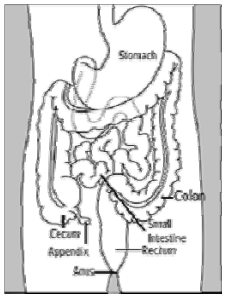
Colon Cancer Treatment

Christina Wu, MD
Division of Medical Oncology
The Ohio State University Wexner Medical Center

Colon cancer

- Incidence
- Risk Factors
- Screening
- Hereditary Syndromes
- Signs and Symptoms
- Diagnostic work-up
- Staging
- Treatment

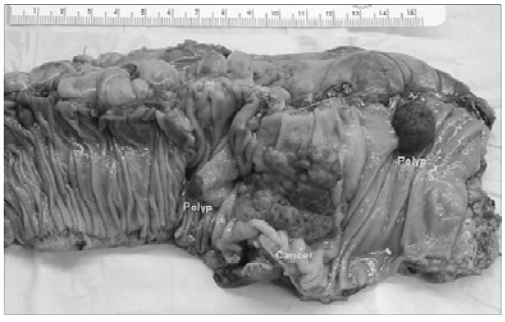
Colon cancer



Wikimedia Commons

Adenocarcinomas that occur anywhere along the large bowel (ascending, transverse, and descending) into the rectum.

Colon cancer



Wikimedia Commons

2012 Estimated US Cancer Cases*

		Men 848,170	Women 790,740		
Prostate	29%			29%	Breast
Lung & bronchus	14%			14%	Lung & bronchus
Colon & rectum	9%			9%	Colon & rectum
Urinary bladder	7%			6%	Uterine corpus
Melanoma of skin	5%			5%	Thyroid
Kidney & renal pelvis	5%			4%	Melanoma of skin
Non-Hodgkin lymphoma	4%			4%	Non-Hodgkin lymphoma
Oral cavity	3%			3%	Kidney & renal pelvis
Leukemia	3%			3%	Ovary
Pancreas	3%			3%	Pancreas
All Other Sites	18%			20%	All Other Sites

Source: American Cancer Society, 2012 — Source: American Cancer Society, 2012.

*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

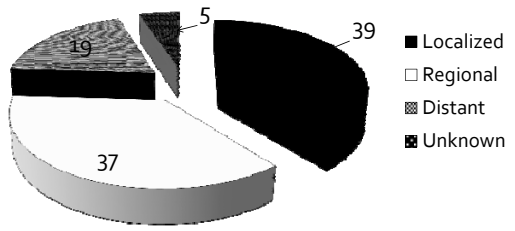
2012 American Cancer Society, Inc

2012 Estimated US Cancer Deaths

		Men 301,820	Women 275,370		
Lung & bronchus	29%			26%	Lung & bronchus
Prostate	9%			14%	Breast
Colon & rectum	9%			9%	Colon & rectum
Pancreas	6%			7%	Pancreas
Liver & intrahepatic bile duct	5%			6%	Ovary
Leukemia	4%			4%	Leukemia
Esophagus	4%			3%	Non-Hodgkin lymphoma
Urinary bladder	3%			3%	Uterine corpus
Non-Hodgkin lymphoma	3%			2%	Liver & intrahepatic bile duct
Kidney & renal pelvis	3%			2%	Brain/other nervous system
All other sites	25%			24%	All other sites

2012 American Cancer Society, Inc

Colorectal Stage Distribution at Diagnosis (%)



19 % patients have Stage IV disease on diagnosis
5 year-survival of Stage IV disease is 12%

Altekruse SF, Kosary CL, Krapcho M, et al. *SEER Cancer Statistics Review, 1975-2007*, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2007/, based on November 2009 SEER data submission, posted to the SEER web site, 2010.

Risk Factors

- **Personal or family history of colorectal cancer or adenomatous polyps before age 50**
- **Inflammatory bowel disease**
  - **Ulcerative colitis >Crohn's disease**
- **History of abdominal radiation**
- **Acromegaly (increased adenomas)**
- **Familial syndromes**
- **High fat and low fiber diets**
- **Obesity**

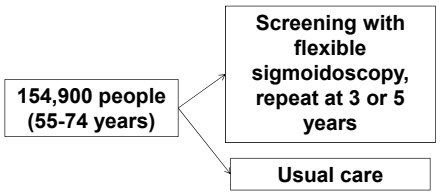
Protective factors

- NSAIDs
- Exercise
- High fiber, low fat diet
- Folic acid supplementation
- Vitamin D and calcium

Screening recommendations:

- 90% colon cancer cases occur after age 50
- Starting at age 50:
  - Fecal occult blood test (annually)
  - Flexible sigmoidoscopy (every 5 years)
  - Colonoscopy (every 10 years)
  - Air contrast barium enema (every 5 years)
- If patients are diagnosed with colon cancer, their 1st degree relatives should start having screening colonoscopies 10 years junior to their age at diagnosis or at age 50, whichever occurs earlier.

Screening decreases mortality



•21% reduction in incidence of colorectal cancer in the intervention group
•26% reduction in deaths from colorectal cancer in the intervention group
•50% reduction in mortality from distal colorectal cancer

Schoen et al. NEJM 2012;366:2345-2357.

