Stereotactic body radiation therapy (SBRT) for pancreatic and non-hepatobiliary gastrointestinal (GI) malignancies

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Abstract In this review article, we review the current literature addressing the use of stereotactic body radiation therapy (SBRT) in non-hepatobiliary gastrointestinal malignancies. For many gastrointestinal malignancies, the desire to treat large fields encompassing nodal drainage and micrometastatic disease has precluded the use of stereotactic body radiation therapy for most definitive cases. However, the use of SBRT in locally advanced pancreatic cancer (LAPC) as well as in the treatment of metastatic abdominal lymph nodes has shown excellent local control rates. In carefully selected patients, local control in LAPC has been achieved with SBRT with minimal side effects. Toxicity in these patients has most closely correlated with the dose and volume of irradiated duodenum and small bowel. Similar patterns of excellent local control with minimal side effects have also been seen in the treatment of abdominal lymph node metastases as well as gastric and rectal cancer recurrence.

Keywords SBRT · Gastrointestinal · Pancreas · Abdominal lymph nodes

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Introduction

With the advent of advanced systems such as improvements in intensity-modulated radiation therapy (IMRT), frameless stereotactic devices, and robot-mounted linear accelerators, the ability to deliver high-dose hypofractionated radiation with accuracy has driven interest in stereotactic body radiation therapy (SBRT). For many GI malignancies, the desire to treat large fields encompassing nodal drainage and micrometastatic disease has precluded the use of SBRT for most definitive cases. Instead, much interest has focused on the use of SBRT for achieving local control in nodal disease, abdominal metastatic disease, and local recurrences. Here, we will discuss the relevant studies in the use of SBRT for gastrointestinal disease—predominantly focusing on the use of SBRT for locally advanced pancreatic cancer.

SBRT for pancreatic cancer

Introduction

Pancreatic cancer remains one of the leading causes of cancer death in the USA. In 2011, the American Cancer Society estimated that there will be 44,030 new cases of pancreatic cancer. This ranks tenth in incidence among all cancers. The estimated 37,660 deaths rank fourth among all cancers indicating the incredibly high mortality rate associated with the disease [1]. Despite far-reaching advances in all fields of oncology over the last 20 years, mortality rate in pancreatic cancer has held steadily with only meager advances in survival. A 5-year survival rate of less than 5 % is due to the high incidence of metastatic disease at presentation combined with the limited effectiveness of systemic therapies. On presentation, around 40 % of patients have

metastatic disease, 40 % have locally advanced unresectable disease, and only 20 % are resectable. Resection offers the only chance of cure, and resectability is typically defined as outlined in Table 1, with some institutional variation. Following resection, the large fields required to treat regional lymph nodes as well as the tumor bed have limited the use of SBRT in the adjuvant setting to patients with close or positive surgical resection margins. The majority of investigations in the use of SBRT for pancreatic malignancies have focused on locally advanced pancreatic cancer (LAPC).

Locally advanced disease

Treatment overview

LAPC has a very high mortality rate and a survival rate similar to metastatic disease. Around 40 % of patients with pancreatic cancer present with locally advanced disease without evidence of distant metastases [2]. Reported median survival time varies between 8 and 14 months with rare long-term survivors.

In patients with locally advanced disease, the role of chemoradiation remains somewhat controversial. However, both rapid local and distant progression have driven interest in combining both local and systemic therapies. Traditionally fractionated chemoradiation has required a 5- to 6-week break from high-dose systemic chemotherapy. Modern trials comparing systemic therapy to systemic therapy with chemoradiation have yielded conflicting results. The Federation Francophone de Cancerologie Digestive and Societe Francaise de Radiotherapie Oncologique (FFCD-SFRO) trial comparing LAPC patients randomized to gemcitabine (GEM) alone or induction chemoradiation with cisplatin and fluorouracil (5-FU) followed by gemcitabine showed a survival benefit in the gemcitabine alone arm (8.6 versus 13 months) [3]. However, this study has been criticized for its use of nonstandard concurrent chemotherapy regimen with cisplatin/and 5-FU which may have led to an unusually high toxicity and dropout rate. The study was closed early at interim analysis due to a lower survival rate in the

