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Postoperative Complications following Intraoperative Radiotherapy in Abdominopelvic Malignancy: A Single Institution Analysis of 113 Consecutive Patients

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Abstract

Background—Intraoperative radiotherapy (IORT) has advantages over external beam radiation therapy (EBRT). Few studies have described side effects associated with its addition. We evaluated our institution's experience with abdominopelvic IORT to assess safety by postoperative complication rates.

Methods—Prospectively collected IRB-approved database of all patients receiving abdominopelvic IORT (via high dose rate brachytherapy) at Johns Hopkins Hospital between November 2006 and May 2014 was reviewed. Patients were discussed in multidisciplinary conferences. Those selected for IORT were patients for whom curative intent resection was planned for which IORT could improve margin-negative resection and optimize locoregional control. Perioperative complications were classified via Clavien-Dindo scale for postoperative surgical complications.

Results—113 patients were evaluated. Most common diagnosis was sarcoma (50/113, 44%) followed by colorectal cancer (45/113, 40%), most of which were recurrent (84%). There were no perioperative deaths. 57% of patients experienced a complication Grade II or higher: 24% (27/113) Grade II; 27% (30/113) Grade III; 7% (8/113) Grade IV. Wound complications were most common (38%), then gastrointestinal (25%). No radiotherapy variables were significantly associated with complications on uni/multi-variate analysis.

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Conclusions—Our institution's experience with IORT demonstrated historically expected postoperative complication rates. IORT is safe, with acceptable perioperative morbidity.

Keywords

Rectal Cancer; Sarcoma; Radiation Therapy; High Dose Rate Brachytherapy; Colorectal Cancer

Introduction

Radiation therapy is an important component in the local management of many cancer types. The primary use of radiotherapy is in locally advanced/invasive and borderline resectable tumors. When considering abdominal radiotherapy, the most common indications are for locally advanced or recurrent colorectal cancer, retroperitoneal/ intra-abdominal sarcomas with close margins, borderline resectable pancreatic cancer, and some urologic and gynecologic malignancies [1–3]. Radiotherapy is administered as an adjunct to surgical resection either preoperatively to facilitate shrinkage of borderline resectable tumors or postoperatively to treat residual tumor cells in the resection bed [1–3].

The mechanism of action by which radiation therapy works to target and kill malignant cells has been described elsewhere [1,4]. In short, several mechanisms are involved which lead to direct damage to cellular DNA and the formation of free radicals, resulting in apoptosis of tumor cells. However, these effects also damage adjacent normal cells and tissue, leading to the potential toxicities that can be seen with radiation therapy [2,4]. External beam radiotherapy (EBRT) is used to deliver fractionated doses, allowing for the highest dose to tumor cells while minimizing the amount of radiation exposure to adjacent normal tissue.

Preoperative EBRT benefits from an undisrupted vascular supply, increasing oxygenation and formation of toxic free radicals, as well as displacement of adjacent normal structures by the tumor, which has not yet been resected [1,2]. Preoperative EBRT may also alter the ability of tumor cells that become disrupted at the time of surgical resection to implant and cause dissemination or recurrence. Postoperative EBRT, on the other hand, can target residual tumor cells in the resection bed, as opposed to preoperatively when a much larger tumor burden is being treated. However, the radiation oncologist must now contend with adjacent bowel and normal tissue which obstruct the path of radiation to the tumor bed and contribute to significant toxicity as a result [1,2].

Intraoperative radiotherapy (IORT) offers several advantages in that it is able to directly target microscopic or gross residual disease, or close tumor margins, immediately following surgical resection [2,3,5]. However, unlike postoperative EBRT, adjacent organs are able to be displaced, protected, and shielded so that the maximum dose can be delivered to at-risk areas identified during resection with lower radiation toxicity than that given by an increased dose of EBRT alone [2,3,5]. In fact, because of this ability to directly administer radiotherapy, the high single-treatment dose given during IORT is equivalent to 2.5 times that dose by EBRT [5,6]. For example, a typical dose given during IORT, 15 Gy, is equivalent to about 37.5 Gy by EBRT, effectively nearly doubling a typical cumulative dose given in preoperative or postoperative EBRT.

