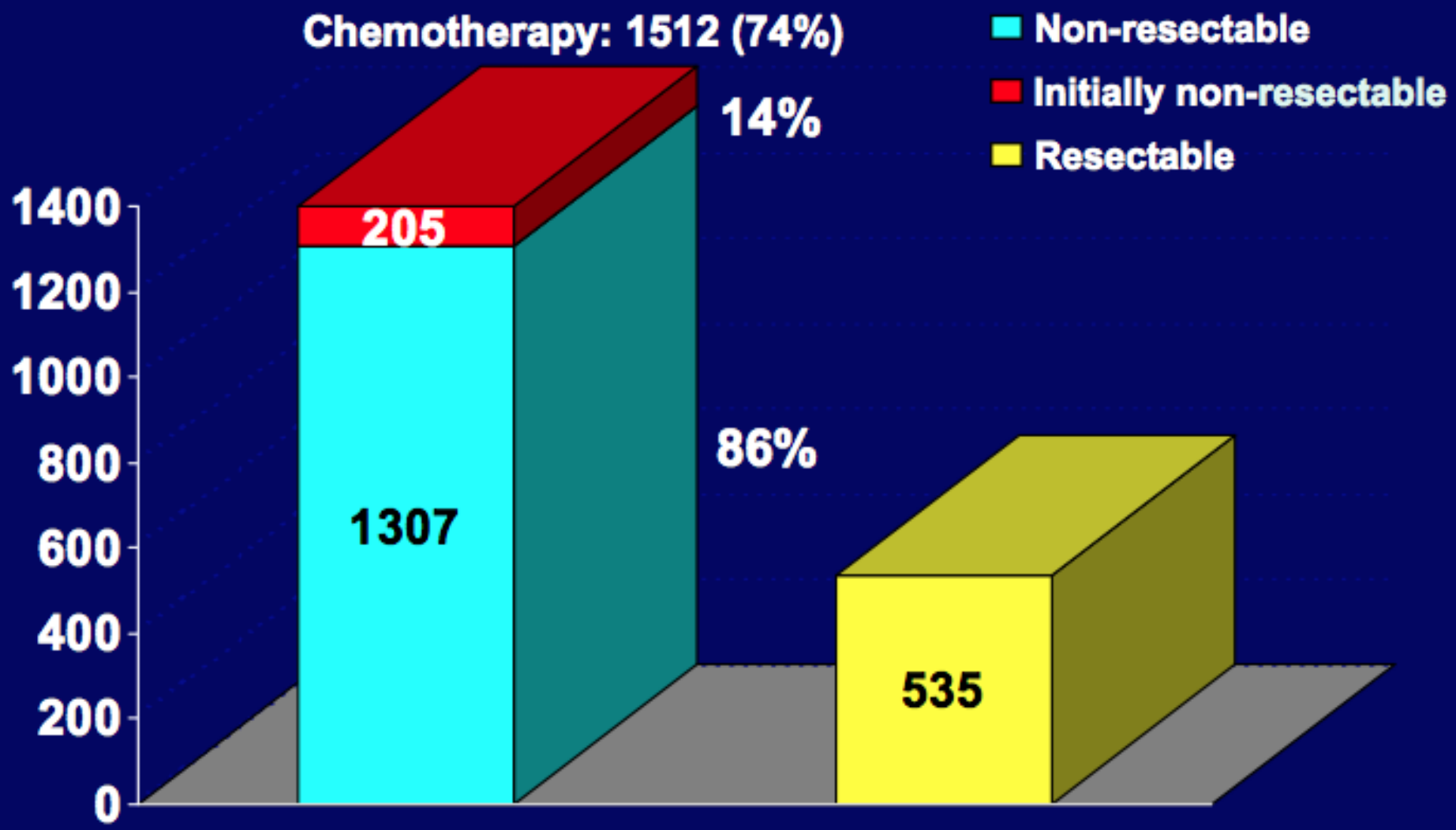
Pre Chemo

Post Chemo



Colorectal liver metastases

Paul Brousse Hospital: 2047 patients (Apr 1988–Dec 2003)





