

ARROCase:

Borderline Resectable Pancreatic Cancer

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Case Presentation:

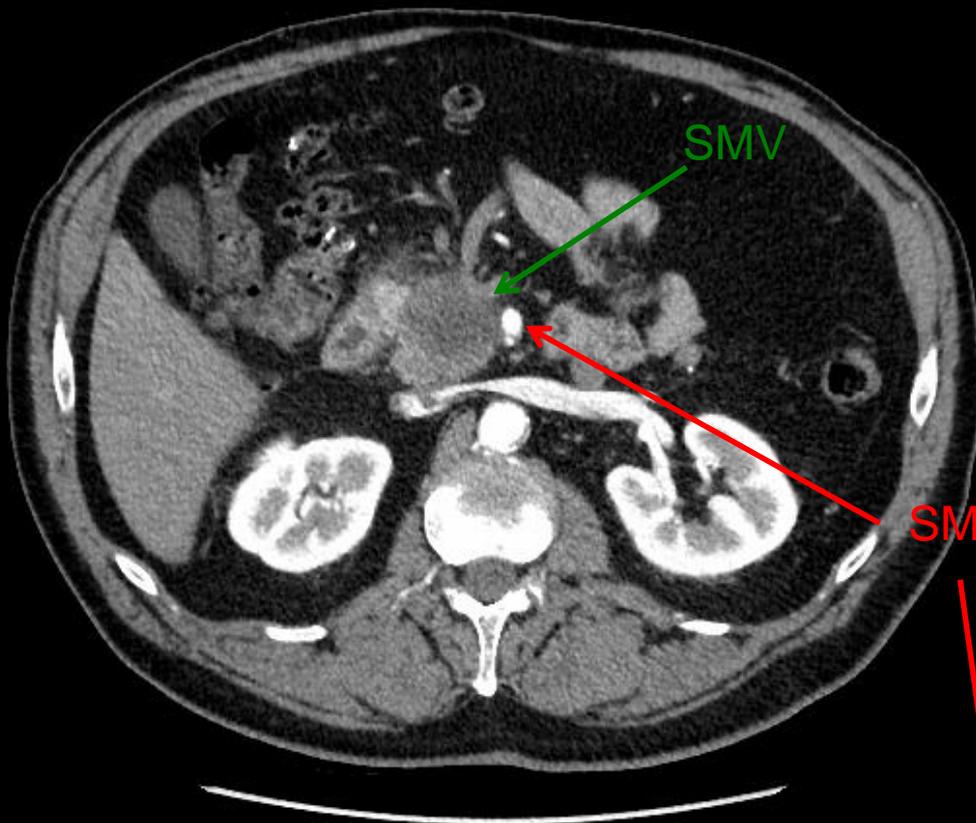
- 60 year old previously healthy male
- Presentation: 6 week history of poorly localized abdominal pain with radiation to his back. No nausea or vomiting episodes.
- Approximately 15 lb weight loss despite normal intake.
- Self-referred to his PCP

Pertinent Exam Findings

- KPS:100
- GENERAL: The patient appears healthy in no distress.
- LYMPHATICS: He has no cervical or supraclavicular lymphadenopathy.
- ABDOMEN: Somewhat obese. He is tender in the right upper quadrant. There are no palpable masses. He has no enlargement of his liver or his spleen. He has no fluid wave.
- HEAD: Examination of his eyes reveals normal, symmetrically reactive to light. No scleral icterus. Oral cavity with no visible lesions.

Workup

- Labs:
 - CBC, LFTs, Basic Chem unremarkable
 - CA 19-9 → 49.1 (H)
- Imaging:
 - CT ABD(pancreas protocol): 4.3x 3.4 cm pancreatic head mass. The mass completely encases the SMV and the portal vein/SMV confluence. The mass abuts the SMA ~120°
 - CT chest, PET → No metastatic disease *Role of PET evolving
- EUS w FNA: No enlarged peripancreatic LN. Celiac axis normal. Bx shows adenocarcinoma
- If neoadjuvant therapy planned, place biliary stent for in cases of biliary obstruction. Also consider diagnostic laparoscopy if neoadjuvant therapy planned.
- Renal perfusion scan prior to radiation therapy
- The patients was considered **borderline resectable** due to SMA abutment <180° and SMV encasement.



