Southeastern Multidisciplinary Approaches to Cancer Symposium

Surgical Therapies for Peritoneal Metastases

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Disclosures

I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:
The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:
Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

This presentation is dedicated solely to research or other issues that do not contain a direct patient care component.

Introduction

- Peritoneum- common site of metastasis for GI malignancies.
  -appendix, gastric, colorectal, pancreas, cholangioca, GEP NET, GIST
- PSM (peritoneal surface metastasis) > worse prognosis
- First PSM resection in the 1980s for ovarian ca
- Response of PSM to systemic cth is lower compared to other metastatic sites
- CRS + systemic cth > better prognosis in selected PSM patients.
- CRS + HIPEC > better prognosis in certain GI malignancies with PSM
- 1990s- drug regimen; methods; surgical techniques for CRS
- OS for CRS + HIPEC patients- PCI score, CC score, site of primary tumor, histologic type

Epidemiology

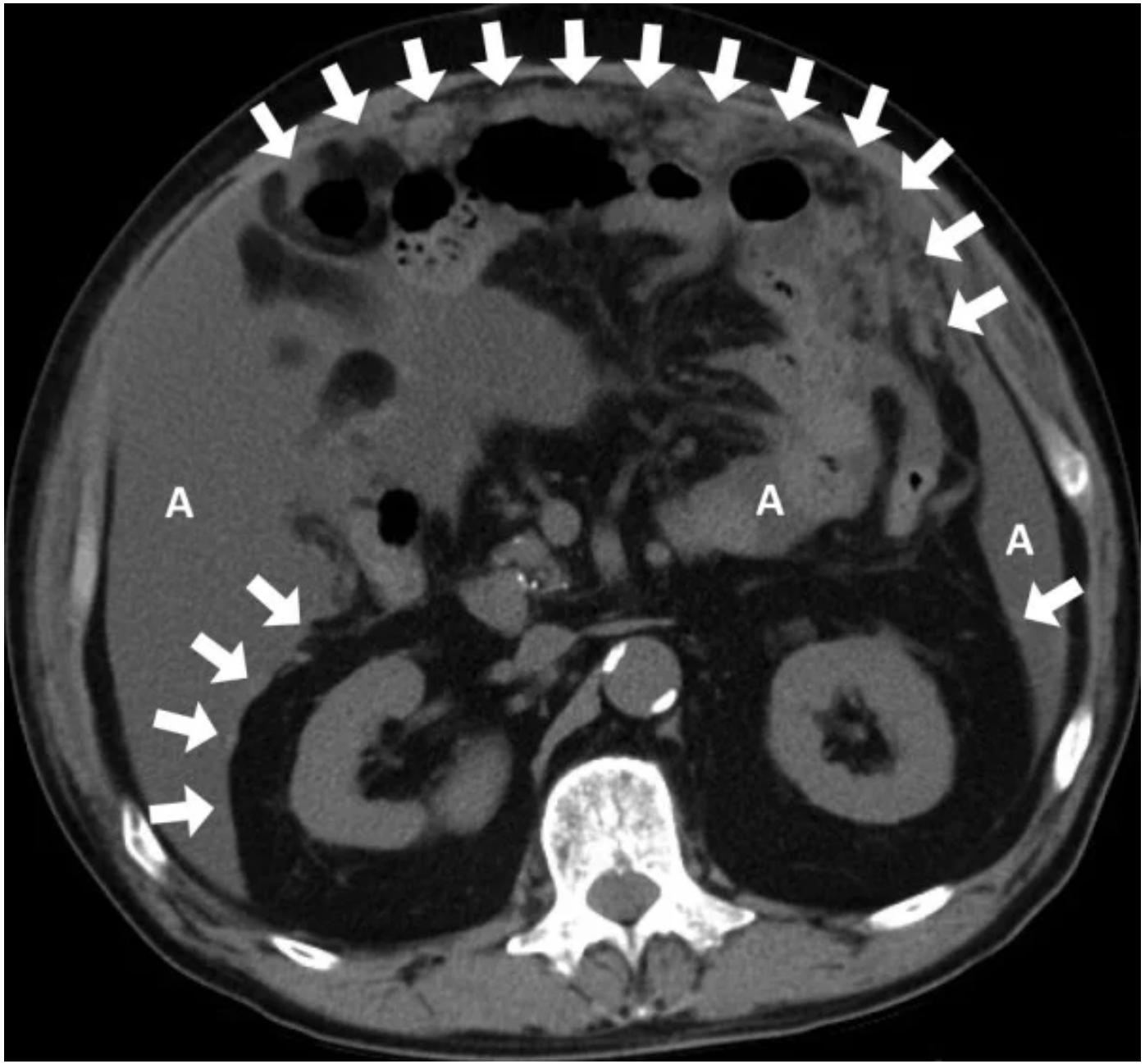
- Primary sites- appendix, colon, stomach, ovaries
- Affects approximately 70,000 to 80,000 patients in the U.S. annually.

PSM Biology

- Tumor-mesothelial interaction
- Adhesion molecules-CD44 and Integrins
- Tumor cells MMP (degrade extracellular matrix to facilitate implantation
- Altered mesothelial cells (cancer associated fibroblasts- cytokines and growth factors promoting invasion, cth resistance and decreased survival
- Mesothelial-Mesenchymal Transition (MMT) facilitates evasion of immune system