Colorectal liver metastases

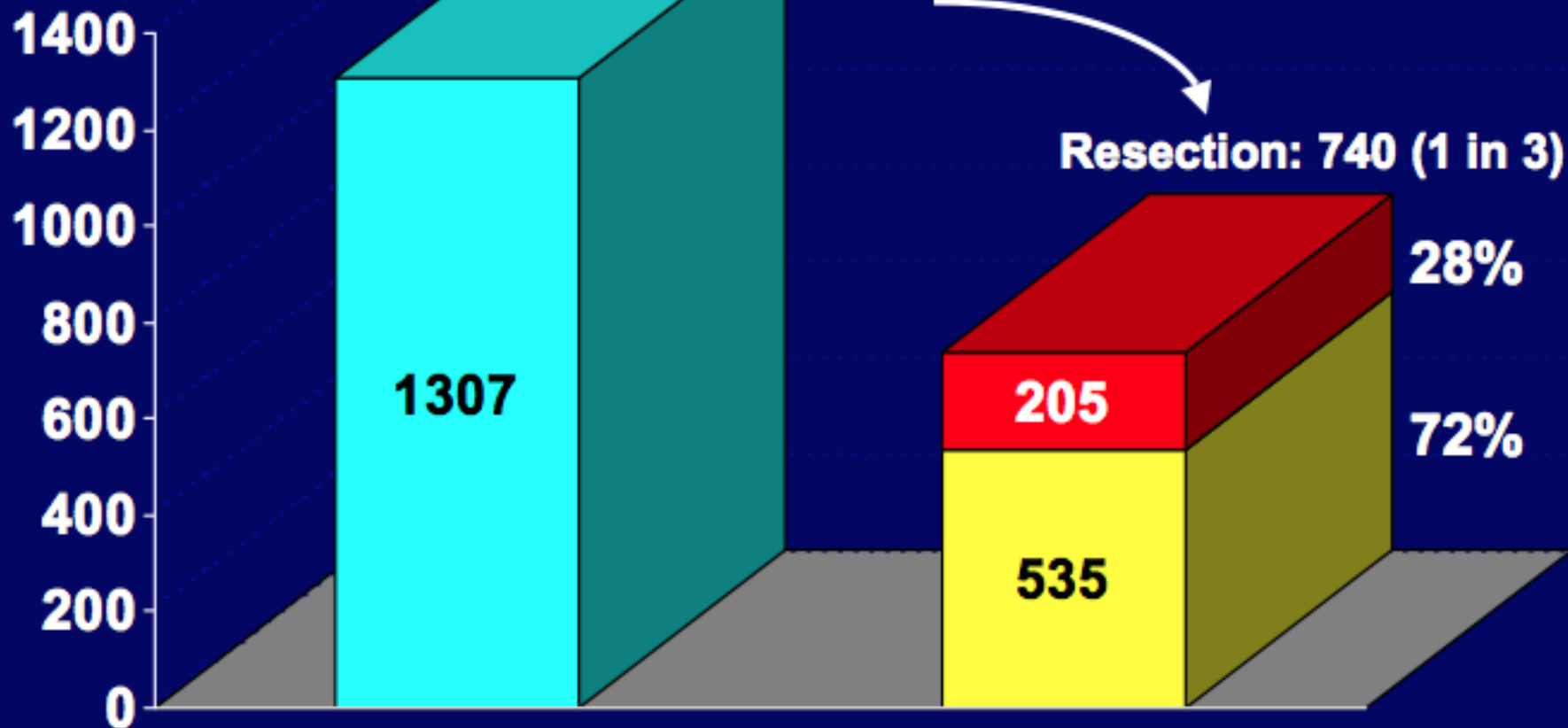
Paul Brousse Hospital: 2047 patients (Apr 1988–Dec 2003)

Chemotherapy: 1512 (74%)

