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High-dose-rate endorectal brachytherapy for locally advanced rectal cancer in previously irradiated patients

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ABSTRACT

PURPOSE: Preoperative high-dose-rate (HDR) endorectal brachytherapy is well tolerated among patients with locally advanced rectal cancer. However, these studies excluded patients who previously received pelvic radiation therapy (RT). Because a favorable toxicity profile has been published for HDR endorectal brachytherapy, we evaluated this technique in patients who have previously received pelvic irradiation.

METHODS AND MATERIALS: We included patients who had received pelvic irradiation for a previous pelvic malignancy and later received preoperative HDR endorectal brachytherapy for rectal cancer. Brachytherapy was delivered to a total dose of 26 Gy in 4 consecutive daily 6.5 Gy fractions.

RESULTS: We evaluated 10 patients who previously received pelvic external beam radiation therapy (EBRT) alone (n=6), EBRT and brachytherapy (n=2), or brachytherapy alone (n=2). The median interval between the initial course of RT and endorectal brachytherapy was approximately 11 years (range, 1-19 years). Two patients experienced a complete pathologic response while 1 patient had a near complete pathologic response. No acute grade ≥3 toxicity was observed. No intraoperative or postoperative surgical complications were observed.

CONCLUSIONS: Preoperative HDR endorectal brachytherapy is an alternative to EBRT for patients with locally advanced rectal cancer who have previously received pelvic RT.

Keywords: Reirradiation; Endorectal brachytherapy; Rectal cancer; High-dose-rate

Introduction

Despite high levels of resectability, local and distant failures are not uncommon for patients with locally advanced rectal cancer (1, 2). Preoperative external beam radiation therapy (EBRT) with or without chemotherapy has a number of benefits over surgery alone or postoperative treatment. In fact, randomized data demonstrate an approximate 50% increase in local control (LC) with preoperative chemoradiation compared with surgery alone in patients with T3, T4, or node-positive disease (1, 3, 4). Currently there is no consensus as to the optimal preoperative EBRT total dose or fractionation schema, although two common regimens include 50–54 Gy in 1.8-Gy fractions with chemotherapy and 25 Gy in 5-Gy fractions without chemotherapy.

The notion of preoperative intracavitary brachytherapy as an alternative to EBRT for locally advanced rectal cancer has become increasingly accepted over recent years. Early data from Yanagi *et al.* showed significantly improved LC in patients treated with preoperative endorectal brachytherapy when compared with historical controls of surgery alone (5). In a Phase I/II trial at McGill University, 49 patients with large T2, T3, or early T4 tumors were treated with endorectal high-dose-rate (HDR) brachytherapy to 26 Gy in four fractions, once daily over 4 consecutive days (6). The authors reported a 32% pathologic complete response (pCR) rate with an additional 36% of patients having only microscopic residual disease. At 29 months' follow-up,

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only one local failure (LF) and five distant metastases were reported. More recent long-term results in 100 patients with a 59-month median follow-up included 5-year LF, disease-free survival (DFS), and overall survival (OS) rates of 5%, 64%, and 68%, respectively (7). These data compare favorably with the 5-year LF rates of the experimental arms of the Dutch, German, European Organization for Research and Treatment, and Fédération Francophone de Cancérologie Digestive trials ranging from 6% to 9% (3, 4, 8, 9). Additionally, the 5-year OS for the radiation arm of these trials was approximately 70%.

Patients who have previously received pelvic irradiation, such as for prostate cancer, are generally not recommended for receiving additional EBRT because of concerns for high risk, long-term complications in tissues that have already received a substantial dose, such as the bowel and bladder. Furthermore, studies examining patients who have undergone definitive radiation therapy for prostate cancer alone have shown an increased incidence of rectal cancer (10, 11). Pelvic reirradiation is typically not recommended for these previously irradiated patients, who are then usually offered surgery alone.

Mohiuddin *et al.* published early Phase I/II data in previously irradiated patients suggesting that pelvic reirradiation to moderate doses (median 34.2 Gy) is feasible (12). Valentini *et al.* later evaluated the feasibility of reirradiation using hyperfractionation based on the relationship between late normal tissue toxicity and fraction size (13). More recently, a single institutional study from MD Anderson also showed that twice-daily (BID) reirradiation for locally recurrent disease increased LC with acceptable late toxicity (14). Although these studies used EBRT, a reirradiation approach employing endorectal brachytherapy would theoretically result in significantly less damage to previously irradiated normal tissues while potentially improving LC by simultaneously permitting dose escalation dose to tumor. To the best of our knowledge, there are no published data using brachytherapy in this regard.

We have treated a series of patients with preoperative endorectal brachytherapy who previously received pelvic irradiation before their diagnosis of rectal cancer. The purpose of this study is to evaluate the safety and efficacy of pelvic reirradiation using preoperative endorectal brachytherapy.

Methods and materials

Patient details

After obtaining approval from our Institutional Review Board, we reviewed our departmental database for all patients with nonmetastatic biopsy-proven T1-4N0-1 rectal adenocarcinoma who received preoperative HDR endorectal brachytherapy alone. Patients who received EBRT in addition to brachytherapy were not evaluated in this study. Patients were included in this study only if they had previously received irradiation to the pelvis (EBRT alone, brachytherapy alone, or combination EBRT and brachytherapy) before their current diagnosis of rectal cancer. All patients in this study were treated with curative intent.

Staging

The initial staging workup included computed tomography (CT) scan of the chest, abdomen, and pelvis, positron emission tomography (PET) scan, colonoscopy, and endoscopic ultrasound, blood chemistries, and carcinoembryonic antigen level.

Simulation and brachytherapy planning

Prior to CT simulation, VisiCoil fiducial markers (Core Oncology, Santa Barbara, CA) were placed endoscopically under endoscopic ultrasound guidance, with a 1-cm margin at the superior and inferior extent of the tumor. Fiducial markers were used during treatment planning to optimize target delineation as well as to ensure accurate placement of the endorectal applicator on a daily basis. At the time of CT simulation, the anal verge was marked with radiopaque wire and the rectum was injected with viscous lidocaine. A semirigid endorectal applicator (Nucletron, an Elekta company [Elekta AB, Stockholm, Sweden]) with eight flexible catheters was placed into the rectal lumen with the patient in a modified lithotomy position. The rectal applicator was then secured to the treatment table with an adjustable clamp. A CT scan using with 3-mm slice interval was obtained from several centimeters superior to the tip of the endorectal applicator to the mid-femur. The tip of the applicator was positioned at least 2 cm cephalad to the superior extent of the visible tumor based on staging endoscopic ultrasound and/or MRI, as shown in Fig. 1. For tumors with semicircumferential involvement, a semicircumferential inflatable standoff balloon was inflated with up to 20 mL of 20% contrasted saline to displace the uninvolved rectum away from the applicator, as shown in Fig. 2. The CT images were then transferred to an Oncentra workstation (Nucletron) and the gross tumor volume, fiducial markers, and pelvic organs at risk were contoured by the physician on the simulation scan. The endorectal applicator and catheters were identified and reconstructed on the simulation CT images by the planning physicist.

An Oncentra workstation was used to generate a treatment plan, including the optimal dwell times and dwell positions within each catheter. Because of the irregular nature of rectal tumors, the treatment catheters were loaded differentially to maximize dose to the target volume and minimize dose to the uninvolved pelvic organs. A total dose of 26 Gy delivered in 4 consecutive daily fractions of 6.5 Gy