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Dose accumulation during vaginal cuff brachytherapy based on rigid/deformable registration vs. single plan addition

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ABSTRACT

PURPOSE: To compare dose summation using a single plan (SP) approach for vaginal cuff brachytherapy (VBT) against dose summation after a rigid or deformable registration for each VBT fraction, in women with early stage endometrial cancer receiving postoperative VBT.

METHODS AND MATERIALS: A retrospective analysis of 19 patients who received VBT as the sole adjuvant treatment was undertaken. For the purposes of the study, every VBT fraction was re-segmented and re-planned under the same conditions. CT-planning images were registered, initially following a rigid method and then using deformable registration. The transformation vectors were reused to warp the dose files, followed by the dose summation. Three dose accumulation scenarios were studied: (*1*) an SP approach, (*2*) a rigid dose warping summation (RDWS), (*3*) a deformable dose warping summation (DDWS). Each scenario was analyzed for 3 and 5 fractions to evaluate the effect of fractionation. D0.1cc, D1cc, D2cc, D5cc, D5%, and Dmean values were compared for organs at risk, such as the rectum and bladder.

RESULTS: No statistical significances were observed in rectal parameters between SP and RDWS or between SP and DDWS. Significant SP, RDWS and DDWS Dmean, D0.1cc, and D2cc metric differences for the 5 fractions bladder scenario were observed (p = 0.0242, 0.0196, and 0.0242, respectively).

CONCLUSIONS: A multi-image planning procedure for a VBT course leads to limited differences between different summation methods. SP is an effective and acceptable surrogate for absorbed doses in organs at risk.

Keywords: Cylinder; Endometrium; Rigid registration; Deformable registration; Dose accumulation

Introduction

Endometrial carcinoma (EC) is the third most common cancer diagnosed in women and is the most common female genital tract malignancy worldwide (1). Early-stage EC treatment involves surgery (total abdominal hysterectomy and bilateral salpingo-oophorectomy with or without pelvic lymph node dissection) followed by adjuvant radiotherapy in selected cases. Prospective randomized studies have shown that radiotherapy (RT) reduces the risk of pelvic relapse but does not improve the overall survival in patients with early EC (2, 3). The PORTEC-2 trial demonstrated that patients with intermediate-risk EC can be safely treated with postoperative brachytherapy in the absence of whole pelvis external beam radiotherapy, decreasing toxicity (4). The vaginal cuff remains the most common site of relapse. Subsequently, there has been a shift away from external beam irradiation and an increase in the use of vaginal cuff brachytherapy (VBT) in these patients.

With the adoption of three-dimensional (3D) image-based planning, there has been concern regarding the movement of pelvic organs, as well as interfraction variation between implants. The cervical cancer literature suggests the benefit of

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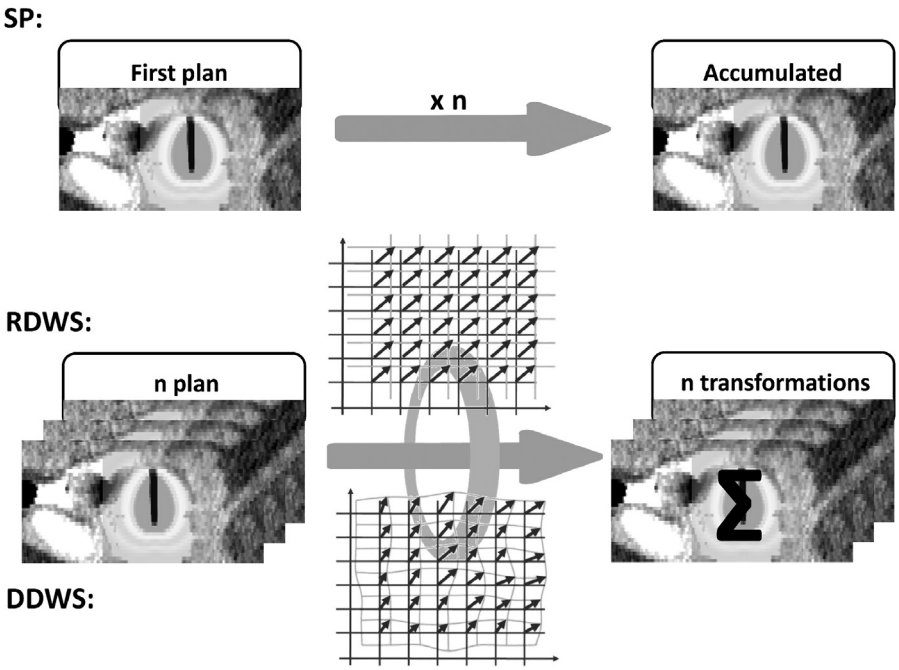

