

Pancreas SBRT

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Case Presentation

- 70 year old gentleman presents with refractory abdominal pain, bloating, and 16 lb weight loss over 1 month

Patient History

- Past Medical/Surgical History
 - Liver cysts
- Family History
 - Father with CAD, Mother DM, no malignancy
- Social History
 - Retired English teacher
 - Occasional EtOH use (<2 drinks per week)
 - Non-smoker, no drug use

Physical Examination

Vitals: Ht 72 cm, Wt 157 lbs, BP 142/88, HR 65,
Temp 97.8, SpO2 98% on RA

Gen: Well-appearing male in NAD

Lungs: Clear with symmetric air movement

Heart: RRR, S1S2 normal, no murmurs

Abd: Soft, non-distended, left-mid tender

Skin: No jaundice

Lymph: No cervical, supraclavicular, axillary, or
inguinal LAD noted

Laboratory Studies

- CBC
 - Within normal limits
- Chemistries
 - Within normal limits
 - Cr 0.95
- Liver panel
 - AST 15, ALT 26, AP 115
 - Albumin 4.1
- **Ca 19-9 is 250**

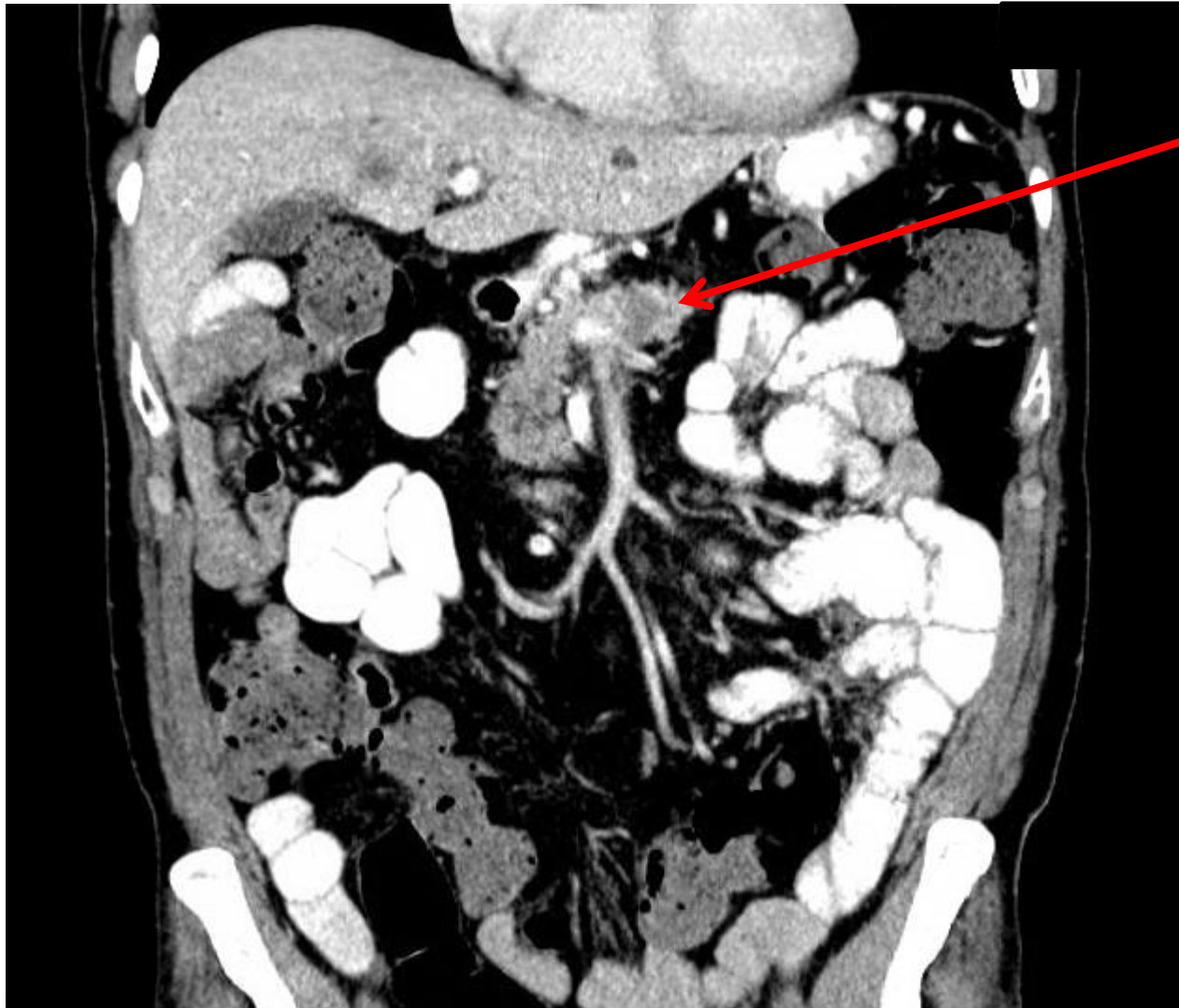
CT Scan – Pancreatic phase (ax)



