The Renaissance of Cytoreduction and HIPEC

Nicholas Sich, MD, MS, FACS, FSSO

11/2/2025

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Overview:

- No Disclosures
- **Scope of Practice of Complex General Surgical Oncology**
- Overview of Cytoreductive Surgery and HIPEC
- Current/Expanding Indications for Management of Stage IV Cancer
- Palliative Indications
- Future State/Horizons for Previously Inoperable Patients

“Hi! Do you take care of _____???”

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Surgical Oncology / HPB Surgery: The Whipple Guy

- Hepatopancreaticobiliary Surgery
  - Pancreas Cancer
  - Liver Cancer
  - Bile Duct/Ampullary Tumors
- Upper Gastrointestinal Cancers:
  - Esophagus, Stomach, Small Bowel
- Solid Organ Metastatic Cancers:
  - Lung, Kidney, Head & Neck

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Surgical Oncology / Complex General:

- Lower Gastrointestinal Cancers
  - Colon Cancer, Rectal Cancer, Anal Cancer
- Sarcoma:
  - Extremity Soft Tissue Sarcoma
  - Retroperitoneal Sarcoma
  - Peripheral Nerve Sheath Tumors, Desmoid Tumors
- Skin
  - Melanoma, Merkel Cell, Squamous, Basal
- Endocrine:
  - Thyroid/Parathyroid, Adrenal
- Peritoneal Surface Malignancies:
  - Ovarian Cancer, Endometrial Cancer
  - Appendix Cancer, Colon Cancer, Mucinous Tumors
  - Gastric Cancer, Sarcoma
  - Palliative Surgical Malignancies
- Breast Cancer

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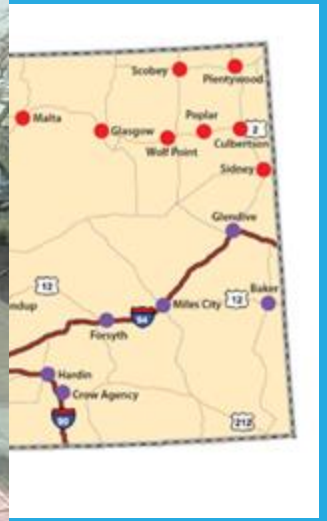
The Obligatory ‘About Me’ Slide



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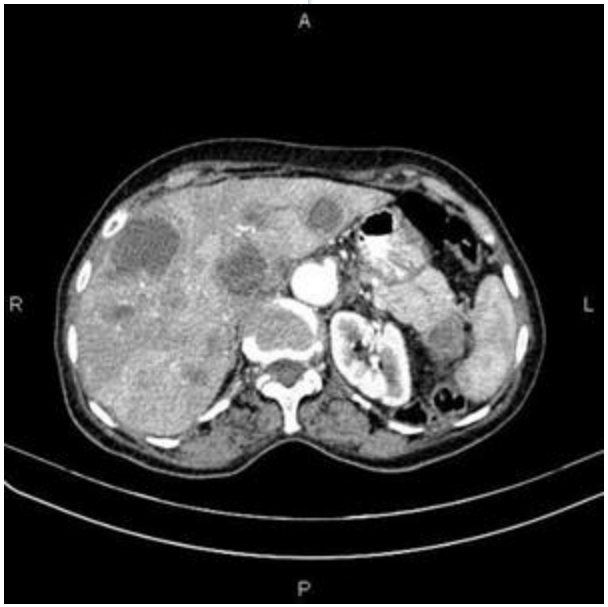
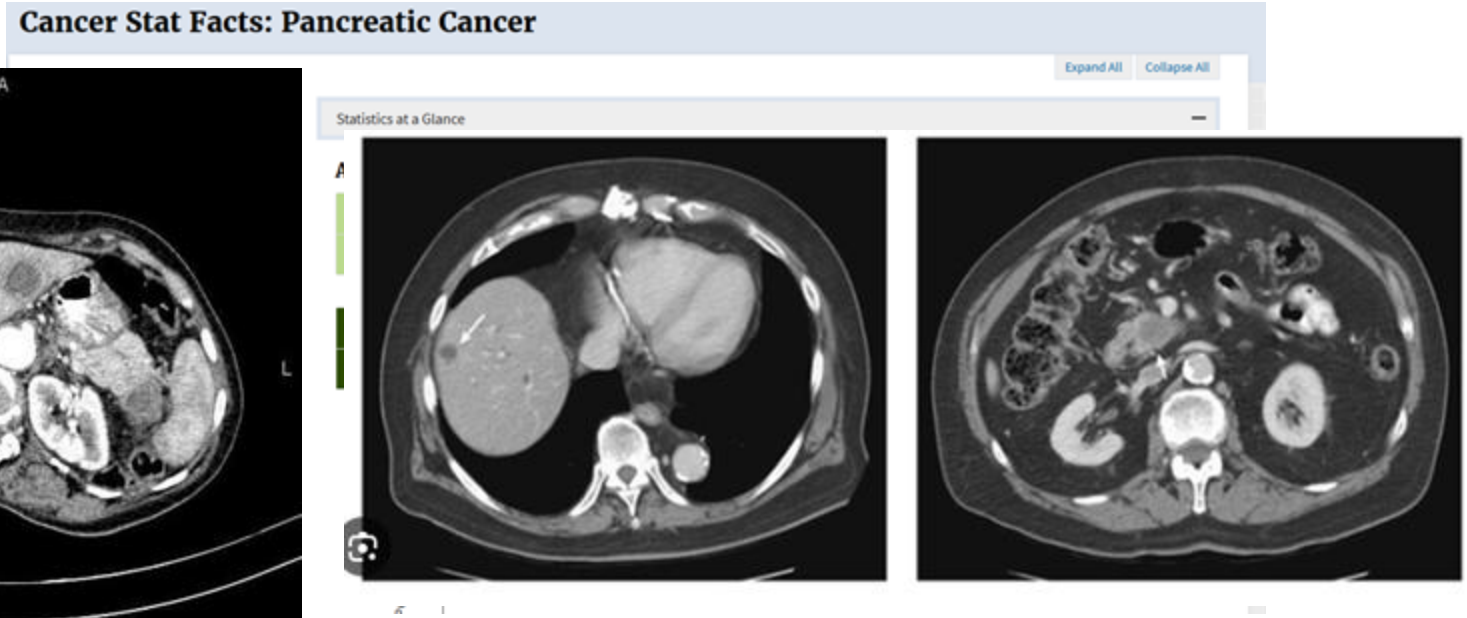
Stage IV Disease vs. “Stage IV” Disease