Hereditary Syndromes

FAP

- Familial adenomatous polyposis (FAP)
- Germline mutation in the adenomatous polyposis coli (APC) gene
- 1% of all colon cancer
- Autosomal dominant
- Patients have hundreds to thousands of colonic polyps, which place them at high risk for mutation into tumors at a young age (45 years)
- Extracolonic tumors: CNS tumors, small bowel cancer, thyroid cancer, pancreatic cancer, gastric cancer pediatric hepatoblastoma

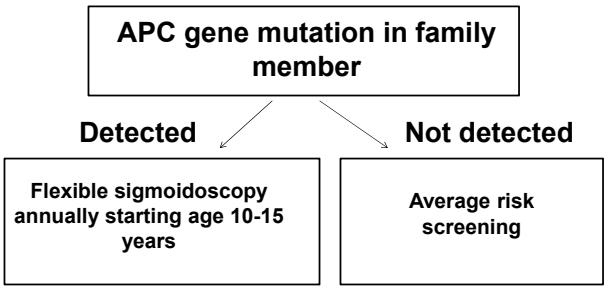
FAP

Wikimedia Commons

FAP- Personal history

- Treatment: proctocolectomy or colectomy
- Surveillance:
  - Endoscopic evaluation of remaining bowel
  - Upper endoscopy
  - Annual thyroid exam

FAP- Family history



HNPCC

- Hereditary Non-Polyposis Colorectal Cancer (HNPCC) or Lynch syndrome
- Germline mutation in genes involved in mismatch repair enzymes
  - Important in surveillance and repair of errors that occur during DNA synthesis
  - MLH1, MSH2, MSH6, PMS2
- 2-3% of all colon cancer
- Autosomal dominant
- Patients present at young age

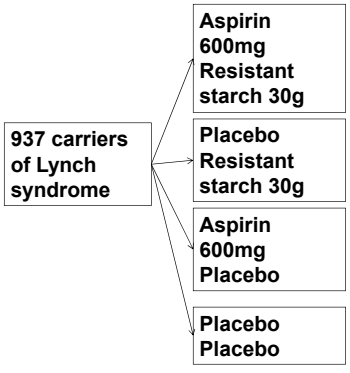
Amsterdam criteria for HNPCC

- ≥ 3 family members with colorectal cancer (≥ 2 first degree relatives)
- ≥ 2 successive family generations affected
- Colorectal cancer before age 50 in at least 1 family member
- FAP excluded

HNPCC

- Extracolonic tumors: breast, pancreas, gastric, gynecologic, and genitourinary cancers
- Screening recommendations:
  - Colonoscopy, age 20-25
  - EGD and duodenoscopy, age 30-35
  - Urinalysis, age 25-30
- Consider prophylactic hysterectomy and bilateral salpingo-oophrectomy

CAPP2 study



Aspirin intervention, follow-up at 55.7 months:
•**HR 0.63**
(95% CI 0.35-1.13, p=0.12)

2 year intervention with aspirin:
•**HR 0.41**
(95% CI 0.91-0.86, p=0.02)

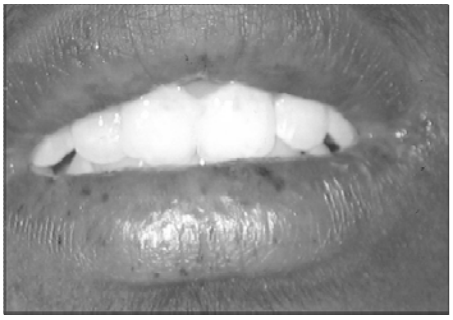
Primary outcome: Development of colon cancer

Burn et al. Lancet 2011;378:2081-2087.

Peutz-Jegher syndrome

- Germline mutation of serinine threonine kinase (STK11)
- Autosomal dominant
- Diagnosis: (2 of the following)
  - Freckling at the mouth, lips, fingers, and genitals
  - More than 2 hamartomatous polyps of small intestine
  - Family history
- Extracolonic tumors: breast, ovarian, testicular, pancreas, small intestine, stomach

Peutz-Jegher syndrome



http://www.gfmer.ch/genetic_diseases_v2/gendis_detail_list.php?cat3=231

Peutz-Jeghers syndrome

- Surveillance:
  - Mammogram, age 25
  - Upper endoscopy and colonoscopy, late teens
  - Pancreas imaging?, age 25-30
  - Small bowel imaging, age 8-10
  - Testicular exam, age 10
  - Pelvic exam and Pap smear, age 18-20

Signs and symptoms

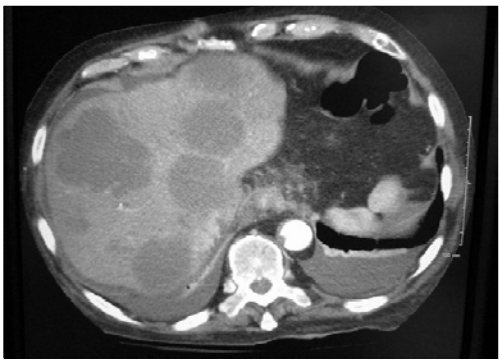
Signs and Symptoms

- Weight loss
- Fatigue
- Anemia
  - Microcytic ,due to iron deficiency
- Abdominal pain
- Melena
- Rectal bleeding
- Change in bowel movements
  - Constipation or diarrhea

