

Assessment of dose to vaginal mucosa for gynecologic template interstitial high-dose-rate brachytherapy using Monte Carlo simulation

Devin Van Elburg, PhD^{1,2}, Tyler Meyer, PhD^{1,2,3}, Kevin Martell, MD³, Sarah Quirk, PhD⁴, Michael Roumeliotis, PhD⁵

¹Department of Physics & Astronomy, University of Calgary, Calgary AB, Canada, ²Medical Physics Department, Tom Baker Cancer Centre, Calgary AB, Canada, ³Department of Oncology, Tom Baker Cancer Centre, University of Calgary, Calgary AB, Canada, ⁴Department of Radiation Oncology, Brigham & Women's Hospital, Harvard Medical School, Boston, MA, USA, ⁵Department of Radiation Oncology & Molecular Radiation Sciences, Johns Hopkins University, Baltimore, MD, USA

Institution of research: Tom Baker Cancer Centre, Calgary, AB, Canada, T2N 4N2

Abstract

Purpose: This study investigated reliable vaginal mucosa dose-volume histogram (DVH) metrics in gynecologic template interstitial high-dose-rate brachytherapy (HDR-BT) for the purpose of standardized dose reporting.

Material and methods: Gynecologic template (Syed/Neblett) interstitial HDR-BT patients treated from September 2016 to November 2022 at the study institute were included in the cohort. Each patient implant included a vaginal mucosa contour defined by a 5 mm expansion from vaginal cylinder, then another volume with clinical target volume subtracted. DVH metrics were investigated between $D_{0.1cc}$ to D_{4cc} . Clinical plans were re-calculated using Monte Carlo (MC) simulations both in heterogeneous material and in water.

Results: The patient cohort included 61 patients with clinical plans using conventional homogeneous dose calculation (TG43). Heterogeneous vs. water MC dose differences were between -1.1% and -1.4% for all metrics investigated. DVH metrics D_{1cc} and smaller resulted in > 5% discrepancies between TG43 and MC dose (to water) calculation due to the proximity of source positions in/nearby the vaginal mucosa. Reliability improved when DVH metric volume was larger (D_{2cc} and D_{4cc}). Both D_{2cc} and D_{4cc} presented very high linear correlation between TG43 and MC reported doses for the vagina, and average \pm standard deviation dose difference was $4.6 \pm 2.9\%$ and $-3.0 \pm 1.9\%$, respectively. Dose differences decreased when the clinical target volume was removed: $-1.5 \pm 3.5\%$ and $-0.8 \pm 2.1\%$ for D_{2cc} and D_{4cc} , respectively.

Conclusions: For perineal template gynecologic HDR-BT procedures, the 2 cc volume is the smallest representative volume that reliably reports vaginal dose and at minimum should be reported to establish dose and outcome evaluation.

J Contemp Brachytherapy 2023; 15, 5: 317-324

DOI: <https://doi.org/10.5114/jcb.2023.131781>

Key words: brachytherapy, interstitial radiotherapy, gynecologic cancers, dosimetry calculations.

Purpose

Patients diagnosed with gynecologic (GYN) cancers are often indicated for treatment with radiotherapy. A substantial subset of these patients is treated with both external beam radiation therapy and high-dose-rate brachytherapy (HDR-BT). For patients with primary disease of the cervix, endometrium, or vagina as well as complex recurrences, HDR-BT may be delivered by perineal template interstitial procedures. These procedures are complex and, due to the variation in target volume location, require individualized dosimetry that is often compromised, compared with well-established trial

outcomes where majority of patients are treated for less advanced disease with standard applicators to deliver brachytherapy [1, 2].

In treatment with standard intra-cavitary brachytherapy applicators for cervical cancer, such as tandem and ring applicators, toxicity to normal tissue structures is comprehensively reported [1, 3]. In many perineal template-based implants, doses to uninvolved normal tissue structures, such as the bladder and rectum are similarly reported [2], as the planned dose gradients from catheters to normal tissues may be similar to standard brachytherapy applicators. For the vaginal mucosa, perineal template interstitial implant procedures may be indicated for

Address for correspondence: Devin Van Elburg, Department of Physics & Astronomy, University of Calgary, Calgary AB, Canada, T2N 1N4, ✉ e-mail: devin.vanelburg@ucalgary.ca

Received: 01.06.2023

Accepted: 19.09.2023

Published: 03.10.2023

a broader selection of gynecologic cancers, which are not dosimetrically similar. These implants often have needles directly abutting or penetrating the vaginal tissue. To deliver dose to target, brachytherapy sources dwell within the thin catheter lumen that contacts the mucosa, resulting in higher doses than is typical from standard brachytherapy applicators.

Vaginal mucosa dose in GYN HDR-BT is not standardized and not specified in the most recent consensus guidelines from recognized bodies, such as the American Brachytherapy Society (ABS) [2, 3] and GEC-ESTRO GYN working group [4, 5]. Vaginal toxicity is an ongoing area of investigation, and it has been correlated with surrogate dose points reported in the literature. The ICRU Report 89 [6] recommends the recto-vaginal reference point dose as well as the posterior-inferior border of symphysis (PIBS) and PIBS ± 2 cm points. These reference points are included in the planning aims and dose reported in the EMBRACE II study. In intra-cavitary and hybrid intra-cavitary/interstitial applicator treatment, a dose-effect relationship has been demonstrated between recto-vaginal reference point and grade two vaginal stenosis [7]. Both the recto-vaginal reference point and PIBS points are defined with respect to a conventional applicator and with a single channel centered in the vagina, which have radial dose distributions, and therefore point dose estimation is representative of circumferential dose within the vagina. However, the recto-vaginal reference point and PIBS points cannot be directly translated in the case of template interstitial HDR-BT, where these points do not represent predictable and representative dosimetry.

