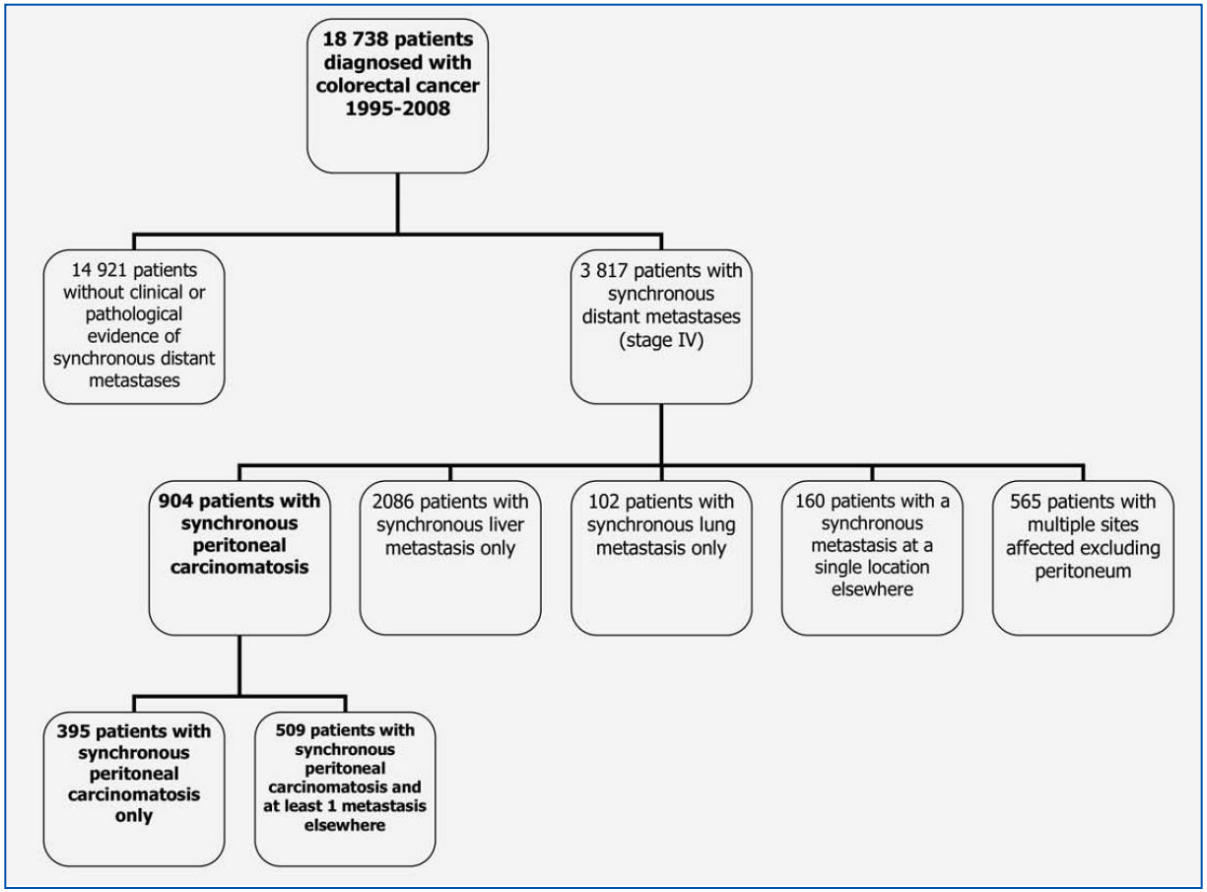
Hospital Barmherzige Brueder Regensburg
Department of General- and Visceral Surgery

Treatment of metastatic disease confined to the peritoneum

Pompiliu Piso

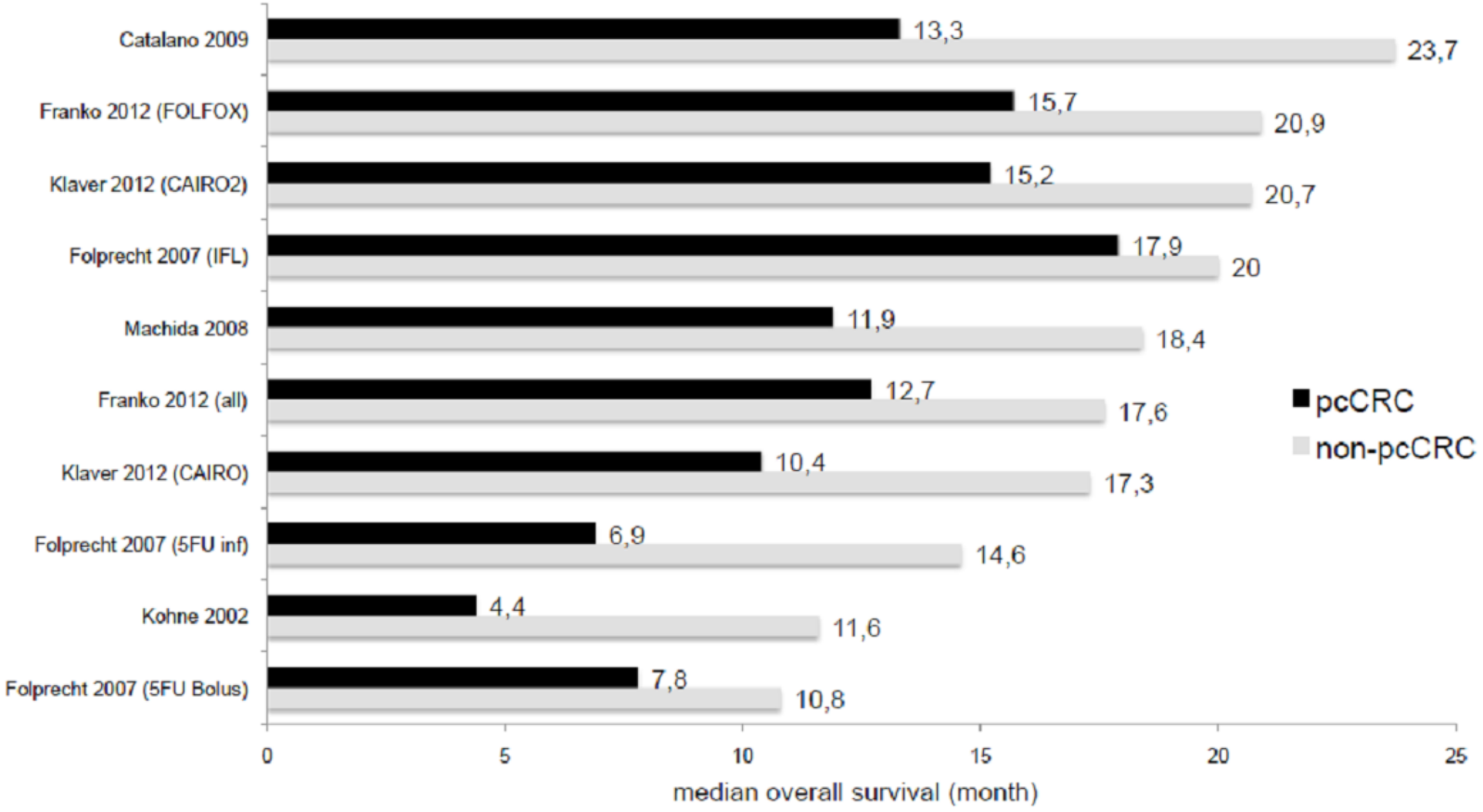
4.8% synchronous PC, Lemmens et al, Int J Cancer 2011



4.2% of 12.000, Segelmann et al, Br J Surg 2012

30% intraoperative diagnose, Glehen et al, Cancer 2010

Only 2% of all patients had PC



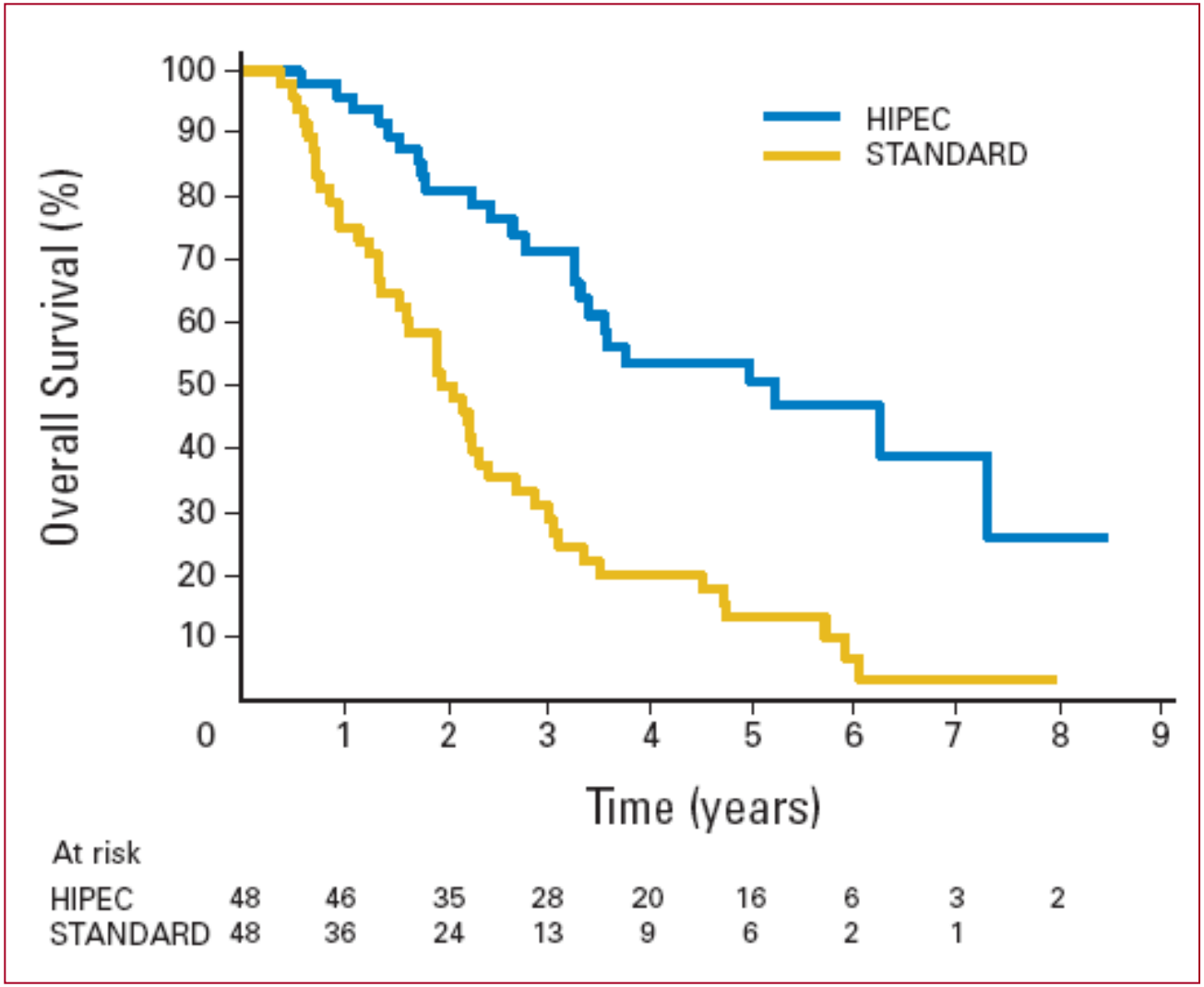
Franko J et al. Curr Colorectal Cancer Rep 2013

