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Dose warping uncertainties for the accumulated rectal wall dose in cervical cancer brachytherapy

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ABSTRACT

PURPOSE: Structure-based deformable image registration (DIR) can be used to calculate accumulated dose volume histogram parameters for cervical cancer brachytherapy (BT). The purpose of this study is to investigate dose warping uncertainties for the accumulated dose to the 2 cm^3 receiving the highest dose ($D_{2\ cm^3}$) in the rectal wall, using a physically realistic model (PRM) describing rectal wall deformation.

METHODS AND MATERIALS: For 10 patients, treated with MRI-guided pulsed dose rate BT (two times 24 × 0.75 Gy, given in two applications BT1 and BT2), the planning images were registered with structure-based DIR. The resulting transformation vectors were used to accumulate the total rectum dose from BT. To investigate the dose warping uncertainty, a PRM describing rectal deformation was used. For point pairs on $rectum_{BT1}$ and $rectum_{BT2}$ that were at the same location according to the PRM, the dose for BT1 and BT2 was added (D_{PRM}) and compared to the DIR-accumulated dose (D_{DIR}) in the BT2 point. The remaining distance after DIR between corresponding point pairs, defined as the residual distance, was calculated.

RESULTS: For points within the $D_{2\ cm^3}$ volume, more than 75% was part of the $D_{2\ cm^3}$ volume according to both PRM and DIR. The absolute dose difference was <7.3 Gy_{EQD2}, and the median (95th percentile) of the residual distance was 8.7 (22) mm.

CONCLUSIONS: DIR corresponded with the PRM for on average 75% of the $D_{2\ cm^3}$ volume. Local absolute dose differences and residual distances were large. Care should therefore be taken with DIR for dose-warping purposes in BT.

Keywords: Cervical cancer; Brachytherapy; Deformable image registration; Dose accumulation; Uncertainties

Introduction

Locally advanced cervical cancer is commonly treated with concurrent chemotherapy and radiotherapy. The radiation treatment consists of external beam radiotherapy (EBRT) combined with a brachytherapy (BT) boost in multiple applications to the tumor area. After each BT implantation, the 3D dose distribution is calculated using image-guided treatment planning. Planning aims include a recommended dose to 90% of the high-risk clinical target volume (CTV_{HR}) from EBRT and BT of 90−95 Gy_{EQD2}, expressed as equivalent dose in 2 Gy fractions (EQD_2) (1). The dose to the most irradiated 2 cm^3 of the rectum ($D_{2\ cm^3}$), which is associated with rectal toxicity, should not exceed 75 Gy_{EQD2} (2, 3).

It is recommended by the International Commission on Radiation Units and Measurements (ICRU) to assume that the high dose volumes are at the same location on the rectal wall for the evaluation of the cumulative rectum $D_{2\ cm^3}$ of multiple BT applications, meaning that the dose volume histogram (DVH) parameters can simply be added (1). With the ICRU formalism, $D_{2\ cm^3}$ is possibly overestimated, which may lead to errors in establishing the dose-response relationship in the rectum. To avoid overestimating the cumulative $D_{2\ cm^3}$, it may be preferable to sum the 3D dose distributions instead.

When summing the total dose, it is necessary to use deformable image registration (DIR) to account for rectal deformation due to differences in filling and/or the presence

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of air and the effect of the applicator on the position of the rectum. Earlier studies investigated the added value of DIR when calculating cumulative rectal $D_{2\ cm^3}$, and they found small differences (<10%) with direct addition of the $D_{2\ cm^3}$ (4–7). Because of the DIR-related uncertainty, they concluded that there was limited benefit of dose accumulation with DIR over direct addition of DVH parameters.

Indeed, little is known about the reliability of DIR for accumulation of the BT dose in the rectum. Jamema *et al.* analyzed uncertainties when accumulating the BT dose in the rectum, by comparing intensity-based with structure-based matching (6). They found that dose accumulation based on structure-based matching is more reliable than intensity-based matching since intensity-based DIR led to implausible deformation and a systematic underestimation of the dose. Dose accumulation accuracy may improve further when the matching is performed based on a physically realistic model (PRM) that includes an estimate of the biomechanical properties because such properties are not taken into account in the structure-based DIR. As of yet, no studies have investigated the dose warping uncertainties for accumulated BT doses through landmark identification. Such anatomical landmarks cannot be identified through visual assessment on BT planning images (CT/anatomical MRI). We propose to investigate the uncertainties for dose accumulation based on structure-based matching by identifying corresponding point pairs on the rectum wall using a model describing rectal deformation.

