ELSEVIER

Brachytherapy ■ (2015) ■

BRACHYTHERAPY

Uncertainties of deformable image registration for dose accumulation of high-dose regions in bladder and rectum in locally advanced cervical cancer

Swamidas V. Jamema[1,*], Umesh Mahantshetty[2], Else Andersen[3], Karsten Ø. Noe[4], Thomas S. Sørensen[5], Jesper F. Kallehauge[3], Shyam K. Shrivastava[2], Deepak D. Deshpande[1], Kari Tanderup[3,5]

[1]*Department of Medical Physics, Tata Memorial Hospital, Mumbai, India*
[2]*Department of Radiation Oncology, Tata Memorial Hospital, Mumbai, India*
[3]*Department of Oncology, Aarhus University Hospital, Aarhus, Denmark*
[4]*Computer Graphics Lab, The Alexandra Institute, Aarhus, Denmark*
[5]*Aarhus University, Aarhus, Denmark*

ABSTRACT

PURPOSE: To compare the dose accumulation for bladder and rectum by deformable image registration (DIR) and direct addition (DA) of dose volume histogram parameters in magnetic resonance image−guided adaptive brachytherapy (IGABT). Two DIR algorithms, contour- and intensity-based, also have been analyzed.

METHODS AND MATERIALS: Patients (n = 21) treated with IGABT for carcinoma cervix under the IntErnational study on MRI-guided BRachytherapy in locally Advanced CErvical cancer protocol were analyzed. Each patient underwent two HDR-BT applications, 1-week apart with two fractions of 7 Gy each delivered per application. For each application, magnetic resonance imaging, volume delineation, reconstruction, treatment planning (BT1 and BT2), and dose evaluation were carried out. BT1 and BT2 images were registered using an intensity-based DIR, followed by deformable dose accumulation (DDA), which was then compared with DA. To compare the intensity-based DIR to other DIR approaches, nine patients were further evaluated using an in-house contour-based DIR algorithm for bladder dose accumulation.

RESULTS: Mean (±standard deviation; range) percentage variation between DA and DDA was found to be 2.4% (±3.3;−1.8, 11.5) and 5.2% (±5.1;−1.7, 16.5) for the rectum and bladder, respectively. The differences between the DA and DDA were found to be statistically significant for both rectum (p = 0.008) and bladder (p = 0.0003). Intensity-based DIR algorithm resulted in a larger mean deviation between DDA and DA as compared with contour-based DIR, although statistically insignificant (p = 0.32). The difference between DDA and DA was 2.4 ± 2.0% and 1.3 ± 1.2%, for intensity- and contour-based DIR, respectively.

CONCLUSIONS: DA of dose volume histogram parameters provides a good estimate to the dose to the organs at risk; DIR based on image intensities may lead to systematic underestimation of dose due to implausible DIR.

Keywords: Deformable image registration; Deformable dose accumulation; Cervix brachytherapy

Introduction

Recent advances in magnetic resonance (MR) image−based brachytherapy (BT) have brought a paradigm shift in the radiotherapeutic management of cervical cancer. Mono-institutional series have shown promising results in favor of MR-image based BT in terms of increased local control and reduced toxicities (1−4). An ongoing multicentric collaborative trial, IntErnational study on MRI-guided BRachytherapy in locally Advanced CErvical cancer

Received 22 June 2015; received in revised form 25 August 2015; accepted 28 August 2015.

Financial disclosure: Aarhus University Hospital was supported by research grants from the Danish Cancer Society, Danish Council for Strategic Research, and CIRRO—the Lundbeck Foundation Center for Interventional Research in Radiation Oncology.

Varian Medical Systems Inc supported the study through access to research software (SmartAdapt).

* Corresponding author. Department of Medical Physics, Tata Memorial Hospital, Mumbai, 400012, India. Tel.: +91 98692 39536; fax: +91 22 2740 5085.

E-mail address: svjamema@gmail.com (S.V. Jamema).

1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2015.08.011

(EMBRACE), will reveal more information on the dose–effect relationship on local control and morbidity using image-guided adaptive brachytheraphy (IGABT; www.embracestudy.dk).

Georg *et al.* (5) investigated a possible correlation between the dose volume parameters D_{2cm^3}, D_{1cm^3}, and $D_{0.1cm^3}$ (minimal dose to the most irradiated 2, 1, and 0.1 cm^3, respectively) and morbidity for rectum and urinary bladder. There are a range of uncertainties in the process of IGABT which have been systematically reported, including contouring (6, 7), applicator reconstruction (8–10), planning (11), interfraction variation (12), and overall uncertainties (13). Many groups have been working and reporting on these uncertainties and possible solutions. One of the uncertainties is deformation of organs (14) which has an impact on the dose accumulation in organs at risk (OARs). These clinical uncertainties may introduce uncertainties in establishing the dose–response relationship.

