Seminars in Colon and Rectal Surgery 25 (2014) 44–47

Contents lists available at ScienceDirect

Seminars in Colon and Rectal Surgery

journal homepage: www.elsevier.com/locate/yscrs

Intraoperative and stereotactic ablative radiation therapy in recurrent rectal cancer

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A B S T R A C T

Despite significant advances in primary management of rectal cancer, local recurrence, although increasingly uncommon, presents a therapeutic challenge. Multimodality therapy, including surgery, radiation therapy, and chemotherapy, is often called for despite, in most cases, having been used in the primary setting. Technical advances in radiation planning and delivery have contributed to development of ways to deliver high-radiation doses to exactly where it is needed, preventing damage to surrounding normal structures. In combination with modern surgical and chemotherapeutic options, these specialized radiation therapy techniques, including intraoperative radiation therapy and stereotactic ablative radiation therapy, have contributed to excellent local control and survival outcomes for these patients.

1. Introduction

Recurrence rates following modern combined-modality therapy for locally advanced rectal cancers is fortunately very low at 6–10%.[1,2] When it does happen, we are faced with a challenging clinical situation with significant clinical symptoms affecting quality of life, including pelvic pain, bleeding, and bowel obstruction. Advances in imaging, treatment planning, and treatment delivery have made radiation treatments safer now than ever before. This has enabled maximal avoidance of surrounding normal structures, facilitating high-radiation doses often delivered in a single or a few fractions. Intraoperative radiation therapy (IORT) and stereotactic ablative radiation therapy (SABR) have been incorporated as part of a multimodality approach to improve outcomes in this patient population.

The choice of therapy in the recurrent setting depends on prior therapy and the extent of the recurrent disease. If limited to pelvic recurrence without distant disease (which is not uncommon), local modalities such as surgery with or without additional radiation therapy may permit successful salvage. Limited distant metastases (to the liver or lung) may or may not be a relative contraindication depending on location and potential for curative resection (or ablative therapy like SABR) of the distant metastases. Surgical resection still remains a dominant modality in the management of pelvic recurrences. Obtaining margin negative resection is challenging,[3–7] often requiring extensive resections like pelvic exenteration or partial sacrectomy, and outcomes after resection alone are poor.[8] Most patients have already been treated with external-beam radiation therapy (EBRT), which may preclude or limit its utility in the recurrent setting either before or after resection. Radiation therapy alone (with or without concurrent chemotherapy), without surgery, in the recurrent setting can provide durable palliation but long-term survival is often not realistic.[9] Specialized radiation techniques, like IORT and SABR, are being increasingly used in these situations often in combination with maximal surgical debulking to achieve durable local control and extended survival.

2. Patient evaluation

Optimally, these patients are managed by an experienced multidisciplinary team, including colorectal surgery, plastic and reconstructive surgery, gynecologic oncology, urology, neurosurgery, radiation oncology, and medical oncology among others. In addition to patient history and physical examination, imaging including CT scans, PET scans, and MRI help to characterize the extent of disease. The tumor is, in most situations, more extensive than indicated by physical and radiological examinations, and often the resectability can only be determined intraoperatively with due consideration to extent of adjacent organ, vascular, lymphatic, and/or nerve root involvement. Due to prior surgery, the tumor growth is not confined by specific facial compartments, as these fasciae have been compromised during prior surgery.

3. Treatment considerations

3.1. No prior pelvic radiation therapy

When the patient is radiation naïve, he or she is typically managed similar to locally advanced rectal cancer with

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http://dx.doi.org/10.1053/j.scrs.2013.09.007

Table 1
Results after IORT in recurrent rectal cancer.

Series	No. of patients	Overall survival	Local control
Haddock (Mayo)	607	5 yr—30%	3 yr—65%
Dresen (Netherlands)	147	5 yr—32%	5 yr—54%
Alektiar (MSKCC)	74	5 yr—23%	5 yr—39%
Guo (Cleveland)	32	3 yr—49%	3 yr—56%
Bussières (France)	73	3 yr—31%	3 yr—31%

preoperative chemoradiation followed by surgery (see article by Dr. Minsky). Subsequent to this trimodality therapy, there may be a role for additional IORT (see below) depending on tumor extent and margin status.

3.2. Surgical considerations

Oncologically, sound resections may not be feasible or realistic in certain situations, such as circumferential pelvic mass, encasement of iliac vessels, extensive pelvic bone involvement, and extensive unresectable extrapelvic disease.[10,11] Consideration for palliative RT including SABR may be appropriate in these situations. Surgical resection alone can provide long-term survival only if complete resections with negative margins can be achieved.[4–8,12,13] This often requires extensive debilitating resections with multiple permanent stomas, causing chronic quality-of-life impairment including pain. It may be possible to preserve urinary and fecal continence when the integrity of the pelvic floor muscles is not compromised.[14,15] In patients who have not received prior radiation, preoperative combined-modality chemoradiation therapy can allow for higher complete resection rates and possibly reduce the extent of surgical resections and preserve quality of life.[16–20] Radiation alone may not be optimal as a preoperative strategy compared to chemoradiation therapy.[21]

Palliation for obstructive symptoms may require tumor resection if enteric bypass, stent placement, or endoscopic laser ablation is not successful or feasible.