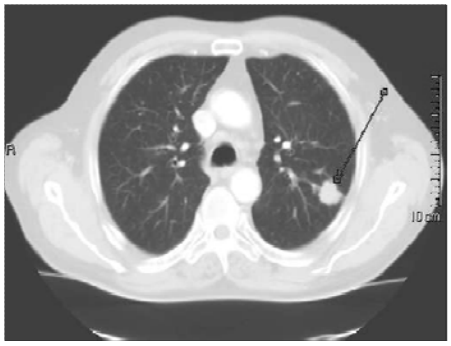
Diagnostic work-up

- CBC + differential
- Comprehensive metabolic panel
- Serum CEA
- Colonoscopy with biopsy

- CT chest/abdomen/pelvis
- PET/CT scan



Wikimedia Commons



Wikimedia Commons

Staging

Stage	Tumor	Node	Metastasis
I	T1-2	N0	M0
II	T3-4	N0	M0
III	Any T	**N1-2**	M0
IV	Any T	Any N	**M1**

Staging Affects Survival

Category	*SEER*				*SEER*	
TN	*Relative survival, 5-year (%)*	*SE*	*TNM stage, 6th ed*	*TNM stage , 7th ed*	*Observed survival, 5-year (%)*	*SE*
T1N0	97.4	0.6	I	I	78.7	0.5
T2N0	96.8	0.6	I	I	74.3	0.4
T3N0	87.5	0.4	IIA	IIA	66.7	0.6
T4aN0	79.6	1.0	IIB	IIB	60.6	0.8
T4bN0	58.4	1.3	**IIB**	**IIC**	45.7	1.0
T1-2N1a	90.7	1.5	IIIA	IIIA	73.7	1.2
T1-2N1b	83.0	2.0	IIIA	IIIA	67.2	1.6
T1-2N2a	79.0	3.6	**IIIC**	**IIIA/IIIB**	64.7	3.0
T3N1a	74.2	0.8	IIIB	IIIB	58.2	0.6
T4aN1a	67.6	2.0	IIIB	IIIB	52.2	1.5

AJCC 7th edition

Treatment

- **Surgery**
- **Chemotherapy**

- **Radiofrequency ablation**
- **Radiation therapy**

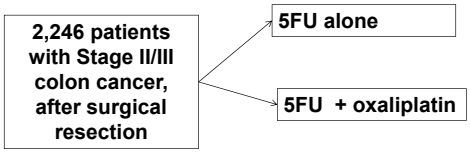
Resectable disease

- **Stage I**
- **Stage II**
  - **High risk: Tumor perforation, lymphovascular invasion, perineural invasion, high-grade histology, <12 lymph nodes sampled**
- **Stage III (lymph node involvement)**

Resectable disease

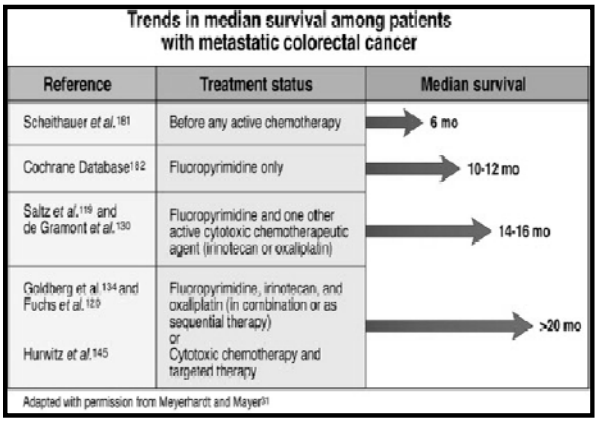
- **Adjuvant chemotherapy**
  - **Goal: Eradicate micrometastases, reduce the risk of recurrence of cancer and improve survival**
- **5-Fluorouracil (5FU)**
- **Capecitabine (Xeloda)**
- **Oxaliplatin**

MOSAIC trial



Stage	Intervention	Probability of surviving at 6 years
III	5FU	69%
	5FU +oxaliplatin	73% (20% reduction in risk of death)
II	5FU	87%
	5FU +oxaliplatin	87%

Andre et al. J Clin Oncol 2009;27:3109-3116,



Wolpin BM and Mayer RJ. Gastroenterology 2008.

Goals in Patients with Advanced Disease

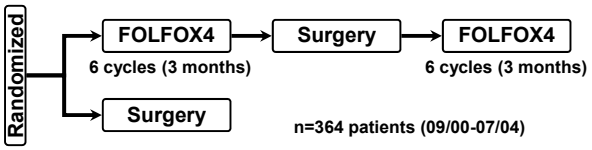
- **Resection if possible**
- **Conversion therapy if initial resection not possible**
- **Extension of length of life**
- **Maintenance of quality of life**

Metastatic disease

- Palliative chemotherapy
  - 5FU or capecitabine
  - Oxaliplatin
  - Irinotecan
- Biologic agents
  - VEGF pathway- bevacizumab, aflibercept
  - EGFR pathway- cetuximab, panitumumab
  - Regorafenib

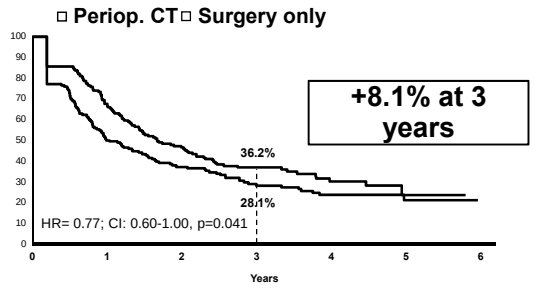
- Metastectomy
- Radiation therapy
- Radiofrequency ablation

EORTC 40983 – Peri-operative FOLFOX in Resectable Liver Metastasis



Nordlinger B, et al. Lancet 2008;371(9617):1007-16.