chemoradiation arm. More recently, the Eastern Cooperative Oncology Group (ECOG) Study 4201 randomized LAPC patients between gemcitabine alone versus induction gemcitabine followed by chemoradiation followed by maintenance gemcitabine. This “sandwich” chemoradiation had a survival benefit versus gemcitabine alone of 11.1 versus 9.2 months [4]. However, the study was closed early due to lack of accrual. A retrospective analysis of LAPC patients treated in phase II–III studies with gemcitabine followed by chemoradiation revealed that 29.3 % of patients developed metastatic disease after 3 months of induction chemotherapy [5]. This underscores the likelihood that a high percentage of LAPC patients have occult micrometastatic disease. This also suggests that we may be able to select for patients who would benefit from chemoradiation by restaging after induction chemotherapy.

The survival benefit seen in the FFCD-SFRO trial among patients treated with systemic chemotherapy compared to upfront chemoradiation highlights that pancreatic cancer is an aggressive disease with an early predisposition for development of distant metastases. However, subsequently, the Groupe Cooperateur Multidisciplinaire en Oncologie (GERCOR) study has suggested that there may be a subset of patients that benefit from the addition of consolidative chemoradiation after a course of induction chemotherapy. The current standard of care typically involves induction chemotherapy with restaging after 2 to 3 months, followed by consideration of consolidative radiation therapy in the absence of distant metastases. This prevents both unnecessary localized treatment and extended breaks from systemic chemotherapy in patients who are destined to develop metastatic disease despite optimal systemic therapy. This has led to strong interest in the investigation of SBRT as a method of achieving local control while shortening the time interval to delay or break systemic chemotherapy.

Outcomes with early SBRT experience for SBRT

Initial investigations into SBRT for LAPC were disappointing. In a study from Aarhus University, patients treated with

Table 1 Resectability criteria in pancreatic cancer

Resectable	Borderline resectable	Locally advanced	Metastatic
No evidence of metastatic disease	No evidence of metastatic disease	No evidence of metastatic disease	Evidence of metastatic disease
Lack of or minimal encroachment of the superior mesenteric artery (SMA) and celiac axis (typically seen as preservation of a fat plane around the vessels radiographically)	Partial encasement of the SMA or celiac axis	>50 % encasement of the SMA or celiac	
Resection → chemotherapy/chemoradiation	Questionable margin-negative resection	Invasion of the aorta or inferior vena cava	
	Neoadjuvant therapy (chemo/chemoradiation) → evaluation of resectability	Induction chemotherapy → RT	Chemotherapy