Fig. 1. Schematic representation of the 3 dose-accumulation strategies analyzed. (*1*) SP approach: doses were calculated in the first fraction and further replicated in the next fractions. (*2*) Dose calculation at each fraction followed by a registration, and dose accumulation, either rigid (RDWS) or deformable (DDWS). SP = single plan; RDWS = rigid dose warping summation; DDWS = deformable dose warping summation.

individualized plans for each brachytherapy fraction (5–7). Evidence for image-based planning with each VBT fraction is not as clear, with some reports suggesting an absence of benefit (8). Although their study aimed to evaluate the usefulness of repeated organs at risk (OARs) dose–volume histogram (DVH) calculations in multi-fractionated treatments, ours involved analyzing the different dose accumulation methods.

Deformable registration and dose accumulation is an important field of research in radiotherapy (9, 10). Dose summation with fractionated VBT should be considered to ascertain the dose distribution around the implant and OARs as accurately as possible. Variations in organ position, shape, and volume can cause discrepancies between planned and delivered doses. These anatomic changes could be heightened by brachytherapy applicators. Applying standard procedures to calculate the total does not factor in anatomic deformations, given that only the first fraction doses are taken into account, or at best, treatment fractions are rigidly registered. Deformable registration may overcome these limitations, improving both anatomic alignment and dose accumulation.

We analyzed the variation in dose to the rectum and bladder according to three accumulation strategies: single plan (SP), rigid registration, and b-spline deformable registration (Fig. 1). As there is no current consensus on the optimal number of fractions to be delivered, each type of accumulation strategy was calculated, mimicking a 3 or 5 fractions treatment.

Methods and materials

Patient data

Brachytherapy CT scans of 19 consecutive patients, who had received postoperative 3D HDR-VBT, with single-channel vaginal cylinders for EC, and who had at least five brachytherapy CT scans available for review, were retrospectively studied. Eighteen patients had exclusive postoperative VBT for early stage EC (Ia, one patient; Ib, 13 patients; Ic, four patients) and one patient had salvage VBT. The median age was 68 years. Brachytherapy was performed with the largest diameter cylinder that comfortably could fit the vaginal vault and was consistently in all subsequent applications. The intention was for the cylinders to remain positioned parallel to the patient craniocaudal axis. A CT scan was carried out immediately after the cylinder insertion.

CT simulation, segmentation, and planning

Pelvic CT scans were obtained for every brachytherapy fraction with 2-mm slice thickness. A Foley catheter was inserted into the bladder through which dilute contrast was instilled.

To achieve the best possible comparison and for the purposes of the study, OARs were re-contoured by the same researcher, and each brachytherapy fraction was re-planned (Oncentra v.4.1, Nucletron, an Elekta company [Elekta AB, Stockholm, Sweden]) under the same conditions for an

iridium-192 remote after-loading unit (MicroHDR, Nucletron, [Elekta]), regardless of the actual delivered treatment (5 VBT fractions of 4.5−5 Gy/fx were administered to each patient). An active length of 2.5 cm was used and optimized to deliver a fraction dose of 5 Gy at 5 mm deep into the vaginal vault. The entire bladder volume was segmented. To ensure uniformity, the rectum was defined from 1 cm above the cylinder tip to 1.5 cm below the last activated dwell source position, meaning the rectal length was always the same.

Dose accumulation

Three strategies were used: (*1*) using the first plan alone multiplied by the number of evaluated fractions, (*2*) using a rigid registration, and (*3*) using a b-spline deformable registration of every individual CT-based plan (Fig. 1). To simulate two different VBT fractionation regimens, one of them was created using the first three applications and the other with the five applications. The image manipulation workflow is shown in Fig. 2. Figure 3 outlines the image registration and dose-accumulation procedures.