Alternatively, several other groups have taken the approach of dose-volume histogram (DVH) statistics to calculate vaginal mucosa hot spots [8-14]. Many of these studies used hot spot doses of all or a combination of $D_{0.1cc}$, $D_{0.5cc}$, D_{1cc} , and D_{2cc} [9-14], and defined the vagina as the volume extending to a depth of 1 to 5 mm from the surface of the vaginal applicator [9, 11, 12], or the full vagina as seen on computed tomography (CT) or magnetic resonance imaging (MRI) [8, 10, 13, 14]. In these intra-cavitary applicator-based gynecological brachytherapy studies, these hot spot metrics have been correlated with vaginal toxicity [8, 13, 14]. For example, Susko *et al.* found that for ring and tandem and for tandem and ovoid HDR-BT patients, a threshold dose of 108 Gy to D_{2cc} of the vaginal mucosa differentiated patients experiencing vaginal toxicities, where at two years, 36.2% and 70.5% of patients experienced grade 2 or greater vaginal toxicities below and above the 108 Gy threshold, respectively, and 9.9% and 30.0% experienced grade 3 or greater toxicities, respectively [14]. DVH-based vaginal dose-effect relationships have been found for intra-cavitary techniques, but have not been investigated for interstitial techniques explicitly, which may be important given that representative vaginal dose reporting was lacking for these patients.

Vaginal dose evaluation at points or small volumes is problematic for interstitial brachytherapy techniques due to the very steep dose gradient and consequently, the uncertainties introduced when evaluating these metrics. The aim of the present work was to identify small vol-

ume DVH metrics that reliably report the high-dose to the vaginal mucosa. A reliable dose metric is one that is consistent in different dose calculation methods.

Across all studies and standard clinical practice, the American Association of Physics in Medicine (AAPM) Task Group 43 [15] (TG43) dose calculation is used to report dose. It is generally accepted that the differences in dose accuracy are likely to have minimal clinical impact between model-based dose calculation algorithms or Monte Carlo (MC) simulation compared with TG43 for GYN treatments [16-19]. Previous investigations have focused on target coverage and the rectum, bladder, and sigmoid doses. Investigations have not clearly examined vaginal dose hot spots or dose comparison in these treatment areas with a highest dose gradient area. Most studies concentrated on applicator-based techniques [16, 18, 19]. One study reporting the results of MC simulation for GYN perineal template interstitial HDR-BT procedures, did not examine vaginal dose [17].

AAPM Task Group 186 [19] provides the framework for evaluating model-based dose calculation algorithms (MBDCAs) in brachytherapy and quantifying performance compared with standard TG43 formalism. In this report, a 2% agreement tolerance is recommended between the MBDCAs and consensus TG43 parameters under reference conditions, and discrepancies above 2% should be carefully investigated.

In the current work, we evaluated vaginal dose in GYN perineal template interstitial HDR-BT treatments using MC simulation. This is important to characterize that an appropriate dose reporting strategy may be developed as vaginal toxicity is correlated to small volume dose metrics, and interstitial HDR-BT treatments have high-dose gradients in the vagina.

Material and methods

Patient and treatment characteristics

Gynecologic perineal template interstitial HDR-BT patients treated from September 2016 to November 2022 at the study institute were included in the study. All implants were performed using Syed/Neblett GYN templates and flexi-needles (Best Medical International, Springfield, VA, USA) under ultrasound guidance. Each patient received post-implant MRI/CT imaging for treatment planning. CT image resolution was $0.3 \times 0.3 \times 1.5$ mm³. Treatment planning was performed using Oncentra Brachy v. 4.6 (Elekta, Stockholm, Sweden). Structures routinely contoured included gross tumor volume (GTV), clinical target volume (CTV), intermediate-risk clinical target volume (IR-CTV), bladder, rectum, and sigmoid. For this study, vaginal contours were created retrospectively in the original, clinical structure sets by expanding vaginal cylinder by 5 mm and removing the cylinder (vagina_{5mm}). This contour was a simple geometric expansion that may include target volume. An additional normal tissue vaginal contour was created by subtracting CTV from vaginal expansion contour (vagina_{5mm-CTV}). Figure 1 shows the vagina_{5mm} contour and CTV for a representative patient CT with interstitial implant. Oncentra DVH

calculation settings were set to the highest granularity: 800 bins, 200,000 sample points, and high-dose limit of 2× dose prescription. The high-dose limit was incrementally increased to 4×, 8×, and 16× as needed, when small volume dose metrics exceeded dose limit.