Diagnosis/Staging

- High resolution CT/MRI/PET
- Diagnostic laparoscopy
- Scoring system (PCI score)
- Colorectal/appendiceal –PCI score cut off 12-15; Gastric- PCI score cut off 6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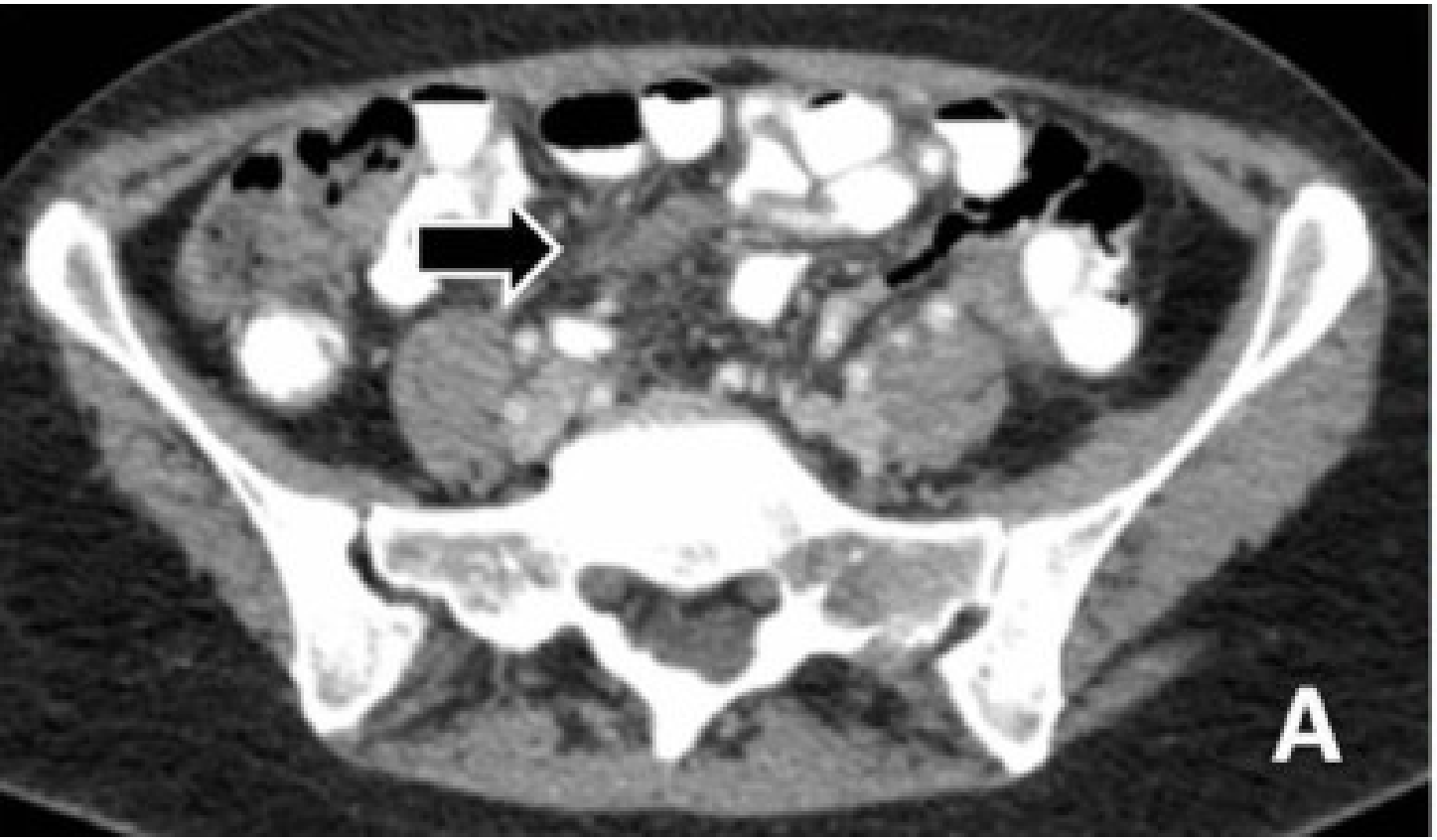
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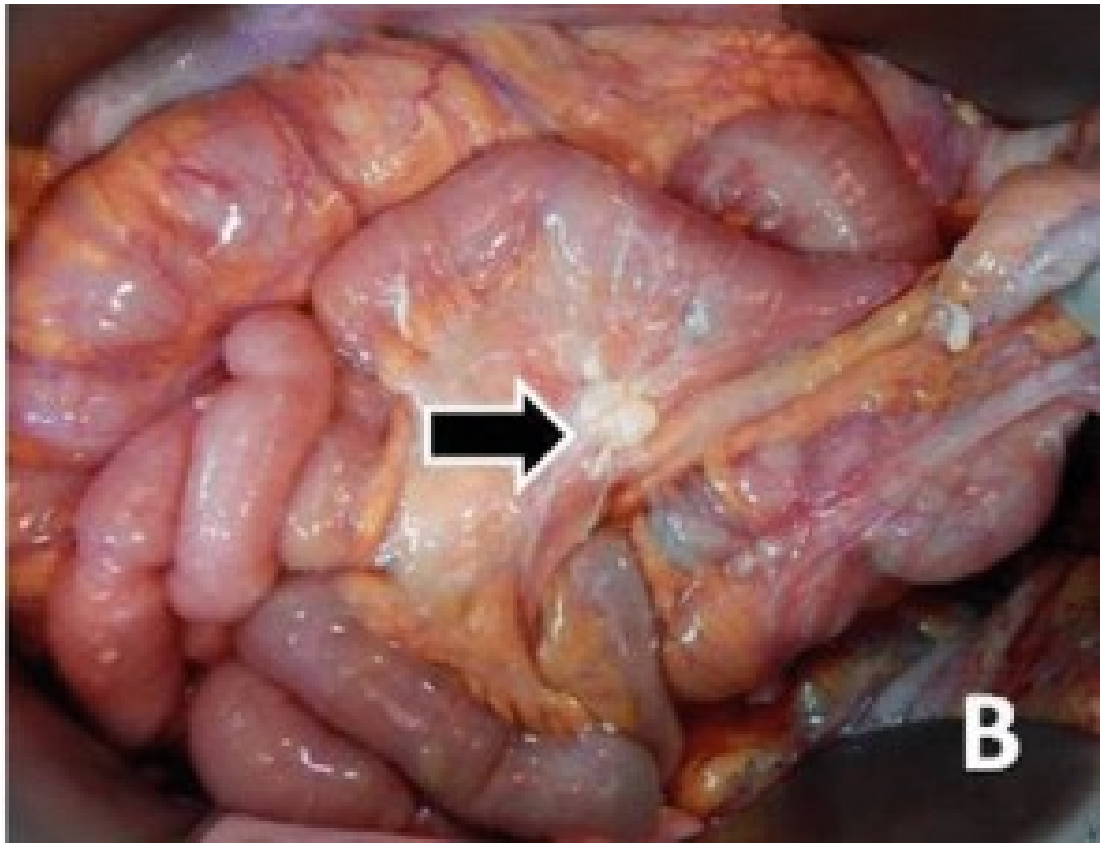
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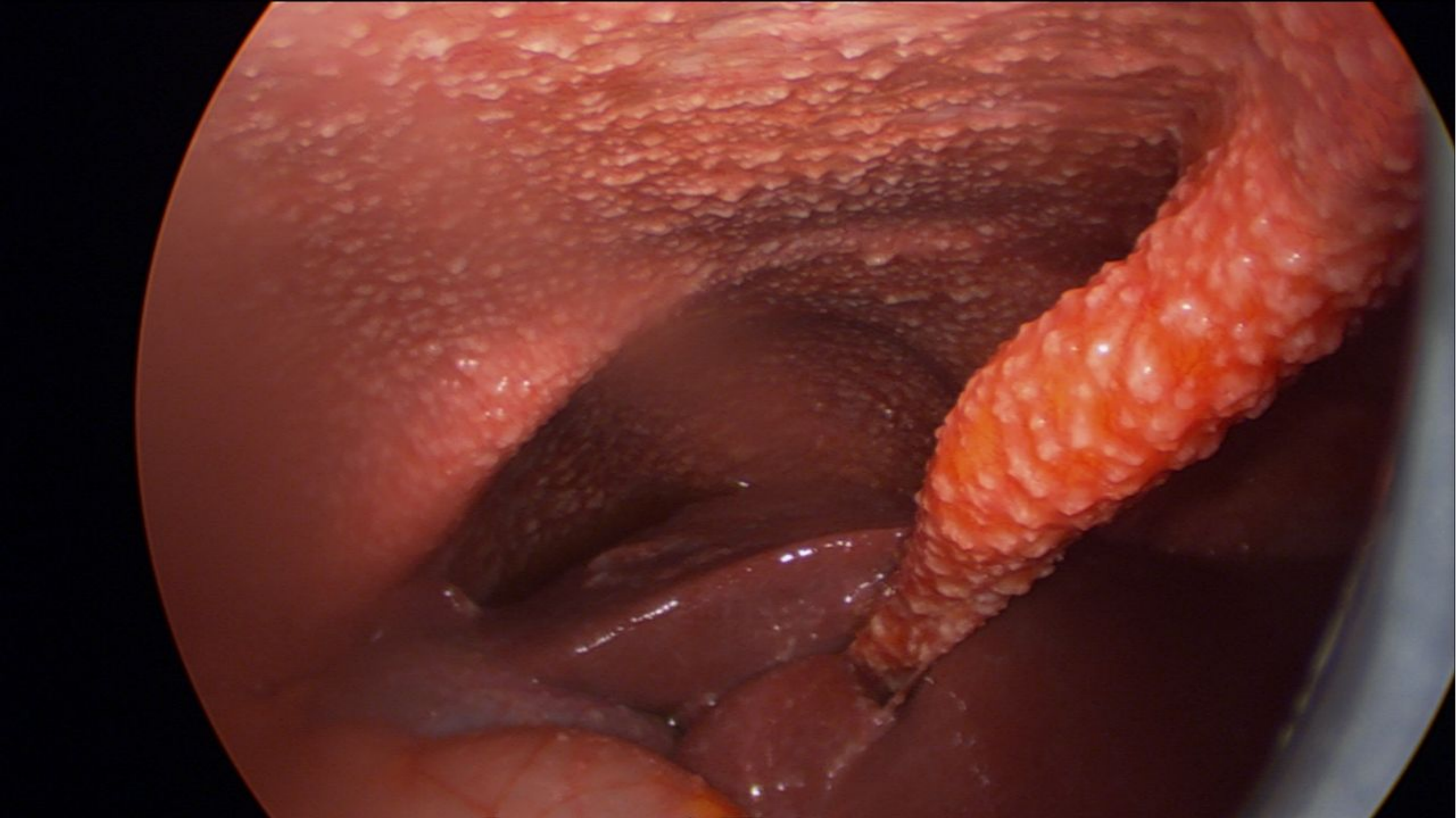
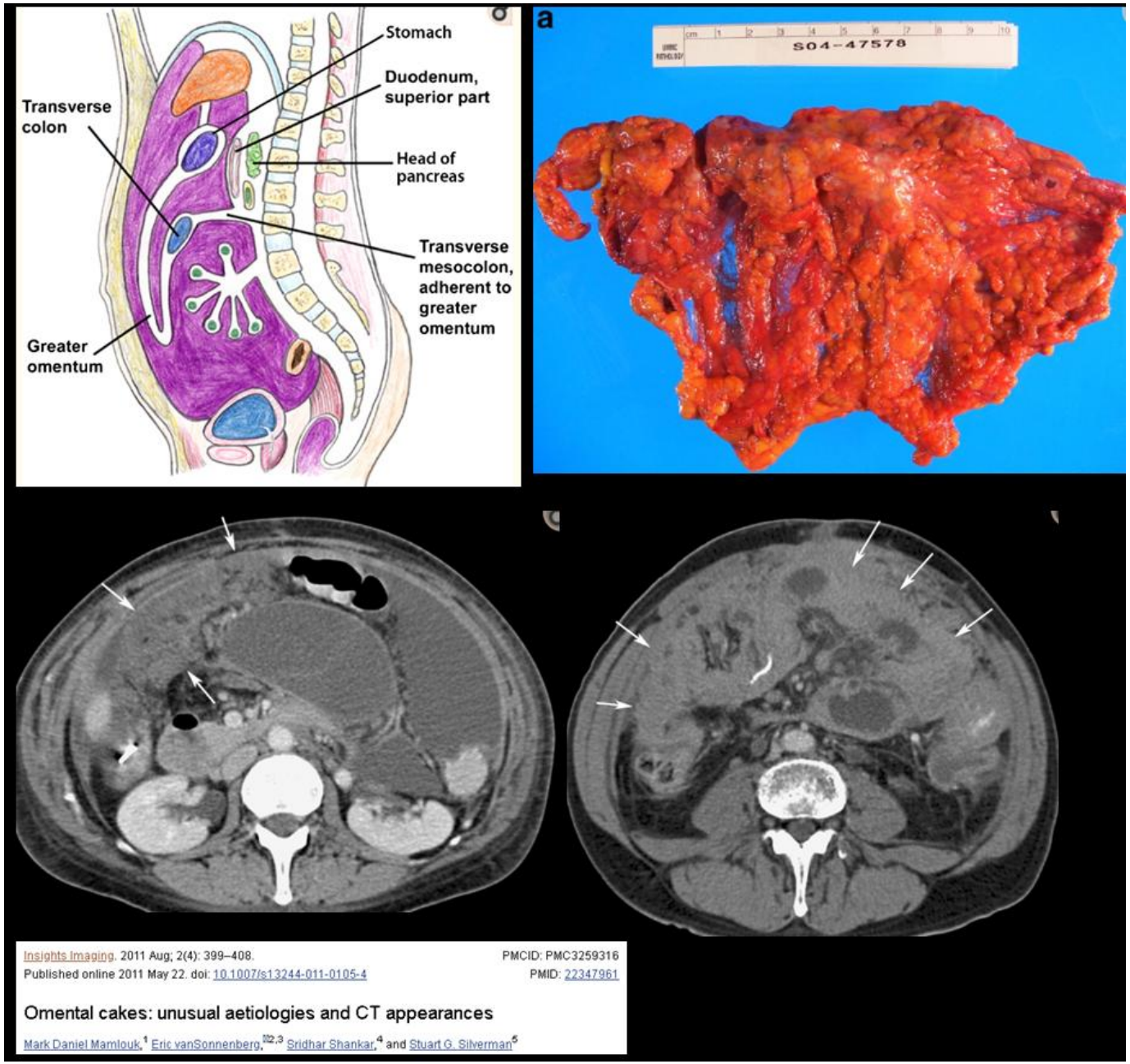