Hypoenhancing
pancreatic
body mass

Presumed
splenic a.
involvement

CT Scan – Pancreatic phase (cor)



Hypo-enhancing
pancreatic body mass

Diagnostic work up

- CT scan with pancreas protocol
 - 15 mm mass in the mid-body of the pancreas with pancreatic ductal dilation and superior mesenteric vein encasement, and apparent involvement of the splenic artery posterior to the pancreas. **The tumor abuts the celiac artery.** Multiple hepatic cysts are seen diffusely. No hepatic metastases identified.
 - “Borderline resectable” (<180 contact with CA)
- EUS – pancreatic body mass FNA shows Adenocarcinoma
- CT chest – negative

Epidemiology

- Female~Male, peak incidence: 65-80 yo
- Despite #12 cancer incidence, #4 deaths
 - 53,070 cases, 41,780 deaths est. in 2016
- Risk factors: cigarette smoking, diets high in animal fat, prior abdominal radiation (i.e. testicular CA), chronic DM, chronic pancreatitis, obesity
- 10% familial : BRCA2, Peutz-Jeghers, HNPCC, Hereditary pancreatitis, MEN I, VHL, AT

Diagnostic workup

- Per NCCN, imaging should include a dedicated pancreatic CT or MRI
 - CT angiography with thin slices (<1mm) using dual-phase contrast (pancreatic and portal phase) is preferred
- Biopsy via EUS versus CT-guidance
 - Reduced risk for peritoneal seeding
- Diagnostic laparoscopy considered in selected patients
- CA 19-9 at baseline not diagnostic, but may be helpful for response assessment

Resectability status

Resectability status	Arterial (celiac, SMA, common hepatic)	Venous (SMV, PV)
Resectable	No contact	No contact or <180° contact without vein irregularity
Borderline resectable	<ul style="list-style-type: none"> • CH contact w/o celiac • SMA <180° contact • Contact with CA <180° • Presence of variant anatomy 	<ul style="list-style-type: none"> • Contact with SMV/PV >180° without irregularity • Contact with IVC
Unresectable	<ul style="list-style-type: none"> • Contact with CA/SMA >180° • Contact with first jejunal branch of SMA 	<ul style="list-style-type: none"> • Unresectable due to tumor involvement or occlusion • Involvement of first jejunal branch of SMV

See radiology reporting template in NCCN guidelines (adapted from Al-Hawary et al., Radiology, 2014)

Treatment paradigm

- Pancreas SBRT is one of several potential treatment paradigms for unresectable or borderline resectable pancreatic cancer
 - Chemotherapy alone
 - Definitive chemoradiotherapy
 - Chemotherapy → chemoradiotherapy
 - Chemotherapy → SBRT

Neoadjuvant therapy

- Patient underwent 4 cycles of gemcitabine and nab-paclitaxel
- Response by CT
 - “Small mass within the mid-body of the pancreas appears less conspicuous. There is decreased compromise of the portal venous components evidenced by decreased dilation of the splenic vein as well as decreased dilation of the pancreatic duct.”
- Response by CA 19-9 of 250 → 27

Why Pancreas SBRT

- Local control is important in advanced pancreatic cancer
 - Pain, bleeding, obstructive jaundice
- Chemoradiotherapy is arduous
 - 50.4-59.4 Gy over 5-6 weeks
 - Concurrent 5FU or capecitabine
 - Acute GI toxicities in up to 30%
 - LC improved over chemotherapy alone per LAP-07
- SBRT can offer equal or better LC, less acute toxicity, and shorter treatment course

Single fraction SBRT

- First, dose-escalation study of pancreas SBRT by Stanford (Koong et al., IJROBP 2004)
 - Escalated 15, 20, then 25 Gy x1 fraction
 - 7 patients treated at 25 Gy with no GI grade 3 or greater acute toxicity.
- Single and multi-fraction regimens were later tried, with finding that multi-fraction regimens had less SBRT-related toxicity