Table 2 Local control rates and survival

Study	Patients	Fractionation	System	Local Control	OS
Koong Stanford 1 [7]	15 LAPC ECOG PS <2	3–15 Gy × 1 5–20 Gy × 1 7–25 Gy × 1	CK	All pts treated at 25 Gy had distant metastases with no local progression	MS—11 months TTP—2 months
Koong Stanford 2 [8]	19 enrolled LAPC 3 developed distant disease before boost	45 Gy in 1.8 Gy/fx with concurrent 5-FU or capecitabine → 25 Gy × 1 within 1 month	IMRT by LINAC SRS boost by CK	FFLP—94 % 1 reported local failure after endoscopy at 34 weeks after SRS—bx negative	MS—33 weeks OS 6 months 80 % OS 12 months 15 %
Schellenberg Stanford 3 [9]	16 LAPC	GEM on days 1, 8, and 15 → SBRT 25 Gy × 1 on day 29 → GEM weekly 3 on 1 off until progression or toxicity	CK	13 out of 16 distant mets first 3 recurrences at 14, 16, and 21 months Only seen by CT/PET	MS—11.4 months OS 1 year—50 % OS 2 years 18 % TTP—9 months
Chang Stanford Retro [11]	77 LAPC or comorbid conditions 8 pts with mets and low distant burden No tumors >7.5 cm Includes 40 pts from prior studies	25 Gy × 1 in all pts Some received chemo or EBRT first	CK	FFLP at 6 months—91 % FFLP at 12 months—84 % PFS at 6 months—26 % PFS at 12 months—9 %	OS 6 months—56 % OS 12 months—21 %
Schellenberg Stanford 4 [12]	20 pts with LAPC	GEM × 1 cycle → SBRT day 29–25 Gy × 1 via 9 field IMRT with 2–3 mm margin with respiratory gating and gold seed fiducials → 3 on 1 off GEM	IMRT	FFLP—94 % at 1 year by serial CT 88 % by PET 5 progressed locally (4 out of 5 by PET only)	MS—11.8 months OS at 1 year—50 % OS at 2 years—20 %
Mahadevan BID 1 [10]	Retrospective 36 LAPC 8–3 × 8 Gy 25–3 × 10 Gy 3–3 × 12 Gy	24, 30, or 36 Gy in 3 fractions → GEM until progression, toxicity, or 6 cycles	CK	LC at 24 months—78 %	MS—14.3 months PFS—9.6 months
Mahadevan BID 2 [13]	Retrospective	2 cycles of GEM → restaging → third cycle and planning → SBRT during week off between the third and fourth cycles (3 × 8–12 Gy) → GEM until tolerance or progression 8 patients developed mets before SBRT	CK	Local control at 21 months—85 %	MS—20 months
Polistina [14]	23 LAPC	6 × weekly GEM → 30 Gy in 3 fx on 3 consecutive days within 1 month of chemo → GEM 14 pts—1 × 20–25 Gy 5 pts—3 × 24–30 Gy	28 pts—3 × 8 Gy 11 pts—3 × 10 Gy 0 pts 3 × 12 Gy CK	8 % became resectable Local response ratio—82.6 % (14 PR, 2 CR, 3 stable)	MS—10.6 months
Goyal Case Western [15]	19 LAPC		CK	LC—88 % FFLP at 6 months—88 % FFLP at 1 year—65 % TTP—11.43 months	MS—14.37 months

Table 2 (continued)

Study	Patients	Fractionation	System	Local Control	OS
Hoyer [6]	22 LAPC	15 Gy × 3 in 5–10 days	LINAC	6 LF—5 with distant disease 1 isolated local failure	MS—5.4 months Survival at 1 year—5 % TTP 4.8 months OS 10.3 months
Rwigyema [16]	Retro 71 total 40 LAPC 11 LR 8 metastatic 12 adjuvant for + surgical margins	67–1 fx SRS (43–24 Gy, 13–22 Gy, 5–25 Gy, 4–20 Gy, 2–18 Gy)	CK or trilogy	FFLP >24 Gy—73 %, <24 Gy—45 %	
Didolkar [17]	85 patients 71 LAPC 14 LR	15–30 Gy in 3 fractions PLUS GEM (most)	CK	78 had CR, PR, or stable disease	OS from diagnosis 18.6 months OS from SBRT 8.6 months

Illustration of the results of studies using SBRT for locally advanced pancreatic adenocarcinoma. There are no current phase three randomized trials. With the exception of Hoyer et al., all studies show very good local control with limited progression locally. However, the durability of this control is unclear due to rapid progression of metastatic disease CK CyberKnife, CR complete response, FFLP freedom from local progression, GEM gemcitabine, LAPC locally advanced pancreatic cancer, LC local control, LF local failure, LR local recurrence, MS median survival, OS overall survival, PFS progression-free survival, PR partial response, PS performance status, SRS stereotactic radiosurgery, TTP time to progression, TTLP time to local progression, mets metastases