Definition of Resectability

<i>Resectable</i>	<i>NCCN Version 2.2012</i>
SMA, Celiac,	No abutment
Hepatic Artery (HA)	No abutment
SMV/PV	No abutment, distortion, tumor thrombus or encasement

Definition of Resectability

<i>Borderline Resectable</i>	<i>NCCN Version 2.2012</i>
SMA, Celiac	<180° abutment
Hepatic Artery (HA)	<ol style="list-style-type: none">1. Gastro-duodenal artery encasement up to the Hepatic artery or2. Direct abutment of hepatic artery w/o extension to celiac axis
SMV/PV	<ol style="list-style-type: none">1. Impingement and narrowing of the lumen2. Encasement or short segment venous occlusion *

* Many institutions that perform venous resections with reconstruction consider short segment occlusion of the SMV as technically resectable.

Definition of Resectability

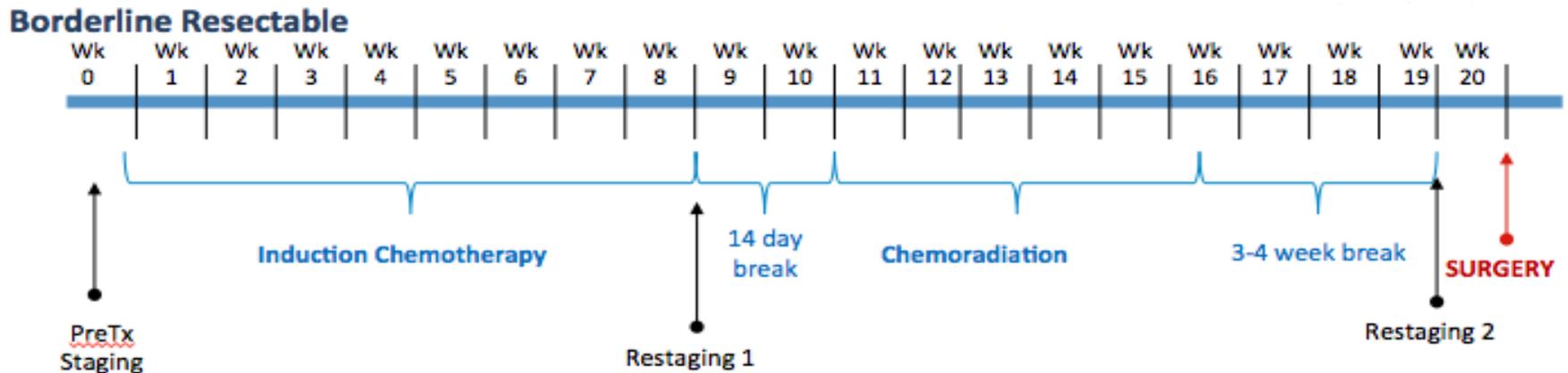
<i>Unresectable</i>	<i>NCCN Version 2.2012</i>
SMA, Celiac	>180°
SMV/PV	Unreconstructable SMV/PV
Other	<ol style="list-style-type: none">1. Aortic invasion or encasement2. LN metastases beyond the field of resection

Treatment Decision Point

- Consultation with Surgical Oncology, Medical Oncology, Radiation Oncology
- Potential treatment options
 - Surgery followed by adjuvant chemo-radiation
 - Induction chemotherapy, chemoradiation, followed by surgery
 - Induction chemotherapy followed by surgery
- Potential advantages to a neoadjuvant approach
 - Increased access to multimodality therapy
 - Identification of patients at high risk for early metastases who are not likely to benefit from surgical resection
 - Improved tumor oxygenation and free radical formation
 - Potential increased margin negative resection and downstaging of borderline resectable patients
 - Improved radiation target delineation
 - Decreased incidence of pancreatiko-jejunal anastomotic leak postoperatively

Treatment Algorithm → Borderline Resectable Pancreatic Cancer

- The optimal treatment algorithm for borderline resectable pancreatic cancer is not defined.
- Treatment often begins with two months of systemic therapy followed by restaging and chemo-radiation.
- MCW treatment algorithm:



Courtesy of MCW Pancreatic Cancer Research Group

Chemotherapy

- Induction Chemotherapy

- Phase II trial for induction Gemcitabine/Cisplatin prior to Gem/XRT in resectable disease. (Varadhachary et al, JCO 2008)
- Increasing use of FOLFIRINOX (Bolus 5-FU,Leucovorin,Irinotecan, oxaliplatin) induction in medically fit patients secondary to survival benefit observed in the metastatic setting over single agent gemcitabine (Conroy et al, N Engl J Med 2011)

- Chemoradiation

- gemcitabine (400mg/m² weekly) or
- capecitabine (825 mg/m² twice daily on radiation treatment days) frequently used

Radiation Planning- IMRT

Simulation:

- Supine with arms up in alpha cradle or other immobilization. PO and IV contrast if available.
- Consider 4D-CT to evaluate motion. Superior/inferior displacement may be >1.5 cm

Contours: No consensus for preoperative treatment volumes.

- Some institutions treat primary tumor with a margin
 - MCW → CTV includes : Primary mass, SMA origin with ~ 7mm margin, SMA and SMV vessels adjacent to the pancreatic head, Enlarged lymph nodes, +/- Celiac axis depending on tumor location. Carve out bowel and bone. Do not routinely include porta hepatic or peri-aortic LN regions.
- PTV: CTV + 1cm depending on institutional protocol
 - MCW: Daily IGRT for all patients. Respiratory gating used if motion >1.0 cm (40-60% phase), ITV of primary mass created if motion < 1.0 cm
- OAR: Small bowel, large bowel, duodenum, stomach, liver, kidneys (preferentially spared if renal perfusion scan reveals dominance), cord