Outcomes for pancreatic SBRT

Study	Number patients	Dose	Number fractions	Local control (%)	Median survival (mo)
Koong et al., 2005	16	25	1	94	8.25
Hoyer et al., 2005	22	45	3	57	5.7
Mahadevan et al., 2010	36	24-36	3	78	14.3
Schellenberg et al., 2011	12	25	1	94	11.8
Goyal et al., 2012	20	22-30	1-3	81	14.4
Lin et al., 2015	20	35-45	5	80	20
Moningi et al., 2015	88	25-33	5	61	14.4-18.4
Shaib et al., 2016	13	36-45	3	NR	11

Adapted from Kim et al., J Gastro Onc, 2016

All studies on unresectable patients, except Moningi, which included borderline resectable as well

Phase II Multicenter Trial

- Herman, et al., Cancer 2014
 - Phase II Multi-institutional Study
 - Johns Hopkins, MSKCC, Stanford
- Locally advanced, N=49, Median F/U 13.9mos
 - ≤ 3 wks Gemcitabine \rightarrow SBRT \rightarrow Gemcitabine
 - SBRT 33Gy/5fx, centrally reviewed
 - 83% local progression free survival, median OS 13.9 mos
 - 2% \geq acute gr 2, 11% \geq late grade 2 toxicity

Cost effectiveness of pancreas SBRT

Stanford cost-effectiveness study (Murphy et al., 2012)

- Compared cost effectiveness of 4 models:
 - Gem alone
 - Gem + conventional RT
 - Gem + IMRT
 - Gem + SBRT
- SBRT + gem added 0.20 QALY at inc. cost of \$13,700 compared with gem alone
- **Unlike IMRT, SBRT + gem increases the clinical effectiveness beyond gem alone at a potentially acceptable cost.**

SBRT Simulation

- Implanted Fiducials
 - Gold markers implanted endoscopically
 - Minimum 2, but 3-5 recommended to account for potential migration or loss
 - Plan for simulation 5-14 days following implant to allow seeds to “settle”
- Motion management via expiratory breath hold or abdominal compression
- Patient immobilization
 - NPO
 - Supine in vac-lock, arms up on wing board
 - IV contrast & small bowel contrast

Biliary Stent versus Fiducial Markers

- van der Horst et al. IJROBP 2014
 - Eleven PA patients with stents and fiducials
 - Daily CBCT registered to planning CT by bony anatomy, stent, or fiducials
- Stent better than bony anatomy in 67% of fractions
- Found that stent-tumor relation was not rigid, with deviations up to 8.4mm
- Conclusion: fiducials > stent > bony anatomy

Treatment Planning

- Planned with VMAT, minimize tx time
- Prescription
 - 25-33Gy in 5 fractions
 - Consider SIB 35-50Gy to areas of vessel involvement
 - Range of fractionations from daily to BIW/TIW

Dose Constraints*

Organ	Constraint	Organ	Constraint
Duodenum		Kidneys (combined)	
V30	<0.5 cc	Mean dose	<10 Gy
V18	<5 cc	Spinal Cord	
V12.5	<10 cc	V30	<0.035 cc
Stomach		Spinal Cord +5 mm	
V30	<0.5 cc	V25	<0.5 cc
V25	<5 cc		
Liver			
Mean dose	<15 Gy		

