New school technology meets old school technique: Intensity modulated proton therapy and laparoscopic pelvic sling facilitate safe and efficacious treatment of pelvic sarcoma

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Abstract

Purpose: Small bowel tolerance may be dose-limiting in the management of some pelvic and abdominal malignancies with curative-intent radiotherapy. Multiple techniques previously have been attempted to exclude small bowel from the radiation field, including the surgical insertion of an absorbable mesh to serve as a temporary pelvic sling. This case highlights a clinically meaningful application of this technique with modern radiotherapy.

Methods and Materials: A patient with locally invasive, unresectable high-grade sarcoma of the right pelvic vasculature was evaluated for definitive radiotherapy. The tumor immediately abutted small bowel. The patient underwent laparoscopic placement of a mesh sling to retract the abutting small bowel and subsequently completed intensity modulated proton therapy.

Results: The patient tolerated the mesh insertion procedure and radiotherapy well with no significant toxicities. The combination approach achieved excellent dose metrics, and the patient has no evidence of progression 14 months out from treatment.

Conclusions: The combination of mesh as a pelvic sling and proton radiotherapy enabled the application of a curative dose of radiotherapy and should be considered for patients in need of curative-intent radiation when the bowel is in close proximity to the target.

Introduction

Curative-intent radiotherapy often is a necessary component in the management of unresectable abdominal and pelvic malignancies, and small bowel is the primary dose-limiting organ[1]. Radiotherapy-induced enteritis and small bowel injuries such as fistulas, strictures, and perforations are related to dose and volume of organ exposed[2,3]. Severe toxicity can be fatal. As a result, while some patients may be placed at higher risk for toxicity when target coverage is prioritized, more commonly patients may experience greater risk for recurrence when the target is undercovered to protect the bowel. Several non-invasive and invasive methods have been employed to displace small bowel out of the radiation field[4]. Additionally, advanced radiotherapy techniques may be synergistic with displacement methods by enabling dose escalation and dosimetric sparing of close but no longer abutting critical structures. Herein the authors describe a case of locally invasive pelvic sarcoma in which a pelvic sling was used to retract small bowel away from the tumor and facilitate definitive intensity modulated proton therapy (IMPT).

Case Presentation

A 66-year-old woman was evaluated in the Department of Radiation Oncology in June 2020 for newly diagnosed high-grade sarcoma likely arising from the distal right external iliac vasculature. Six months previously she had been found to have a deep venous thrombosis of the proximal right common femoral vein on ultrasound and had been initiated on anticoagulation. At the time of evaluation in radiation oncology, the patient was experiencing mild right pelvic pain and increased right lower extremity swelling. CT and MRI demonstrated a 7.9 x 5.8 x 10.4 cm tumor of the right pelvic sidewall and groin that encased her right external iliac and common femoral vessels with occlusion and invasion of the venous system. The tumor also directly abutted a 23 mm segment of her small bowel with a thin fat plane between the two (Figure 1a). PET/CT demonstrated a hypermetabolic lesion without regional adenopathy or distant disease (Figure 2a). The patient's medical history was significant for right-sided ductal carcinoma in-situ of breast origin managed with lumpectomy and adjuvant radiation, right-sided renal cell carcinoma managed with partial nephrectomy, active tobacco smoking, and diabetes mellitus.

The patient previously had been evaluated by orthopedic oncology, and surgical resection was predicted to involve resection of right femoral nerve and vascular reconstruction over a long segment with the possibility to include an external hemipelvectomy. Given her medical comorbidities, tobacco use, the extent of surgery, and risk of progression, the patient had been deemed a poor candidate for resection. Definitive radiotherapy was offered as an alternative to surgery, although there was concern for delivering curative-intent dose given the proximity of the small bowel to the tumor. The patient was counseled that with standard techniques radiotherapy alone likely could be delivered only palliative intent. To offer a potentially curative approach, the patient was referred to colorectal surgery for laparoscopic placement of mesh to retract the small bowel from the superior extent of the tumor. Mesh placement was selected over other techniques such as tissue expander placement or hydrogel insertion given the unstable location and absence of tissue planes in the inferolateral abdominopelvic cavity. The patient consented to the procedure and subsequent radiotherapy.

