

# Liver-Directed Therapy for Primary and Metastatic Hepatic Malignancies

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## Overview

- Liver Directed Therapies
- Hepatic Resection
  - General Criteria for Resectability
- Metastatic Malignancies
  - Colorectal
  - Neuroendocrine
  - Non-colorectal, non-neuroendocrine
- Primary Cancers
  - HCC
  - Extra- and Intra-Hepatic Cholangiocarcinoma

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## Liver Directed Therapies

- Resection
- Ablation
  - RFA
  - Cryoablation
  - Chemical
- Chemoembolization (TACE)
- Hepatic artery infusion
- Microwave ablation
- Selective Internal Radiation Therapy (SIRT)

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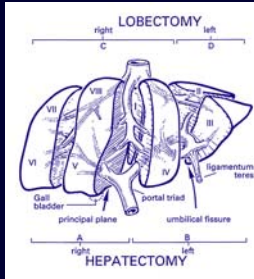
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## Hepatic Resection



- Mortality < 5%
  - Zero mortality in many series
- Hemorrhage control and reduction in need for transfusion
  - Low CVP anesthesia
  - Novel methods of parenchymal transection
  - Hemodilution
- Liver dysfunction and failure

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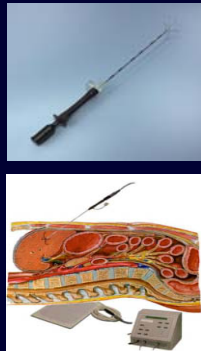
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## Radiofrequency Ablation

- High-frequency alternating current creates heat that destroys tumor cells
- Operative (open or laparoscopic) or percutaneous approach
- Spares hepatic parenchyma



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## RFA Benefits and Limitations

- Less invasive
- Fewer complications
- Decreased expense
- Simultaneous treatment with systemic therapies
- Does not preclude subsequent resection
- Size limitation
- “Heat sink” effect
- Adjacent organs may require open approach



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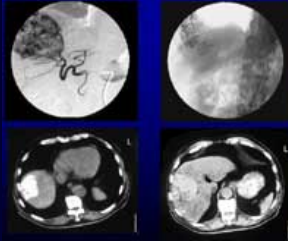
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## Transarterial Chemoembolization (TACE)

- Relies on hepatic artery as primary blood supply for tumor
- Directed chemotherapy followed by embolization of tumor's arterial blood supply
- Minimally invasive
- Safe
- Can be repeated



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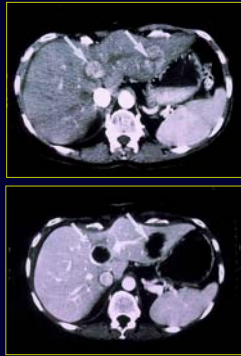
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## Chemical Ablation

- Only HCC in cirrhotic livers
  - Soft tumor with hard surrounding liver allows diffusion into tumor only
- Ethanol ablation most common
  - PEI (percutaneous ethanol ablation)
- Acetic acid also used
- Safe and minimally invasive
- Multiple treatments needed



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## Hepatic Artery Infusion



- Metastases derive most blood from hepatic artery
- Improved progression-free survival in liver in pts s/p hepatic resection
  - No overall survival benefit
- Enthusiasm waned w/ modern systemic therapy
- NSABP C-09
  - CAPOX with or without HAI in resected pts
- Now what?

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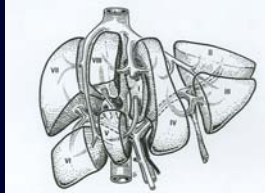
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## Hepatic Resection General Criteria for Resectability

- Preservation of functional hepatic parenchyma
  - Preservation of two contiguous liver segments
  - Normal liver: 25% liver remnant
  - Cirrhotic liver 50-75% depending on Child class
- Operative risk
- Ability to obtain a negative margin
  - R0 resection
- Good performance status
  - ECOG 0-1



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## Resection (and Other Liver-Directed Therapy) for Metastatic Disease Prognostic Indicators and Surrogates for Tumor Biology

- Disease-free interval
  - >12 months better prognosis
- Number of metastases
- Number of organs
  - 1 vs greater than one
- Site of metastases
  - Visceral vs non-visceral
- Response to systemic therapy

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## Which of the following patients is a good candidate for hepatic resection for metastatic disease?

