Cytoreductive Surgery and HIPEC

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Lacks Cancer Center
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• A surgery that clears all visible and palpable areas of tumor from the abdomen and pelvis
• **Heated Intra-Peritoneal Chemotherapy** in direct contact with tissues while avoiding systemic reactions
What types of cancer?

- Mucinous appendiceal neoplasms
- Colorectal cancer with peritoneal spread
- Peritoneal mesothelioma
- Ovarian/Primary peritoneal cancers
- Less common subtypes*

Peritoneal spread portends worse outcomes\(^1,^2\)
Traditional chemotherapy has less access

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Preoperative evaluation

- Functional status
- Morbidities
- PCI
- PSDSS

Peritoneal Cancer Index

<table>
<thead>
<tr>
<th>Regions</th>
<th>Lesion Size</th>
<th>Lesion Size Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Central</td>
<td></td>
<td>LS 0: No tumor seen</td>
</tr>
<tr>
<td>1 Right Upper</td>
<td></td>
<td>LS 1: Tumor up to 0.5 cm</td>
</tr>
<tr>
<td>2 Epigastrum</td>
<td></td>
<td>LS 2: Tumor up to 5.0 cm</td>
</tr>
<tr>
<td>3 Left Upper</td>
<td></td>
<td>LS 3: Tumor &gt; 5.0 cm or confluence</td>
</tr>
<tr>
<td>4 Left Flank</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 Left Lower</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Pelvis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 Right Lower</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Right Flank</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 Upper Jejunum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 Lower Jejunum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 Upper Ileum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 Lower Ileum</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PCI
Contraindications

• Patient is too frail to tolerate a major abdominal surgery
• Metastatic spread outside the abdominal/pelvic cavities
• Major liver involvement
• PCI > 20
Surgery

• Midline incision from xiphoid to pubic symphysis
• Remove all gross disease (many organs may be resected)
• Strip peritoneal and diaphragmatic surfaces
• Place catheters for inflow/outflow and temporarily close the skin
• Heat circuit to 41°C, instill mitomycin C for 90 minutes, then drain fluid
• Perform anastomosis (if any) and closure
In hospital recovery

- Prolonged ileus (may require TPN)
- Significant IV fluid requirements
- Expect 10-14 days in the hospital
- More extensive resections have higher complication rates
Life after HIPEC

• Once recovered (6-9 months), no lasting effect from the HIPEC itself.
• Dependent on which organs need to be resected
• Will usually have fatigue for several weeks, even months before back to full strength
• No additional restrictions
• Some histologies require additional, systemic chemotherapy
## Is HIPEC (un)safe?

