UCI University of California, Irvine

Colorectal Cancer in The Abdomen

Oliver Eng, MD, FACS, FSSO
Associate Professor of Surgery
Associate Director, Peritoneal Surface Malignancy Program
Associate Program Director, Complex General Surgical Oncology Fellowship
Co-Director, Student Clerkship
Vice Chair, Protocol Review and Monitoring Committee, Chao Family Comprehensive Cancer Center

Disclosures

- Speaker, Tempus Labs., Inc.
- Medical Advisory Board, Verywell Health/Health.com

Colorectal Cancer

- 3rd most common cancer diagnosed in the United States

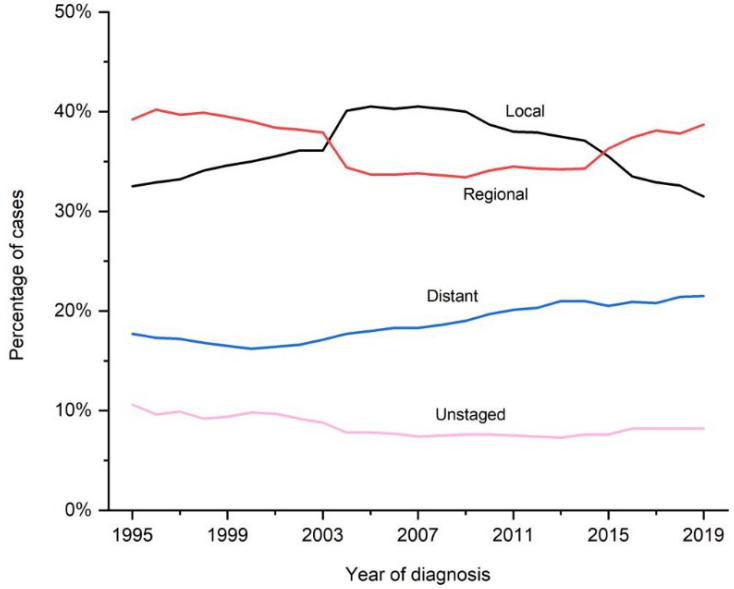
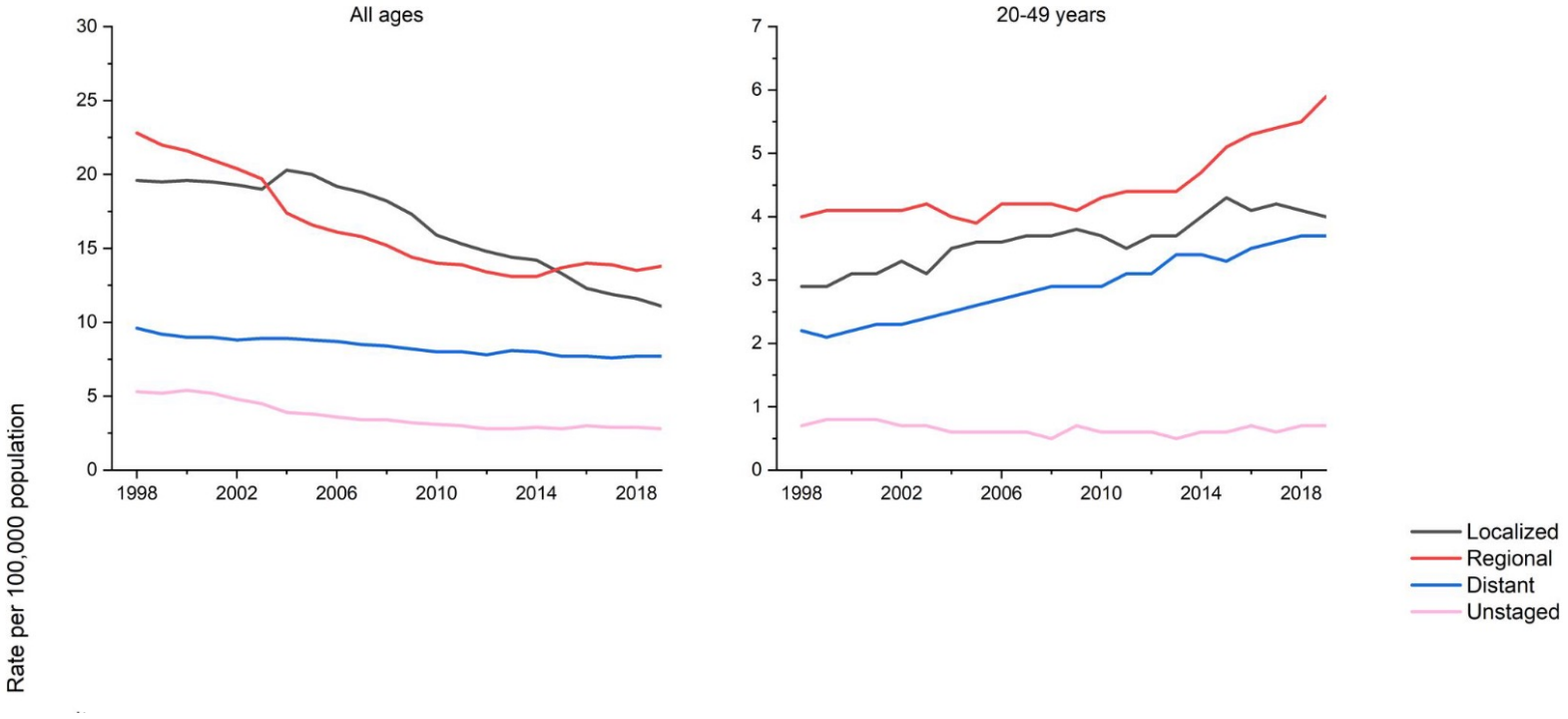


FIGURE 4 Trends in colorectal cancer stage distribution (%), 1995–2019, United States. Excludes appendiceal cancer. *Source*: North American Association of Central Cancer Registries, 2022.

Siegel et al, CA Cancer J Clin, 2023

Colorectal Cancer



Siegel et al, CA Cancer J Clin, 2023

Colorectal Cancer that Has Spread - Metastasis

- Management has evolved over the past several decades

- Concept of ”Metastasectomy”
  *Arch. Surg. **1997**—”Hepatic Resection for Metastatic Colorectal Cancer Results in Cure for Some Patients”*

- Reduction of Disease Burden → Resectability → Survival

Jamison et al, Arch Surg 1997

Abdomen - Peritoneum

Abdomen - Peritoneum

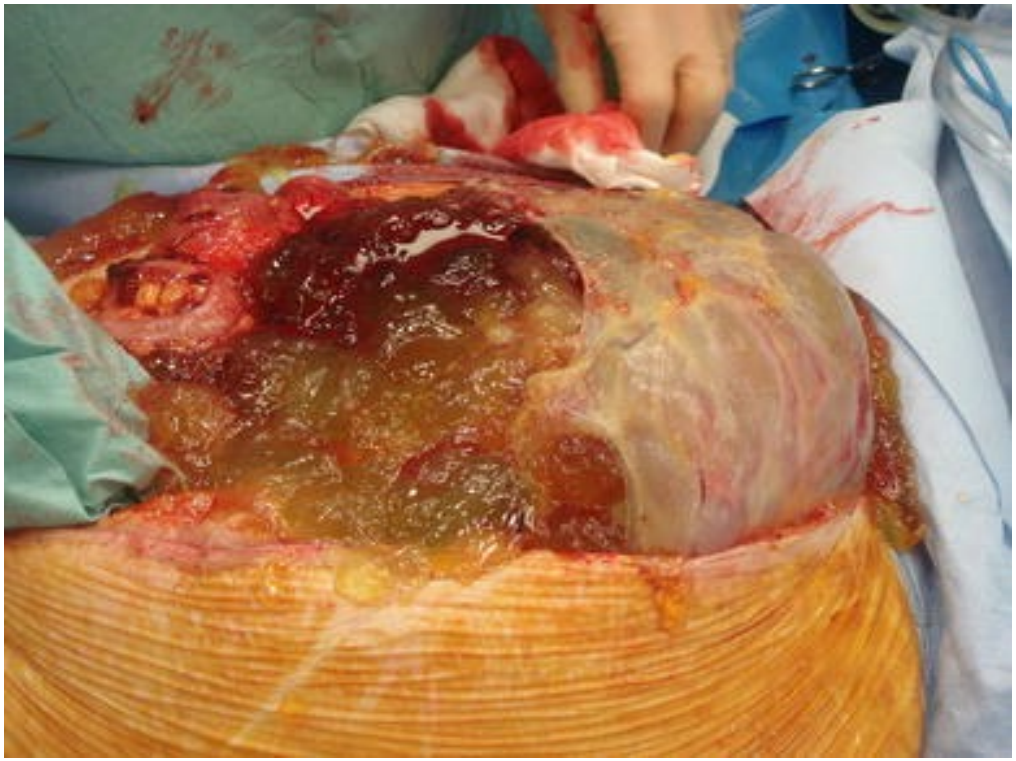
- Imaging under-representation
- Limited in detection <1cm diameter
- Imaging correctly predicted disease burden in 50% of patients

Table 4
Inter-rater agreement (κ)[a] between radiologists 1 and 2 for DW-MRI and CT for sites of disease.

