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Original article

Multiple-CT optimization of intensity-modulated proton therapy – Is it possible to eliminate adaptive planning?

Xianliang Wang [a,b,c], Heng Li [a], Xiaorong Ronald Zhu [a], Qing Hou [b], Li Liao [d], Bo Jiang [e], Yupeng Li [a], Pei Wang [c], Jinyi Lang [c], Xiaodong Zhang [a,*,1]

[a] Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, USA; [b] Key Laboratory of Radiation Physics and Technology, Institute of Nuclear Science and Technology, Sichuan University; [c] Department of Radiation Oncology, Sichuan Cancer Hospital & Institute, Chengdu, China; [d] Global Oncology One, Houston, USA; [e] Department of Radiotherapy, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China

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ABSTRACT

Background and purpose: We hypothesized that a plan's robustness to anatomical changes can be improved by optimizing with multiple CT scans of a patient. The purpose of this study was to determine whether an intensity modulated proton therapy (IMPT) plan could be developed to meet dose criteria on both planning and adaptive CT plans.

Material and methods: Eight lung cancer patients who underwent adaptive IMPT were retrospectively selected. Each patient had two CTs: a primary planning CT (PCT) and an adaptive planning CT (ACT), and IMPT plans associated with the scans. PCT and ACT were then used in combination to optimize one plan (MCT plan). The doses to the target and organs at risk from the PCT plan, ACT plan, P-ACT plan (PCT plan calculated on ACT data), and MCT plans calculated on both CTs were compared.

Results: The MCT plan maintained the $D_{95\%}$ on both CTs (mean, 65.99 Gy on PCT and 66.02 Gy on ACT). Target dose coverage on ACT was significantly better with the MCT plan than with the P-ACT plan ($p = 0.01$). MCT plans had slightly higher lung V_{20} (0.6%, $p = 0.02$) than did PCT plans. The various plans showed no statistically significant difference in heart and spinal cord dose.

Conclusions: The results of this study indicate that an IMPT plan can meet the dose criteria on both PCT and ACT, and that MCT optimization can improve the plan's robustness to anatomical change.

Intensity-modulated proton therapy (IMPT), with its sharp distal fall-off of the Bragg peaks, offers dose advantages over intensity-modulated photon therapy [1–3]. Effective use of the characteristics of proton beams can improve local control of tumors and reduce side effects to organs at risk (OARs) [4–6]. However, the high dose gradients of IMPT makes this modality particularly sensitive to range and setup uncertainties and patient anatomical changes [7,8]. These uncertainties can make the actual dose in the patient differ from the dose estimated in the treatment plan, in turn could lead to undesirable clinical results. One way to solve the problem of uncertainties in IMPT is to account for them in the optimization process.

The state of art robust optimization takes range and setup uncertainties into account; the optimization objective function for a given iteration is calculated using the worst-case dose distribution or probability methods [9–13]. A robust optimization plan, therefore, is significantly less sensitive to range and setup uncertainties than a conventional optimization plan [14,15]. However, anatomical changes, which are not accounted for in robust optimization, can still lead to large dose deviations from the planned dose during the course of the treatment [16].

Anatomical changes during radiotherapy can be roughly classified as inter-fractional (e.g., daily anatomical variation) or intra-fractional (e.g., respiratory motion). Studies of reducing the dose effects caused by anatomical changes in IMPT are mostly focused on the intra-fractional motion [17–22]. However, the dose differences caused by respiratory motion have been found to be smaller than those caused by daily anatomical variations [16,17]. Because the methods used for minimizing dose effects caused by respiratory motion cannot effectively solve the problem posed by daily anatomical variations, the treatment plan must be constantly adjusted during the course of treatment to ensure that the dose prescription covers the target volume [23,24]. However, this adaptive planning process itself (e.g., image registration, dose accumulation) introduces difficult-to-quantify uncertainties to

* Corresponding author at: Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, 1840 Old Spanish Trail, Houston, TX, USA.
E-mail address: xizhang@mdanderson.org (X. Zhang).
[1] Department and institution address where the research was conducted: Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, 1840 Old Spanish Trail, Houston, TX, USA.

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the actual dose delivered to the patient, and the process of adaptive planning is very time consuming. Thus, adaptive planning not only increases the work burden for physicians and physicists but also increases the economic burden for patients. Given the need for accuracy in dose delivery, the reduction in adaptive planning is an urgent problem for clinical practice.