- 45 y/o M w/ metastatic melanoma to bilateral lungs and liver
- 88 y/o F w/ severe COPD requiring home O2 w/ a single liver metastasis from colon ca resected 5 yrs ago
- 56 y/o F w/ synchronous primary breast cancer and a single liver metastasis
- 70 y/o M w/ 10 liver metastases and multiple nodal metastases from neuroendocrine carcinoma
- 60 y/o F w/ 2 liver metastases from colon cancer treated 3 years ago, s/p systemic therapy w/ a good radiographic response

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## Colorectal Liver Metastases

“Hepatic resection for metastases from colorectal cancer is of dubious value”

*Silen, 1989*



- Standard of care
- Increasingly offered to patients
- ~ 10,000-15,000 patients are candidates for curative resection yearly
  - 5-yr survival of 30-40%
  - around 4000 pts/year have long-term survival

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## Hepatic Resection Classic Contraindications

- 4 or more lesions
- Bilobar disease
- Extrahepatic disease
- Synchronous metastases
- Surgical margin < 1 cm
- Inadequate remnant liver
- Portal lymph node involvement



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## Hepatic Resection for CRC Mets Current Contraindications

**NONE**

(well...sort of)

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## Hepatic Resection for CRC Mets

### Current *Absolute* Contraindications

- *Unresectable* extrahepatic disease
- Inadequate remnant liver (despite staged resection, PVE)
  - Over 70% of liver, or 6 segments
- Inability to obtain R0 resection (?)

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### No Prospective Randomized Trial Exists

- In retrospective series, resected patients have survival significantly better than all other groups
  - Patients *with resectable disease* who do NOT undergo resection have median survival 12 months shorter than resected patients
  - 16% 10-yr survival; actual 20 year survivors

*Scheele, Br J Surg 1990*

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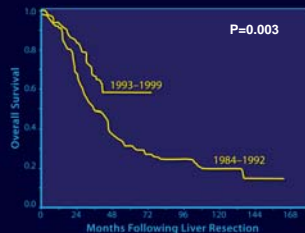
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### “Trends in Long-Term Survival Following Liver Resection for Hepatic Colorectal Metastases”

*Choti et al, Ann Surg 2002*



	'84-'92	'93-'99
Number of Pts	93	133
Overall Survival (%)		
3-Yr	48	67
5-Yr	31	58
Median Survival (mo)	36	na

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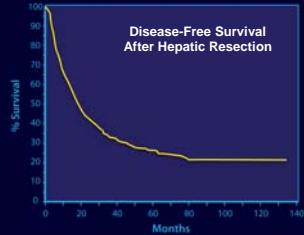
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## “Survival After Hepatic Resection for Colorectal Metastases: A 10-Year Experience”

*Wei et al, Ann Surg Oncol 2006*



	'77-'93	'92-'02
Number of Pts	123	423
Overall Survival (%)		
5-Yr	34	47
10-Yr	na	28
Disease-Free Survival (%)		
5-Yr	na	27
10-Yr	na	22

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## Increasing Application (and Success) of Hepatic Resection

- Better patient selection
  - Advances in imaging
  - Response to chemotherapy
- Improved operative safety
- Use of innovative modalities
  - Neoadjuvant chemotherapy
  - Portal vein embolization
  - Local ablative therapies
  - Staged resection

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## “Clinical Score for Predicting Recurrence After Hepatic Resection for Metastatic Colorectal Cancer”

*Fong et al, Ann Surg 1999*

- 1001 consecutive cases
- 13 years, single institution
- 5-yr survival 37%
- 10-yr survival 22%
- Clinical Risk Score (CRS) devised to assist selection of pts for resection

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## Predictors of Recurrence: Factors Useful in Risk Score

	Hazard	Coefficient	p value
Positive Margin	1.7	0.5	0.004
Extrahepatic Disease	1.7	0.5	0.003
> 1 Tumor	1.5	0.4	0.0004
CEA > 200ng/mL	1.5	0.4	0.01
Size > 5 cm	1.4	0.3	0.01
Node (+) Primary	1.3	0.28	0.02
DFI < 12 months	1.3	0.25	0.03
Bilateral Tumor	0.9	-0.1	0.4

Fong et al, Ann Surg 1999

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## Clinical Risk Score for Tumor Recurrence

Score	Survival (%)			
	2-yr	3-yr	5-yr	Median (mo)
0	79	72	60	74
1	76	66	44	51
2	73	60	40	47
3	67	42	20	33
4	45	38	25	20
5	45	27	14	20

Fong et al, Ann Surg 1999

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### Case 1

72 y/o woman s/p  
partial colectomy  
8 yrs ago. T3N0.  
CEA =124.

There is a single  
7 cm metastasis.




