Laparoscopic & Robot assisted Pancreas Resection

Ronald M. Van Dam, MD PhD
European Surgical Center Aachen Maastricht

Maastricht University & RWTH Aachen
COI disclosure

Medtronic unrestricted grant ORANGE II trial

Johnson & Johnson unrestricted grant
Laelaps & Laelive Project NL & DE

Shareholder The Organoid Factory
Laparoscopic & Robot assisted Pancreas Resection

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European Surgical Center Aachen Maastricht

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Minimal Invasive Pancreatic Surgery (MIPS)

Background & facts

MIPS Implementation in NL

Laparoscopic and robot assisted

Distal pancreatectomy

Pancreatoduodenectomy

Conclusions
Indications

- Pancreatic cancer
- Neuroendocrine tumor (pNET)
- Intraductal Papillary Mucinous Neoplasm (IPMN)
- Mucinous cystic neoplasm (MCN)
- (Focal) chronic pancreatitis
Kind of resection

- Pancreatoduodenectomy
  - Portal vein resection
- Enucleation
- Central pancreatectomy
- Distal pancreatectomy (DP)
  - +/- spleen preservation
  - RAMPS (Strasberg)
  - DP with celiac artery resection (Appleby)

- Distal pancreatectomy spleen preservation
  - With splenic vessel resection (Warshaw)
  - Without splenic vessel (Kimura)
Lymph nodes (PDAC)

Kayahara et al.
Fujita et al.

Strasberg et al. J Cancer 2012
Extensive resections

Radical Antegrade Modular Pancreatosplenectomy (RAMPS)

- Higher R0 rate

Strasberg et al. J Cancer 2012
Extensive resections

DP-ceeliac artery resection (Appleby)

- Involvement celiac axis
Warshaw

Distal pancreatectomy, spleen preserving, resecting splenic a/v
Kimura
Distal pancreatectomy, spleen and vessel preserving
Splenic preservation

Life threatening post splenectomy infections

• 5% life time risk!
  • In children risk 10 – 15%
  • Vaccination
  • 2 years of prophylactic antibiotics
    • Pneumo-meningococci, Haemophilus sp, encapsulated bacteria
  • Mortality risk 200 times higher
Once upon a time...
Standardization of Care

- DVT Prophylaxis
- Strict fluid regimen
- Epidural
- Short acting anaesthesia
- Avoid pre-Med
- No drains
- CHO Loading
- Short Incision
- Eras
- Mobilise early
- Early return to oral diet
- Bairhugger
- Routine analgesia
- Ileus prophylaxis
- Remove Catheter early
- No NG Tubes

Fearon et al. Clin Nutr 2005
Minimization of impact

Multidisciplinary
Multimodal
Percutaneous
Minimal Invasive
Personalized
Reduced impact by MI Pancreas Surgery

• Do we need the short term benefit in Oncology?

• Abdominal wall integrity

• More access to adjuvant therapy?

• Long term survival?
Reduced impact by MI Pancreas Surgery

- Technically demanding

- Intensive training needed (team)

- Hospital volume / centralization (n=20)

- More complications in the easier cases
Outcomes MIPS consistently better 2010 - 2018

• Less blood loss
• Less pain
• Mortality and recurrence comparable
• Shorter LOS

• Theatre times considerably longer
• Less or more complications!

MAJORITY LEVEL 3 EVIDENCE

> 100 series, > 5000 pancreas resections
Shorter LOS?
What determines length of stay

The patient, the operation, the stress response

Expectations

Planning and geography

1 – 2 d

Recovery criteria fulfilled

Patient willing to go home

Patient goes home
New objective outcome parameter

Functional recovery

= ready for discharge
<table>
<thead>
<tr>
<th>Functional Recovery</th>
<th>Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tolerance of solid food</td>
<td>✔</td>
</tr>
<tr>
<td>No IV fluids</td>
<td>✔</td>
</tr>
<tr>
<td>Oral analgetics only</td>
<td>✔</td>
</tr>
<tr>
<td>Mobile at pre op level</td>
<td>✔</td>
</tr>
<tr>
<td>Normal / improving lab</td>
<td>✔</td>
</tr>
<tr>
<td>Willing to go home</td>
<td></td>
</tr>
</tbody>
</table>
Minimal Invasive Pancreas Resection

1994
Lap distal - Cushieri

1994
Lap distal - Gagner

2008 LDP
Maastricht UMC

2010 Robot PD
Giulianotti

2014 - 2019
NL LAELAPS programs
LDP & LPD & RPD

2019
IMIPS / IHPBA
‘Guidelines’

2016
LEOPARD 2 – LPD RCT

2015
LEOPARD 1 – LDP RCT

Slow adoption

Anatomy
Complications
Learning curves
It is all in the detail
LAEALPS programs

• In the past, uncontrolled introduction of minimally invasive surgery has led to unfavourable outcomes (e.g. colorectal surgery)

• Structured nationwide implementation approach is needed
  o Can results from expert centers be reproduced on a national scale?