Monte Carlo simulations

Computed tomography images with clinically approved structure sets, new vaginal contours, and clinical treatment plans were exported and used to simulate MC-based dose distributions in EGS-NRC brachytherapy package *egs_brachy* [20]. Contoured structures were assigned tissue compositions, and are shown in Supplementary information (Table S1). Tissue compositions used are specified in ICRU 46 [21], except for cylinder material, Delrin® (Piedmont Plastics, Charlotte, NC) or homopolymer polyoxymethylene, which has a density of 1.41 g/cc [22], and air was set as defined in the TG43 report [15]. The air and lumen of interstitial needles in the implant were not modeled. For the rest of the body, *egs_brachy* assigned voxels to either air, female soft tissue, or cortical bone based on voxel CT number.

For the MC simulation, volume corrections were applied to remove iridium-192 (^{192}Ir) source volumes from patient volumes. Dose calculation grid size was the same as the CT image matrix size ($0.3 \times 0.3 \times 1.5 \text{ mm}^3$). For each patient plan, 1×10^9 histories were simulated. Across all prescriptions, physical doses were converted to equivalent dose in 2 Gy fractions (EQD₂) using an $\alpha/\beta = 10$ for targets and $\alpha/\beta = 3$ for OARs. The total EQD₂ dose was reported to include external beam radiation therapy dose (typically 45 Gy in 25 fractions). *Egs_brachy* simulations were performed once with tissues modeled and once with all media set to water (MC and MC_{water}, respectively) to distinguish between dosimetric differences observed when modeling heterogeneous media versus homogeneous water using the same dose calculation software.

Dose reporting and data analysis

Since vaginal dose DVH metrics are not well-defined for GYN perineal interstitial HDR-BT, hot spot dose metrics were calculated in Oncentra (referred to as TG43) and MC simulations as the minimum dose to 0.1 cm³, 0.5 cm³, 1 cm³, 2 cm³, and 4 cm³ (D_{0.1cc}, D_{0.5cc}, D_{1cc}, D_{2cc}, and D_{4cc} respectively). Standard DVH metrics were calculated for other relevant structures as well: D₅₀, D₉₀, and D₉₈ for high-risk CTV; D₉₀ and D₉₈ for intermediate-risk CTV; D₉₀ and D₉₈ for GTV; D_{0.1cc} and D_{2cc} for the bladder, rectum, and sigmoid.

Dose differences were reported between TG43 and MC, TG43 and MC_{water}, and MC and MC_{water} to isolate differences due to modeling heterogeneous tissue versus homogeneous water, and due to different calculation software when the media was homogeneous water. Across the patient cohort, all dose metrics were reported as average and standard deviation in both absolute difference and percent difference relative to each calculation method.

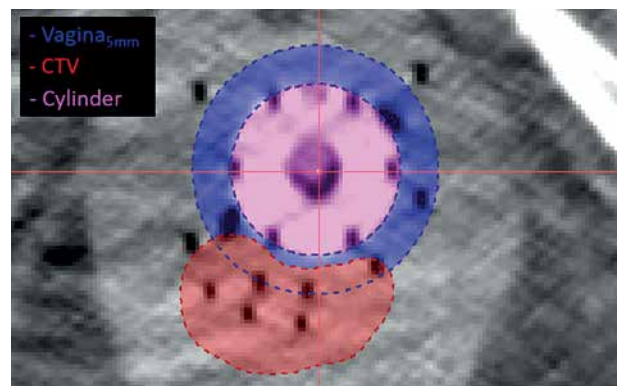


Fig. 1. Axial CT image of a representative patient. The vagina_{5mm} contour is a geometric expansion of 5 mm thick shell around the vaginal cylinder. To represent normal vaginal tissue, the contour vagina_{5mm-CTV} is created by removing the CTV volume from the vagina contour volume

Results

Patient and treatment characteristics

Between September 2016 and November 2022, 61 GYN perineal template interstitial HDR-BT patients were treated at the study institution and included in this research. Of the 61 patients, the primary disease sites included 32 cervical, 11 vaginal, and 18 endometrial. Across all site groups, the most common prescriptions were 24 Gy in 3 fractions ($n = 33$) and 18 Gy in 3 fractions ($n = 20$). The remaining nine patients had prescribed doses and fractionation in the range of 5 to 7.75 Gy in 3 to 6 fractions, respectively. For the 61 patients, a total of 82 separate clinically treated plans existed to account for adapted plans or new implants for subsequent fractions. A total of 164 total simulations were completed, once for heterogeneous and once for homogeneous water [23]. The average \pm standard deviation number of needles used in these implants was 18 ± 5 , which universally included seven needles in the cylinder (six peripheral and one central).

Vaginal dose reporting

Dose differences between TG43 and MC_{water} are shown in Figure 2 for a representative patient. Figure 2 includes structure volumes and dose distributions on CT image datasets (Figure 2A) as well as dose maps calculated in MC_{water} (Figure 2B) and TG43 (Figure 2C). Clear discrepancies in the dose distributions were observed as the MC software removed dose inside the cylinder and sources, which is explained in more detail in the Discussion section.

