SBRT for Pancreatic cancers

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SBRT biliary tract

- Pancreatic Ca
- Liver Ca
- Cholangio
Background

• R0 resection is the only curative option for resectable or borderline resectable pancreatic cancers

• Even after R0 resection the 5 year survival is dismal 15-25%
NAT - Rationale

• Patients not been physiologically compromised by a major surgical procedure.

• Avoidance of major surgery in aggressive tumor biology

• Early treatment of micrometastatic disease which is likely to increase the underlying micrometastatic burden postop.

• Intact tumor mass is well perfused and the cytotoxic effects of chemotherapy and/or radiation are not compromised by the creation of a more hypoxic, inflammatory, and fibrotic surgical bed.

• Downstaging of tumor thereby improving the likelihood of an ultimate R0 resection.
Definitions

• **Resectable:**
  • no extension to celiac, CHA, SMA
  • patent SMV-PV confluence
  • stage I, II (T1-3, Nx, M0)

• **Borderline:**
  • arterial abutment (< 180deg)
  • venous abutment or encasement (with option for reconstruction)
  • stage III (minimal T4)

• **Locally Advanced:**
  • celiac, SMA encasement (> 180deg)
  • stage III (T4, Nx, M0)

R1 resections
Poorer outcomes

Resectable cancers - Causes of poor outcome

- Rate of R0 resection **70% margin positive** (Sohn 2000, Howard 2006)
  - The failure to consistently achieve microscopic surgical clearance contributes to the high rates of disease relapse:

  - TMH (M Bal). Pancreatic ca (77% +ve in NAT naïve vs. 40% post NAT)
  - 67% for the entire group. Posterior margin (43%) SMA (29%) DBD (14%) and PN (14%)

Pancreatic Cancer Surgery
*The New R-status Counts*

Annals of surgery 2016

n=561

R0- 112(20%)
R1(<1mm)- 123 (21.9%)
R1 (direct)- 326 (58%)

In R0N0M0 5-year survival was 62.2%,
R0 resection – changing concepts

Transection Margins
Reported R1 resection rate – 25%
in older studies

Circumferential resection Margins (includes all margins)
Reported R1 resection rate – 75%
In newer studies
Evidence - NAT

- 3 Metaanalysis (2 BRPC, 1 RC +BRPC)

- 1 ph 3 RCT
Metaanalysis – (NACRT borderline resectable tumors)

• Festa et al (2013)

• Radiological downstaging of the lesion is uncommon

• If no distant or local progression all patients should be explored surgically

• A clear benefit of this regimen could be to spare surgery to patients with progressive disease during the frame-time chemo-radiotherapy is being delivered
Neoadjuvant therapy for patients with borderline resectable pancreatic cancer: A systematic review and meta-analysis.

• Cochrane database 1966-2015, 18 studies (N=959)
• CR= 2.8% PR= 28.7% SD= 45.9%, tumor progression under therapy = 16.9%
• Resection = 65.3% –76.5%), R0 = 57.4%
• mean of median survival = 17.9 months all patients, 25.9 months resected, and 11.9 months for unresected patients.

• Conclusion- The resection and R0 resection rates and survival in the group of borderline resectable tumor patients after neoadjuvant therapy are similar to the resectable tumor patients

Tang et al. Pancreatology 2016
Dutch meta-analysis 2018 contd....

<table>
<thead>
<tr>
<th></th>
<th>Upfront Sx</th>
<th>NAT</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOS in months</td>
<td>14.8 (11.6–25.3) months N= 1746</td>
<td>18.8 (range 9.4–50.2) months Post NAT</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>18.8 (range 9.4–50.2) months Post NAT</td>
<td></td>
</tr>
<tr>
<td>819 RC BRPC 927</td>
<td>17.5 (12–25.3) months</td>
<td>18.2 (10–50.2) months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12.8 (11.6–16.3) months</td>
<td>19.2 (11–32) months</td>
<td></td>
</tr>
<tr>
<td>R0 resection post NAT</td>
<td>-</td>
<td>26.1 months</td>
<td></td>
</tr>
<tr>
<td>Overall resection rate</td>
<td>81.3%</td>
<td>66%</td>
<td>0.001</td>
</tr>
<tr>
<td>R0 Resection rate</td>
<td>66.9% RC-71.4% BRPC- 63.9%</td>
<td>86.8% RC-85% (Gain of 14%) BRPC-88.6% (Gain of 22%)</td>
<td>0.001</td>
</tr>
<tr>
<td>pLN rate</td>
<td>63.8%</td>
<td>43.8%</td>
<td>0.001</td>
</tr>
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Preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer (PREOPANC-1): A randomized, controlled, multicenter phase III trial. Dutch Group (Versteinje JCO 2022)

<table>
<thead>
<tr>
<th></th>
<th>Arm A</th>
<th>Arm B</th>
<th>HR</th>
<th>P</th>
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<tbody>
<tr>
<td>5yr OS</td>
<td>6.5</td>
<td>16.5</td>
<td>0.71</td>
<td>0.025</td>
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<tr>
<td>R0 rate</td>
<td>31%</td>
<td>65%</td>
<td></td>
<td>0.001</td>
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<tr>
<td>DFS</td>
<td>7.9</td>
<td>11.2</td>
<td>0.67</td>
<td>0.010</td>
</tr>
<tr>
<td>DMFI</td>
<td>10.2</td>
<td>17.1</td>
<td>0.63</td>
<td>0.012</td>
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<tr>
<td>LRFI</td>
<td>11.8</td>
<td>NR</td>
<td>0.47</td>
<td>0.001</td>
</tr>
<tr>
<td>Resection rate</td>
<td>72%</td>
<td>62%</td>
<td></td>
<td>0.15</td>
</tr>
<tr>
<td>mOAS for operated patients</td>
<td>16.8</td>
<td>29.9</td>
<td></td>
<td>0.001</td>
</tr>
</tbody>
</table>

No significant difference was observed in grade ≥ 3 adverse events between both groups (p = 0.17).
Preopanc – Long term outcomes