Non-resectable

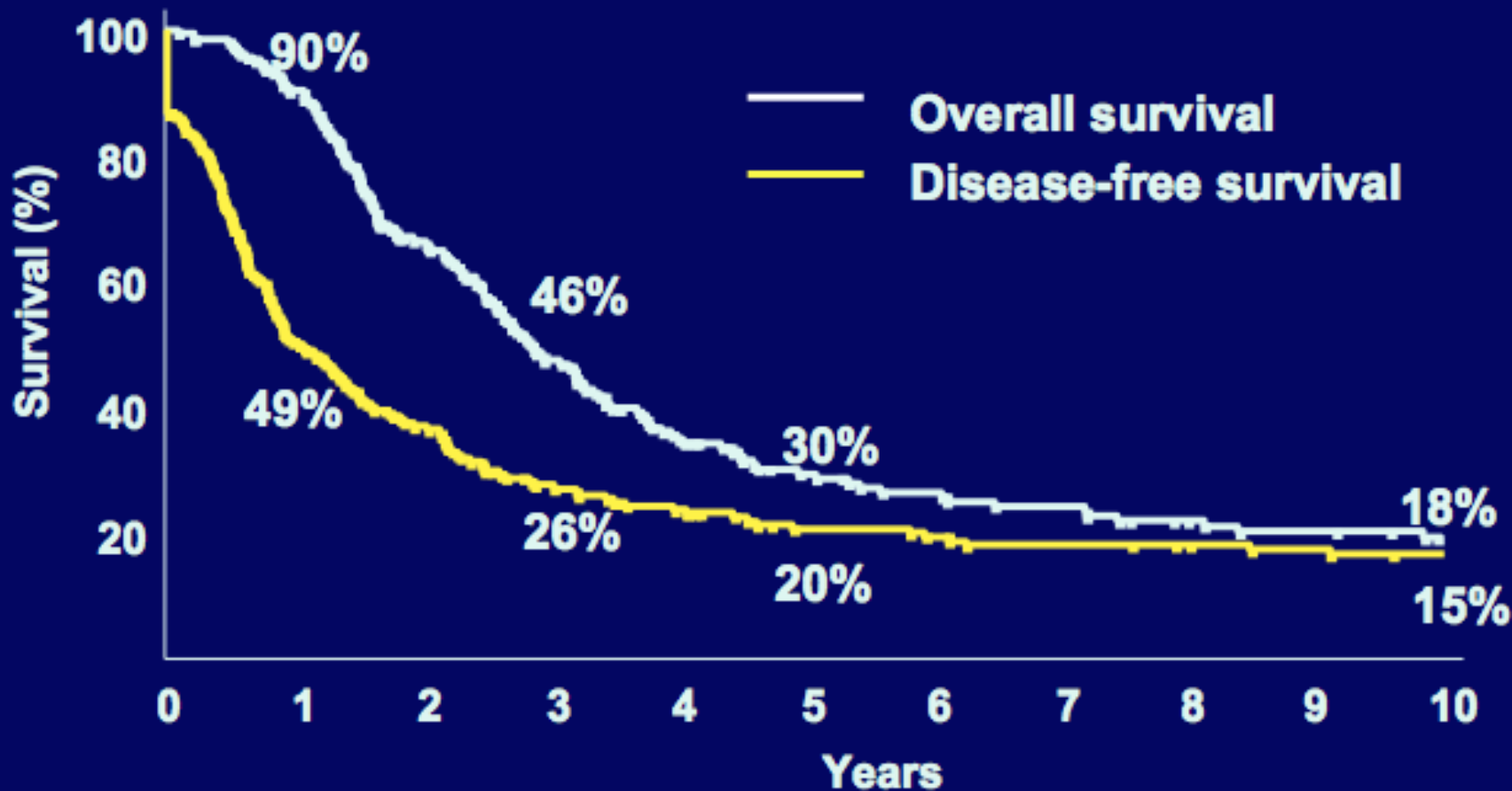
Initially non-resectable

Resectable



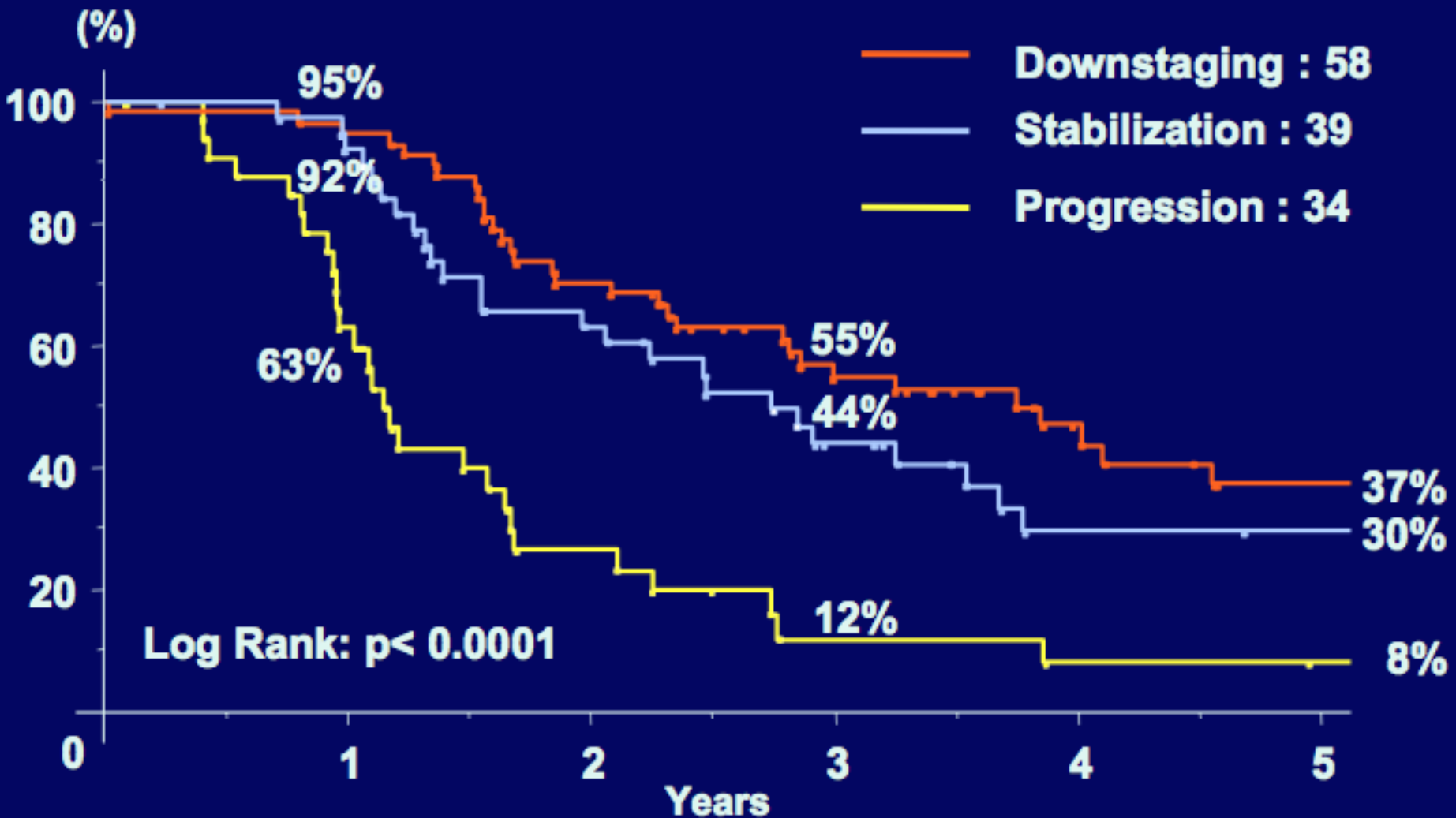
Survival after liver resection of non-resectable colorectal metastases after systemic chemotherapy

Paul Brousse Hospital - 205 patients (Apr 88 – Dec 2003)





Overall survival after resection of multiple liver metastases according to chemotherapy response



Chemotherapy Regimen

- **FOLFOX – 5FU/Leucovorin/Oxaliplatin**
- **FOLFIRI – 5FU/Leucovorin/Irinotecan**
- **FOLFIRI + cetuximab (K-ras mutation)**
- **FOLFIRI + panitumumab (K-ras mutation negative)**

Chemotherapy Disadvantages

- **Chemotherapy-associated steatohepatitis (CASH)**
 - **Irinotecan**
 - **Independent predictor of peri-operative infectious complications**
- **Sinusoidal obstruction syndrome**
 - **Oxaliplatin**

Chemotherapy Disadvantages

- **Nodular regenerative hyperplasia**
 - **5-FU + oxaliplatin**
- **Bevacizumab (Avastin)**
 - **May increase vascular lesions**
 - **Decrease hepatic regeneration**