Dose differences between MC, MC_{water}, and TG43 for the vaginal expansion and representative normal vaginal tissue contour (vagina_{5mm} and vagina_{5mm-CTV}) are reported in Table 1 and Figure 3. For both MC and MC_{water}, the mean vaginal dose was less than TG43, indicating that standard clinical distributions over-estimated the vaginal hot spot dose. In general, the discrepancy between MC simulations and Oncentra was the greatest for the smaller volume DVH metrics, and the discrepancy decreased

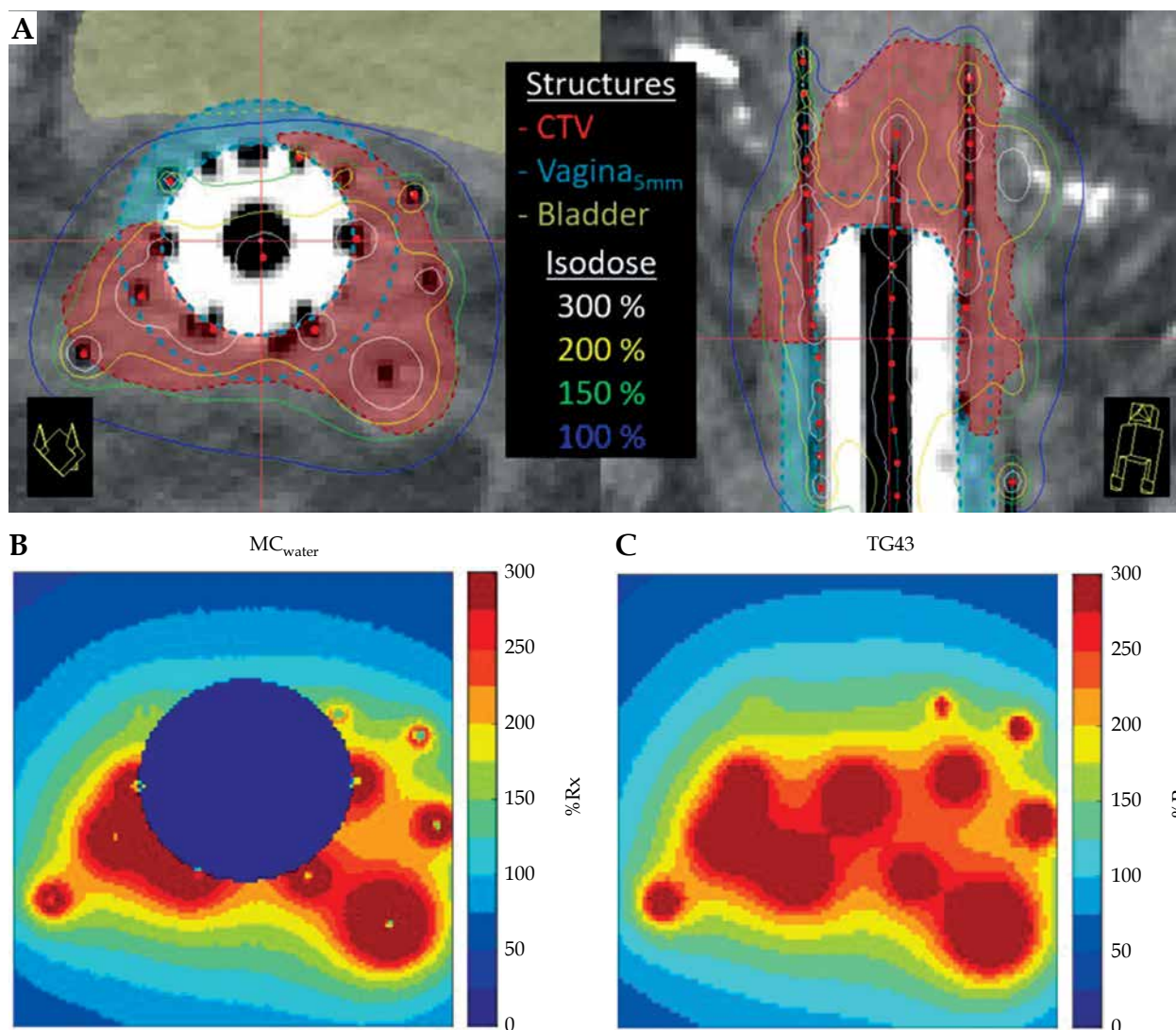


Fig. 2. Axial and sagittal CT slices of the implant with the largest difference between TG43 and MC_{water} vagina_{5mm} D_{2cc} . Isodose lines are relative to 8 Gy prescription dose, **B)** MC_{water} and **C)** TG43 calculated dose on the same axial slice in **(A)**. MC and MC_{water} simulations do not calculate dose inside the cylinder and sources

as the volume increased. For the vagina_{5mm-CTV} D_{2cc} and D_{4cc} and vagina_{5mm} D_{4cc} , the mean \pm one standard deviation dose differences between MC_{water} and TG43 were within $\pm 5\%$, demonstrating reasonable agreement for dose volume metrics conventionally used to report normal tissues doses in GYN HDR-BT. Of the 61 patients simulated, an agreement between MC_{water} and TG43 was within $\pm 5\%$ for 62.3% and 86.9% of patients for the vaginal expansion (vagina_{5mm}) D_{2cc} and D_{4cc} , respectively, and 83.6% and 98.4% of patients for the vaginal normal tissue (vagina_{5mm-CTV}) D_{2cc} and D_{4cc} , respectively.