CT images and doses were exported for the rigid and deformable registration from OncentraT (Eleckta) to the 3D-SLICER v.4.2 package with the SlicerRT module (11, 12). 3D-SLICER is a multi-platform, free, and open-source software package for visualization and medical imaging computing. All registrations used the first plan as the reference volume, and CTs from the subsequent applications

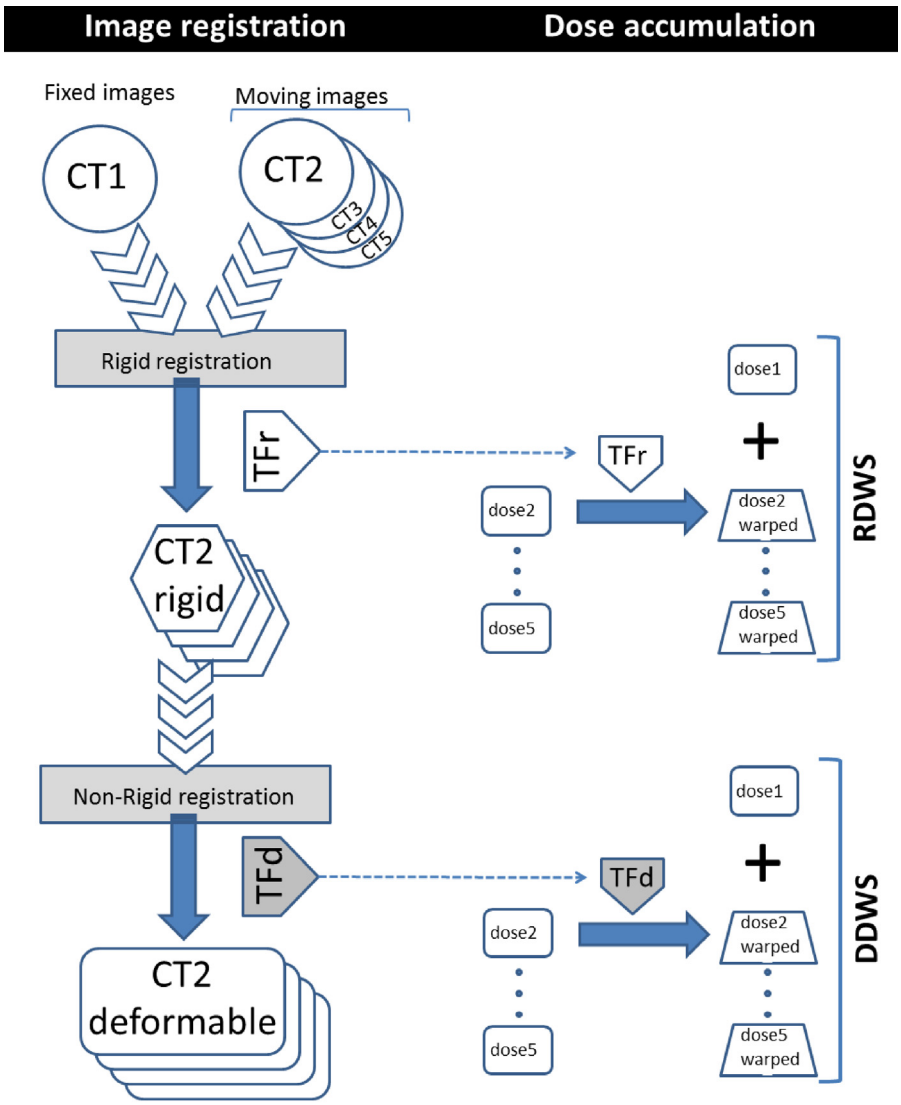

Fig. 2. General workflow. Image registration: CT sets ($n = 2-5$) related to the first CT study are rigidly registered for each patient. The result is a TFr and a new set of images. These sets of rigid registered images form in turn the moving images for the deformable registration procedure. Finally, a TFd and a set of non-rigidly deformed images are produced. Dose accumulation: transformation fields, either rigid or deformable, are applied to the planning dose files, to create warped dose files, which are summed to the first, still unmodified dose file, producing RDWS and DDWS. TFr = rigid transformation field; TFd = deformable transformation field; RDWS = rigid dose warping summation; DDWS = deformable dose warping summation.