Timing of Resection After Chemotherapy

- **Chemotherapy related morbidity dependent of # of treatment cycles**
- **Surgery should be considered after 4-6 cycles based on re-staging imaging**
- **Bevacizumab break 5-6 weeks before resection**



Adjuvant Chemotherapy After Resection

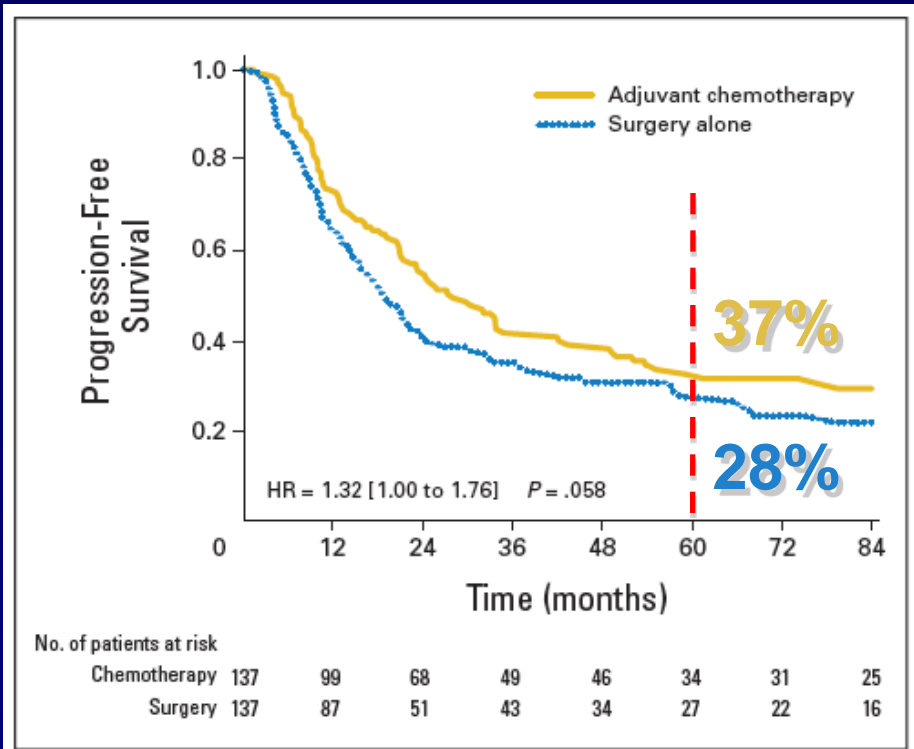


Fig 2. Progression-free survival by treatment group. HR, hazard ratio.

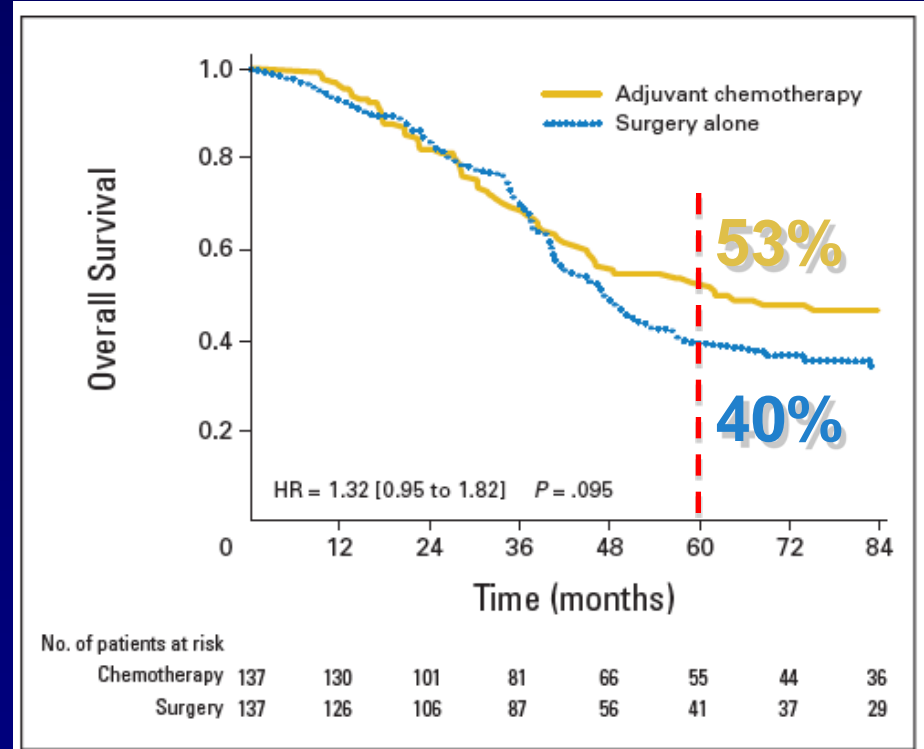


Fig 3. Overall survival by treatment group. HR, hazard ratio.