Progression-Free Survival in Eligible Patients



MOSAIC: Oxaliplatin difference in 3-yr DFS for stage III: +7.2%

Nordlinger et al. Lancet 2008

Complications of Chemotherapy

	With chemotherapy	Without chemotherapy
Post-operative complications	25.2 %	16 %
Post-op deaths	1 pt	2 pt

Treatment-Associated Liver Toxicity

- 5-FU: steatosis
- Irinotecan: steatohepatitis
- Oxaliplatin: sinusoidal/vascular injury
- Bevacizumab
  - Potential wound healing complications
  - Wait 6-8 wks before surgical resection
- Cetuximab: no known acute/chronic effects
- Incidence of postoperative complications increases with prolonged use

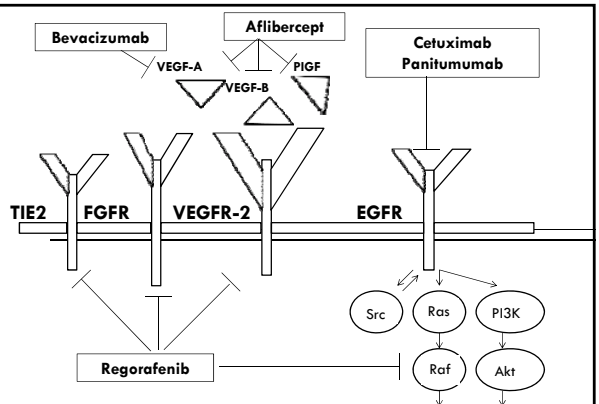


Figure 1. Signaling pathways that are targeted in colon cancer.

Survival for patients with metastatic colorectal cancer (mCRC)

Treatment	Median survival
No treatment	6 months
5-Fluorouracil	10-12 months
FOLFOX or FOLFIRI	14-16 months
Chemotherapy and bevacizumab	20-24 months

Anti-VEGF therapy

- Agents: Bevacizumab or aflibercept
- Administered: intravenously
- Side effects:
  - Hypertension
  - Proteinuria
  - Poor wound healing
  - Bowel perforation
  - Arterial thromboembolic events

Bevacizumab + IFL

Patients with untreated mCRC n= 813

IFL (irinotecan + bolus 5FU) n= 411

15.6 months OS 6.2 months PFS

20.3 months OS 10.2 months PFS

IFL + bevacizumab n= 402

Hurwitz H, et al. N Engl J Med 2004;350:2335-2342.

Anti-EGFR therapy

- Agents: Cetuximab or panitumumab
- Administered: intravenously
- Side effects:
  - Hypomagnesemia and hypocalcemia
  - Acneiform rash
    - Tx: Minocycline, hydrocortisone cream, sunblock
  - Hypersensitivity reaction
  - Pulmonary fibrosis

BOND-1

Patients with mCRC refractory to irinotecan n= 329

Cetuximab n= 111 patients

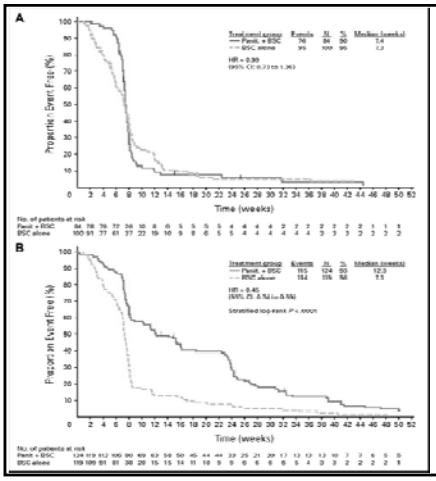
10.8% ORR 1.5 mo TTP

No Impact on Overall Survival

22.9% ORR 4.1 mo TTP

Cetuximab and Irinotecan n= 218 patients

Cunningham D et al. NEJM 2004;351:337-345.



KRAS results available for 92% patients

Progression-free survival by treatment within *KRAS* groups. Progression-free survival by randomized treatment in (A) mutant and (B) wild-type *KRAS* groups.

Amado R G et al. JCO 2008;26:1626-1634

Regorafenib

- Administered: orally
- Side effects:
  - Hand-foot syndrome
  - Hypertension
  - Diarrhea
  - Hepatotoxicity

In summary, colon cancer…

- 3rd most common cancer
- Screening starts at age 50
- Familial syndromes:
  - FAP, HNPCC, Peutz-Jegher syndrome
- Diagnostic work-up and staging
- Adjuvant chemotherapy to prevent cancer recurrence
- New targeted therapies for metastatic disease

Colon Cancer

Sherif R.Z. Abdel-Misih, MD, FACS
Assistant Professor - Clinical
Department of Surgical Oncology
The Ohio State University Wexner Medical Center

Outline

Surgical Treatments

Surgical Dogma

Surgical Advances

Surgical Treatments

- Primary Tumors
  - Surgical resection remains mainstay of curative therapy
  - Resection
    - Minimally invasive (Laparoscopic, Robotic)
- Metastatic Disease
  - Surgical resection
  - Local therapies
    - Ablation (RFA/Microwave)
  - Regional therapies
    - SIRT (selective internal radiation therapy – Y-90)
    - Isolated hepatic perfusion (IHP)
    - Hepatic artery infusion pump (HAIP)
    - Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