Insights Imaging. 2011 Aug; 2(4): 399–408.
Published online 2011 May 22. doi: 10.1007/s13244-011-0105-4
PMCID: PMC3259316
PMID: 22347961

Omental cakes: unusual aetiologies and CT appearances

Mark Daniel Mamlouk,[1] Eric vanSonnenberg,[2,3] Sridhar Shankar,[4] and Stuart G. Silverman[5]

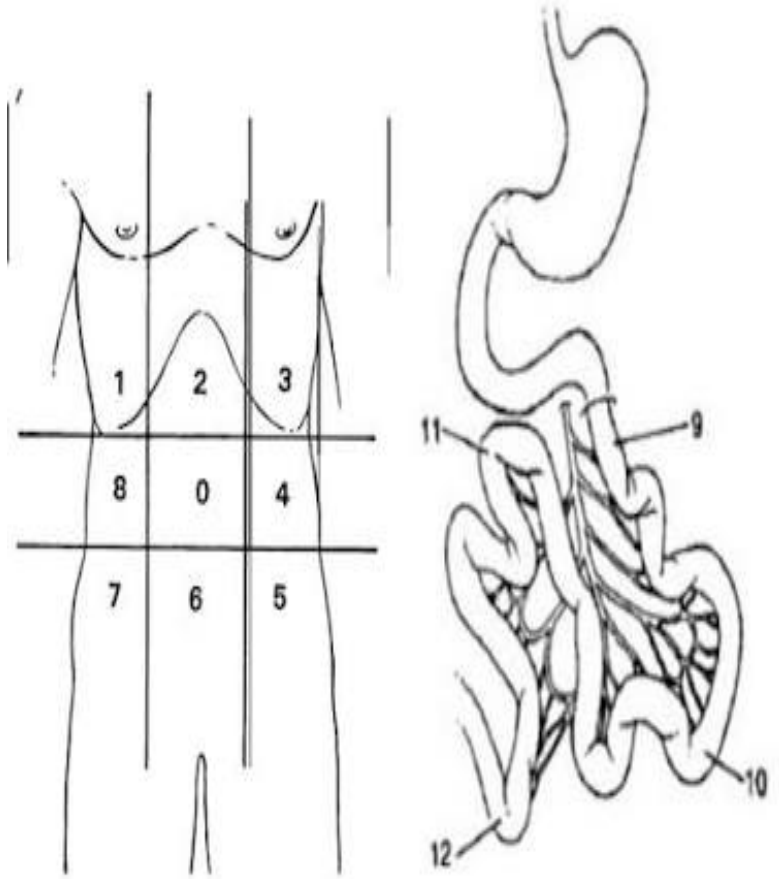
CRS (Cytoreductive Surgery)

