



Factsheet for the Press (Physics)

DEVELOPMENT OF A COMPREHENSIVE ONLINE ADAPTIVE SOLUTION TO ACCOUNT FOR INTER- AND INTRA-FRACTIONAL VARIATIONS

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Context: The fundamental goal of radiation therapy (RT) is to deliver an effective radiation dose to the tumor while maximally avoiding irradiating its surrounding normal structures. The effective dose is normally delivered in multiple sessions (fractions) based on radiobiological considerations. For example, the current standard RT for prostate cancer is to deliver the treatment doses in 35-44 fractions with one fraction delivered per day. It has been well documented that, during the multi-fraction process, patient setup cannot be reproduced in every fraction and the location, shape and size of patient anatomic structures can change significantly during the irradiation (e.g., due to respiration) and from fraction to fraction. Because of the large geometric variations during each treatment session (intra-fraction variation) and among treatment sessions (inter-fraction variation), a margin of 1 - 2 cm is commonly added around the tumor to form the planning target volume (PTV), in order to ensure that the tumor is adequately treated. This large PTV margin results 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. The problem of these large intra- and inter-fraction variations has been one of the major factors limiting the effectiveness of RT. In the last two decades, tremendous effort has been spent in RT community to develop technology and methodology to account for these variations. In this work, we developed a comprehensive solution, online adaptive replanning technique based on daily respiration-gated diagnostic-quality CT, to effectively account for inter- and intra-fraction variations. This solution enables "image-plan-treat", a new paradigm for RT that permits shrinking PTV margins and can facilitate accurate RT delivery particularly important for hypofractionations and/or dose escalations.

Purpose: The following method was employed to develop a comprehensive solution: (1) respiratory-gated imaging and delivery to account for intra-fractional respiratory motion and (2) fast online adaptive replanning to handle the inter-fractional variation. Initial planning for IMRT treatment is based on a gated 4D CT (space and time resolution). The fast online replanning is performed using RealArt (Prowess Inc.) based on daily diagnostic-quality CTs acquired with an in-room CT scanner (CTVision, Siemens). The entire solution was validated with phantom measurements and retrospectively tested with 10 selected pancreatic cancer cases. With this solution the Planning Target Volume (PTV) margin can be reduced as small as 3mm, significantly improve tumor targeting for RT.

Findings:

- 1) Intra- and/or inter-fraction variations in RT can be significant for tumor sites such in thorax, abdomen and pelvis. The current standard RT practice cannot fully address these variations,



even using the most advanced delivery techniques such as IMRT and image-guided RT (IGRT).

- 2) We have developed a fast online adaptive replanning technique that can effectively address the interfraction variation and can be performed within the similar or slightly longer time frame required for the current IGRT practice.
- 3) The online adaptive replanning based on respiration-gated daily CT can account for both intra- and inter-fractional variations, significantly improving tumor targeting by reducing PTV margin to as small as 3 mm.

Impact: The comprehensive solution of online adaptive replanning with respiration gating can substantially reduce PTV margin to as small as 3 mm, resulting in reductions of normal tissue dose by a factor of 5 in RT for pancreatic cancer. Such dose reductions will decrease radiation related toxicities and/or allow dose escalation, improving treatment outcome.

Indicative of a bigger trend in oncology? The online adaptive replanning will enable the “image-plan-treat”, allowing each treatment session to have a new optimal plan based on the images of the day. The online replanning technique combined with the management of respiration motion would reduce/eliminate the effect of intra- and inter-treatment geometric variations and the need for big margins, enabling higher doses to be delivered to the target to enhance cure without increasing normal tissue toxicity. Therefore, this solution represents not only a major paradigm shift but also the future of RT.

“This ambitious work describes the next step in the quest of conformably irradiating a tumour in a highly deforming geometry. The authors have developed an innovative framework in the treatment of pancreatic cancers than enables online planning and delivery for the geometry of the day.”

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