Minimally Invasive Surgery

- Technological advances allowed less invasive approaches more feasible
- Requires technical expertise and resources
- Initially questioned quality of oncologic resection and outcomes

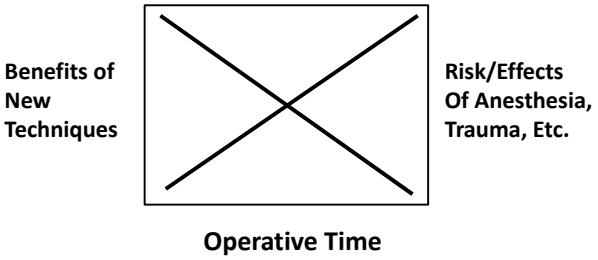
Minimally Invasive Surgery (MIS) Considerations

- Tumor Related
  - Location (Right/Sigmoid easier)
  - Size/Invasion
  - Localization
- Patient Related
  - Body habitus
  - Previous surgery
  - Comorbidities

MIS: Conversion to Open

- Occurs in 10-25 % cases
  - Body habitus
  - Prior surgery
  - Inflammation
  - Tumor size
  - Anatomic
- Not surgical failure
- Early conversion preserves outcomes

Benefits of Minimally Invasive Surgery (MIS)



MIS: Data and Literature

- What are the benefits?
  - Return of bowel function (1-2 days earlier)
  - Decreased pain (less narcotics)
  - Length of stay (1 day less)
  - Earlier return to work/activities
  - Expectation bias may play a role

MIS: Outcomes

- Cost
  - Increased OR/time costs
  - ?Balance by shorter hospital stay
- Oncology
  - Are cancer outcomes preserved with MIS?

COST (Clinical Outcomes of Surgical Therapy)

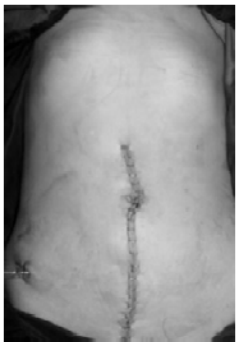
- 872 patients with colon adenocarcinoma
- Recurrence
  - 16% Laparoscopic
  - 18% Open
- Survival
  - 86% Laparoscopic
  - 85% Open
- Hospital Stay
  - 5 days Laparoscopic
  - 6 days Open

N Engl J Med 2004;350:2050-9

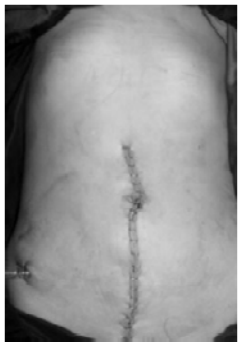
COST Trial
(Clinical Outcomes of Surgical Therapy) Trial

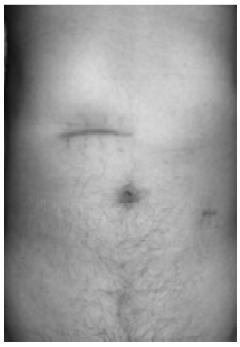
- 5 year data
- Disease-free 5 year survival
  - 68.4% Open
  - 69.2% Laparoscopic
- Overall survival
  - 74.6% Open
  - 76.4% Laparoscopic
- Recurrence
  - 21.8% Open
  - 19.4% Laparoscopic
- Replicated in other large trials (CLASICC - UK, COLOR - European)

MIS: Cosmesis



MIS: Cosmesis





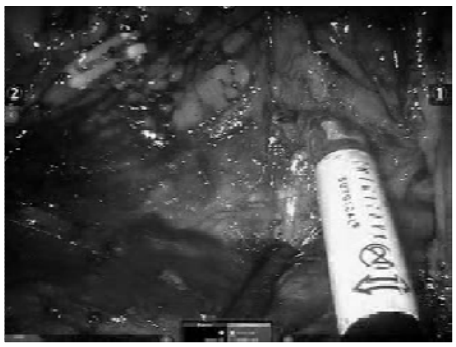
Robotic Surgery Benefits

- Same patient benefits as MIS
- Technical
  - Allows HD 3-D visualization
  - Facilitates fine, precise movement within confined spaces (pelvis, ENT)
- 39 pts Rectal adenocarcinoma
  - Oncologic principles feasible
    - (-) Margins, LN harvest adequate, TME
  - Safe (12.8% morbidity, 0 Mortality)
  - OR time increased (285 min.)
  - Length of stay (median 4 days)

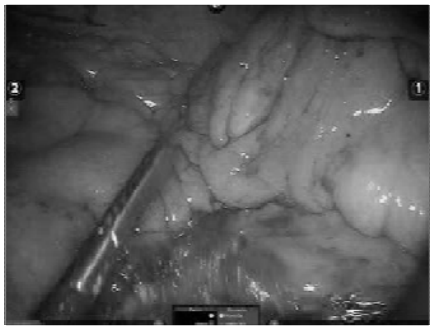
Hellan M. et al. Annals Surg Onc 2007; 14(11):3168-3173