- Removal of visible disease (multivisceral resection and peritonectomy)
- Complete cytoreduction is the preferred goal but CC-1 may be acceptable (survival benefit)
- Patient selection

HIPEC (Hyperthermic Intraperitoneal Chemoperfusion)

- Hyperthermia (41-43 degrees Celsius)
  - direct cytotoxicity
  -increased penetration
  -synergistic effect
- Direct application
- Blood-peritoneal barrier (decreased toxicity; high dose cth)

Peritoneal Cancer Index Score



00: Central
01: Right upper
02: Epigastrium
03: Left upper
04: Left flank
05: Left lower
06: Pelvis
07: Right lower
08: Right flank
09: Upper Jejunum
10: Lower jejunum
11: Upper ileum
12: Lower ileum

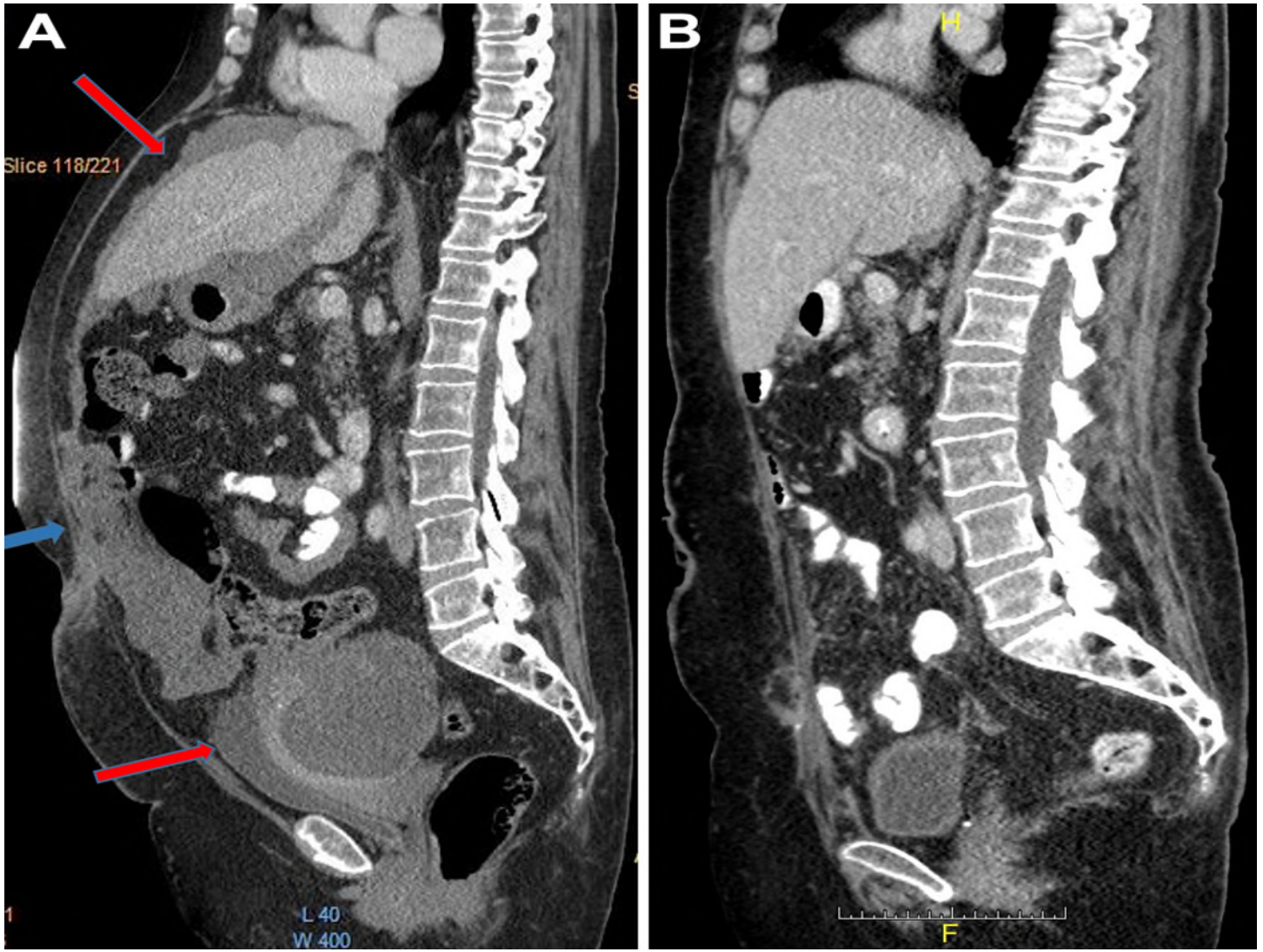
COMPLETENESS OF CYTOREDUCTION SCORE

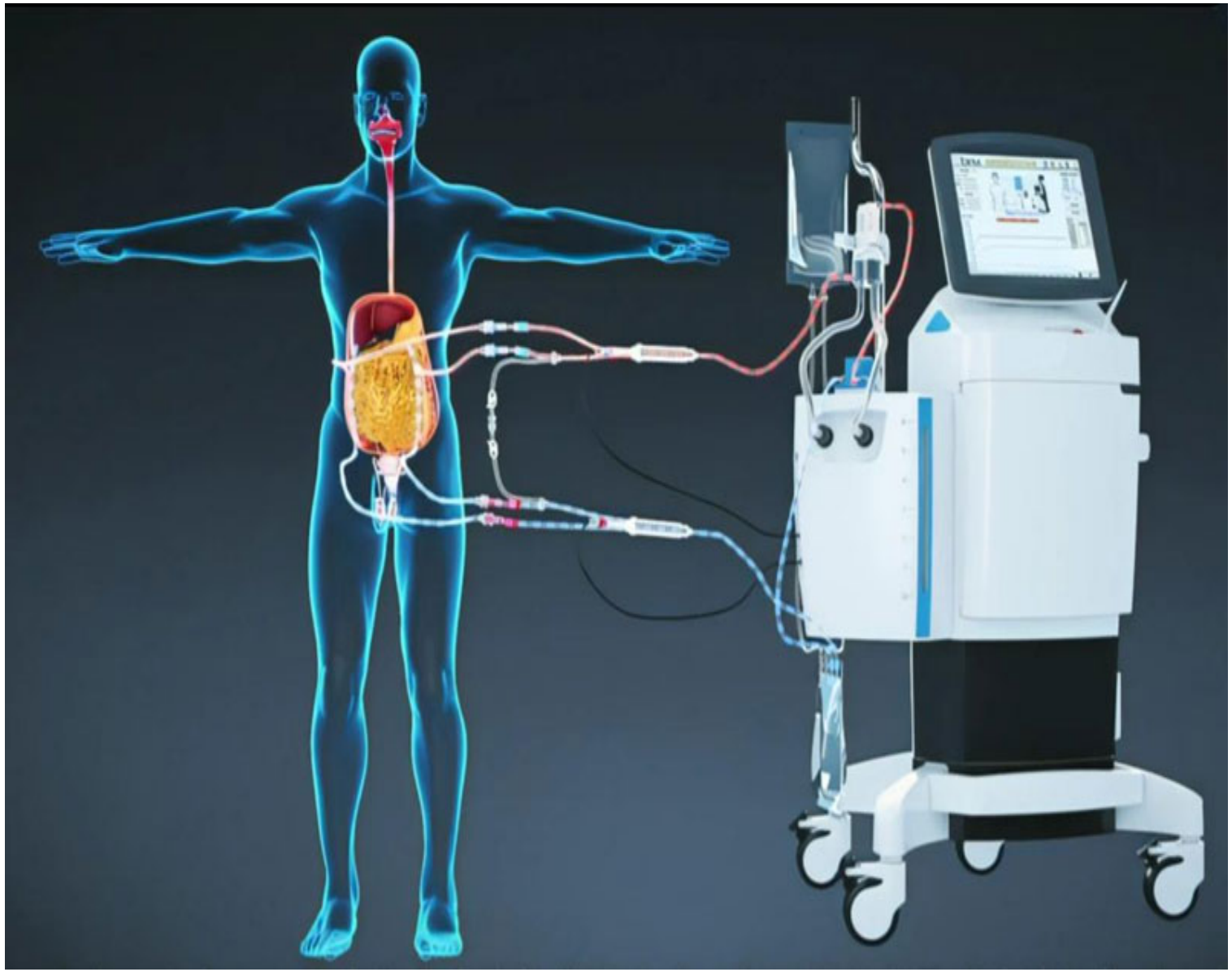
CC-0
No peritoneal nodule was seen

CC-1
Tumor nodules persisting after cytoreduction are less than 2.5mm in diameter

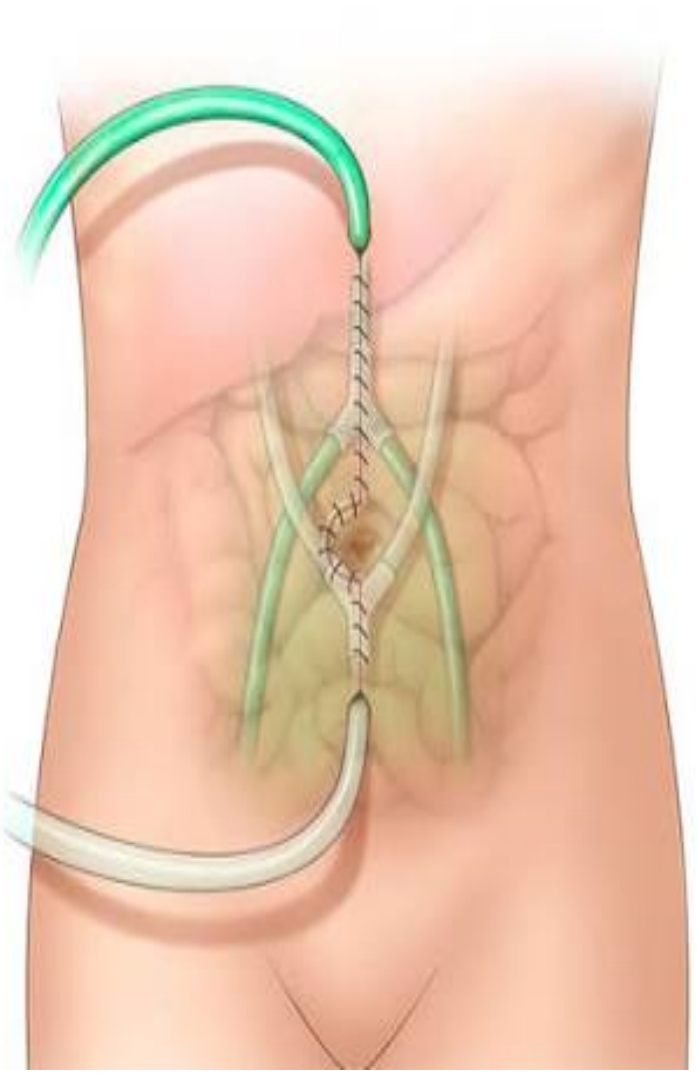
CC-2