The surgical procedure was performed under general anesthesia, and prophylactic cefazolin and metronidazole were administered. Three 5 mm trocars were placed for the camera and two working ports, and laparoscopic mobilization of the bowel was performed. To exclude the bowel from the planned radiation field, a 16 x 20 cm absorbable mesh was inserted through a

4 cm low midline incision. The mesh was secured with absorbable suture laterally to the underside of the abdominal wall, superiorly to the retroperitoneum, and medially to the right border of the sigmoid colon and rectum. Care was taken to avoid the iliac vessels and ureter. The procedure and post-operative course proceeded well and without complication. The patient endorsed mild new abdominal pain after her procedure in addition to her baseline right pelvic pain. She otherwise felt well and was discharged one day after the procedure.

After one week with no apparent complications such as infection or bowel obstruction, the patient was simulated for radiation planning in the supine position using a lower extremity vacuum bag to immobilize the legs and pelvis. Intravenous contrast was utilized. The treatment planning CT confirmed that retraction of the bowel had been achieved (Figure 1b). Fluid had layered between the mesh and small bowel, enhancing displacement. The nearest edge of small bowel was 10 mm away from the gross tumor. The diagnostic MRI was fused to the planning CT to improve target delineation.

IMPT to be delivered in 15 fractions was planned, treating the tumor to 6750 cGyE with expansions to cover areas at risk for sub-clinical disease to 5700 cGyE and 4500 cGyE (Figure 3a). To reduce the risk of incisional dehiscence, care was taken to avoid beams entering through the midline incision and laparoscopic port sites. A two-field arrangement was used and consisted of ipsilateral posterior-oblique and anterior-oblique beams. Hounsfield unit overrides for the mesh were considered unnecessary due to the composition, size, and geometry of the mesh material in this plan. Multifield optimization was performed using a pencil beam superposition convolution algorithm and a uniform estimate of 1.1 for relative biologic effectiveness (RBE). The plan was designed to be robust to 5 mm of setup uncertainty, 3% range uncertainty, and inter-field displacements of 2 mm. The D99% of the gross tumor volume (GTV) was 6783 cGyE, and the minimum and maximum point doses were 6257 cGyE and 7766 cGyE, respectively. An internal subvolume was permitted to receive additional dose, and approximately 45% of the GTV received ≥7500 cGyE. No beam ranged out towards the small bowel. Instead, a crisp lateral penumbra was achieved by utilizing the smallest appropriate spot size of our delivery system for each field, and this was leveraged to maximize small bowel sparing. A 4.5-cm range shifter attached to the end of the treatment nozzle was needed for the anterior oblique beam in order to cover the proximal regions of the target, while no range shifter was required for the posterior oblique field. The small bowel D0.03 cc was 4397 cGyE, D1 cc was 3553 cGyE, and V3000 cGyE was 2.77 cc. Other organs at risk (OARs) were well spared with all plan normal tissue constraints met. Additionally, the final plan dose was re-computed using an in-house developed Monte Carlo dose calculation engine[5,6]. This system also generates the non-uniform effective biological dose by combining the physical dose with a model of proton RBE that is based on the calculated distribution of linear energy transfer (Figure 3b). These Monte Carlo dose calculations confirmed that the small bowel D0.03 cc was consistent with treatment goals of less than 4500 cGyE.

The patient commenced radiotherapy three weeks following placement of the mesh, and treatment was completed without interruption. Weekly CT verification scans demonstrated consistent displacement of the small bowel from the high-dose radiation region (Figure 3c). Throughout radiotherapy the patient experienced expected mild decreased appetite, nausea, fatigue, and dermatitis, all of which resolved shortly after completing radiation.

PET-MRI performed three months following completion of radiotherapy demonstrated a complete metabolic response with decreased size of the mass (6.7 x 4.9 x 9.5 cm), absence of restricted diffusion and contrast enhancement, and no evidence of locoregional progression or distant metastasis (Figure 1b). The patient reported resolution of her pain as well as no new bowel-related toxicities. Imaging surveillance of the pelvis, most recently with MRI at 14 months following completion of radiotherapy (Figure 1c), demonstrated continued decreased size of the mass (now 5.1 x 2.9 x 5.9 cm) and no evidence of locoregional progression. Clinically the patient remains on anticoagulation and experiences mild discomfort associated with fluctuating right lower extremity lymphedema. No bowel-related toxicities were reported at follow up.