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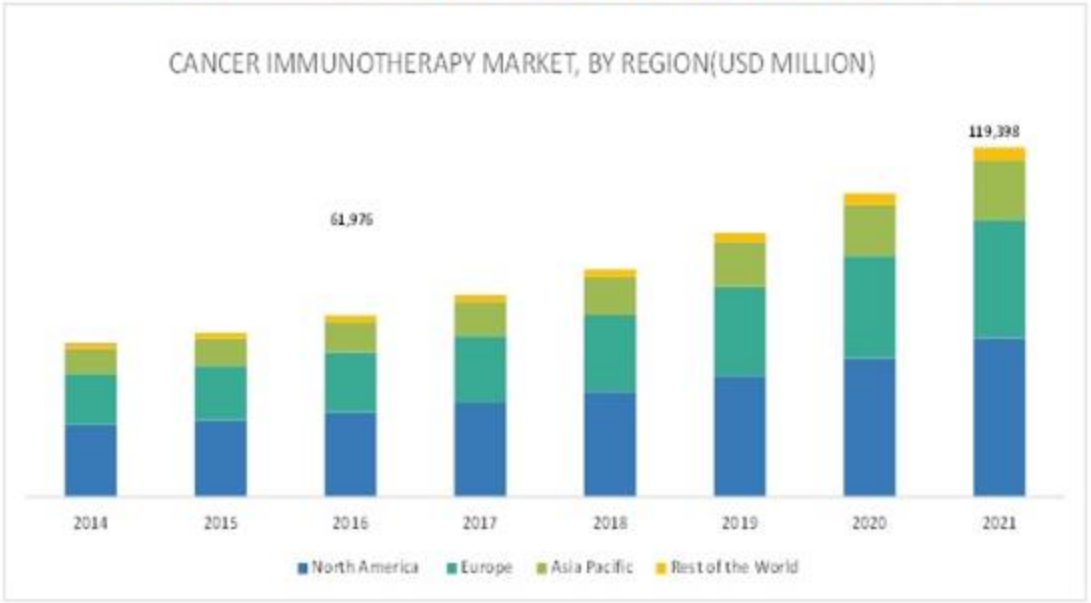
Stage IV Disease vs. “Stage IV” Disease

Global Cancer Immunotherapy Market, by Region, 2016-2021 (USD million)



- Advent of Immunotherapy
  - dMMR Testing
  - MSI Testing
  - PDL Testing
  - HER2 Testing
- Ubiquitous Adoption of Genetics
- Advances in Chemotherapy
- Advances in **Tolerance** of Chemotherapy
- Near Universal Multi-Disciplinary Cancer Patient Management

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What are you and your patients getting with “MDC” Review?

Surgeons

Medical Oncology

Radiation Oncology

Diagnostic Radiology

Interventional Radiology

Interventional Gastroenterology

Disease Specific Pathology

Genetics

Social Workers

Cancer Nurse Navigation

COC Registrars

Clinical Trial Eval

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MDC: Individualized Cancer Care of A New Age

Critical Reviews in Oncology/Hematology
Volume 173, May 2022, 103654

Surgical management of pancreatic cancer liver oligometastases

Rebekah Macfie, Yael Berger, Umut Sarpel, Spiros Hiotis, Benjamin Golas, Daniel Labow, Noah Cohen

The Mount Sinai Hospital, United States

Received 26 October 2021, Revised 8 March 2022, Accepted 9 March 2022, Available online 14 March 2022, Version of Record 31 March 2022.

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Published in final edited form as: J Hepatobiliary Pancreat Sci. 2023 Feb 7;30(8):1025–1035. doi: 10.1002/jhbp.1303

Oncologic resection of pancreatic cancer with isolated liver metastasis: Favorable outcomes in select patients

Minako Nagai [1,2], Michael J Wright [1], Ding Ding [1], Elizabeth D Thompson [3], Ammar A Javed [1], Matthew J Weiss [4], Ralph H Hruban [3], Jun Yu [1], Richard A Burkhart [1], Jin He [1], John L Cameron [1], Christopher L Wolfgang [5], William R Burns [1]

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Ovarian Cancer

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2024
Ovarian Cancer

recommendation based on the regimen selected for NACT or postoperative chemotherapy.

