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Intraoperative high-dose-rate brachytherapy using dose painting technique: Evaluation of safety and preliminary clinical outcomes

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ABSTRACT

PURPOSE: Intraoperative radiation therapy (IORT) allows delivery of tumoricidal doses of radiation to areas of potential residual microscopic disease while minimizing doses to normal tissues. IORT using high-dose-rate (HDR) brachytherapy allows dose modulation and delivery of concomitant boosts to high-risk areas. This study describes a novel technique of HDR-IORT with dose painting (DP) (HDR-IORT-DP) and evaluates the clinical outcomes.

METHODS AND MATERIALS: Sixteen patients with recurrent cancers received HDR-IORT-DP at the time of radical resection. Of these patients, 13 had colorectal cancer, 2 had head and neck cancer, and 1 had a gynecologic malignancy. All received external beam radiation previously. Negative margin (R0) was obtained in 12 patients (75%) and microscopically positive margins (R1) in 4 patients (25%).

RESULTS: The median total target and boost area were 45 and 8.5 cm^2, and HDR-IORT and boost dose were 1500 and 1750 cGy, respectively. Median followup was 14.9 months. The 2-year local control and overall survival were 80% and 20%, respectively. Eleven patients (69%) developed distant metastasis and were deceased at the time of the last followup. A total of 13 patients (19%) developed Grade 3 toxicity related to HDR-IORT; no grade 4+ toxicities were observed.

CONCLUSIONS: HDR-IORT-DP technique is feasible, safe, and allows for dose escalation in locally advanced or recurrent previously irradiated tumors. To our knowledge, this is the first clinical report on HDR-IORT-DP. Further studies are warranted to evaluate efficacy in a larger patient cohort. Local control was encouraging in our patients.

Keywords: Intraoperative radiotherapy; High-dose-rate brachytherapy; Reirradiation; Dose painting

Introduction

Management of recurrent neoplasms remains a clinical challenge. Despite aggressive surgery, chemotherapy, and/or radiotherapy, locally advanced cancers recur in 15−50% of patients (1). Locoregional relapse after resection of colorectal cancer is associated with poor prognosis, with median survival of 11−15 months, and often as few as 5% of patients survive 5 years (2). Intraoperative radiotherapy (IORT) has been advocated (3) as a component of an aggressive multidisciplinary management in T4 or recurrent tumors. It seems to provide improvement in tumor local control (LC), while limiting dose to normal adjacent structures and minimizing toxicity; this has been the rationale for its use. It is given as a single fraction with doses ranging from 10 to 20 Gy, which has been estimated to have the cell-killing equivalence of two to three times the dose using conventional external beam radiotherapy (EBRT) (3).

IORT can be delivered by several different techniques: electron beam therapy, orthovoltage radiotherapy, and high-dose-rate (HDR) brachytherapy. Most centers use intraoperative electron radiotherapy (IOERT) where the radiation is delivered by a linear accelerator thorough a rigid cone directed to the tumor bed. For HDR brachytherapy technique, a flexible applicator is placed in direct contact to the area to be treated and source guide tubes are

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connected to an afterloader system to deliver the radiation via a ^{192}Ir source.

At our institution, IORT is delivered with HDR brachytherapy using the Harrison–Anderson–Mick (HAM) applicator (Mick Radio-Nuclear Instruments, Inc., NY) that allows a very conformal treatment even on curved and deep body surfaces (4). The use of HDR-IORT is also ideal in particular sites, such as the lateral pelvic sidewall or deep in the pelvis, as well as in pediatric patients, where an electron rigid cone could be relatively inaccessible. Usually, a square/rectangular area is treated. This multiple-channel applicator and the use of computerized treatment planning systems allow for dose optimization by varying source positions and dwell times. The dose can be sculpted inside of the target area permitting dose escalation or de-escalation, allowing for planned nonhomogenous dose distributions or dose painting (DP). This DP technique allows the sites highly suspicious for positive microscopic disease or close margins to be treated to higher doses, while minimizing dose to areas of subclinical spread; normal organs could also be more effectively spared from high or unnecessary doses of radiation.

