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Intensity-modulated radiation therapy for pancreatic and prostate cancer using pulsed low–dose rate delivery techniques

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ABSTRACT

Reirradiation of patients who were previously treated with radiotherapy is vastly challenging. Pulsed low–dose rate (PLDR) external beam radiotherapy has the potential to reduce normal tissue toxicities while providing significant tumor control for recurrent cancers. This work investigates treatment planning techniques for intensity-modulated radiation therapy (IMRT)-based PLDR treatment of various sites, including cases with pancreatic and prostate cancer. A total of 20 patients with clinical recurrence were selected for this study, including 10 cases with pancreatic cancer and 10 with prostate cancer. Large variations in the target volume were included to test the ability of IMRT using the existing treatment planning system and optimization algorithm to deliver uniform doses in individual gantry angles/fields for PLDR treatments. Treatment plans were generated with 10 gantry angles using the step-and-shoot IMRT delivery technique, which can be delivered in 3-minute intervals to achieve an effective low dose rate of 6.7 cGy/min. Instead of dose constraints on critical structures, ring structures were mainly used in PLDR-IMRT optimization. In this study, the PLDR-IMRT plans were compared with the PLDR-3-dimensional conformal radiation therapy (3DCRT) plans and the PLDR-RapidArc plans. For the 10 cases with pancreatic cancer that were investigated, the mean planning target volume (PTV) dose for each gantry angle in the PLDR-IMRT plans ranged from 17.6 to 22.4 cGy. The maximum doses ranged between 22.9 and 34.8 cGy. The minimum doses ranged from 8.2 to 17.5 cGy. For the 10 cases with prostate cancer that were investigated, the mean PTV doses for individual gantry angles ranged from 18.8 to 22.6 cGy. The maximum doses per gantry angle were between 24.0 and 34.7 cGy. The minimum doses per gantry angle ranged from 4.4 to 17.4 cGy. A significant reduction in the organ at risk (OAR) dose was observed with the PLDR-IMRT plan when compared with that using the PLDR-3DCRT plan. The volume receiving an 18-Gy (V_{18}) dose for the left and right kidneys was reduced by 10.6% and 12.5%, respectively, for the pancreatic plans. The volume receiving a 45-Gy (V_{45}) dose for the small bowel decreased from 65.3% to 45.5%. For the cases with prostate cancer, the volume receiving a 40-Gy (V_{40}) dose for the bladder and the rectum was reduced significantly by 25.1% and 51.2%, respectively. When compared with the RapidArc technique, the volume receiving a 30-Gy (V_{30}) dose for the left and the right kidneys was lower in the IMRT plans. For most OARs, no significant differences were observed between the PLDR-IMRT and the PLDR-RapidArc plans. These results clearly demonstrated that the PLDR-IMRT plan was suitable for PLDR pancreatic and prostate cancer treatments in terms of the overall plan quality. A significant reduction in the OAR dose was achieved with the PLDR-IMRT plan when compared with that using the PLDR-3DCRT plan. For most OARs, no significant differences were observed between the PLDR-IMRT and the PLDR-RapidArc plans. When compared with the PLDR-3DCRT plan, the PLDR-IMRT plan could provide superior target coverage and normal tissue sparing for PLDR reirradiation of recurrent pancreatic and prostate cancers. The PLDR-IMRT plan is an effective treatment choice for recurrent cancers in most cancer centers.

Introduction

Local recurrences in patients with cancer who were previously irradiated pose a significant clinical challenge. Reirradiation

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therapy is a common treatment option in those patients who are unable to tolerate surgery and chemotherapy. However, reirradiation of patients who were previously treated with radiotherapy is vastly more challenging, particularly when attempting to deliver potentially curative doses more than 5000 cGy. The cumulative dose delivered to the surrounding critical organs places them at a high risk for severe toxicity.[1] There is no consensus standard of re-treatment dose constraints for most normal tissues.[2,3] The dangers of re-treatment must be considered because of the radiation resistance of cancer cells.[4] For the purpose of re-treating recurrent disease with larger doses, a new method is needed to enhance repair of radiation damage in normal tissues while maintaining a therapeutic dose to the tumor.

