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Adaptive radiotherapy

Development of an online adaptive solution to account for inter- and intra-fractional variations ☆

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ABSTRACT

Purpose: The current IGRT repositioning cannot fully account for the organ deformation and rotation. We introduce a comprehensive solution using gated IMRT with online adaptive replanning to manage both inter- and intra-fractional variations.

Methods and materials: The solution includes (1) generating respiration-gated IMRT plans based on 4DCT, (2) acquiring daily gated CT in treatment position prior to the treatment using a diagnostic-quality in-room CT (CTVision, Siemens) with the same gating window as that for the planning CT, (3) performing online repositioning or adaptive replanning based on the gated CT of the day, and (4) delivering the treatment with gating. The entire solution is demonstrated with RT data from 10 selected pancreatic cancer cases. The dosimetric impact of various advanced delivery technologies was investigated.

Results: The online adaptive replanning based on the CT of the day combining with gating significantly improves normal tissue sparing during RT for pancreatic cancer. As the complexity of the delivery technology increases from no IGRT to with IGRT, gating and online adaptive replanning, the inter- and intra-fractional variations can be accounted for with increased adequacy.

Conclusion: The online adaptive replanning technique based on daily respiration-gated diagnostic-quality CT combined with gated delivery can effectively correct for inter- and intra-fraction variations during radiation therapy.

The large inter- and intra-fraction variations during the delivery of radiation therapy (RT) have been well recognized as one of the major factors limiting the effectiveness of RT for many tumor sites [1,2]. Abdominal targets, such as the pancreas are examples of the treatment sites that can experience more than 2 cm inter- and intra-fractional variations [2–6]. To account for such large variations, a large margin between the planning-target volume (PTV) and the clinical-target volume (CTV) is conventionally used to ensure an adequate coverage of the CTV. For example, the PTV-to-CTV margins are usually 1–1.5 and 1.5–2.0 cm for prostate and pancreas, respectively, with the conventional RT delivery [1,2]. The large PTV-to-CTV margins result in the irradiation of normal structures with high doses. The normal tissue toxicity is commonly the limit for delivering a curative dose to the tumor.

In the last two decades, tremendous effort has been spent in RT community to develop technology and methodology to account for the inter- and intra-fraction variations. The respiration motion is the major source for intra-fraction variations in thorax and abdomen. The recently developed respiration gating is one the effective techniques to reduce the effect of respiration motion by synchronizing the RT delivery with respiration [7]. The development of image-guided RT (IGRT) in recent years has allowed us to image the patient in the treatment position and has made it possible to address the inter-fraction variations [1,8]. Because of this great promise, IGRT is being rapidly introduced into the clinical setting. The current standard practice of IGRT is to reposition the patient based on the rigid-body registration of the planning CT and the daily treatment CT acquired before the treatment. This repositioning method is not capable of addressing organ deformation and rotation and independent motion between different organs, which are the major components of inter-fractional motion for many tumors including pancreatic tumor [9,10].

The ideal method to account for inter-fractional variation is to generate a new IMRT plan from a full optimization based on the image taken immediately before treatment. However, such a process is too lengthy to be realistically implemented with today's treatment planning technology, while the patient is lying on the table. Recently, several approaches have been proposed or developed [11–15] to address this issue. For example, our group has developed a two-step process of online adaptive replanning [15,16]. This process includes segment aperture morphing (SAM) and segment weight optimization (SWO). SAM corrects for both deformation

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and translation of the target by means of multi-leaf collimator adjustments, therefore the requirement of a couch shift is eliminated. SWO improves on the SAM plan by determining the optimum monitor units for each segment.

In this work, we introduce a comprehensive solution including (i) using respiration-synchronized diagnostic-quality imaging to guide online repositioning or adaptive replanning to manage inter-fractional variations and (ii) using respiration-gated delivery to address the intra-fraction respiration motion. Pancreatic cancer is used as a testing model to demonstrate the implementation and dosimetric advantages of this solution.

Methods and materials

Data from 10 pancreatic cancer patients treated in our institution were selected to demonstrate the solution. These data include planning CTs, treatment plans, and daily treatment CTs.

Management of intra-fractional respiration motion

The process started with a 4DCT scan acquired and sorted into 10 phases in a respiration cycle using a CT scanner (LightSpeed, GE). The target (whole pancreas or pancreatic head) was delineated based on the CT at the end of exhale (50% phase), which was then populated onto the CTs of other respiratory phases using a deformable image registration tool (ABAS, CMS/Elekta). The ABAS-generated contours were carefully reviewed and manually modified if necessary. Internal target volume (ITV) for three breathing phases at the end of exhale (ITV_3) was generated based on the union of the target contours of the three phases of 40%, 50%, and 60%. (Note that for simplicity, we only use these three phases in this work, although other phases may be used to design a gated plan.) A margin that was estimated to account for residual respiration motion and other non-respiration intra-fractional variations (e.g., the motion cause by the table rotation for treatment CT acquisition, physiological organ motion, and contour delineation uncertainty) was added to ITV_3 to form the PTV. To investigate the effect of reducing respiration motion on the target volume, the ITV for all 10 breathing phases (ITV_{10}, the union of the target contours in the 10 phases) was also generated for the 10 cases studied.

