Combining Novel Direction Modulated Brachytherapy Tandem-and-Ovoids Applicators for Treatment Planning of Multi-Institutional Cervical Cancer Cases: Removing Needles in Intracavitary-Interstitial Techniques

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A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science at Virginia Commonwealth University

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Abstract

Purpose: Lack of standard guidelines for optimal needle insertion during high-dose-rate (HDR) intracavitary-interstitial (IC-IS) brachytherapy of the cervix means a sophisticated and technical skillset of inserting needles next to IC applicators must be developed to enhance plan quality. This study sought to evaluate the performance of two separate direction modulated brachytherapy (DMBT) tandem applicators used in conjunction with one set of novel DMBT ovoids, uniquely designed to effectively obviate the need for IS needles.

Materials and Methods: A cohort of 32 retrospective clinical HDR brachytherapy plans, from three institutions, were re-planned with Varian's BrachyVision® (v16.1) treatment planning system (BV-TPS), using the latest VEGO® inverse optimization algorithm, with dose heterogeneity accounted for through the AcurosBV®. All plans consisted of IC-IS cases, with a range of 2-4 freehand-loaded needles, with an average prescription dose of 709±53 cGy, and with an average high-risk clinical target volume (HRCTV) of 36.73±17.15 [range 9.8-69.6] cm^3. Two DMBT tandem models of 5.4-mm and 8.0-mm thicknesses along with a novel DMBT ovoids design, introduced for the first time, with 9 equi-angled grooves and 10-mm-diameter thickness. During re-planning, the conventional tandems, ovoids/rings, and all the needles were replaced by one of the two DMBT tandem models and a set of DMBT ovoids. A two-step inverse optimization process was performed to achieve the lowest possible OAR D2cc doses while 1) keeping equivalent target coverage (ΔHRCTV-D90 to within ±0.5%) and 2) maintaining the general pear-shape dose distribution used by the original plans. For all plans, this process was repeated using each of the two DMBT tandem-and-ovoids combinations for a total re-planning of (32×2=) 64 cases.

Results: On average, -48.62±28.83 (-41.67±34.69) cGy, -44.32±25.84 (-43.01±26.78) cGy, and -41.73±24.35 (-33.57±25.01) cGy reductions in D2cc across bladder, rectum, and sigmoid, respectively, were achieved for the 8-mm (5.4-mm) DMBT tandem-and-ovoids combinations while the average ΔHRCTV-D90 was +4.3±2.9 cGy (+3.63±2.74 cGy). Additionally, D2cc reductions in terms of EQD2 [Gy] were calculated and showed significant reductions of -4.18±2.47 (-3.48±2.81) Gy, -2.79±1.75 (-2.67±1.71) Gy, and -3.38±1.90 (-2.74±2.03) Gy for bladder, rectum, and sigmoid, respectively with an average net increase in total dwell times of 248.54±77.40 (179.13±59.92) seconds at the luxury of avoiding IS needle insertions.

Conclusions: It is clinically feasible to obviate the need for IS needles by incorporating the DMBT tandem-and-ovoids while producing lower OAR D2cc doses and maintaining equivalent target coverage.

1. Introduction

1.1. Background

The history of brachytherapy began in 1896 following the discovery of X-rays by Wilhelm Röentgen and radioactivity by Henri Becquerel. Shortly after, Pierre Curie and Alexander Graham Bell recommended the use of radioactive isotopes for cancer treatment. Brachytherapy was started for the treatment of malignant tumor in 1901 using a small radium tube containing 0.398 g of radium sulfate at St. Louis Hospital in Paris. In 1903, the first gynecological brachytherapy was described by Margareth Cleaves in New York and Robert Abbe from St. Luke Memorial Hospital performed the first radium implant after the excision of tumor that introduced the idea of afterloading technique of radium treatment in the United States [1]. With the discovery of the radium isotope, clinical trials and experiments have increased rapidly and after World War II, radioisotopes such as Cobalt-60 (Co-60), Gold-198 (Au-198), Tantalum-182 (Ta-182), and Cesium-137(Cs-137) were introduced and replaced Radium-226 in intracavitary therapy. In 1958, Iridium-192 (Ir-192) replaced these sources because of its high specific activity and was first used clinically by Ulrich Henschke at the Memorial Sloan Kettering Cancer Center [1]. Using Ir-192 as a source made it possible to produce smaller sources that could travel inside brachytherapy applicators and deliver doses in shortest times. With an average photon energy of 380 keV, Ir-192 could also provide a steeper dose gradient compared to the external beam radiation therapy. In addition, as the source is placed near or within the target, brachytherapy could deliver maximum dose to the target with minimizing the dose to organs at risks (OARs) which is one of the reasons that it has still been considering one of the standard treatment modalities for the treatment of cancer patients.