Table 18. Prospective Comparative Trials Testing HIPEC for Ovarian Cancer

Trial	Patients	Treatment Arms	HIPEC Method & Regimen	Surgical/Safety Outcomes, Arm A vs. B	Efficacy Outcomes, Arm A vs. B
Phase III non-R Single center Greece 2003–2009 Spiliotis 2011[914]	Recurrent after CRS + systemic chemo FIGO Stage IIIC–IV[a]	Arm A (n = 24): Secondary CRS →HIPEC →Postop chemo Arm B (n = 24): Secondary CRS →Postop chemo	Open technique 90-min perfusion at 42.5°C Cisplatin 50 mg/m²	PCI median: 21.2 vs. 19.8; NS CC-0 or CC-1: 83% vs. 66%; *P* < .01 Major or minor postoperative complications, grade 2–3[b]: 40% vs. 20%; *P* < .04	OS, median (months)[c]: 19.4 vs. 11.2; *P* < .05
Phase III RCT Single center Greece 2006–2013 Spiliotis 2015[915]	Recurrent after primary surgery + chemo FIGO stage IIIC, IV[d]; 63%, 37%	Arm A (n = 60): Secondary CRS →HIPEC →Postop chemo Arm B (n = 60): Secondary CRS →Postop chemo	Open/Closed technique: 66%/33% 60-min perfusion at 42.5°C For platinum-sensitive (n = 34): • Cisplatin 100 mg/m² + paclitaxel 175 mg/m² For platinum-resistant (n = 26): • Doxorubicin 35 mg/m² + paclitaxel 175 mg/m² • Doxorubicin 35 mg/m² + mitomycin 15 mg/m²	Extent of disease: • PCI <5: 12% vs. 13% • PCI 5 to <10: 40% vs. 37% • PCI ≥10: 48% vs. 50% Cytoreduction: • CC-0: 65% vs. 55% • CC-1: 20% vs. 33% • CC-2: 15% vs. 12%	OS, mean (months): mean 26.7 vs. 13.4; *P* = .006
Phase III RCT Multicenter Korea 2010–2016 Lim ASCO 2017[916]	Primary Stage III/IV Optimal CRS (<1 cm residual)	Arm A (n = 92): Primary CRS →HIPEC →Postop chemo Arm B (n = 92): Primary CRS →Postop chemo	90-min perfusion at 41.5°C Cisplatin 75 mg/m²	Extent of surgery: NS Residual disease: NS Blood loss, transfusion, neutropenia, thrombocytopenia: NS Hospital stay: NS Operative time (minutes): 487 vs. 404; *P* < .001 Postop morbidity/mortality: NS[e]	PFS, 5-y rate: 21% vs. 16%;NS OS, 5-y rate: 51% vs. 49%;NS Patients with NACT: PFS, 2-y rate: 37% vs. 30% OS, 5-y rate: 48% vs. 28%

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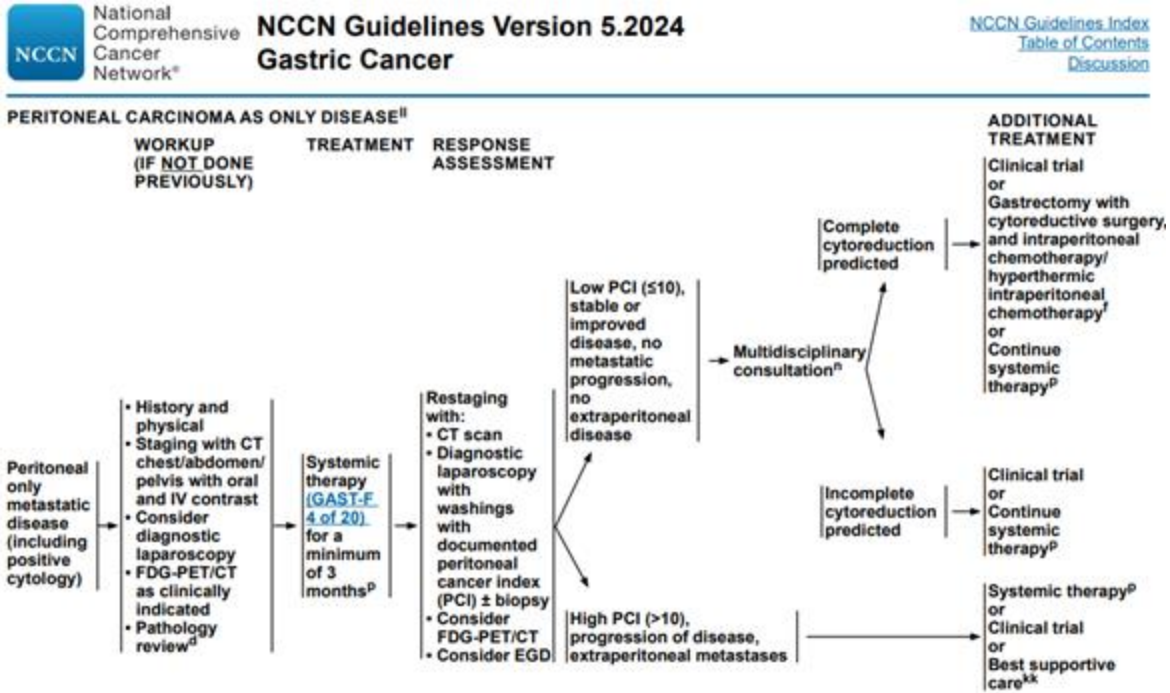
Gastric Cancer