Glehen O et al, J Clin Oncol 2004
Univariate Analysis (n = 506), International Registry

Variable	Median (months)	Log-Rank p
Preoperative systemic chemotherapy		
Yes vs. No	19.2 vs. 20.4	0.35
Adjuvant systemic chemotherapy		
Yes vs. No	25.2 vs. 15.6	0.02

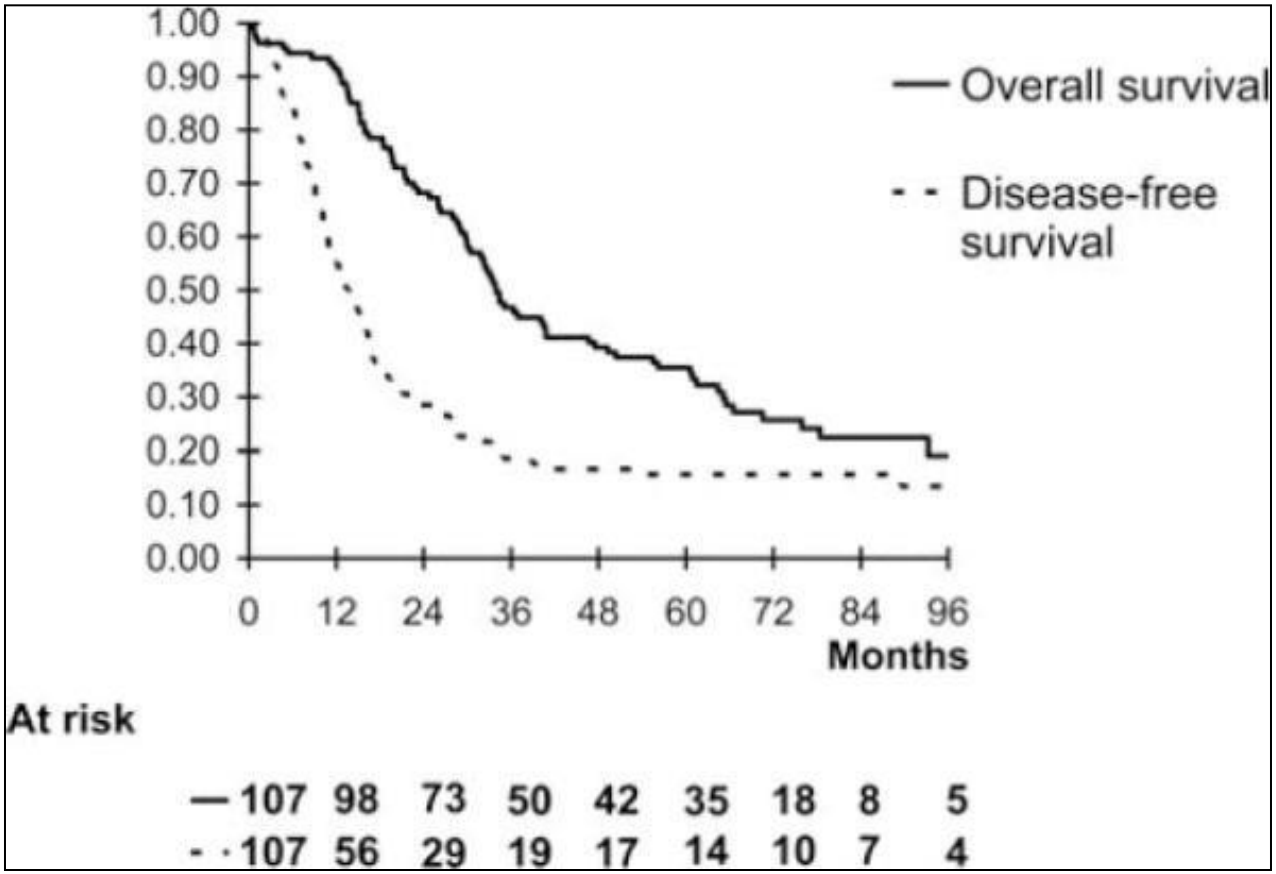
Elias D et al, J Clin Oncol 2010
Univariate Analysis (n = 523), French Registry

Variable	Median (months)	Log-Rank p
Preoperative systemic chemotherapy		
Yes vs. No	30 vs. 30	0.85
Adjuvant systemic chemotherapy		
Yes vs. No	31 vs. 27	0.04



Elias D et al. J Clin Oncol 2009

Is There a Possibility of a Cure in Patients With Colorectal Peritoneal Carcinomatosis Amenable to Complete Cytoreductive Surgery and Intraperitoneal Chemotherapy?

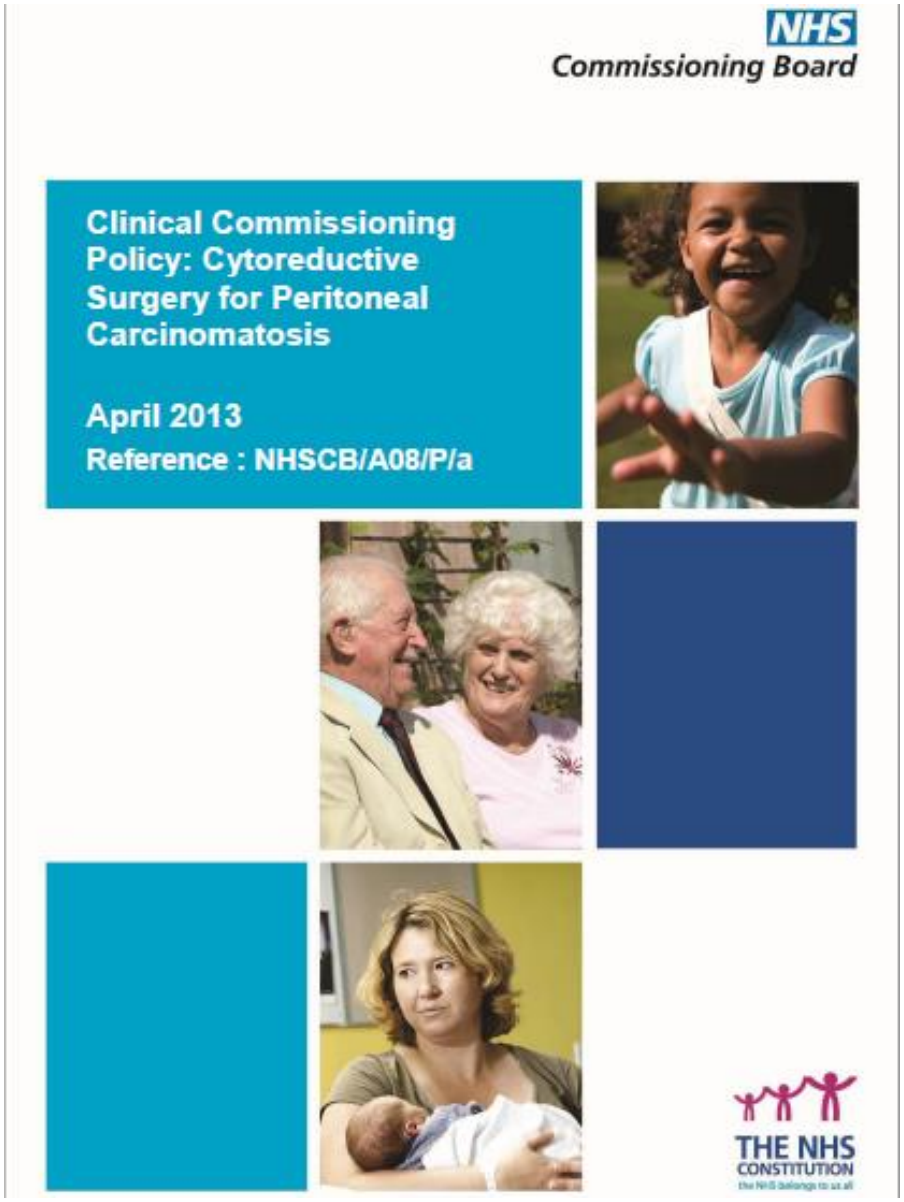


Goere D et al. Annals of Surgery 2013

Multimodal Treatment for PC arising from CRC

JOURNAL OF CLINICAL ONCOLOGY	Verwaal et al. 2003 (15), 2008 (16)	1b	Prospective randomized
JOURNAL OF CLINICAL ONCOLOGY	Elias et al. 2009 (17)	3b	Matched-pair
Cancer	Franko 2010 et al. (18)	3b	Matched-pair
Annals of SURGICAL ONCOLOGY	Matheme et al. 2004 (19)	3b	Matched-pair
JOURNAL OF CLINICAL ONCOLOGY	Glehen et al. 2004 (20)	2b	Multinational register
JOURNAL OF CLINICAL ONCOLOGY	Elias et al. 2010 (21)	4	French register
ANNALS OF SURGERY	Cao et al. 2009 (22)	2a	Systematic meta-analysis
ANNALS OF SURGERY	Elias et al. 2010 (13)	2b	Matched-pair
Annals of SURGICAL ONCOLOGY	Elias 2004 et al. (e5)	2b	Prospectiv randomized
Annals of SURGICAL ONCOLOGY	Esquivel et al. 2007 (6)	3a	Consensus conference
Cancer	Glehen et al. 2010 (e6)	2b	Large multicentric retrosp.

P Piso, D Arnold, Dtsch Arztebl Int 2011, 108:402-8



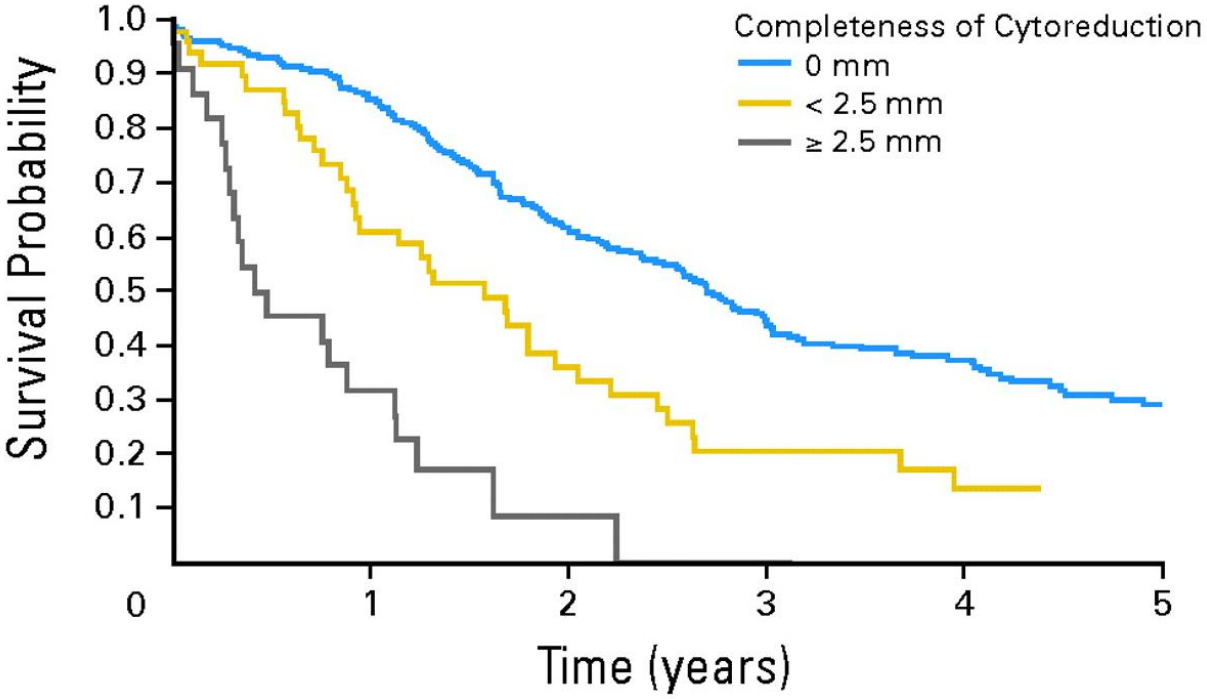
http://www.england.nhs.uk/wp-content/uploads/2013/04/a08-p-a.pdf

