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Anatomic structure-based deformable image registration of brachytherapy implants in the treatment of locally advanced cervix cancer

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ABSTRACT

PURPOSE: To examine the impact of anatomic structure-based image sets in deformable image registration (DIR) for cervical cancer patients.

METHODS AND MATERIALS: CT examinations of 7 patients previously treated for locally advanced cervical cancer with external beam radiation therapy and from three to five fractions of high-dose-rate brachytherapy (HDR-BT) were used. Structure-based image sets were created from ''free'' structures already made for planning purposes, with each structure of interest assigned a unique, homogeneous Hounsfield number. Subsequent HDR fractions were registered to the pre-treatment external beam radiation therapy and/or the first HDR fraction using commercially available software by rigid alignment (RIG) followed by DIR. Comparison methods included quantification of external contour displacement between source and target images and calculation of mean voxel displacement values. Registration results for structure-based image sets were then compared and contrasted to intensity-based registrations of the original grayscale images.

RESULTS: Utilization of anatomic structure-based image sets resulted in better initial rigid matching (A-RIG) with more importance on applicator positioning and soft tissue structures. Subsequent DIR of anatomic structure-based images allowed for intermodality registrations, whereas all intermodality registrations using original CT images failed to produce anatomically feasible results.

CONCLUSIONS: We have investigated the use of structure-based CT image sets for image registrations and have produced anatomically favorable registrations with excellent matching of external contours as compared to registrations of original grayscale images. Commercial software registrations using treatment-planning structures required no manual tweaking on a per-patient basis, suggesting results are reproducible and broadly applicable.

Keywords: Cervix cancer; Brachytherapy; Uncertainty; Deformable image registration; EBRT; HDR

Introduction

Concurrent chemoradiation involving external beam radiation therapy (EBRT) followed by high-dose-rate intracavitary brachytherapy (HDR-BT) is an effective treatment modality for locally advanced cervical cancer (1–3). The introduction of 3D image-guided adaptive brachytherapy has allowed for significantly improved outcomes (4, 5), although local failures and late toxicities remain an issue (6–8). With the tight margins and steep dose gradients of HDR-BT, planning often becomes a difficult balancing act between coverage of high-risk clinical target volumes (HRCTVs) and constraining surrounding organs at risk

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(OAR). Currently, dose constraints are based on limiting absolute volumes of OAR to a specified dose, assuming the same portion is exposed to the highest dose region each fraction. This approach may overestimate the maximum true OAR dose (9), potentially limiting dose prescribed to the HRCTV (10) and unpredictable dosimetric effects with or without a parametrial boost (11−14). In addition, it is known that there are large deformations caused by the insertion of the applicator, an issue further complicated by the dynamic range of organ motion in the pelvic region and known contouring discrepancies of the target volume (15). In the interest of adaptive radiotherapy, a better understanding of these clinical uncertainties to allow for higher prescription doses and decreased probability and severity of morbidities would be of great value.

Standard treatment protocols recommend image-guided treatment planning by CT or MRI studies taken throughout the course of treatment, with MRI preferred for target delineation and CT an acceptable modality of choice for applicators and surrounding OAR (16−18). Therefore, each patient has multiple images used for treatment-planning purposes; each associated with its own unique dose distribution. The generation of cumulative 3D dosimetric information requires dose accumulation, which means deformable image registration (DIR) of serial images must occur. Correlation of serial images for dose accumulation purposes in the pelvis is challenging for a number of reasons, including but not limited to: (1) the insertion of an applicator introducing large deformations and intensities not present in EBRT images, along with the assumption that the applicator is in the same position with respect to the HRCTV and OAR (19−21); (2) physiologic intrafraction and interfraction variability of the HRCTV, bladder, rectum, and especially sigmoid volumes (22), further complicated by interphysician contouring discrepancies most significant in the sigmoid and HRCTV (15, 23, 24), and (3) shrinkage of the HRCTV that occurs over time, most notably throughout the external beam portion of treatment, making it difficult to determine how to account for the voxels that disappear during the course of treatment (15, 22, 25, 26). Because of the anatomic complexity in this clinical scenario, current prevailing methodology for dose summation uses dose addition of dose volume histogram parameters without DIR, which has been shown to provide a good estimate of dose to OAR (27). Therefore, before using alternative methods such as deformable dose summation, it is important to scrutinize geometric and visual data thoroughly before considering the application of registration results to dosimetry, as resulting dosimetry is only as valuable as the quality of the underlying registrations.

There has been a paucity of data discussing optimization of workflow for multimodality registrations in the pelvic region (28). However, in recent years, interest in hybrid landmark-driven, intensity-based algorithms has increased due to the limitations of pure image intensity-based algorithms (27,29−33). Fortunately, recent developments have provided strategies to evaluate the quality of DIR algorithms, including evaluations based on geometric data alone (34, 35). In this study, we present and evaluate the quality of a hybrid contour-based deformable registration process using commercial software for locally advanced cervical cancer patients undergoing EBRT and HDR-BT.

Methods and materials

Patient material

A retrospective, nonrandomized, institutional review board−approved study of image-based treatment planning was initiated in 2011. Thirty-three clinical cases were available for analysis, each patient previously treated by EBRT and from three to five HDR-BT treatments administered according to the Groupe Européen de Curiethérapie and European Society for Therapeutic Radiology and Oncology working group and American Brachytherapy Society guidelines (17, 36, 37). HDR-BT generally began during Week 4 of EBRT, provided appropriate tumor reduction after EBRT. Administration of HDR-BT occurred once to twice weekly (separated by 72 hours) with no EBRT or chemotherapy on the day of insertion for an overall treatment time of fewer than 8 weeks. Tandem and ring or tandem and ovoid applicators were selected for individual patients, and the same type of applicator was used throughout the course of treatment. Radiopaque contrast was used to fill the Foley catheter in the bladder and pulled down against the urethra. Each fraction included a planning CT, with each CT imaging study including a corresponding RT structure set and an RT Dose file in DICOM format. Velocity (Velocity Medical Systems, Atlanta, GA), an oncology imaging and treatment-planning program by Velocity Medical Solutions, was used for this project to perform registrations of serial images. In this study, we report on the first 7 patients completed, combining for 22 unique HDR to HDR registrations and 15 unique HDR to EBRT registrations to produce the data.

Structure-based image sets

Anatomic structure-based image sets were generated from manually contoured structures by creating multimodality binary image sets using in-house software, with each structure of interest assigned its own unique, homogenous CT value for points within the contoured structure, zero otherwise (28). Structures of interest include the bladder, rectum, sigmoid, femoral heads, uterus, applicator, and packing. Patients whose imaging studies contained excessive artifact hindering clear structure delineation were excluded. For intermodality registrations, the applicator and packing were excluded from the HDR-BT structure-based image sets to allow for registration of images with high-contrast applicators to the pretreatment EBRT. Although it would be ideal to include the HRCTV in the