	DW-MRI (κ)	CT (κ)
Omentum	**0.899**	0.458
Gastrohepatic ligament	0.316	0.000
Morrison's pouch	**0.683**	0.182
Spleen	0.038	0.040
Liver parenchyma	**0.646**	**0.649**
Liver surface	**0.695**	0.270
L diaphragm	0.385	0.064
R diaphragm	**0.690**	0.323
Mesentery	0.534	0.191
Cul de sac	**0.806**	**0.806**
Bladder peritoneum	0.041	0.000
Pelvic or para-aortic lymph nodes	0.571	0.092

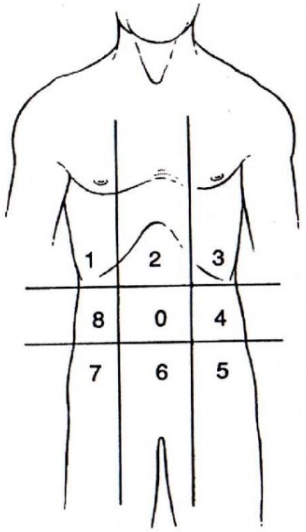
[a] $\kappa > 0.61$ represents substantial inter-rater agreement.

Fehniger et al, Gyn Onc 2016
Low et al, ASO 2015



Mirnezami et al, Tech in Coloproctology 2009

Peritoneal Cancer Index

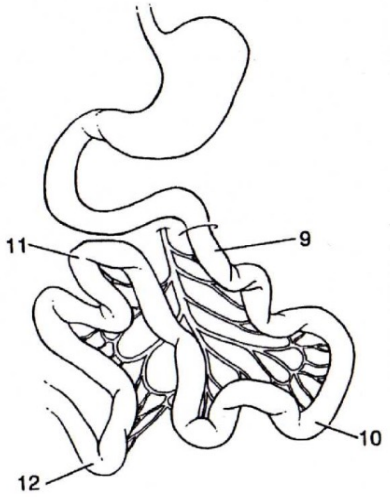


Regions	Lesion Size
0 Central	____
1 Right Upper	____
2 Epigastrium	____
3 Left Upper	____
4 Left Flank	____
5 Left Lower	____
6 Pelvis	____
7 Right Lower	____
8 Right Flank	____
9 Upper Jejunum	____
10 Lower Jejunum	____
11 Upper Ileum	____
12 Lower Ileum	____

PCI ☐

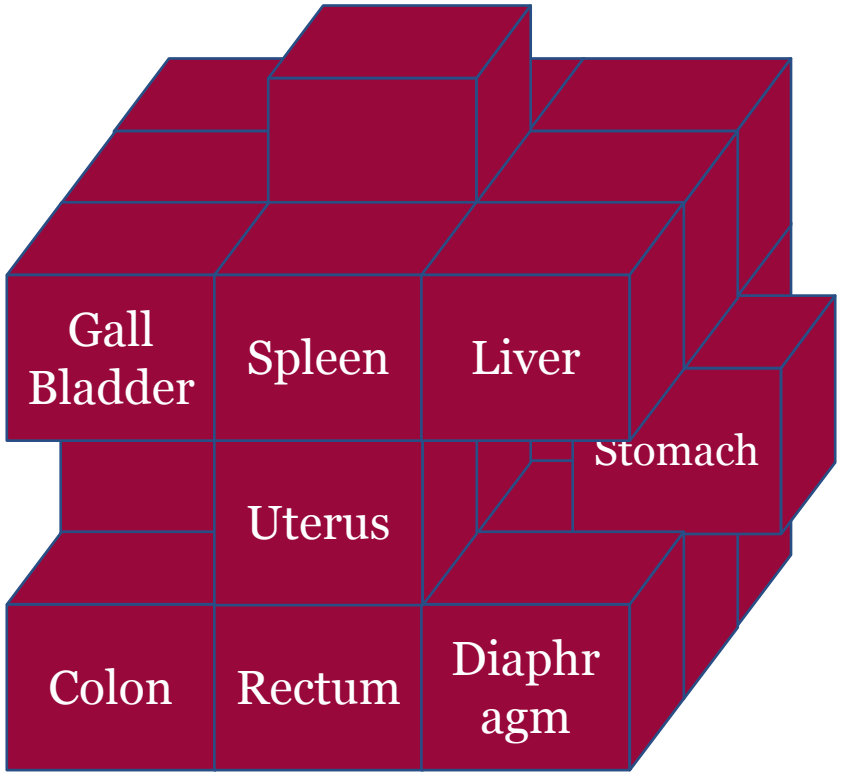
Lesion Size Score

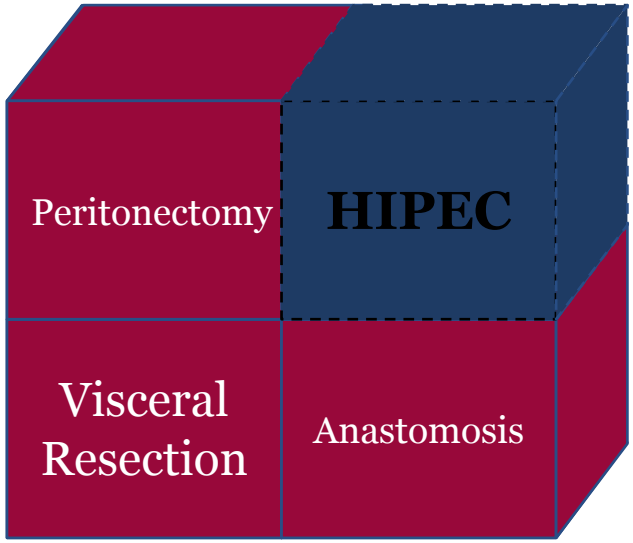
LS 0 No tumor seen
LS 1 Tumor up to 0.5 cm
LS 2 Tumor up to 5.0 cm
LS 3 Tumor > 5.0 cm or confluence

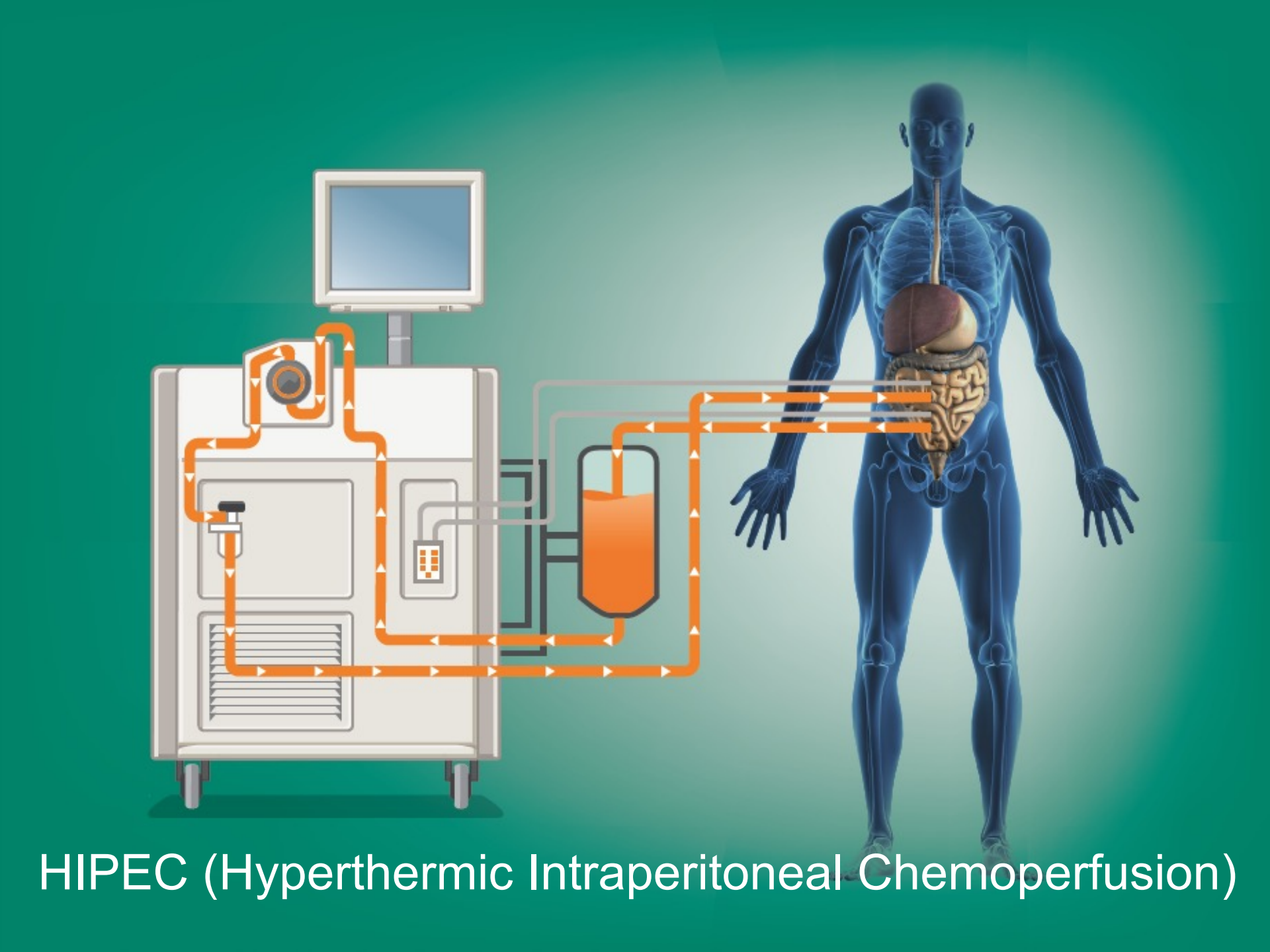


Sugarbaker, 1996

Cytoreductive Surgery (CRS)