In modern radiotherapy, including conventional radiotherapy, 3-dimensional conformal radiation therapy (3DCRT), intensity-modulated radiation therapy (IMRT), and volumetric-modulated arc therapy (RapidArc), a dose of 200 cGy is delivered at a dose rate of 300 to 600 cGy/min. It takes a few minutes to treat a patient with multiple gantry angles/fields in most cases. Some radiochemical processes, including the generation of free radicals, occur in this short time. However, this interval is too short for most clinically relevant biological repair processes to occur.[5] By reducing the dose rate and increasing the treatment time, cellular repair processes can occur during irradiation. Low–dose rate brachytherapy has been used for the treatment of locally recurrent breast cancer and head and neck cancer.[6,7] Some institutions have reported that a similar pulsed low–dose rate (PLDR) external beam radiotherapy has been developed for treatment of recurrent cancers, such as malignant tumors, breast carcinoma, and glioblastoma multiforme.[8,9] Low–dose rate radiotherapy takes advantage of a second intriguing radiation phenomenon known as low-dose hyperradiosensitivity, which is increased radiosensitivity to doses less than 30 to 50 cGy, depending on cell types. Data are reported on the low dose response of many human cell lines,[10] most of which have confirmed low-dose hyperradiosensitivity.[11,12] A low–dose rate external beam can be obtained from aging Cobalt-60 sources, which are seldom used in the clinic. Another method is to divide a daily treatment fraction into a number of equal subfractions delivered in a pulsed manner separated by a fixed interval.[5] A team at the University of Wisconsin developed a technique, which they termed pulsed reduced–dose rate radiotherapy.[1,5,8,9] The treatment plans included opposed lateral fields, wedge-pair fields, and multiple field techniques using 3-dimensional conformal planning. A standard dose of 200 cGy was divided into 10 beams administered at 3-minute intervals, resulting in an effective dose rate of 6.67 cGy/min. The dose rate of the accelerator was reduced to 100 cGy/min during the treatment. The monitor units (MUs) of each pulsed beam were calculated to deliver an average dose of 20 cGy to the target volume.

Advanced radiation therapy using the RapidArc delivery technique (Varian Medical Systems, Palo Alto, CA) has been investigated at Fox Chase Cancer Center, Philadelphia, PA.[4] Of 20-cGy pulsed full or partial arcs, 10 were separated by 3-minute intervals with an apparent dose rate of 6.67 cGy/min and the maximum subfractional dose of 35 cGy. The PLDR-RapidArc technique can provide superior target coverage and lower doses to normal tissues. Considering that IMRT has received widespread application in China in recent years, and most hospitals do not have the hardware and software to adopt the RapidArc technique, it is useful to investigate the IMRT technique for PLDR treatment. In this study, we investigated treatment planning techniques for IMRT-based PLDR treatment of different sites, including cases with pancreatic and prostate cancer. In the optimization, we use simple ring structures plus reference constraints to ensure that the maximum dose of each gantry angle in the target volume does not exceed 35, and the mean dose is maintained at 20 cGy approximately.

Methods and Materials

Patient cases and planning objectives

A total of 20 patients with clinical recurrence were selected for this study, including 10 cases with pancreatic cancer and 10 with prostate cancer. Table 1 lists the planning target volume (PTV) for each patient and the field setup in each plan. The mean volume of PTV is 552.50 ± 230.80 cm^3 (range: 301.60 to 1063.70) for cases with pancreatic cancer and 195.90 ± 66.40 cm^3 (range: 92.60 to 345.20) for cases with prostate cancer. The large variation of PTV was intended to test the ability of IMRT, using the existing treatment planning system and optimization algorithm, to deliver uniform doses in individual gantry angles/fields for PLDR treatments.

