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Deformable registration

Assessment of cumulative external beam and intracavitary brachytherapy organ doses in gynecologic cancers using deformable dose summation

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Purpose: Due to inter-fraction variation in applicator position, organ displacement and deformation, doses to targets and normal tissues may not be accurately represented by adding the doses from external beam radiation therapy (EBRT) and intracavitary brachytherapy (ICBT) using rigid image registration. Deformable image registration permits organ and applicators to be spatially matched in 3D, enabling more accurate tracking of the accumulated volumetric dose to the target as well as organs at risk (OAR). This study assesses the dosimetric impact of using deformable image registration to determine the cumulative EBRT and ICBT doses to the rectum and bladder.
Methods and materials: Data from 20 patients with stage IB1-IVA cervical cancer were analyzed. Nine of the patients were treated with ICBT and EBRT which included a nodal or parametrium boost while eleven were treated with ICBT and EBRT with no boost. Dose summation was performed in two stages. For the first stage, only the ICBT fractional doses were added using both "parameter adding" and deformable registration techniques. In the second stage, the ICBT and EBRT doses were combined using "parameter adding" in two ways. Partial "parameter adding" considers the cumulative ICBT dose from deformable registration as one parameter while full "parameter adding" uses fractional ICBT parameters. The cumulative minimum doses to 2cc (D2cc) of the rectum and bladder were compared between deformable registration and "parameter adding" techniques.
Results: Dose summation of ICBT fractions only using deformable registration yielded D2cc values that were (10.1 ± 9.5)% lower for the rectum and (7.2 ± 6.3)% lower for the bladder compared to "parameter adding". When ICBT and EBRT doses were summed deformably, the group without EBRT boost had D2cc that were (0.0 ± 4.6)% and (−1.2 ± 2.9)% lower for the rectum and bladder respectively compared to partial "parameter adding". With EBRT boost, the differences were (−2.9 ± 4.0)% and (−3.2 ± 3.3)% for the rectum and bladder respectively. For full "parameter adding", the differences from deformable sum were (2.7 ± 5.0)%, (2.6 ± 5.0)% without EBRT boost and (0.6 ± 4.8)%, (−1.5 ± 3.7)% with EBRT boost.
Conclusion: Comparison of deformable dose summation with the technique of "parameter adding" suggests that "parameter adding" can be used as a good approximation of D2cc when adding ICBT and EBRT doses with or without boost. With EBRT boosts, deformable dose summation may more accurately represent dose to normal critical structures but these differences remain small compared to "parameter adding".

The treatment of locally advanced cervical carcinoma involves a combination of external beam radiotherapy (EBRT) and intracavitary brachytherapy (ICBT). For the current study, the focus is on ICBT using the tandem and ovoid applicator only. Amongst centers in the United States, dose and fractionation schedules vary; the American Brachytherapy Society recommends an EBRT dose of 45–50.4 Gy (44.3–49.6 Gy EQD2) and high dose rate (HDR) brachytherapy dose of 5.3–7 Gy in 4–6 fractions [1] for a total EQD2 dose of 90 Gy.

The clinical practice of brachytherapy has moved from an orthogonal film based system with prescription to Point A and normal tissue point dose reporting as per the International Commission on Radiation Units and Measurements (ICRU) Report 38 [2] to image based brachytherapy with computed tomography

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(CT) or magnetic resonance imaging (MRI). CT and MRI allow construction of a quantitative geometric model that gives a more accurate representation of tumor extent and nearby dose-limiting structures though most centers also continue to report doses to ICRU defined points [3]. While planning with 3D imaging is commonplace, there has been a move to also describe dose in three dimensions, rather than by the ICRU point dose specifications. The Groupe Européen de Curiethérapie–European Society for Therapeutic Radiology and Oncology (GEC–ESTRO) working group has published volume-based recommendations for dose prescriptions [4]. To date, maximum doses to normal tissue from EBRT and ICBT have been summed and reported using "parameter adding" as it is not possible to derive a composite plan dose-volume histogram (DVH) using only the EBRT DVH and the ICBT DVH.

In the era of adaptive therapy, both for EBRT and brachytherapy, accurate representation of delivered dose to the tumor as well as normal tissues is important for planning future treatments which must take into account deficiencies in the prior dose distribution. The complicating factor with EBRT and ICBT treatments is that the device can significantly alter the pelvic anatomy of both the primary tumor as well as normal tissues. There are two approaches to deal with this uncertainty: (1) rigidly register the EBRT treatment planning scan to each individual ICBT treatment datasets, or (2) deformably register the two different datasets together. With rigid registration, datasets are co-registered based on bony anatomy. The image from one dataset is rigidly transformed with six degrees of freedom (three translational and three rotational) to another. Deformable image registration is not limited to the 6 degrees of freedom and permits different sub-sections of the image to move and scale independently, enabling better estimates of the spatial relationship between the volume elements of corresponding structures across image data sets. Deformable image registration is potentially useful for adaptive re-planning [5,6] and as a tool for computer assisted target and organ segmentation for a number of treatment sites [7–9]. One important application of deformable image registration is radiation dose summation [10]. Deformable registration has been applied to assess target and organ coverage during whole pelvic intensity modulated radiation therapy (IMRT) and the dosimetric consequences of applying deformable registration to two ICBT fractions on the bladder [11]. The present study aims to determine whether deformable registration of EBRT and multiple ICBT treatments results in differences in reported D2cc for the rectum and bladder.