To our knowledge, this is the first clinical report on HDR-IORT using a DP technique (HDR-IORT-DP). The aim of this study is to describe the HDR-IORT-DP technique and report on the preliminary clinical outcomes of patients treated with this approach.

Methods and materials

Beginning in 2007, the DP technique was introduced for HDR-IORT cases at Memorial Sloan–Kettering Cancer Center; thus the treatment plans for all patients who received IORT after January 2007 were reviewed to identify IORT plans using DP. A total of 207 patients with locally advanced or recurrent neoplasms, who underwent IORT between January 12, 2007 and August 25, 2010 were identified. Among this group, 16 patients (7.7%) received HDR-IORT-DP and comprised our study group: 13 patients had recurrent colorectal cancer, 2 patients had recurrent cancer of the head and neck region, and 1 had a gynecologic malignancy. All patients in this group had undergone surgical resection and EBRT previously and had areas within the field that were identified by the surgeon to be at higher risk of microscopic residual disease or were adjacent to critical structures such as the ureter, where adequate shielding could not be achieved owing to geometric constraints. DP was indicated in these cases to either achieve modulation of the dose and delivery of a concomitant boost to higher-risk areas within the resection bed, while delivering a lower dose to the regions closest to normal structures or to achieve even more conformal dosimetry to a more complicated geometric region within the square or rectangular treatment region created by the HAM applicator. At the time of HDR-IORT-DP, patients were undergoing radical resection with expected close margins owing to locally advanced/recurrent nature of the tumors. Final resection margins were negative (R0) in 12 patients (75%) and microscopically positive margins (R1) in 4 patients (25%). Patient and treatment characteristics are shown in Table 1.

The HDR-IORT-DP was delivered using the HAM applicator, a flexible pad of silicone rubber that has 8-mm thickness and 22 cm in length (Fig. 1). Multiple catheters (3–24) are embedded parallel to each other spaced 10-mm apart, while a fixed source-to-tissue distance of 5 mm is maintained. All procedures were performed in a dedicated shielded operating room. The HDR-IORT-DP technique can be summarized as follows: After tumor resection, the decision to proceed with IORT is based on the radiation oncologist's and the surgeon's impression of the risk for close or microscopically positive margins. If deemed necessary, the area at risk is mapped out by the surgeon and radiation oncologist, and the HAM applicator is chosen with the number of channels to cover the target area appropriately. A sterile, transparent, and flexible template that mimics the HAM applicator and varies in number of channels from 3 to 24 is used to define the ''DP'' regions within the treatment area (Fig. 2). The region for dose escalation and/or de-escalation is demarcated by the radiation oncologist using a surgical pen. The same template is also used when changes in the shape of the radiation field are desired. The template containing this information is given to the physicist to incorporate within the intraoperative treatment planning system. The orientation of the applicator and the template must be established to implement such dose prescriptions correctly. The dose to a larger area (Dose 1) and to the boost region (Dose 2) is determined by the radiation oncologist and prescribed to 0.5 cm from the applicator's surface. The HAM applicator is positioned in direct contact with the area at risk using either sutures or packing to hold the applicator in place (Fig. 3a). Packing is also used to displace normal

Table 1
Patient and dosimetric characteristics

Age, y	62.5 (24–85)
Gender	
Male	10
Female	6
Type of cancer	
Colorectal	13
Head and neck	2
Gynecologic	1
Margin	
R0	12
R1	4
Total area treated (cm^2)	45 (8–136)
Boost area (cm^2)	8.5 (4–42)
Number of channels	7 (3–18)
Number of dwell positions	9 (7–13)
Treatment time (min)	36.5 (12–98)
Dose 1 (cGy)	1500 (1250–1750)
Dose 2 (cGy)	1750 (1750–1850)