**Graph A**

- **Legend:**
  - Blue line: Upfront surgery
  - Red line: Neoadjuvant CRT

- **HR 0.73 (95% CI: 0.58 to 0.96); P = .025**

- **Time (months):**
  - OS (%)
  - No. at risk:
    - Upfront surgery: 127 (0), 103 (0), 75 (0), 51 (0), 40 (0), 32 (0), 20 (1), 16 (2), 11 (4), 7 (8), 5 (6)
    - Neoadjuvant CRT: 119 (0), 96 (0), 73 (0), 53 (0), 46 (0), 39 (0), 34 (0), 29 (2), 24 (5), 17 (10), 11 (15)

**Graph B**

- **Legend:**
  - Blue line: Resectable, upfront surgery
  - Red line: Resectable, neoadjuvant CRT
  - Green line: Borderline, upfront surgery
  - Orange line: Borderline, neoadjuvant CRT

- **HR 0.79 (95% CI: 0.54 to 1.18); P = .23**
- **HR 0.67 (95% CI: 0.45 to 0.99); P = .046**

- **Time (months):**
  - OS (%)
  - No. at risk:
    - Resectable, upfront surgery: 68 (0), 55 (0), 40 (0), 30 (0), 23 (0), 22 (0), 14 (1), 10 (2), 7 (3), 5 (4), 4 (4)
    - Resectable, neoadjuvant CRT: 66 (0), 53 (0), 26 (0), 20 (0), 16 (2), 14 (4), 9 (8), 5 (11)
    - Borderline, upfront surgery: 59 (0), 48 (0), 33 (0), 21 (0), 17 (0), 10 (0), 6 (0), 6 (0), 4 (1), 2 (2), 1 (2)
    - Borderline, neoadjuvant CRT: 54 (0), 45 (0), 34 (0), 25 (0), 21 (0), 17 (0), 14 (0), 13 (0), 10 (1), 8 (2), 8 (4)
Neoadjuvant CRT and chemotherapy for Resectable and Borderline Resectable Pancreatic Cancer: The New Standard
Efficacy of Preoperative mFOLFIRINOX vs mFOLFIRINOX Plus Hypofractionated Radiotherapy for Borderline Resectable Adenocarcinoma of the Pancreas
The AO21501 Phase 2 Randomized Clinical Trial
155 Assessed for eligibility

- 29 Excluded
- 26 Ineligible
- 3 Patient decision

126 Randomized

70 Randomized to receive mFOLFOXIRINOX
- 65 Initiated intervention as assigned
  - 5 Did not receive assigned intervention
    - 1 Adverse events
    - 1 Disease progression
    - 3 Withdrawal
  - 20 Completed intervention as assigned
  - 45 Discontinued intervention
    - 13 Adverse events
    - 9 Disease progression
    - 6 Physician decision
    - 5 Withdrawal
    - 4 Locally advanced disease at surgery
    - 2 Metastases discovered at surgery
    - 2 Alternative therapy
    - 2 Other complicating disease
    - 1 Death
    - 1 Other

65 Included in analysis
- 5 Excluded from analysis
- 5 Not treated

56 Randomized to receive mFOLFOXIRINOX plus radiotherapy
- 55 Initiated intervention as assigned
  - 1 Did not receive assigned intervention
    - 1 Withdrawal
  - 10 Completed intervention as assigned
  - 45 Discontinued intervention
    - 12 Disease progression
    - 8 Adverse events
    - 6 Physician decision
    - 5 Withdrawal
    - 4 Locally advanced disease at surgery
    - 2 Treatment arm closed
    - 2 Other
    - 1 Other complicating disease

55 Included in analysis
- 1 Excluded from analysis
- 1 Not treated
Alliance

• Interim 17/30 NACT arm
• 10/30 RT arm

• 30/126 patients completed assigned interventions
• Lower doses of RT
• 39 patients in 27 centres

• 28% RT deviations in QA arm – poor contouring ASTRO 2022
NCCN guidelines

BORDERLINE RESECTABLE<sup>d,e</sup> NO METASTASES, PLANNED NEOADJUVANT THERAPY

WORKUP

- Biopsy, positive
- Neoadjuvant therapy

Planned neoadjuvant therapy<sup>f</sup>

- Biopsy, EUS with FNA preferred<sup>g</sup>
- Consider staging laparoscopy<sup>h</sup>
- Placement of stent (preferably a short metal stent) if biliary ductal obstruction is present

Surgical resection<sup>i</sup>

Unresectable at surgery<sup>j</sup>

No jaundice

Jaundice

Disease progression precluding surgery<sup>k</sup>

See Locally Advanced Unresectable (PANC-7) or Metastatic Disease (PANC-9)

TREATMENT

See Adjuvant Treatment and Surveillance (PANC-1)

See Locally Advanced Unresectable (PANC-7)

See Metastatic Disease (PANC-9)

Stenting or biliary bypass
± duodenal bypass (category 2B for prophylactic duodenal bypass)
± open ethanol celiac plexus block (category 2B)

Cancer not confirmed
- Repeat biopsy
- Neoadjuvant therapy (follow pathway)

Cancer not confirmed
(exclude autoimmune pancreatitis [AIP])

See Planned Resection (PANC-1)
Sequencing of NAT

BRPC
NACT 4-6# followed by CRT or SBRT

LAPC
NACT 6-8# followed by CRT or SBRT + Contd CT
What chemotherapy....