Tumor nodules persisting after cytoreduction are between 2.5 mm and 2.5 cm in diameter

CC-3
Tumor nodules persisting after cytoreduction are greater than 2.5cm in diameter


A
Slice 118/221
L 40
W 400
B
H
F



Set up for the chemoperfusion




35
THINK
THINK
HCG
The HIPEC system is an
advanced technology

Colorectal cancer PSM

- Synchronous PSM- 6-7% of patients; Metachronous PSM-6%
- Treatment options for CRC with PSM
  -palliative systemic chemotherapy
  -palliative surgery
- Verwaal et al (CRC + PSM + bowel obstruction)- CRS/HIPEC > palliative surgery + systemic cth
- Elias et al (CRS/HIPEC with CC-0)- median OS 40 months
- Gore et al- (CRS/HIPEC with CC-0)- 5 yr DFS 16%
- PRODIGE-7 (CRS + HIPEC vs CRS)- median OS 41.7 mths vs 41.2 mths , p=0.99
- Prognostic factors for OS/DFS- CC score, PCI, no of regions with PSM; histology (signet ring and mucinous ca)

Appendiceal PSM

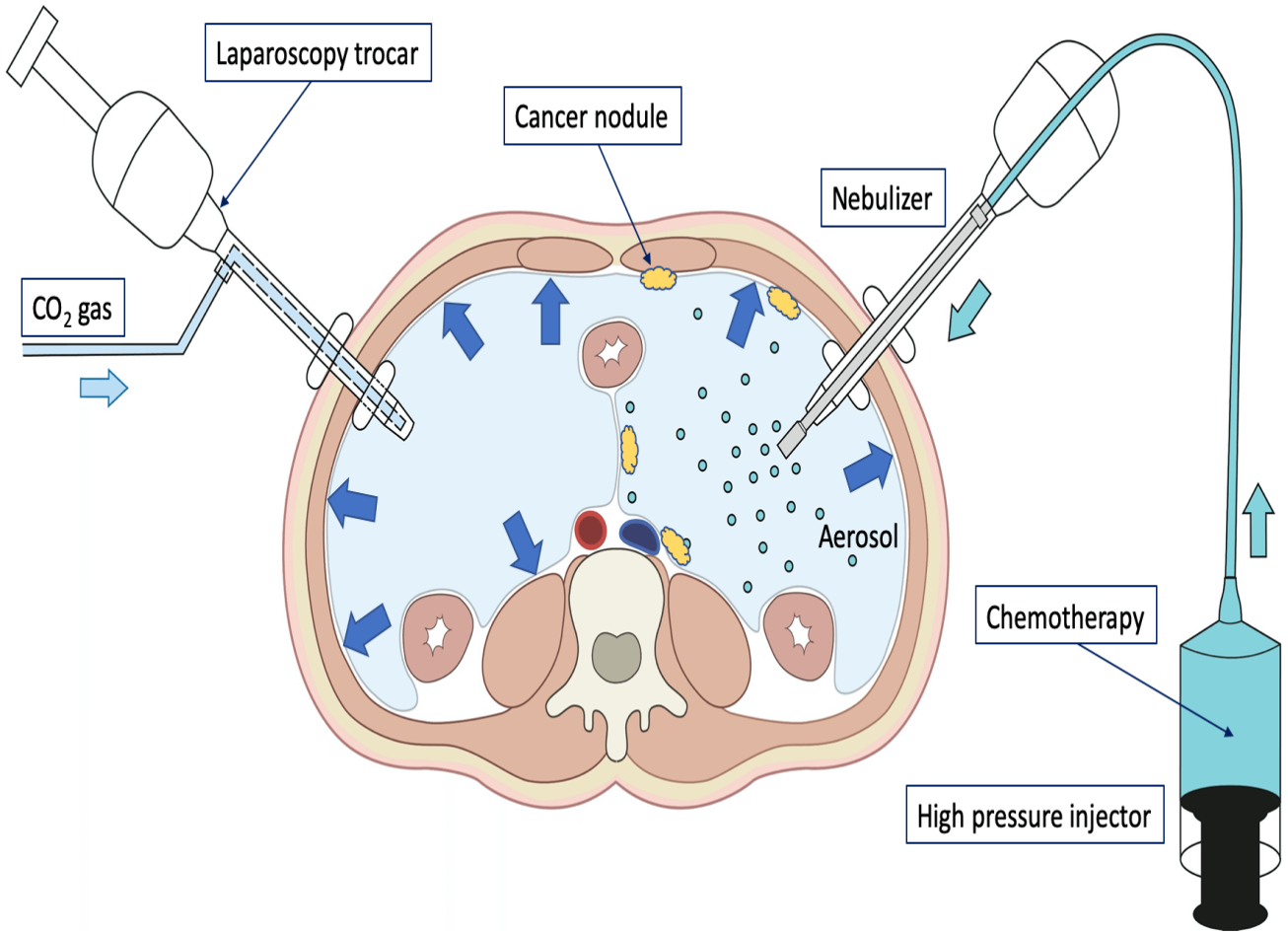
- PMP- CRS/HIPEC is gold standard of treatment
- CRS + HIPEC with CC-0 -5 yr OS (85%) , 10 yr OS (75%)