• Ultimately, RCTs needed in trained centers
LAELEAPS

Longitudinal Assessment and Realization of
Laparoscopic Pancreatic Surgery
in the Netherlands
LAELEPS 1  Distal pancreatectomy
LAELEPS 2  Pancreatoduodenectomy
LAELEPS 3  Robot pancreatectomy

Longitudinal Assessment and Realization of Laparoscopic Pancreatic Surgery in the Netherlands
32 pancreatic surgeons from 17 centers
detailed **technique description, video training, and proctoring on-site**


N = 201, 71 MIDPs in the 9 years before training and 130 in the 22 months following training
(7-fold increase, P < 0.001)

Significant results ODP vs MIDP:

- Conversion rate 38% vs 8% (P < 0.001)
- Median intraoperative blood loss 350 mL vs 200 mL (P = 0.03)
- Spleen preservation 75% vs 48% (P < 0.001)
- Length of hospital stay 9 vs 7 days, P < 0.001)

No significant difference in:

- Operating time (P = 0.98)
- Clavien-Dindo grade ≥3 complications (P=0.24)
- R0 resection rate (P = 0.67)
- Lymph node retrieval (P = 0.54)
- 30-day mortality was 3% vs 0% (P = 0.12).

*de Rooij et al. Ann Surg 2016*
LEOPARD RCT
open vs. minimally invasive distal pancreatectomy

A multicenter patient-blinded RCT in 14 Dutch centers,
N=111 between April 2015 and March 2017
51 MIDP vs 57 ODP analysed

Significant results MIDP vs ODP:
- Time to functional recovery 6 vs 4 days (P < 0.001)
- Length of hospital stay 8 vs 6 days (P < 0.001)
- Operative blood loss 400 vs 150 mL (P < 0.001)
- Operative time 217 vs 179 minutes (P = 0.005)
- Delayed gastric emptying grade B/C 20% vs 6% (P = 0.04)
- 90-day mortality was 0% vs 2%
- Conversion 8%

No significant difference MIDP vs ODP:
- Clavien-Dindo grade ≥3 complications 25 vs 38% (P = 0.21)
- Pancreatic fistulas grade B/C 39 vs 23% (P = 0.07)
- Cost (P = 0.41)

de Rooij et al. Ann Surg 2019
Outcomes After Minimally-invasive Versus Open Pancreatoduodenectomy

A Pan-European Propensity Score Matched Study


Primary outcome was 30-day major morbidity (Clavien-Dindo ≥3).

Significant results MIPD vs OPD:
- Mean operative time 415.8 vs 324.2 minutes (P < 0.001)
- Pancreatic fistula grade B/C 22.6% vs. 12.7% (P < 0.001)
- Bile leakage grade B/C 3.0% vs 5.1% (P = 0.047)
- Length of hospital stay 18.2 vs 17.4 days (P < 0.001)

No significant difference MIPD vs OPD:
- Mortality 4% vs 3.3% (P = 0.576)
- Major morbidity 28% vs 30% (P = 0.526)
- Hemorrhage 9.5% vs 7.3% (P = 0.156)
- DGE grade B/C 10.6% vs 13.1% (P = 0.167)

Klompmaker et al. Ann Surg 2018
Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial

RCT
4 centres in the Netherlands ≥20 LPDs before trial participation
After LAELAPS 2 training
50 LPD vs 49 OPD

DSMB stopped trial due to 10% vs 2% mortality (p=0.20)
99 out of 136 patients (73%)

MIPD vs OPD
• Operative time 410 vs. 274 minutes (P < 0.0001)
• Complications Clavien-Dindo ≥ grade 3
  • 50% vs 39% (p = 0.26)
• Pancreatic fistula grade B/C
  • 28% vs 24% (P = 0.69)
• DGE grade B/C 34% vs 20% (P = 0.13)
• Hemorrhage 10% vs 14% (P = 0.51)
• Length of hospital stay 11 vs 10 d (P = 0.86)

Hilst et al. Lancet GEH 2019
Laparoscopic Pancreaticoduodenectomy Should Not Be Routine for Resection of Periampullary Tumors

Safi Dokmak, MD, Fadhel Samir Ftériche, MD, Béatrice Aussilhou, MD, Yacine Bensafta, MD, Philippe Lévy, MD, Philippe Ruszniewski, MD, Jacques Belghiti, MD, Alain Sauvanet, MD