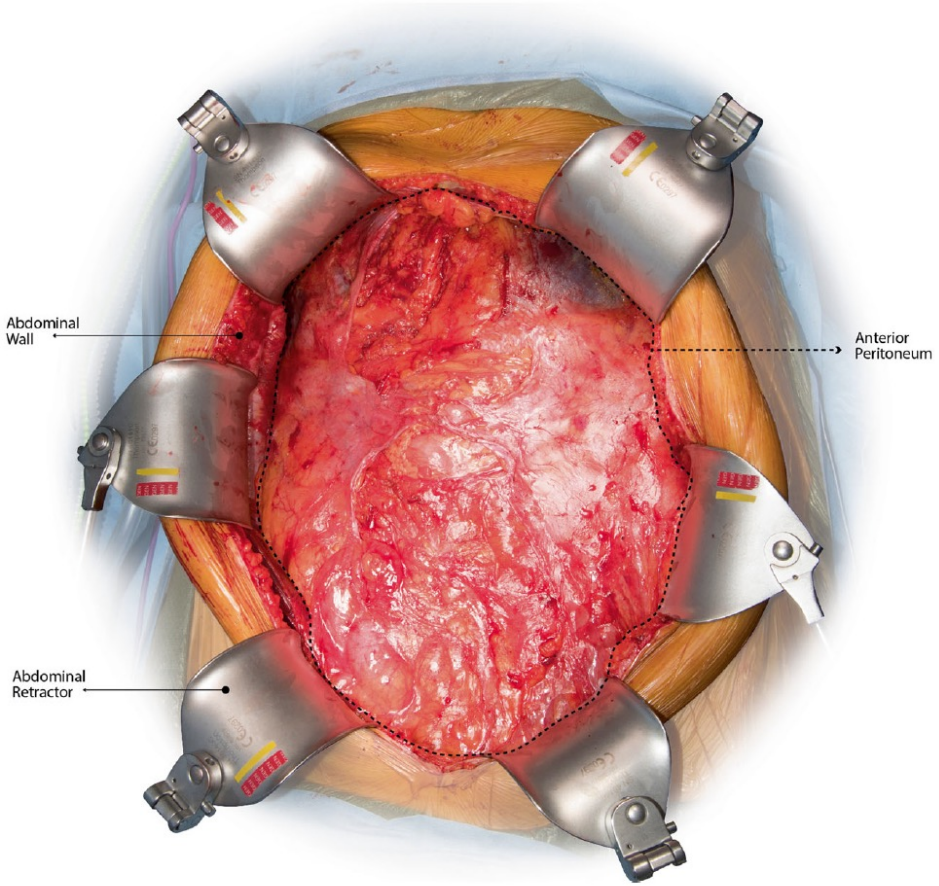


HIPEC (Hyperthermic Intraperitoneal Chemoperfusion)

Cytoreductive Surgery—How do we do it?

Cytoreductive Surgery—How do we do it?

Fig. 1 Anterior peritonectomy



Izquierdo et al, JOGS 2019

Cytoreductive Surgery—How do we do it?

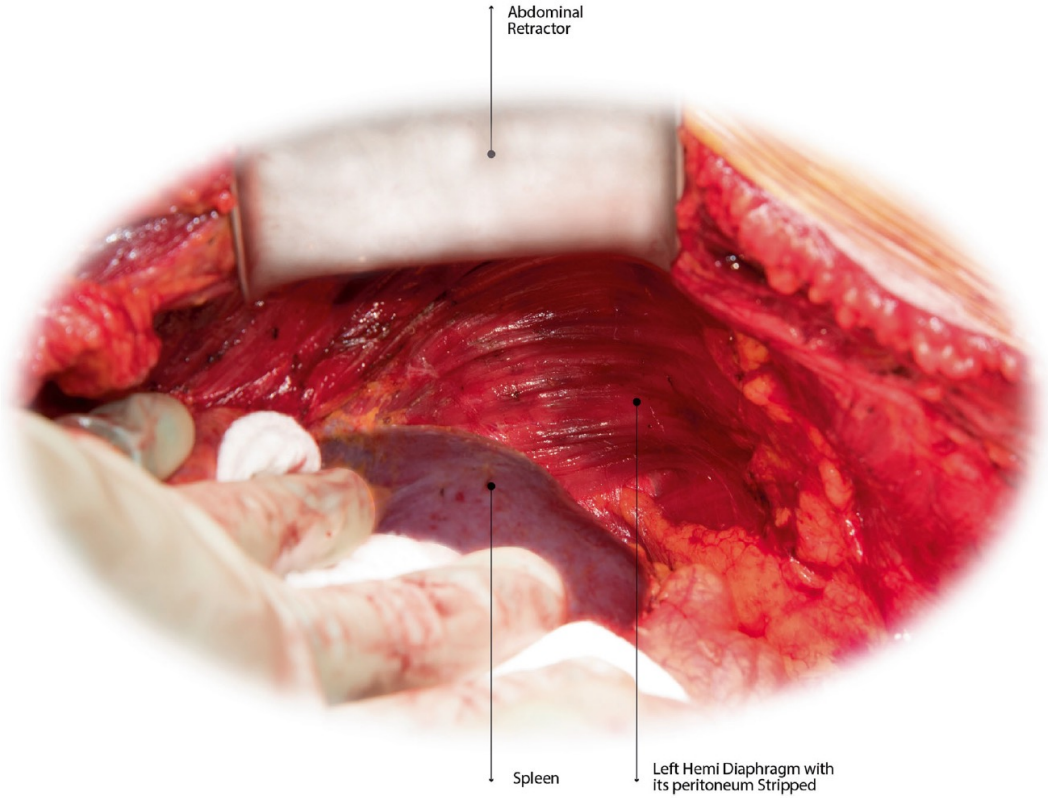


Fig. 2 Completed left upper quadrant peritonectomy

Izquierdo et al, JOGS 2019

Cytoreductive Surgery—How do we do it?

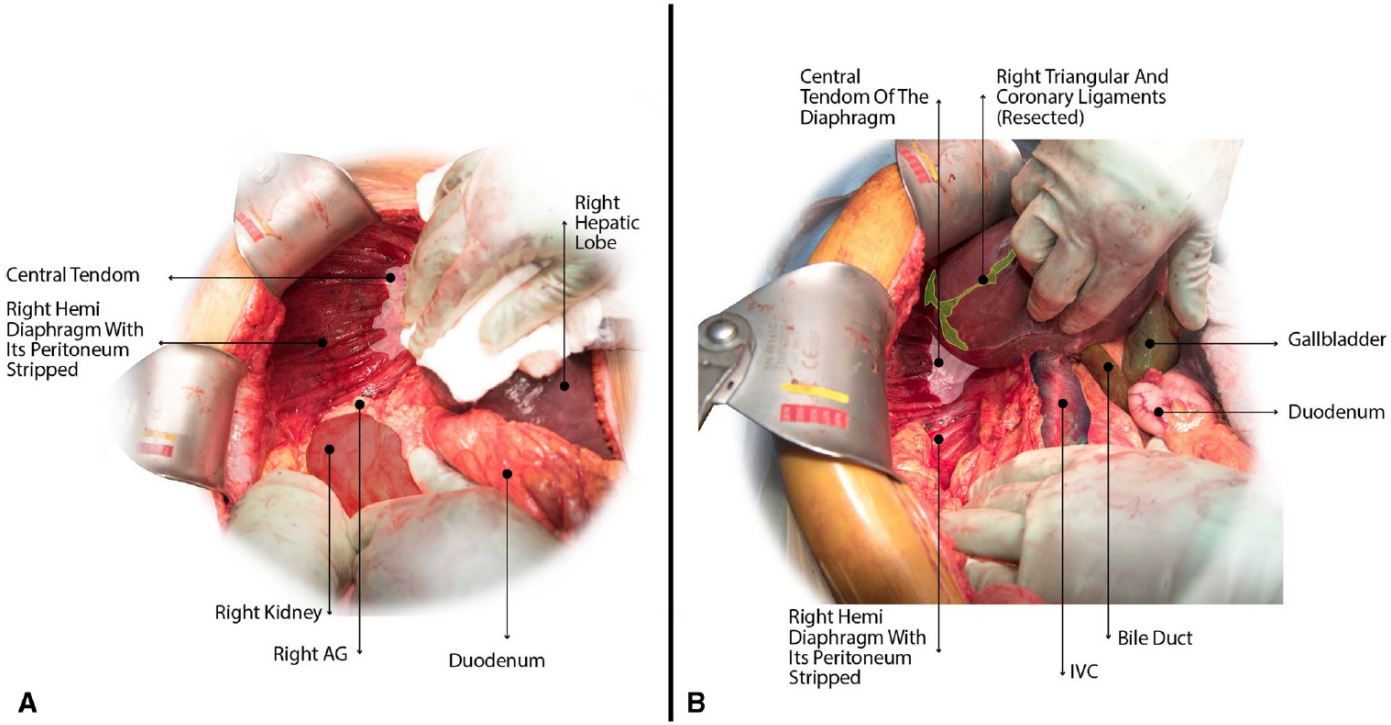


Fig. 3 **a**, **b** Completed right hemidiaphragmatic peritonectomy

Izquierdo et al, JOGS 2019

Cytoreductive Surgery—How do we do it?