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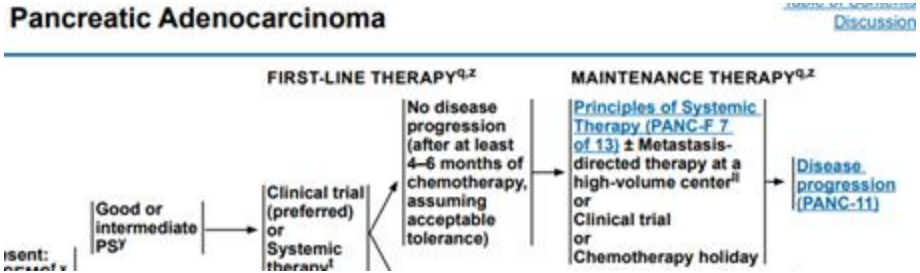
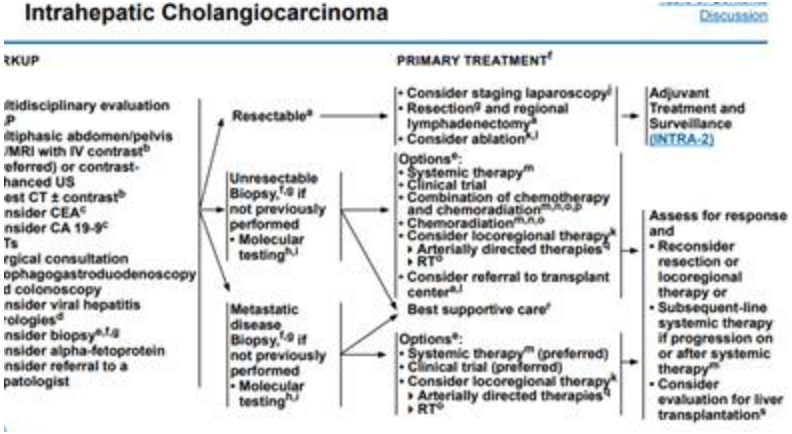
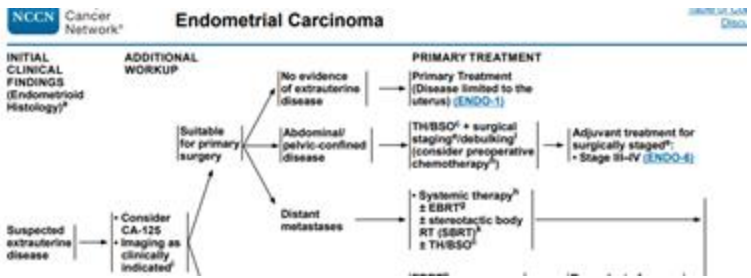
Stage IV Disease vs. “Stage IV” Disease

The Panel currently believes that complete CRS and/or intraperitoneal chemotherapy can be considered in experienced centers for selected patients with limited peritoneal metastases for whom R0 resection can be achieved. However, the significant morbidity and mortality associated with HIPEC, as well as the conflicting data on clinical efficacy, make this approach very controversial.







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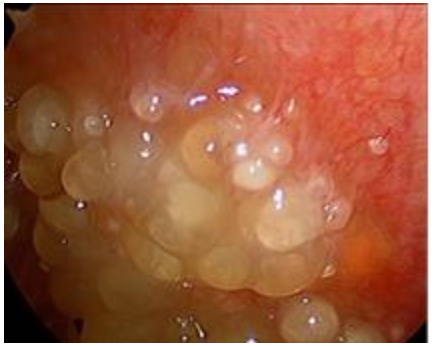
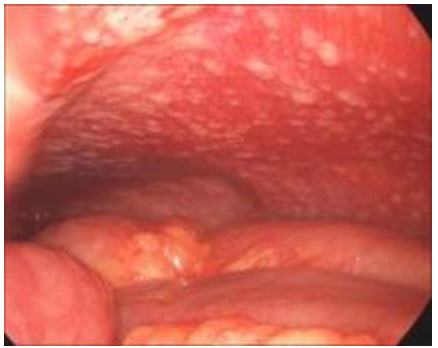
Peritoneal Carcinomatosis

- Peritoneal carcinomatosis (PC) represents a common form of tumor progression from primary abdominal tumors
- Usually remains in the peritoneal cavity
- Frequently terminal
- Accompanied by malignant ascites >50%
- 10-35% of recurrent colorectal cancer cases (higher for T4)
  - PC is the sole site of disease
- Untreated PC from CRC has a median survival of 7 months, which can be extended to 12 months with chemo





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Peltz J, et al., *BMC Cancer* 2010
Jayne DG et al., *Brit J Surg* 2002

What is Cytoreductive Surgery?

Hepatopancreaticobiliary Surgery
Surgical Oncology

Operative Report

[redacted]
Primary Care Physician: [redacted]
DOB: [redacted] Age: [redacted]

Admit Date: [redacted] Admit Diagnosis: Adenocarcinoma of jejunum (HCC) [C17.1]
Adenocarcinoma of small bowel (HCC) [C17.9]
Acute hypoxic respiratory failure (HCC) [J96.01]

Procedure Information

Date of Surgery: [redacted]

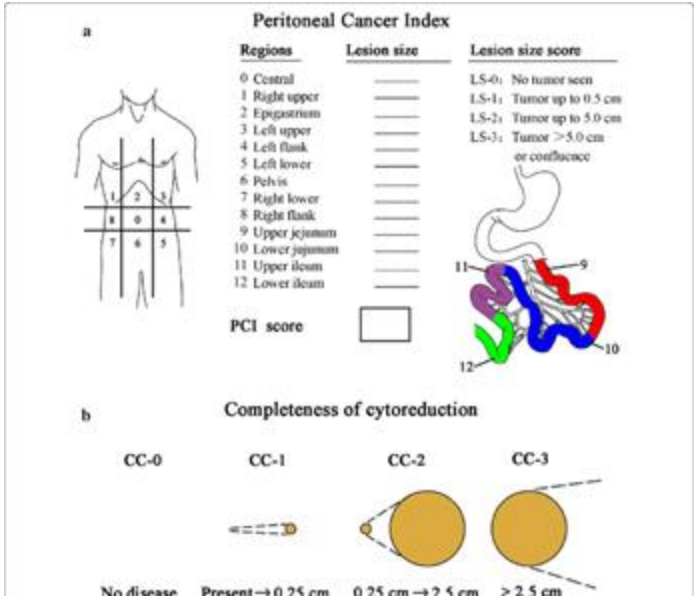
PREOPERATIVE DIAGNOSIS:
Small Bowel Proximal Jejunal Adenocarcinoma, Peritoneal Carcinomatosis