- Resection
- HIPEC
- PIPAC

- Resection

Completness of Cytoreduction:

Complete cytoreduction: CCR-0 (CCR-1)



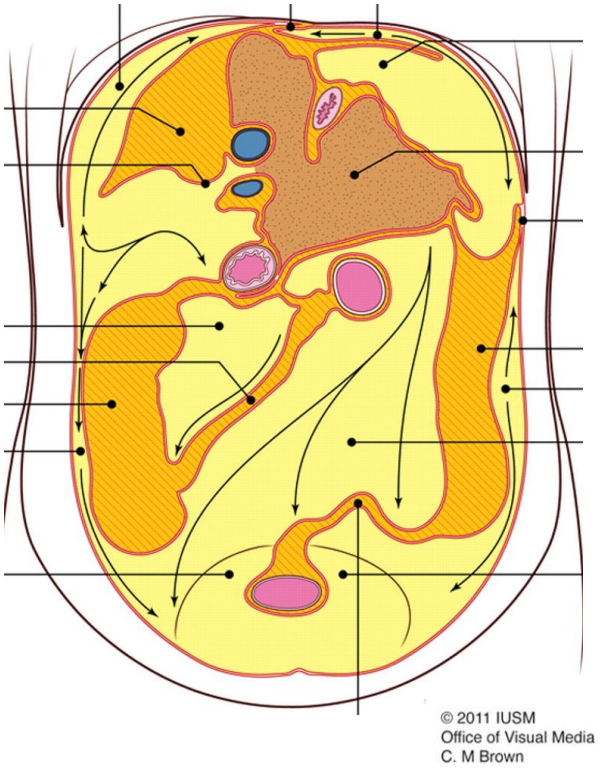
D Elias, Journal of Clinical Oncology 2010