This study reviews our institution's experience in initiation and incorporation of IORT into the treatment paradigm of locally advanced or recurrent intra-abdominal malignancies. We assess the safety of IORT with regards to postoperative acute and long term surgical complications and demonstrate that surgical complication rates with IORT are acceptable and non-inferior to historical previously published rates in comparable advanced malignancies.

Materials and Methods

Study Population

All patients receiving IORT to the abdomen, pelvis and retroperitoneum region were included in this study beginning from the initiation of the IORT program at Johns Hopkins Hospital in November 2006 until May 2014. Abdominopelvic IORT included retroperitoneal IORT. Patients were discussed and determined to be appropriate candidates for IORT in a multidisciplinary collaboration which included pathology, surgical oncology, medical oncology, and radiation oncology. All patients were discussed in their respective disease-based multidisciplinary conferences (MDC) such as sarcoma MDC, colorectal MDC, etc. Patients selected for intraoperative radiation therapy were patients in whom curative intent resection was being attempted. IORT in these cases was determined to potentially improve margin-negative resection and optimize locoregional control. The medical records of all patients were reviewed for patient characteristics, comorbidities, indications, radiotherapy administration details and postoperative complications. Degree of comorbidity was assessed using the Charlson Comorbidity Index (CCI). It is important to note that CCI gives a score of 2 for non-metastatic solid tumors and 6 for metastatic tumors, so all patients in this study had a minimum CCI score of either 2 or 6 before factoring in other comorbidities. All forms or variations of EBRT, including intensity modulated radiotherapy (IMRT), image-guided radiotherapy (IGRT), and 3-D conformational radiotherapy (3D-CRT), were classified together as EBRT.

IORT Technique

IORT details were obtained from radiation oncology procedure notes in the medical record. Our institution's technique, known as high dose rate brachytherapy (HDR-IORT) has been previously described in detail [5]. This technique combines IORT with brachytherapy, a form of radiation in which a local radiation source is implanted inside or next to the area requiring treatment. Briefly, high-dose-rate brachytherapy catheters are threaded through flexible silicone applicators known as Freiburg Flaps that can be cut and shaped to accurately resemble the target area being irradiated. The room is then cleared and radiation therapy administered. Freiburg flaps offer an advantage over the comparatively rigid cone applicators used in intraoperative electron beam radiotherapy (IOERT) and IORT with low energy photons [5]. The flaps also deliver a more concentrated dose at the surface of the target area compared to IOERT, which delivers more homogeneous doses throughout the tissue depth [3,7]. Number of fields, dosages, treatment area, and treatment depths were determined by the treating radiation oncologist on an individual basis. Most patients received either preoperative or postoperative EBRT as well, and this is detailed in the results.

Complications

Perioperative complications were classified according to the Clavien-Dindo classification system for postoperative surgical complications [8]. Grade 1 complications were not included as they are self-resolving or require only routine postoperative medications and nursing care, so they may go undocumented. All Grade 2 and higher complications were analyzed and grouped by organ system. Complications arising in the first 30 days postoperatively were classified as acute complications, while complications arising more than 30 days postoperatively or persisting past the first 30 days were classified as chronic.

Statistical Analysis

Tests for interactions between different variables were performed using the chi-square test. *P* value less than 0.05 was considered statistically significant. Statistical analyses were performed using the STATA 10.0 statistical software [9].

Results

Surgical and Patient Characteristics

There were 113 patients who underwent intraoperative radiation therapy between November 2006 and May 2014 who met all inclusion criteria and were included for analysis. Table 1 describes patient and surgical characteristics. Gender distribution was nearly equal (49% Male, 51% Female) and the mean age at surgery was 55.8 years. The median CCI score was 7, and the highest was 12. One patient appears twice, as they had two separate instances of IORT for recurrent rectal cancer.