POSTOPERATIVE DIAGNOSIS:
Small Bowel Proximal Jejunal Adenocarcinoma, Peritoneal Carcinomatosis

PROCEDURE PERFORMED:
Cytoreductive Surgery:

1. Low Anterior Resection (Dr. Wagner primary, Sich Assist)
2. Right Ureteral Segmental Resection and Reconstruction over Stent (Dr. Borchert primary, Sich/Wagner Assist), Cysto
3. Additional Sigmoid Resection and End Colostomy
4. Complete Omentectomy
5. Splenectomy
6. Multi-Focal Partial Superficial Capsular Hepatectomies (Right Liver)
7. Right Full Thickness Partial Diaphragm Resection with Simple Linear Closure (10x5cm)
8. Left Full Thickness Partial Diaphragm Resection with Simple Linear Closure (1x1cm)
9. RUQ Complete Peritoneal Stripping (20x20cm)
10. LUQ Partial Peritoneal Stripping (10x10cm)
11. Pelvic Peritoneal Stripping and Paracolic Gutter Peritoneal Stripping (10x10cm)
12. Jejunal Primary Resection and Anastomosis
13. Additional Ileal Resection for Devascularized Segment and Mesenteric Metastasectomy with Additional Anastomosis
14. En Bloc Right Hemicolectomy, Abdominal Wall Resection RLQ, Partial Gastrectomy, Partial Cholecystectomy, Divestment of Duodenum with Primary Suture Repair of Serosa

SURGEON:
Nicholas Sich MD
Surgical Oncologist



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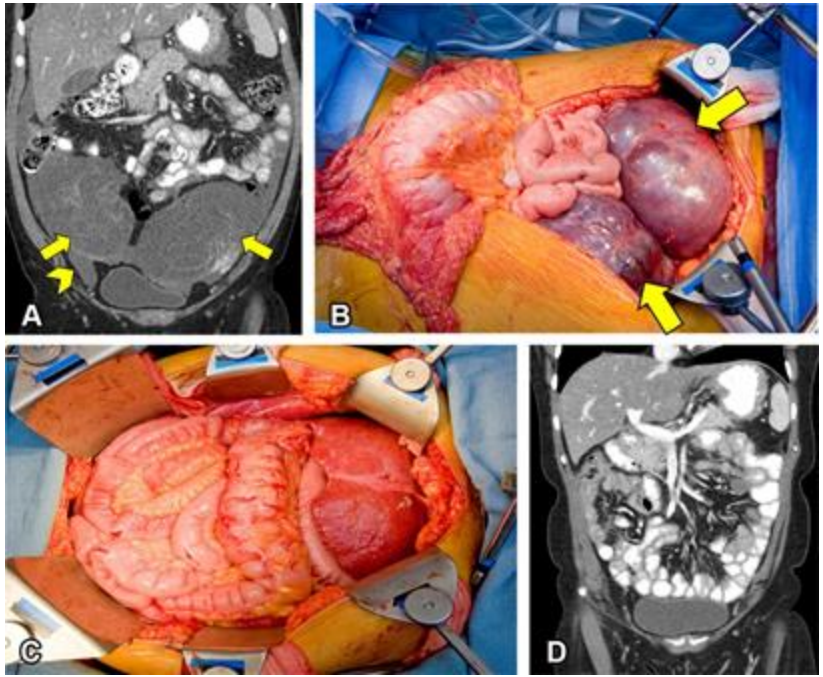
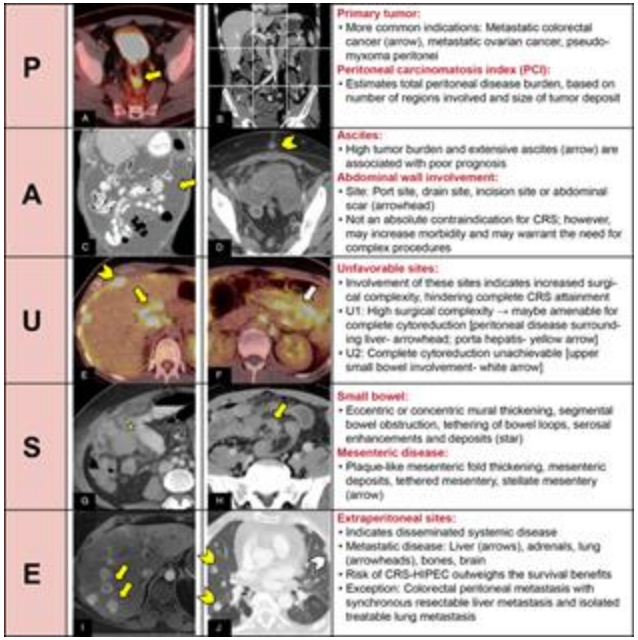
What is Cytoreductive Surgery?