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**Case 1**  
**What is this patient's Clinical Risk Score?**

- a) 0
- b) 1
- c) 2
- d) 3
- e) 4

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**Case 1**  
**What therapy would you recommend?**

- a) Hepatic resection
- b) Hospice
- c) Systemic therapy only
- d) RFA
- e) Hepatic artery infusion and systemic therapy

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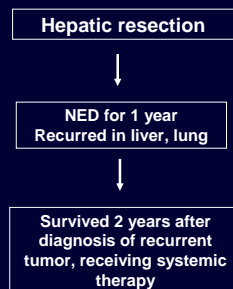
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**Case 1 Follow-Up**



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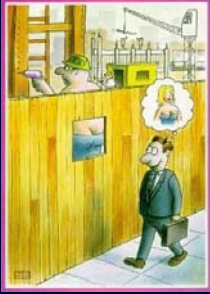
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## What Happened?



- Two main possibilities:
  - CRS not reliable in a different institution
  - No prognostic criteria are definitive enough to exclude a curative resection (and vice versa)

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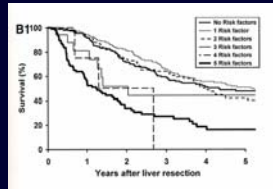
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## Are Risk Scoring Systems Reliable and Valuable?

- 662 pts w colorectal liver mets treated at Mayo clinic from 1960-1995
- Applied 3 different scoring systems to Mayo cohort to validate the models
- Conclusion: models only marginally better than chance in predicting recurrence and survival



Fong CRS applied to Mayo cohort

Zakaria et al, Ann Surg 2007

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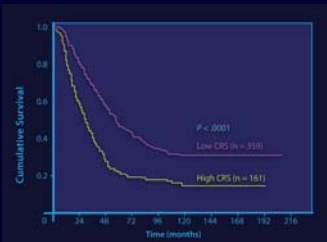
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## “Actual 10-Year Survival After Resection of Colorectal Liver Metastases Defines Cure”

Tomlinson et al, J Clin Oncol 2007

- 612 pts with 10 yr follow-up
- 102 (17%) actual 10 yr survivors
- 1/3 died of recurrent disease after 5 yrs



Overall survival by CRS

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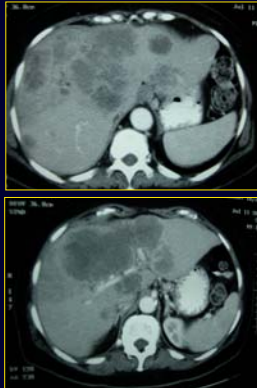
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**Case 2**

66 y/o woman s/p transverse colectomy 1 year ago.  
T3N0  
CEA =2000.



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**Case 2**

**The best therapy at this time is:**

- a) Immediate hepatic resection
- b) TACE and systemic therapy
- c) Systemic therapy then possible resection
- d) Resection w/ RFA, hepatic artery infusion
- e) Total hepatectomy and orthotopic liver transplantation

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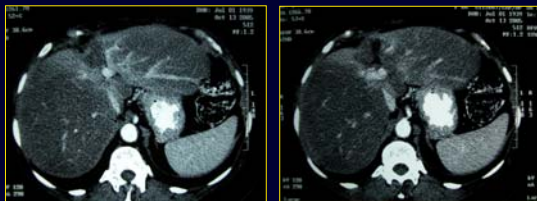
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**After Pre-Op Systemic Therapy**



- Case 1
  - Pt underwent left hepatectomy
  - Path showed 2.5 cm metastatic adenocarcinoma w/ 2 subcentimeter satellites, margins neg

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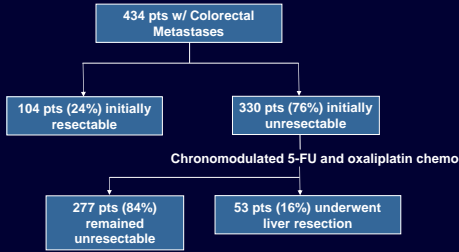
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**“Resection of Nonresectable Liver Metastases from Colorectal Cancer After Neoadjuvant Chemotherapy”**  
*Bismuth et al, Ann Surg 1996*




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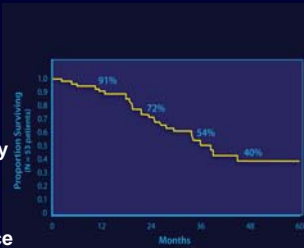
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**Neoadjuvant Chemotherapy**

- 40% 5-yr overall survival
- 34 pts (66%) recurred in liver at mean of 42 mo
  - Repeat hepatectomy performed in 15 (44%)
- 25 pts (47%) w/ extrahepatic recurrence
- 93 resections inc. liver, lung, abdominal



*Bismuth et al, Ann Surg 1996*

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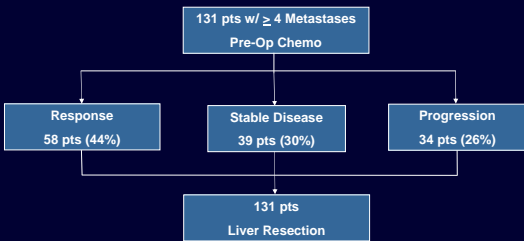
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**“Tumor Progression While on Chemotherapy: Contraindication to Liver Resection for Multiple Metastases?”**  
*Adam et al, Ann Surg 2004*