In a fractionated brachytherapy schedule, the absolute dose to OAR volumes is derived by adding dose volume histogram (DVH) parameters from each fraction. The underlying assumption is that the high-dose region is located in the exact same part of the organ in each BT fraction. This approach has previously been called the "worst case assumption" in the European Group of Curietherapie and the European Society for Therapeutic Radiology and Oncology recommendations because DVH parameter addition will overestimate the dose if the high-dose region moves to a new location (15).

Interapplication variations result in deformation of organs, which may lead to uncertainties in dose accumulation while directly adding the DVH parameters. To provide better estimates of accumulated doses, deformable image registration (DIR) algorithms have been introduced in the recent past, to take into account the variation in the anatomy such as bladder filling and organ motion (16–18). In the recent past, dose accumulation based on DIR has been reported for the bladder (16); however, for the rectum, no data have been reported yet, and in general, the literature is sparse for multifractionated IGABT.

With an aim to estimate, compare, and report, the dose accumulation for the bladder and rectum by DIR and direct addition (DA) of DVH parameters in a multifractionated high dose rate magnetic resonance image-guided adaptive brachytheraphy schedule, we undertook this study.

Methods and materials

Patient material

An analysis of 21 patients treated with IGABT under the EMBRACE protocol was carried out. The treatment protocol of EMBRACE including application, imaging, volume delineation, planning, and dose evaluation was discussed in our previous publication in detail (19). European Group of Curietherapie and the European Society for Therapeutic Radiology and Oncology guidelines for reporting (20, 21) imaging, target volume delineation (21), and applicator reconstruction (22) were followed. Total external beam radiotherapy (EBRT) and BT dose was calculated in terms of biological Equivalent dose (EQD2) using α/β ratios of 3 and 10 Gy, for OARs and targets, respectively (21). We aimed for a total D_{90} for the HR CTV of at least 84-Gy EQD2, which corresponds to 45 Gy of EBRT plus 4×7 Gy BT dose. The EQD2 dose to the OARs was limited by dose constraints of total 90, 75, and 75 Gy for the bladder, rectum, and sigmoid, respectively. Every patient had two applications, 1-week apart with two fractions of 7 Gy each delivered per application. For each application, the patient had undergone MR imaging (MR_1, MR_2), volume delineation, applicator reconstruction, treatment planning (BT_1 and BT_2), and dose evaluation. For MR image acquisition, the patients were transferred to an MRI unit (1.5 T, GE, Signa, UK). Fast Spin Echo (FSE) T1 axial, FSE T2 axial, para-coronal, and parasagittal sequences of 3–4 mm slice thickness and 0–1 mm gap were obtained (23). As per departmental protocol, FSE T2 axial images were used for both target delineation and reconstruction. The same sequence of images with dose distribution was later used for DIR and deformable dose accumulation (DDA).

DDA using intensity-based DIR

The algorithm used in the present study for DIR is based on an optimized derivative of Lucas–Kanade Optical Flow (SmartAdapt; Varian Medical Systems, Palo Alto, CA, USA) (24). The algorithm is solely driven by image intensities and does not apply any constraints related to organ contours or anatomic landmarks. In this article, this algorithm is henceforth referred as "intensity-based DIR."

Initially, we performed a rigid registration based on the applicator, followed by DIR of a region of interest, which included the rectum and bladder separately, followed by evaluation of organ wall alignment (only anterior rectal and posterior bladder wall was considered). This evaluation was based on how closely the organs were aligned in the high-dose region (spatial location of D_{2cm^3}), as they were marked as a contour in this series of patients. No manual adaptation of the anterior bladder wall or the posterior rectal wall alignment, or the alignment in the longitudinal (sup–inf) direction was carried out. In automatic DIR, even if the alignment of the anterior rectal wall, posterior bladder wall, and the whole organ rectum or bladder was not within the criteria of (+/− 2 mm), no manual adjusting was carried out. The manual adjustment of the deformation field vectors was done, by aligning the organ walls with the help of mouse-clicks only in the region of high dose, D_{2cm^3}. With dose gradients of for example 6% per mm in organ walls, we considered that the intensity-based DIR method would be associated with too large uncertainties if we evaluated D_{2cm^3} on organ walls which were >2 mm displaced.

To evaluate the impact of the registration on the dose accumulation, we performed two registrations for each patient with