• Modified FOLFIRINOX 3-4# (GI- ASCO 2013)

• NAB - PACLI

• Concurrent Gemcitabine – traditionally given

• Concurrent Capecitabine – Promising (SCALOP trial)
Neoadjuvant Rx – New standard of care
Evidence

• 3 Metaanalysis (2 BRPC, 1 RC +BRPC)

• 1 ph 3 RCT
Metaanalysis – (NACRT borderline resectable tumors)

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Tang et al. Pancreatologty 2016
From 3DCRT to SBRT

55-60gY/25#/5weeks
Dose escalated concurrent chemo-radiation in borderline resectable and locally advanced pancreatic cancers with tomotherapy based intensity modulated radiotherapy: a phase II study

Shirley Lewis¹, Supriya Chopra Sastri², Supreeta Arya³, Shaesta Mehta⁴, Prachi Patil⁴, Shyamkishore Shrivastava⁵, Reena Phurailatpam⁶, Shailesh V. Shrikhande⁶, Reena Engineer⁵

Overall (n=30)
Borderline resectable (n=18)
Locally advanced (n=12)

55-60gY/25#/5weeks
SBRT - Pancreas

• Why

• When

• How
SBRT - Why

<table>
<thead>
<tr>
<th></th>
<th>SBRT</th>
<th>LCRT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment time</td>
<td>1-2 weeks</td>
<td>5 weeks</td>
</tr>
<tr>
<td>Effective RT dose</td>
<td>$&gt;83 \text{ Gy}$</td>
<td>$55 \text{ Gy/25#}$</td>
</tr>
<tr>
<td>Small bowel toxicity</td>
<td>Same</td>
<td></td>
</tr>
<tr>
<td>Radiological downstaging</td>
<td>Seen</td>
<td>Not seen</td>
</tr>
<tr>
<td>R0 resection (BRPC)</td>
<td>90%</td>
<td>60%</td>
</tr>
</tbody>
</table>

SBRT offers a number of potential advantages, including a higher BED, reduced volume of normal tissue irradiated, and reduced overall treatment time.

- No direct / Randomized evidence to say SBRT is superior to fractionated IMRT
- SBRT > 5Gy with motion Mx
Evolution of SBRT
Lack of fractionation
Inadequate motion management techniques
Absence of image guidance using fiducial markers
Lack of specific dose constraints for OARs
• Median volume treated - 136cc, whereas the by the Stanford group was 41cc

• PTV was encompassed by the 67% isodose surface.
• High-dose (>8 Gy) /#
• Rapidly activates the cell membrane acid sphingomyelinase (ASMase) that hydrolyses sphingomyelin to generate the proapoptotic second messenger ceramide
• Thus initiating transmembrane signaling of apoptosis
<table>
<thead>
<tr>
<th>Stage</th>
<th>Arterial</th>
<th>Venous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resectable</td>
<td>Clear fat planes around CA, SMA, and HA</td>
<td>No SMV/portal vein distortion</td>
</tr>
<tr>
<td>Borderline resectable</td>
<td>Gastroduodenal artery encasement up to the hepatic artery with either short segment encasement or direct abutment of the hepatic artery without extension to the CA. Tumor abutment of the SMA not to exceed greater than 180° of the circumference of the vessel wall</td>
<td>Venous involvement of the SMV or portal vein with distortion or narrowing of the vein or occlusion of the vein with suitable vessel proximal and distal, allowing for safe resection and replacement</td>
</tr>
<tr>
<td>Unresectable*</td>
<td>Aortic invasion or encasement. Based on tumor location: Pancreatic head—More than 180° SMA encasement, any CA abutment, IVC</td>
<td>Unreconstructible SMV/portal vein occlusion</td>
</tr>
<tr>
<td></td>
<td>Pancreatic body/tail—SMA or CA encasement greater than 180°</td>
<td></td>
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Questions?

• Role in BRPC
• Role in LAPC

• Is it safe
• Is it well tolerated
• Is it effective
• Comparison with IMRT
Challenges of SBRT in Pancreas

• The head of Pancreas, where majority of the tumor is in close proximity to the Duodenum

• RT dose of >50Gy (1.8-2Gy daily) results in ulcerations stenosis, bleeding and perforation

• The Pancreas moves with respiration and peristalsis
SBRT for BRPC

Indicated to improve resectability in the Neoadjuvant setting
• 30 patients completed NAT and were offered surgical exploration.

• 17 (56.7 %) reported no acute adverse effects during SBRT. No grade 3 or higher toxicity was observed from SBRT.

• 29 (96.7 %) underwent exploration.

• Twenty-one (70%) patients underwent R0 resection none requiring vessel resection

• One (3.3 %) patient was resected with microscopic positive margins.
**SBRT for LAPC and BRPC Is Effective and Well Tolerated**

Chuong 2013

<table>
<thead>
<tr>
<th></th>
<th>BRPC</th>
<th>LAPC</th>
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</thead>
<tbody>
<tr>
<td>Median 1Yr OS</td>
<td>72.2%</td>
<td>68.1%</td>
</tr>
<tr>
<td>Median PFS</td>
<td>16.4 mths</td>
<td>15 months</td>
</tr>
<tr>
<td>1 Yr PFS</td>
<td>9.7 mths</td>
<td>9.8 mths</td>
</tr>
</tbody>
</table>

**BRPC with R0 resection**

<table>
<thead>
<tr>
<th></th>
<th>Operated</th>
<th>Not operated</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOS</td>
<td>19.3 mths vs</td>
<td>12.3 mths p.03</td>
</tr>
<tr>
<td></td>
<td>84.2%</td>
<td>58.3%</td>
</tr>
<tr>
<td>Median 1Yr OS</td>
<td>56.5%</td>
<td>25% p.0001</td>
</tr>
<tr>
<td>Median PFS</td>
<td></td>
<td>81%</td>
</tr>
<tr>
<td>1 Yr PFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 yr local control non Sx pts</td>
<td></td>
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</tr>
</tbody>
</table>

No acute grade 3 toxicity, and late grade 3 toxicity was minimal (5.3%).

Dose painting
35Gy/5#
25Gy/5#
Surgical positive margin rate was lower after neoadjuvant therapy (3.3% vs. 16.2%, P=0.006). Median OS - 33.5 months in NAT vs. 23.1 months in upfront resection patients who received adjuvant treatment (P=0.057).
Median overall survival approaching 3 years, far superior to contemporary outcomes.