Peritonectomy Procedures

PeritonectomyRUQ

Lesser omentectomy
CHE

Right colectomy



PeritonectomyLUQ

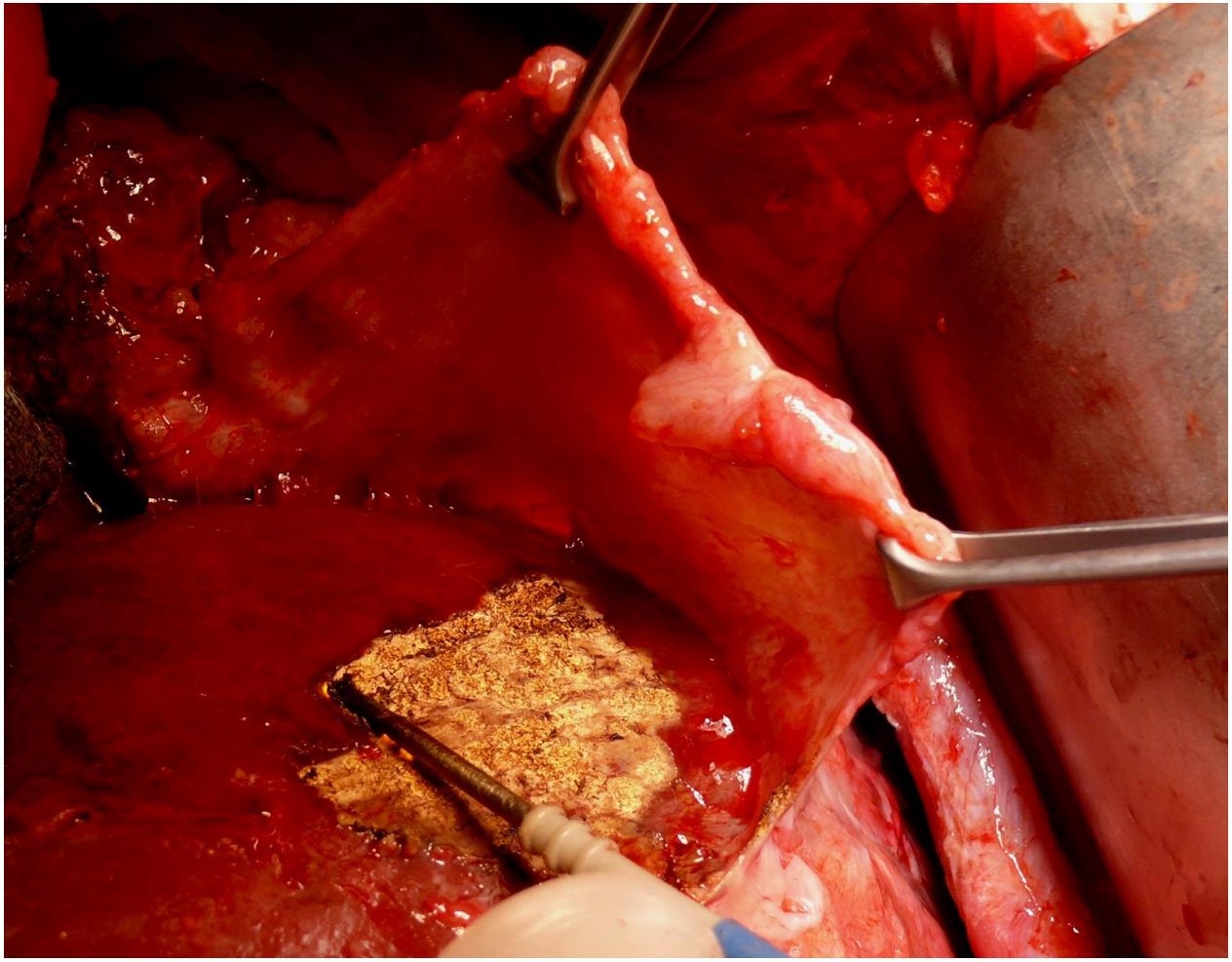
Omentectomy
Splenectomy

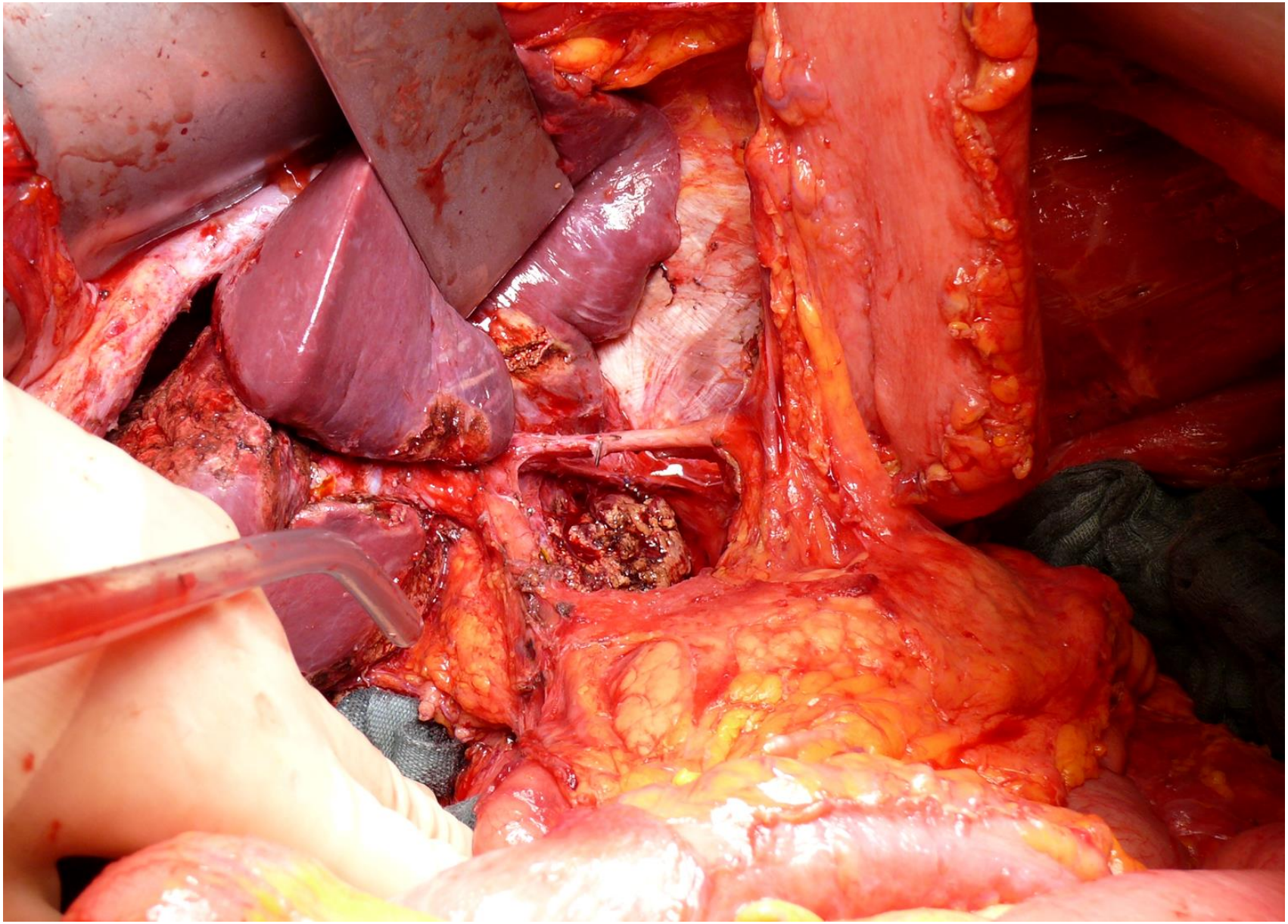
Gastrectomy

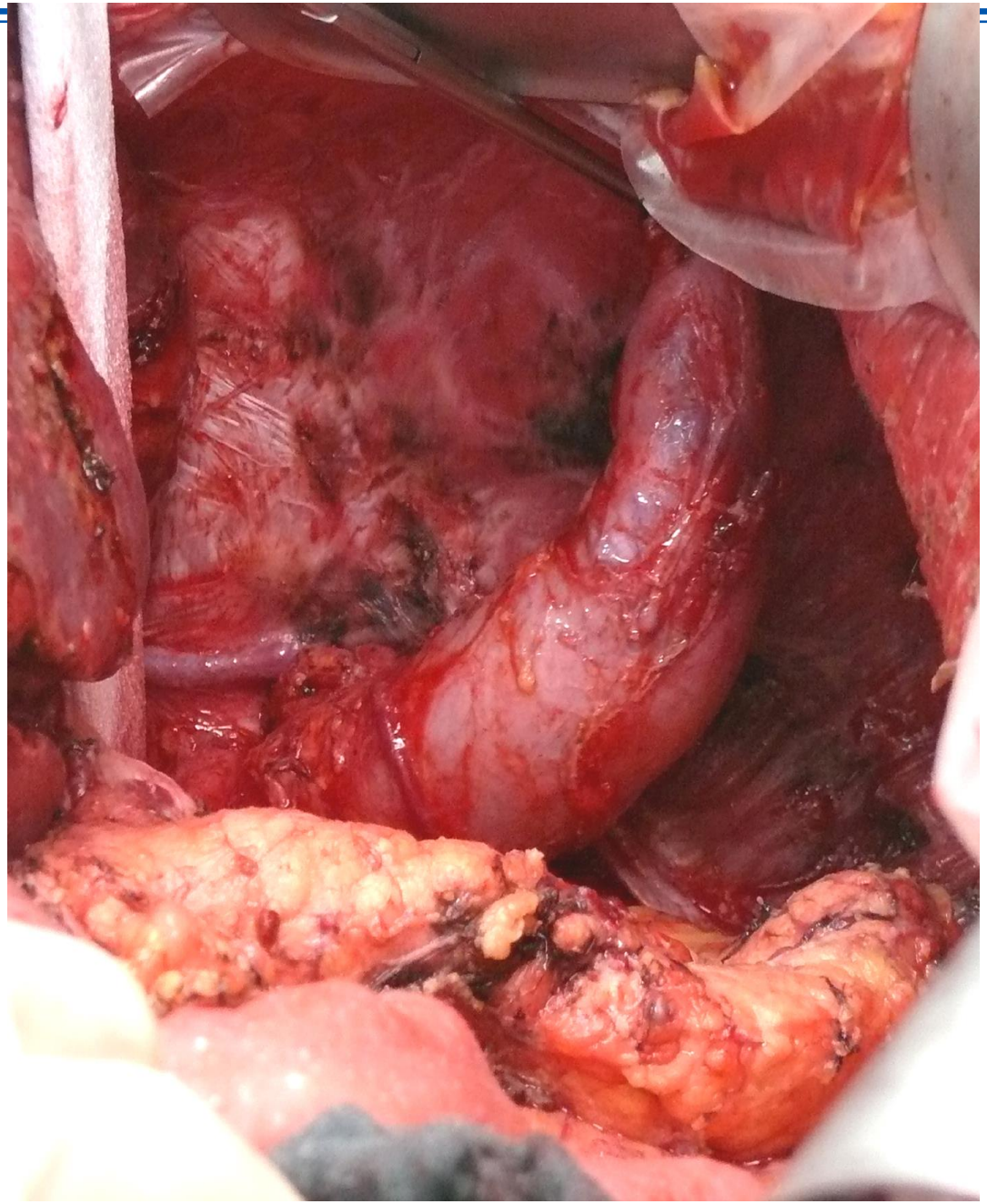
Anterior parietal
peritonectomy

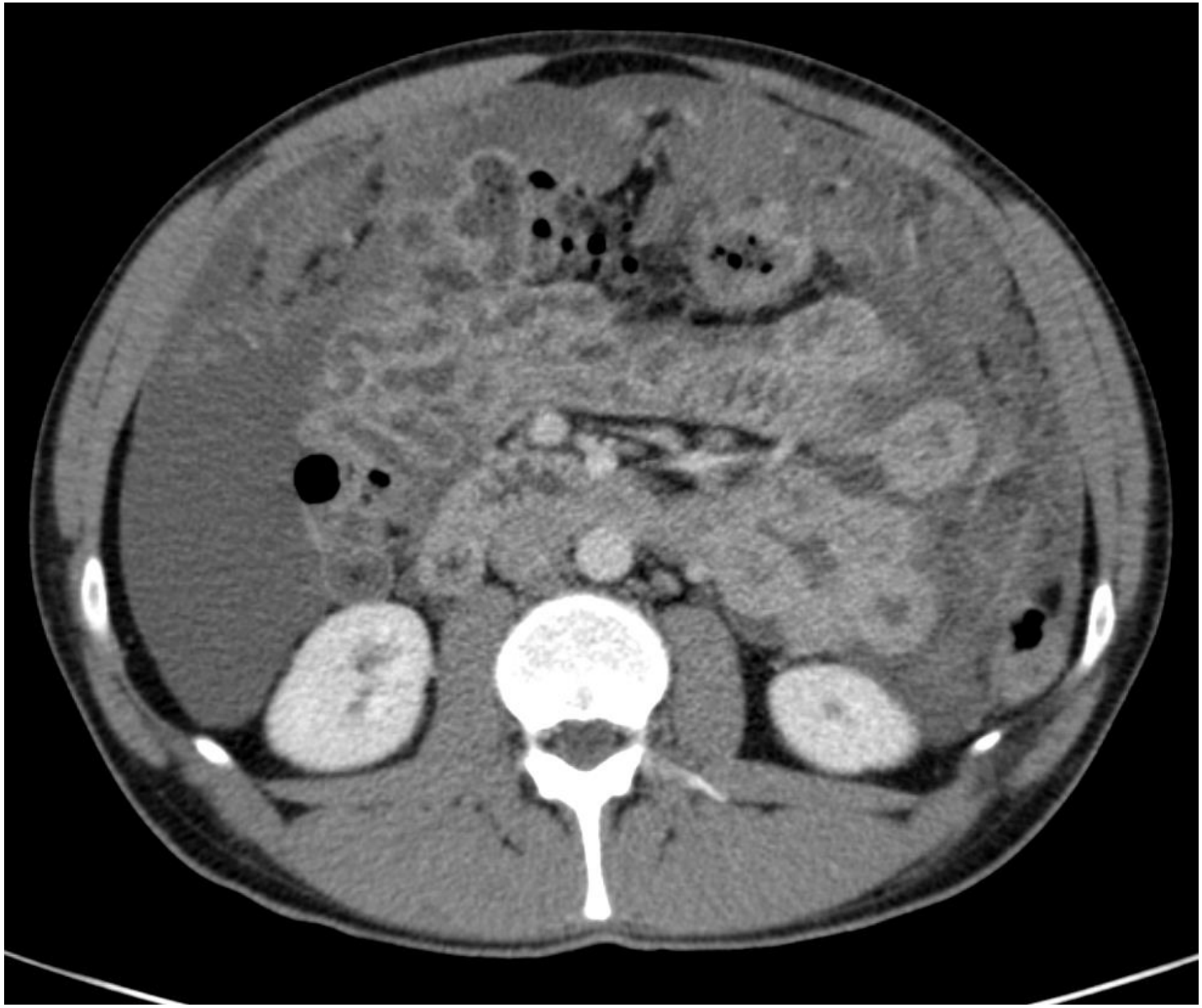
Peritonectomy small pelvis,
Rectosigmoid resection,
Hysterectomy

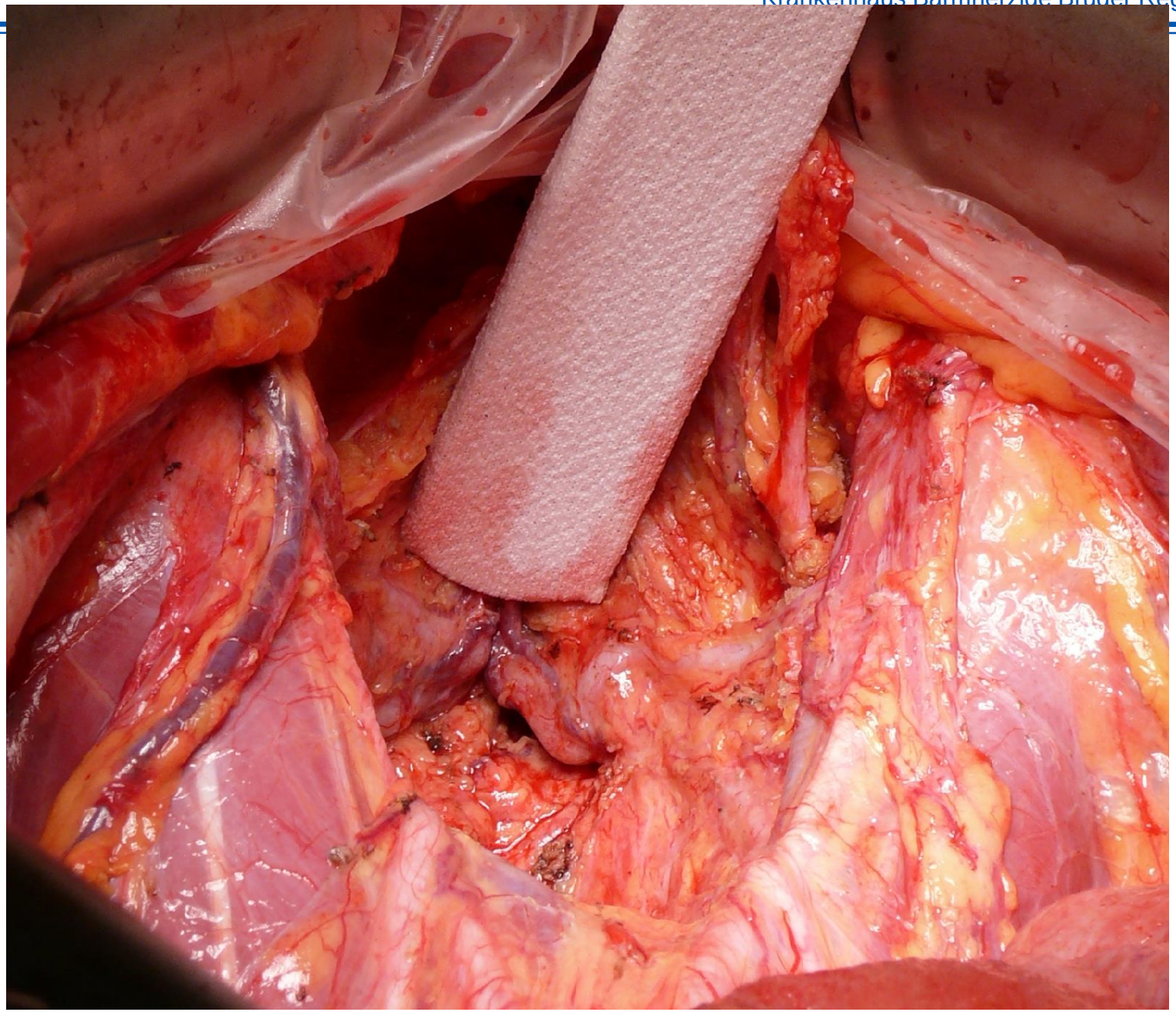
Sugarbaker et al,
Ann Surg 1999
Tirkes T et al.
Radiographics 2012











Selection for multimodality treatment

No extensive small bowel disease,
max. one bowel stenosis
(PET-CT, CT, laparoscopy)