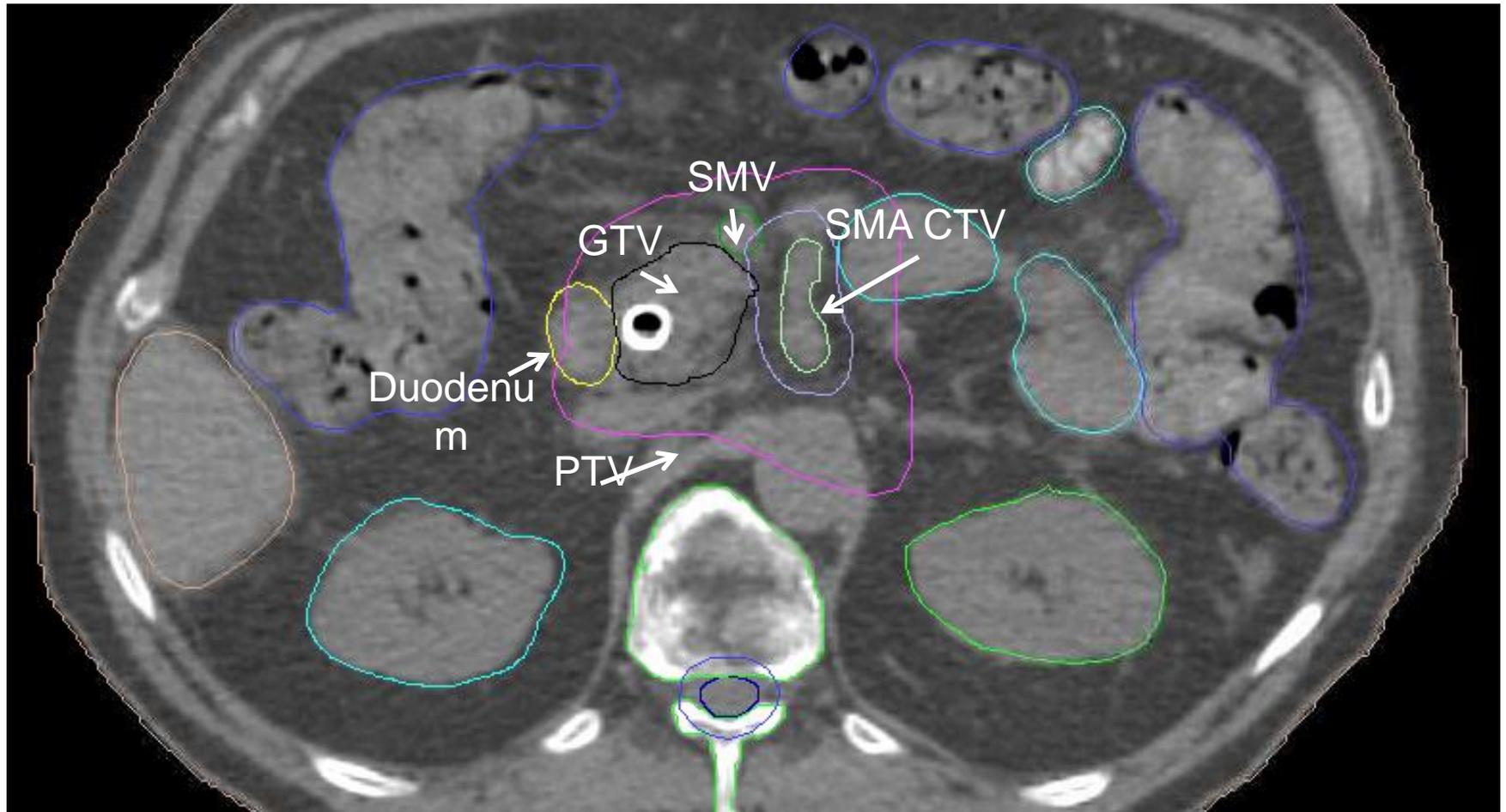
Case Treatment

- Induction Chemotherapy
 - 4 cycles of FOLFIRINOX → Restaging shows no evidence of progression with decline in CA19-9 from 49.1 to 21. CT Imaging revealed some decrease in size of primary mass with stable SMA/SMV relationship.
- Chemoradiation
 - 50.4 Gy at 1.8 Gy/ Fx to >95% PTV using IMRT with concurrent capecitabine (825 mg/m² twice daily on radiation treatment days) Restaging showed no evidence of progression with stable SMA/SMV relationship
- Pancreaticoduodenectomy (whipple) performed with SMV resection and Internal Jugular Vein interposition graft
 - Final path: ypT2N1b, 2.5 cm tumor with >50% tumor necrosis, 2/39 LN involved, margins negative. Tumor distance from SMA margin 5 mm.