1.2. Prognosis, Diagnosis and Treatment in Cervical Cancer

Cervical cancer is the third-most common cancer among women worldwide, with an annual incidence of 530,000 cases and 250,000 deaths. In the developing world, it is the second leading cause of cancer death among women [2]. The incidence of cervical cancer in developed countries has decreased by 70% over the past 50 years, with the adoption of improved screening methods in cervical cytology [3]. Even more reduction in its incidence is anticipated with the implementation of human papilloma virus (HPV) vaccine, as HPV infection is associated with the development of cervical and other anogenital cancers [4]. FIGO (Fe´de´ration Internationale de Gyne´cologie et d'Obste´trique) staging is the most widely used staging system. Lymph-node involvement is related to stage, with from 15 % to 20 % in Stage IB, 30 % in Stage

IIB, and more than from 40 % to 50 % in Stage III. MRI is regarded as the gold standard for tumor assessment and PET-CT is considered a non-invasive examination to assess nodal and distant disease [5] For locally advanced cervical cancer, the standard of care has evolved from external beam radiation therapy (EBRT) alone, to EBRT plus brachytherapy, to combined EBRT plus brachytherapy with concurrent chemotherapy [6]. The external beam radiation therapy delivers treatment to the pelvic lymph nodes, parametria, and primary tumor, to a dose adequate to control microscopic disease. The addition of brachytherapy serves to boost the gross tumor and improves disease control and survival [7].

1.3. Brachytherapy in Cervical Cancer Treatment

The first treatment of cervical cancer with Radium was performed by American surgeon Robert Abbe in 1910 [8]. Since then, the basics of cervical cancer brachytherapy procedure have been the same. An intracavitary applicator with two main components is implanted to allow the radionuclide to treat the tumor using the applicator. Specifically, a tandem is placed within the cervix, through the intrauterine canal and a ring (or ovoids) are placed against the cervix, against the vaginal fornices. Together, the tandem and ring/ovoids give rise to a 3D pear-shaped radiation dose distribution which ideally covers the target or cancer cells. The three first historical systems were the Stockholm (1910), Paris (1919) and Manchester (1938) systems. The Stockholm system was fractionated in two to three fractions, each lasting approximately 20 h to 30 h, separated by 1 to 2 weeks. The use of larger amounts of radium decreased application times from 18 h to 10 h. The uterus contained from 30 mg to 90 mg of radium and the vaginal applicators (cylinders or boxes) from 60 mg to 80 mg. Unlike the Stockholm system, the Paris system was delivered in a single session and used equal amount of Radium in the uterus and vagina [5]. The Manchester system was the first system to define treatment in terms of absorbed dose to a point which is representative of the target [9]. Instead of prescribing absorbed dose to a malignant region, absorbed dose was limited to the area where the uterine vessels cross the ureter. It was considered that the tolerance of this area is the main limiting factor in the irradiation of the cervix. Prescribing a fixed dose to this point, known as Point-A, was the main concept of the Manchester system. Point A was defined as a point 2 cm lateral to the central canal of the uterus and 2 cm up from the mucus membrane of the lateral fornix, in the axis of the uterus. During the era of X-ray radiographs, dose calculations were done with the help of radiographs and localization of Point A was difficult because the surface of the ovoids was not visible. Therefore, they revised this system in 1953 to locate Point A from 2 cm up from the flange or lowest most source of intrauterine tandem and 2 cm lateral from the central canal. This concept of absorbed dose to a single point (Point-A), made this system the most acceptable technique for the treatment of cervical cancer and 46% of clinics still prescribing dose to Point-A according to a 2014 survey conducted by the American Brachytherapy Society (ABS) [10].

Implementation of image-guided brachytherapy (IGBT) in the last few decades has increased with the introduction of use of 3D imaging (computed tomography (CT) & magnetic resonance imaging (MRI)) as IGBT helps to visualize the extent of tumor growth and the proximity of OARs [11-12]. Moreover, the introduction of volumetric based tumor targets and OARs has made it possible to move from prescription from Point-A to dose to 3D volumes in terms of dose-volume histogram (DVH) metrics [13]. Definitions for volume-based targets were recommended by the Groupe Européen de Curiethérapie and the European Society for Radiotherapy & Oncology (GEC-ESTRO) in 2005 and are summarized in the International Commission on Radiation Units and Measurement's report #89 (ICRU-89) [5]. These include the gross tumor volume, intermediate-risk clinical target volume and the high-risk clinical target volume (HRCTV) where the HRCTV was defined as the gross tumor volume, the whole cervix, and adjacent residual pathologic tissue, if present. Multiple retrospective studies have validated moving away from a Point-A prescription to a volume-based approach. Also, the most well known, RetroEMBRACE found that women treated with IGBT has improved local control and reduced treatment-related toxicity compared to women treated with classical, x-ray radiography-based brachytherapy [14]. The popularity of IGBT has increased significantly over the past few decades. According to the ABS 2014 survey, Use of MRI in brachytherapy has increased from 2% to 34% between 2007 to 2014 as most of the centers adopted IGBT (CT and/or MRI) techniques [10].

