

Stereotactic Body Radiation Therapy in Pancreas Adenocarcinoma Demonstrates Minimal Acute and Late Toxicity



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Purpose/Objectives

- Stereotactic body radiation therapy (SBRT) has been increasingly utilized to improve local control in pancreatic cancer (PCA)
- Initial reports of single-fraction PCA SBRT described significant treatment-related toxicity, which is now minimized with treatment modification such as fractionation and active breathing control (ABC)
- We evaluated institutional rates of acute and late toxicity in PCA SBRT and aimed to identify potential modifiable treatment factors

Methods

- PCA patients (n=321) treated with 5-fraction SBRT from 2010-2016 were retrospectively analyzed
- Acute and late gastrointestinal adverse events (AE), defined respectively as occurring within and beyond 90 days of treatment, were assessed using the CTCAE v3.0
- Grade ≥3 adverse events were categorized as either unlikely or potentially attributable to SBRT by group consensus of 3 physicians
- Multivariate logistic regression was used to assess toxicity outcomes with respect to performance status, ABC use, surgical resection, induction chemotherapy duration, and dose to sum of proximal organs-at-risk (duodenum, stomach, and bowel)

Results

Table 1: Baseline Characteristics

Characteristic	N (%)
Median age at treatment (range), yrs	66 (36-90)
Male (%)	174 (54)
ECOG performance status (%)	
ECOG 0	119 (37)
ECOG 1	179 (56)
ECOG 2	23 (7)
Stage of disease (%)	
Locally advanced	82 (58)
Borderline resectable	187 (26)
Other	52 (16)
Setting of SBRT (%)	
Neoadjuvant/upfront	273 (85)
Adjuvant	16 (5)
Salvage	29 (9)
Location of tumor (%)	
Head	201 (67)
Body/tail	88 (33)
≥4 months induction chemotherapy (%)	157 (49)
Surgical resection (%)	47 (15)
Volumetric-modulated arc therapy (%)	260 (81)
Active breathing control (%)	260 (81)
Dose prescription (%)	
33Gy in 5 fractions	213 (66)
Other dose in 5 fractions	108 (34)

Table 2a: Rates of Acute Toxicity

Acute Toxicity n=321	Unlikely SBRT Attributable			Potentially SBRT Attributable			Total Grade ≥3 (%)
	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)	
Dehydration	-	-	-	-	-	-	-
Diarrhea	-	-	-	1 (0.3)	-	-	1 (0.3)
Dyspepsia	-	-	-	-	-	-	-
Fatigue	-	-	-	1 (0.3)	-	-	1 (0.3)
Nausea	-	-	-	-	-	-	-
Weight Loss	-	-	-	-	-	-	-
Vomiting	-	-	-	-	-	-	-
Abdominal Pain	-	-	-	5 (1.0)	-	-	5 (1.6)
Ulcer	-	-	-	1 (0.3)	-	-	1 (0.3)
GI Bleed	1 (0.3)	-	-	2 (0.6)	-	2 (0.6)	5 (1.6)
Gastritis	1 (0.3)	-	-	3 (0.9)	-	-	4 (1.2)
Fistula	-	-	-	-	-	-	-
Sepsis	1 (0.3)	-	-	-	-	-	1 (0.3)
Bowel Obstruction	4 (1.2)	1 (0.3)	1 (0.3)	3 (0.3)	-	-	9 (2.8)
Biliary Obstruction	1 (0.3)	-	1 (0.3)	1 (0.3)	-	-	3 (1.0)
Abscess	1 (0.3)	-	-	-	-	-	1 (0.3)
Enteritis	1 (0.3)	-	-	-	-	-	1 (0.3)
Perforation	1 (0.3)	1 (0.3)	-	-	-	-	2 (0.6)
Esophagitis	-	-	-	-	-	-	-
Other	-	-	2 (0.6)	-	-	-	2 (0.6)

Table 3: Predictors of Potentially SBRT-Attributable Grade ≥3 AEs

Variable	p-value	OR: 95% CI
ECOG < 2	>0.05	---
Surgical Resection	>0.05	---
ABC	>0.05	---
Chemo > 4 months	>0.05	---
Dosimetric Variable (sum of proximal OAR)		
V15 ^a	0.031	1.010: 1.001–1.020
V15 < 75cc ^b	0.043	0.249: 0.065–0.954
V20 ^a	0.023	1.022: 1.003–1.041
V20 < 45cc ^b	0.012	0.167: 0.041–0.676
V25 ^a	0.027	1.033: 1.004–1.064
V25 < 9cc ^b	0.129	0.402: 0.124–1.300
V30 ^a	0.036	1.045: 1.003–1.089
V30 < 1.5cc ^b	0.134	0.438: 0.149–1.290
V33 ^a	0.060	1.051: 0.998–1.107
V33 < 1.1cc ^b	0.035	0.306: 0.101–0.922