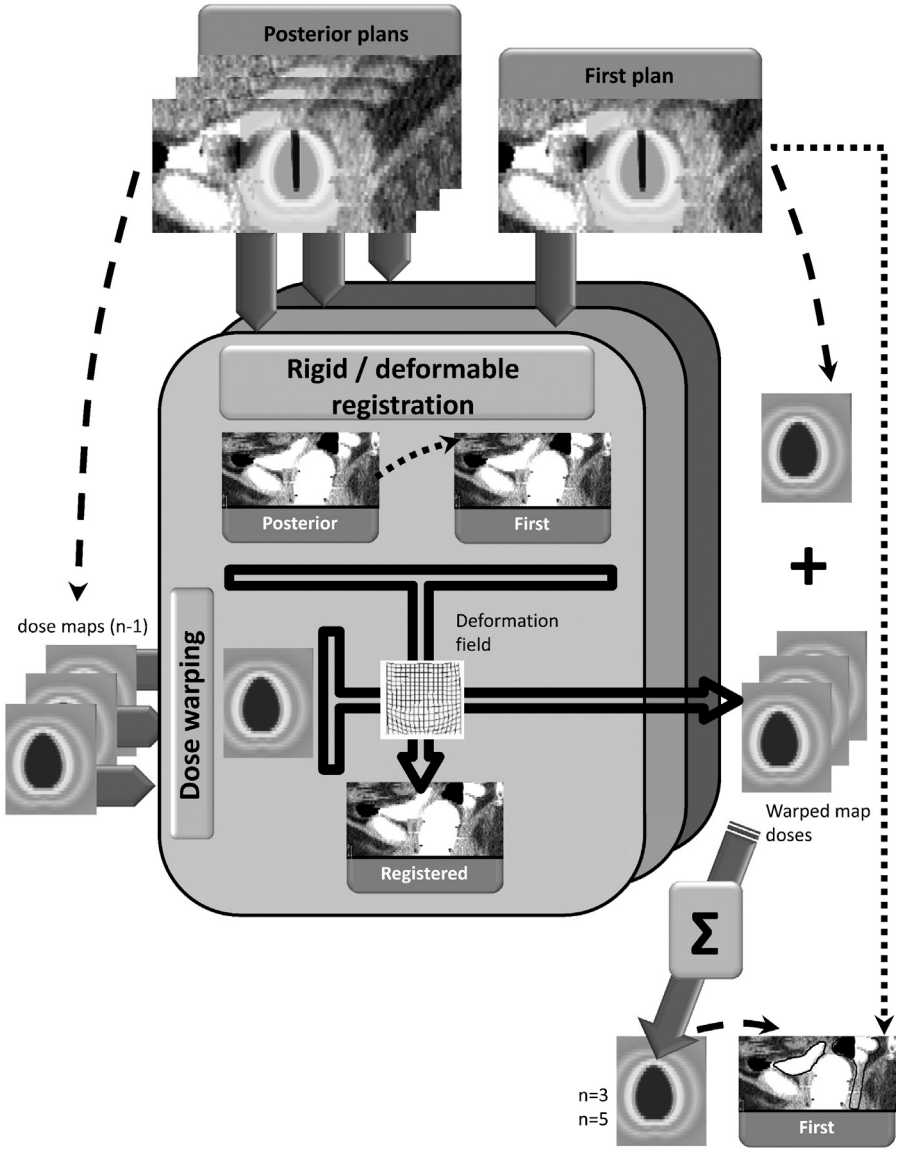

Fig. 3. Schematic diagram of registration and cumulative dose calculation. Both types of registration, rigid and deformable, share the same scheme. The first CT-planning images were used as the fixed volumes, with the later CTs used as the moving volumes. The deformation fields that were created were used to transform and warp the corresponding dose maps. Warped doses were summed up to the first dose map and DVHs were carried out from the first fraction OARs. This procedure was carried out for two lengths of VBT courses (3 and 5 fractions). DVH = dose−volume histogram; OARs = organs at risk; VBT = vaginal cuff brachytherapy.

were taken as the moving volumes. Reference volumes, by definition, remain unchanged, and moving volumes are transformed in later steps. After a coarse manual image alignment, an automatic rigid registration produced a new set of images from the moving volumes that were used as the moving sets for the deformable registration. This involved the use of an intensity-based alignment method which used the mutual information metric to examine the common information contained in the two images. The b-spline method was used for the deformable registration (13) (Parameters: 100,000 samples; $5 \times 5 \times 3$ control points; 1500 iterations). The transformation fields produced from the two registration procedures were saved and used to warp doses. Both rigid and deformable registrations were performed using the 3D-SLICER General BRAINSFit Registration module. To reduce processing time, images were cropped around the vaginal cylinder and the nearby OARs, the contoured rectum, and the bladder. Registration was checked by visual inspection.