Only in patients with low risk of pancreas fistula

<table>
<thead>
<tr>
<th>Complication</th>
<th>Laparoscopic (n = 46)</th>
<th>Open (n = 46)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, n (%)</td>
<td>1 (2)</td>
<td>0</td>
<td>0.28</td>
</tr>
<tr>
<td>Overall morbidity, n (%)</td>
<td>34 (74)</td>
<td>27 (59)</td>
<td>0.12</td>
</tr>
<tr>
<td>Clavien III–IV, n (%)</td>
<td>13 (28)</td>
<td>9 (20)</td>
<td>0.32</td>
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<tr>
<td>Pancreatic fistula, n (%)</td>
<td>22 (48)</td>
<td>19 (41)</td>
<td>0.52</td>
</tr>
<tr>
<td>Grades of pancreatic fistula</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>2 (4)</td>
<td>4 (9)</td>
<td>0.39</td>
</tr>
<tr>
<td>B</td>
<td>9 (20)</td>
<td>12 (26)</td>
<td>0.61</td>
</tr>
<tr>
<td>C</td>
<td>11 (24)</td>
<td>3 (6)</td>
<td>0.007</td>
</tr>
<tr>
<td>Delayed gastric emptying, n (%)</td>
<td>8 (17)</td>
<td>7 (15)</td>
<td>0.77</td>
</tr>
<tr>
<td>Bleeding, n (%)</td>
<td>11 (24)</td>
<td>3 (7)</td>
<td>0.02</td>
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<td>Reintervention, n (%)</td>
<td>11 (24)</td>
<td>5 (11)</td>
<td>0.09</td>
</tr>
<tr>
<td>Biliary fistula, n (%)</td>
<td>2 (4)</td>
<td>2 (4)</td>
<td>1</td>
</tr>
<tr>
<td>Drained collections, n (%)</td>
<td>2 (4)</td>
<td>3 (7)</td>
<td>0.40</td>
</tr>
<tr>
<td>Gastroenteric anastomosis fistula, n (%)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>1</td>
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<tr>
<td>Pulmonary complications, n (%)</td>
<td>5 (11)</td>
<td>4 (9)</td>
<td>0.74</td>
</tr>
<tr>
<td>Readmission, n (%)</td>
<td>4 (9)</td>
<td>4 (9)</td>
<td>1</td>
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<tr>
<td>Hospital stay, d, mean (range)</td>
<td>25 (6–104)</td>
<td>23 (7–115)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Dokmak et al. JACS 2015
summary

MIPS more and more popular

MI Distal pancreatectomy
  Better in RCT but more fistulas

MI Pancreatoduodenectomy
  Higher mortality in stopped RCT (volume / learning curve?)

  Higher morbidity and more fistulas in high risk patients
Robot-assisted Laparoscopic Surgery

- Less physically challenging for surgeon
- Better views/magnification
- Better instrument range of motion and control
- Better rates of spleen preservation
- Shorter hospital stay
- Lower total complication rate

BUT

- No RCT
- Alone in 1-2 consoles / not at table
- Hidden patient
- Learning curves 20-40
- Longer operative times
- Higher costs
- No tactile feedback

Zureikat et al. 2013, Walsh et al. 2017, Yu et al. 2019
Safety and efficacy for robot-assisted versus open pancreaticoduodenectomy and distal pancreatectomy: A systematic review and meta-analysis

Wenyan Zhao¹, Chengyang Liu², Shuqiang Li³, Donghua Geng¹, Yong Feng¹, Ming Sun³, *

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Study Design</th>
<th>Comparator 1</th>
<th>Comparator 2</th>
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<tbody>
<tr>
<td>Baker et al. [9]</td>
<td>2016</td>
<td>USA</td>
<td>Retrospective</td>
<td>RAPD</td>
<td>OPD</td>
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<td>Zureikat et al. [17]</td>
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<td>USA</td>
<td>Retrospective</td>
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<td>Chen et al. [14]</td>
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<td>Retrospective</td>
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<td>Retrospective</td>
<td>RAPD</td>
<td>OPD</td>
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<td>Walsh et al. [18]</td>
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<td>USA</td>
<td>Prospective</td>
<td>RAPD</td>
<td>OPD</td>
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<td>Hammill et al. [19]</td>
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<td>OPD</td>
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<td>Xourafas et al. [23]</td>
<td>2017</td>
<td>USA</td>
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<td>RADP</td>
<td>ODP</td>
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<td>Lee et al. [21]</td>
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<td>USA</td>
<td>Prospective</td>
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<td>ODP</td>
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<td>Duran et al. [20]</td>
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<td>Spain</td>
<td>Retrospective</td>
<td>RADP</td>
<td>ODP</td>
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<td>Waters et al. [22]</td>
<td>2010</td>
<td>USA</td>
<td>Retrospective</td>
<td>RADP</td>
<td>ODP</td>
</tr>
</tbody>
</table>