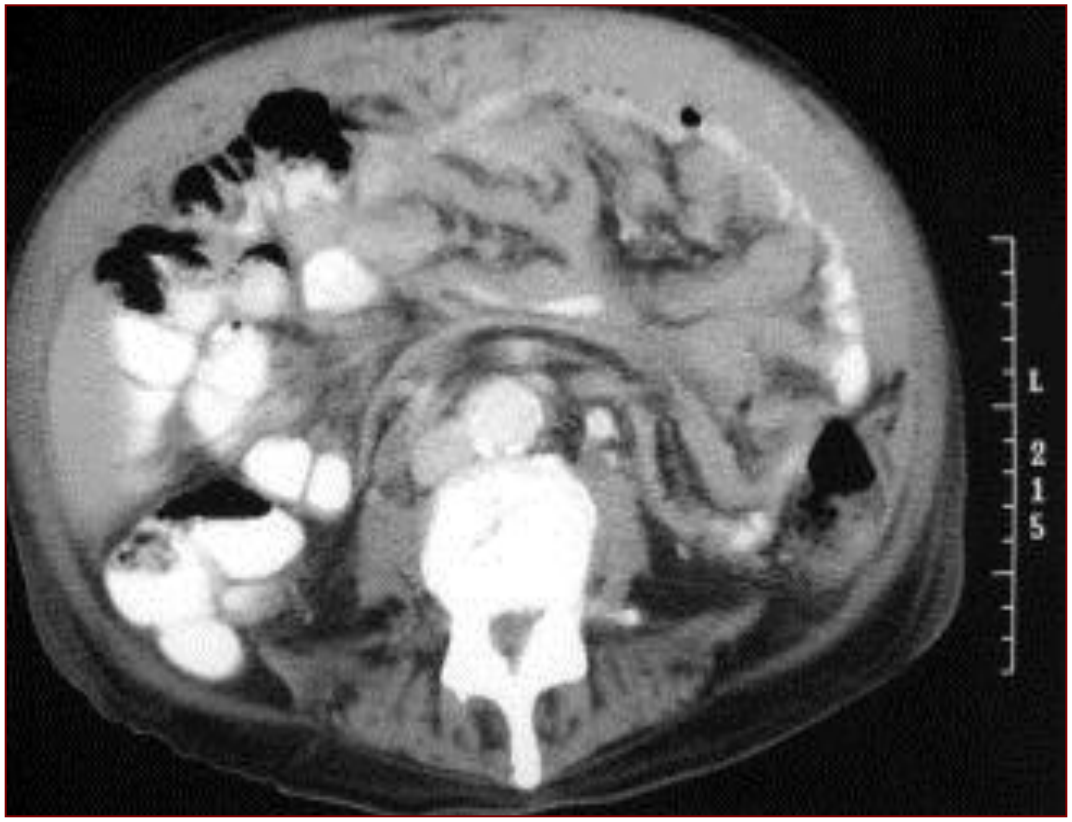
No biliary/ureteral obstruction
due to tumor penetration

No involvement of the
gastrohepatic ligament > 5cm (CT)

Good Performing status
(ECOG 1 or 2)
No severe co-morbidities

Piso, Cancer J, 2009

Small bowel involvement



Piso et al, Int J Colorect Dis 2007, Esquivel et al, Ann Surg Oncol 2007

Laparoscopy own data – exclusion of small bowel disease

- 2011: 111 CRS+HIPEC
- 2012: 122 CRS+HIPEC
- 2013: 125 CRS+HIPEC

- 148 Laparoscopies
  - 70% were excluded from major surgery
  - 75% CCR0-1 of those having CRS after laparoscopy

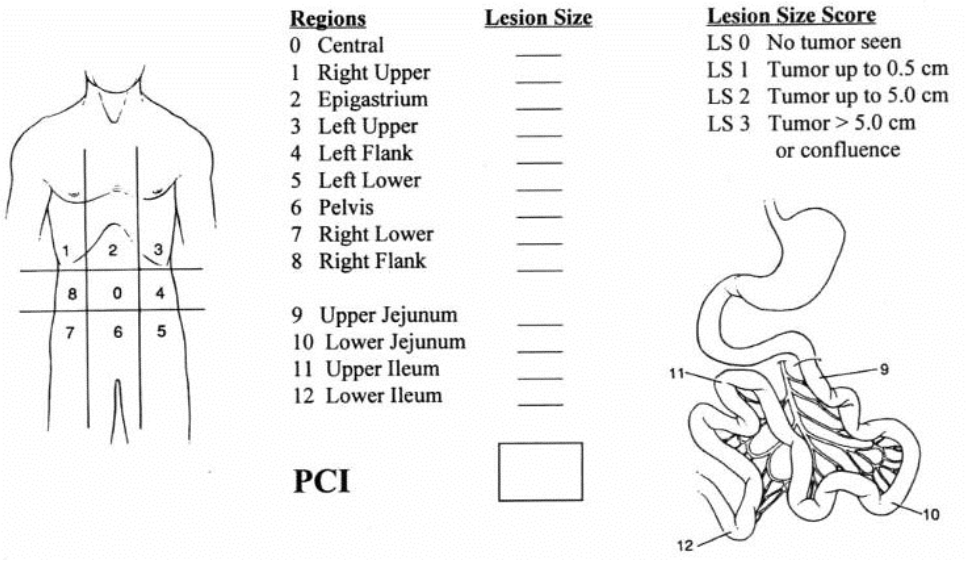
Selection for multimodality treatment

PCI<20
(CT, PET-CT)

No extra-abdominal metastases

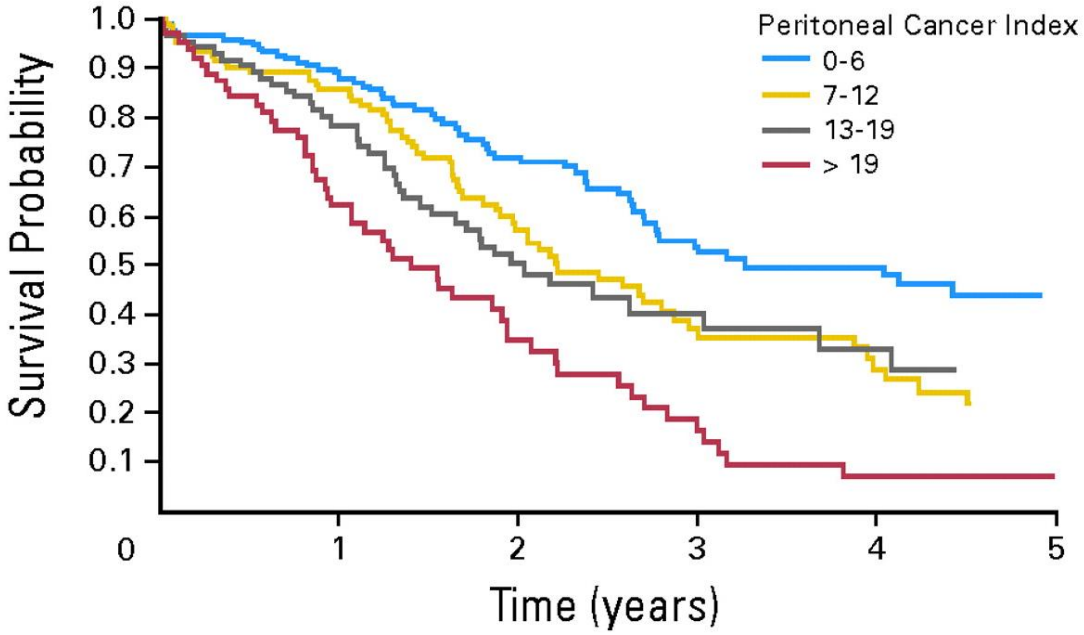
Up to 3 peripheric resectable liver metastases

