Physics and Imaging in Radiation Oncology 6 (2018) 89–93

Contents lists available at ScienceDirect

Physics and Imaging in Radiation Oncology

journal homepage: www.elsevier.com/locate/phro

Original Research Article

Pre-clinical experience of an adaptive plan library strategy in radiotherapy of rectal cancer: An inter-observer study

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ARTICLE INFO

Keywords:
Plan library
Rectum
Adaptive radiotherapy
Inter-observer study

ABSTRACT

Background and purpose: The clinical target volume (CTV) in radiotherapy of rectal cancer is subject to large deformations. With a plan library strategy, the treatment may be adapted to these deformations. The purpose of this study was to determine feasibility and consistency in plan selection for a plan library strategy in radiotherapy of rectal cancer.

Material and methods: Thirty rectal cancer patients were included in this retrospective study with in total 150 CBCT scans. A library of CTVs was constructed with in-house built software using population statistics on daily rectal deformations. The library consisted of five plans based on: the original CTV, two larger, and two smaller CTVs. An inter-observer study (study-I) was performed to test the consistency in plan choices between four observers (all RTTs). After five months the observers were asked to re-evaluate (study-II) the same set of scans based on refined guidelines.

Results: In study-I the observers reached accordance with the majority choice in 69% of cases. This improved to 87% in study-II. The consensus meeting revealed that inconsistency in choices mainly arose from inadequate instructions, which were later clarified and formulated more accurately.

Conclusion: Plan selection based on daily CBCT scans for rectal cancer patients is feasible, and can be performed consistently by well-trained RTTs.

1. Introduction

Clinical target volume (CTV) shape variation is a major geometric uncertainty [1] in radiotherapy of rectal cancer. To account for this, large planning target volume (PTV) margins are needed. Despite intensity modulated radiation therapy (IMRT) and on-line position verification which can reduce the dose to the normal tissues and organs at risk, for example; small bowel [2,3], large PTV margins are still necessary. Several studies have shown a clear relationship between dose to the small bowel and acute radiation enteritis, as well as late toxicity, such as chronic diarrhea, bowel stricture, perforation and hemorrhage [4–6]. By implementing an adaptive strategy with a plan library for radiotherapy in rectal cancer patients, CTV shape variations can be partly accounted for. This allows a reduction in PTV margins, which could lead to a reduction of dose to the small bowel and to other healthy tissue.

The concept of a plan library involves the a priori creation of a number of plans based on changing patient anatomy and then selecting one of these plans on a daily basis [7]. For example: a planning CT (pCT) is a snap shot of the pelvic region at a certain point in time. Within the pelvic region organs like bladder, rectum and small bowel can show organ filling which is not representative for the filling on treatment days [8]. Despite strict protocols for bladder and rectum filling, radiation side effects, non-compliance and dysfunction due to the presence of tumor tissue, will lead to day-to-day variations [9]. With a library of treatment plans it is possible to choose the best fitting plan based on the patient's anatomy for that particular day.

The plan library approach has been successfully applied in several institutes for bladder and cervical cancer [10,11]. For these sites, libraries were created by interpolation of structures of interest defined on CT scans in full and empty bladder state. However, for rectal cancer patients this approach was not feasible, as a major source of uncertainty was not bladder, but rectal filling [9]. For our study, the library was therefore based on patient population data studied by Nijkamp et al. [1]. They concluded that the systematic CTV shape variation was heterogeneous and ranged from 0.2 cm SD close to bony anatomy to 1.0 cm SD at the upper-anterior edge of the mesorectum. This heterogeneous error distribution is reflected in the libraries that were created for this

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https://doi.org/10.1016/j.phro.2018.06.003
Received 6 February 2018; Received in revised form 28 May 2018; Accepted 1 June 2018

current study [12]. In this novel method the libraries were generated using ± 1 and 2 SDs of the patient population data from the original CTV. Thus broadly speaking, this plan library strategy was used to correct for a major part of the systematic error, while the margins compensated for random variations in filling, plus organ deformations.

In 2016 de Jong el al. [13] reported an inter-observer study on plan selection for rectal cancer patients. Our study is comparable to the study of de Jong et al. since we both preformed an inter-observer study for a plan library strategy in rectal cancer. However, there is an important difference in the methods that were used to create the plan library. De Jong et al. used plans with different PTV margins at the ventral side of the upper mesorectum position. Their PTV margins were varied based on rectal and bladder filling on the planning CT. In our study the library was generated by in-house developed software containing; population statistics, different rectal regions and different rectal movement [12]. So the aim of this study was to investigate the feasibility of plan selection in rectum cancer patients and to determine inter-observer consistency in plan selection, given the sometimes challenging image quality of CBCT data.