1.4. Directional Modulated Brachytherapy (DMBT) Tandem and Ovoids

In the case of cervical cancer, the tandem-based applicator provides a cylindrically symmetric, pear-shaped dose distribution. The benefit of brachytherapy is its ability to deliver a high dose of radiation to the tumor while minimizing exposure to OARs. However, this is only true if the tumor is small and contained within the uterus. For large cervix tumors which extend into the nearby paravaginal and parametrial regions, it is not possible to adequately treat the tumor extent without overdosing the OARs. In these cases, the option is to use the intracavitary tandem-based implant with interstitial needles to safely increase the dose to the tumor. Some of the challenges of using these intracavitary-interstitial (IC-IS) hybrid applicators are related to insufficient infrastructure in smaller nonacademic settings, lack of skills and experience of the physicians inserting the needles and patient discomfort. To overcome these challenges utilization of emerging technology in High Dose Rate (HDR) brachytherapy for cervical cancer is inevitable [15]. The theoretical concept of Directional Modulated Brachytherapy was first proposed by Han et al., 2014 for HDR of cervical cancer to create more conformal dose by using anisotropic source with the help of 3D imaging [16]. Multiple studies have proposed direction modulated brachytherapy (DMBT) tandem applicator against standard applicators, in the setting of image guided adaptive brachytherapy of cervical cancer over the last few years [17-19]. The purpose of this study is to evaluate potential of two direction modulated brachytherapy (DMBT) tandem applicators combined with one DMBT ovoids of unique designs to effectively removing the need for IS needles in a range of IC-IS cases found in multi-institutional clinics by achieving the improvements in OAR doses, recto-vaginal (RV-RP) dose, the doses to the posterior-inferior-border-of-symphysis (PIBS) reference points, and the equivalent total OAR doses delivered in 2 Gy fractions.

2. Methodology

2.1. DMBT Tandem and Ovoids

The experimental DMBT tandem and ovoids are designed with multiple channels around the periphery of a non-ferromagnetic tungsten-alloy rod (ρ = 18.0 g/cm3) as shown in Figure 1 [19] and Figure 2. The tungsten-alloy is composed of 95% tungsten, 3.5% nickel, and 1.5% copper [18] and was chosen for its high physical density to allow better OAR dose sparing than titanium or plastic and for being MRI compatible to minimize susceptibility artifact [20]. In this study, two DMBT tandem models of thickness 5.4mm and 8mm are evaluated. Each of them consists of 6 channels with a channel diameter of 1.3mm and length of 80mm as shown in Figure 3. Also, only one unique DMBT ovoids model is introduced and evaluated for the first time where each ovoid consists of 9 channels with channel diameter of 1.3mm and length of 30mm as shown in Figure 4.

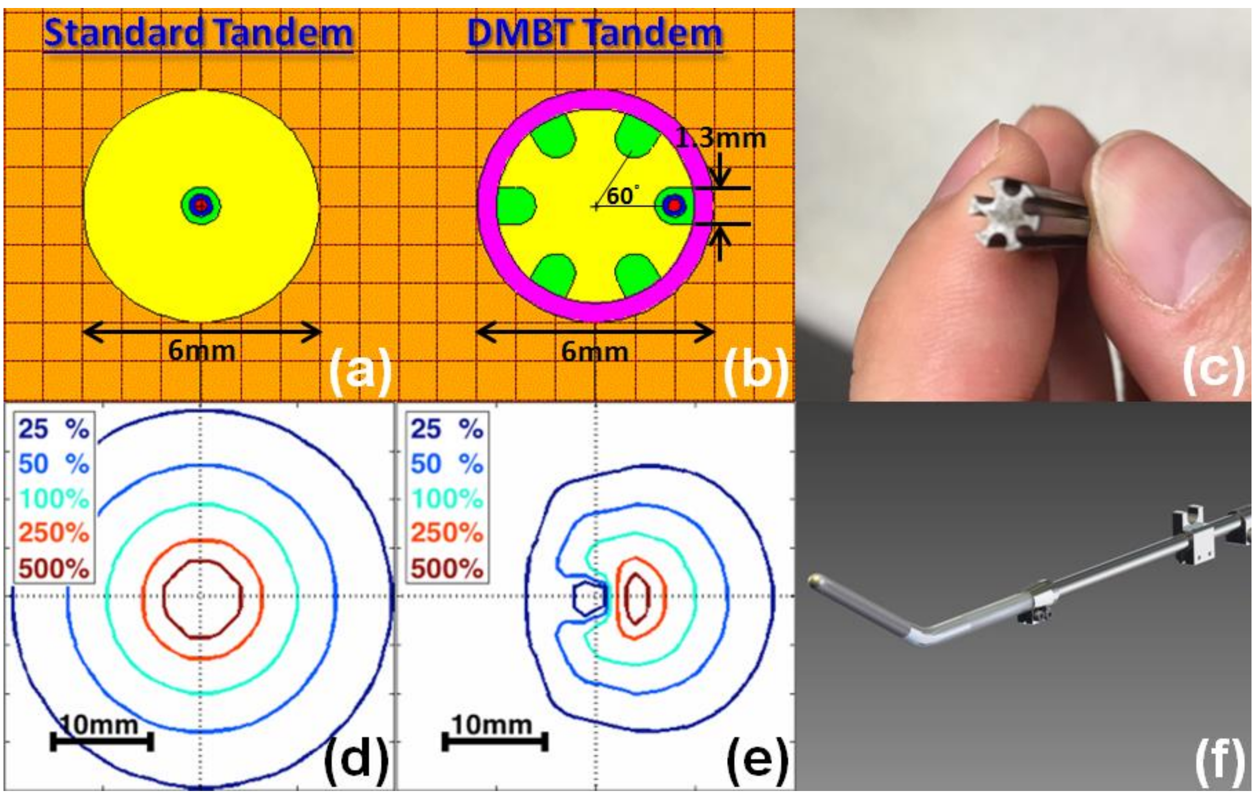

Figure 1: (a) A conventional tandem (b) The direction-modulated brachytherapy (DMBT) tandem. (c) Six channeled DMBT tandem (d) Isotropic dose distribution by conventional tandem. (e) Anisotropic dose distribution by DMBT tandem. (f) A prototype of a DMBT tandem.