Registered doses and images were exported to the CERR software package for dose summation and DVH analysis. Written in Matlab language, CERR is a free software platform for radiotherapy research (14). Registered doses were summed with the first application dose, producing a total rigid dose warping summation (RDWS) and a total deformable dose warping summation (DDWS). RDWS was defined as the total dose summation of the rigid warped doses and the first fraction dose. This means that only translations

Table 1
Rectum metric values based on summation method and the number of fractions considered

Number of fractions	Rectum metrics	Raw values (median, IQR) (Gy)				Δ% (Median)		Abs (Δ%) ≥ 20% (%)	
		SP	RDWS	DDWS	*p*	RDWS	DDWS	RDWS	DDWS
3fx	Dmean	4.83 (3.13)	3.76 (3.20)	4.74 (3.74)	0.104	−3.60	−3.55	21.1	21.1
	D0.1cc	20.46 (3.48)	21.98 (5.00)	20.50 (3.08)	0.268	5.18	2.75	42.1	5.3
	D1cc	16.50 (2.88)	16.66 (3.92)	16.62 (3.20)	0.611	2.05	1.83	31.6	5.3
	D2cc	14.82 (3.12)	14.74 (3.12)	14.82 (3.64)	0.516	1.80	1.01	31.6	5.3
	D5cc	11.94 (3.00)	12.10 (2.52)	12.10 (3.88)	0.458	0.66	0.47	15.8	21.1
	D5%	14.10 (2.76)	14.18 (4.00)	14.58 (4.64)	0.694	2.18	0.73	21.1	5.3
5fx	Dmean	8.05 (5.21)	5.66 (4.89)	7.92 (6.34)	0.692	2.35	−5.54	26.3	21.1
	D0.1cc	34.10 (5.80)	33.62 (9.88)	35.22 (6.32)	0.143	10.72	3.08	42.1	5.3
	D1cc	27.50 (4.80)	27.26 (7.88)	28.74 (6.56)	0.368	6.14	3.02	42.1	5.3
	D2cc	24.70 (5.20)	24.50 (7.92)	25.42 (7.64)	0.409	4.26	1.49	36.8	10.5
	D5cc	19.90 (5.00)	18.58 (5.24)	20.34 (8.08)	0.887	1.77	0.55	26.3	15.8
	D5%	23.50 (4.60)	24.02 (6.16)	24.50 (7.40)	0.694	3.98	0.78	36.8	5.3

IQR = interquartile range; Δ% = increase in percentage; Abs (Δ%) ≥ 20% (%) = percentage of cases exceeding an absolute variation of 20% or more related to the SP approach; *p* = *p*-values of the Friedman's test; SP = single plan; RDWS = rigid dose warping summation; DDWS = deformable dose warping summation; 3fx = 3 fractions; 5fx = 5 fractions.

Columns show the raw data, the percentage of median variation of rigid (RDWS) and deformable dose summations (DDWS) compared with the SP procedure, and the percentage of cases exceeding an absolute variation of 20% or more related to the SP approach.

and rotations were allowed. Results were highly influenced by bone structure signal. DDWS was defined as the total dose summation of the deformable warped doses and the first fraction dose. This procedure means that rectum and bladder deformation, due to brachytherapy applicators or natural processes in the body, such as bladder distention or rectal gas pockets or rectal feces, are taken into account. In addition to the rigid and deformable dose accumulation, a third simulation was performed using an SP. For the SP method, the dose metrics of the first fraction were multiplied by the number of fractions. Two different clinical settings were simulated for each type of registration, one with the first three implants and the second with all five implants. All image and dose files were exported using the DICOM-RT standard (15) that facilitates information sharing and the interoperability of different radiation therapy systems.

Statistical analysis

The effect of different simulations and scenarios on OARs was evaluated by comparing DVH parameters (D0.1cc, D1cc, D2cc, D5cc, D5%, and Dmean). The percentage change of these parameters, after a rigid or deformable deformation, was compared with the calculated values obtained by a simple multiplication from the first CT plan. To analyze the influence of the length of brachytherapy courses on dose warped parameters compared with the SP approach, the differences between dose-warped parameters and SP parameters were calculated, for both the 3 and 5 fractions setting. Dose metric differences were normalized in relation to the prescribed total dose (15 Gy or 25 Gy, according to number of fractions) and in relation to the SP values. Differences in results were also assessed by the use of non-parametrical tests (16). The Wilcoxon signed-rank test was used to compare two-paired groups. The Friedman's test was undertaken to compare multiple-paired observations. Post hoc multiple comparisons were calculated using the Dunn-Bonferroni method. A difference was deemed statistically significant at $p < 0.05$. Analyses were done with the SPSS v.21 (IBM Corp., Armonk, NY) and Stata v.12 (StataCorp LP, College Station, TX).