36% of patients who received FOLFIRINOX (Oxaliplatin, leucovorin, irinotecan, 5-fluorouracil) chemotherapy and SBRT underwent surgical resection, despite having “unresectable” disease at diagnosis.
SBRT in LAPC

30-40% of all panc ca
<table>
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<tbody>
<tr>
<td>The pooled 1- year OS ranged from.</td>
<td>51.6%</td>
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<tr>
<td>The median OS</td>
<td>5.7 - 47 months (median 17)</td>
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<tr>
<td>Severe side effects</td>
<td>&lt;10%</td>
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<tr>
<td>LRC rate at 1 year</td>
<td>72.3%</td>
</tr>
<tr>
<td>LRC appeared to correlate with the total SBRT dose and the number of #</td>
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</table>
RT for LAPC

• Concurrent CTRT Vs. Chemo alone – Mixed results no definite evidence

• NACT followed by CTRT – Advantageous for non metastatic, 30% develop mets

• CTRT to 55 Gy with concurrent continuous infusion 5-FU improved survival compared to continued chemotherapy (median survival of 15.0 vs. 11.7 months, P=0.0009 (Huguet et al)

LAP07

• 15.2 mths CTRT vs. 16.5 mnths with chemotherapy, P=0.83).
• CTRT had - improved local control (68% vs. 54%)
  - prolonged time to second line treatment (6.1 months compared to 3.7 months, P=0.02). likely improves quality of life.
IMRT Vs SBRT
Chapman et al 2018

- Retrospective study
- 91 pts SBRT = 75 IMRT = 16
- 70% BRPC 30% LAPC
- RT dose 30Gy/5# or 50Gy/25#

- SBRT and IMRT appear to have similar rates of resection, perioperative outcomes, and survival outcomes
IMRT Vs SBRT for unresectable LAPC Park 2017

- Retrospective study
- SBRT n=44, IMRT n=226 treated from 2008 to 2016
- SBRT (five fractions, 30–33 Gy) or IMRT (25–28 #, 45–56 Gy) with concurrent chemotherapy

Not inferior to Long course in outcomes or toxicity
Radiation in the era of FOLFIRINOX and gemcitabine/nab-paclitaxel

• The phase III PRODIGE4/ACCORD11 -FOLFIRINOX nearly doubled median overall survival compared to gemcitabine (11.1 vs. 6.8 months, P<0.0001)

• MPACT trial - superiority of gemcitabine and nab-paclitaxel compared to gemcitabine alone in the metastatic setting, with median overall survival of 8.5 vs. 6.7 months, respectively

• Recent Metaanalysis - Addition of RT improved mPFS and MOS to 15 and 24 months.
Association of Ablative Radiation Therapy With Survival Among Patients With Inoperable Pancreatic Cancer

Marsha Reynold, MD, PhD; Eileen M. O’Reilly, MD; Anna M. Varghese, MD; Megan Fiasconaro, MSc; Melissa Timmins, MD; Paul R. Papanicolaou, MD; Abraham Wu, MD; Carla Heli, MD; John G. Curran, MD
Figure 1. Overall Survival and Cumulative Incidence of Locoregional Progression

A. Overall survival from the time of A-RT

B. Cumulative incidence of locoregional failure from the time of A-RT

No. at risk
All 119 81 23 6

No. at risk
All 117 73 15 2


Figure 2. Overall Survival and Cumulative Incidence of Locoregional Progression by CA19-9 Percent Change

A. Overall survival by postinduction CA19-9 decrease

B. Cumulative incidence of locoregional failure by postinduction CA19-9 decrease

No. at risk
<80th Percentile 19 9 3 0
80th Percentile 77 54 12 4

No. at risk
<80th Percentile 19 7 1 0
80th Percentile 76 48 10 1

P = .07

P = .09
Aggressive chemotherapy + Dose escalated SBRT + R0 resection (venous / arterial reconstruction)

4-6# FOLFIRINOX + High dose SBRT

Better Overall outcomes!!
Early initiation of systemic treatment

- FOLFIRINOX /NAB-Paclitaxel
- 4-8#

Shortening the time taken to deliver CTRT

- SBRT
- High precision RT
- More effective RT higher doses up to 75Gy/1 week
NACT- Advantages

1. Increases the proportion of patients with resectable disease receiving multimodality therapy.

2. May reduce tumor volume and downstage tumors enabling surgical resection with a lower risk of an R1 resection.

3. May also allow earlier treatment of radiographically occult micrometastasis.

4. May identify patients with a favorable cancer biology that have the greatest benefit from surgical resection.
• 20 patients treated with either SBRT or dose-escalated hypofractionated IMRT (DE-IMRT) were re-planned
• 70 Gy/5# - GTV
• 40 Gy/5#- PTV

Mean iGTV coverage
50 Gy - 91% (0.07%),
60 Gy - 61.3% (0.08%)
70 Gy - 24.4% (0.05%)

Max PTV coverage
70 Gy - 33%.
60 Gy - 77.5%
Predicting response to SBRT and Sx resection

Predictors - chemotherapy regimen, amount of arterial involvement and age. Radiation dose (GTV D95)

Cheng et al Advances in Radiation Oncology: 2018
Different combined regimens of chemotherapy with SBRT for LAPC

Factors associated with OS

<table>
<thead>
<tr>
<th>Treatment modality</th>
<th>OS</th>
<th>CI</th>
<th>p</th>
<th>DED&lt;sub&gt;10&lt;/sub&gt;</th>
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<tr>
<td>Nonchemotherapy</td>
<td>33</td>
<td>11.2</td>
<td>10.5-11.8</td>
<td>&lt;.001</td>
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<tr>
<td>Induction chemotherapy</td>
<td>45</td>
<td>12.2</td>
<td>11.3-13.0</td>
<td>0.60</td>
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<tr>
<td>Adjuvant chemotherapy</td>
<td>205</td>
<td>13.6</td>
<td>13.0-14.2</td>
<td>0.42</td>
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<tr>
<td>Induction and adjuvant chemotherapy</td>
<td>136</td>
<td>13.3</td>
<td>13.0-14.0</td>
<td>0.50</td>
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<tr>
<td>DED&lt;sub&gt;10&lt;/sub&gt;</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≥60 Gy</td>
<td>225</td>
<td>13.1</td>
<td>10.0-17.1</td>
<td>&lt;.001</td>
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<tr>
<td>&lt;60 Gy</td>
<td>194</td>
<td>11.5</td>
<td>10.0-11.5</td>
<td>2.59</td>
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Factors associated with PFS