Discussion

For curative-intent radiotherapy, it is incumbent upon the radiation oncologist to identify and, when possible, overcome barriers to safely achieving a curative-intent dose to gross disease. For disease abutting a critical, radiosensitive organ, the options to undertreat disease or exceed the tolerance of the organ can lead to suboptimal outcomes. However, in some circumstances the radiosensitive organ can be displaced using interventional or surgical methods to provide curative-intent dosing while minimizing toxicity. A common example is the insertion of a hydrogel spacer for displacement of the rectum from the prostate[7]. Combined modality therapy often can leverage complementary features of surgery and radiation to maximize the chance for success. A relevant example is the use of radiotherapy to facilitate limb-persevering surgery for soft tissue sarcomas. The key difference is that while radiation often is utilized to improve the outcomes of curative-intent surgery, this report highlights an example of using surgery to improve curative-intent radiotherapy.

While small bowel mobility in the pelvis may ameliorate toxicities from expected high dose exposure over short segments, extended segments and/or doses far exceeding tolerance remain concerning, particularly if the at-risk section of the bowel is not freely mobile. Various techniques have been employed to exclude small bowel from abdominal and pelvic radiation fields, including non-invasive measures such as prone positioning, use of a bellyboard, and bladder filling. The effectiveness of these techniques is limited, leading to innovation of invasive methods to displace bowel such as insertion of mesh, tissue expanders, and/or silicon prostheses as well as generation of a pelvic sling from native peritoneum or omentum[4,8-13]. A theoretical downside of any invasive technique is the development of adhesions, which may restrict small bowel mobility. A short duration between procedure and radiation treatment could mitigate this concern, particularly with displacement adequate enough such that the small bowel cannot be fixed in high dose regions.

Placement of mesh prior to radiotherapy is discussed most in the literature, and Table 1 highlights the diseases, organs that have been displaced, and select outcomes. It has been shown to improve radiotherapy dosimetry with superior small bowel sparing compared to prior to insertion[14]. Traditionally mesh was placed using a laparotomy, which is generally well tolerated but carries risks of complications including pelvic infection/abscess, wound dehiscence, and small bowel obstruction, herniation, and fistula formation[15-18]. Laparoscopic surgical techniques permit insertion to be performed in a minimally invasive manner, which reduces operative morbidity and decreases recovery times[14,19]. Although the risks are modest, displacing small bowel through invasive techniques may be of most value when otherwise there are unacceptably high risks of small bowel toxicities or treatment failure[13,20]. The technique of using mesh as a pelvic sling is nearly four decades old and was pioneered during previous eras that lacked access to modern highly conformal radiotherapy techniques and high-quality image guidance[10]. In this patient's situation, no radiation technology yet exists that safely can deliver a definitive radiation dose to a sarcoma abutting the small bowel without additional measures.

The risk of radiation-induced enteropathy increases significantly at 4500-5000 cGy, which can be dose-limiting when treating tumors of the pelvis[21]. Herein the authors describe a case of definitive treatment of a radio-resistant tumor with previously immediately adjacent small bowel to an equivalent dose in 200 cGyE fractions of over 10000 $cGyE_3$ and 8000 $cGyE_{10}$[22-24]. Insertion of the mesh provided some physical separation between the tumor and bowel, while IMPT permitted a sufficiently steep dose gradient to achieve small bowel D0.03 cc of less than 5300 $cGyE_3$. IMPT has been shown previously to provide clinically relevant dose reductions of pelvic organs at risk relative to photon therapy and may have significant utility in situations where abrupt dose fall-off is crucial[27]. More widely available intensity-modulated radiation therapy could be employed in similar settings with sufficient anatomic separation for dose fall-off. Due in part to the challenge of achieving high target dose, soft tissue sarcoma uncommonly is treated with curative-intent radiotherapy alone. Retrospective analysis of definitive radiotherapy for soft tissue sarcoma suggests improvement in clinical outcomes with doses of 6300 cGy or higher, achieving 60% local control and 52% overall survival at five years in this group[25]. In the plan from this case, the intermediate dose-volume in this case was prescribed to over 6500 $cGyE_{10}$. The patient's active smoking and diabetes mellitus placed her at increased risk of radiation-induced complications[26]. Despite her comorbidities, radiotherapy was delivered safely without significant early or late toxicities to date. At 14 months since radiotherapy, locoregional control has endured with no distant metastases.