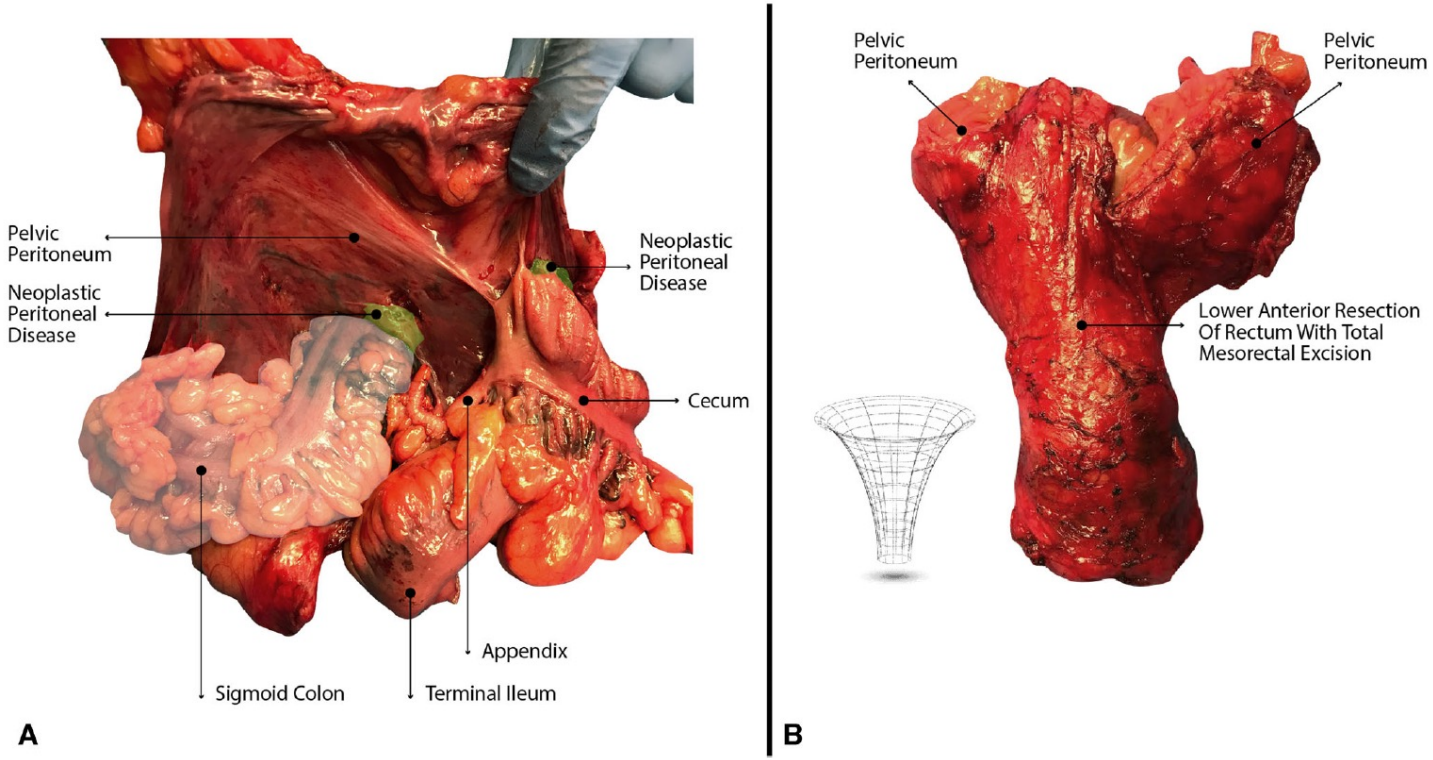


Fig. 4 **a**, **b** Pelvic peritonectomy with visceral resection

Izquierdo et al, JOGS 2019

Cytoreductive Surgery—How do we do it?

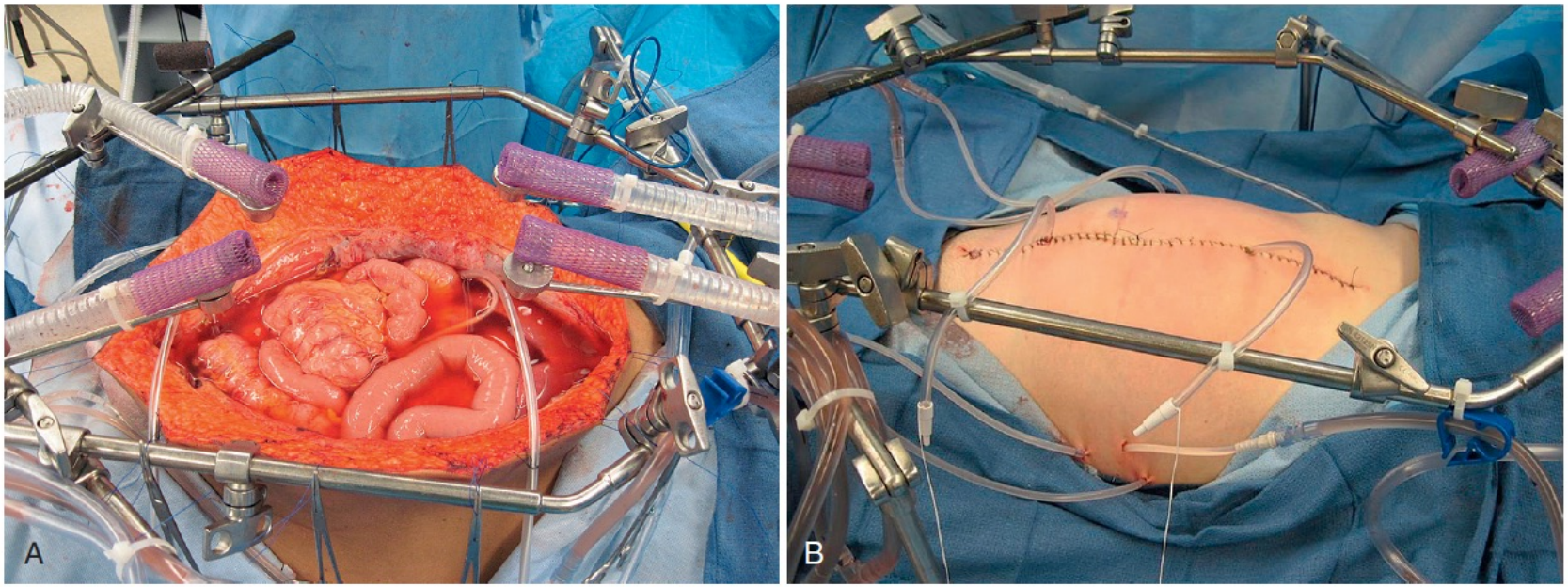


FIGURE 1 **A,** Hyperthermic intraperitoneal chemotherapy administered with an open technique allows continued manipulation of the abdominal and pelvic contents to achieve uniform distribution of heat and chemotherapy. A vapor barrier above the chemotherapy solution is created by four smoke aspirators. **B,** The closed method for hyperthermic perioperative chemotherapy is preferred by some surgeons.