^a continuous variable ^b categorical variable

Table 2b: Rates of Late Toxicity

Late Toxicity n=281	Unlikely SBRT Attributable			Potentially SBRT Attributable			Total Grade ≥3 (%)
	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)	
Ulcer	-	-	-	5 (1.7)	-	-	5 (1.7)
GI Bleed	-	-	-	6 (2.1)	-	-	6 (2.1)
Gastritis	-	-	-	-	-	-	-
Fistula	-	-	-	2 (0.7)	1 (0.4)	-	3 (1.1)
Sepsis	2 (0.7)	1 (0.4)	-	-	-	-	3 (1.1)
Bowel Obstruction	9 (3.2)	2 (0.7)	-	2 (0.7)	-	-	13 (4.6)
Biliary Obstruction	3 (1.1)	-	-	4 (1.4)	-	-	7 (2.5)
Abscess	5 (1.7)	1 (0.4)	-	1 (0.4)	-	-	7 (2.5)
Enteritis	1 (0.4)	1 (0.4)	-	-	1 (0.4)	-	3 (1.1)
Perforation	-	-	-	-	-	-	-
Esophagitis	1 (0.4)	-	-	-	-	-	1 (0.4)
Pain	1 (0.4)	-	-	-	-	-	1 (0.4)
Other	-	-	-	-	-	-	-

Conclusion

Our institution's PCA SBRT treatment protocol is well tolerated. Our experience may provide insight into dosimetric constraints to proximal organs-at-risk associated with Grade ≥3 toxicity.

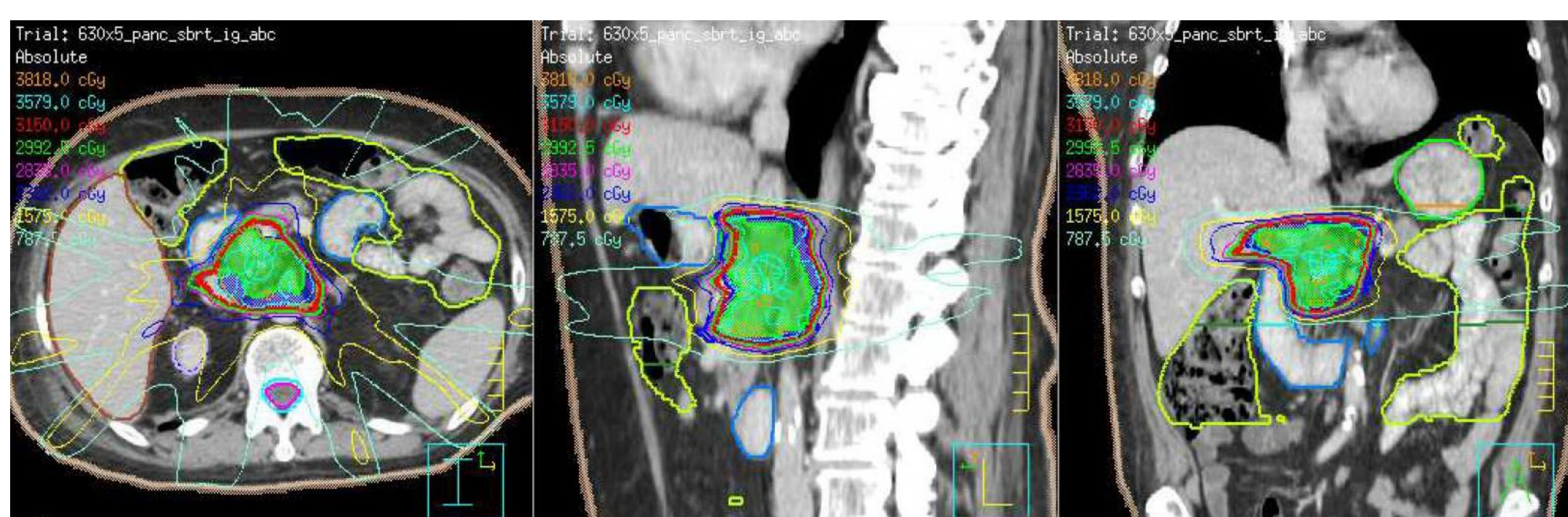


Figure 1: Sample pancreas SBRT treatment plan