Sarcomas and colorectal cancer made up the indication for surgery in a combined 84.1% of all patients (44% sarcoma, 40% colorectal cancer). All other indications made up 16%, and these included urologic cancers (4%), gynecologic cancers (4%), anal cancer (4%) and pancreatic cancer (3%). The majority of patients had recurrent disease (75%). 84% of colorectal cancers and 68% of sarcomas were recurrent tumors. Therefore, 32% of sarcomas received IORT for a primary, nonrecurrent tumor. Sarcomas often require multivisceral organ resection during surgery [10], and the primary sarcomas which received IORT were chosen due to the concern for potentially positive margins even after EBRT and extensive multivisceral resection was performed. Additionally, primary sarcomas receiving IORT were generally higher grade (69% intermediate or high grade, with 13% no grade reported). The histology of those primary sarcomas which received IORT included leiomyosarcoma (31%), dedifferentiated liposarcoma (19%), and the remainder an assortment of different histologies including epitheloid sarcoma, malignant solitary fibrous tumor, malignant peripheral nerve sheath tumor, pleomorphic sarcoma, and synovial sarcoma. The main criteria for IORT in all of these patients was invasion of the sarcoma into pelvic, and retroperitoneal structures that would leave close margins of resection. A smaller number of colorectal cancers receiving IORT were primary tumors (16%), and these were all T4 rectal cancers invading adjacent structures which were predicted to have close margins on resection.

The most common location for tumors was in the pelvis (53%) followed by the retroperitoneum (33%) and intraperitoneal abdomen (14%). 64% of sarcomas were in the

retroperitoneum, and 87% of all retroperitoneal tumors were sarcomas ($p < 0.001$). Conversely, 71% of all colorectal cancers were in the pelvis, and colorectal cancer made up 53% of all pelvic tumors ($p < 0.001$). Nearly all patients (96%) had either an R0 or R1 resection (R0: 51%, R1: 45%). This is a high rate of R0 resection and the final resection margin would not be known until postoperatively, but these patients also had locally invasive disease and were determined to be at risk for positive margins after resection during preoperative multidisciplinary discussion. Additionally, the majority of these R0 resections also received preoperative EBRT (72%), which may have allowed for higher rates of microscopically negative margins. In terms of wound closure, 39% of patients had a tissue flap without mesh, 7% had a tissue flap with mesh, and 54% had no flap.

Radiation Therapy Characteristics

The majority of patients (80%) underwent external beam radiation therapy (EBRT) either preoperatively or postoperatively (Table 2). 73% of all patients underwent preoperative EBRT and IORT, while 6% of all patients underwent EBRT postoperatively, and 20% did not undergo either preoperative or postoperative EBRT. All colorectal cancer patients who received EBRT received it preoperatively; none received postoperative EBRT. 84% of colorectal cancer patients had preoperative EBRT. The few colorectal patients who did not receive preoperative EBRT (8/54, 16%) were those presenting with recurrent disease who had previously received EBRT to the tumor area during prior treatment of their initial disease in the past; however they were determined to be unable to receive additional EBRT during the perioperative period of this present recurrence. The mean total treatment area irradiated during IORT was 55.2 cm² with a median of 40 cm². Most patients had a single IORT field (89%) while 10% of patients had two fields and one patient had three. The most common doses administered were 12 (45%), 10 (38%), and 15 (12%) Gy per field. Finally, 75% of patients had IORT administered only to the surface while 25% of patients were given radiation to a depth of 5mm. The technique of delivering radiation to the surface vs deeper into the tissue is dependent on the amount of time the brachytherapy catheters remain in the dwell position. To deliver radiation to 5mm depth below the surface, the radiation source remains in the dwell position for a longer period of time than if radiation is delivered to the surface alone. This also results in a higher surface dose and can potentially result in increased complications and/or decreased healing. On statistical analysis, there were no significant interactions between type of cancer and location of tumor with relation to treatment depth, number of fields, or dose administered.

Complications

Complication rates are outlined in Table 3. There were no deaths in the first 30 days after surgery and IORT. Only complications of Grade II or higher were included in the current analysis. 43% (48/113) experienced no complication of Grade II or higher. 57% (65/113) of patients had at least 1 complication of any type (acute and/or chronic). 24% (27/113) experienced a Grade II complication as their highest grade, 27% (30/113) Grade III, and 7% (8/113) Grade IV. 27% of patients had a chronic complication; of these, 90% of the patients had only one chronic complication. In those with acute complications, the majority (68%) experienced only 1 complication, with the maximum number of acute complications being 3. With regards to complication types overall, the most common type was wound

complication (38% of all patients) followed by gastrointestinal (25%) then genitourinary (15%). Wound complications also had the highest rate of Grade III/Grade IV complication (65% of wound complications) compared to other complication types. In the 31 patients who experienced chronic complications, the most common chronic complication type was gastrointestinal (12/31, 39%) followed equally by wound (8/31, 25%) and neurologic (8/31, 26%). The chronic complications were gastrointestinal (enterocutaneous fistulas and small bowel obstruction, 40%), chronic non-healing wounds/sinuses (27%), chronic neuropathic pain (27%), and genitourinary (7%, 1 patient developed bladder fistula after lymphocele/abscess and 1 patient who developed erectile dysfunction).