Deraco et al, Cameron's Current Surgical Therapy

CRS/HIPEC in CRC with PM

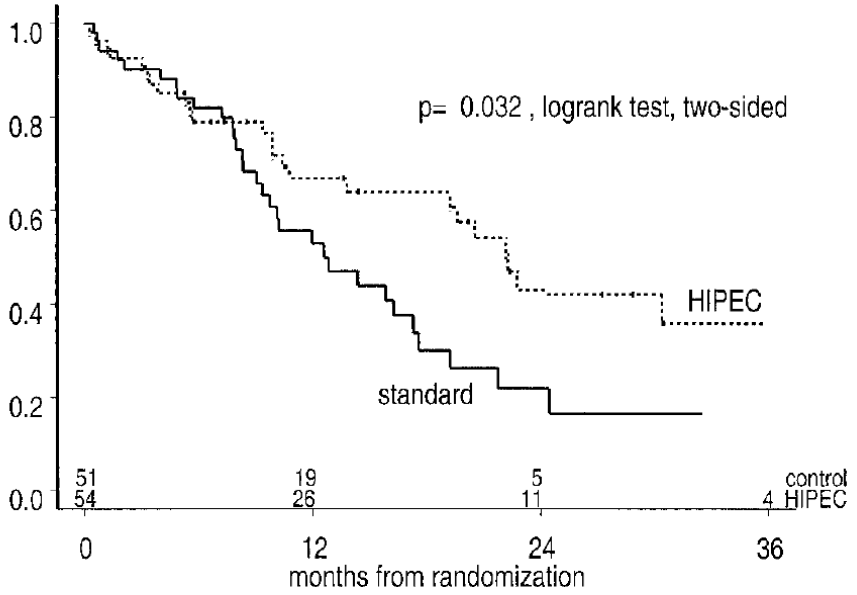


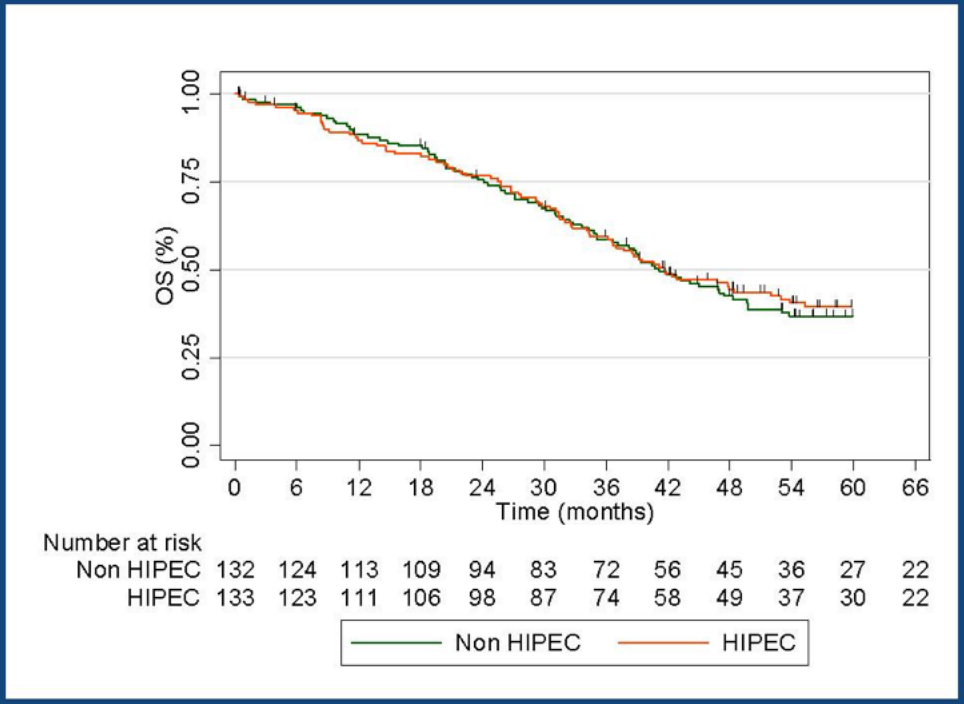
Fig 2. Kaplan-Meier survival curve, comparing standard treatment to hyperthermic intraperitoneal chemotherapy (HIPEC).

- At median follow-up of 21.6 months, CRS/HIPEC arm median OS was **22.3 vs. 12.6** months in the control arm
- Complete cytoreduction: median OS of **48 months**, with **45%** alive at 5 years

Verwaal et al, JCO 2003
Verwaal et al, ASO 2008

PRODIGE 7

Overall survival (ITT)



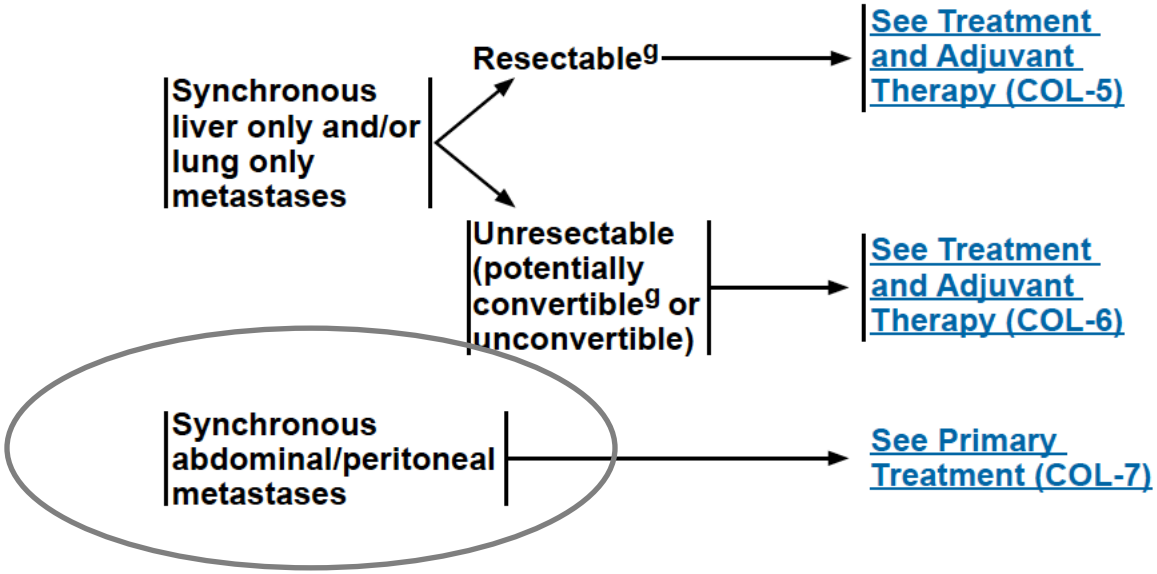
Median Follow Up: 64 months [95% CI:58.9-69.8]

	HIPEC	Non-HIPEC	P-value
Median Survival (months) [95% CI]	41.7 [36.2-52.8]	41.2 [35.1-49.7]	0.995
1-year Survival	86.9%	88.3%	
5-year Survival	39.4%	36.7%	

HR=1.00: 95%CI [0.73 - 1.37] p=0.995

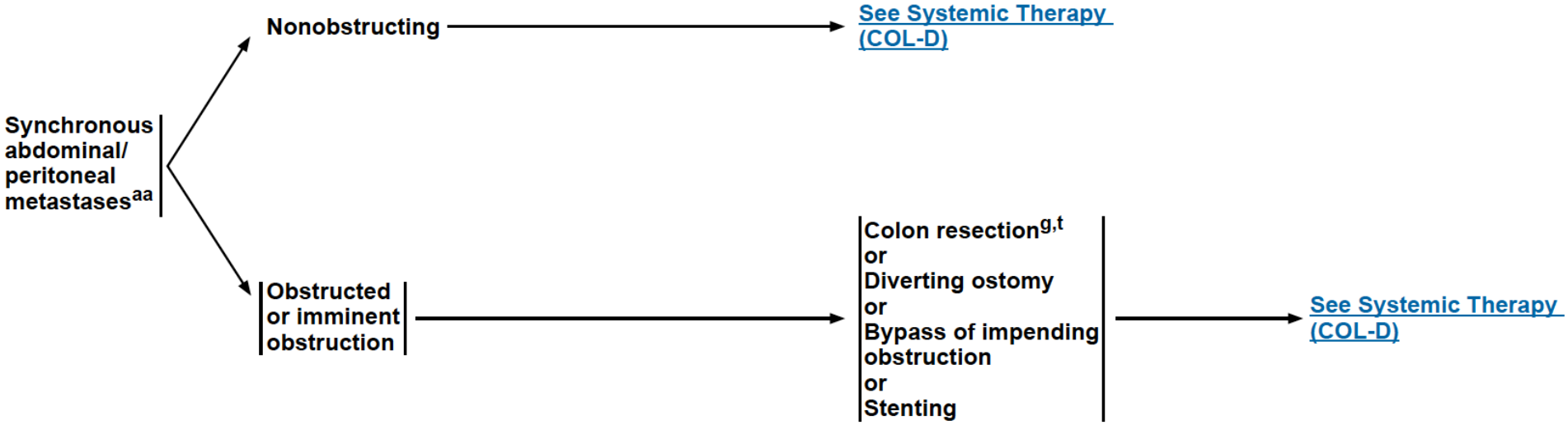
Quenet et al, JCO 2018, presentation at ASCO 2018 (supp.)

NCCN Colon Cancer Guidelines



[b]See Principles of Imaging (COL-A).
[e]See Principles of Pathologic Review (COL-B 4 of 5) -
[g]See Principles of Surgery (COL-C 2 of 3).

NCCN Colon Cancer Guidelines



Consider colon resection only if imminent risk of obstruction, significant bleeding, perforation, or other significant tumor-related symptoms.

[aa]Complete cytoreductive surgery and/or intraperitoneal chemotherapy can be considered in experienced centers for select patients with limited peritoneal metastases for whom R0 resection can be achieved.

NCCN Colon Cancer Guidelines—2024

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2024
Colon Cancer

perioperative systemic therapy and control arms, respectively. Grade ≥3 systemic therapy-related toxicity was observed in 35% of patients and ORR were 28% (radiologic response) and 38% (major pathologic response) following neoadjuvant therapy.

The panel currently believes that complete cytoreductive surgery 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.