Results

Rectum parameters

No statistically significant differences were observed when RDWS and DDWS were compared with the SP approach. Results were similar in both the 3 and 5 dose fractions. Table 1 shows the raw dose values expressed as a median and an interquartile range based on each dose summation scenario. Variation in the DDWS values was lower than the RDWS values compared with the SP doses. All the same, the median registered metrics differed from the SP summation procedure between a −5.54% and 10.72%. On average, an absolute dose metric variation of 20% or more was observed in about a third of cases when all the RDWS parameters were taken into account, but the values were smaller in the DDWS scenario.

Bladder parameters

Table 2 shows the bladder DVH parameters. The Friedman test produced significant differences when evaluating bladder Dmean (3 fractions, $p = 0.014$; 5 fractions, $p = 0.002$). Dmean post hoc test analysis revealed a significant difference between the DDWS and SP settings (3 fractions, $p = 0.001$; 5 fractions, $p = 0.002$) and between the DDWS and RDWS settings (5 fractions, $p = 0.045$). Friedman's test also found significance for the 5 fractions setting in the D0.1cc and D1cc parameters ($p = 0.0196$ and 0.0242, respectively), with borderline significance for D5cc and

Table 2
Bladder metric values based on the number of fractions considered

Number of fractions	Bladder metrics	Raw values (median, IQR) (Gy)				Δ% (Median)		Abs (Δ%) ≥ 20% (%)	
		SP	RDWS	DDWS	*p*	RDWS	DDWS	RDWS	DDWS
3fx	Dmean	2.42 (1.02)	2.42 (1.49)	2.21 (1.41)	0.014	−6.86	−11.93	26.3	31.6
	D0.1cc	15.42 (3.48)	16.86 (4.20)	15.50 (3.28)	0.532	1.57	−3.29	36.8	10.5
	D1cc	13.02 (3.12)	13.50 (3.08)	12.30 (3.08)	0.368	3.38	−2.55	31.6	0
	D2cc	12.06 (2.64)	12.06 (2.84)	11.18 (2.92)	0.331	1.44	−2.44	26.3	0
	D5cc	10.26 (1.92)	10.34 (2.28)	9.18 (3.12)	0.34	−2.07	−3.53	26.3	5.3
	D5%	10.38 (1.80)	10.58 (2.40)	9.86 (2.80)	0.076	1.84	−1.60	21.1	10.5
5fx	Dmean	4.04 (1.70)	4.07 (2.94)	3.63 (2.26)	0.002	−9.08	−14.77	31.6	31.6
	D0.1cc	25.70 (5.80)	27.54 (8.68)	25.30 (4.60)	0.0196	7.32	−4.04	36.8	5.3
	D1cc	21.70 (5.20)	22.62 (3.08)	21.10 (4.12)	0.0242	5.69	−4.51	31.6	5.3
	D2cc	20.10 (4.40)	19.82 (5.80)	18.42 (4.32)	0.364	2.09	−5.23	31.6	10.5
	D5cc	17.10 (3.20)	17.42 (4.72)	15.58 (4.72)	0.0534	2.73	−6.50	31.6	26.3
	D5%	17.30 (3.00)	17.50 (5.04)	16.06 (3.72)	0.0534	2.40	−6.14	31.6	21.1

IQR = interquartile range; Δ% = increase in percentage; Abs (Δ%) ≥ 20% (%) = percentage of cases exceeding an absolute variation of 20% or more related to the SP approach; *p* = *p*-values of the Friedman's test; SP = single plan; RDWS = rigid dose warping summation; DDWS = deformable dose warping summation; 3fx = 3 fractions; 5fx = 5 fractions.

Columns show the raw data, the percentage of median variation of rigid (RDWS) and deformable dose summations (DDWS) compared with the SP procedure, and the percentage of cases exceeding an absolute variation of 20% or more related to the SP approach.

D5% (both, $p = 0.0534$). We were unable to find paired differences between the two groups during post hoc analysis. We believe that the opposite median percentage sign (Δ%) between RDWS and DDWS (Table 2) is irrelevant, given the small differences in absolute values.