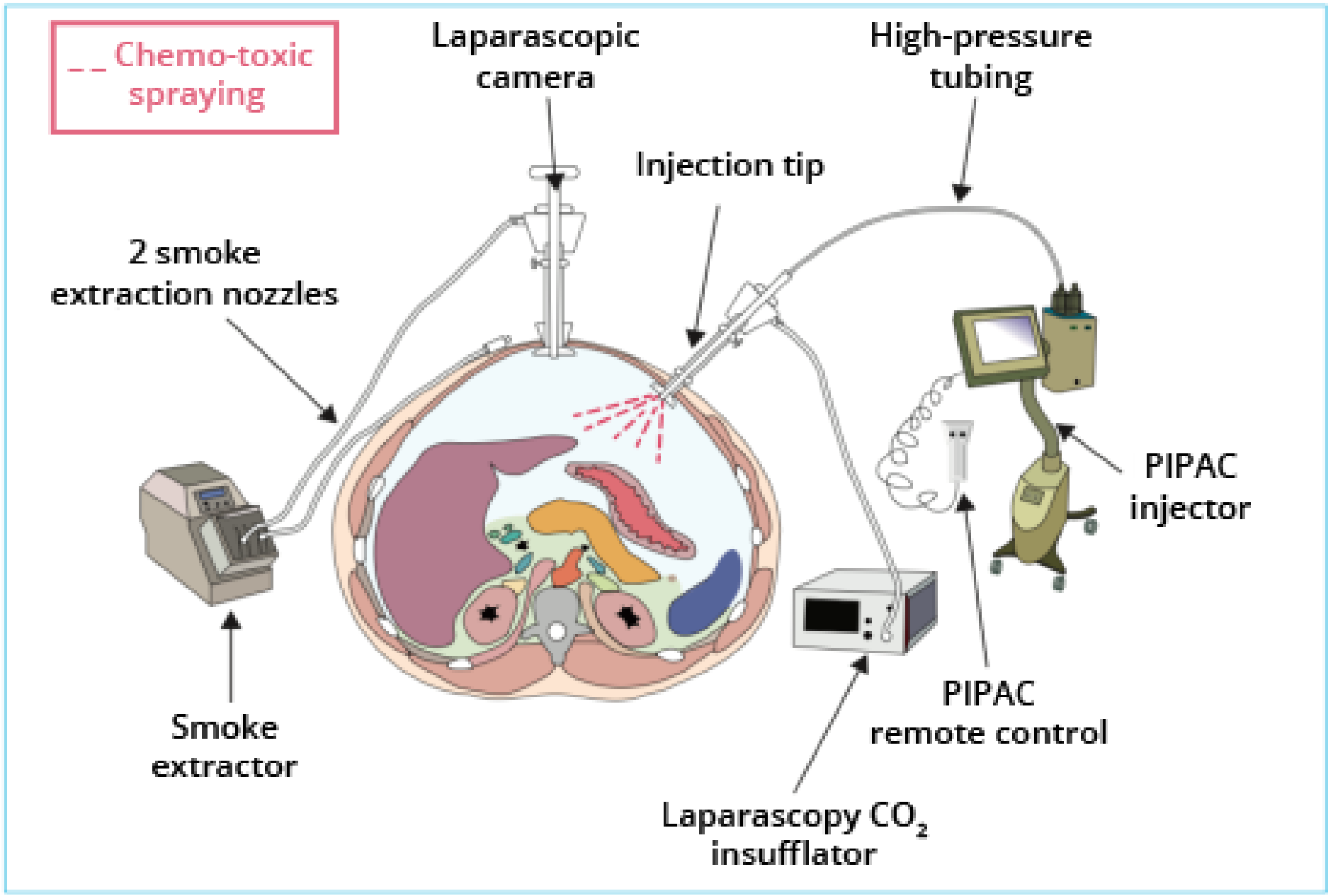
Gastric carcinoma PSM

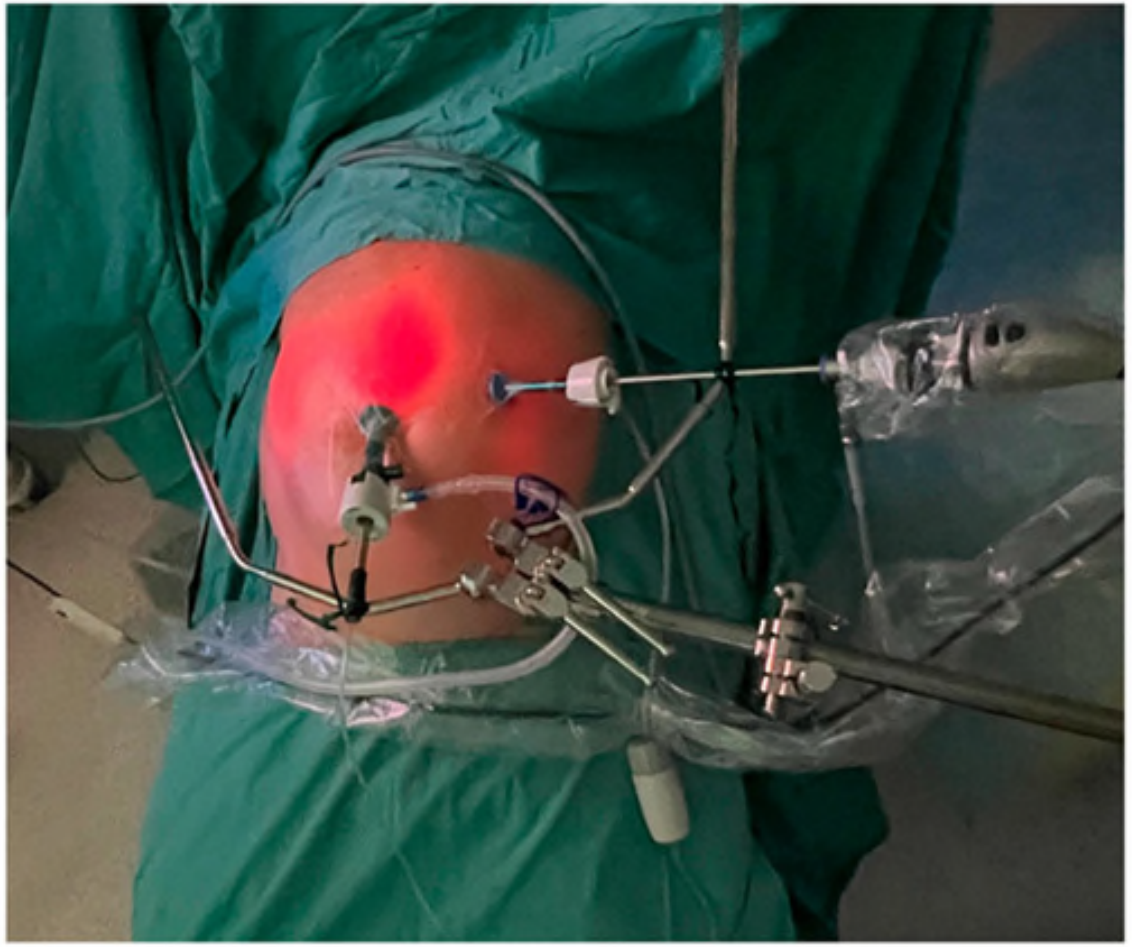
- Gastric ca with PSM- median OS 8-10 mths
- CRS +HIPEC combined with neoadjuvant and adjuvant systemic therapy > better DFS & OS
- Yokemura et al; Glehen et al;
- CRS + HIPEC with CC-0- median OS 15 mths ; 5 yr OS 23%
- Prognostic factors: CC-0 , PCI <6 (median OS > 40 mths)
  - CC-0 vs incomplete cytoreduction (40.7 mths vs 10.7 mths , p=0.003)
  -PCI ≤ 6 vs PCI > 6 (median OS 44.3 mths vs 13.4 mths, p value = .005
- Other prognostic factors- signet ring cell histology; poor differentiation; lymph node metastasis; lack of response to preop systemic cth