High-quality modern proton radiotherapy is essential to provide the optimal plan, and an experienced multidisciplinary team is needed. The penumbra increases as protons traverse greater distances of matter owing to increased multicoulomb scattering[28], so thoughtful beam arrangements and weighting are essential. Beam spot size further drives the sharpness of the lateral penumbra in pencil-beam scanning[29]. In this case, the smallest beam spots were used in the region where the target and primary OAR are in closest proximity to maintain a crisp lateral penumbra in this region. In addition to careful beam arrangements, the planned dose was evaluated using both analytic and Monte Carlo dose calculations to ensure that the dose modeling was sufficiently accurate. Furthermore, a biological dose model was utilized to analyze and correct via re-optimization for regions of excessively high biological dose caused by the combination of high physical dose and the increased LET of end-of-range protons. Robust optimization should be used routinely to ensure adequate target coverage and OAR protection. Lastly, verification scanning is critical to assess for changes in target, OARs, and patient habitus that could perturb the radiation plan. This was particularly important in this case, as fluid within the sling was partly responsible for the displacement and certainly could have changed. This patient's tumor and small bowel position was stable throughout verifications and the dose distribution remained true to plan.

Conclusions

In a case of locally invasive high-grade sarcoma of pelvis, a mesh was placed laparoscopically without complication and was used to retract small bowel that previously abutted the tumor, permitting definitive high-dose IMPT to be delivered with excellent dose metrics, no late bowel-related toxicities, and locoregional control at 14 months from treatment. This combination of an established surgical technique and modern proton radiotherapy should be considered in the setting of definitive radiotherapy, particularly for patients with anatomically unfavorable tumor locations and/or increased risk of bowel toxicity.

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Figure Captions

Figure 1. a) MRI prior to mesh insertion showing direct abutment of the tumor and small bowel over a 23 mm segment; b) treatment planning CT after mesh insertion, which resulted in 10 mm or more separation between tumor and small bowel.

Figure 2. a) PET-CT at diagnosis showing a large centrally necrotic right pelvic mass; b) follow-up PET-MRI at 3 months post-treatment demonstrating complete metabolic response and decreased size of the mass with no evidence of locoregional progression or distant metastasis; c) follow-up MRI at 14 months post-treatment re-demonstrating no evidence of progression.

Figure 3. Radiotherapy plan treating gross tumor to 6750 cGyE with expansions to 5700 cGyE and 4500 cGyE to cover areas at risk for sub-clinical disease; target is contoured in magenta, small bowel in green, and large bowel in orange: a) treatment planning CT using uniform estimate of 1.1 for relative biologic effectiveness (RBE); b) treatment planning CT using in-house model estimate of non-uniform RBE; c) verification CT using uniform estimate of 1.1 for RBE.

Declaration of interests

☒The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Tables

Reference	Number of patients	Primary histologies	Organ(s) excluded	Median follow-up (months)	Radiographic exclusion of small bowel (%)	Toxicities possibly related to mesh placement	Rate of radiation enteritis (%)
Soper et al., 1985[29]	6	Cervical, endometrial	Small bowel	5	100	None	0
Devereux et al., 1988[8]	60	Rectal, gynecologic	Small bowel	28 (mean)	n/a	None	0
Feldman et al., 1988[4]	16	Rectal, sacral chordoma	Small bowel	15 (mean)	81	Fungal infection	0
Sener et al., 1989[18]	8	Colorectal, urologic	Small bowel	12	n/a	Pelvic abscess, wound dehiscence, small bowel herniation, small bowel obstruction x2	12
Dasmahapatra and Swaminathan, 1991[16]	45	Rectal	Small bowel	34	100	Small bowel obstruction x2	0
Rodier et al., 1991[30]	60	Cervical, endometrial, rectal, bladder, retroperitoneal sarcoma, ovarian, vulvar	Small bowel	18 (mean)	93	Small bowel obstruction x5	7
Beitler et al., 1997[15]	20	Rectal	Small bowel	18 (mean)	n/a	Pelvic abscess, perineal seroma, toxic perineal wound, pulmonary embolus, lower extremity deep venous thrombosis	7
Joyce et al., 2009[14]	6	Prostate, bladder	Small bowel	n/a	100	Pulmonary edema	n/a
Yoon et al., 2013[13]	5	Retroperitoneal sarcoma, pelvic sarcoma, Wilms tumor	Small bowel, colon, ureter, bladder, pancrea	18	100	Lower extremity deep venous thrombosis	0