Table 1
The PTV for the 20 patients investigated and the gantry (couch) angles for each plan. For example, 30 (C90) means 30° gantry angle and 90° couch angle in PLDR-IMRT plans. In PLDR-RapidArc plans, 179.9/180.1 stands for the start/stop gantry angle

Patient	PTV (cc)	Setup of treatment fields (gantry and couch)		
		PLDR-3DCRT (deg.)	PLDR-IMRT (deg.)	PLDR-RapidArc (deg.)
Pancreas 1	862.0	170, 80, 30, 330, 280	160, 85, 65, 35, 330, 300, 270, 200, 30 (C90), 330 (C90)	179.9/180.1
Pancreas 2	486.0	180, 80, 30, 330, 280	160, 85, 60, 30, 330, 300, 280, 195, 30 (C90), 330 (C90)	179.9/180.1
Pancreas 3	530.3	180, 80, 30, 330, 280	160, 80, 60, 35, 330, 305, 285, 200, 30 (C90), 330 (C90)	179.9/180.1
Pancreas 4	424.6	160, 70, 0, 315, 270	170, 80, 55, 30, 0, 345, 330, 315, 300, 285	179.9/180.1
Pancreas 5	512.8	170, 80, 40, 340, 270	170, 80, 60, 40, 20, 330, 305, 280, 30 (C90), 330 (C90)	179.9/180.1
Pancreas 6	468.9	170, 60, 20, 340, 290	170, 80, 60, 40, 20, 330, 305, 280, 30 (C90), 330 (C90)	179.9/180.1
Pancreas 7	301.6	170, 60, 20, 320, 270	170, 80, 60, 40, 20, 330, 305, 280, 30 (C90), 330 (C90)	179.9/180.1
Pancreas 8	1063.7	170, 70, 20, 330, 270	170, 100, 75, 35, 325, 300, 280, 260, 30 (C90), 330 (C90)	179.9/180.1
Pancreas 9	477.2	190, 105, 60, 0, 310	180, 110, 90, 70, 50, 30, 0, 330, 300, 270	179.9/180.1
Pancreas 10	397.6	180, 90, 30, 330, 270	170, 80, 55, 30, 340, 320, 300, 280, 30 (C90), 330 (C90)	179.9/180.1
Prostate 1	92.6	180, 90, 0, 270	110, 90 (C20), 90 (C340), 60, 20, 340, 300, 270 (C20), 270 (C340), 250	179.9/180.1
Prostate 2	175.1	180, 90, 0, 270	100, 75 (C20), 75 (C340), 45, 15, 345, 315, 285 (C20), 285 (C340), 260	179.9/180.1
Prostate 3	345.2	180, 90, 0, 270	110, 90 (C20), 90 (C340), 60, 20, 340, 300, 270 (C20), 270 (C340), 250	179.9/180.1
Prostate 4	139.0	180, 90, 0, 270	110, 90 (C20), 90 (C340), 60, 20, 340, 300, 270 (C20), 270 (C340), 250	179.9/180.1
Prostate 5	171.3	180, 90, 0, 270	100, 75 (C20), 75 (C340), 45, 15, 345, 315, 285 (C20), 285 (C340), 260	179.9/180.1
Prostate 6	211.3	180, 90, 0, 270	110, 90 (C20), 90 (C340), 60, 20, 340, 300, 270 (C20), 270 (C340), 250	179.9/180.1
Prostate 7	191.0	180, 90, 0, 270	110, 90 (C15), 90 (C345), 60, 20, 340, 300, 270 (C15), 270 (C345), 250	179.9/180.1
Prostate 8	232.0	180, 90, 0, 270	110, 90 (C10), 90 (C350), 50, 20, 340, 310, 270 (C10), 270 (C350), 250	179.9/180.1
Prostate 9	220.5	180, 90, 0, 270	110, 90 (C20), 90 (C340), 60, 20, 340, 300, 270 (C20), 270 (C340), 250	179.9/180.1
Prostate 10	180.8	180, 90, 0, 270	110, 90 (C20), 90 (C340), 60, 20, 340, 300, 270 (C20), 270 (C340), 250	179.9/180.1