45 Gy in three fractions via traditional linear accelerators (LINAC) developed a marked decrease in performance status and significant toxicity without benefits to survival or durable local control [6]. The development of systems such as Cyberknife allowed for delivery of a high dose of radiation with a rapid fall off of dose to normal tissue. An initial phase I study out of Stanford published in 2004 demonstrated the feasibility and safety of SBRT for LAPC [7]. In this study, 15 patients with LAPC and an ECOG performance status of ≤ 2 were treated with 15, 20, or 25 Gy in a single fraction via CyberKnife. One out of three patients treated with 15 Gy, two out of four patients treated with 20 Gy, and zero out of six patients treated with 25 Gy progressed locally. Having no local progressions at 25 Gy, the dose escalation study was discontinued prior to reaching dose-limiting toxicity [7]. No benefit was seen in survival. They followed this with a phase II study combining conventionally fractionated chemoradiation with a stereotactic radiosurgery (SRS) boost [8]. Sixteen patients were treated with 45 Gy in 1.8 Gy per fraction to the tumor and regional lymphatics with concurrent 5-FU or capecitabine. Within 1 month of chemoradiation, patients were given an SRS boost of 25 Gy to the tumor using CyberKnife. This resulted in excellent local control with 15 out of 16 patients being free from local progression until death. However, they also saw no improvement over standard treatment in time to progression (17.5 weeks) or median survival (33 weeks). This rapid progression to distant metastasis emphasizes the importance of delivery of systemic chemotherapy without delay. In their next trial, 16 patients underwent one cycle of GEM followed by 25-Gy SRS to the gross tumor followed by gemcitabine until progression or death [9]. All 16 patients received SRS with a median of four cycles of chemotherapy. Three patients failed locally at 14, 16, and 21 months following SBRT. Median survival was 11.4 months with 50 % of patients alive at 1 year. These survival rates were again comparable to traditional chemoradiation. A benefit in local control with no benefit in progression-free survival or overall survival was seen in a number of small phase I and II trials as well as retrospective studies summarized in Table 2.

With the results of the analysis of the GERCOR trials indicating a 29.3 % metastatic rate after 3 months of induction chemotherapy, strategies evolved to both address the need for systemic therapy and avoid radiation in patients unlikely to benefit. In a retrospective study from the Beth Israel Deaconess, 47 patients with LAPC were given two cycles of gemcitabine followed by restaging [10]. Patients without metastatic disease were given a third cycle of gemcitabine while undergoing planning. Patients were then treated with 24–36 Gy in three fractions followed by maintenance gemcitabine. Eight patients (17 %) developed metastatic disease prior to undergoing SBRT. This study showed

Table 3 Reported toxicities

Study	Treatment	Toxicity	Notes
Koong Stanford 1 [7]	SRS 15–25 Gy	No grade 3 Grade 1/2: nausea and diarrhea	
Koong Stanford 2 [8]	45 Gy in 1.8 Gy/Fx with 5-FU/Cape→25 Gy×1 SRS	Acute—grade 3: gastroparesis, duodenal ulcers	
Schellenberg Stanford 3 [9]	GEM→SRS 25 Gy→GEM	Acute—3 pts pain and gastritis, 1 gastric outlet obstruction Late—7 out of 15 pts surviving >4 months had toxicity—5 developed duodenal ulcers, 1 pt required stent, and 1 pt had a bowel perforation	Most closely correlated to duodenum receiving 12.5 Gy
Chang Stanford Retro [11]	25 Gy×1 in all pts Varying chemo regimens	Acute—grade 3: 1 GI ulcer Late—grade 2: 3 small bowel ulcers; grade 3: 3 gastric ulcers, 3 strictures	
Schellenberg Stanford 4 [12]	GEM→25 Gy via IMRT→GEM	Acute—grade 3: none Late—grade 3/4: 1 duodenal perforation, 3 small bowel ulcers	
Mahadevan BID 1 [10]	24–36 Gy→GEM	Acute—grade 3: 2 nausea Late—grade 3/4: 2 GI bleeds	
Mahadevan BID 2 [13]	GEM→24–36 Gy→GEM	Acute—grade 1: 22 fatigue; grade 2: 9 nausea Late—grade 3: 2 GI bleeding, 1 gastric outlet obstruction	
Polistina [14]	GEM→30 Gy→GEM	No grade 2 or higher toxicities	
Goyal Case Western [15]	1×20–25 Gy or 3×8–10 Gy	Acute—2 nausea/fatigue Late—grade 3: 1 asymptomatic pyloric ulcer, 3 small bowel ulcers	
Hoyer Denmark [6]	45 Gy SBRT	Marked decrease in PS 79 % had grade 2 or higher symptoms—mainly nausea 94 % had pain ≥grade 2	
Rwigema [16]	SRS 18–25 Gy	4 pts—severe mucositis or ulceration of stomach or duodenum Acute—grade 3: 1 nausea, 1 abdominal pain, 1 gastroparesis Late—only grade 1 toxicity	
Didolkar [17]	15–30 Gy SBRT	Acute—grade 3/4: 19 upper GI toxicity (duodenitis, gastritis, diarrhea)	