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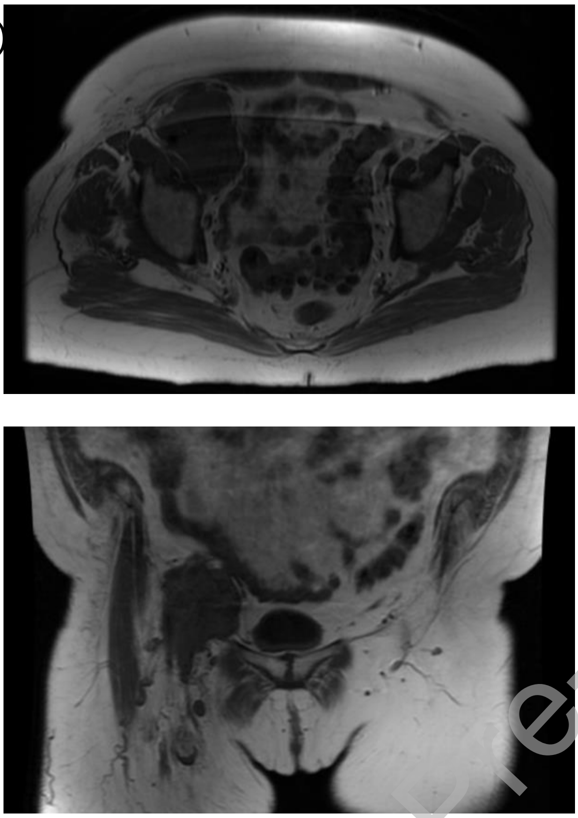
Table 1. Selected studies of mesh used to retract small bowel prior to radiotherapy in the management of pelvic and abdominal malignancies.

Figure 1

1a)



1b)

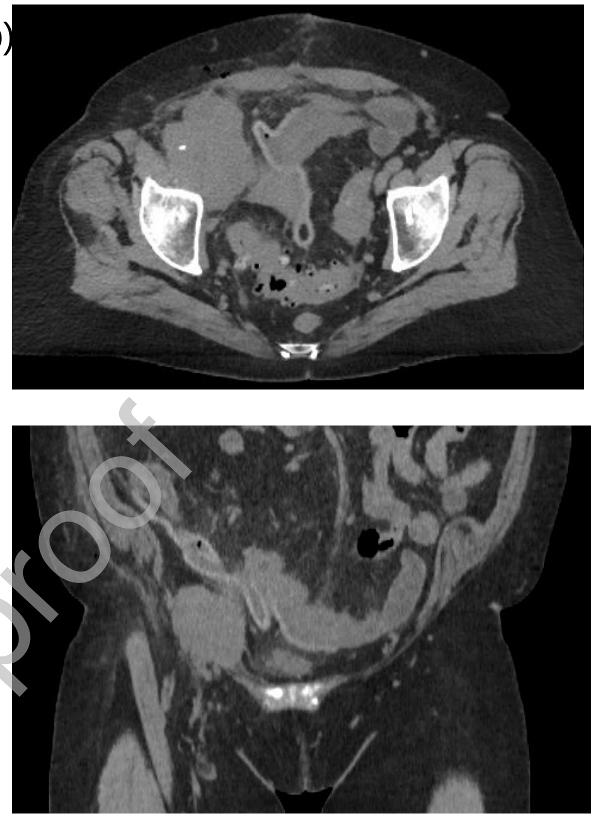


Figure 2

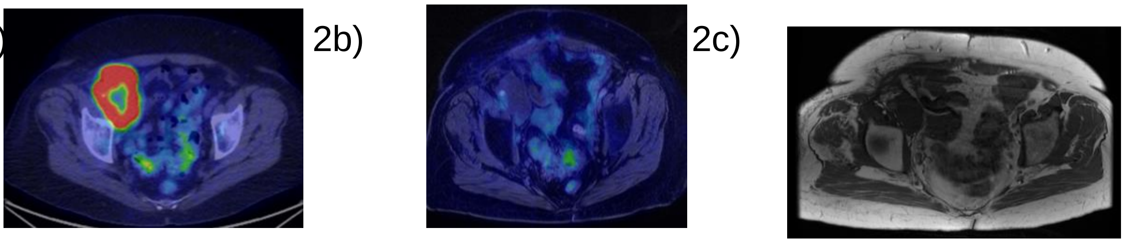


Figure 3

3a) 3b) 3c)