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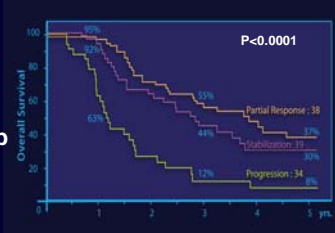
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## Tumor Progression on Chemo

- 28% 5-yr overall survival
- 37% 5-yr overall survival for patients w/ response to preop chemo
- Disease control before surgery crucial to prolonged survival



Adam et al, Ann Surg 2004

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## Pre-Op Systemic Therapy Questions

- Indications
- Optimal timing of surgery
  - Complete response or just enough to render resectable?
  - Borderline resectability—resect 1<sup>st</sup>?
- Ability to accurately determine response
- CASH (Chemotherapy-Associated Steatohepatitis)
  - Fatty infiltration → fibrosis → frank cirrhosis
- Costs
  - 6 mo course of treatment: \$180,000

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## Should All Lesions Be Resected After Pre-Op Systemic Therapy?

- Remnants of uncertain malignant potential (RUMP)
  - Only 3/22 pts (14%) had pathologic CR
  - Median 20% viable neoplasm (range 0-60%) recovered per lesion

Znajda et al, J Gastrointest Surg 2006



- “Missing” liver metastases
  - 15 pts undergoing hepatic resection after chemo
  - 11 “missing” mets @ exploration
  - Only 27% recurrence at 31 months after radiologic CR

Elias et al, J Surg Oncol 2004

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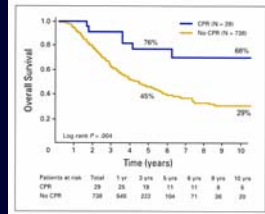
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## Complete Pathologic Response After Pre-Op Chemo

- 767 pts underwent pre-op chemo between 1985-2006
- 29 (4%) w/ complete PR
  - Improved 5 and 10-yr survival
- No relationship to pts who had a complete CR



Adam et al, J Clin Oncol 2008

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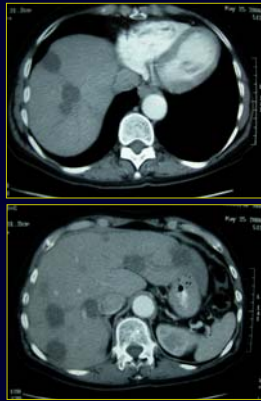
### Case 3

64 y/o woman who presented w/ abdominal pain and bloating in 1/06.

CT showed multiple liver mets.

CEA =3900.

Primary cancer identified as rectum. Asymptomatic.




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### Case 3

The best therapy at this time is:

- Immediate synchronous hepatic and colon resection
- Systemic therapy then synchronous hepatic and colon resection
- Hepatic artery infusion and systemic therapy
- Systemic therapy then staged hepatic and colon resection using portal vein embolization
- Systemic therapy and TACE

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### Case 3 Follow-Up

- Underwent systemic therapy
  - FOLFOX + bevacizumab
- Proctectomy w/ multiple wedge resections of left hemiliver mets on 1/07
- Additional systemic therapy
- Portal vein embolization 4/07
- 2<sup>nd</sup> stage hepatectomy 5/07



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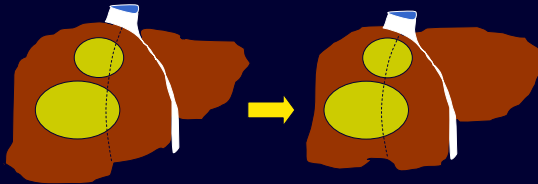
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### Portal Vein Embolization

•Obstruct portal venous flow to side of liver ipsilateral to lesion



•Induce contralateral hypertrophy  
•Increase size of future liver remnant



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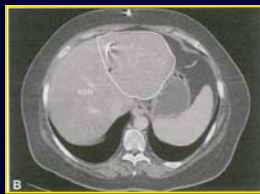
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### Portal Vein Embolization



Pre-PVE



Post-PVE

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**“Preoperative Portal Vein Embolization for Extended Hepatectomy”**  
*Hemming et al, Ann Surg 2003*

	PVE Group (n=31)	Non-PVE (n=21)	p value
Gender M:F	19:12	13:8	NS
Age (range)	61 (31-82)	59 (33-76)	NS
O.R. Time, min	285	270	NS
Blood Loss, mL	640	660	NS
Liver Failure	3 (10%)	7 (33%)	0.03
Peak Bilirubin	2.6 ± 1.2	5.0 ± 5.1	0.01
FFP Requirement	0.7 ± 1.4 u	2.9 ± 3.9 u	0.006
Length of Stay	8.7 ± 2.3 d	11.3 ± 5.7 d	0.03