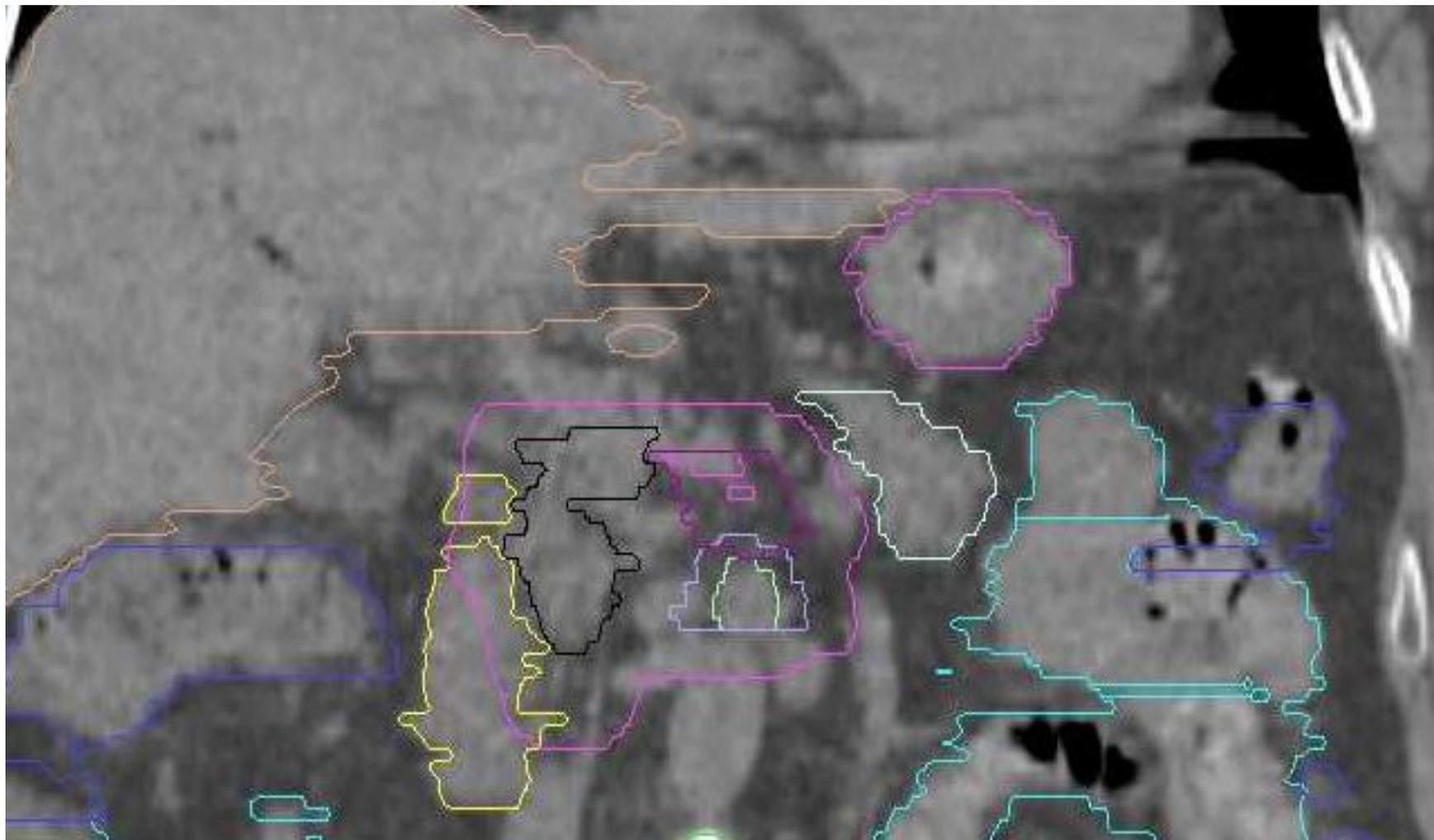
On Treatment Issues

- Premedication
 - Ondansetron 8mg 30-60 minutes pretreatment then as needed
 - Daily proton pump inhibitor 30-60 minutes before breakfast
- Dyspepsia
 - Gaviscon liquid 15-30 ml QID between meals and before bed.
 - Simethicone prn
- Creon taken with meals and snacks
- Rule out cholangitis for RUQ pain, fever