3.3. IORT

IORT enables the delivery of radiation to the site of highest risk of local failure (the tumor bed) while decreasing the radiation dose to surrounding normal tissues, which in most situations has received prior radiation therapy. Large single doses (about 15 Gy) are typically delivered immediately or within a few days after surgical debulking. Unique radiobiological mechanisms may play a role with these high doses.[22]

Several reports have documented the beneficial role of IORT as a component in the management of recurrent rectal cancer[20,23–27] (Table 1). The Mayo Clinic experience (Haddock) is the largest reported series (607patients) using electrons, treated between 1981 and 2008. The median IORT dose was 15 Gy (range 7.5–30 Gy). The median survival was 36 months with a 5-year survival of 30%. Local control at 3 years was 65%. Neuropathy was observed in 15% of patients and was related to IORT dose (more common with >12.5 Gy). Toxicity (grade 3 or higher) attributable to IORT was observed in 11% of patients. The MSKCC series (Alektiar) used high-dose-rate intraoperative brachytherapy (Fig. 1) in 74 patients between 1992 and 1998. The dose of IORT ranged from 10 to 18 Gy. The 5-year local control and overall survival rates were 39% and 23%, respectively. The incidence of peripheral neuropathy was 16%. At the Cleveland Clinic (Guo), intraoperative Intrabeam® Photon RadioSurgery (PRS) system was utilized for IORT (Fig. 2). Median tumor bed surface dose was 14.4 Gy (range 13.4–23.1 Gy). The 3-year local control and survival rates were 56% and 49%, respectively.

Optimal outcomes after IORT follows complete resection.[28] Incomplete resection compromised 5-year local control and disease-free survival rates compared to complete resection (21% and 7% vs. 47% and 21%, respectively).

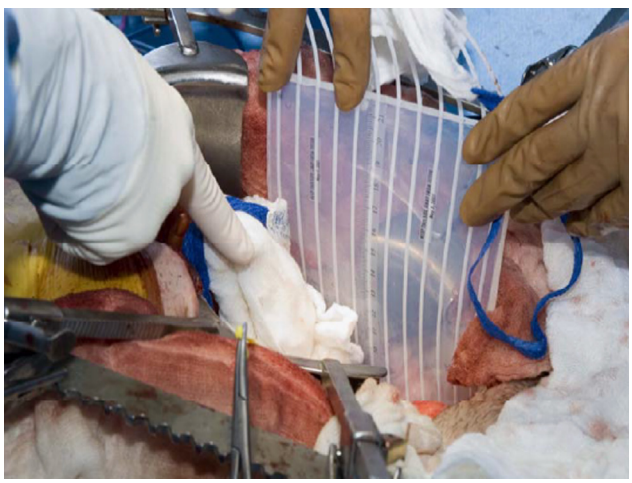

Fig. 1. Harrison–Anderson–Mick (HAM) applicator being positioned in the tumor bed after resection of a presacral recurrence.

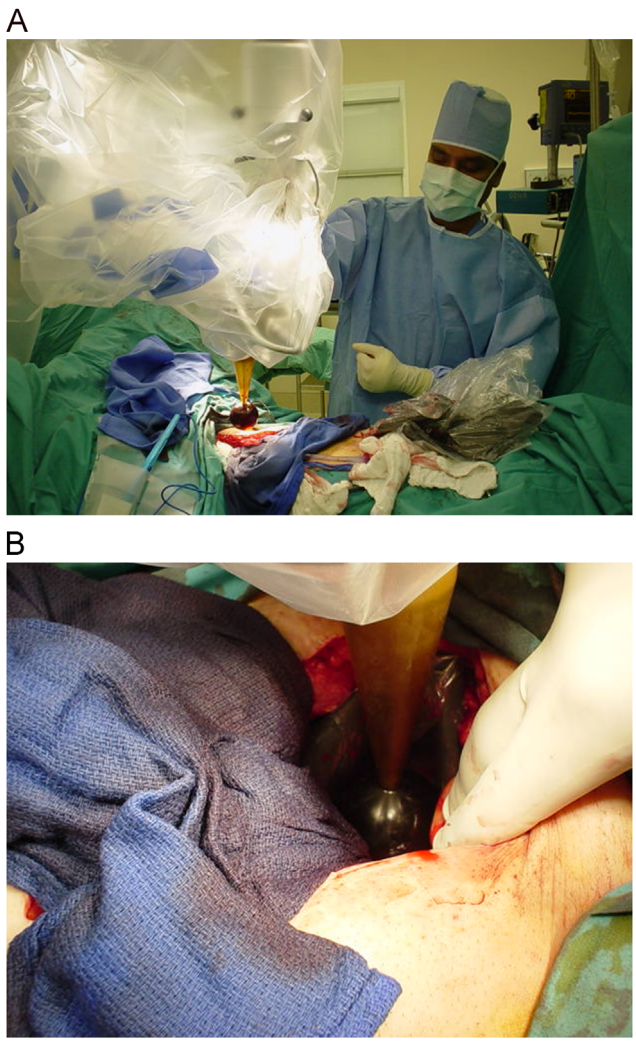

Fig. 2. Intrabeam® Photon RadioSurgery (PRS) system being positioned in the tumor bed after surgical debulking.