Mean dose differences for all vaginal DVH metrics (Table 1) were 1.1% to 1.4% less in MC than MC_{water} , which was considerably less than the differences of over 4% observed between MC and TG43, revealing that the largest differences in clinically reported dosimetry was not due to the presence or absence of tissue modeling. In all other structures, MC and MC_{water} differences in mean

DVH metrics (shown in Figure 4) were within 1%, consistent with previously published results [17].

Correlation between the MC_{water} and TG43 dose for vagina_{5mm} $D_{0.1cc}$ and D_{2cc} is presented in Figure 5. TG43 and MC_{water} demonstrated a strong linear correlation ($R^2 = 0.989$) for D_{2cc} . For the smallest point volume ($D_{0.1cc}$), the linear correlation was weaker ($R^2 = 0.561$) showing that the relationship between TG43 and MC_{water} vagina_{5mm} $D_{0.1cc}$ was less reliable.

Monte Carlo statistical uncertainty

Average statistical uncertainty for all vaginal DVH metrics, averaged over all 176 simulations (1×10^9 histories), was less than 0.8%. The largest statistical uncertainty for the vagina_{5mm} and vagina_{5mm-CTV} metrics for a single patient were 1.0% and 2.2%, respectively, both for D_{4cc} . Average statistical uncertainty for all other DVH metrics were less than 1.5%.

Table 1. Percentage of dose differences between MC, MC_{water}, and TG43 calculation methods, averaged over all patients in the cohort. Absolute doses calculated in TG43 are given for reference

DVH metric	Absolute Oncentra dose, average ±STD (Gy ₃ EQD ₂)	Percentage of dose difference average ±STD (%)			
		MC vs. TG43	MC _{water} vs. TG43	MC vs. MC _{water}	
Vagina _{5mm}	D _{0.1cc}	2,090 ±1,310	-43.9 ±14.8	-43.1 ±14.9	-1.4 ±0.8
	D _{0.5cc}	567 ±258	-15.8 ±7.4	-14.9 ±7.4	-1.2 ±0.4
	D _{1cc}	379 ±148	-8.8 ±4.6	-7.8 ±4.6	-1.1 ±0.4
	D _{2cc}	274 ±96	-5.6 ±3.0	-4.6 ±2.9	-1.1 ±0.5
	D _{4cc}	199 ±65	-4.1 ±2.0	-3.0 ±1.9	-1.1 ±0.4
Vagina _{5mm-CTV}	D _{0.1cc}	579 ±556	-21.5 ±20.4	-20.4 ±20.6	-1.3 ±0.7
	D _{0.5cc}	222 ±117	-7.2 ±9.1	-6.1 ±9.2	-1.2 ±0.3
	D _{1cc}	169 ±71	-4.4 ±5.8	-3.2 ±5.8	-1.2 ±0.3
	D _{2cc}	133 ±45	-2.7 ±3.5	-1.5 ±3.5	-1.2 ±0.3
	D _{4cc}	106 ±33	-1.9 ±2.2	-0.8 ±2.1	-1.1 ±0.3

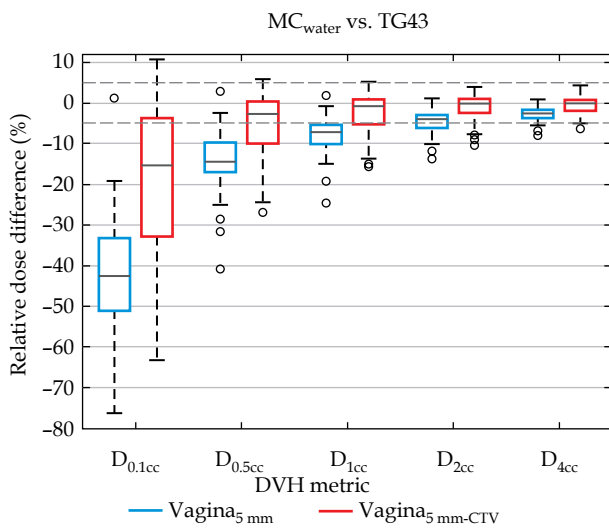


Fig. 3. Relative dose difference between MC_{water} and TG43 for each vaginal DVH metric. Dashed lines indicate ±5% range. The interquartile range for the vagina_{5mm-CTV} D_{2cc} and D_{4cc} and the vagina_{5mm} D_{4cc} were within ±5% agreement. Whiskers represent the range, while outliers are data points outside 3× interquartile range

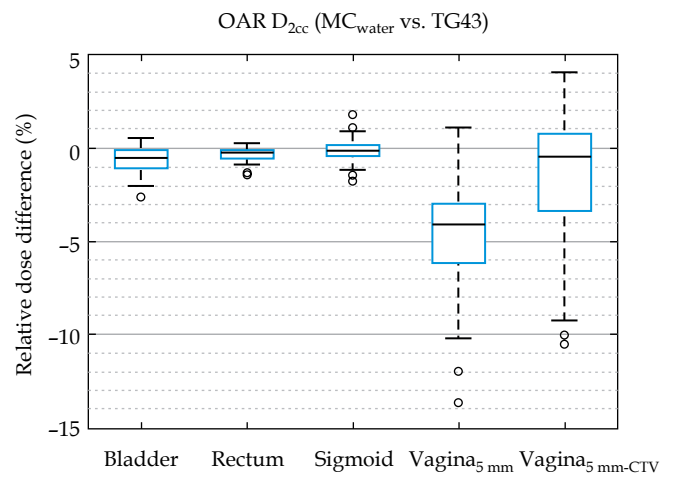


Fig. 4. Relative dose difference of D_{2cc} for OAR structures between MC_{water} relative to TG43. Boxes show interquartile range and whiskers indicate the range, while outliers are points outside 3× interquartile range