2. Materials and methods

2.1. Patients and treatment

Thirty rectal cancer patients were included in this retrospective study. The patient group consisted of nineteen males and eleven females with an average age of 67 years. See supplementary material 1 for patient characteristics. Patients received short-course-radiotherapy (SCRT), 5xGy with on-line position verification using daily CBCT. All patients received full bladder instructions: i.e. to empty the bladder and drink a fixed amount (350 ml) of water 1 h before pCT and each treatment fraction. All pCT scans were acquired with a flat table top. The patient was scanned in supine position with a knee support. The scan length included the L4-L5 junction as the cranial border and the trochanter minor as the caudal border. Delineations on the pCT were performed according to the guidelines by Roels et al. [14]. The CTV contained the mesorectum-upper and -lower (separately [9]), presacral area, pelvic lymph node areas (internal iliac lymph node areas and obturator lymph node areas), GTV and if indicated the anal sphincter complex. Delineated organs at risk were femur, bowel area, bladder and vulva/testis. Treatment was delivered (Elekta Synergy, Elekta Oncology Systems Ltd., Crawley, West Sussex, UK) using dual VMAT arcs with 10 MV within 5–7 min including online CBCT registration (120 kV, 32 mA, 40 ms, in 660 frames, over 360 degrees) on bony anatomy of the pelvic area. In total 150 CBCT scans were available for this study.

2.2. Creating a plan library

As explained by Hartgring et al. [12] the method to create plan library CTVs was based on 3D population statistics of the shape variation of the rectum CTV [1]. The population statistics were derived from shape variation data of thirty-three SCRT patients with daily repeat CT scans on which the rectum CTV was delineated. Rather than using patient specific data from several scans only one single pCT was used for structure generation.

The plan library CTVs were created by expanding or contracting the delineated CTV perpendicular to its surface, proportional to the local statistics of shape variation of the population and a global scaling factor, assuming 100% correlation between all regions of the surface. The scaling factor was tuned such that the largest distance between the CTVs was 1 cm. This was done to generate structures with a desired distance from each other.

Besides the original CTV four additional CTVs were created, see Fig. 1 and supplementary material 2; two smaller with a maximum of -1, -2 cm (belonging to treatment plan −1 and plan −2) and two larger with a maximum of +1, +2 cm (belonging to treatment plan 1 and

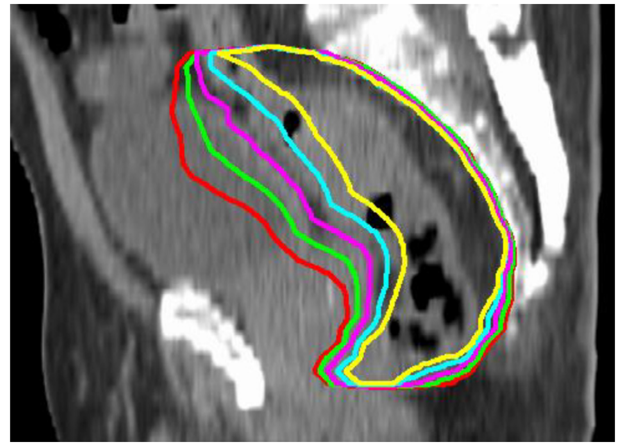

Fig. 1. Example of generated plan library structures (CTVs) on a sagittal planning CT. Purple is the original CTV (Plan 0), aqua is plan -1, yellow is plan -2, green is plan 1 and red is plan 2. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

plan 2) than the original CTV (belonging to treatment plan 0). In total five CTVs were available for plan selection.

By introducing plan library for rectal cancer patients we were able to reduce the PTV margin from 2.5 cm to 1.5 cm in the upper-mesorectum region. This meant that healthy tissues could be spared by selecting plans 0 to −2. Selecting plan “1” gave comparable PTV margins to the original PTV margins without a plan library approach.

2.3. Observer studies

The purpose of the observer studies was to test feasibility of plan selection in rectal cancer patients and to determine the inter-observer consistency in plan selection. For this we performed a baseline measurement (study-I) with four observers (all RTTs). The observers had differing levels of experience in CBCT image registration, one with less experience (three years) and the other three with extensive experience (> 10 years). The aim of study-II was to identify the reproducibility of the plan library approach.

The observers selected plans individually for 150 CBCT scans based on a priori set of instructions. The guidelines consisted of four steps: first, choose the best plan based on the coverage of the whole mesorectum, using the CTV structures. Second, check if that CTV encompassed the tumor (GTV). Third, focus on the ventral part of the mesorectum (less movement is seen at the dorsal part) [9] and fourth, coverage of presacral region is less important due to fewer recurrences in this area, except when the GTV lies within the presacral region [15,16]. We investigated and evaluated the feasibility of plan selection in rectal cancer patients in study-I by scoring the amount of times observers were able to select the correct plan on the CBCT scan images. We defined “correct plan” as: A plan chosen by the majority was determined for each scan. Majority was reached if at least three of the four observers chose the same plan. If only two observers choose the same plan the majority choice was discussed in the consensus meeting and the radiation oncologist made the final decision.

Due to variation in rectal filling, and corresponding differences in movement, we divided the mesorectum in three rectal regions: presacral, upper-mesorectum and lower-mesorectum, see supplementary material 3. For these three regions the optimal plan was selected as well as a plan which covered the whole mesorectum (overall plan). Using this practical approach evaluation of influence by one rectal region in selecting an overall plan would become insightful. The plan number difference between the optimal plan selected for a rectal region and an overall selected plan could been explained as followed: if the observer