Specific complications for each category of wounds are outlined in Table 4. Abscesses were the most common type of wound complication (16 patients, 37% of all wound complications), followed by surgical site infection causing dehiscence/ opened by the surgeon to drain (14 patients, 33% of wound complications), and delayed/non-healing wound (14 patients, 33% of wound complications). One patient experienced necrotizing fasciitis resulting in evisceration and required re-operation. The most common gastrointestinal complication was small bowel obstruction or ileus which did not resolve without intervention (i.e. nasogastric decompression or surgical intervention; 15 patients, 54% of GI complications). 7 patients developed enteric fistulas (enterocutaneous, entero-enteric, etc; 25% of GI complications), and 5 patients (18% of GI complications) had GI tract inflammation (3 enteritis, 1 gastritis, 1 esophagitis + duodenal ulcer). The most common genitourinary complication was obstruction resulting in hydroureter/hydronephrosis (6 patients, 35% of GU complications) followed by prolonged inability to void (3 patients, 18% of GU complications). Neuropathy consisted of neuropathic pain in 8 patients (62% of neurologic complications) and weakness/numbness/paresthesia in 5 patients (39% of neuro complications). It is difficult to determine the complications that are due exclusively to surgery or IORT, and it is likely that they are due to a combination of the two factors. However, certain complications are likely related more closely to surgical factors, such as abscesses, surgical site infections, wound dehiscence, and small bowel obstruction/ileus. Others are more likely a toxicity of IORT treatment including delayed/non-healing chronic wounds, GI tract inflammation, and neuropathy.

Several factors contributed to increased rates of specific complication types. In comparing the two most frequent cancer diagnoses (sarcoma and colorectal cancer), there was a greater number of genitourinary complications in colorectal cancer than in sarcomas, and this difference was statistically significant (8% sarcoma vs 27% colorectal cancer, $p = 0.015$; Table 5). Additionally, a tumor located in the pelvis was also more likely to result in genitourinary complications compared to any other location (25% pelvis vs 13% abdomen and 0% retroperitoneum, $p = 0.003$; Table 5). Flap closure of the wound, with or without mesh, increased the rate of wound complications compared to closure without a flap (50% flap vs. 32% no flap, $p = 0.053$; Table 5).

No other interactions between diagnoses or location were observed. None of the radiotherapy variables assessed including IORT dose, number of fields, treatment area, treatment depth or administration of EBRT significantly affected either the risk of complications overall, individual complication types, the grade of complications, or the

number of complications. Additionally multiple multivariate models showed no variables related to IORT administration to be significantly associated with increased risk of overall complications

Discussion

The implementation of IORT has been investigated extensively in sarcomas and locally advanced/ recurrent rectal cancers [1–3,11]. Our results reflect this, with 85% of all patients having a diagnosis of either colorectal cancer or sarcoma, and 86% of colorectal patients presenting with recurrent disease. Radiation therapy and IORT are especially well-suited for these cancers because of their propensity to occur locally. Because of this, the main outcome measure to define the success or failure of IORT in studies thus far has been the locoregional recurrence rate. These rates must also be evaluated in the context of patients with comparable diagnoses and disease stages, as this will affect the recurrence rates.