<table>
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<tr>
<th>Treatment modality</th>
<th>PFS</th>
<th>CI</th>
<th>p</th>
<th>DED&lt;sub&gt;10&lt;/sub&gt;</th>
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<tbody>
<tr>
<td>Nonchemotherapy</td>
<td>6.4</td>
<td>5.0-6.2</td>
<td>&lt;.001</td>
<td>1</td>
</tr>
<tr>
<td>Induction chemotherapy</td>
<td>6.2</td>
<td>6.0-6.8</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td>8.6</td>
<td>8.2-9.0</td>
<td>0.28</td>
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<tr>
<td>Induction and adjuvant chemotherapy</td>
<td>8.1</td>
<td>7.4-8.8</td>
<td>0.33</td>
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</tr>
</tbody>
</table>
CONKO-007: Chemoradiotherapy vs Chemotherapy Alone for Unresectable Locally Advanced Pancreatic Cancer

CCO Independent Conference Highlights*
of the 2022 ASCO Annual Meeting, June 3-7, 2022, Chicago, Illinois

*CCO is an independent medical education company that provides state-of-the-art medical information to healthcare professionals through conference coverage and other educational programs.
CONKO-007: Study Design

- Randomized phase III trial

Patients with unresectable locally advanced pancreatic cancer; no prior radiotherapy or chemotherapy; ECOG PS ≤2. (N = 402)

Induction CT: Gemcitabine or FOLFIRINOX

CRT: Gemcitabine + RT†
(n = 167)

Randomized
(n = 336)

CT: Gemcitabine or FOLFIRINOX†
(n = 169)

Computed tomography scan for evaluation of resectability; if R0 resectable, could proceed to surgery; if not, could receive additional chemotherapy

*Gemcitabine 1000 mg/m²/d on Days 1, 8, 15, 29, 36, 43, 57, 64, and 71 or FOLFIRINOX on Days 1, 15, 29, 43, 57, and 71.
†Irradiation 28 x 1.8 Gy with total dose 50.4 Gy; gemcitabine 300 mg/m²/d on Days 1, 8, 15, 22, and 29 followed by gemcitabine 1000 mg/m²/d on Days 57, 64, and 71. *Primary endpoint was changed from OS after interim analysis due to insufficient recruitment.

- Primary endpoint: R0 resection rate†
- Secondary endpoints: OS, DFS, rate of resections, survival following resection
- Median follow-up: 55.13 mo

## CONKO-007: R0 Resection Rate, All Randomized Patients

<table>
<thead>
<tr>
<th>Outcome, n (%)</th>
<th>CT (n = 167)</th>
<th>CT + CRT (n = 169)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection performed</td>
<td>60 (36)</td>
<td>62 (37)</td>
<td>.91</td>
</tr>
<tr>
<td>pCR</td>
<td>1 (0.6)</td>
<td>11 (7)</td>
<td>.0055</td>
</tr>
<tr>
<td>Resection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• R0</td>
<td>30 (18)</td>
<td>43 (25)</td>
<td>.1126</td>
</tr>
<tr>
<td>• R1</td>
<td>16 (10)</td>
<td>5 (3)</td>
<td>.0133</td>
</tr>
<tr>
<td>• R2, Rx</td>
<td>14 (8)</td>
<td>14 (8)</td>
<td>1.0000</td>
</tr>
<tr>
<td>CRM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Negative</td>
<td>15 (9)</td>
<td>29 (17)</td>
<td>.0348</td>
</tr>
<tr>
<td>• Positive</td>
<td>27 (16)</td>
<td>11 (7)</td>
<td>.0057</td>
</tr>
<tr>
<td>• Missing data</td>
<td>4 (2)</td>
<td>8 (5)</td>
<td></td>
</tr>
<tr>
<td>Deceased with 30 days post resection</td>
<td>5 (3)</td>
<td>4 (2)</td>
<td>.7494</td>
</tr>
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</table>
## CONKO-007: R0 Resection Rate, Patients Who Underwent Surgery After Randomized Treatment

<table>
<thead>
<tr>
<th>Outcome, n (%)</th>
<th>CT (n = 60)</th>
<th>CT + CRT (n = 62)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pCR</td>
<td>1 (2)</td>
<td>11 (18)</td>
<td>.0043</td>
</tr>
<tr>
<td><strong>Resection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• R0</td>
<td>30 (50)</td>
<td>43 (69)</td>
<td>.0418</td>
</tr>
<tr>
<td>• R1</td>
<td>16 (27)</td>
<td>5 (8)</td>
<td>.0081</td>
</tr>
<tr>
<td>• R2, Rx</td>
<td>14 (23)</td>
<td>14 (23)</td>
<td>1.0000</td>
</tr>
<tr>
<td><strong>CRM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Negative</td>
<td>15 (25)</td>
<td>29 (47)</td>
<td>.0147</td>
</tr>
<tr>
<td>• Positive</td>
<td>27 (45)</td>
<td>11 (18)</td>
<td>.0016</td>
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<tr>
<td>• Missing data</td>
<td>4 (7)</td>
<td>8 (13)</td>
<td></td>
</tr>
<tr>
<td>Deceased with 30 days post resection</td>
<td>5 (8)</td>
<td>4 (6)</td>
<td>.7413</td>
</tr>
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</table>
## CONKO-007: OS by Subgroups

