

Clinical Investigation: Gastrointestinal Cancer

Comparison of Various Online Strategies to Account for Interfractional Variations for Pancreatic Cancer

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Summary

Nine different types of online methods that include IGRT repositioning and adaptive radiation therapy replanning for pancreas irradiation were compared retrospectively on daily kV CT images. The full-scale reoptimization would deliver the best dosimetry but would require a large amount of contour generation, which is impractical. A simpler approach such as SAM (segment aperture morphing) that does not require the delineation of the whole contour set could approximate the full-scale reoptimization results.

Purpose: To identify practical techniques to address the large interfractional variations for pancreas irradiation by comparing various used/proposed online strategies.

Methods and Materials: The daily computed tomography (CT) images acquired using a respiration-gated in-room CT (CTVision; Siemens) for 10 pancreatic cancer patients treated with image guided radiation therapy (IGRT) were analyzed. The contours of the pancreas and organs at risk on each daily CT set were generated by populating from the planning CT using a deformable registration tool (ABAS; Elekta) with manual editing. Nine online strategies were considered: (1) standard IGRT (ie, IGRT with 0-mm additional margin [AM]); (2) IGRT with 2-mm AM; (3) IGRT with 5-mm AM; (4) IGRT with plan renormalized to maintain 95% planning target volume (PTV) coverage; (5) full-scale reoptimization; (6) reoptimization starting from the original plan; (7) segment aperture morphing (SAM) from the original plan, based on PTV shape change; (8) SAM plus segment weight optimization; and (9) reoptimization starting from the SAM plan. One-way analysis of variance was applied to plan qualities for the 9 strategies to assess statistical significance in difference.

Results: The 3 IGRT strategies (1-3) lead to either inadequate PTV coverage or higher doses to critical structures, indicating that the additional margins alone are not adequate to account for the changes. The full-scale reoptimization results in the best plan but requires the delineation of several structures, which is time consuming. The SAM strategy (7) was the fastest one, because it requires delineating only 1 structure (target), and its plan quality was comparable to that for the full-scale reoptimization.

Conclusion: Online replanning strategies can lead to either reduced organs-at-risk dose and/or improved target coverage as compared with the current practice of IGRT. The SAM-based online replanning is comparable to full-scale reoptimization and is efficient for practical use.
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Introduction

Pancreatic cancer is the fourth most common cause of cancer death in United States. The prognosis is poor, approximately 5% at 5 years (1). Efficacy of definitive radiation therapy for pancreatic cancer is restricted by the dose limits of the surrounding organs at risk (OARs), mainly the duodenum, small and large bowels, stomach, kidneys, and liver (2). If surrounding OARs can be better spared, dose could be escalated, which would improve tumor control. One of the factors that hinder this is the intra- and interfractional variations, which necessitate the use of large treatment margins (eg, 1.5-2.0 cm). The current practices of respiratory motion management (3) and daily online image guided radiation therapy (IGRT) repositioning (4) cannot completely account for the intra- and interfractional variations. The remaining uncertainties, such as rotations, deformations, and other residual errors, can require margins as large as 10 mm (5). A better way to address interfractional variations is online adaptive replanning, whereby a new plan is generated either from scratch or by modifying the original plan according to the anatomy of the day right before treatment delivery.

Generation of a new plan from scratch using the image of the day would handle all the interfractional variation and thereby eliminate all the interfractional margins; however, this is time consuming, preventing daily implementation with currently available technology. There have been other alternatives proposed for daily plan adaptation that are not very time consuming yet provide significant dosimetric improvement (6). However, those methods are mostly specialized toward specific sites, such as prostate, and may not be applicable directly to pancreas cases. A recently reported strategy (7) that consists of 2 distinct steps of intervention, (1) segment aperture morphing (SAM); and (2) segment weight optimization (SWO), has been shown to perform better than the IGRT repositioning for pancreatic tumors (5). It would be interesting to see how a SAM+SWO strategy can compare with SAM alone and with full-blown reoptimization. Segment aperture morphing modifies the shapes of the segments in the treatment plan on the basis of the variation in the target's projection in the beam's-eye view of daily versus planning target volumes (PTVs) and therefore only requires the daily target volume to be present. This is a distinct advantage of SAM compared with full-blown reoptimization or SWO, which requires delineation of all targets and OARs. Such extensive delineation would be very time consuming, a major obstacle for online intervention.