Relapse rates for rectal cancer have historically been as high as 50% [12] with improved rates recently due to total mesorectal excision (TME) and incorporation of EBRT [13–15]. However, in recurrent and locally advanced rectal cancer, obtaining margin negative resection often requires extensive surgery including abdominoperineal resection (APR) and pelvic exenteration along with radiation, and IORT is able to increase radiation to at risk areas beyond doses given by EBRT alone while attempting to minimize further GI toxicity. Outcomes reported from preoperative EBRT combined with IORT in locally advanced primary colorectal cancer have demonstrated local control rates as high as 95%, disease-specific survival rates of 63% and overall 5 year survival rates of 46%. [1,16,17]. Benefits in recurrence and survival have also been reported in locally recurrent colorectal cancer [18–21]. Recent systematic reviews and meta-analyses of IORT in colorectal cancer have concluded that data thus far points to improvements in local control rates and, to a lesser extent, overall survival [22,23]. The main outcome evaluating the determination of success in IORT thus far is the presence or absence of locoregional recurrence. However, a key factor for locoregional recurrence with or without IORT remains resection margins, and some studies have questioned the utility of implementing IORT in the context of R0 resections [18,22,24]

In retroperitoneal sarcomas, locoregional recurrence occurs in 20–75% of patients, even after macroscopic complete resection. Surgery often requires extensive multivisceral resections and multiple re-resections, leading to attempts to integrate radiation therapy into the treatment paradigm. Multiple institutions have reported benefits in local control with postoperative EBRT [25–27]. A single prospective randomized trial of 35 patients comparing IORT and postoperative EBRT to postoperative EBRT alone showed significant improvements in locoregional control and a modest decrease in complications with IORT, but no difference in survival [28]. More recent studies using preoperative EBRT with and without IORT have shown favorable local control rates with this combination. [29–31].

Along with decreases in local recurrence rates, however, some studies in colorectal cancer have shown increases in postoperative morbidity and complication rates with IORT, especially in terms of wound complications, hemorrhagic complications, and genitourinary

complications. One meta-analysis in colorectal cancer demonstrated that IORT did not increase risk of anastomotic, urologic, or overall complications compared to surgery alone [22]. However, pooled analysis did show a borderline increased risk of wound complications (OR 1.86, 95% CI 1.03 – 3.38) [22]. A systematic review of IORT in colorectal cancer found the incidence of reported severe complications with IORT to vary between 30–40%, and the most common types of complications to be gastrointestinal, dermatologic (primarily wound), and infections related to surgery. These complication rates are also not inferior to what has been reported for surgery alone in comparable patient cohorts. Surgery for locally recurrent rectal cancer, which often requires en-bloc multi-visceral resections, has postoperative morbidity rates between 30–60% [32]. One study also reported a major complication rate of 27% for extended radical resection in recurrent rectal cancer [33]. Similarly, large retroperitoneal sarcomas requiring extensive multivisceral resection also have significant perioperative morbidity rates independent of the incorporation of IORT. One study in primary retroperitoneal sarcomas evaluated outcomes of compartmental resection, which is an aggressive approach that treats the retroperitoneum like an extremity compartment and attempts to achieve wide margins by resecting organs adjacent to the sarcoma regardless of whether they are involved by tumor [34]. They reported a complication rate of 16%, although half of these required reoperation. Additionally, there were 13 perioperative deaths (4%) and 3 intraoperative deaths [34]. A recent phase I/II clinical trial of preoperative IMRT with IORT in retroperitoneal sarcomas reported a severe postoperative complication rate of 33%, with no postoperative mortality [30]. Therefore, as in locally advanced/ recurrent rectal cancer, retroperitoneal sarcomas which are aggressive enough to receive consideration for IORT have similar complication rates to the extensive surgical resections required to remove these tumors.

Our institution's experience with IORT thus far demonstrated an overall complication rate of 57%. The rate of high grade complications (at least Grade III or IV) was 34%, and the most common complication type was wound complication (38% of all patients), followed by GI complications (25%). These rates are in line with what would be expected and acceptable for our patient cohort, which was made up of locally aggressive and difficult to resect tumors, a high proportion of which were recurrent (75%) and required extensive multi-visceral resection. Therefore, our results demonstrate similar complication rates when performing aggressive surgical resection with IORT compared to previously published data on aggressive surgical resection alone. Certain disease factors and surgical variables were associated with increased rates of specific complication types. These included colorectal cancer diagnosis, which had significantly increased rates of genitourinary complications, as did tumor location in the pelvis. This is not surprising, as colorectal cancers were significantly more likely to be located in the pelvis. Additionally, the use of flaps for wound closure was associated with increased rates of wound complications. However, this may be confounded by the fact that patients requiring flap closure were often the more complicated cases, which resulted in difficult wound closure and thus more wound complications. A particularly positive finding is that none of the IORT variables assessed were associated with increases in overall complications or any specific type of complications. This is a promising result which indicates that IORT is safe, with an acceptable complication risk within the full

range of dosages, treatment areas, number of fields, and treatment depths employed in this study.