<table>
<thead>
<tr>
<th>Outcome</th>
<th>OS, Mo</th>
<th>5-Yr OS, % (Range)</th>
<th>HR (95% CI), CT vs CT + CRT</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- No (n = 214)</td>
<td>14</td>
<td>0</td>
<td>0.573 (0.443-0.743)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>- Yes (n = 122)</td>
<td>19</td>
<td>17.5 (11.1-27.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>All surgical patients (N = 122)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- CT arm (n = 60)</td>
<td>19</td>
<td>12.0 (5.3-27.5)</td>
<td>0.896 (0.595-1.350)</td>
<td>.601</td>
</tr>
<tr>
<td>- CT + CRT arm (n = 62)</td>
<td>20</td>
<td>24.0 (14.7-39.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>All surgical patients treated with FOLFIRINOX (N = 112)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- CT arm (n = 56)</td>
<td>21</td>
<td>13.0 (5.7-29.6)</td>
<td>0.857 (0.555-1.324)</td>
<td>.487</td>
</tr>
<tr>
<td>- CT + CRT arm (n = 56)</td>
<td>22</td>
<td>26.9 (16.7-43.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Resection status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- R0 (n = 73)</td>
<td>26</td>
<td>27.3 (17.4-43.8)</td>
<td>R0 vs R1: 2.155 (1.249-3.717)</td>
<td>.006</td>
</tr>
<tr>
<td>- R1 (n = 21)</td>
<td>17</td>
<td>8.0 (1.4-45.0)</td>
<td>R0 vs incom/p/no: 2.486 (1.786-3.460)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>- Incomplete/no surgery (n = 242)</td>
<td>16</td>
<td>0</td>
<td>R0 vs no random: 4.163 (2.943-5.889)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>- No randomization (n = 159)</td>
<td>9</td>
<td>0</td>
<td>R1 vs incom/p/no: 1.154 (0.710-1.874)</td>
<td>.563</td>
</tr>
<tr>
<td><strong>Resection status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- CRM- (n = 44)</td>
<td>36</td>
<td>35.9 (22.6-57.0)</td>
<td>CRM- vs CRM+: 2.293 (1.356-3.876)</td>
<td>.002</td>
</tr>
<tr>
<td>- CRM+ (n = 38)</td>
<td>18</td>
<td>9.0 (2.6-31.7)</td>
<td>CRM+ vs incom/p/no: 3.115 (2.034-4.770)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>- Incomplete/no surgery (n = 242)</td>
<td>16</td>
<td>0</td>
<td>CRM- vs no random: 5.197 (3.352-8.058)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>- No randomization (n = 159)</td>
<td>9</td>
<td>0</td>
<td>CRM+ vs incom/p/no: 1.358 (0.926-1.992)</td>
<td>.117</td>
</tr>
</tbody>
</table>
Future directions

• MRI guided
Stereotactic MR-guided adaptive radiation therapy (SMART) for pancreatic cancer

At each fraction, OAR (re-)contouring is done within a distance of 3 cm from the PTV surface allows good OAR sparing and adequate target coverage while requiring only limited online (re-)contouring from clinicians.
Dose escalation with proton or photon radiation treatment for pancreatic cancer

Myriam Bouchard, Richard A. Amos, Tina M. Briere, Sam Beddar, Christopher H. Crane

*Department of Radiation Physics, The University of Texas M.D. Anderson Cancer Center, Houston, USA
Department of Radiation Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, USA

Radiotherapy and Oncology 92 (2009) 238–243

optimal choice of radiation therapy modality for safe dose escalation depends on the pancreatic tumor position in relation to OAR anatomy. IMRT and passive scattering PT showed advantageous results, but for different tumor positions. 3DCRT plans presented considerably inferior target coverage compared

Fig. 5. Bowel and internal target volume dose-volume histograms for tumor position #1, comparing 72-Gy IMRT, 72-Gy PT and 50-Gy four-field box.

Percentages of ITVs and CTvs receiving doses >72 Gy ($V_{72 Gy}$) according to tumor positions.

<table>
<thead>
<tr>
<th>Position #</th>
<th>ITV $V_{72 Gy}$</th>
<th>CTV $V_{72 Gy}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial (#1)</td>
<td>IMRT 97.1%</td>
<td>Protons 94.4%</td>
</tr>
<tr>
<td>Head (#1-3)</td>
<td>75.9 ± 20.0%</td>
<td>86.5 ± 6.2%</td>
</tr>
<tr>
<td>Body (#4-7)</td>
<td>93.1 ± 3.1%</td>
<td>77.8 ± 4.3%</td>
</tr>
<tr>
<td>Tail (#8-11)</td>
<td>86.3 ± 14.1%</td>
<td>89.8 ± 6.5%</td>
</tr>
</tbody>
</table>
SBRT dose regimens

• 40-50Gy/ 5#

• 67.5Gy/15

• Is there a difference?

• BED is what matters
• BED >90 Gy desirable upto 100Gy
50Gy/5# vs 67.5/15# - ASTRO 2022

• Two institutes comparison

• No difference in outcomes
SBRT Pancreas

SOP
• Patients with active duodenal or gastric ulcers are not acceptable for SBRT.

• Patients with direct tumor invasion of the bowel or stomach based on endoscopy or if organ at risk (OAR) constraints cannot be met: Consider for Hypofractionated IGRT (HIGRT)

• Patients should have 4D CT simulation / fluoroscopy to assess tumor motion

• Patients should be treated with SBRT only if motion management techniques are available
Duodenal infiltration by tumor

Not a contraindication for SBRT
More fractionated regimens preferred

MD Anderson/ Mayo
67.5/15#
55Gy / 10#
Keeping the BED >85Gy
Fiducial placement

- 1-5 (preferably ≥ 3) fiducial markers (Civco, Visicoil, Gold anchor) should be placed for targeting purposes in or directly at the tumor periphery and/or within 1 cm of the tumor (normal pancreas) under EUS (preferred) or CT guidance.
CT guided Gold marker placement
Simulation

• Counsel regarding the procedure and advise breathing exercises

• Supine position with a customized immobilization device (e.g. Vac-Lok)

• Empty stomach / four hours fasting/ Prokinetic and carminative protocol

• Oral contrast: Diatrizoate Meglumine 2.5ml diluted in 50ml of water is given 20 minutes prior to the scan. Ensure no unusual distension of stomach/duodenum/bowel.