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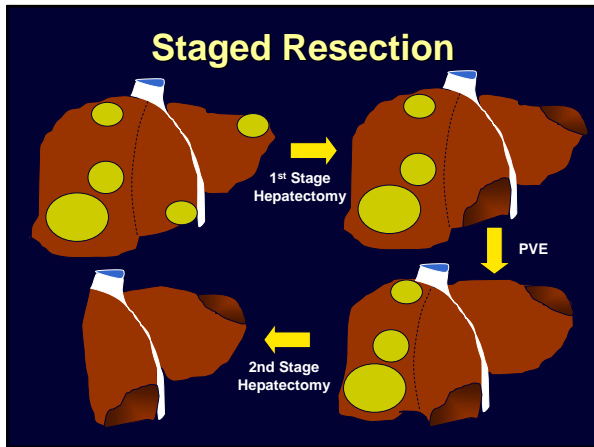
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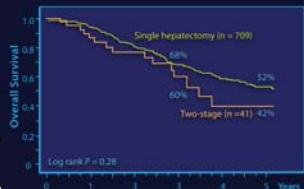
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**Long Term Results of 2-Stage Hepatectomy**

- 59 pts (out of 262) w/ initially unresectable mets who required two hepatectomies
  - Mean no. of mets 9
- 2-stage approach feasible in 41 of 59 patients (69%)
- 5-yr survival 31% by intention-to-treat



Patients at risk	Total	1 yr	2 yrs	3 yrs	4 yrs	5 yrs
Single hepatectomy	709	549	366	252	176	120
Two-stage	41	29	21	11	6	4

*Wicherts et al, Ann Surg 2008*

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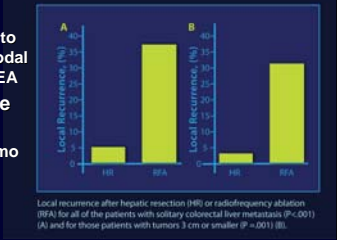
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## RFA vs. Resection Colorectal Metastases

- 180 pts treated w/ resection vs RFA
  - Comparable w/ respect to primary tumor stage, nodal status, DFI, met size, CEA
- Higher local recurrence after RFA
  - 37 vs 5% at median 31 mo
- Worse overall and disease-free survival
  - 27 vs. 71% overall 5-yr survival
  - 0 vs. 50% 5-yr DFS



Aloia et al, Arch Surg 2006

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## RFA for Colorectal Metastases Current Uses

- Patients with small lesions (<3 cm ideal) who are unresectable due to underlying liver disease
- Patients with intra-hepatic recurrence s/p hepatectomy, who are not candidates for repeat hepatectomy
  - Should be NED elsewhere

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“It is obvious that biological behaviour prevails over surgical enthusiasm in deciding the fate of patients with colorectal liver metastases”



Scheele, 1990

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**“In the world of Surgical Oncology  
Biology is King  
Selection is Queen  
Technical maneuvers are the Prince  
and Princess**

Occasionally the Prince or Princess tries to usurp the throne; they almost always fail to overcome the powerful forces of the King and Queen”

*Cady, 1997*

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## **Neuroendocrine Metastases**

- Can aggressive therapy prolong survival?
  - Generally indolent behavior
  - Extensive hepatic and extra-hepatic metastases
- Palliation of symptoms
- Multiple Treatment Options:
  - Resection +/- Ablative Therapies
  - TACE
  - Systemic Therapy

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### **Case 4**

55 y/o F s/p resection of a “pancreatic endocrine tumor” in 2004.

One large liver metastasis, two smaller ones.

Elevated gastrin, urinary 5-HIAA.

Progressed on Octreotide + IFN trial.



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**Case 4**  
**The best approach now is:**

- a) Resection
- b) TACE then resection
- c) RFA
- d) Liver transplantation
- e) Hepatic artery infusion

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**Does hepatic resection improve survival in metastatic neuroendocrine tumors?**

Series	No. of Subjects	Treatment	3-Year Survival (%)	5-Year Survival (%)
Musunuru 2006	17	Medical	31	NA
	18	TAE	31	NA
	13	Surgery	83	60
Sarmiento 2003	170	Surgery	75	61
Norton 2003	16	Surgery	NA	82
Chamberlain 2000	18	Medical	39	NA
	33	TAE	83	50
	34	Surgery	83	76
Chen 1998	23	Medical	40	29
	15	Surgery	92	73

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**TACE followed by Resection?**