All the contours of organs at risk (OAR), including the duodenum, stomach, liver, kidneys, and bowels, were drawn on the 50%-phase CT. An IMRT plan was generated using a planning system (Prowess Inc.) based on the 50%-phase CT. The plan was delivered under respiration gating with beam turning on during 40% and 60% phases in each breathing cycle [17]. During the image acquisition of planning and daily treatment CTs and treatment delivery, the patient was asked to breathe freely and his/her breathing pattern was monitored in real time. If an unstable or a different breathing pattern from that recorded during the planning CT acquisition is observed, the gated treatment CT acquisition or the treatment delivery will be interrupted.

Management of inter-fractional variations

Prior to each treatment delivery, a gated CT was acquired during 40–60% phases using an in-room CT (CTVision, Siemens) with the patient in the treatment position. This gated treatment CT was registered with the planning CT (of the same breathing phases) based on soft-tissue alignment using a software tool (AT, Siemens). The translational shifts required to reproduce the patient position as that at the planning CT acquisition were calculated. The patient was then repositioned following the shifts prior to the delivery of each treatment fraction.

All pancreatic cancer patients analyzed in this study were treated with gated in-room CT guided gated IMRT following the above process. In the situation that the inter-fractional organ deformation and rotation and/or independent motion between different organs are severe, i.e., cannot be adequately accounted for by the PTV margin, the following online adaptive replanning (adaptive RT or ART) process [15,16] is proposed: (1) generating contours of target and OAR based on the daily gated CT by auto-segmentation using ABAS, (2) morphing segment apertures based on new contours and optimizing weights of the new apertures to generate the adaptive plan, (3) computing and comparing dose distributions between the adaptive plan and the original plan with patient repositioning, (4) transferring and performing QA tests (independent MU calculation and validation of planning data transfer) for the adaptive plan with an in-house developed software tool, and (5) delivering the adaptive plan under gating. This online adaptive replanning process was implemented in a commercial product (RealART, Prowess Inc.) and was tested with the daily CT acquired for the 10 selected pancreatic cancer cases.

Dosimetric impact of different delivery technologies

To demonstrate the impact of using the advanced delivery technologies, we have generated IMRT plans for five randomly selected pancreatic cancer patients for the four RT delivery options with different levels of complexity: (1) no IGRT for patient positioning and no gating for respiration motion, (2) IGRT repositioning based on soft-tissue alignment but no gating, (3) IGRT repositioning based on soft-tissue alignment and with gating to manage respiration motion, and (4) online adaptive replanning and gating. Different PTV margins were determined and used in these plans. For delivery option (1), a margin of 15 mm was used to account for the inter- and intra-fraction variations based on the data in this work and those reported previously [2–5,9]. Since the use of IGRT reduces/eliminates inter-fractional translational motion, a 12 mm margin was used for option (2) to account for the remaining inter-fractional organ deformation and/or rotation and the intra-fractional motion. For option (3), a margin of 10 mm was used to compensate for the remaining inter-fractional organ deformation and/or rotation and the residual respiration motion. Since online adaptive replanning can completely account for inter-fractional variations including deformation and rotation, the major sources of uncertainty in option (4) would be the variations in residual respiration motion and in the organ delineation. A margin of 3 mm was determined for option (4).

For each selected patient, four IMRT plans with five beams were generated based on the planning CT using the same planning system (Panther 4.71, Prowess Inc.) with a prescription dose of 50.4 in 1.8 Gy fractions. The dosimetric criteria for all IMRT plans were: the PTV covered by 100% of the prescription dose (V_{100}) ⩾95% of PTV, maximum dose ⩽53 Gy for duodenum, maximum dose ⩽43 Gy for spinal cord, the volume irradiated by at least 45 Gy (V_{45Gy}) ⩽50% and maximum dose ⩽52 Gy for stomach and bowels, the volume irradiated by at least 30 Gy (V_{30Gy}) ⩽30% for liver, and the volume irradiated by at least 15 Gy (V_{15Gy}) ⩽25% for kidneys. A series of dose–volume quantities for the PTV and OARs were compared among four plans.

Results and discussion

Management of intra-fraction motion

From the 4DCT acquired, it was found that the respiratory organ motion is mostly along the superior–inferior (SI) direction. The average respiration motion (peak-to-peak amplitudes) of liver, left kidney, right kidney, and pancreas along SI directions were 7.9 ± 3.2, 7.1 ± 3.1, 5.7 ± 3.2, and 5.6 ± 2.7 mm, respectively, for the 10 pancreas cases studied. On average, the ITV was reduced