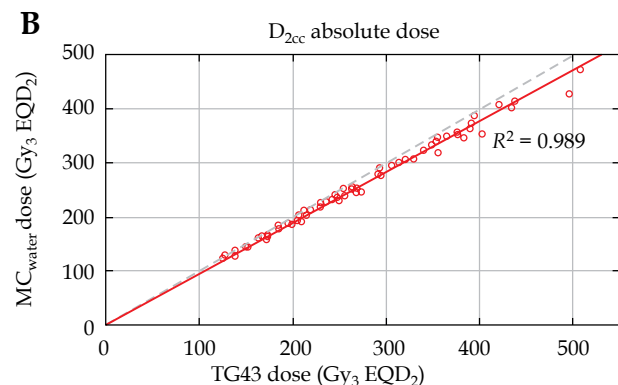
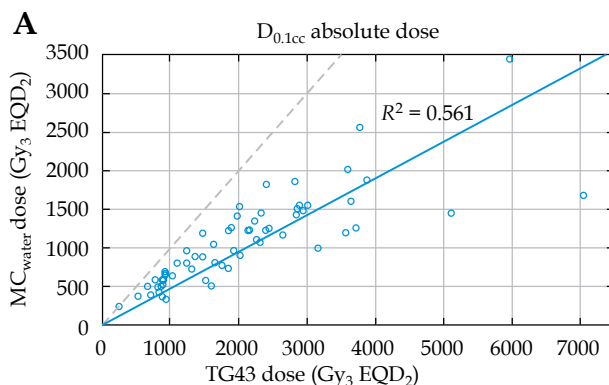


Fig. 5. MC_{water} vs. TG43 dose for vagina_{5mm} D_{0.1cc} (A) and D_{2cc} (B). Black dotted line is x = y. Linear fits are given for both distributions. Considerable scatter is observed with D_{0.1cc} and worsens as dose increases, but when DVH volume is increased to D_{2cc} the relationship between MC_{water} and TG43 dose is much more correlated

Discussion

This study investigates the dose reported to the vaginal mucosa for clinical GYN perineal template interstitial HDR-BT treatments. Due to interstitial nature of the technique, the reported doses are much different compared with standard GYN HDR-BT applicator treatments. Differences between MC-based dose and TG43-based dose were compared to evaluate discrepancies in conventional clinical dose reporting. For vaginal dose-volumes, the 2 cc represents the smallest volume with the expected correlation and within 5% average accuracy between dose calculation algorithms. The large uncertainties in small dose volumes result in unreliable plan quality evaluation, which may contribute to previous dose-effect relationship studies not determining correlations for volumes below D_{2cc} [14].

Independent investigation is required because the previously established dose-effect relationships are not representative of the dose delivered to the mucosa for interstitial procedures that is established in the report of this study. For template interstitial implants, the doses can be particularly high when the target volume is in or nearby the conventional vaginal mucosa structure due to the proximity of needles that must be loaded to achieve adequate therapeutic dose to the target. The combination of small DVH metric volumes and high-dose gradient regions leads to challenging dosimetry. To establish dose-effect relationships for doses that may be delivered in interstitial procedures, a reliable dose metric is required for dose reporting. In this investigation, volumes of 0.1 cc, 0.5 cc, and 1 cc yielded poorly correlated estimates, and only evaluating 2 cc and 4 cc volumes produced accurate and reproducible dosimetry.

The authors acknowledge that vaginal dose may not be a high priority for planning in interstitial HDR-BT, especially when the tumor resides within the vaginal mucosa directly, and the primary goal is to cover the target with margins considering uncertainties at the expense of delivering dose to the healthy vaginal tissue. However, vaginal doses should still be reported to indicate potential severe toxicities. Given the complex dose distributions and lack of standard and representative dose reporting in interstitial HDR-BT, reporting vaginal doses to volumes of at least 2 cc is reliable and representative of the hottest dose to the vaginal mucosa. These hot spot volumes will occur near the surface of the needles or cylinder, and may not be contiguous but truly represent the hottest dose in complex interstitial dose distributions, while standard points based on cylinder position do not.

The clinical standard will continue to have clinicians reviewing brachytherapy treatment plans using TG43-based dose calculation. The 2 cc volume metric satisfies the conditions for accuracy and precision at all dose levels investigated across large cohort of patients. It should be reiterated that the TG43-based dose calculation is generally a slight overestimate of the MC-based dose calculation. To establish dose-effect relationships for the mucosa, reporting small volume metrics from TG43-based calculations will result in difficulty establishing the correlation with outcomes. If MC-based dose calculation

becomes the clinical standard, smaller volume metrics may be reported.