MIS: Robotic Surgery

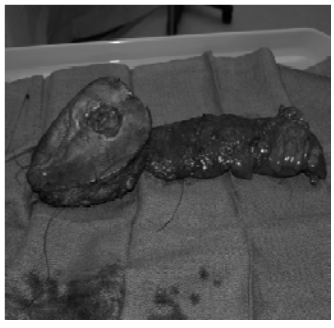
MIS: Robotic Surgery

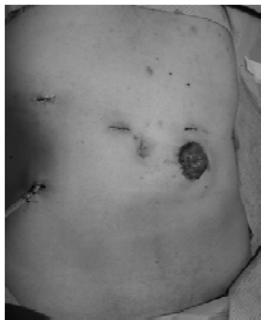


MIS: Robotic Surgery



MIS: Robotic Surgery





Colon Cancer Metastases

- Liver most common site
  - Approximate 50% incidence
  - Often only site
- Surgical resection remains mainstay of curative therapy
  - <20% amenable to resection
- Adjuncts to surgical resection
  - Ablation therapy (RFA, Microwave)
  - Minimally invasive approaches

Colon Cancer therapies

- Chemotherapy (marked advances)
- Surgery (Primary tumor, metastatic disease, isolated hepatic perfusion)
- Locoregional therapy
  - SIRT (Selective internal radiation therapy; y-90)
  - HAIP (Hepatic artery infusion pump)
  - Ablation therapy
  - HIPEC

Chemotherapy advancement

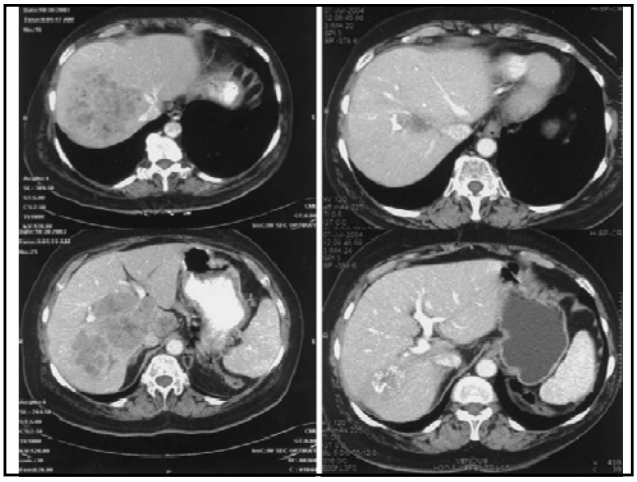
1996

- 5FU / Leucovorin

- Prolonged patient survival
- Induce disease/tumor shrinkage
- May allow resection in previously unresectable patients (response > 50%)
- Chemotherapy toxicities

2013

- Avastin(bevacizumab)
- Aflibercept (Eylea)
- Erbitux (cetuximab)
- Vectibix (panitumumab)
- Eloxatin (oxaliplatin)
- Camptosar (irinotecan)
- 5FU
- Xeloda (capecitabine)
- Tarceva (erlotonib)
- FUDR
- Leucovorin
- Levamisole
- Mitomycin-C



"Unresectability"

- Relative (eye of the beholder)
  - Expertise, Resources, Attitude
- Surgery Risk
  - Anatomic
  - Techniques
  - Mortality (20% in '80's →<5%
- Better Chemotherapy and imaging → Better patient selection

Surgical Dogma

- 'Unresectable'
  - Bilobar disease
  - >4 lesions
  - Extrahepatic/Metachronous disease
  - Lesions > 5cm
- SSO/SSAT/AHPBA Consensus
  - Dogma no longer valid; Important factors to consider for resection
    - Margin (-) resection
    - Complete resection/treatment of all intrahepatic/extrahepatic disease
    - Functional liver remnant with inflow/outflow/biliary drainage of >2 contiguous sectors(segments)

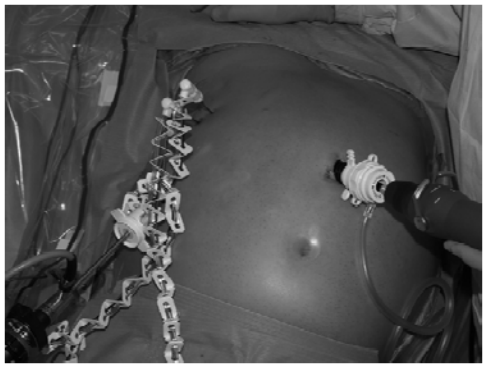
Locoregional therapies

- Ablation
- SIRT
- Isolate Hepatic Perfusion (IHP)
- Hepatic artery infusion pump (HAIP)
- Hyperthermic Intraperitoneal Chemotherapy (HIPEC)
- Indications
  - Unresectable disease
  - Medically unfit for hepatectomy
  - Poor biology (widespread extrahepatic disease, distant metastases, etc.)