- Patient motivation
- Infrom consent
- At least acceptable QoL predictable

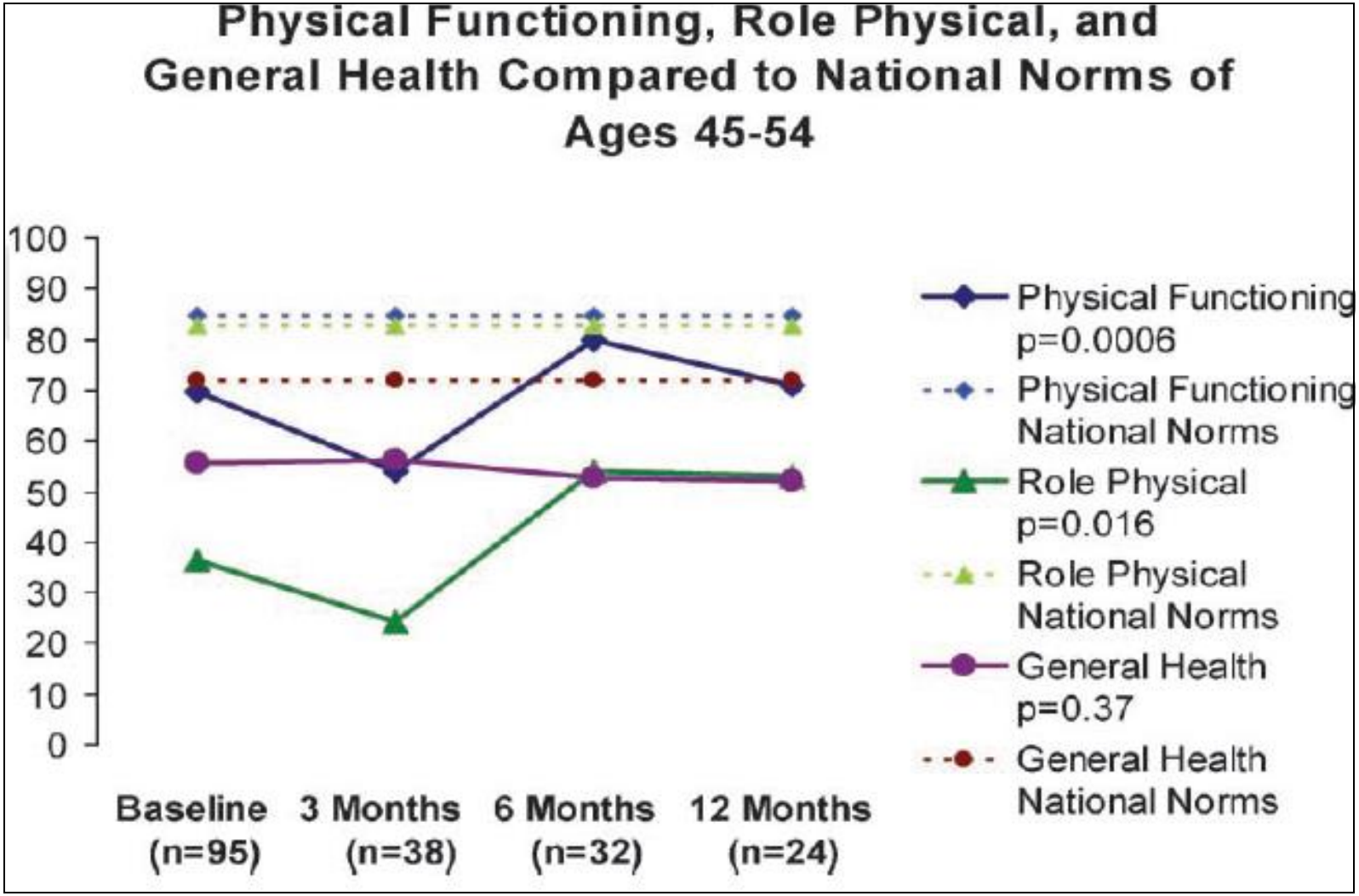


Piso, Cancer J, 2009

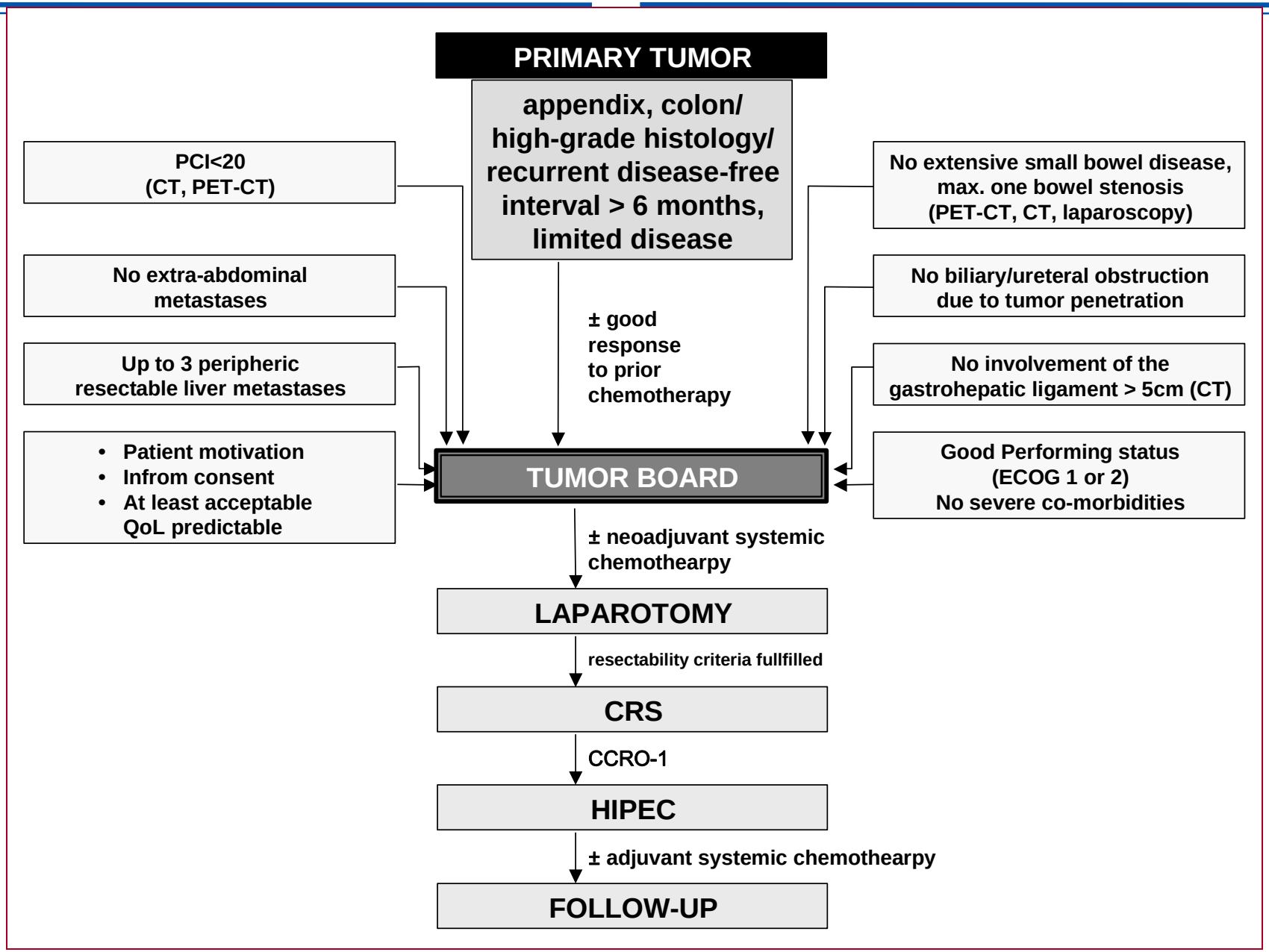
Peritoneal Cancer Index:
Tumorextent: PCI < 20



D Elias, Journal of Clinical Oncology 2010



McQuellon, Piso et al J Surg Oncol 2008



Piso, Cancer J, 2009

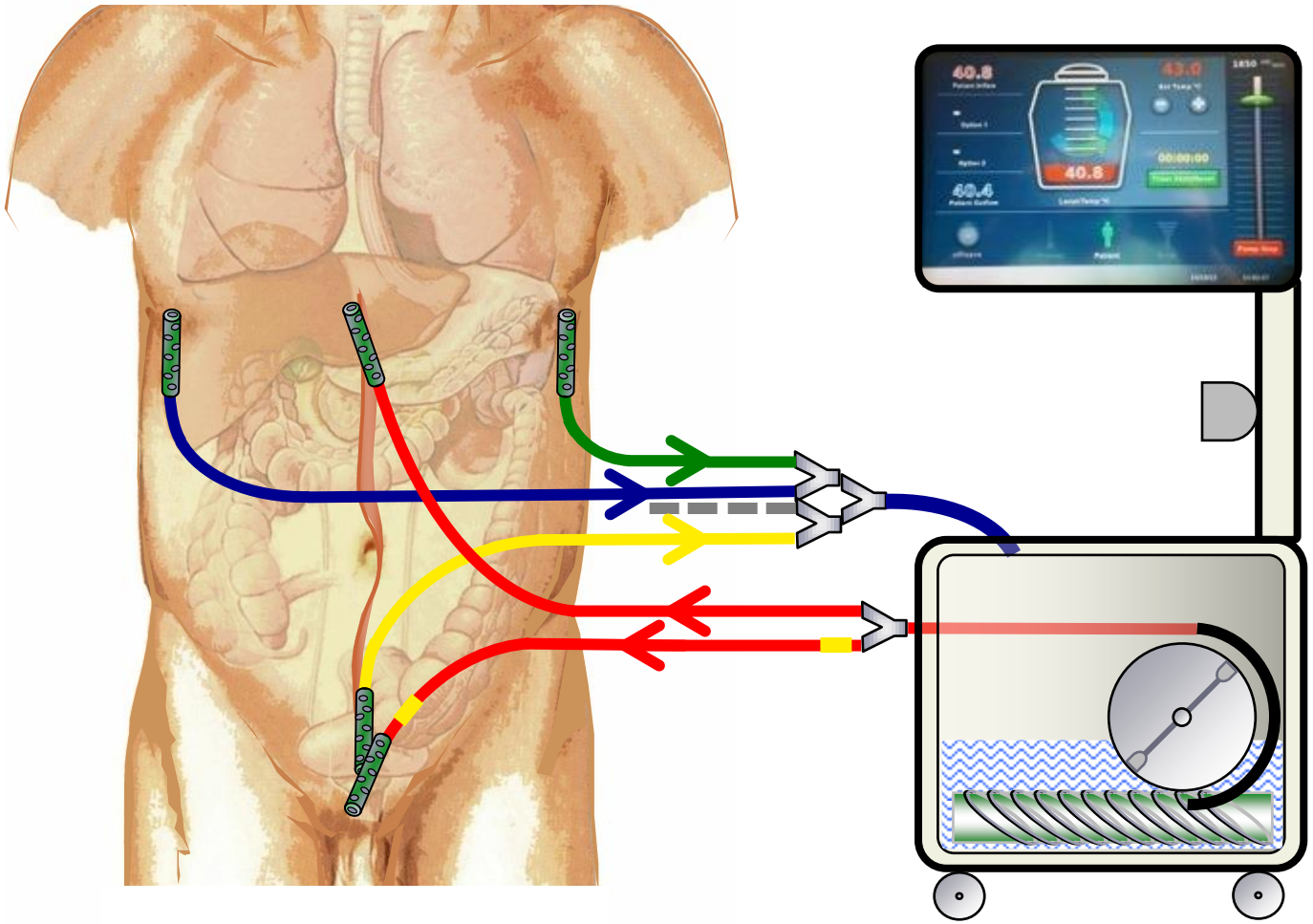
- HIPEC

- HIPEC only for CCR0/1
- Bidirectional protocole with oxaliplatin EU
- Mitomycin protocole USA

Table 1 | Properties of cytotoxic agents used during intraoperative or early postoperative intraperitoneal chemotherapy

Drug	Molecular weight (Daltons)	Intraperitoneal dose (mg/m^2)	Area under concentration-time curve ratio*	Drug penetration distance	Thermal enhancement
Platinum compounds					
Cisplatin[84]	300.1	90–250	13–21	1–3 mm	+
Carboplatin[85]	371.3	350–800	1.9–5.3	0.5 mm	+
Oxaliplatin[86]	397.3	460	3.5	1–2 mm	+
Antimicrotubule agents					
Paclitaxel[87]	853.9	20–175	NA	More than 80 cell layers	Not studied
Docetaxel[88]	861.9	40–156	207	NA	+
Topoisomerase interactive agents					
Mitoxantrone[89]	517.4	28	15.2	5–6 cell layers	±
Doxorubicin[90]	543.5	60–75	162	4–6 cell layers	+