Methods and materials

The datasets of 20 patients with carcinoma of the cervix (stages IB1-IVA) were used. This retrospective study was approved by the Institutional Review Board at the University of Pennsylvania. The stage at presentation is as follows: IB1 (3), IB2 (5), IIA (1), IIB (6), IIIA (1), IIIB (3) IVA (1). The median patient age was 43 years (range, 29–77 years). All patients received a dose of 44.3–49.6 Gy (EQD2) to the pelvis with EBRT using intensity-modulated radiotherapy or 3D conformal radiotherapy and 4–5 fractions of HDR brachytherapy (5.5–6 Gy/fx) via tandem and ovoids [1]. The choice of number of fractions was decided based on availability of treatment slots. The EBRT plan was normalized such that at least 95% of prescription dose covers at least 98% of the target volume. An EBRT boost was administered to 9 patients with pathologically or radiographically involved nodes. The boost regions were para-aortic (patients 1 and 10), left iliac node (patient 18), right iliac node (patient 12), left parametrial (patient 11) and bilateral parametrial (patients 6, 14, 16 and 17). The combined dose for all patients ranged from 80.0 to 91.4 Gy (EQD2) to point A. Eighteen patients received concurrent cisplatin chemotherapy. All patients underwent CT planning for both the EBRT and each ICBT fraction. There was no bowel preparation but patients were prepared by drinking two eight ounce bottles of water prior to simulation and daily treatment. Additionally, the bladder and rectum were contoured and the minimum doses to 2cc of the most irradiated part of the organs (D2cc) were obtained for each ICBT plan. The entire bladder was contoured, and the rectum was contoured from the anus to the rectosigmoid junction. We used the method of whole organ contouring for each OAR as that method serves as an accurate estimate of D2cc [12].

Image pre-processing and deformable image registration

Commercially available deformable image registration software MIM Maestro (MIM Software, Cleveland, OH, USA) was used in this study. Since the software deforms one CT to another by matching image intensities [13], inconsistent CT numbers between image pairs may compromise the accuracy of the image registration. For this reason, images are pre-processed to correct for air pockets, artifacts, contrast material and variation in CT number within the rectum and bladder as they may not show meaningful correspondence between different image sets. This pre-processing step includes overriding the CT numbers of the rectum and bladder contours to 1000 Hounsfield units which is similar to dense bone thereby artificially enhancing the contrast between the OAR walls and its adjacent soft tissue. In addition, vaginal packing or balloons used in ICBT are also contoured and the CT numbers assigned 0 Hounsfield units (water equivalent). For registration between ICBT and EBRT image sets only, the applicator was contoured and assigned water CT number. The degree to which the OAR walls between different image sets matched was evaluated by computing the Dice similarity coefficient (DSC) between the reference (A) and deformed (B) contours:

$$\mathrm{DSC} = \frac{2|A \cap B|}{|A| + |B|}$$

The DSC is a measure of the spatial overlap between the contours and has the maximum value 1 if contours A and B completely overlap and 0 if there is zero overlap. The first ICBT CT and contours was used as the reference data set to which all other images were deformed into.

Accumulation of ICBT and EBRT doses

The deformation fields derived from image registrations were applied to the dose distributions for summation purposes. All doses were converted to equivalent 2 Gy/fraction doses (EQD2) on a voxel by voxel basis using the linear-quadratic model with $\alpha/\beta = 3$ Gy for late effects [14] and then summed. D2cc results using "parameter adding" for summing only ICBT were calculated by numerically adding individual D2cc ICBT DVH parameters. "Parameter adding" of ICBT and EBRT doses were performed in two ways. For partial "parameter adding", fractional ICBT doses were initially added using deformable registration and the D2cc parameter from the cumulative ICBT doses was then added to the nominal EBRT dose prescriptions. In this way, only one cumulative ICBT dose distribution was combined with one EBRT dose distribution and differences between the deformable sum and "parameter adding" results are attributable to the characteristic differences between the ICBT and the EBRT dose distributions and not due to inter-fraction variation in ICBT dose. For full "parameter adding" the fractional ICBT D2cc and EBRT dose prescriptions were added numerically. Due to the variability in the spatial location of the EBRT boost, the EBRT boost component is not included in "parameter adding" but included in the deformable sum.