It is important to note that our patients were chosen for IORT from patients evaluated in multidisciplinary conferences which allow for input from experts of all disciplines involved. These collaborations are crucial and necessary. Without this multidisciplinary approach, one would expect higher complication rates, especially in smaller centers or centers that do not have similar volume or experience in administering IORT.

There are several limitations to our study. First, this study is a retrospective chart review and may suffer from incomplete or missing documentation in the chart. Second, we described the perioperative outcomes, complication rates, and effects on types of complications of variables related to IORT therapy. However, we do not have a comparable cohort of patients during this time period which did not receive IORT therapy to compare the effects of IORT to surgery $\pm$ EBRT alone. All patients that were determined to be candidates for and potentially benefit from IORT during this time period were evaluated by radiation oncology and received IORT if appropriate. Our paper combined various disparate cancer diagnoses, although the most common were sarcomas and colorectal cancers. These patients were self-selected through their clinical workup and diagnosis as patients identified as suffering from locally aggressive cancers which would benefit most from IORT. Additionally, we are not offering a direct comparison between a treatment group of IORT + surgery and a control group of surgery alone. This would require a controlled trial or case control study directly comparing these 2 treatment arms, and is beyond the scope of this current paper. By presenting previously published data on complication rates in resection of locally advanced/recurrent rectal cancer and intra-abdominal sarcoma, our intention was simply to place the complication rates presented in our study within the appropriate context of what is considered an acceptable postoperative morbidity for this patient cohort. Lastly, we have not discussed the effects on local control, disease free survival and overall survival in this paper, however this data is still being collected and assessed and will be addressed in the future.

Conclusions

We have described the patient and treatment characteristics of IORT patients treated at Johns Hopkins Hospital over the 8 year period beginning in November 2006. Our study is one of the largest series on IORT that has been published to date. Our most common diagnoses were sarcoma, followed by colorectal cancer. The rate of high grade complications (at least Grade III or IV) was 34%, and the most common complication type was wound complication, followed by gastrointestinal. Wound complications were most common, and this is likely due to the frequency of extensive, radical resections which required complex flap closure of the wound. GI complications were the next most common type. Several disease and treatment characteristics were associated with increased rates of specific types of complications, including colorectal cancer and pelvic tumor location association with genitourinary complications, and flap closure association with wound complications. None of the variables dealing with administration of IORT were associated with increased rates of overall complications or specific complication types, indicating that IORT is safe and has

acceptable perioperative morbidity in line with expected postoperative complication rates in similar patient cohorts.

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Synopsis

Intraoperative Radiotherapy (IORT) is an emerging component in the management of abdominopelvic malignancy, especially in rectal cancer and sarcoma. We analyzed all patients who received abdominopelvic IORT at Johns Hopkins Hospital between 2006 and 2014 to determine postoperative complication rates with the addition of IORT. Sarcoma and colorectal cancer were the most common diagnoses. We found complication rates comparable to historic rates in similar patients who receive surgery without IORT, and determined that the addition of IORT in select patients is safe, with an acceptable postoperative morbidity.

Table 1

Demographics of entire sample set (n = 113)

Variable	n (%)
Gender	
Male	55 (49)
Female	58 (51)
Age: mean (range)	56 (15–84)
Charlson Comorbidity Index: Median (range)	7 (2–12)
Diagnosis	
Sarcoma	50 (44)
Colorectal	45 (40)
Other*	18 (16)
Urologic	5 (4)
Gynecologic	5 (4)
Anal	5 (4)
Pancreas	3 (3)
Tumor Location	
Pelvis	60 (53)
Retroperitoneum	37 (33)
Abdomen	16 (14)
Recurrent Disease	
Yes	85 (75)
No	28 (25)
Flap reconstruction	
None	61 (54)
Native flap	44 (39)
Mesh	8 (7)
Resection margins	
R0	58 (51)
R1	51 (45)
R2	4 (4)