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal</th>
<th>Year</th>
<th>Morbidity</th>
<th>Mortality</th>
<th># of Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Passot</td>
<td>J Surg Oncol</td>
<td>2016</td>
<td>50%</td>
<td>2%</td>
<td>1125</td>
</tr>
<tr>
<td>Robella</td>
<td>Minerva Chir</td>
<td>2014</td>
<td>35.70%</td>
<td>7.10%</td>
<td>70</td>
</tr>
<tr>
<td>Bakrin</td>
<td>J Surg Oncol</td>
<td>2013</td>
<td>31.30%</td>
<td>0.80%</td>
<td>566</td>
</tr>
<tr>
<td>Gonzalez</td>
<td>Eur J Surg Oncol</td>
<td>2013</td>
<td>26%</td>
<td>7%</td>
<td>42</td>
</tr>
<tr>
<td>Bakrin</td>
<td>Eur J Surg Oncol</td>
<td>2013</td>
<td>20.60%</td>
<td>5.60%</td>
<td>36</td>
</tr>
<tr>
<td>Bakrin</td>
<td>Ann Surg Oncol</td>
<td>2012</td>
<td>11.60%</td>
<td>0.37%</td>
<td>246</td>
</tr>
<tr>
<td>Deraco</td>
<td>BJOG</td>
<td>2012</td>
<td>26.30%</td>
<td>5.30%</td>
<td>55</td>
</tr>
<tr>
<td>Tentes</td>
<td>J Oncol</td>
<td>2012</td>
<td>51.20%</td>
<td>4.70%</td>
<td>43</td>
</tr>
<tr>
<td>Fagotti</td>
<td>Gynecol Oncol</td>
<td>2011</td>
<td>35%</td>
<td>0%</td>
<td>41</td>
</tr>
<tr>
<td>Dovern</td>
<td>Eur J Gynaecol Oncol</td>
<td>2010</td>
<td>3.4-50%</td>
<td>2.90%</td>
<td>546</td>
</tr>
<tr>
<td>Roviello</td>
<td>J Surg Oncol</td>
<td>2010</td>
<td>23%</td>
<td>0%</td>
<td>53</td>
</tr>
<tr>
<td>Carrabin</td>
<td>Bull Bancer</td>
<td>2010</td>
<td>55.60%</td>
<td>0%</td>
<td>22</td>
</tr>
<tr>
<td>Pavlov</td>
<td>Eur J Surg Oncol</td>
<td>2009</td>
<td>17.80%</td>
<td>1.80%</td>
<td>52</td>
</tr>
<tr>
<td>Fagotti</td>
<td>Gynecol Oncol</td>
<td>2009</td>
<td>28%</td>
<td>0%</td>
<td>25</td>
</tr>
<tr>
<td>DiGiorgio</td>
<td>Cancer</td>
<td>2008</td>
<td>21.30%</td>
<td>4.20%</td>
<td></td>
</tr>
<tr>
<td>Cotte</td>
<td>World J Surg</td>
<td>2007</td>
<td>13.60%</td>
<td>2.50%</td>
<td>81</td>
</tr>
</tbody>
</table>

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Is HIPEC worthwhile?

- Mucinous appendiceal neoplasms\(^1\):  
  - 25 months v 77 months
- Colorectal Cancer\(^2\):  
  - 24 months v 63 months
- Peritoneal Mesothelioma\(^3\):  
  - 23 months v 56 months
- Refractory ascites\(^4\):  
  - Effective for 95%
- Ovarian\(^5\):  
  - 38.3% v 72.5% 5 year survival
Level I evidence for HIPEC: Randomized trials*

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal</th>
<th>Year</th>
<th>Tumor Site</th>
<th>DSS</th>
<th># of Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verwaal</td>
<td>Ann Surg Oncol</td>
<td>2008</td>
<td>CRC</td>
<td>12.6 v 22.2</td>
<td>105</td>
</tr>
<tr>
<td>Spiliotis</td>
<td>Ann Surg Oncol</td>
<td>2015</td>
<td>Ovarian</td>
<td>13.4 v 26.7</td>
<td>120</td>
</tr>
</tbody>
</table>

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Ongoing Studies (CRC)

- **COLOPEC\(^1\):**
  - Dutch study: pT4 or perforated CRC, randomized to HIPEC + adjuvant v adjuvant

- **Ripley, et al\(^2\):**
  - High risk colon cancer with standard treatment +/- 2\(^{nd}\) look surgery

- **Prophylchip\(^3\):**
  - French study: FOLFOX to high risk, then randomize +/- HIPEC: data 2019

- **Promenade:**
  - Italian study: Systemic therapy with randomizing HIPEC to high risk CRC patients

- **HIPEC T4:**
  - Spain: Locally advanced colon cancers treated with HIPEC at first surgery

- **Coeliochip:**
  - French RENAPE group: role of laparoscopy
Future of CRS/HIPEC

• Prophylaxis for high risk pts?
• Expand for additional types of cancer (gastric, sarcoma, pancreatic)?
• Minimally invasive?
• Standardized protocols?
  – NCCN guidelines
  – American Society of Peritoneal Surface Malignancies¹
• Trial designs²?
  – Phase I: Hard to know if toxicity is due to drug or surgery
  – Phase II: Difficult to compare, no measurable response, lack of large databases
  – Phase III: Technique variability and cost are difficult to control
• Quality control?