Representative Target Volumes



Representative Target Volumes

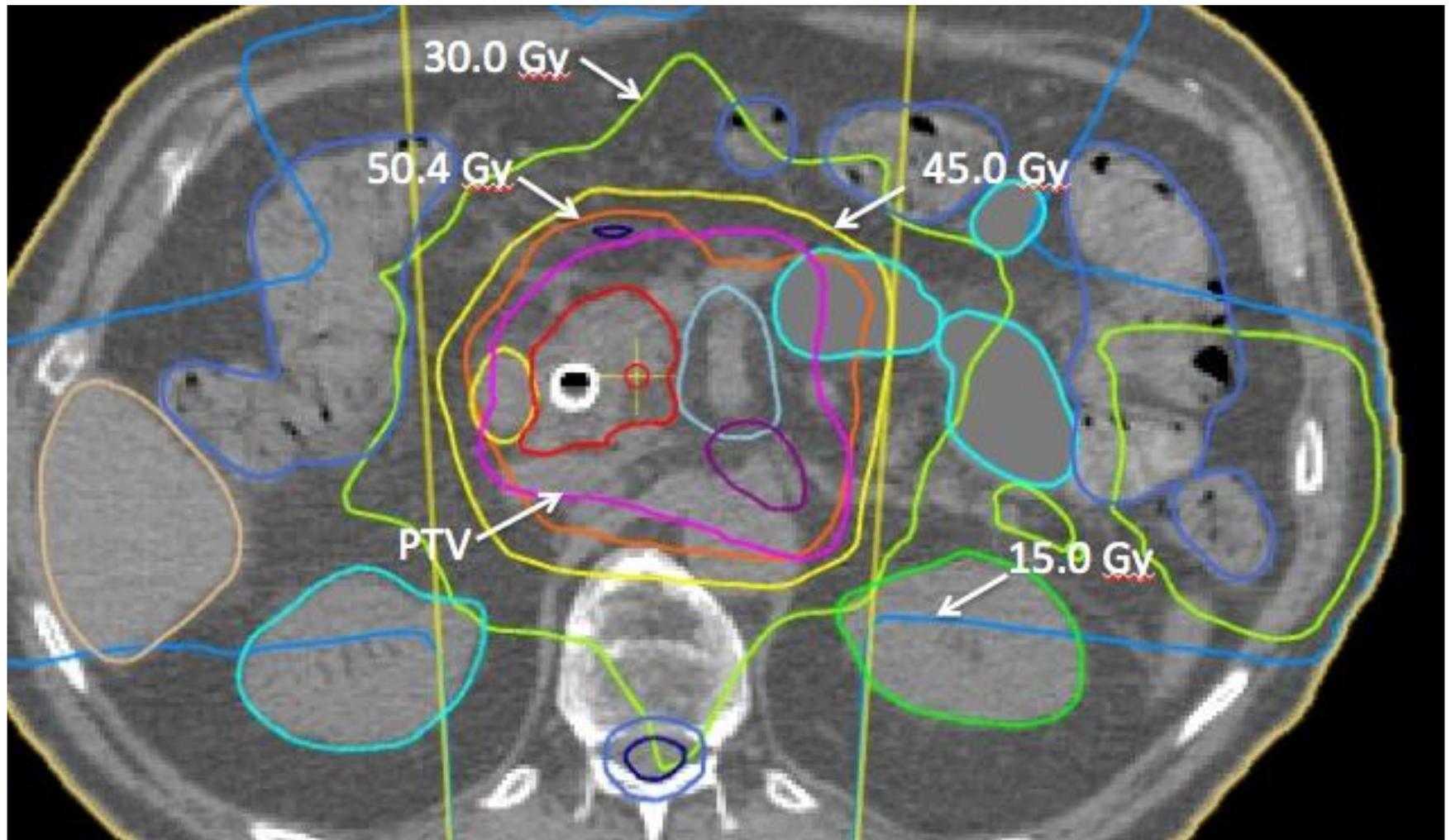


IMRT Constraints

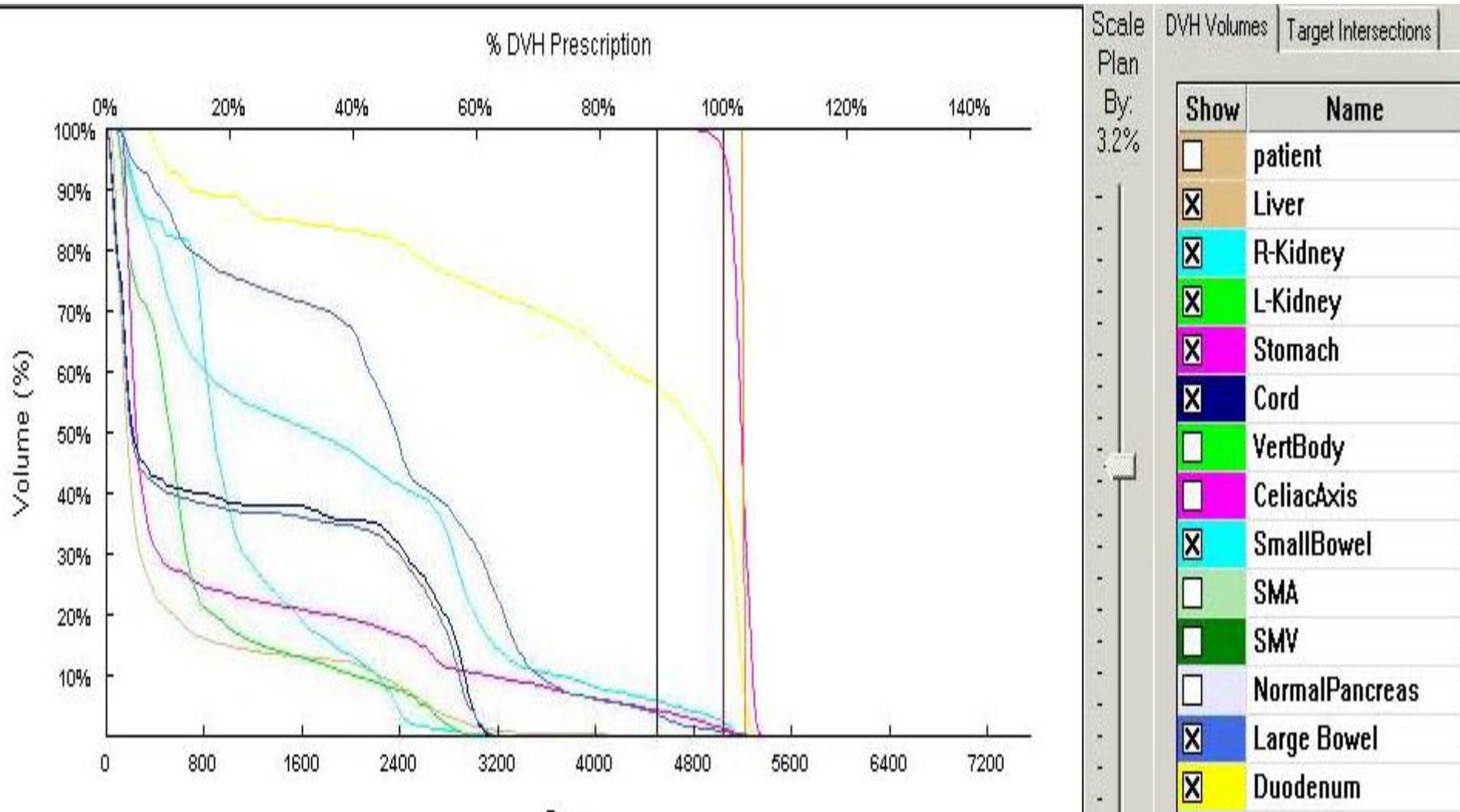
Table 2. Dose Constraints for IMRT Optimization

Structure	Constraints	%
PTV	5040 cGy (1.8 Gy/Fx)	> 95%
Liver	Volume at 3000 cGy	< 30%
Liver mean dose	<2800 cGy	-
L Kidney and R Kidney	1500 cGy	<25%
Stomach	4500 cGy	<25%
Stomach Max Dose	5300 cGy	-
Duodenum Max Dose	5300 cGy	-
Small Bowel	4500 cGy	<25%
Small Bowel Max Dose	5300 cGy	-
Large Bowel	4500 cGy	<50%
Large Bowel Max Dose	5300 cGy	-

Representative Isodose Distribution



Dose Volume Histogram



Case Specific Teaching Points

- Multidisciplinary management is essential for patients with borderline resectable pancreatic cancer.
- In the setting of SMA abutment or SMV encasement, a surgery first approach may risk an R1/R2 resection.
- In this case, the patient was able to achieve margin negative resection following neoadjuvant therapy despite initial vascular involvement.
- Katz et al reported on 160 patients with borderline resectable pancreatic cancer. Following neoadjuvant treatment, 66 (41%) of patients underwent surgical resection and 94% of resected patients had negative margins (1)

References

1. Katz et al. *Borderline Resectable Pancreatic Cancer: The Importance of This Emerging Stage of Disease* J Am Coll Surg 2008;206:833–848
2. Evans et al. *Borderline Resectable Pancreatic Cancer: Definitions and the Importance of Multimodality Therapy.* Ann Surg Oncol 2010. 17:2803–2805
3. Varadachary et al. *Preoperative Gemcitabine and Cisplatin Followed by Gemcitabine-Based Chemoradiation for Resectable Adenocarcinoma of the Pancreatic Head.* J Clin Oncol 2008. 26:3487-3495