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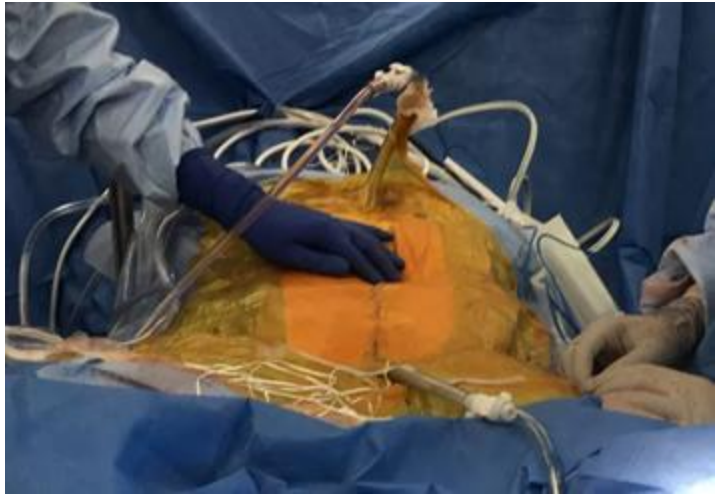
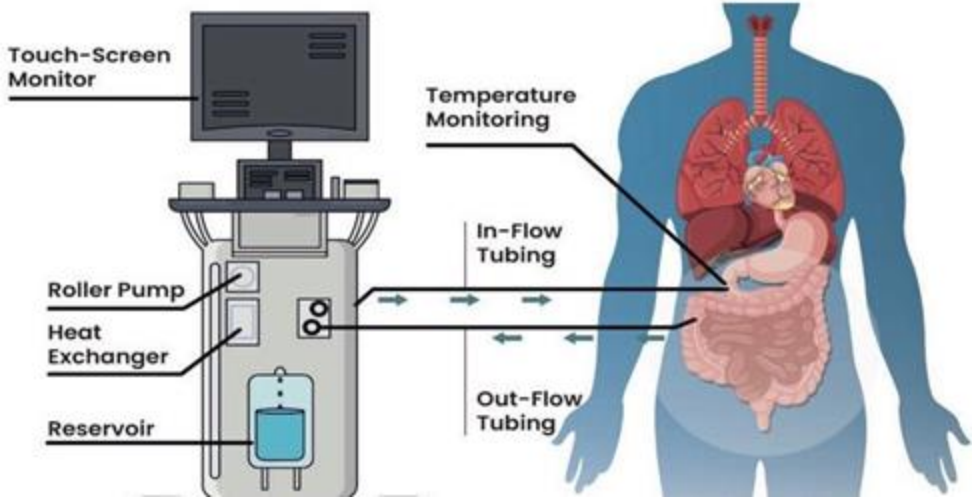
Images Courtesy of Srinivas Rao et al., Gastrointestinal Imaging May 1 2025 Vol 45(5)

What is HIPEC?





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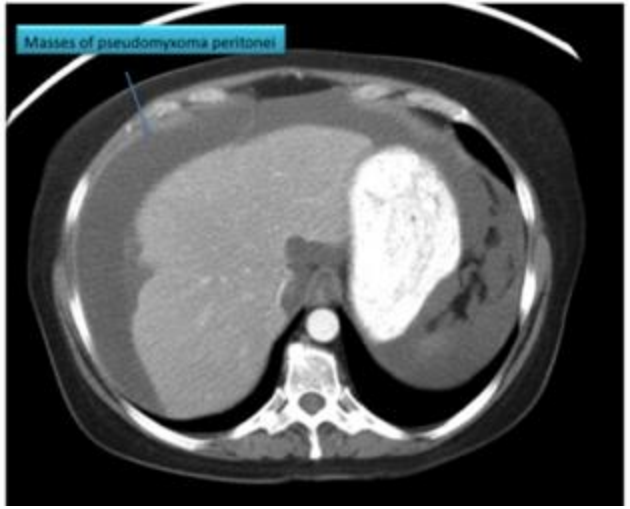
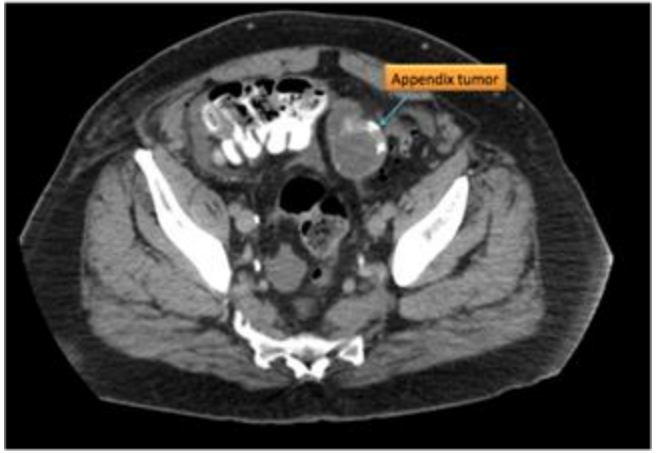
Cancers We Treat

- Pseudomyxoma Peritoneii
- Appendiceal Cancer
- Colon Cancer
- Gastric Cancer
- Peritoneal Mesothelioma
- Sarcomas
- Gynecologic Cancers
- Primary Peritoneal Carcinoma
- Mucinous Tumors
- Breast Cancer
- Bile Duct Cancers
- Neuroendocrine Tumors