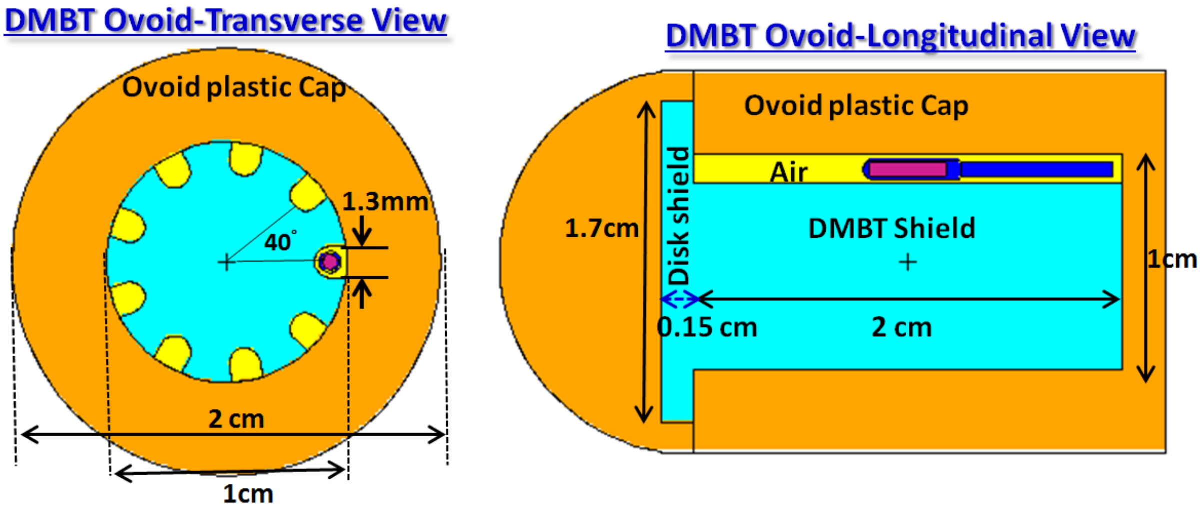

Figure 2: (a) A cross-sectional view of a DMBT ovoid. (b) A longitudinal view of a DMBT ovoid provided by Varian.

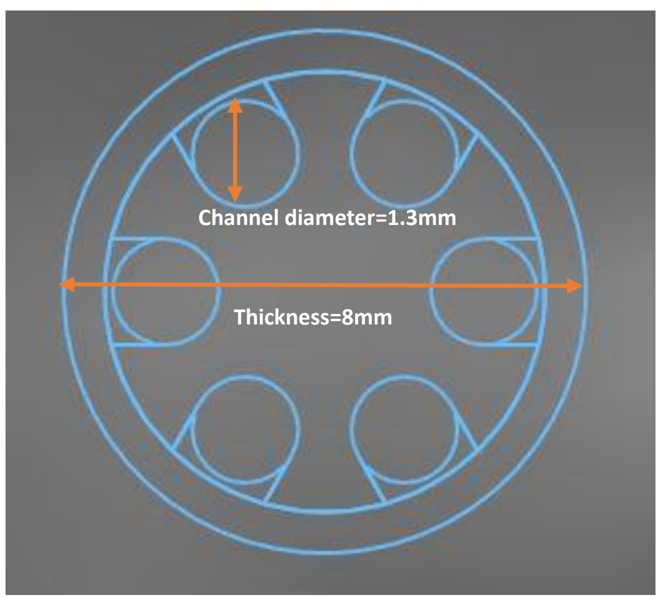

Figure 3: Definitions of the physical dimensions of the DMBT tandem.

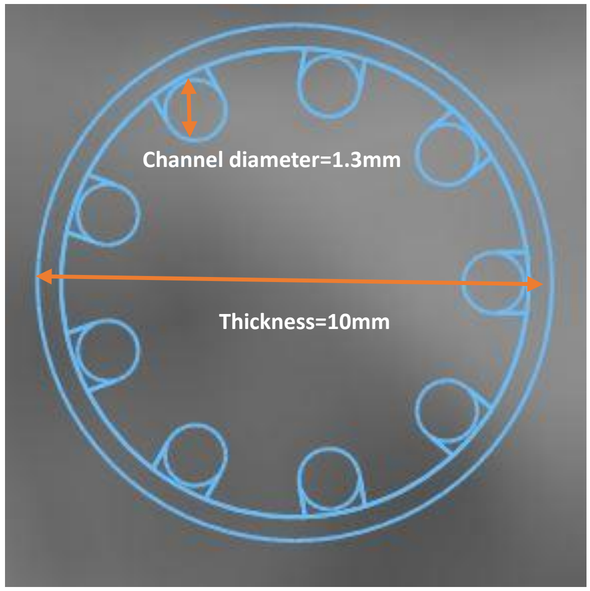

Figure 4: Definitions of the physical dimensions of the DMBT ovoid.