Table 2

IORT variables

Variable	n (%)
No EBRT	23 (20)
EBRT	90 (80)
Preop	83 (92)
Post-op	7 (8)
Number of IORT Fields	
1	96 (89)
2	11 (10)
3	1 (1)
Missing/Unknown	5
Treatment Area (cm²): Mean (range)	55 (2–376)
<u>Dose Per Field</u>	
Single Field (n = 96)	
Dose, Gy	
10	36 (38)
12	44 (46)
12.5	1 (1)
13	1 (1)
15	13 (13)
20	1 (1.0)
Double field, cm2 (n = 11)	
Dose, Gy	
10, 10	4 (36)
12, 12	5 (45)
8, 10	1 (9)
8, 8	1 (9)
Triple Field (n = 1)	
Dose, Gy	
10	1 (100)
Missing/Unknown	5
Treatment Depth	
0 (surface only)	81 (75)
5mm	27 (25)
Missing/Unknown	6

Table 3

Complications after IORT (Only Grade II or Higher by Clavien-Dindo)

Variable	n (%)
Complications:	
No Complications	48 (43)
Any complication	65 (57)
Acute	56 (50)
Chronic	30 (27)
In patients with acute complications, the number of complications (n = 56)	
1	38 (68)
2	13 (23)
3	5 (9)
In patients with chronic complications, the number of complications (n = 30)	
1	27 (90)
2	3 (10)
Highest Grade of Complications (n = 65)	
Grade 2	27 (42)
Grade 3	30 (46)
Grade 4	8 (12)
Complications	
Wound	43 (38)
GI	28 (25)
GU	17 (15)
Neuropathy	13 (11)
Other	6 (5)
Wound Complications (n = 43)	
Grade 2	15 (35)
Grade 3	24 (56)
Grade 4	4 (9)
GI Complications (n = 28)	
Grade 2	13 (46)
Grade 3	14 (50)
Grade 4	1 (4)
GU Complications (n = 17)	
Grade 2	10 (59)
Grade 3	6 (35)
Grade 4	1 (6)
Neuropathy/Pain (n = 13)	

Variable	n (%)
Grade 2	11 (85)
Grade 3	2 (15)
Grade 4	0
Other (n = 6)	
Grade 2	0
Grade 3	2 (33)
Grade 4	4 (67)

Table 4

Specific Complications by Type

Specific Complication	Number of Patients with Complication	Percent of Complication Type
<u>Wound</u>	<u>43</u>	<u>100</u>
Abscess	16	37
SSI - wound opened by surgeon or dehiscence	14	33
Delayed healing or chronic non-healing wound	14	33
Wound necrosis requiring debridement	2	5
SSI - antibiotic treatment only	2	5
Necrotizing fasciitis with evisceration	1	2
<u>Gastrointestinal</u>	<u>28</u>	<u>100</u>
SBO or prolonged ileus not resolving spontaneously	15	54
Enteric fistula	7	25
GI tract inflammation	5	18
enteritis	3	
gastritis	1	
esophagitis + duodenal ulcer	1	
Duodenal stump leak	1	4
Anastomotic stricture	1	4
<u>Genitourinary</u>	<u>17</u>	<u>100</u>
Obstruction resulting in hydroureter/hydronephrosis	6	35
Prolonged inability to void	3	18
UTI/pyelonephritis	2	12
Incontinence	2	12
Ureteral stricture	1	6
Bladder fistula	1	6
Cystitis/hematuria	1	6
Erectile dysfunction	1	6
<u>Neuropathy</u>	<u>13</u>	<u>100</u>
Pain	8	61
Weakness/numbness/paresthesia	5	39

Table 5

Significant Factors for Complication Types on Univariate Analysis

	Complication Rate (%)	p-value
<u>Factors in GU Complications</u>		
Diagnosis:		
Colorectal	27	0.015
Sarcoma	8	
Tumor Location:		
Pelvic	25	0.003
Intra-abdominal	13	
Retroperitoneal	0	
<u>Factors in Wound Complications</u>		
Flap Wound Closure:		
Flap	50	0.053
No Flap	32	