• A 4DCT scan (when available) / Fluoroscopic tracking of markers - to assess respiratory motion. If the tumor motion > 5mm, respiratory motion management is required.
Dosimetric analysis
debh v/s dibh
<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>Std Dev</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>D15 Exp- D15 Insp</td>
<td>3.46</td>
<td>4.1</td>
<td>0.421</td>
</tr>
<tr>
<td>D20 Exp- D20 Insp</td>
<td>5.95</td>
<td>9.72</td>
<td>0.085</td>
</tr>
<tr>
<td>D33 Exp- D33 Insp</td>
<td>0.49</td>
<td>0.84</td>
<td>0.1</td>
</tr>
<tr>
<td>D35 Exp- D35 Insp</td>
<td>0.33</td>
<td>0.16</td>
<td>0.075</td>
</tr>
<tr>
<td>D36 Exp- D36 Insp</td>
<td>0.08</td>
<td>0.17</td>
<td>0.145</td>
</tr>
<tr>
<td>B20 Exp- B20 Insp</td>
<td>17.49</td>
<td>51.69</td>
<td>0.312</td>
</tr>
<tr>
<td>B33 Exp- B33 Insp</td>
<td>5.6</td>
<td>14.25</td>
<td>0.245</td>
</tr>
<tr>
<td>S15 Exp- S15 Insp</td>
<td>12.42</td>
<td>11.41</td>
<td>0.007</td>
</tr>
<tr>
<td>S20 Exp- S20 Insp</td>
<td>5.25</td>
<td>5.95</td>
<td>0.021</td>
</tr>
<tr>
<td>L12 Exp- L12 Insp</td>
<td>51.8</td>
<td>38.17</td>
<td>0.002</td>
</tr>
<tr>
<td>K12 Exp- K12 Insp</td>
<td>4.01</td>
<td>12.1</td>
<td>0.321</td>
</tr>
</tbody>
</table>

P-value calculated using PAIRED T-test in Parametric variables normally distributed ( P< 0.05)
IR camera calibration
4DCT – tracking the pattern of respiration
Monitoring breath hold

Breath-hold technique
- Deep expiratory breath-hold (DEBH)
- Comfortable breath-hold (CBH)
- Deep inspiratory breath-hold (DIBH)
Basic Original Report

Australasian Gastrointestinal Trials Group (AGITG) and Trans-Tasman Radiation Oncology Group (TROG) Guidelines for Pancreatic Stereotactic Body Radiation Therapy (SBRT)

Andrew Oar MBBS MIPH FRANZCR a,b,*,
40 Gy in 5 fractions (BED₁₀Z72 Gy, BED₃Z147 Gy) to as much of the PTV as possible. To meet dose constraints to OARs, under coverage of the PTV near gastrointestinal structures is required. We recommend the dose to 90% of an evaluable PTV (PTV less gastrointestinal PRV) is greater than 100% of the prescription dose (40 Gy). Compromises to coverage may be needed when tumors are proximal to hollow viscous. If D90% (minimum dose covering 90% of the volume) is less than 90% of prescription dose, reduced-dose SBRT, conventional chemoradiotherapy, or chemotherapy alone should be considered (Table 1). Maximum doses (D₀.₅ cm³) of 33 Gy in 5 fractions (BED₁₀Z 54 Gy, BED₃Z 103 Gy) to the duodenum and small bowel have a low incidence of toxicity.
• SBRT should be delivered as 5 fractions
• with a maximum of 4 treatments per week, with 2
• consecutive days permitted but not 3.
• A minimum of
• 24 hours between fractions is also recommended.
Predictors of outcome in patients receiving stereotactic body radiation therapy for borderline resectable and locally advanced pancreatic cancers

Akanksha Anup, Manish Bhandare, Vikram Chaudhari, Rahul Krishnatr Shailesh Shrikhande, Vikas Ostwal, Anant Ramaswamy, Akshay Bahet Mukta Ramadwar, Reena Engineer

On multivariate analysis, Eastern Cooperative Oncology Group (ECOG) < 2 [hazard ratio (HR): 2.77 (1.2–6.2; 0.014)], head location [3.7 (1.4–9.6; 0.007)], and radiological response post-NACT-SBRT [4.38 (1.08–17.7; 0.039)] were significant predictors of outcome in both the cohorts. No grade ≥3 late radiotherapy (RT)-related toxicities were seen.
TARGET DELINEATION
GTV
Vessels (Tumor vessel interface)
Duodenum
Small bowel
GTV + 3mm
TVI + 3mm
GI + 3mm (PRV GI)
High Dose PTV
Intermediate Dose PTV
Plan evaluation
<table>
<thead>
<tr>
<th>BRPC (ALLIANCE)</th>
<th>BED (α/β = 10)</th>
<th>BED (α/β = 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>33Gy/5 # (SBRT)</td>
<td>54.8</td>
<td>105.6</td>
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<tr>
<td>25Gy/5 # (HIGRT)*</td>
<td>37.5</td>
<td>66.7</td>
</tr>
<tr>
<td>BRPC (TMH)</td>
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<td></td>
</tr>
<tr>
<td>36Gy/5 #</td>
<td>61.9</td>
<td>122</td>
</tr>
<tr>
<td>42Gy/5 #</td>
<td>77.2</td>
<td>159</td>
</tr>
<tr>
<td>45Gy/5 #</td>
<td>85.5</td>
<td>180</td>
</tr>
<tr>
<td>LAPC (TMH)</td>
<td>50Gy / 5 #</td>
<td>100</td>
</tr>
<tr>
<td>BRPC/ LAPC</td>
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<td></td>
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<tr>
<td>Frank duodenal</td>
<td>67.5Gy/15#</td>
<td>97.88</td>
</tr>
<tr>
<td>infiltration</td>
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</tr>
</tbody>
</table>

*(Large tumors, Mucosal infiltration, non-availability of IGRT/Motion management or if OAR constraints not achievable with 33Gy/5#)*
<table>
<thead>
<tr>
<th>OAR</th>
<th>Constraints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenum</td>
<td>V20 &lt; 20 cc</td>
</tr>
<tr>
<td>Small bowel</td>
<td>V35 &lt; 1 cc*</td>
</tr>
<tr>
<td></td>
<td>Dmax &lt; 40Gy</td>
</tr>
<tr>
<td></td>
<td>V20 &lt; 20 cc</td>
</tr>
<tr>
<td>Stomach</td>
<td>V35 &lt; 1 cc*</td>
</tr>
<tr>
<td></td>
<td>Dmax &lt; 40 Gy*</td>
</tr>
<tr>
<td>Kidneys</td>
<td>V12 &lt; 25%*</td>
</tr>
<tr>
<td>Liver</td>
<td>V12 &lt; 50%*</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>V20&lt;1cc*</td>
</tr>
</tbody>
</table>