The purpose of this study is therefore to accumulate the total BT dose to the rectal wall using structure-based DIR and to investigate dose warping uncertainties using a PRM describing rectal deformation.

Methods and materials

Patients

Ten cervical cancer patients treated with EBRT (45–50 Gy in 1.8–2.0 Gy/fraction) and a pulsed dose rate BT boost, delivered in two applications BT1 and BT2 of 18 Gy each in pulse doses of 75 cGy every hour, were included in this study. EBRT was planned with volumetric modulated arc therapy. For BT, an intrauterine device with ovoids and if needed interstitial needles were used. The interval between the BT applications was <2 weeks. The planning aim was a cumulative D_{90} of 90–95 Gy_{EQD2} from EBRT and BT on the CTV_{HR}. To spare the rectum, the planned cumulative $D_{2\ cm^3}$ from EBRT and the BT applications should not exceed 75 Gy_{EQD2}. Prior to the BT delivery, T_2-weighted Turbo Spin Echo MRI (voxel size: 0.5 × 0.5 × 3.3 mm^3) was acquired on an Ingenia 3T MRI scanner (Philips Healthcare, Best, The Netherlands) (8). On the MRI scans, the rectum was delineated from the rectosigmoid junction to the level of the anal sphincter. Rectum volumes at the time of BT1 and BT2 are described in Supplementary Table 1. BT planning was performed using Oncentra Brachy 4.5 (Elekta, Veenendaal, The Netherlands), using a library for applicator reconstruction, after which the plan was manually optimized. Typical dose distributions are shown in Fig. 1.

Implementation of the PRM

We used a PRM describing rectal deformation to localize corresponding point pairs on the rectum wall because there is a lack of corresponding anatomical landmarks that can be distinguished on the BT planning MRI (9, 10). The principles of the PRM were previously described by Meijer *et al.* (11) and Hoogeman *et al.* (12). This model was already used to quantify rectum displacements (12, 13) and to relate dose surface maps to toxicity (14, 15).

The model is based on physiological characteristics of the rectum (11, 12, 16). The rectum is attached on the dorsal side to the sacrum by the mesorectum. The rectum wall has an inner lining of circular smooth muscle which will stretch and elongate with increased rectal filling. This stretching, which is assumed to always be perpendicular to the central axis is accompanied by an overall narrowing of the rectum wall. Due to this trade-off between rectal wall thickness and stretching of the rectum muscularis, the amount of tissue in the rectal wall is constant in every intersection perpendicular to the central axis. Since displacements along the length of the axis can be neglected, the central axes of the rectum of BT1 and BT2 ($rectum_{BT1}$, $rectum_{BT2}$) are assumed to be fixed in length.

The central axes were constructed using a minimum distance field as described by Zhou *et al.* (17), to find for each lateral plane the voxel with the shortest distance to the boundary (Matlab R2014b, Mathworks Inc., MA) (Fig. 2). Subsequently, the axis was smoothed using a moving average filter with a span of 0.5 cm.

For both $rectum_{BT1}$ and $rectum_{BT2}$, orthogonal planes were constructed at five evenly spaced positions on the axis. For areas of high curvature in the rectum, the planes might intersect. To avoid intersecting planes, only five planes were constructed, and the planes were rotated away from each other if the local curvature of the central axes exceeded a fixed maximum. Next, 100 points were evenly distributed over the intersection curve of each plane with the rectal wall. It was assumed that the rectum is fixed at the dorsal side. This fixed dorsal point was point 1, and it was found by sampling the point on the intersection curve for which the left-right coordinate was closest to that of the central axis. All corresponding point pairs were stored to be used for the DIR evaluation.

DIR and dose accumulation

The dose from BT1 and BT2 was accumulated in EQD_2 using DIR to take into account rectal deformation. First, the BT doses were converted to EQD_2 on a voxel-by-voxel level using LQ-model based equations with an α/β value