2.2. Patient Cohort

A cohort of 32 retrospective clinical HDR brachytherapy plans was provided by three institutions: Virginia Commonwealth University (VCU), University of Michigan (UMich), and University of California San Diego (UCSD). The treatment plans were selected by considering three main conditions. First, plans containing IC-IS cases were considered. Second, plans that originally had conventional tandem-ovoid (12) and Conventional tandem-ring (20) and then replanned by DMBT tandem-ovoid and DMBT tandem-ring were selected to replace those conventional ovoids/ring by DMBT ovoids. Third, CT simulated only patients were selected as the number of patients simulated with MRI imaging were not adequate. Considering the above conditions, we were able to select 32 previously treated CT based (IC-IS) plans (T&O and T&R) belonging to 12 patients. HRCTV sizes range from 9.8 cm3 to 69.58 cm3 with an average of 36.73 cm3. Prescription doses ranged from 600 cGy to 800 cGy. FIGO stages ranged from IB3 to IIIC2. A summarized table of the patient cohort can be seen in Table 1.

Patient No	Fraction	FIGO Stage	Prescription Dose (cGy)	HRCTV Volume (cc)	Technique	Applicator	# Needles
1	1	IIB	600	41.95	IC-IS	T&O	3
	2		600	51.22	IC-IS	T&O	4
2	1	IIB	600	23.71	IC-IS	T&O	2
3	1	IIIC1	800	23.8	IC-IS	T&O	2
4	1	IIB	700	53.49	IC-IS	T&O	4
	2		700	59.66	IC-IS	T&O	4
5	1	IIIC1	700	20.69	IC-IS	T&R	2
	2		700	28.2	IC-IS	T&R	2
	3		700	19.87	IC-IS	T&R	2
	4		700	24.46	IC-IS	T&R	2
6	1	IB3	800	19.75	IC-IS	T&R	2
	2		800	17.79	IC-IS	T&R	2
7	1	IIB	800	20.32	IC-IS	T&R	2
	2		800	14.11	IC-IS	T&R	2
	3		800	9.8	IC-IS	T&R	2
8	1	IIIC2	700	57.25	IC-IS	T&O	2
	2		700	31.26	IC-IS	T&O	2
	3		700	48.62	IC-IS	T&O	2
	4		700	59.59	IC-IS	T&R	2
9	1	IIB	700	26.73	IC-IS	T&R	2
	2		700	24.88	IC-IS	T&R	2
	3		700	30.06	IC-IS	T&R	2
10	1	IIB	700	35.72	IC-IS	T&R	3
	2		700	43.7	IC-IS	T&R	3
	3		700	33.3	IC-IS	T&R	3
11	1	IB3	700	69.58	IC-IS	T&R	2
	2		700	19.09	IC-IS	T&R	2
	3		700	31.99	IC-IS	T&R	2
	4		700	56.3	IC-IS	T&R	2
12	1	IIIC1	700	59.48	IC-IS	T&O	4
	2		700	58.48	IC-IS	T&O	4
	3		700	60.55	IC-IS	T&O	2

Table 1: Data on 12 patient cohorts was used in this study. 12 plans belonged to 6 patients using T&O while the remaining 20 plans belonged to 6 patients using T&R.

2.3. Sources and Afterloaders

Varian's VariSource, GammaMed Plus and Bravos devices were used in this study where the sources were Ir-192. For each plan treatment date was set to the calibration date of both sources which was 9/10/2020. The activity and source strength of the VS2000 Ir-192 model were 10 Ci and 40300 cGy•cm2/h respectively. The activity and source strength of the GMP Ir-192 model were 10 Ci and 40700 cGy•cm2/h respectively.

The activity and source strength of the Bravos Ir-192 model were same as GMP Ir-192 which were 10 Ci and 40700 cGy•cm2/h respectively.

2.4. System and software

In this study Varian BrachyVision v.16.1, Varian, Palo Alto, CA treatment planning system was used. This research version of TPS provides a library of 9 DMBT digitized tandem models and only one model of DMBT ovoids. Our research group has quantified 9 DMBT tandem models of varying physical dimensions to improve in plan quality via organs at risk (OAR) dose reductions from a large cohort of patient cases collected from three institutions. All 9 DMBT tandem models were each able to generate notable D2cc reductions to OARs approximately 50 cGy, without compromising target coverage. 8mm and 5.4mm thick tandems provided the highest reduction of D2cc in all OARs and thus selected for this study to see whether they could provide additional improvement along with only one model of DMBT ovoids.