- **Potential benefits:**
  - May decrease tumor size, facilitate resection
    - Decrease release of vasoactive amines
  - Use in combination with resection and/or ablation to help cytoreduce tumor
- **Limitations:**
  - Tumor progression

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**“Neuroendocrine Hepatic Metastases: Does Aggressive Management Improve Survival?”**  
 Touzios et al, Ann Surg 2005

	Resection/ Ablation	TACE +/- Resection/ Ablation	Non- Aggressive
Symptom Improvement (%)	95*	88*	42
30-Day Mortality (%)	5.3	5.6	8.7
Survival Median, mo	>96*	50*	20
5 Yrs (%)	72*	50*	25

*p < 0.05 compared to Non-aggressive*

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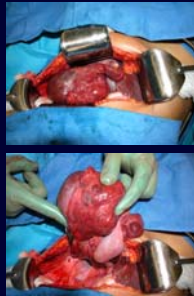
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**Non-colorectal, Non-neuroendocrine Metastases**

- Diverse group of malignancies
- Limited but growing body of data
- Patients w/ metastases from GU primaries have best survival
- Breast cancer best studied




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**Modern Series**  
**Liver Resection for Non-Colorectal, Non-Neuroendocrine Metastasis**

Series	Number	5-Yr Survival (%)	Operative Mortality (%)
Harrison 1997	96	37	0
Hemming 2000	37	45	0
Laurent 2001	39	35	0
Yamada 2001	33	12	9
Takada 2001	14	NR	7
Karavias 2002	18	NR	0
Weitz 2005	141	28	0
Ercolani 2005	142	34	0

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**“Hepatic Resection for Noncolorectal  
Nonendocrine Liver Metastases: Analysis of  
1452 Patients”**

Adam et al, Ann Surg 2006

Tumor Type	Number	5-Yr Survival (%)	Median Survival (mo)
All	1452	36	35
Adrenal	28	66	63
Testicular	78	51	82
Ovarian	65	50	98
Breast	454	41	45
Renal	85	38	36
Stomach	64	27	15
Ocular Melanoma	104	21	19
Pulmonary	32	8	16

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**Case 5**

62 y/o F s/p  
mastectomy 14 yrs  
ago for node  
positive ER neg  
cancer. Received  
radiation and  
chemo.

Elevated CA 2729  
noted. Biopsy-  
proven ER + liver  
metastasis.




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**Case 5**

**Select the most appropriate therapy:**

- a) Systemic therapy only
- b) Systemic therapy followed by resection if good response
- c) RFA and systemic therapy
- d) Immediate hepatic resection
- e) Hospice

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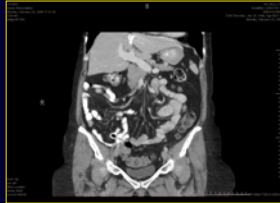
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## Case 5 Follow-Up

- Started on Femara
- Excellent response
- Underwent segmental liver resection
  - Path: 3 cm metastatic carcinoma c/w breast primary, margin neg



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## “Is Liver Resection Justified for Patients With Hepatic Metastases From Breast Cancer?”

*Adam et al, Ann Surg 2006*

- 108 patients w/ breast cancer liver mets
  - 1984-2004
- Hepatic resection offered to all pts provided that:
  - Curative resection feasible
  - Extrahepatic disease controlled
- 84% received chemo between diagnosis and hepatic resection of liver mets
- Partial response to treatment in 78%
- 83% underwent post-resection systemic therapy

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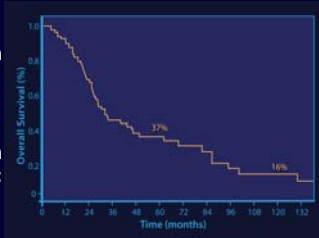
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## Liver Resection for Breast Cancer Overall Survival

- Median follow-up 38 months
- Overall survival from hepatic resection:
  - Median 32 months
  - 5-yr survival 37%
- Overall survival from liver mets diagnosis:
  - Median 46 months
  - 5-yr survival 41%



*Adam et al, Ann Surg 2006*

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## Hepatic Resection for Breast Cancer Liver Metastases Published Results (Modern Series, >10 Subjects)

Series	No. of Subjects	Median Survival (mo)	5-Year Survival (%)	Mortality (%)
Selzner 2000	17	25	22	6
Yoshimoto 2000	25	34	NR	--
Pocard 2001	65	47	46	0
Carlini 2002	17	53	46	0
Vlastos 2004	31	63	61	0
Sakamoto 2005	34	36	21	0
d'Annibale 2005	18	32	30	0
Ercolani 2005	21	42	25	0
Adam 2006*	454	45	41	NR

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## Hepatic Resection for Breast Cancer Prognostic Factors for Overall Survival