Scenarios where dose evaluation occurs very close to a source are subject to great uncertainties due to extrapolation of TG43 data in short distances and uncertainties in the source model [19]. Other groups have observed large discrepancies of > 20% between MBDCAs and TG43-based treatment planning systems near ^{192}Ir source [18, 24]. For GYN perineal template interstitial HDR-BT cases, the vaginal mucosa often contains many interstitial needles, and proximity of sources to vaginal dose calculation points are likely subject to high uncertainties.

Discrepancies in vaginal dose calculation in this work result in part from the removal of dose deposited inside the source from dose distributions in MC, which is observed in the dose distributions shown in Figure 2 and is further detailed in Section 2 of the Supplementary information. These discrepancies would occur regardless of MC or TG43 implementation, assuming that the MC removes intra-source doses while TG43 implementations do not. In the context of GYN interstitial HDR-BT, Desbiens *et al.* [17] observed that exclusion of non-biological material (such as the cylinder and air pockets) is important in both MC and TG43. The HDR source is also non-biological material that for interstitial HDR-BT can represent a considerable portion of volume on the order of DVH metric volume. The simulated ^{192}Ir flexi-source has a volume of approximately 8 mm³: 13 source positions dwelling inside the vaginal contour accounts for 0.1 cm³. Larger volume metrics, such as D_{2cc} are greater than the order of source volume in the vaginal mucosa, and are therefore more reliable. Removing the CTV from the vaginal contour further increases reliability of TG43-calculated vaginal dose, since the CTV should contain the highest-weighted dwell positions. Modeling the interstitial needle lumen and removing it from the patient volume may further impact vaginal dose calculation.

Dose calculation deviations between TG43-based treatment planning software have been shown to be 4-8% (one standard deviation) for DVH metrics between 0.1 cc and 2 cc [25]. Treatment planning systems differ in region-of-interest reconstruction and interpolation strategies, which cause DVH metric uncertainties [25-27], especially when these small volumes are situated in high-dose gradient regions [25, 27] where uncertainties over 10% can be observed [25]. However, small volume DVH uncertainties between TG43 treatment planning systems are comparable to inter-observer variability [25], and improve when CT slice thickness is reduced [27], as this facilitates more accurate catheter reconstruction and structure contouring. All these findings suggest that small volume dose evaluation near HDR sources is unreliable, which we explicitly investigated for vaginal dose assessment in the current study.

In this study, a 5 mm expansion of the vaginal cylinder was used as a surrogate for the vaginal mucosa contour, as several groups have done previously [9, 11, 12]. The true vaginal mucosa is a complex structure with variable depths and folds and can be contoured in CT and MRI. However, contouring the vaginal mucosa on a per-patient basis for the sake of dose reporting may not

be practical, especially when vaginal doses are typically not considered a high-priority planning aim. Cylinder expansion offers a quick, robust, and practical alternative vaginal mucosa volume. In this study, we demonstrated the problem with small volume vaginal dose reporting below 2 cc for perineal template interstitial implants.

This study shows that modeling the HDR source and removing its volume from the patient geometry causes large discrepancies in small volume vaginal dose metrics between MC and TG43. Excluding non-biological material, such as source volumes from the vaginal contour, better resembles the clinical vaginal dose. When evaluating vaginal dose in GYN perineal template interstitial HDR-BT, it is recommended that clinics with TG43 dose calculation use vaginal dose metric volumes of at least 2 cc and withdraw the CTV volume from the vaginal contour. This removes the influence of source modeling and facilitates reliable calculation of the vaginal hot spot dose in TG43-based treatment planning systems compared with MC. Reliable vaginal dose metrics are essential if dose-effect relationships for vaginal toxicities are to be established.

Conclusions

For gynecologic perineal template HDR-BT procedures, the 2 cc volume is the smallest representative volume that reliably reports dose to the vaginal mucosa. The correlation between TG43 dose and MC-based dose calculation for D_{2cc} of the vagina is very high and, on average, within 5%. At a minimum, D_{2cc} should be reported for the normal vaginal mucosa for dose and outcome evaluation. Dose reporting using accurate metrics is critical to establish dose-effect relationships for brachytherapy procedures with high-doses due to the proximity of the radiation source to the vaginal mucosa.

Funding statement

This work was supported by the Alberta Innovates Graduate Studentship and the Canadian Institutes of Health Research.

Acknowledgements

Approval to access patient CTs and plans was granted by the Health Research Ethics Board of Alberta (HREBA) Cancer Committee (Ethics ID: HREBA.CC-19-0222).

Disclosure

Authors Roumeliotis and Meyer have ownership interest in Okolo Health, a brachytherapy company. The other authors report no conflict of interest.

Supplementary material is available on the journal's website.