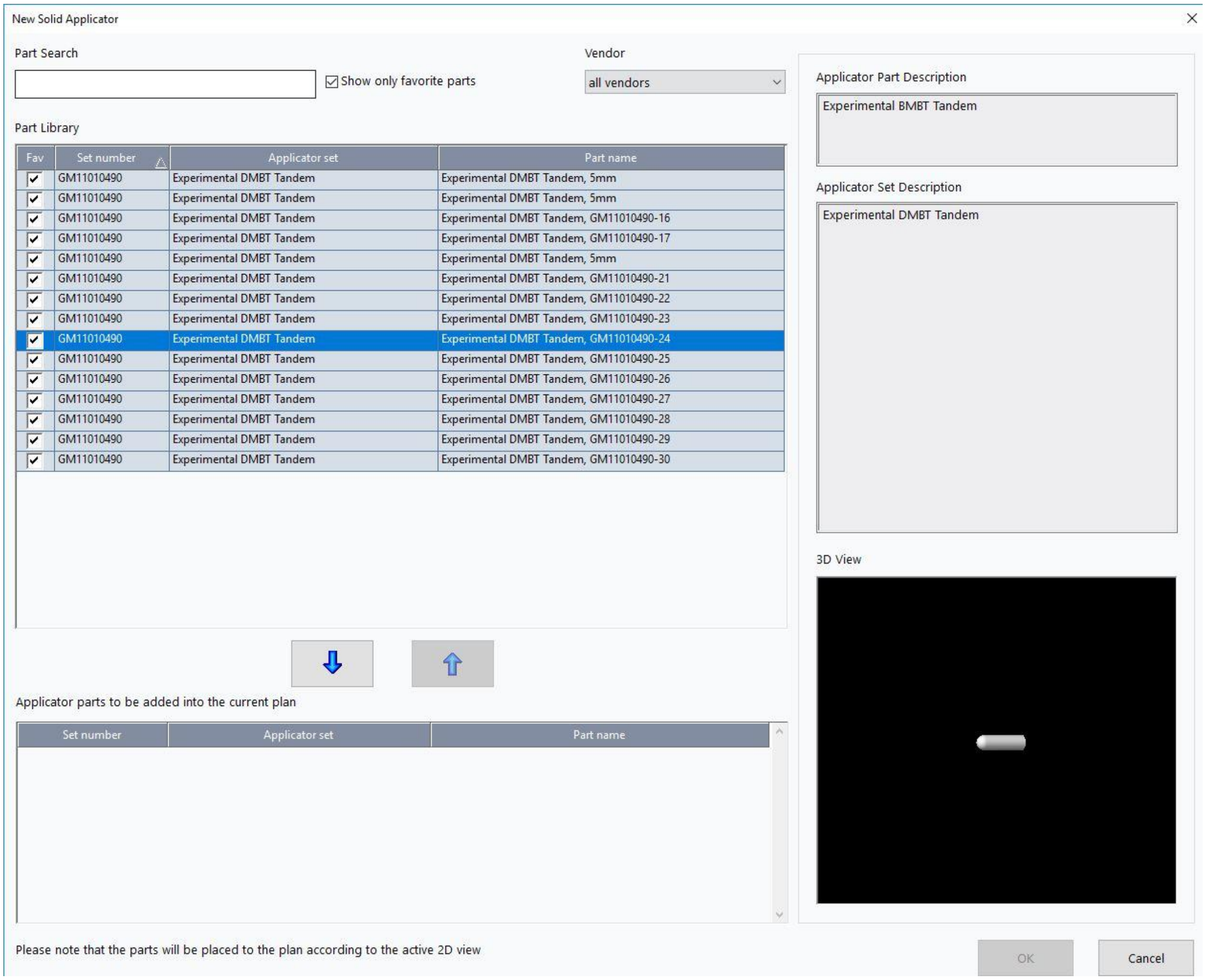

Figure 5: Library of digitized DMBT tandem and ovoids in brachy vision TPS.

3. Treatment Planning

Among 110 multi-institutional clinical HDR treatment plans that were imported in our research version TPS and replanned to 990 plans by DMBT tandems, only 64 plans (32 plans have DMBT tandem of thickness 5.4mm and 32 plans have DMBT tandem of thickness 8mm) were selected for the replacement of Ovoids/Ring by DMBT ovoids. Our research group replanned these 64 plans by aligning the DMBT tandem in place of conventional tandem, setting dwell position in all 6 channels of DMBT tandems, removing conventional tandem and needles, specifying recto-vaginal point, generating structure, and optimizing plan. These plans were analyzed to demonstrate how much better coverage was possible to provide for High-Risk Clinical Target Volume (HRCTV) and at the same time how much dose to organs at risks (OARs) can be lower by utilizing only DMBT tandems when needles were removed. The next step of treatment planning for these 64 plans was to align DMBT ovoids in the place of conventional ovoids/ring.

3.1. DMBT ovoids alignment

In case of replacing conventional ovoids, DMBT ovoids were aligned in the same position as the conventional ovoids and dwell positions in all 18 channels are set at the same level of conventional ovoids dwell position. In case of ring replacement, DMBT ovoids are aligned at the middle of right side and left side of the ring. After proper alignment, dwell positions were set at the middle of each of the 9 channels of DMBT ovoids.