- Disease-free interval
  - DFI <12 months vs. > 12 months
    - 9 vs. 27 months *Selzner et al, Surgery 2000*
  - DFI < 48 months vs. > 48 months
    - 55% vs. 86% 3-Yr Survival *Pocard et al, Ann Chir 2001*
- Presence of extrahepatic metastases  
*Sakamoto et al, World J Surg 2005*
- Response to systemic therapy
  - 42% response vs 0% progression 5 yr survival
- Margin status *Adam et al, Ann Surg 2006*
  - 43% R0/R1 vs 10% R2 5-yr survival

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## Hepatocellular Carcinoma Multiple Treatment Options

- Resection
- Total hepatectomy w/ orthotopic liver transplantation (OLT)
- Trans-arterial chemoembolization (TACE)
- Radiofrequency Ablation (RFA)
- Percutaneous ethanol injection (PEI)
- Systemic therapy




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## Hepatocellular Carcinoma Hepatic Resection

- Historical “gold standard” but changing
- Significant limitation of preserving enough function hepatic parenchyma
  - Limits applicability in cirrhotic patients
- High morbidity
- Invasive

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## Hepatocellular Carcinoma Hepatic Resection: Selected Series

Series	Number	3-Yr Survival (%)	5-Yr Survival (%)
Franco 1990	72	51	NR
Nagasue 1993	229	51	23
Llovet 1999	77	62	51
Zhou 2001	1000 (<5cm)	77	65
	1366 (>5cm)	48	37
Ercolani 2003	224	63	43
Shimozawa 2004	135	73	55

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## Hepatocellular Carcinoma Liver Transplantation

- Best outcomes
  - Improved chance for cure by obtaining wide margins and removing liver at risk for future tumor
  - Treats underlying liver disease and portal hypertension
    - Survival limited by cirrhosis and progressive liver failure
- Primary limitation is organ donor supply

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## Liver Transplantation For HCC Best Reported Outcomes

AUTHOR, JOURNAL, YR	CENTER	N	ACTUARIAL SURVIVAL	
			1-YR	5-YR
Mazzaferro, <i>NEJM</i> 1996	Milan, Italy	48	84%	74%
Llovet, <i>Hepatology</i> 1998	Barcelona, Spain	58	84%	74%
Bismuth, <i>Sem Liver Dis</i> 1999	Villejuif, France	45	82%	74%
Jonas, <i>Hepatology</i> 2001	Berlin, Germany	120	90%	71%
Yao, <i>Hepatology</i> 2001	San Francisco	64	87%	73%

Adapted from Bruix and Llovet, *Hepatology* 2002

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## RFA vs Other Ablative Therapies Selected RCTs

Series	No. of Subjects	Treatment	Treatments Per Tumor	Overall Survival (%)
Lencioni 2002	52	RFA	1.1	98
	50	PEI	5.4	88
Lin 2004	62	RFA	1.3	74
	62	PEI	4.9	51
	63	PAI	2.5	53
Shiina 2005	118	RFA	2.1	74
	114	PEI	6.4	57

Adapted from Lau et al, *Ann Surg* 2009

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## RFA as Primary Treatment of Resectable HCC

•180 pts w/ HCC  $\leq$  5 cm randomized to either percutaneous RFA or resection

	Percutaneous RFA	Hepatic Resection	p value
<b>Overall Survival</b>			
1 Yr (%)	95.8	93.3	NS
4 Yrs (%)	67.9	64.0	
<b>Disease Free Survival</b>			
1 Yr (%)	85.9	86.6	NS
4 Yrs (%)	46.4	51.6	

Chen et al, *Ann Surg* 2006

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## Hepatocellular Carcinoma Chemoembolization (TACE)

- Not considered curative
  - Prolongs survival
- Bridge to resection or transplant
- Primary therapy in pts who are not resection or transplant candidates
- Appropriate for large and hypervascular tumors

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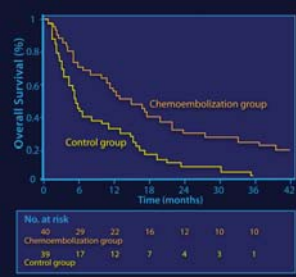
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## TACE as Primary Treatment of Unresectable HCC



	TACE	Control
Number of Pts	40	39
Overall Survival (%)		
1-Yr	57	32
2-Yr	31	11
3-Yr	26	3

*P=0.02*

Lo et al, Hepatology 2002

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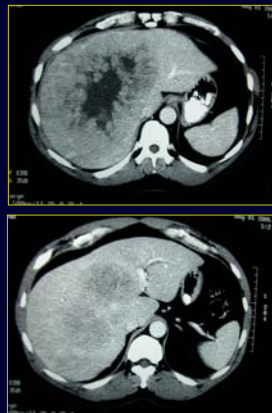
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### Case 6

60y/o M with hepatitis B, no cirrhosis, preserved liver function, and a large liver mass. AFP =3000.