References

- Pötter R, Tanderup K, Kirisits C et al. The EMBRACE II study: The outcome and prospect of two decades of evolution within the GEC-ESTRO GYN working group and the EMBRACE studies. *Clin Transl Radiat Oncol* 2018; 9: 48-60.
- Beriwal S, Demanes DJ, Erickson B et al. American Brachytherapy Society consensus guidelines for interstitial brachytherapy for vaginal cancer. *Brachytherapy* 2012; 11: 68-75.
- Viswanathan AN, Thomadsen B. American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part I: General principles. *Brachytherapy* 2012; 11: 33-46.
- Pötter R, Haie-Meder C, Van Limbergen E et al. Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy – 3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. *Radiother Oncol* 2006; 78: 67-77.
- Schmid MP, Fokdal L, Westerveld H et al. Recommendations from gynaecological (GYN) GEC-ESTRO working group – ACROP: Target concept for image guided adaptive brachytherapy in primary vaginal cancer. *Radiother Oncol* 2020; 145: 36-44.
- Pötter R, Kirisits C, Erickson B et al. Prescribing, recording, and reporting brachytherapy for cancer of the cervix. *J ICRU* 2013; 13: NP.
- Kirchheimer K, Nout RA, Lindegaard JC et al. Dose-effect relationship and risk factors for vaginal stenosis after definitive radio(chemo)therapy with image-guided brachytherapy for locally advanced cervical cancer in the EMBRACE study. *Radiother Oncol* 2016; 118: 160-166.
- Anneke P, Mailleux H, Sfumato P et al. Multivariate normal tissue complication probability modeling of vaginal late toxicity after brachytherapy for cervical cancer. *Brachytherapy* 2018; 17: 922-928.
- Carrara M, Cusumano D, Giandini T et al. Comparison of different treatment planning optimization methods for vaginal HDR brachytherapy with multichannel applicators: A reduction of the high doses to the vaginal mucosa is possible. *Phys Medica* 2017; 44: 58-65.
- Glaser SM, Kim H, Beriwal S. Multichannel vaginal cylinder brachytherapy-Impact of tumor thickness and location on dose to organs at risk. *Brachytherapy* 2015; 14: 913-918.
- Lapuz C, Dempsey C, Capp A et al. Dosimetric comparison of optimization methods for multichannel intracavitary brachytherapy for superficial vaginal tumors. *Brachytherapy* 2013; 12: 637-644.
- Mendez LC, Paudel M, Wronski M et al. Dosimetric comparison of interstitial brachytherapy with multi-channel vaginal cylinder plans in patients with vaginal tumors. *Radiat Oncol* 2017; 12: 10-14.
- Susko M, Craciunescu OI, Meltsner SG et al. Vaginal toxicity from vaginal brachytherapy and Capri-based systems. *Int J Radiat Oncol* 2016; 96: E287-E288.
- Susko M, Craciunescu O, Meltsner S et al. Vaginal dose is associated with toxicity in image guided tandem ring or ovoid-based brachytherapy. *Int J Radiat Oncol* 2016; 94: 1099-1105.
- Rivard MJ, Coursey BM, DeWerd LA et al. Update of AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations. *Med Phys* 2004; 31: 633-674.
- Hyer DE, Sheybani A, Jacobson GM et al. The dosimetric impact of heterogeneity corrections in high-dose-rate 192Ir brachytherapy for cervical cancer: Investigation of both conventional Point-A and volume-optimized plans. *Brachytherapy* 2012; 11: 515-520.
- Desbiens M, Amours MD, Afsharpour H et al. Monte Carlo dosimetry of high dose rate gynecologic interstitial brachytherapy. *Radiother Oncol* 2013; 109: 425-429.
- Mikell JK, Klopp AH, Gonzalez GMN et al. Impact of heterogeneity-based dose calculation using a deterministic grid-based boltzmann equation solver for intracavitary brachytherapy. *Int J Radiat Oncol Biol Phys* 2012; 83: e417-e422.

19. Beaulieu L, Carlsson Tedgren A, Carrier JFF et al. Report of the Task Group 186 on model-based dose calculation methods in brachytherapy beyond the TG-43 formalism: Current status and recommendations for clinical implementation. *Med Phys* 2012; 39: 6208-6236.
20. Chamberland MJP, Taylor REP, Rogers DWO et al. egs_brachy: a versatile and fast Monte Carlo code for brachytherapy. *Phys Med Biol* 2016; 61: 8214-8231.
21. White DR, Griffith RV, Wilson IJ et al. ICRU Report 46, Photon, Electron, Proton, and Neutron Interaction Data for Body Tissues. *J ICRU* 1992.
22. Röchling/Piedmont Plastics. Technical data sheet - Sustarin(R) H (Acetal Homopolymer "Delrin"), n.d. <https://www.piedmontplastics.com/resources/literatures/rochling-sustarinR-h>. Accessed September 2023.
23. Belliveau JG, Thind K, Banerjee R et al. The impact of inter-fraction changes for perineal template-based interstitial gynecologic brachytherapy implants. *J Contemp Brachytherapy* 2019; 11: 122-127.
24. Amoush A, Luckstead M, Lamba M et al. A comparison of HDR near source dosimetry using a treatment planning system, Monte Carlo simulation, and radiochromic film. *Med Dosim* 2019; 38: 160-164.
25. Kirisits C, Siebert FA, Baltas D et al. Accuracy of volume and DVH parameters determined with different brachytherapy treatment planning systems. *Radiother Oncol* 2007; 84: 290-297.
26. Pepin MD, Penoncello GP, Brom KM et al. Assessment of dose-volume histogram precision for five clinical systems. *Med Phys* 2022; 49: 6303-6318.
27. van der Meer MC, Bosman PAN, Pieters BR et al. Sensitivity of dose-volume indices to computation settings in high-dose-rate prostate brachytherapy treatment plan evaluation. *J Appl Clin Med Phys* 2019; 20: 66-74.