* Mandatory constraints
V 35 Duodenum <1cc
V 35 Bowel <1cc
CASE 1
68Y/male, diabetic
BRPC (Portal vein, SMV and SMA abutment)
Post 2 cycles Gemcitabine + Nab Paclitaxel
GTV
GTV+3mm
TVI
PRV GI

PTV 1
PTV 2
PTV 3
GTV
GTV+3mm
TVI
PRV GI
PTV 1
PTV 2
PTV 3

Following 3 # CT,

SBRT - to the tumor and abutting vessel and a 3 mm PTV margin to 33 Gy (6.6 Gy x 5)

The cumulative incidence of Local failure (LF) at 12 months from resection was 50% (95% CI: 20-80). All LF were outside to the PTV33.
Figure 1. (A) Patient with borderline resectable tumor due to SMV encasement treated to the primary tumor alone. A local-only recurrence occurred at the SMA 7 months from surgery as the first site of failure. (B) CT at time of recurrence fused to planning CT revealing the recurrence volume marginal to the original PTV (arrow).
Figure 2. (A) Patient with borderline resectable tumor due to common hepatic artery abutment treated to the primary tumor alone. A local only recurrence occurred 12 months following surgery at the celiac artery as the first site of failure. (B) CT at time of recurrence fused to planning CT revealing the recurrence volume marginal to the original PTV (arrow)
Optional elective PTV to 25 Gy (5 Gy x 5) customized to the nodal space and mesenteric vessels
### Table 2  Suggested dose constraints for pancreas SBRT

<table>
<thead>
<tr>
<th>Organ</th>
<th>Standardized name</th>
<th>Parameter</th>
<th>Constraint</th>
<th>Per protocol, Gy</th>
<th>Minor variation, Gy</th>
<th>Major variation, Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenum</td>
<td>Duodenum</td>
<td>Dmax (0.5 cm$^3$)</td>
<td>&lt;33</td>
<td>35</td>
<td>35</td>
<td>&gt;35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>V30</td>
<td>&lt;5*</td>
<td>5-10*</td>
<td>10*</td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>Stomach</td>
<td>Dmax (0.5 cm$^3$)</td>
<td>&lt;33</td>
<td>35</td>
<td>35</td>
<td>&gt;35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>V30</td>
<td>&lt;5*</td>
<td>5-10*</td>
<td>10*</td>
<td></td>
</tr>
<tr>
<td>Small bowel</td>
<td>SmallBowel</td>
<td>Dmax (0.5 cm$^3$)</td>
<td>&lt;33</td>
<td>35</td>
<td>35</td>
<td>&gt;35</td>
</tr>
<tr>
<td></td>
<td></td>
<td>V30</td>
<td>&lt;5*</td>
<td>5-10*</td>
<td>10*</td>
<td></td>
</tr>
<tr>
<td>Large bowel</td>
<td>LargeBowel</td>
<td>Dmax (0.5 cm$^3$)</td>
<td>≤35 Gy</td>
<td>35-38 Gy</td>
<td>38</td>
<td>&gt;38</td>
</tr>
<tr>
<td>Duodenum PRV†</td>
<td>Duodenum_PRV</td>
<td>Dmax (0.5 cm$^3$)</td>
<td>&lt;38 Gy</td>
<td>38-40 Gy</td>
<td>40</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Small bowel PRV†</td>
<td>SmallBowel_PRV</td>
<td>Dmax (0.5 cm$^3$)</td>
<td>&lt;38 Gy</td>
<td>38-40 Gy</td>
<td>40</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Large bowel PRV†</td>
<td>LargeBowel_PRV</td>
<td>Dmax (0.5 cm$^3$)</td>
<td>&lt;38 Gy</td>
<td>38-40 Gy</td>
<td>40</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Stomach PRV†</td>
<td>Stomach_PRV</td>
<td>Dmax (0.5 cm$^3$)</td>
<td>&lt;38 Gy</td>
<td>38-40 Gy</td>
<td>40</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Spinal cord PRV</td>
<td>SpinalCord_05</td>
<td>Dmax (0.5 cm$^3$)</td>
<td>&lt;20 Gy</td>
<td>25</td>
<td>&gt;25</td>
<td></td>
</tr>
<tr>
<td>Combined kidneys</td>
<td>Kidneys_Comb</td>
<td>V12$^\dagger$</td>
<td>&lt;25$^S$</td>
<td>25-30$^S$</td>
<td>30$^S$</td>
<td></td>
</tr>
<tr>
<td>Single kidney</td>
<td>Kidney_L</td>
<td>V10$^\dagger$</td>
<td>&lt;10$^S$</td>
<td>10-25$^S$</td>
<td>&gt;25$^S$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Kidney_R</td>
<td>V12$^\dagger$</td>
<td>≤40$^S$</td>
<td>≤50$^S$</td>
<td>&gt;50$^S$</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>Liver</td>
<td>V12$^\dagger$</td>
<td>&lt;40$^S$</td>
<td>≤50$^S$</td>
<td>&gt;50$^S$</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** Dmax = maximum dose; PRV = planning organ-at-risk volume; SBRT = stereotactic body radiation therapy.

* Unit is cm$^3$.
† Minimum PRV expansion should be 3 mm; however, larger expansions should be considered in a setting of increased organ movement or uncertainty.
$^S$ Unit is Gy.
$^\dagger$ Unit is percent.
Summary

• SBRT is feasible for all intact pancreatic cancers

• Better integrated with Chemotherapy regimens
History

• 58 y/o gentleman
• P/W Pain in epigastric region, significant weight loss
• Investigations
  - Triphasic CECT TAP: Hypoattenuating lesion involving head and body of pancreas
  - CT guided biopsy of pancreatic mass: MDAC
  - CA 19.9: 16.46
Celiac Axis: >180° encasement
Aorta: <180° encasement
SHA: >180° encasement
SMA: >180° encasement
PV: <180° encasement

LAPC, unlikely to come up for Surgery
Post 6# m FOLFIRINOX
- Decrease in disease volume
- Persistent encasement of CA, CHA, SMA
- Unresectable
- Clinical improvement - Pain relief +, Wt gain +
PTV_35/5: GTV+3mm
PTV_45/5: GTV+3mm – PRV_GI
PTV_50/5: GTV – PRV_GI
THANK YOU