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**The next step in management is:**

- a) Biopsy and sorafenib
- b) Biopsy then resection
- c) No biopsy; immediate resection
- d) No biopsy; TACE then resection if good response
- e) No biopsy; TACE then RFA

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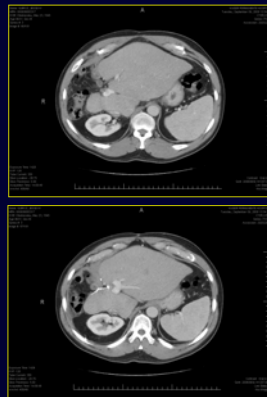
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**Case 6 Follow-Up**

- Underwent serial TACE
- AFP down to 110
- Extended rt hepatectomy w caudate resection
  - Path: 13.5 cm HCC, 90% necrosis, no LVI
- 2+ years NED



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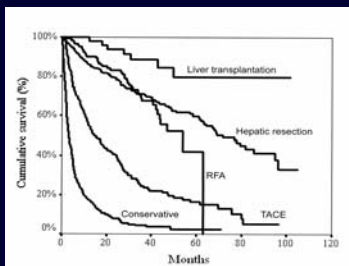
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**HCC**

**Results By Treatment Modality**

•1366 patients w/ HCC and chronic hepatitis, 1991-2004, Univ Hong Kong



from Chan et al, Ann Surg 2008

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## Peripheral Intrahepatic Cholangiocarcinoma

- Primary therapy is liver resection
- Survival s/p resection
  - median 8-50 months
  - 5-yr 13-44%
- Prognostic factors:
  - LVI
  - Regional nodal mets
  - R1/R2 resection
  - Tumor size



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## Extra-hepatic Cholangiocarcinoma Primary Treatment

Dependent on location of tumor in extra-hepatic bile duct

Lower 1/3

Pancreaticoduodenectomy

Middle 1/3

Extra-hepatic bile duct resection with regional node dissection

Upper 1/3 (Hilar)

En bloc hepatectomy with extra-hepatic bile duct resection and regional LND

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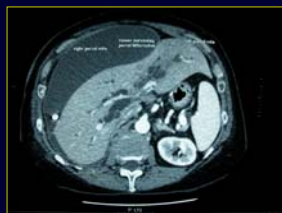
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## Extra-hepatic Cholangiocarcinoma Critical Determinants of Resectability

- Presence of distant metastases
  - Lung, liver, peritoneum
- Vascular involvement
  - Hepatic artery, portal vein
- Extent of tumor within biliary system
- Hepatic lobar atrophy



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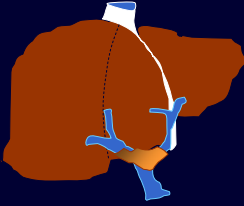
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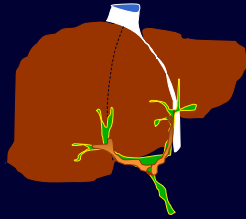
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## Hilar Cholangiocarcinoma Local Criteria for Unresectability

•Main portal vein involvement



•Bilateral duct involvement up to secondary biliary radicals




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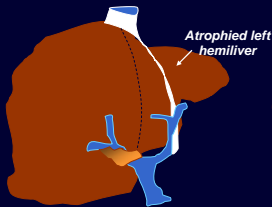
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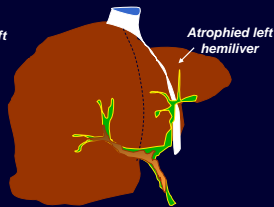
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## Hilar Cholangiocarcinoma Local Criteria for Unresectability II

•Unilateral lobar atrophy with  
contralateral portal vein involvement



•Unilateral lobar atrophy with  
contralateral involvement of  
secondary biliary radicals




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## Primary Resection for Bile Duct Cancer Selected Series

Series	Number of Patients	5-Yr Survival (%)	Median Survival, mo
Jarnagin 2001	80	27	35
Rea 2004	46	26	28
Zervos 2004	31	26	--
Jang 2005	151	32	27
Hemming 2005	53	35	40
Nagino 2006	132	27	--
Murakami 2007	43	44	26
Baton 2007	59	20	--

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## Liver Directed Therapy

### Summary

- Hepatic resection clearly of value in metastatic colorectal cancer
  - Few absolute contra-indications
- Evidence favors resection for metastatic NET
- Consider resection for other metastatic tumors with evidence of favorable tumor biology
- Multiple approaches for HCC

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