Differences observed by VBT fractionation regimens: The normalized differences from the SP summation for each type of dose deformation accumulation, based on the number of fractions, are described in Table 3. RDWS and DDWS values calculated with 5 fractions showed greater differences than the corresponding values calculated with 3 fractions. All the same, only the differences between RDWS and DDWS for the Dmean, D0.1cc, D1cc, and D2cc values for the 5-fractions bladder doses were statistically significant ($p = 0.036$, 0.018, 0.027, and 0.044, respectively) (Table 3).

Discussion

The results shown for dose deformation and dose accumulation do not support a customized dosimetric plan for each fraction. Under optimal circumstances, VBT is delivered using a customized plan with each fraction, although the American Brachytherapy Society stated that this may not be necessary assuming a fixed geometry of the implant for every insertion based on the first fraction (17). The results presented here demonstrate small dosimetric differences

Table 3
Normalized rectum and bladder dose differences between registered (rigid dose warping summation and deformable dose warping summation) doses and the single plan values, for both the 3 and 5 fractions settings (median and interquartile values)

OAR metrics	RDWS (median, IQR) (%)		DDWS (median, IQR) (%)		3fx Significance (*p*-value)	5fx Significance (*p*-value)
	3fx	5fx	3fx	5fx		
Rectum						
Dmean	−1.21 (6.68)	−0.79 (9.05)	−1.03 (2.47)	−1.33 (4.27)	0.936	0.748
D0.1cc	6.4 (50.67)	14.88 (46.88)	2.13 (4.53)	3.2 (8.16)	0.355	0.629
D1cc	2.4 (30.67)	6.56 (28.32)	2.13 (4.53)	3.2 (8.16)	0.643	0.687
D2cc	1.87 (25.07)	4 (24.16)	1.07 (5.07)	1.6 (8.32)	0.658	0.748
D5cc	0.53 (16.8)	1.28 (15.52)	0.27 (3.73)	0.48 (9.28)	0.679	0.968
Bladder						
Dmean	−0.76 (3.93)	−0.97 (5.23)	−2.28 (3.03)	−2.42 (2.52)	0.147	0.036
D0.1cc	1.87 (34.13)	7.52 (51.52)	−3.47 (9.07)	−4.16 (7.36)	0.077	0.018
D1cc	3.2 (25.07)	4.8 (38.24)	−1.87 (10.13)	−4.32 (9.28)	0.126	0.027
D2cc	1.07 (21.87)	1.6 (31.04)	−1.87 (10.13)	−4.16 (7.68)	0.171	0.044
D5cc	1.07 (18.4)	1.76 (21.76)	−2.13 (11.2)	−3.52 (10.24)	0.277	0.077

RDWS = rigid dose warping summation; IQR = interquartile range; DDWS = deformable dose warping summation; *p*-value = results of the Wilcoxon test; OAR = organs at risk.

Dose metric differences were normalized in relation to the total prescribed dose (15 Gy or 25 Gy) and in relation to the single plan values. The right column shows the comparisons (*p*-value) between rigid and deformable values based on the number of fractions.

between the simple SP approach and the two other complex summation methods. Despite statistical significance observed between the planning methods in selected parameters, we do not believe these differences are clinically relevant.

Issues with our work are derived from unsolved deformable registration and dose deformation problems (18), mainly when it comes to non-correspondence and the difficulties in validating calculated doses against measured doses.

Deformable registration relies on the assumption that every point of one image corresponds to some point in the other image, and the presence of bowel gas or different fecal volumes leads to this assumption breaking down (19). The main cause of non-correspondence during pelvic registration is the inability to deal with gas pockets. Methods of dealing with this rectal inconsistency between image studies include creating ''artificial gas'' (20), detecting and painting of bowel gas pockets (21), or using an opposite approach, deflating the gas pockets (19). None of these have been implemented in the software package used. Because the non-correspondence issue remains a much more complex problem than dose calculation (22), it needs to be better characterized before dose deformation can be widely used in clinical situations.

Image registration results could be validated quantitatively, through identifying natural or implanted landmarks in the body, and qualitatively, using check-board displays, side-by-side comparison, or image overlay among other procedures. All the same, there is a lack of similar dose deformation validation procedures, and there are no metrics on which to base the dose deformation accuracy (18). Recent studies (23–25) have established the basis for comparing between calculated and measured deformed doses. Tissue-equivalent deformable gel dosimeters have been described, which can be used to evaluate deformable registration and dose deformation accuracy by direct measurement (23, 24, 26). Our results were obtained without an experimental dose deformation validation, as they were not available during the study. This type of dosimeters is not in widespread use because careful techniques are needed, as well as additional equipment—magnetic resonance or optical CT scanners—to read doses.