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### Table 11: Summary of HIEPC-related procedures in different PC institutions or countries (Published researches).

<table>
<thead>
<tr>
<th>Country / No. Institutions</th>
<th>Major Institutions</th>
<th>No. patients</th>
<th>Mode</th>
<th>HIPEC-MMC alone</th>
<th>HIPEC-MMC+DDP</th>
<th>HIPEC-L-OHP alone</th>
<th>HIPEC-other</th>
<th>Temperature (°C)</th>
<th>Duration (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA, 17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wake Forest University of Baptist Medical Center [13, 20, 48, 56, 66, 67]</td>
<td>&gt;709</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>40.75 (38.5-43)</td>
<td>90 (60-90)</td>
</tr>
<tr>
<td></td>
<td>University of Pittsburgh Medical Center (University of Pittsburgh) [37, 52, 56, 68]</td>
<td>190</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>42 (40-42)</td>
<td>100 (90-100)</td>
</tr>
<tr>
<td></td>
<td>Washington Hospital Center [13, 49, 55]</td>
<td>&gt;81</td>
<td>C</td>
<td>10 or 12.5 mg/m²</td>
<td></td>
<td></td>
<td></td>
<td>42 (40-43)</td>
<td>90 (30-90)</td>
</tr>
<tr>
<td></td>
<td>Cancer Treatment Centers of America [79, 72]</td>
<td></td>
<td>O/C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>40-43</td>
<td>30-120</td>
</tr>
<tr>
<td></td>
<td>Loma Linda University Medical Center [79, 72]</td>
<td></td>
<td>O/C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>40-43</td>
<td>30-120</td>
</tr>
<tr>
<td></td>
<td>Medical College of Wisconsin [79, 72]</td>
<td></td>
<td>O/C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>40-43</td>
<td>30-120</td>
</tr>
<tr>
<td></td>
<td>Mercy Medical Center [79, 72]</td>
<td></td>
<td>O/C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>40-43</td>
<td>30-120</td>
</tr>
<tr>
<td></td>
<td>Moores Cancer Center, University of California [79, 72]</td>
<td></td>
<td>O/C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>40-43</td>
<td>30-120</td>
</tr>
<tr>
<td></td>
<td>Rutgers University [79, 72]</td>
<td></td>
<td>O/C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>40-43</td>
<td>30-120</td>
</tr>
<tr>
<td></td>
<td>St Agnes Hospital [13, 36]</td>
<td>&gt;30</td>
<td>O/C</td>
<td>10-20 mg/m²</td>
<td></td>
<td></td>
<td></td>
<td>42</td>
<td>90</td>
</tr>
</tbody>
</table>

Note: C: closed abdomen technique for HIPEC; O: open abdomen technique for HIPEC; Y: yes; MMC: mitomycin C; DDP: cisplatin; 5-FU: fluorouracil; L-OHP: oxaliplatin; CPT-11: irinotecan
Michigan HIPEC Oncology Collaborative

• Benefits of a collaborative:

• Canadian Experience
  – Dube, et al. 2015 Guidelines on the use of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in patients with peritoneal surface malignancy arising from colorectal or appendiceal neoplasms

• Goals of a HIPEC collaborative
  – Standardization of patient selection, technique
  – Improvement in quality control/oncologic outcomes
  – Increased collaboration amongst providers
  – Data sharing for research
  – Framework for prospective trials
  – Establish centers of excellence

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Proposed steps for establishing MHOC

• Invite current providers from Michigan
  – Mathew Chung (Spectrum Health) 2005
  – *Richard Berri (St. John Providence) 2011
  – Jill Onesti (Mercy Health) 2015
  – *Vandad Raofi (Beaumont) 2016
  – Gitonga Munene (Western Michigan University) 2016
  – Tolutope Oyasiji or Smit Singla (McLaren) 2016/2017

• Establish standards
  – Areas of agreement v areas of controversy

• Set quality metrics

• Arrange and maintain database

• Process for new institutions