The main goals of this work were: (1) to evaluate dosimetric gains for online replanning; and (2) to compare several possible alternative methods in terms of their dosimetric advantages and practicality. Nine online strategies of various forms of reoptimization, SAM+SWO replanning, and IGRT repositioning are explored for pancreas irradiation.

Methods and Materials

A total of 249 daily kilovoltage (kV) computed tomography scans (CTs) acquired for 10 pancreatic cancer patients during IGRT using a CT-on-Rails and linear accelerator combination (CTVision; Siemens Health care, Malvern, PA) were included in this retrospective analysis. All patients received 50.4 Gy to the PTV in the head of pancreas in 28 fractions. The daily CTs had a resolution of approximately $1 \times 1 \times 3$ mm. The respiratory motion was

either <3 mm or was managed with respiratory gating. The image sets of the 4-dimensional CT for phases 40% to 60% (end-expiration) were used to generate the original treatment plan.

The original volumes of the pancreas head, which is the clinical target volume (CTV), duodenum, liver, small bowel, large bowel, spinal cord, stomach, and kidneys were drawn by a physician. To generate daily contours, these contours were transferred to the daily CT sets using a deformable registration based autosegmentation tool (ABAS; Computerized Medical System, St Louis, MO) followed by manual editing to ascertain the accuracy of contours. The autosegmentation results were not very accurate for the abdomen region, and most of the contours had large errors that needed to be corrected. The use of respiratory gating in both imaging (planning and daily CT) and treatment delivery enables small margins. A "PTV3mm" structure was generated on both the planning CT and the daily CTs by expanding the CTV by a 3-mm margin to account for all the remaining uncertainties including residual interfractional errors, delineation errors, IGRT error, and Mechanical errors. This PTV3mm on the daily images needs to receive full coverage and was used as the target for all daily plan optimizations. The interfractional errors—if not accounted for by an online strategy—would require an additional margin (AM) on top of the PTV3mm. In this work, we considered 3 different AMs: 0 mm, 2 mm, and 5 mm.

For each case, intensity modulated radiation therapy (IMRT) plans were generated based on the planning CT and daily CT sets with a planning system (Panther; Prowess Inc., Chico, CA) using the same dose volume constraints. Efforts were made to achieve high target dose uniformity ($\sim \pm 5\%$) and low OAR sparing (eg, lowest possible duodenum dose, especially in the >50 -Gy region). All plans were normalized to have 95% of targets (PTV3mm + AM) receive 50.4 Gy.

Nine plans for 9 online strategies were generated for each daily CT set: (1-3) IGRT_0, IGRT_2 and IGRT_5 plans: generated from original plans with AM = 0 mm, 2 mm, and 5 mm, respectively, based on standard IGRT repositioning (ie, translating the plan on the basis of the best anatomic match between plan and daily CT, without any modification to the plan); (4) IGRT_ReNorm plan: same as IGRT_0 plan but renormalized to achieve 95% coverage of PTV3mm; (5) ReOpt_0 plan: generated by full-scope reoptimization starting from scratch; (6) ReOpt_OR plan: generated by reoptimization starting from the original plan (multileaf collimator [MLC] positions and monitor units [MUs]); (7) SAM plan: generated from the SAM algorithm; (8) SWO plan: generated with the SWO for the SAM plan; and (9) ReOpt_SAM plan: generated by reoptimization starting from the SAM plan (scenario 7).

The first 3 scenarios, mimicking the current clinical IGRT practice (with different margins), use original plans (no replanning or plan modification). The IGRT_ReNorm plan, obtained from rescaling the IGRT_0 plan, does not require replanning (only changing MU, not segment shapes) but only needs the delineation of the target (PTV3mm) for the rescaling.

Scenarios 5-9 require replanning (including plan modification). Scenario 5 (ReOpt_0) requires the full set of contours, including both targets and OARs. Scenario 6 (ReOpt_OR), starting optimization from an existing plan (ie, the original plan), takes advantage of a reduced search space and a quicker convergence to an optimum solution and is less likely to be stuck to a local minimum, as compared with that from scratch. Typically the reoptimization starting from an existing plan takes approximately one-third to one-quarter of the reoptimization time compared with that started from scratch. Scenario 7, the SAM plan, was generated

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