➤ Positive trend toward PFS and OS

Treating Patients with Colon Cancer Liver Metastasis: A Nationwide Analysis of Therapeutic Decision Making

Hari Nathan, MD, PhD¹, John F. Bridges, PhD², David P. Cosgrove, MD³, Luis A. Diaz, Jr, MD³, Daniel A. Laheru, MD³, Joseph M. Herman, MD, MSc⁴, Richard D. Schulick, MD¹, Barish H. Edil, MD¹, Christopher L. Wolfgang, MD, PhD¹, Michael A. Choti, MD¹, and Timothy M. Pawlik, MD, MPH, PhD¹

- **Immediate resection (IR) vs. CTx and liver resection (C-LR) vs. Palliative CTx (PC)**
- **Experienced surgeons more likely to choose PC over C-LR (OR 1.94, P=0.005)**
- **Surgical oncologist were significantly more likely than HPB surgeon to choose C-LR (OR 2.53) or PC (OR 4.15)**

Summary

- **CLM patients are heterogenous and treatment should be individualized**
- **Must achieve POTENTIAL CURE**
- **Peri-operative CTx recommended for resectable CLM**
- **Most patients should receive post-operative chemotherapy**



**Annual incidence of colorectal cancer
in the U.S. is:**

A. 50,000

B. 100,000

C. 150,000

D. 200,000

E. 250,000

The dominant site of colorectal metastasis is:

A. Anything goes

B. Liver

C. Lung

D. Bone

The expanded resectability criteria includes the following except:

A. R0 resection

B. Adequate future liver remnant

C. Preservation of biliary drainage and vascular inflow and outflow

D. Preserve at least 2 adjacent liver segments

E. Less than 4 metastases

References

- Grothey, Axel. Neoadjuvant and adjuvant treatment for colorectal cancer. *Current Surgical Therapy*, 10th Ed, pp 464-481.
- U.S. Cancer Statistics Working Group. *United States Cancer Statistics: 1999–2008 Incidence and Mortality Web-based Report*. Atlanta (GA): Department of Health and Human Services, Centers for Disease Control and Prevention, and National Cancer Institute; 2012
- Howlader N et al. *SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations)*, National Cancer Institute. Bethesda, MD
- O'Connell JB, Maggard MA, Ko CY. Colon cancer survival rates with the new American Joint Committee on Cancer Sixth Edition Staging. *J Natl Cancer Inst.* 2004;96:1420-1425.
- Pawlik, TM, Schulick RD and Choti MA. Expanding criteria for resectability of colorectal liver metastases. *The Oncologist*, 2008;13:51-64.

References

- Ueno S et al. Is delayed liver resection appropriate for patients with metachronous colorectal metastases? *Ann Surg Oncol*, 2011;18:1104-1109.
- Benoist, S and Nordlinger B. The role of preoperative chemotherapy in patients with resectable colorectal liver metastases. *Ann Surg Oncol*, 2009; 16:2385-2390.
- Adam R et al. Is perioperative chemotherapy useful for solitary, metachronous, colorectal liver metastases? *Ann Surg* 2010;252:774-787.
- Manfredi S et al. Epidemiology and management of liver metastases from colorectal cancer. *Ann Surg*, 2006;244:254-259.
- Mitry E et al. Adjuvant chemotherapy after potentially curative resection of metastases from colorectal cancer: a pooled analysis of two randomized trials. *J Clin Oncol*, 2008;26:4906-4911.
- Nathan H et al. Treating patients with colon cancer liver metastases: A nationwide analysis of therapeutic decision making. *Ann Surg Oncol*, 2012; 19:3668-3676.