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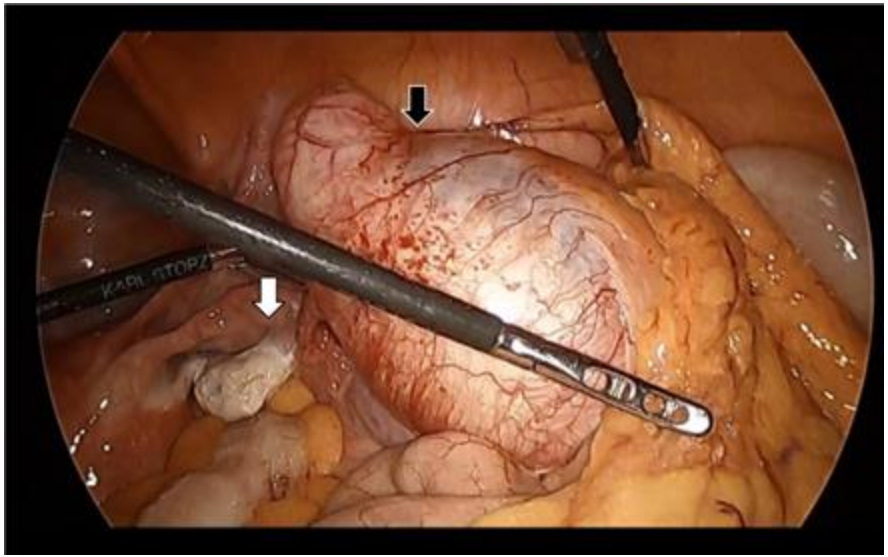
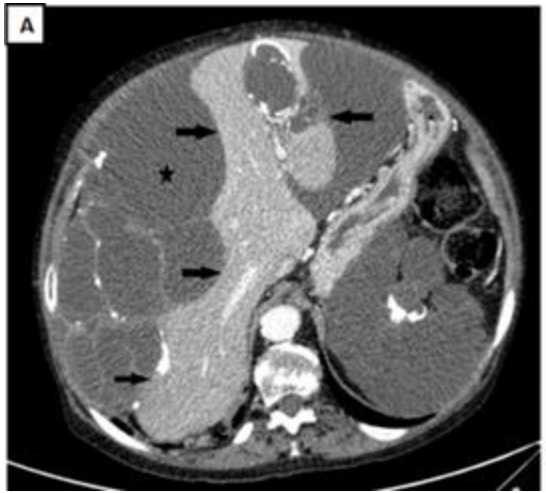
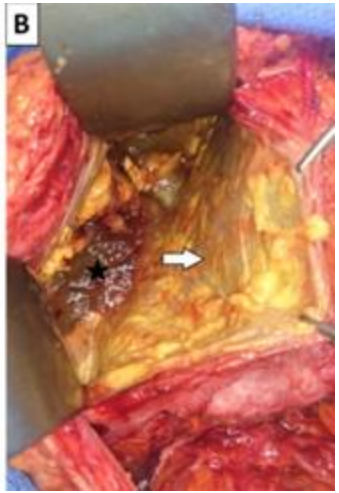
Appendix Cancer, LAMN







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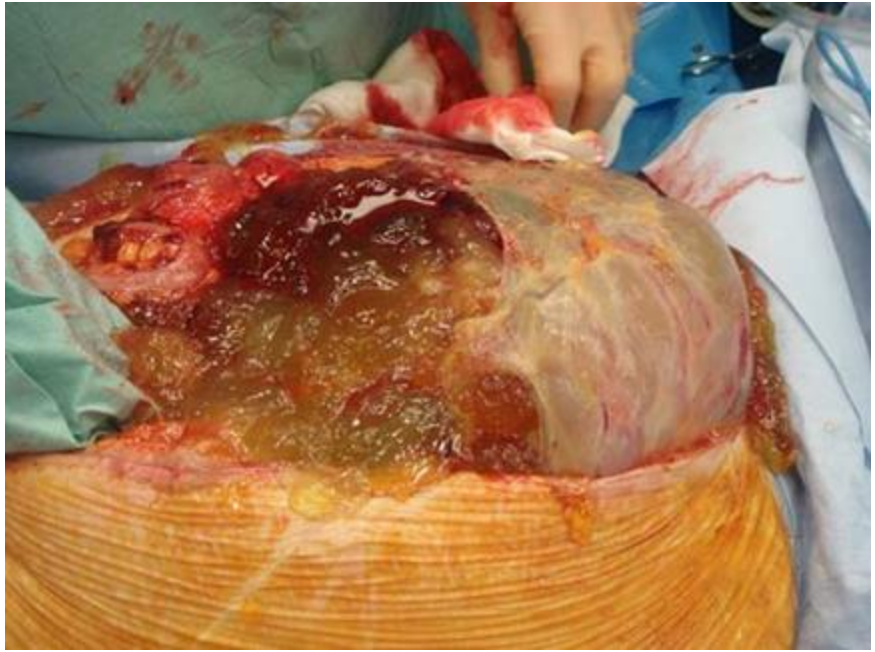
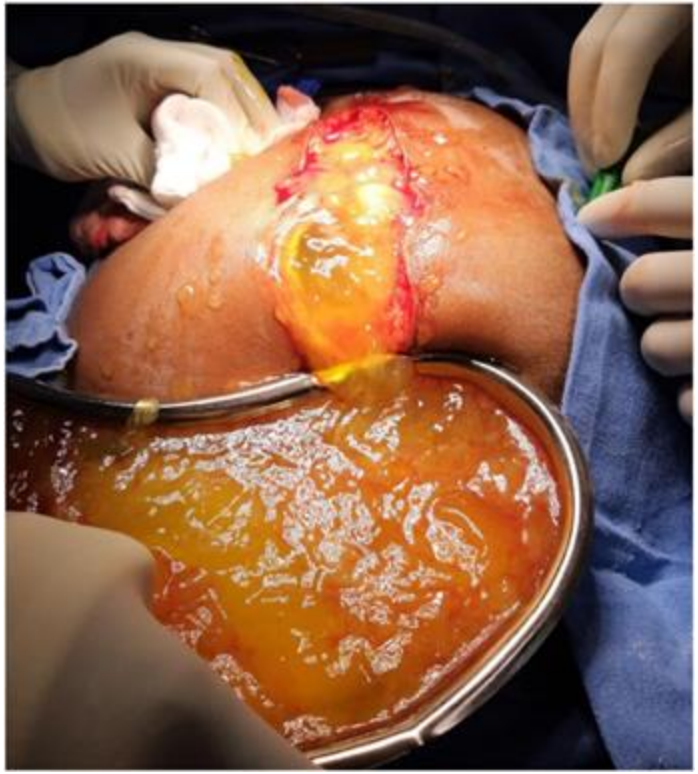
Pseudomyxoma Peritonei (PMP)