Grading done by RTOG toxicity scale in most studies. Toxicities reported are main limited to small bowel and gastric issues such as nausea, vomiting, and abdominal pain. Multiple studies report both gastric and small bowel ulceration. While acute toxicity appears limited, long-term toxicity data are limited by short survival times due to metastatic disease

GEM gemcitabine, SRS stereotactic radiosurgery

a median overall survival of 20 months in patients that underwent SBRT. It is unclear if this benefit was due to optimization of chemotherapy and SBRT delivery or the removal of patients with rapid progression of metastatic disease from the treatment group. Regardless, the median overall survival of 20 months far outpaces the 8- to 14-month survival typically seen in patients with LAPC.

Toxicity

Initial studies with SBRT and LAPC showed unsatisfactory toxicity with high rates of nausea, pain, and mucositis of the duodenum and stomach. In an early experience from Aarhus University, 22 patients were treated with 45 Gy in three fractions using a standard LINAC with multi-leaf collimator [6]. They documented a significant deterioration in performance status and increased nausea and pain. They also reported an 18 % rate of severe mucositis of the stomach or duodenum with one patient experiencing perforation. Using the Cyberknife system, the Stanford group showed a much improved toxicity profile. In an initial phase I dose escalation study, they achieved 100 % local control at 25 Gy in one fraction with only grade 2 toxicities [7]. This can likely be attributed to the size of tissue irradiated. In the study out of Aarhus, the median volume irradiated was 136 cc (range, 38–376 cc) [6], whereas the initial phase I study out of Stanford had a median volume of 28.9 cc (range, 19.2–71.9 cc) [7]. This reduction in volume of irradiated tissue likely reduced the volume of duodenum irradiated. In a series of SBRT studies using CK from multiple institutions, the toxicity profile has been similar with few grade 3 toxicities [7, 8, 11, 12].

However, an increased toxicity has been seen in patients treated with SBRT given during the off week of chemotherapy or when SBRT has been used as a boost following conventional chemoradiation. In a phase II study from Stanford, 16 patients were treated with conventionally fractionated chemoradiation with concurrent 5-FU or capecitabine followed by an SRS boost of 25 Gy in one fraction via Cyberknife. These patients developed significant rates of gastroparesis as well as duodenal ulcers 4–6 months after treatment [8]. In patients treated with gemcitabine before and after radiation, 5 out of 15 patients surviving greater than 4 months after SBRT developed duodenal ulcers [9]. These were most closely correlated to patients receiving greater than 12.5 Gy to the duodenum. However, the study was underpowered to show significance.

As one of the greatest benefits of SBRT in LAPC is the ability to deliver radiation with minimal delay of systemic chemotherapy, reduction of this toxicity seen with sandwich therapy is essential. At the Beth Israel Deaconess, their practice is to both fractionate therapy and dose escalate based on proximity of the cancer to the duodenum. In

Table 4 Dose constraints to organs at risk

Study	Prescription	Duodenum	Spinal cord	Liver	Stomach	Kidney	Bowel
Chang [11] Stanford Composite	25 Gy SRS to isodose covering 95 % PTV (GTV +2–3 mm)	<5 % of volume to receive <22.5 Gy <50 % of volume to receive <12.5 Gy	Max dose, <5 Gy	50 % of volume, <5 Gy 70 % of volume, <2.5 Gy V_{21} , <30 % V_{15} , <50 %	<4 % of volume <22.5 Gy 50 % isodose line should not reach nonadjacent lumen wall Rx dose based on abutment of duodenum/stomach: 1/3 of stomach or duodenum abutted: 8 Gy×3 1 area of abutment: 10 Gy×3 >3 mm separation: 12 Gy×3	75 % volume of each kidney to receive <5 Gy Per kidney, V_{12} <25 %	Max dose, <21 Gy <5 % volume, <20 Gy Max point dose: <10 Gy per fraction
Mahadevan [13] BID	GEM→8–12 Gy×3→GEM	Rx dose based on abutment of duodenum/stomach: 1/3 of stomach or duodenum abutted, 8 Gy×3 1 area of abutment, 10 Gy×3 >3 mm separation, 12 Gy×3	Max dose, 12 Gy				
Rwigema [16]	18–25 Gy SRS (67 pts) 4 pts fractionated	Max dose avg: 15.1 Gy	Max dose avg: 1.8 Gy	Max dose avg: 8.4 Gy	Max dose avg: 15.1 Gy	Max dose avg: R—2.9 Gy, L—3.5 Gy	