Zhao et al. Surg Onc 2018
**Robot PD vs open PD**

### Overall morbidity

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>RAPD Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Odds Ratio M-H Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baker 2016</td>
<td>9</td>
<td>33</td>
<td>49</td>
<td>0.34 [0.12, 0.95]</td>
</tr>
<tr>
<td>Boggi 2016</td>
<td>61</td>
<td>28</td>
<td>36</td>
<td>0.79 [0.31, 2.00]</td>
</tr>
<tr>
<td>Buchs 2011</td>
<td>16</td>
<td>19</td>
<td>39</td>
<td>0.60 [0.28, 1.45]</td>
</tr>
<tr>
<td>Chen 2015</td>
<td>26</td>
<td>69</td>
<td>120</td>
<td>0.57 [0.30, 1.06]</td>
</tr>
<tr>
<td>Hammill 2010</td>
<td>2</td>
<td>16</td>
<td>69</td>
<td>1.10 [0.20, 6.01]</td>
</tr>
<tr>
<td>Lal 2012</td>
<td>17</td>
<td>41</td>
<td>67</td>
<td>3.59 [0.96, 13.48]</td>
</tr>
<tr>
<td>Walsh 2011</td>
<td>8</td>
<td>11</td>
<td>25</td>
<td>0.60 [0.19, 1.90]</td>
</tr>
<tr>
<td>Zhou 2011</td>
<td>2</td>
<td>6</td>
<td>8</td>
<td>0.11 [0.01, 1.07]</td>
</tr>
</tbody>
</table>

Total (95% CI) 270 Events, 413 Total Events, 100.0% Overall morbidity

Heterogeneity: Chi² = 11.16, df = 7 (P = 0.13); I² = 37%

Test for overall effect: Z = 2.28 (P = 0.02)

### Mortality

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>RAPD Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Odds Ratio M-H Fixed 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baker 2016</td>
<td>0</td>
<td>2</td>
<td>49</td>
<td>0.42 [0.02, 9.16]</td>
</tr>
<tr>
<td>Bao 2014</td>
<td>2</td>
<td>2</td>
<td>28</td>
<td>1.00 [0.13, 7.64]</td>
</tr>
<tr>
<td>Boggi 2016</td>
<td>2</td>
<td>0</td>
<td>36</td>
<td>2.24 [0.10, 47.82]</td>
</tr>
<tr>
<td>Buchs 2011</td>
<td>2</td>
<td>1</td>
<td>39</td>
<td>1.81 [0.16, 20.77]</td>
</tr>
<tr>
<td>Chalkonda 2012</td>
<td>1</td>
<td>0</td>
<td>30</td>
<td>3.10 [0.12, 79.23]</td>
</tr>
<tr>
<td>Chen 2015</td>
<td>1</td>
<td>3</td>
<td>120</td>
<td>0.66 [0.07, 6.49]</td>
</tr>
<tr>
<td>Hammill 2010</td>
<td>0</td>
<td>1</td>
<td>69</td>
<td>2.69 [0.10, 71.32]</td>
</tr>
<tr>
<td>Walsh 2011</td>
<td>1</td>
<td>0</td>
<td>25</td>
<td>3.12 [0.12, 80.39]</td>
</tr>
<tr>
<td>Zhou 2011</td>
<td>0</td>
<td>1</td>
<td>8</td>
<td>0.29 [0.01, 8.37]</td>
</tr>
<tr>
<td>Zureikat 2016</td>
<td>4</td>
<td>23</td>
<td>817</td>
<td>0.67 [0.23, 1.95]</td>
</tr>
</tbody>
</table>

Total (95% CI) 519 Events, 1221 Total Events, 100.0% Mortality

Heterogeneity: Chi² = 3.24, df = 9 (P = 0.95); I² = 0%

Test for overall effect: Z = 0.24 (P = 0.81)

*Zhao et al. Surg Onc 2018*
Robot PD vs open PD

Delayed Gastric Emptying

Post op pancreas fistula

Zhao et al. Surg Onc 2018
Conclusions Minimally Invasive Pancreas Surgery

• The nationwide use of MIPS has increased significantly in the Netherlands

• Outcomes of MIPS are comparable to international reports but caution warranted

• Introduction of MIPS and potential volume-outcome relationship confirms its complexity

• Structured training, proctoring and centralization in centers with sufficient volume

• Future for robotics needs to be evaluated