Determining Resectability

The consensus of the panel is that patients diagnosed with potentially resectable mCRC should undergo an upfront evaluation by a multidisciplinary team, including surgical consultation (ie, with an experienced hepatic surgeon in cases involving liver metastases) to assess resectability status. The criteria for determining patient suitability for resection of metastatic disease are the likelihood of achieving complete resection of all evident disease with negative surgical margins and maintaining adequate liver reserve.[565-568] When the remnant liver is insufficient in size based on cross-sectional imaging volumetrics, preoperative portal vein embolization of the involved liver can be done to expand the future liver remnant.[569] It should be noted that size alone is rarely a contraindication to resection of a tumor. Resectability differs fundamentally from endpoints that focus more on palliative measures. Instead, the resectability endpoint is focused on the potential of surgery to cure the disease.[570] Resection should not be undertaken unless complete removal of all known tumor is realistically possible (R0 resection), because incomplete resection or debulking (R1/R2 resection) has not been shown to be beneficial.[412,565]

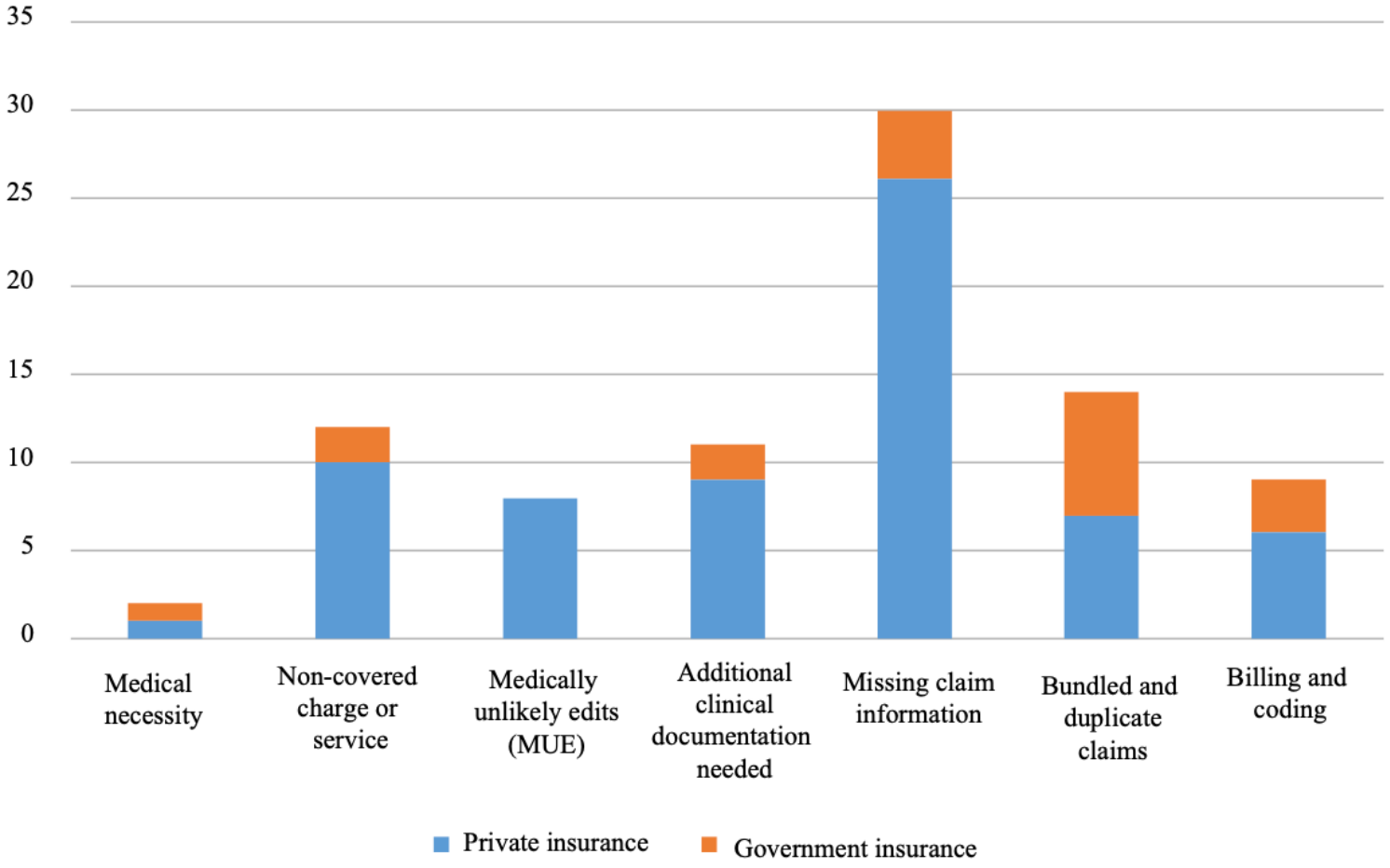
The role of PET/CT in determining resectability of patients with mCRC is discussed in *Workup and Management of Synchronous Metastatic Disease*, below.

Neoadjuvant Therapy and Conversion to Resectability

The majority of patients diagnosed with metastatic colorectal disease have unresectable disease. However, for those with liver-limited unresectable disease that, because of involvement of critical structures, cannot be resected unless regression is accomplished, preoperative systemic therapy is being increasingly considered in highly selected cases in an attempt to downsize colorectal metastases and convert them to a resectable status. Patients presenting with large numbers of metastatic sites within the liver or lung are unlikely to achieve an R0 resection simply based on a favorable response to therapy, as the probability of complete eradication of a metastatic deposit by systemic therapy alone is low. These patients should be regarded as having unresectable disease not amenable to conversion therapy. In some highly selected cases, however, patients with disease that has had significant response to conversion therapy can be converted from unresectable to resectable disease status.[503]

Any active metastatic systemic regimen can be used in an attempt to convert a patient's unresectable disease status to a resectable disease status, because the goal is not specifically to eradicate micrometastatic disease, but rather to obtain the optimal size regression of the visible metastases. An important point to keep in mind is that irinotecan- and oxaliplatin-based chemotherapeutic regimens may cause liver steatohepatitis and sinusoidal liver injury, respectively.[571-575] Studies have reported that chemotherapy-associated liver injury (including severe sinusoidal dilatation and steatohepatitis) is associated with morbidity and complications following hepatectomy for colorectal liver metastases.[571,572,575,576] To limit the development of hepatotoxicity, it is

Insurance Barriers



Ong et al, ASO 2022

› Ann Surg Oncol. 2020 Jun;27(6):1761-1767. doi: 10.1245/s10434-020-08315-x.
Epub 2020 Apr 13.

The Chicago Consensus on Peritoneal Surface Malignancies: Management of Colorectal Metastases