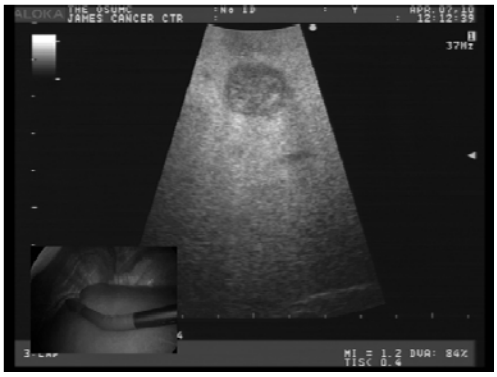
Ablation therapy

- Employs energy (radiofrequency or microwave) to cause tumor necrosis
  - RF uses high frequency AC current
  - Microwave uses electromagnetic waves at microwave energy for tissue heating
- Limited damage to surrounding liver
- Open, laparoscopic, percutaneous approaches
  - Efficacy: Open>Laparoscopic>Percutaneous
  - Inferior to resection in survival and recurrence
- Limited by tumor size (3 cm), anatomy, and heat sink
- Adjunct to major resection

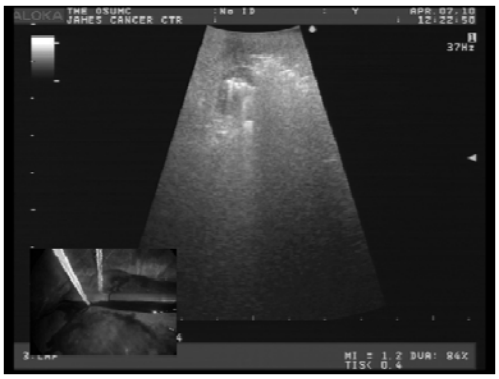
Laparoscopic MWA



Laparoscopic MWA

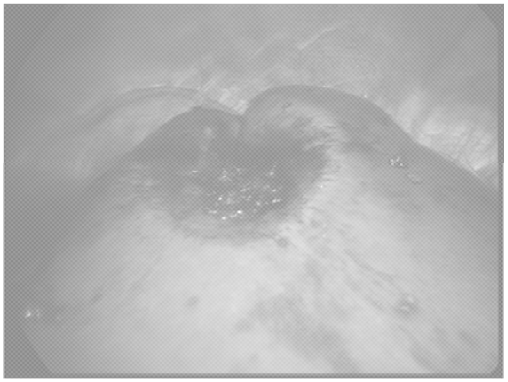


Laparoscopic MWA



Laparoscopic MWA

Laparoscopic MWA



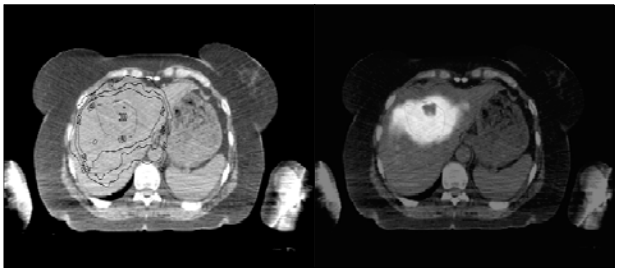
SIRT (yttrium-90 microspheres)

- Radiolabelled particles
  - TheraSpheres – MDS Nordion (HCC)
  - SIRSpheres – SIRTex (CRC)
- High dose radiation to tumor with low dose radiation to liver
- β particle emission with 2-3mm penetration
- Delivered into hepatic artery

SIRT procedure

- Pre-treatment
  - Hepatic angiogram, MAA (shunt study)
  - Embolization of gastroduodenal artery and other vessels as needed
  - LFTs
- Treatment
  - Hepatic artery catheterization and microsphere implantation
- Post-treatment
  - Gamma scan to confirm sphere location

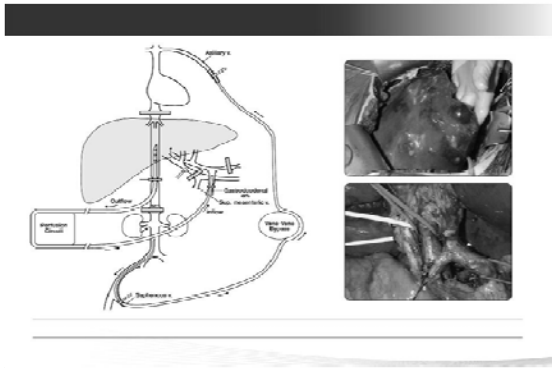
SIRT Post-gamma scan



Isolated Hepatic Perfusion (IHP)

- Goal to provide durable control of isolated diffuse liver metastases of select tumor types
- Hepatic artery major blood supply to liver tumors
- Allows intense treatment to cancer-burdened liver without systemic toxicity
    - Hepatic circulation isolated on a circuit to continuously perfuse chemotherapy under mild hypothermic conditions
- Major operation with associated morbidity

Isolated Hepatic Perfusion (IHP)



Alexander HR et al. Cancer Journal. 2010 Mar-Apr; 16(2):132-41 Slide 42

IHP Technique

- Liver vasculature isolated
- Hepatic temperature probes placed
- 1 hour of hyperthermic (40°C.) perfusion with high dose chemotherapy administration
- Liver flushed of chemotherapy after perfusion
- Vascular catheters removed and vessels repaired

IHP: Treatment Response

- In 114 pts, 59% response rate seen
- Median progression free survival 7 months
- May be useful in conjunction with adjuvant chemotherapy in very select patients

TABLE 4. Treatment Results With IHP for 120 Patients With CRC Liver Metastases Treated With IHP

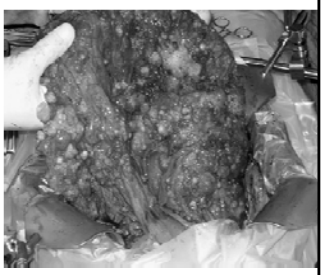
Treatment	n*	CR	PR	%	Hepatic PFS (m)
Overall	114	2	67	59	7.0
IHP (no HAI)	58	0	33	57	5.8
IHP (HAI)	46	2	30	65	13.0†
IHP (TNF alone)	10	0	4		3.0

*Evaluable for response.
†$P < 0.001$ vs. IHP (no HAI) and IHP (TNF alone).