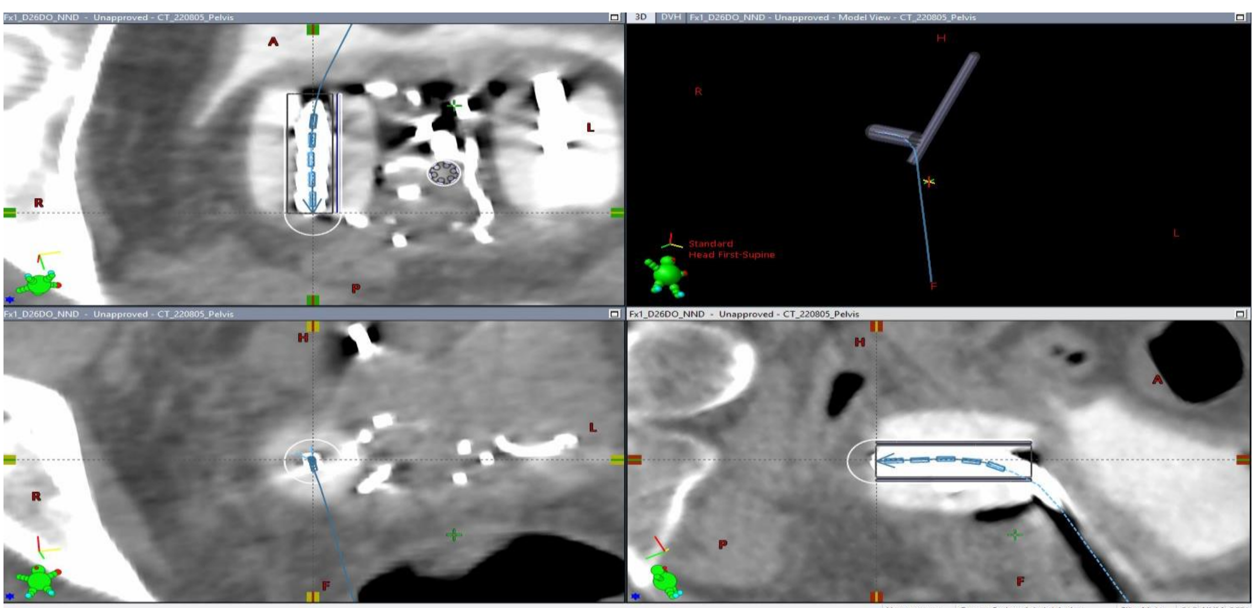

Figure 6: One digitized DMBT ovoid aligned with the original plan's conventional ovoid.

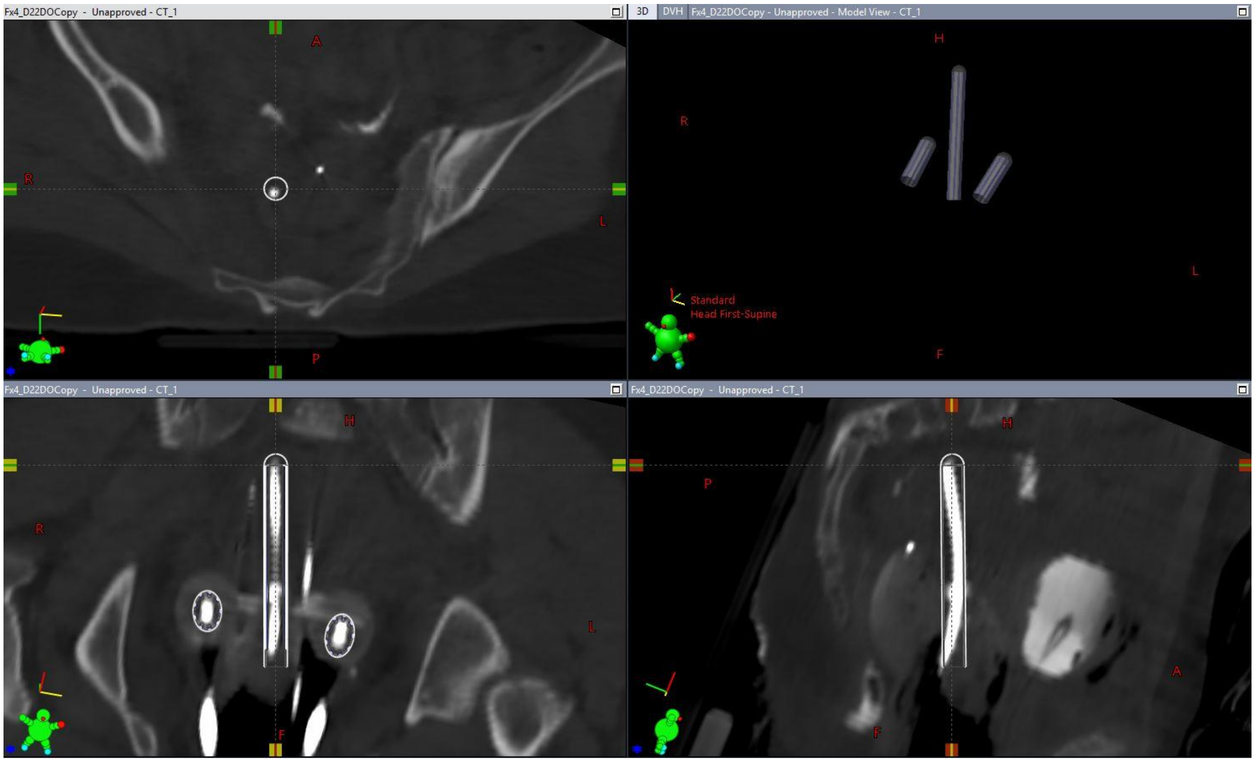

Figure 7: Two digitized DMBT ovoids aligned with the original plan's conventional ovoids.