Illustration of data reported on dose constraints used in LAPC SBRT studies. Consistent across studies is the attempt to limit both the volume of duodenum irradiated as well as the dose

lesions which abut greater than one third of the pancreas–duodenum interface, patients are treated with 8 Gy in three fractions. In lesions <3 mm away from the duodenum, patients are given 10 Gy in three fractions. Patients with lesions >3 mm from the duodenum are given 12 Gy in three fractions. Using these guidelines, they were able to reduce grade 3 toxicities to 7.6 % in patients treated with GEM followed by SBRT followed by GEM [10].

Table 3 illustrates the relevant studies in SBRT and LAPC and their relative toxicities. As systemic therapy has evolved, toxicity profiles have changed with a greater focus on reducing dose and volume of duodenum irradiated. Table 4 illustrates the available data on dose constraints in SBRT for LAPC. Using current SBRT treatment delivery systems, the primary dose-limiting structures are the duodenum and stomach, with less difficulty meeting dose constraints for the spinal cord, kidneys, and liver. In a further analysis of their patient cohort from Stanford, they found

multiple dosimetric predictors of toxicity in their patient cohort treated with 25 Gy in a single fraction [13]. They found that V20, V15, and dMax all correlated significantly with duodenal toxicity. A $V_{15} > 9.1 \text{ cm}^3$ had a toxicity rate of 52 versus 11 % in patients with a $V_{15} < 9.1 \text{ cm}^3$. Similar results were seen in a $V_{20} > 3.3 \text{ cm}^3$ and a $d_{\text{Max}} > 23 \text{ Gy}$. With incomplete understanding of the radiobiologic effects of high-dose fractionation schemes, these recommendations will continue to evolve over time.

Conclusion

SBRT for LAPC is an evolving treatment modality which may provide a means to optimize local treatment while minimizing the treatment gap from chemotherapy. As systemic agents improve over time, the need for adequate local control will increase in importance. Though many current studies indicate SBRT is an effective means of local control in LAPC, long-

Fig. 1 The treatment plan of a patient with a local recurrence of pancreatic intraductal mucinous carcinoma 5 years after Whipple procedure followed by concurrent chemoradiation to 50.4 Gy with 5-FU. Based on his prior irradiation, dose constraints to the spinal cord and

other regional organs at risk were critical. The patient was treated with 8 Gy×5 fractions for a total of 40 Gy via proton SBRT. Interval imaging at 6 months post-SBRT showed a decrease in the size of the mass

term understanding of the effects of SBRT on local control as well as long-term side effect profiles remain limited by patients' short life expectancy due to metastatic disease. Currently, the National Comprehensive Cancer Network recommends that SBRT for locally advanced pancreatic cancer be done on clinical trial due to a lack of randomized data. Future directions include integration of evolving systemic regimens such as the FOLFIRINOX regimen. Figures 1 and 2 illustrate plans for patients with GI malignancies treated using SBRT with both proton and photon radiation respectively.

SBRT for other GI malignancies

Although there are many series on locally advanced pancreatic cancer and both primary and secondary hepatobiliary malignancies, very little data exist on the use of SBRT for other GI malignancies [14]. The few available studies are small series, single-institution experiences primarily focusing on toxicity.

Gastric and rectal recurrences

A study by Kim et al. from Korea investigated the use of SBRT to salvage patients with para-aortic lymph node (PALN) recurrence after a curative resection for gastric cancer

[15]. Seven patients with PALN recurrence were treated with 45 to 51 Gy in three fractions. With a median follow-up of 26 months, two patients were alive with no evidence of disease, three were alive with disease, and two patients died of disease. Five had a complete response, and two showed partial responses. Two patients had grade 1 nausea/vomiting, but no severe complications were detected, either acute or late.