Alexander HR et al. Ann Surg Onc 2009

Peritoneal Metastases (PM)

- PM late manifestation of advanced cancer of various tumor types
- Poor prognosis and outcomes (avg 6 mos. survival)
- Significant treatment challenge
- Limited options



Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for Peritoneal Metastases

- Historical therapy: Chemotherapy, radiation, and palliative surgery
- Aggressive surgical approach: Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC)
- Utilized in very select patients with different tumor types (incl. colon, appendix)

Cytoreductive Surgery (CRS)/HIPEC

- 2 Major components to surgery
  - Cytoreductive surgery (CRS)
    - Address gross (visible) peritoneal tumor burden
    - Goal is to eliminate all gross disease (<2.5mm)
  - HIPEC
    - Address microscopic peritoneal disease after CRS
    - Regional perfusion utilizing hyperthermia and high dose chemotherapy

CRS

- Major Surgery
- Eliminate all gross tumor
  - May require peritonectomies
  - Multi-visceral (organ) resection sometimes necessary
- Completeness of cytoreduction important to outcome
- Increased morbidity and mortality

CRS: Completeness of cytoreduction

- Major determinant of survival
- Glehen et al. – Multi-institutional study of 506 pts receiving CRS/HIPEC
  - Overall median survival 19.2 mos
  - Complete CRS/HIPEC median survival 32.4 mos
  - Incomplete survival 8.4 months
  - P<0.0001

Glehen et al. JCO 2004

CRS: Predictive factors for success

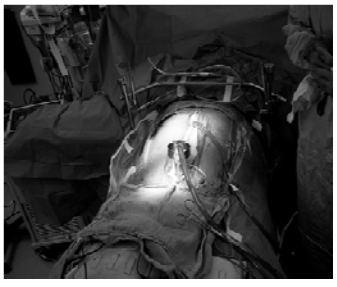
- Peritoneal Surface Malignancy Group determined 8 predictive factors
  - ECOG≤2
  - No evidence of extra-abdominal disease
  - ≤3 small, resectable liver metastases
  - No biliary obstruction
  - No ureteral obstruction
  - No bowel obstruction > 1 site
  - SB involvement
  - Small disease within lesser omentum

Esquivel, J Ann Surg Oncol 2007

HIPEC

- Hyperthermia
  - More toxic to cancer cells
  - Potentiates cytotoxic effects of chemotherapy
  - Direct effect on tumor tissue to soften the tissue and decrease interstitial pressure to improve chemotherapy penetration
- High dose chemotherapy administration with decreased systemic toxicity
- Continuous circulation of heated chemotherapy throughout the abdominal/peritoneal cavity

HIPEC



CRS/HIPEC Complications

- Potential significant complications
- Surgical morbidity 22.9%
- Mortality 4%

Table 5. Details of Major Postoperative Complications (grade 3/4 according to the National Cancer Institute's Common Toxicity Criteria)

Type of Complication	No.	%
Digestive fistula	42	8.3
Hematologic toxicity	12	2.4
Systemic sepsis	10	2
Postoperative bleeding	9	1.8
Intra-abdominal abscess	9	1.8
Respiratory distress	8	1.6
Pneumonia	8	1.6
Urinary fistula	5	1
Line sepsis	5	1
Bowel obstruction	5	1
Pulmonary embolism	2	0.4
Peritonitis	2	0.4
Other	6	1.2
Combined morbidity	116	22.9
Mortality	20	4

Glehen et al. JCO 2004

HIPEC vs. Chemotherapy

- Verwaal et al. showed survival advantage for patients for patients with colorectal PC
  - Median survival 22.3 months (CRS/HIPEC/Chemo-5-FU/Leucovorin)
  - Median survival 12.6 months for chemotherapy with or without palliative surgery
  - P=0.032
- Selection bias?

Verwaal et al. JCO 2003

HIPEC vs. Chemotherapy

- Elias et al. Case control study of 96 patients
- CRS/HIPEC (Oxaliplatin) vs.. Modern chemotx (Oxaliplatin/Irinotecan)
- Median Survival
  - CRS/HIPEC 62.7 mos.
  - Chemotherapy 23.9 mos.
  - P<0.05

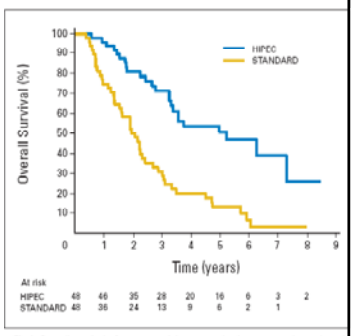


Fig 1. Overall survival of group receiving cytoreductive surgery, hyperthermic intraperitoneal chemotherapy (HIPEC), and systemic treatment versus those receiving standard treatment.

Elias et al. JCO 2009

CRS/HIPEC Summary

- May be an effective therapy in well selected patients with colorectal cancer and GI tumors
- Complete cytoreduction paramount
- Major morbidity/mortality associated with aggressive surgical approach
- Multidisciplinary approach necessary in decision making