The purpose of the current study is to determine if an IMPT plan that is robust to anatomy changes exists. To that end, we hypothesized that the robustness of a plan to inter-fractional anatomical changes can be improved using multiple computed tomography (CT) scans to optimize one treatment plan. We evaluated the multiple CT (MCT) plan on both planning and adaptive CTs to determine if the plan meets dose criteria on both CTs. In addition, we compared the dose characteristics of an MCT plan with those of a plan based on a primary planning CT to ensure that the dose in the MCT plan fell within clinically acceptable parameters. While it is worth noting that the MCT method is clinically infeasible because the adaptive CT is not available till after the patient is under treatment, results of this study are nevertheless critically important as it provides guidance to future direction of robustness optimization and adaptive planning in IMPT.

Materials and methods

Patient data

Eight consecutive patients with lung cancer who were treated with IMPT and underwent adaptive planning in our center from October 2016 to April 2017 were selected for this retrospective study. Table 1 summarizes the characteristics of these patients. Two 4-dimensional (4D) CT data sets were available for each patient: a primary planning CT (PCT) and an adaptive planning CT (ACT). Both CTs were simulated on a GE Light speed 16-slice CT scanner (GE Healthcare, Waukesha, WI). The mean time interval between PCT and ACT was 34 days. Each 4D CT data set included data for 10 respiratory phases along with maximum-intensity projection and average-intensity projection data. The average-intensity projection data set was used as the primary data set for planning. The targets of PCT were contoured in the following way: the internal gross tumor volume was contoured using the gross tumor volume on each respiratory phase or using the maximum-intensity projection and verified through different breathing phases. The clinical target volume (CTV) was defined by expanding the internal gross target volume by 8 mm. The planning target volume (PTV) was obtained as a 5-mm isotropic expansion of CTV.

Prior to the process of delineation, the ACT was registered with the PCT using rigid registration of the bony anatomy on an Eclipse treatment planning system (TPS) (Varian Medical Systems, Palo Alto, CA). The contours of the PCT were copied to the ACT and then modified and confirmed by the treating physicians. The average CTVs for PCT and ACT were 420.19 cm^3 and 418.55 cm^3, respectively.

There was negligible variation in the CTV volume of PCT and ACT (Table 1). However, the range and spread-out Bragg peak (SOBP) for each field varied enormously (Fig. 1), which is an indication for adaptive planning. Deviations in range and SOBP were calculated as $100 \times (N_{ACT} - N_{PCT})/N_{PCT}$, where N was the range or SOBP calculated using the Eclipse TPS.

Table 1
Patient and planning CT characteristics.

Patient number	Age (y)	PCT CTV (cm^3)	ACT CTV (cm^3)	Interval (days)	Tumor location
1	71	1006.60	1000.30	22	Middle right
2	79	199.70	199.00	34	Middle left
3	76	394.20	393.00	54	Left
4	74	429.30	432.20	39	Right
5	75	76.10	75.30	28	Right
6	66	263.30	260.70	37	Left
7	72	510.70	508.30	36	Left
8	52	481.60	479.60	22	Middle

Abbreviations: PCT, primary planning CT; CTV, clinical target volume; ACT, adaptive planning CT.

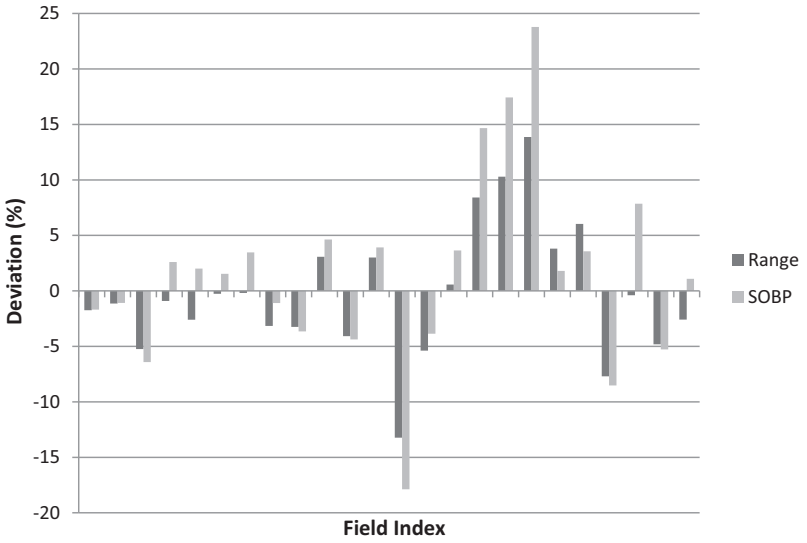

Fig. 1. The percentage deviation of range and spread-out Bragg peak (SOBP) between PCT and ACT for each field.

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