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What HIPEC Can/Cannot Do

Colorectal tumors	
PRODIGE 7. CRS offers a median survival of :	41 months
PROPHYLOCHIP. You start with peritoneal disease and go for 2nd look surgery at 6 months PD will be present in:	36% (26/71)
COLOPEC. You start with a High Risk T4N0/2 tumor. PD will be present at 6 weeks in :	9%
HIPECT4. You start with a High Risk T4N0/2 tumor - Peritoneal recurrence after omentectomy, BSO at 3 years :	15% (10/65)

Gastric tumors	
GASTRIPEC I. With HIPEC	PFS 7 months MFS 10 months

- HIPEC Can't…
  - Improve survival with conventional colon cancer (CRS does)
  - Prevent Peritoneal Metastases

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Palliative CRS/HIPEC

Cytoreductive Surgery with HIPEC is a Safe and Effective Palliative Option in Chemorefractory Symptomatic Peritoneal Metastasis

Chunmeng Zhang [1], Asish Patel [2], Dalton Hegeholz [1], Krista Brown [3], Valerie Shostrom [4], Mallory Pottebaum [1], Jason M Foster [5]

Affiliations + expand

PMID: 35211861 DOI: 10.1245/s10434-022-11323-8

Conclusion: CRS/HIPEC was performed safely in the palliative setting in patients with symptomatic progressive disease receiving multiple lines of chemotherapy. Median survival exceeded 1 year and factors associated with longer survival were optimal CRS and adjuvant chemotherapy. Liver metastasis did not preclude survival benefit in colon cancer patients. CRS/HIPEC can be considered for palliation but should be performed at high-volume centers.

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Palliative CRS/HIPEC Indications

- Malignant Ascites
- Refractory Bowel Obstruction
- Pain
- To Enable Chemotherapy

Two hundred and seventy seven patients were referred for CRS/HIPEC during the study period and 17 underwent 20 palliative procedures. Appendiceal (n = 6) and colorectal cancers (n = 6) were the most common malignancies. Ascites (n = 8) and bowel obstruction (n = 8) were the most common indications for intervention. The postoperative complication rate was 50% and major complication rate was 20%. Partial symptom improvement or resolution of symptoms was achieved in 18 (90%) cases. A durable symptom control at 90 d was achieved in 13 (65%) cases. The median time to symptom recurrence was 5.1 mo (interquartile range: 2-11.4), and the median overall survival was 11.6 mo (interquartile range: 3.8-28.5).

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Expanding Indications: Learning from Gyn-Onc

CRC:

Conclusion: CRS and HIPEC could be a treatment option for a carefully selected CPM patients performed by experienced surgeons. Overall survival of 41.50 months in palliative group compared to 16.8 months from conventional systemic CTx supports CRS and HIPEC even in palliative patients.

Ovarian Stage IV:

Outcomes in select initially diagnosed and unresectable SIV EOC are similar to SIII after NACT plus CRS/HIPEC. SIV EOC may benefit from CRS/HIPEC, and further studies should explore this treatment approach.

Bile Duct:

(p=0.007). Three-year overall survival was 30% and 10% for surgical and chemotherapy group, respectively.

Conclusion: Treatment with CRS and HIPEC for biliary carcinoma with peritoneal metastasis is feasible and may provide survival benefit when compared to palliative chemotherapy.

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CRC/PRODIGY 7

ARTICLES · Volume 22, Issue 2, P256-266, February 2021 Download Full Issue

Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy versus cytoreductive surgery alone for colorectal peritoneal metastases (PRODIGE 7): a multicentre, randomised, open-label, phase 3 trial

François Quénet, MD [a] · Prof Dominique Elias, MD [d] · Lise Roca, MSc [b] · Prof Diane Goéré, MD [d] · Laurent Ghouti, MD [e] · Prof Marc Pocard, MD [f] · et al. Show more

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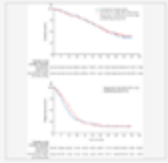
Summary

Background

The addition of hyperthermic intraperitoneal chemotherapy (HIPEC) to cytoreductive surgery has been associated with encouraging survival results in some patients with colorectal peritoneal metastases who were eligible for complete macroscopic resection. We aimed to assess the specific benefit of adding HIPEC to cytoreductive surgery compared with receiving cytoreductive surgery alone.

Figures (3) · Figure Viewer



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What We Don’t Know:

- Chemotherapy regimens for HIPEC remain variable.
- Perfusion times remain variable.
- The heat may be unnecessary.
- We have no idea if the shaking helps.
- Some surgeons still use an open technique (chemo bath); data is variable
- Some surgeons use intravenous chemotherapy during HIPEC
- In spite of the limitations and RCT data which ***specifically*** trends toward CRS being the backbone and HIPEC having limited utility, the procedures indications and patients seeking the operation continue to ***expand***.
- Surgical morbidity and mortality in high volume specialized centers continues to sharply drop; HIPEC used to carry a 8-10% mortality but now is 1-4%. Similar harm reductions in other high risk operations (whipple, major hepatectomy) have led to more aggressive surgical management.

Parting Thoughts:

- We want to cure it, and we're going to try.
- If we can't cure it, we want to turn it into a chronic disease and keep it at bay. Every day our patients don't have to think about cancer is a day that was worth the fight.
- If we can't keep it at bay, we will do everything in our power to either buy a little more time, make our patients a little more comfortable, or both.

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Thank you!

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