Probably, reproduction of our data could need a homogenous cylinder insertion between VBT applications as the influence of some variables, like the applicator angle position (27) or the amount of rectal (28) and vesical distention (29), on VBT dosimetry has been reported. Therefore, when such variables have not been properly taken into account during treatments, results could differ from those presented here.

Applicator geometry variations during intracavitary brachytherapy for cervical cancer produce multiple sets of point A. This variation leads to dosimetric changes (5–7). A 15–20% dose variation to OARs has been associated with interfraction differences in the applicator position (7). The SP approach during brachytherapy for cervical cancer, either using tandem and ovoids, or tandem and ring, has been related to an increase in bladder and rectum D2cc values (30, 31). Similar data are more debated for postoperative EC. Several reports have described no significant dose differences at OARs between SP approaches and re-imaging approaches (32–34). Holloway compared both approaches and found significant small dose differences, which were not considered clinically insignificant (8). Cost-analysis studies have also demonstrated a 35% saving per patient using SP (33).

Although there were small differences in the bladder or rectum doses after dose-warping compared with the SP approach, the 3-fractions scenario was associated with Dmean, D5cc, and D5% bladder dose was underestimated in more than 20% of the cases relative to the SP approach (Table 2) for the 5 fractions. A report from the University of Nebraska Medical Center (32) could not find a significant difference for bladder dose parameters, but a small significant reduction in rectal D2cc and D1cc was evident with the SP approach. According to the authors, such variations did not justify the use of CT-based planning with each VBT fraction. Another report (35) found significantly higher values using the SP approach for all bladder and small bowel metrics studied. No significant differences were seen for rectum and sigmoid. The authors concluded that an SP approach could significantly overestimate doses to bladder and bowel. Results from the Dana-Farber Cancer Institute (8) yielded similar results when the within-patient bladder and rectum dose variations were analyzed by repeated OARs segmentation and DVH calculations. The conclusions were that the small dose differences observed did not support the need to record dose values with each treatment fraction. Evaluated in their entirety, these studies do not believe the dosimetric differences to be clinically significant.

Whereas the previous studies were undertaken with single channel cylinders, or with an unknown type, the Tel Aviv University (34) carried out a study with a multichannel applicator. In this study, no differences for mean and maximum rectal and bladder doses were observed, but an excess of more than 20% mean dose to both OARs was observed in 41% of cases.

The dosimetric results presented here differ from previous reports on the dose summation method. Previous studies did not explain the kind of registration for dose summations, and so it could be inferred that the dose summation was carried out by a direct combination of DVHs. Such direct combinations tend to overestimate and underestimate the delivered dose in the highest and lowest dose regions because DVHs only indicate the volume that received a specific dose during a treatment fraction (36). Instead of adding up all the DVHs, dose accumulation must be undertaken by combining the dose information received by each voxel at every fraction (19), and so a registration method should be used. Our work is the first in the VBT setting to use a rigid and deformable registration, along with dose warping to accumulate fractional doses.

As in other reports that have analyzed the influence of customized plans for each VBT fraction, our results fail to find that dose accumulation methods offer a significant improvement, other than a direct summation of the first fraction. A detailed analysis of our data reveals that doses vary by 20% or more (up to 42% of cases), and the variation is larger for RDWS than for DDWS. Dose variation, as shown in Tables 1and 2, appears to be slightly higher with a rigid registration than with a deformable registration for the rectum. There is a noticeable general reduction in the bladder dose metrics related to the dose-registration and warping procedures, although statistical significance is only achieved in the 5 fractions setting. Data on Table 3 demonstrate that, in spite of the narrow differences seen in the raw values, the dose differences between registered doses using the SP approach increased with the number of VBT fractions. This result could be intuitively expected, given the higher probability of larger anatomic variations with longer VBT fractional courses. The facts presented here suggest that a simple summation using the SP approach is a good surrogate for rigid registration or the more accurate measure offered by complex deformable registration.

Conclusions

Despite the current uncertainties in the field of dose-deformation and dose-accumulation, we believe that our results support the use of a SP approach rather than a customized CT-based plan for each VBT fraction, given the slight differences observed between the SP approach and the two dose summation methods used. Our data are consistent with previously published results produced with different experimental methodologies.

We are of the opinion that the SP approach should become the standard procedure into the clinical setting owing to its simplicity and saving of resources.

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