Ceelen, Flessner in Nature Rev Clin Oncol 2010, 7:108-15



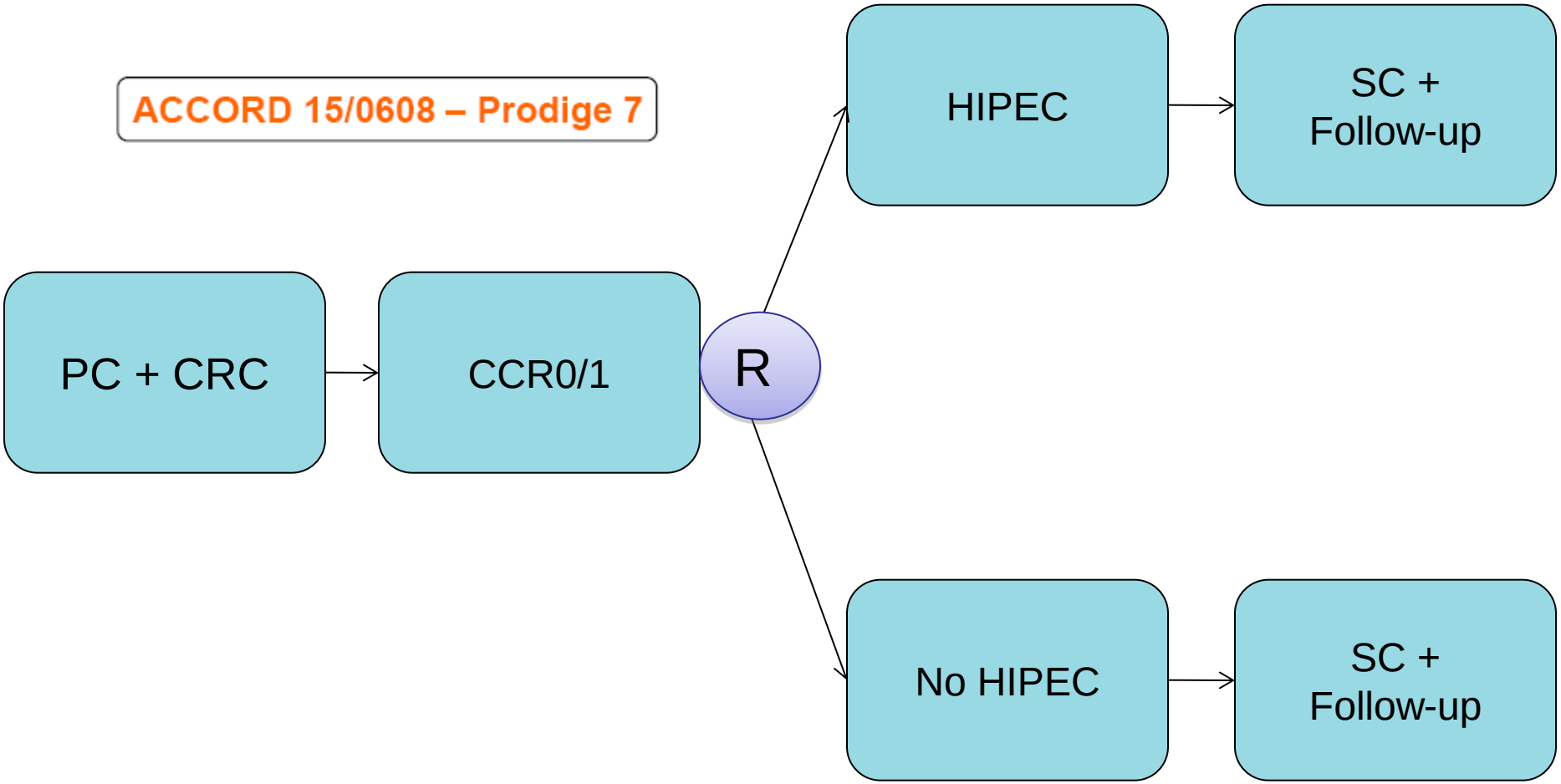
C. Plechinger, Kardialgut, Munich

Oxaliplatin vs. Mitomycin i.p.

- 307 patients
- Matched pair analysis
- Ox. vs. MMC 42% vs. 37% p=0.6 (CTCAE v3.0 grade 3 and 4)
- Mortality 2.5% vs. 0%

Glockzin, Piso in J Surg Oncol 2013, 107:574-8

Phase III trial on role of HIPEC after CCR0/1 for PC from CRC



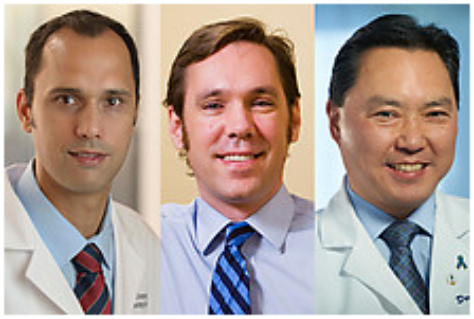
OnCancer
News and Insights from Memorial Sloan Kettering

IN THE CLINIC

Heated Chemotherapy: Using Robust Science to Guide Clinical Decisions

By Esther Napolitano, BS, Science Writer/Editor | Friday, November 15, 2013 9 comments

A procedure called hyperthermic (heated) intraperitoneal chemotherapy, or HIPEC, has shown some promise in early studies for certain types of cancer. Although a number of hospitals in the country are now offering HIPEC, the data to support its use is limited, and some experts argue that more research is needed to evaluate the risks and benefits of the approach, which patients are most likely to benefit, and whether it is better than standard therapies.



Surgeons Oliver Zivanovic, Garrett Nash, and Dennis Chi are leading novel studies of a procedure called hyperthermic intraperitoneal chemotherapy, also known as HIPEC.

Now experts at Memorial Sloan Kettering have set out to attain conclusive scientific evidence to determine the effectiveness of HIPEC in patients with colorectal or appendix cancer, and in women with certain gynecologic cancers.

- PIPAC

PIPAC: Technical aspects

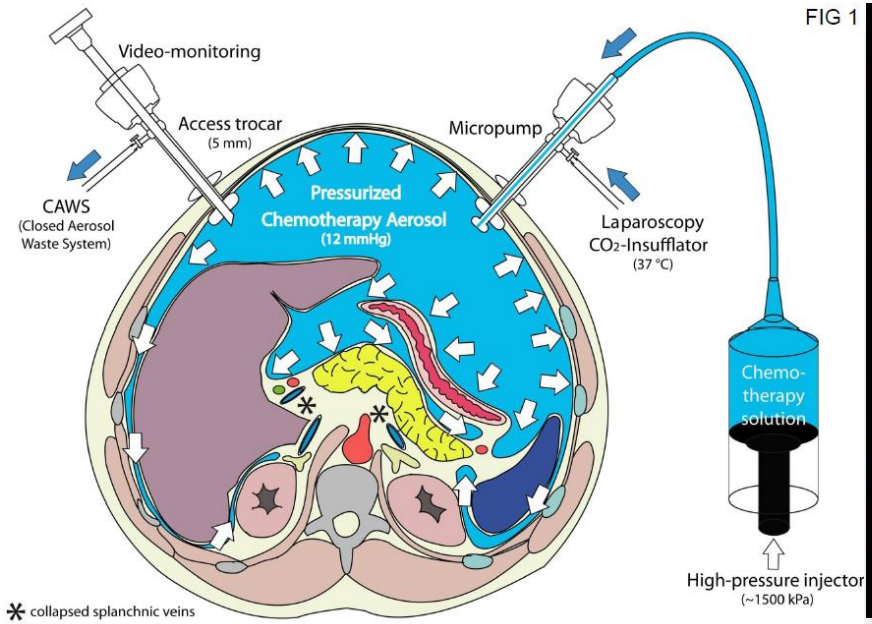
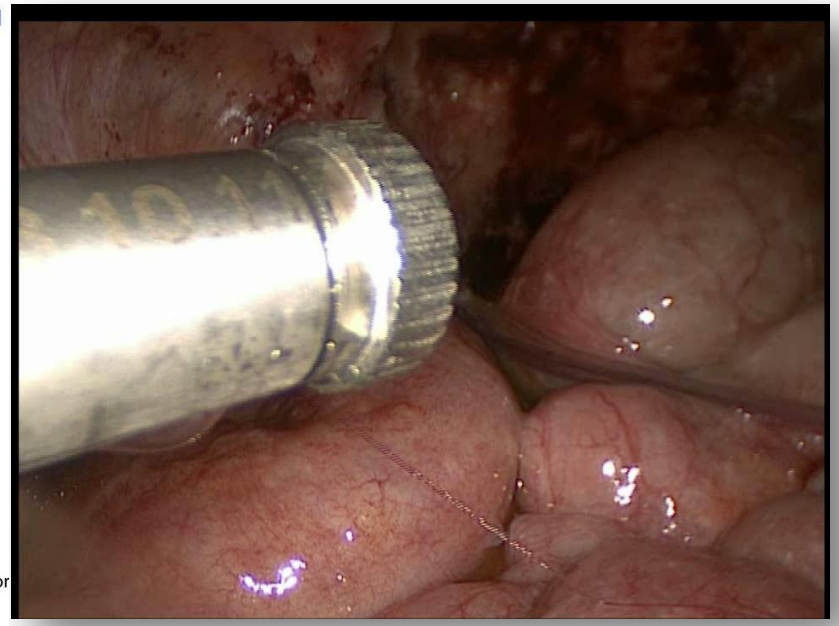


FIG 1



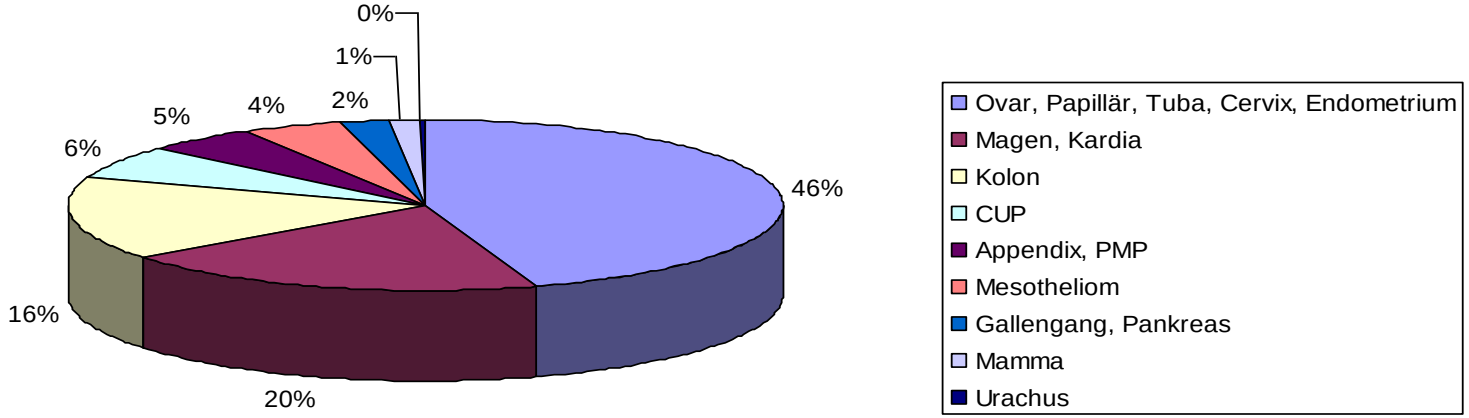
- Laparoscopic approach: 12 mmHg i.-p. pressure, 30 min.
- Chemotherapy: colon: Oxaliplatin 92 mg/m2 body surface;
- Device : MIP®, Reger Medizintechnik (CE-certified, class 2A)
- High-pressure injector: any industry-standard injector up to 20 bar (e.g. Medrad)

1. An artificial hydrostatic intraperitoneal pressure is created
2. Gas/aerosol repartition within a closed volume is homogeneous
3. PIPAC can be repeated

Prof. Raymond, Marien Hospital, Ruhr-University Bochum

5.11.2011 to 2.5.2014: 483 PIPAC + 7 PITAC in 253 patients

556 procedures including primary and secondary non-access (11.9%)



Palliative indication in pretreated, platin-resistant peritoneal carcinomatosis, primary CRS and HIPEC not indicated

Therapy within the framework of regulatory studies PIPAC-OV1 (NCT01809379) and PIPAC-GA1 (NCT01854255) as well of as off-label use according to German AMG.

Mortality zero in the last 383 consecutive procedures
Local toxicity is acceptable, systemic toxicity is minimal
Quality of life appears to be preserved, 1y SR for CRC 70%
PIPAC is not expensive, limited due to max. number of PIPAC sessions

- New concept of locoregional and systemic approach for peritoneal metastases

Cytoreductive surgery plus hyperthermic perioperative chemotherapy to treat peritoneal metastases from colorectal cancer: standard of care or an experimental approach?

Lancet Oncol 2012; 13: e362–69

Paul H Sugarbaker, David P Ryan**

*Joint authors

Washington Cancer Institute, Washington, DC, USA (P H Sugarbaker MD); Department of Medicine, Harvard Medical School, Boston, MA, USA (D P Ryan MD); and

Credits

- Long-term survival in 30% of patients
- Patients with minimum carcinomatosis experience best survival
- Morbidity (12%) and mortality (1%) at experienced centres is acceptable
- Favourable results of treatment continue to be reported from many different institutions in the oncology literature

Debits

- The surgical technology is complex and requires an extended learning curve
- Surgical series contain patients who have received many different chemotherapy regimens and who are at many different timepoints in their treatment
- The one randomised trial was flawed, primarily by the inclusion of patients with appendiceal tumours
- Whether the procedure is causally related to long-term survival or if surgeons select patients likely to survive long term is unclear

Invited commentary: Surgery and chemotherapy for peritoneal carcinomatosis—More about selection and biology than treatment?