PIPAC (Pressurized Intraperitoneal Aerosolized Chemotherapy)

- Palliative
- Intraperitoneal chemotherapy delivery under pressure
- PSM patients who are ineligible for HIPEC
- First report in 2014
- Most commonly used for gastric cancer PSM
- Median OS for gastric cancer with PSM (palliative systemic cth without PIPAC vs with PIPAC: 10.7 vs 15.4 months)
- Can be administered in between systemic chemotherapy
- May facilitate CRS/HIPEC in patients who were initially ineligible

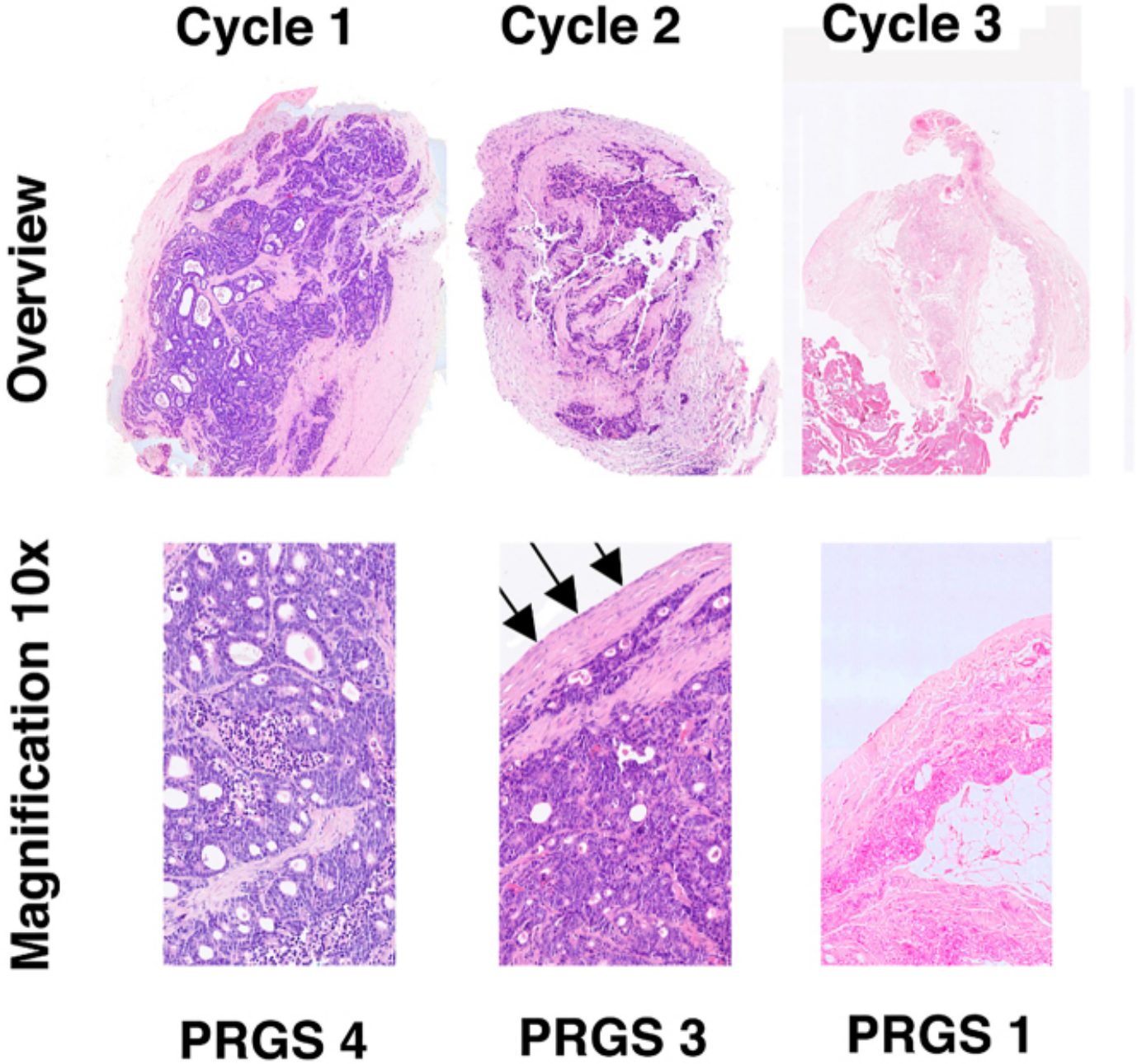

Laparoscopy trocar
Cancer nodule
Nebulizer
CO_2 gas
Aerosol
Chemotherapy
High pressure injector