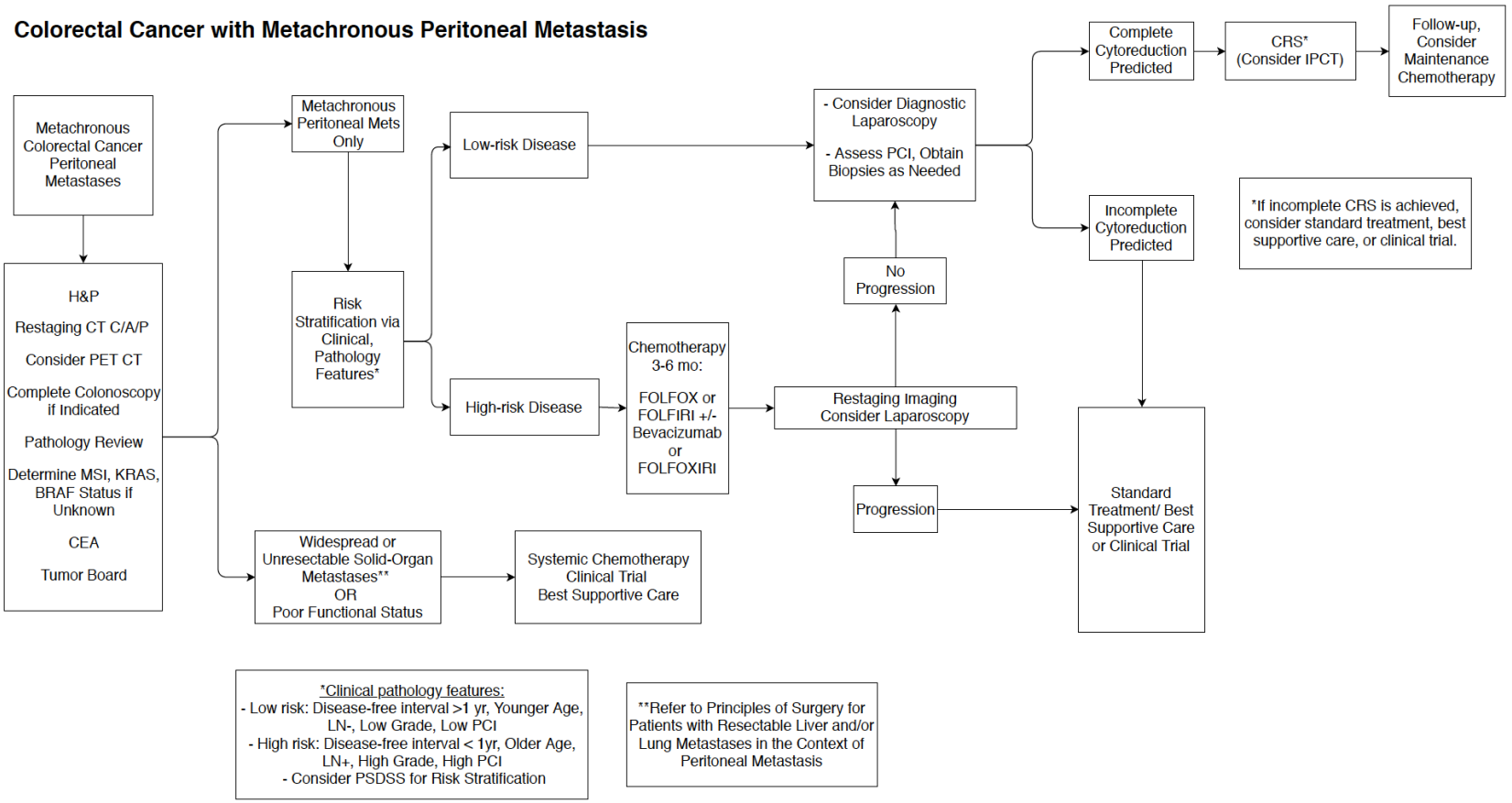
Chicago Consensus Working Group

Collaborators – collapse

Collaborators

Chicago Consensus Working Group: Francisco J Izquierdo, Darryl Schuitevoerder, Alejandro Plana, Scott K Sherman, Michael G White, Joel M Baumgartner, M Haroon A Choudry, Daniel E Abbott, Robert M Barone, Richard N Berri, Carlos H F Chan, Callisia N Clarke, Jordan M Cloyd, James W Fleshman Jr, Georgios V Georgakis, Kamran Idrees, Haejin In, Nelya Melnitchouk, George Salti, Jula Veerapong, Sherif Abdel-Misih, Steven A Ahrendt, Lindsay Alpert, Mazin Al-Kasspooles, Farin Amersi, Amanda K Arrington, Brian Badgwell, Lana Bijelic, Dan G Blazer Iii, Wilbur B Bowne, Charles Komen Brown, Daniel V Catenacci, Clifford S Cho, James C Cusack Jr, Abraham H Dachman, Jeremiah L Deneve, Sean P Dineen, Oliver S Eng, Leopoldo J Fernandez, T Clark Gamblin, Alexandra Gangi, Erin W Gilbert, Martin D Goodman, Anand Govindarajan, Travis E Grotz, Vadim Gushchin, Andrea Hayes-Jordan, Nader Hanna, Carla Harmath, Aliya N Husain, Chukwuemeka Ihemelandu, David Jiang, Fabian M Johnston, John M Kane Iii, Giorgos Karakousis, Kaitlyn J Kelly, Timothy J Kennedy, Xavier M Keutgen, Michael D Kluger, Hedy Lee Kindler, Byrne Lee, Lloyd A Mack, Ugwuji N Maduekwe, Grace Z Mak, Joshua M V Mammen, Marcovalerio Melis, Melvy Sarah Mathew, Ryan P Merkow, Harveshp Mogal, Mecker G Möller, Garrett M Nash, Aytekin Oto, Colette R Pameijer, Sam G Pappas, Patricio M Polanco, Blase N Polite, Sanjay S Reddy, Richard Royal, Armando Sardi, Maheswari Senthil, Namrata Setia, Lucas Sideris, Joseph Skitzki, Konstantinos I Votanopoulos, Joshua H Winer, Shu-Yuan Xiao, Rhonda K Yantiss, Nita Ahuja, Andrew M Lowy, H Richard Alexander Jr, Jesus Esquivel, Jason M Foster, Daniel M Labow, Laura A Lambert, Edward A Levine, Charles Staley, H Sugarbaker, David L Bartlett, Kiran Turaga

Colorectal Cancer with Metachronous Peritoneal Metastasis



THE UNIVERSITY OF CHICAGO

2018 Chicago Consensus on Peritoneal Surface Malignancies

Chicago Consensus Working Group, ASO 2020

Yale School of Medicine /

Surgery ≡ MENU

Home / Research Programs / Peritoneal Surface Malignancy Consortium

Pathways Rapid Reviews Education Team Resources RVU Prior Meetings

The Peritoneal Surface Malignancy Consortium

Our goal is to provide multidisciplinary recommendations for the management of peritoneal surface malignancies across various disease sites. The management of peritoneal surface malignancies remains controversial and poorly represented in national guidelines. Recognizing the need for increased awareness and appropriate management of peritoneal surface disease, our guidelines are meticulously developed with contributions from an esteemed array of PSM experts. Our collaborators include surgical oncologists, medical oncologists, pathologists, radiologists, palliative

Contact Us

If you are looking to get involved in the PSM Consortium, please contact Varun and David for further information.

varun.bansal@yale.edu

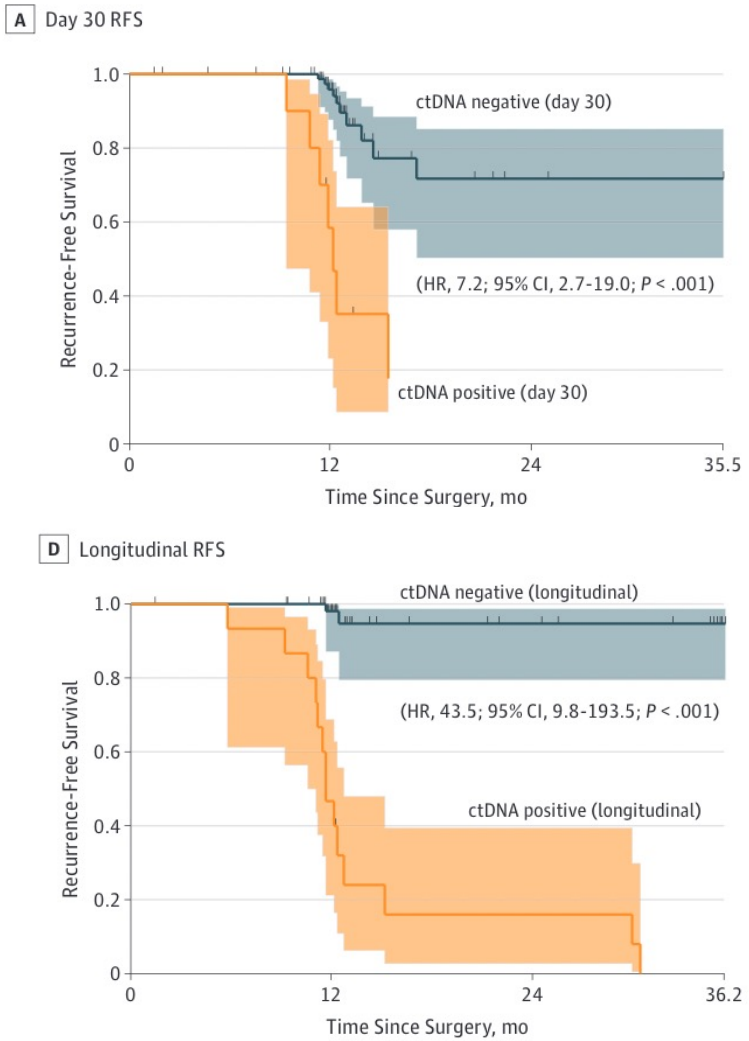
david.su@yale.edu

“Liquid Biopsy”

JAMA Oncol. 2019 Aug 1;5(8):1124-1131. doi: 10.1001/jamaoncol.2019.0528.

Analysis of Plasma Cell-Free DNA by Ultradeep Sequencing in Patients With Stages I to III Colorectal Cancer

Thomas Reinert [1], Tenna Vesterman Henriksen [1], Emil Christensen [1], Shruti Sharma [2], Raheleh Salari [2], Himanshu Sethi [2], Michael Knudsen [1], Iver Nordentoft [1], Hsin-Ta Wu [2], Antony S Tin [2], Mads Heilskov Rasmussen [1], Søren Vang [1], Svetlana Shchegrova [2], Amanda Frydendahl Boll Johansen [1], Ramya Srinivasan [2], Zoe Assaf [2], Mustafa Balcioglu [2], Alexander Olson [2], Scott Dashner [2], Dina Hafez [2], Samantha Navarro [2], Shruti Goel [2], Matthew Rabinowitz [2], Paul Billings [2], Styrmir Sigurjonsson [2], Lars Dyrskjøt [1], Ryan Swenerton [2], Alexey Aleshin [2], Søren Laurberg [3], Anders Husted Madsen [4], Anne-Sofie Kannerup [5], Katrine Stribolt [6], Søren Palmelund Krag [7], Lene H Iversen [3], Kåre Gotschalck Sunesen [5], Cheng-Ho Jimmy Lin [2], Bernhard G Zimmermann [2], Claus Lindbjerg Andersen [1]



Novel Liquid Biopsy Approaches

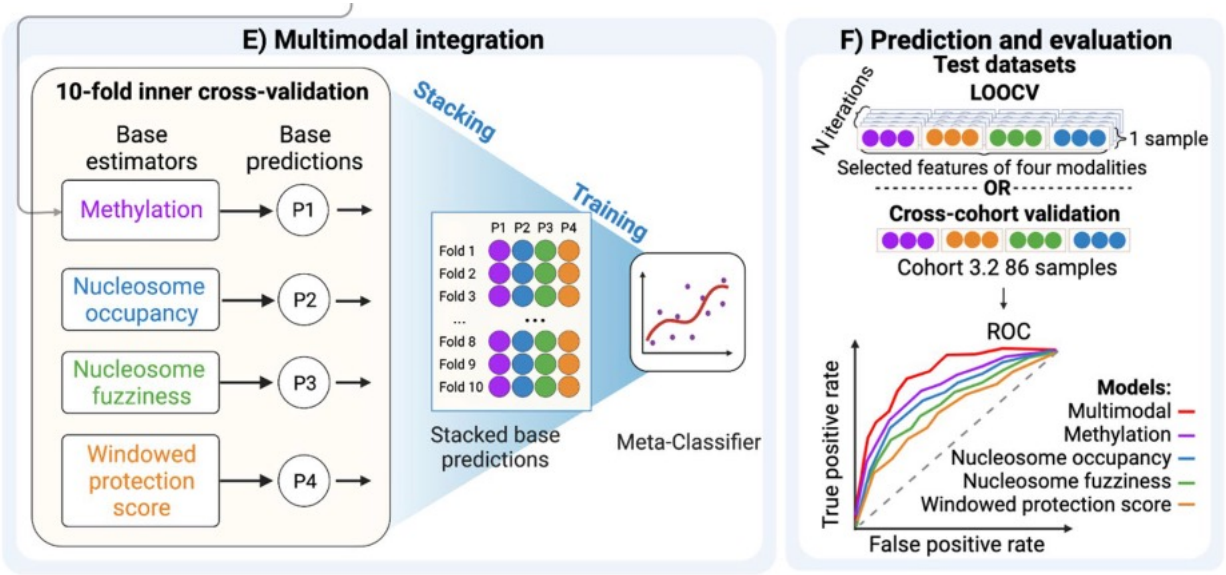
Li *et al. Genome Medicine* (2024) 16:9
https://doi.org/10.1186/s13073-023-01280-6