Murray F. Brennan, MD, *New York, NY*

From the Department of Surgery, Memorial Sloan-Kettering Cancer Center

I am reminded of the question, "Is the glass half full or half empty?" Well, it all depends on whether you are drinking or pouring!

German S3-Guideline CRC 2013

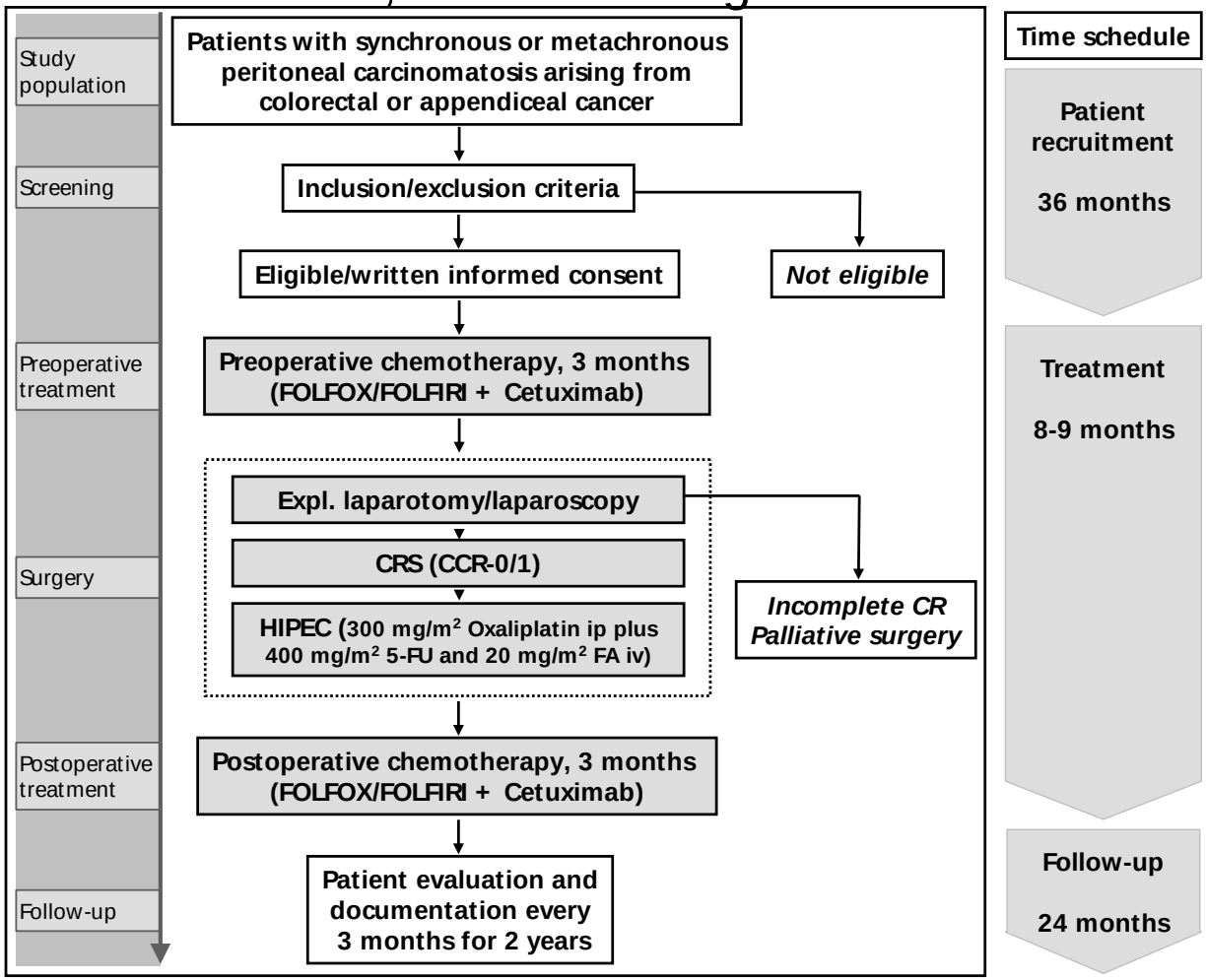
Level of Evidence 2a, strong consensus

- In patients with an **isolated** and **limited** peritoneal carcinomatosis, **without** extraabdominal metastases and **low PCI** (peritoneal cancer index, < 20) cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy can be performed.
- A pre-requisite is **complete macroscopic** cytoreduction.
- The treatment should be performed in **specialized centers**. If possible, patients should be included in **studies**.

http://www.krebsgesellschaft.de/download/ll_krk.pdf

COMBATAC-Studie

EudraCT: 2009-014040-11, ClinicalTrials.gov Identifier: NCT01540344



Glockzin G, Piso P et al. BMC Cancer 2013

Database of the
Peritoneal Oncology Group
German Society of General and Visceral Surgery
since 2011, independent administrator

English | Kontakt | Suche | Impressu

DGAV Deutsche Gesellschaft für Allgemein- und Viszeralchirurgie

Participating hospitals: 52

Start | News | Über die DGAV | Weiter-/Fortbildung | Arbeitsgemeinschaften | Arbeitsgruppen | StuDoQ | Veranstaltungen | SAVC | Mitglieder

Sie sind hier: StuDoQ / HIPEC Register

Suche... ok

- Dateneingabe
- Registrierung zur Teilnahme
- Über StuDoQ
- Zertifizierungen
- HIPEC Register
- NOTES-Register
- QS lap. Sigmaresektion
- QS Kolon-Karzinome
- QS Rektum-Karzinome
- QS Pankreas

HIPEC Register der DGAV

→ Zur Dateneingabe | → Registrierung zur Teilnahme

Liebe Kolleginnen und Kollegen, Liebe Teilnehmer des HIPEC-Registers,

um die Qualität der Peritonektomie und HIPEC Therapie in Deutschland zu verbessern und den Verlauf dieser Patienten besser nachvollziehen zu können, hat die Organgruppe „Peritoneum“ der CAO-V die HIPEC German Registry ins Leben gerufen. In dieser Datenbank sollen die

Aktuelle Anzahl der erfaßten Patienten im HIPEC-Register: **1872**.

Meldungen

Seite 1 Seite 2 Nächste >

21. Februar 2014
Nachrichten aus der DGAV im Februar 2014

Liebe Frau Kollegin,lieber Herr Kollege, heute möchte ich Ihnen erneut einige wichtige Neuigkeiten aus der DGAV mitteilen. I. Veränderungen beim kommenden Deutschen Chirurgenkongress in Berlin Termin: 25.-28.03.2014Es sei...
[mehr]

Peritoneal Surface Malignancy Unit as Center of Competence, @ present 7 in D

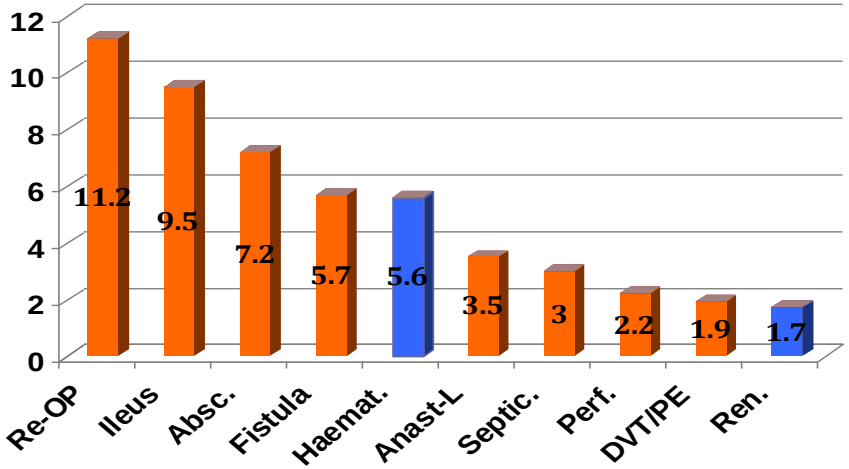
DGAV Deutsche Gesellschaft für Allgemein- und Viszeralchirurgie
Chirurgische Arbeitsgemeinschaft Onkologie – Organgruppe Peritoneum – DGAV · CAO-V

Kompetenzzentrum
Organgruppe Peritoneum

TC Chua, Annals of Surgery 2009
Systematic Review of 155 articles

Mortality:
Mean 2.9, Range 0-17

Grade III/IV morbidity:
Mean 28.8, Range 0-42



Treatment-Related Mortality With Bevacizumab in Cancer Patients: A Meta-analysis
Ranpura et al, JAMA 2011

Colorectal cancer

No. of Studies	No. of FAEs/ Total No. of Participants		Incidence of FAEs, % (95% CI)		RR (95% CI)[a]
	Bevacizumab	Control	Bevacizumab	Control	
5	34/1775	29/1496	2.1 (1.5-3.0)	1.5 (0.4-4.9)	1.05 (0.63-1.74)

Int J Colorectal Dis
DOI 10.1007/s00384-014-1842-x

ORIGINAL ARTICLE

Documented quality of care in certified colorectal cancer centers in Germany: German Cancer Society benchmarking report for 2013

S. Wesselmann · A. Winter · J. Ferencz · T. Seufferlein · S. Post

Table 1 Indicators for audit year 2012, showing medians and target values

	Indicators — audit year 2012	Median	Target value	Sites with target fulfilled
Specialist expertise	Revision operations, colon	8.2 %	<10 %	63.9 %
	Revision operations, rectum	9.5 %	<10 %	52.6 %
	Anastomotic leakage, colon	4.4 %	≤ 6 %	70.9 %
	Anastomotic leakage, rectum	7.6 %	≤ 15 %	84.3 %
	Postoperative mortality within 30 days	2.6 %	<5 %	86.0 %

Take Home Message 1:

It is important to be aware about this type of treatment and its selection criteria when discussing patients with mCRC in tumorboard !

Cross-sectional survey of 487 oncologists in Ontario

Table 3. Predictors of physician awareness of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (S-HIPEC) for pseudomyxoma and colorectal cancer carcinomatosis (CRC-C)

	Pseudomyxoma, *n* = 214				CRC-C, *n* = 214			
Predictors	No. (%)*	Crude *p* value	Adjusted OR (95% CI)	Adjusted *p* value	No. (%)*	Crude *p* value	Adjusted OR (95% CI)	Adjusted *p* value
Type of practice		0.14		0.032		0.08		0.08
Academic	88 (89.8)		2.71 (1.09–6.73)		52 (53.1)		1.72 (0.93–3.18)	
Community	96 (82.8)		1.00 (Ref)		47 (40.5)		1.00 (Ref)	
Specialty		0.039		0.016		0.69		0.36
General surgery	163 (88.1)		3.65 (1.27–10.48)		87 (47.0)		1.53 (0.62–3.80)	
Medical oncology	21 (72.4)		1.00 (Ref)		12 (41.4)		1.00 (Ref)	

Spiegle et al, Can J Surg 2013

www.CPM2014.com
info@cpm2014.com
Twitter: @2014_CPM

Peritoneal Surface Oncology
PSOGI
Group International