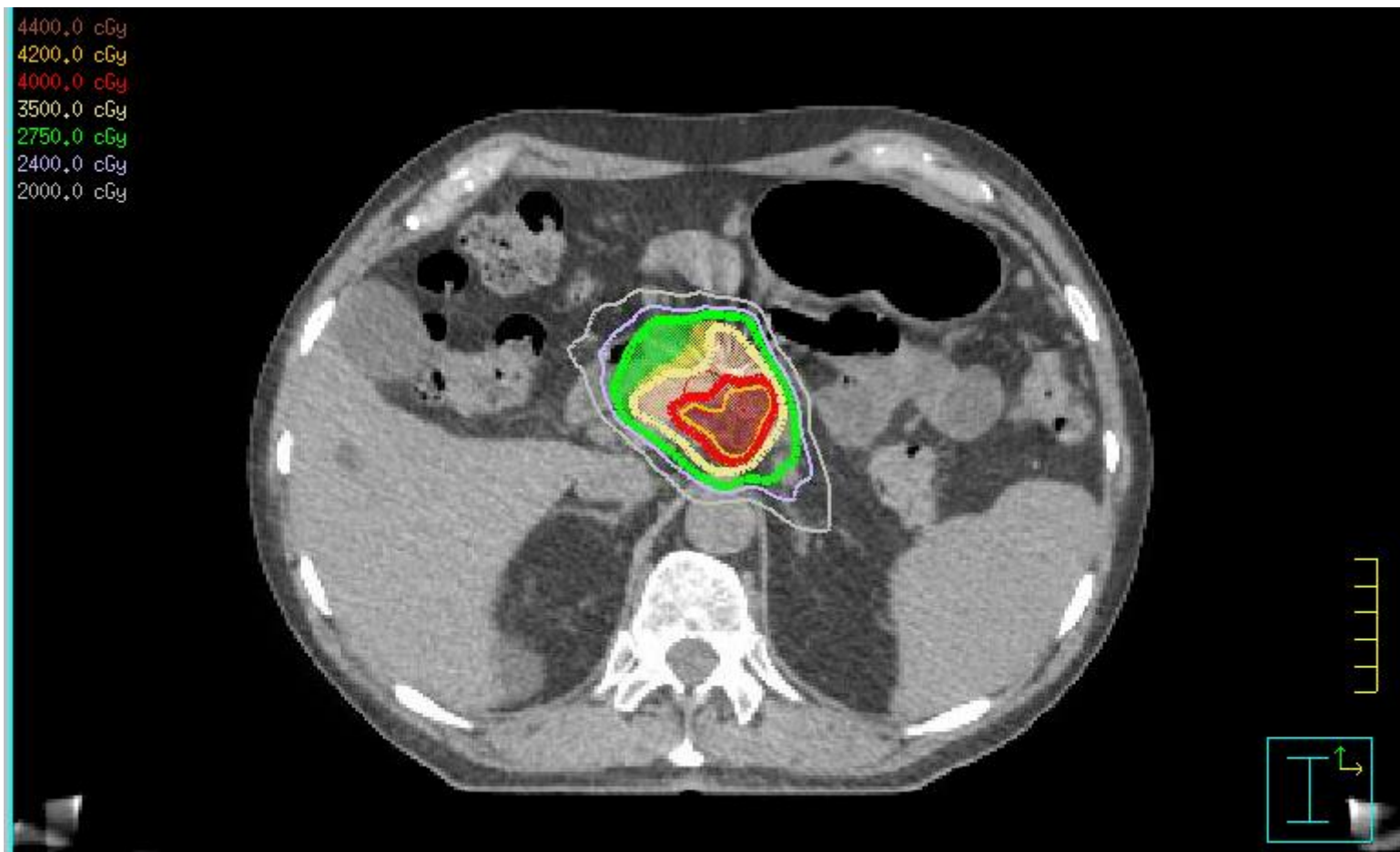
**These are institutional constraints for 5 fraction treatment created as an amalgam of published constraints (Moffitt, JHU) and those used in an institutional trial.*

This patient's plan

- 30Gy in 5 fractions with SIB to vessels (40 Gy/5 fx)
- Multiple scans acquired during CT simulation:
 - If ABC: contrast scan (for volume delineation) and non-contrast scan (for dosimetry planning)
 - If free breathing: helical contrast scan (for volume delineation) and 4DCT (time series for ITV creation, average for planning)

Institutional Method for PTV

- If breath hold: compared contrast-enhanced and non-contrast helical scans, construct PTV based on set up error between the two scans
- If free breathing: measure maximum range of fiducial markers in each of three planes, use travel distance/direction to construct PTV
 - Note this might result in an asymmetric PTV (typically SI size > radial size)









Dose Volume Histogram



Line Type	ROI	Trial or Record	Min.	Max.	Mean	Std. Dev.
◇ —	Stomach	Pancreas SBRT	27.6	2652.6	338.2	330.3
◇ —	Duodenum	Pancreas SBRT	37.3	3175.3	966.2	938.0
◇ —	Liver	Pancreas SBRT	10.0	3709.2	198.1	298.6
◇ —	Cord+5mm	Pancreas SBRT	20.3	1097.0	137.0	257.9
◇ —	Kidney_L	Pancreas SBRT	18.7	2039.6	202.4	371.0
◇ —	Kidney_R	Pancreas SBRT	16.2	958.5	161.1	206.1
◇ —	Kidneys_Total	Pancreas SBRT	16.2	2039.6	181.5	299.8