Genome Medicine

RESEARCH Open Access

Multimodal epigenetic sequencing analysis (MESA) of cell-free DNA for non-invasive colorectal cancer detection

Yumei Li[1,2†], Jianfeng Xu[3†], Chaorong Chen[1†], Zhenhai Lu[4†], Desen Wan[4], Diange Li[5], Jason S. Li[1], Allison J. Sorg[3], Curt C. Roberts[3], Shivani Mahajan[3], Maxime A. Gallant[3], Itai Pinkoviezky[3], Ya Cui[1], David J. Taggart[3*] and Wei Li[1*]



nature communications

Article

https://doi.org/10.1038/s41467-022-32198-z

Molecular characterization of colorectal cancer related peritoneal metastatic disease

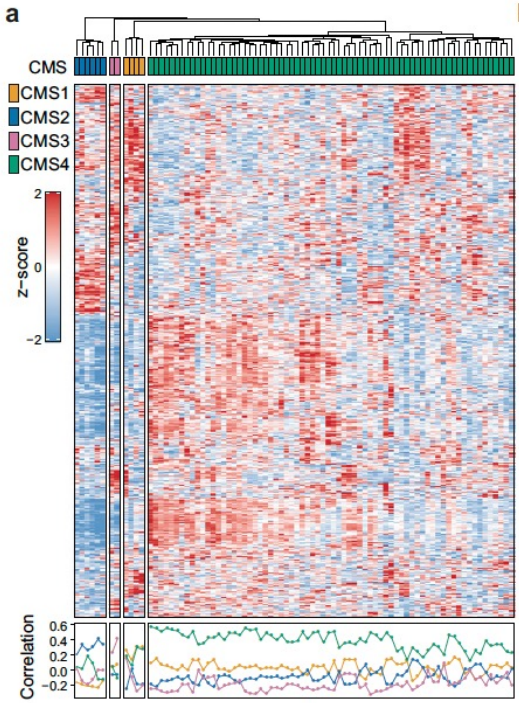
Received: 16 February 2022

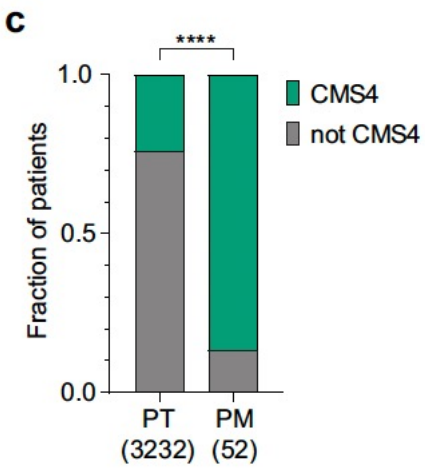
Accepted: 21 July 2022

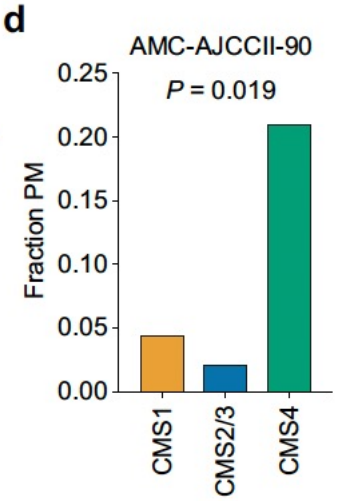
Published online: 04 August 2022

Check for updates

Kristiaan J. Lenos[1,2], Sander Bach[3], Leandro Ferreira Moreno[1,2], Sanne ten Hoorn[1,2], Nina R. Sluiter[3], Sanne Bootsma[1,2], Felipe A. Vieira Braga[1,2], Lisanne E. Nijman[1,2], Tom van den Bosch[1,2], Daniel M. Miedema[1,2], Erik van Dijk[4], Bauke Ylstra[4], Ruth Kulicke[5], Fred P. Davis[5], Nicolas Stransky[5], Gromoslaw A. Smolen[5], Robert R. J. Coebergh van den Braak[6], Jan N. M. IJzermans[6], John W. M. Martens[7], Sally Hallam[8], Andrew D. Beggs[8], Geert J. P. L. Kops[2,9], Nico Lansu[2,9], Vivian P. Bastiaenen[10], Charlotte E. L. Klaver[10], Maria C. Lecca[1,2], Khalid El Makrini[1,2], Clara C. Elbers[1,2], Mark P. G. Dings[1,2], Carel J. M. van Noesel[11], Onno Kranenburg[12], Jan Paul Medema[1,2], Jan Koster[13], Lianne Koens[11], Cornelis J. A. Punt[14], Pieter J. Tanis[10], Ignace H. de Hingh[15], Maarten F. Bijlsma[1,2], Jurriaan B. Tuynman[3,17] & Louis Vermeulen[1,2,16,17]





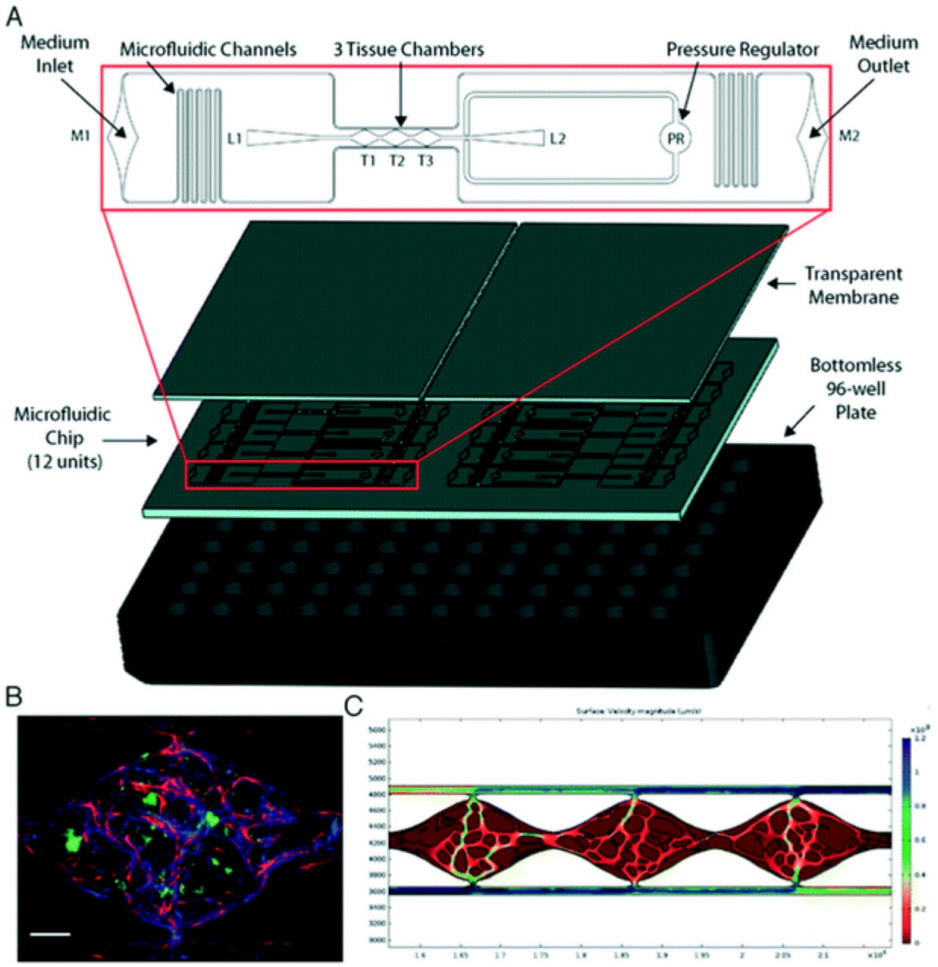


Novel In Vitro Model

› Lab Chip. 2021 Apr 7;21(7):1333-1351. doi: 10.1039/d0lc01216e. Epub 2021 Feb 19.

An in vitro vascularized micro-tumor model of human colorectal cancer recapitulates in vivo responses to standard-of-care therapy

Stephanie J Hachey [1], Silva Movsesyan, Quy H Nguyen, Giselle Burton-Sojo, Ani Tankazyan, Jie Wu, Tuyen Hoang, Da Zhao, Shuxiong Wang, Michaela M Hatch, Elizabeth Celaya, Samantha Gomez, George T Chen, Ryan T Davis, Kevin Nee, Nicholas Pervolarakis, Devon A Lawson, Kai Kessenbrock, Abraham P Lee, John Lowengrub, Marian L Waterman, Christopher C W Hughes



Summary

- Colorectal cancer is one of the most common cancers in the United States
- Management of colorectal cancer that has spread in the abdomen continues to evolve
- We are continually working to change the paradigm

UCI

Thank You!

oeng@hs.uci.edu