Kim et al. also described treatment of 23 patients with recurrent rectal cancer via SBRT [16]. Seven patients had pre-sacral recurrences, while 16 had recurrence in the pelvic side wall. Dose range was from 30 to 51 Gy delivered over three fractions. With a median follow-up of 31 months, the 5-year OS was 23.2 % with a local control rate at 4 years of 74.3 %. They reported grade 1 or 2 toxicities such as nausea, vomiting, and pain in 9 of 23 (39 %) patients. They also reported one grade 4 rectal perforation in a patient who received 51 Gy.

These studies illustrate the safety and potential for excellent local control using SBRT for recurrences in GI malignancies. Though the data are limited at this point, the excellent dose fall off achieved with SBRT can provide an option for reirradiation while minimizing toxicity. However, further study is needed to adequately assess tolerance dosages as illustrated by the grade 4 toxicity in the rectal recurrence series.

Fig. 2 The treatment plan of an 88-year-old man with a gastric neuroendocrine tumor metastatic to the right adrenal gland. He was treated to 35 Gy in five fractions using LINAC-based photon SBRT.

Using SBRT, we were able to achieve excellent coverage of the CTV while limiting dose to the liver, duodenum, and right kidney

Abdominal lymph nodes

A number of series evaluating the use of SBRT for abdominal lymph node metastases from both GI and non-GI primaries have been described in the literature. A study by Bignardi et al. looked at 19 patients with unresectable nodal metastases in the abdomen and retroperitoneum treated with SBRT [17]. Eleven patients had a solitary nodal metastasis, and 8 had a dominant node with up to five total metastases. All patients were prescribed 45 Gy in six fractions, but six cases required a 10 to 20 % reduction in dose due to dose/volume constraints. Eleven patients were treated with a 3D conformal technique and the other eight by volumetric intensity-modulated arc therapy. Actuarial freedom from local progression was 77.8 % at both 12 and 24 months. Toxicity was minimal.

Barney et al. published the SBRT experience for abdominopelvic tumors at the Mayo Clinic [18]. Forty-seven patients received SBRT in the abdomen including the liver (21), lymph nodes (14), and adrenal glands (6). The most common dose prescribed was 50 Gy in five fractions. With a median follow-up of 12 months, 48 target lesions evaluated showed: 18 complete responses (36 %), 12 partial responses (24 %), 12 stable lesions (25 %), and 6 progressive lesions (12 %). Local control estimates at 6 and 12 months were 98 and 87 %, respectively. There was no acute grade 3 or higher toxicities. Five late grade 3 toxicities were reported with one patient death from a duodenal perforation 11 months after SBRT.

A series from Kang et al. used SBRT for the treatment of colorectal metastases confined to one organ [19]. From 2001 to 2006, they treated 59 patients using a median of 42 Gy in three fractions. Twenty-six patients had lymph node metastases, but lung and liver metastases were also included. The 5-year overall survival rate was 29 % with a local control rate of 19 %. Gross tumor volume (GTV) less than 23 ml was shown to be a significantly favorable prognostic factor. There were no acute grade 3 or greater toxicities. There were two grade 4 complications which required bypass surgery.

Though limited, early reports of the use of SBRT for metastatic disease or local recurrences in the abdomen show both excellent local control rates and minimal toxicities. As the technology to perform SBRT becomes more widespread, the worldwide experience with this treatment method should continue to develop.

Conclusion

The use of SBRT for GI malignancies has been shown to be both safe and effective for local control in multiple GI malignancies. In locally advanced pancreatic cancer, excellent results in local control have been achieved, but a questionable toxicity rate and lack of survival benefit have

prevented widespread implementation. There is also a growing experience with the use of SBRT for metastatic and recurrent disease in the abdomen. This evidence, combined with an extensive experience in SBRT for both primary and secondary hepatobiliary cancers, has increased interest in the implementation of SBRT in GI oncology, and we expect this experience to grow rapidly over the coming decade.

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