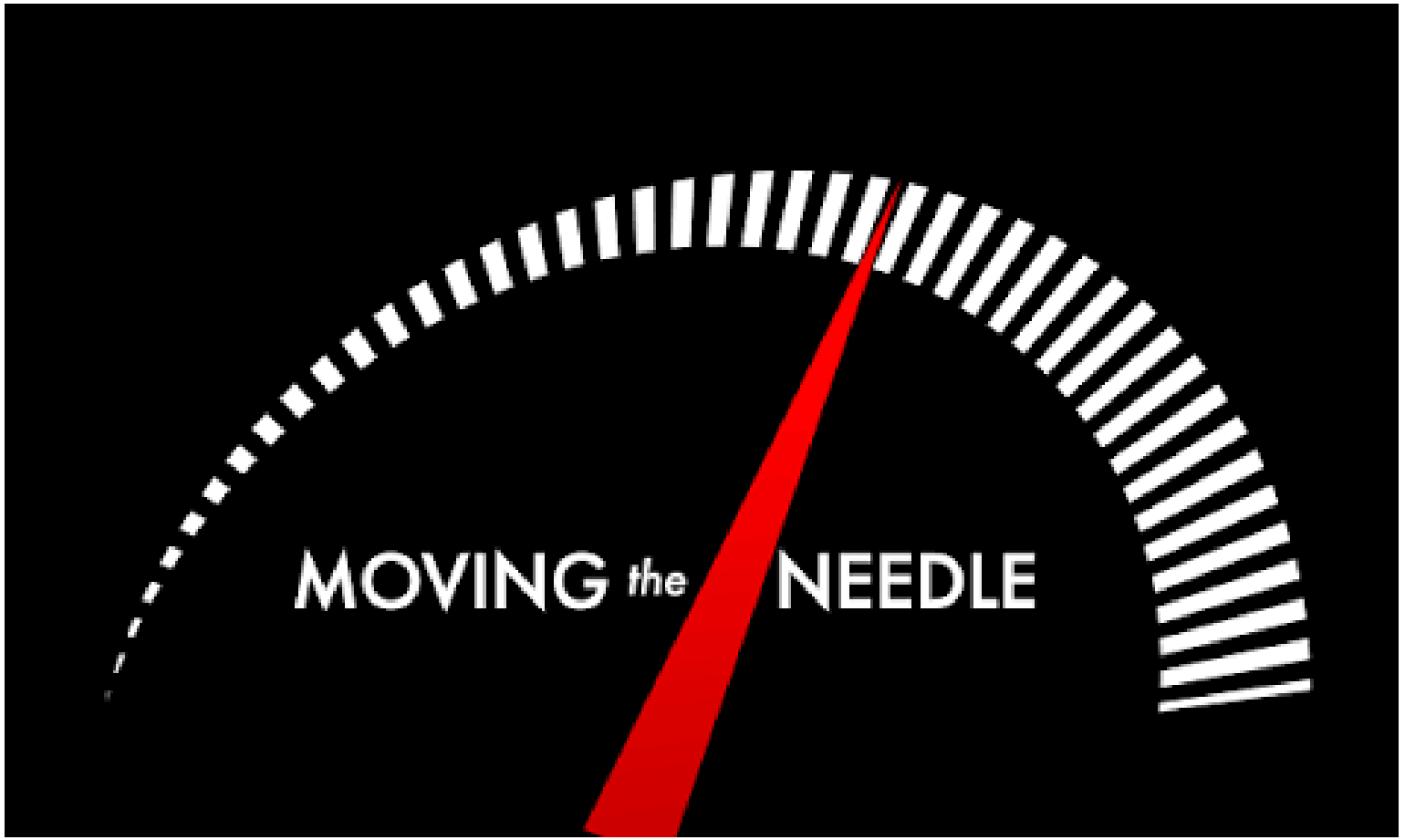


PIPAC set up

Peritoneal Regression Grading System (PRGS)		
Grade	**Tumor cells**	**Regression features**
PRGS 1 – complete response	No tumor cells	Abundant fibrosis and/or acellular mucin pools and/or infarct-like necrosis
PRGS 2 – major response	Few tumor cells (isolated or small clusters)	Fibrosis and/or acellular mucin pools and/or infarct-like necrosis predominant over tumor cells
PRGS 3 – minor response	Predominant tumor cells	Tumor cells predominant over fibrosis and/or acellular mucin pools and/or infarct-like necrosis
PRGS 4 – no response	Visible tumor cells (at lowest magnification)	No regressive changes


Cycle 1
Cycle 2
Cycle 3
Overview
Magnification 10x
PRGS 4
PRGS 3
PRGS 1

Survival Data- Are we moving the needle?



Survival Outcomes for CRS + HIPEC in CRC PSM

Metric/Subgroup	Survival estimate	Key context & clinical significance
Median OS	30-47 mths	12-16 mths for palliative systemic cth
5 yr OS	27-54%	Specialized surgical centers
Median DFS	9-14 mths	Mostly locoregional recurrences
Low Peritoneal Cancer Index (PCI ≤ 10)	69 % 3 yr OS	Disease burden is strongest predictor of OS
High Peritoneal Cancer Index (PCI > 20	Poor or minimal benefit	High disease burden; surgery is rarely recommended in this range.
Complete Cytoreduction (CC-0)	Highest survival tier	No visible macroscopic tumor remains after the surgical resection.
Incomplete Cytoreduction (CC-2/CC-3)	10-14 mths OS	Residual nodules >2.5 mm negate the survival benefits of HIPEC.

Survival outcomes for appendiceal PSM

Malignancy type/ Subgroup	5 yr OS	Median OS	Key clinical insights and context
Overall Appendiceal Cohort	60-70%	139 mths	Outcomes are significantly better than colorectal primaries due to the abundance of low-grade tumors.
Low-Grade Neoplasms (LAMN / DPAM)	82-91%	Not reached	Excel with complete surgery; 10-year survival rates remain high at 75%–85%.
High-Grade Adenocarcinoma (PMCA)	40-55%	43-53 mths	More aggressive biology; behaves similarly to colorectal peritoneal metastases.
Signet Cell Carcinoma	<30%	18-24 mths	Worst prognosis subgroup; highly aggressive with high early recurrence rates.
Complete Cytoreduction (CC-0 / CC-1)	Tier-dependent	Significantly prolonged	Crucial requirement for long-term benefit; incomplete surgery (CC-2/3) drops survival dramatically.

Survival outcomes for gastric PSM

Patient Subgroup / Clinical Metric	OS survival estimates	Key clinical insights and context
All Selected Gastric Patients (Median OS)	15-24 mths	Compares favorably to the ~3–12 month baseline of systemic chemo alone.
5-Year Overall Survival Rate	6%-25%	Long-term survival remains elusive for the vast majority of gastric patients.
Complete Cytoreduction (CC-0)	11-43 mths median OS	Macro-complete surgical removal of all visible tumors is mandatory.
Incomplete Cytoreduction (CC-1 or higher	6-8 mths median OS	Residual disease negates the major benefits of this aggressive surgical intervention.
Low Peritoneal Cancer Index (PCI < 6)	Prolonged survival	Gastric HIPEC is typically reserved strictly for patients with a minimal tumor volume.
High Peritoneal Cancer Index (PCI > 12)	Extremely poor prognosis	Surgery is contraindicated; treatment shifts entirely back to systemic palliation.
Positive Cytology Only (No Gross Tumor)	Superior survival tier	Patients with microscopic cancer cells in abdominal fluid benefit most from HIPEC

Survival Data for PIPAC

Cancer Type/ Clinical Benchmark	Median OS (months)	1-yr OS (%)
Colorectal	9-15	53
Gastric (PIPAC only)	6-8	25
Gastric (PIPAC + systemic CTH)	15	60
HPB	7-9	37
Ovarian/Gynecological	11-14	59
Overall pooled cohort (All cancer types)	11.7	54

Future Directions for HIPEC/CRS and PIPAC

Future directions for CRS/HIPEC

- **Minimally invasive approaches**
- **Precision Medicine & Molecular selection (ctDNA, NGS)**
- **Novel drug delivery models (photoimmunotherapy, CO2 agitation, immunotherapy and targeted therapy)**
- **Standardizing care pathways (prehabilitation and ERAS)**
- **Trial endpoints and sequential therapy (QoL, treatment free interval, prevention of extraperitoneal relapse, PIPAC as bridge to HIPEC/CRS)**

Future Directions for PIPAC

- **Neoadjuvant/Prophylactic use**
- **Electrostatic precipitation (ePIPAC)**
- **Improved technology (micronebulizers, ultra thin devices)**
- **Immunotherapy**
- **Standardized bidirectional therapy**

Thank You