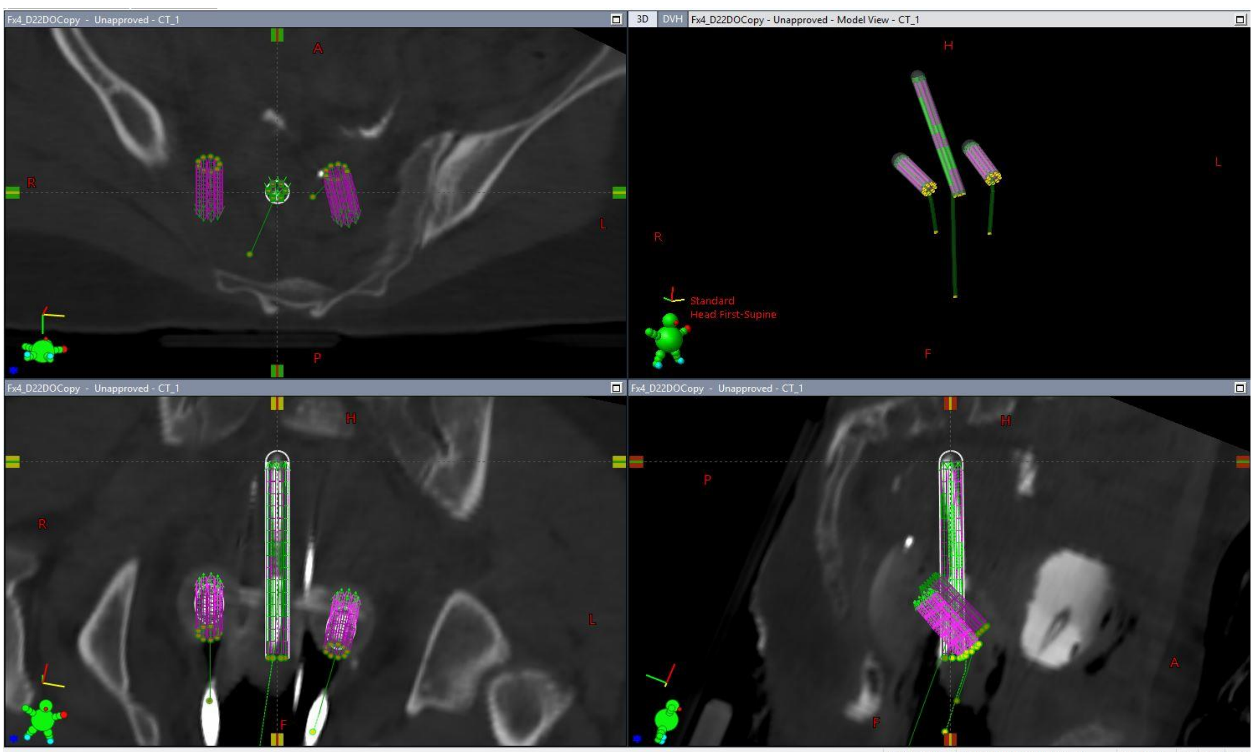

Figure 8: Dwell positions are set to all 6 channels of DMBT tandem and 18 channels of DMBT ovoids for the replacement of conventional tandem and ovoids.

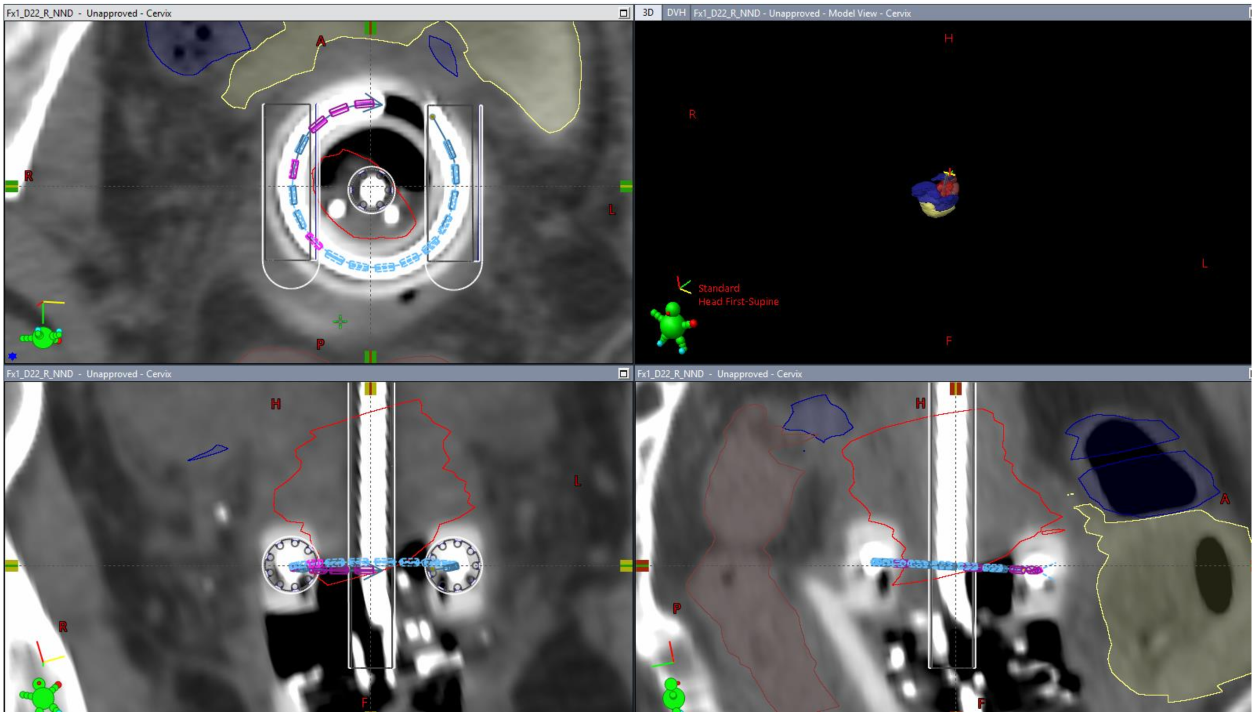

Figure 9: Digitized DMBT ovoids aligned with the original plan's ring.

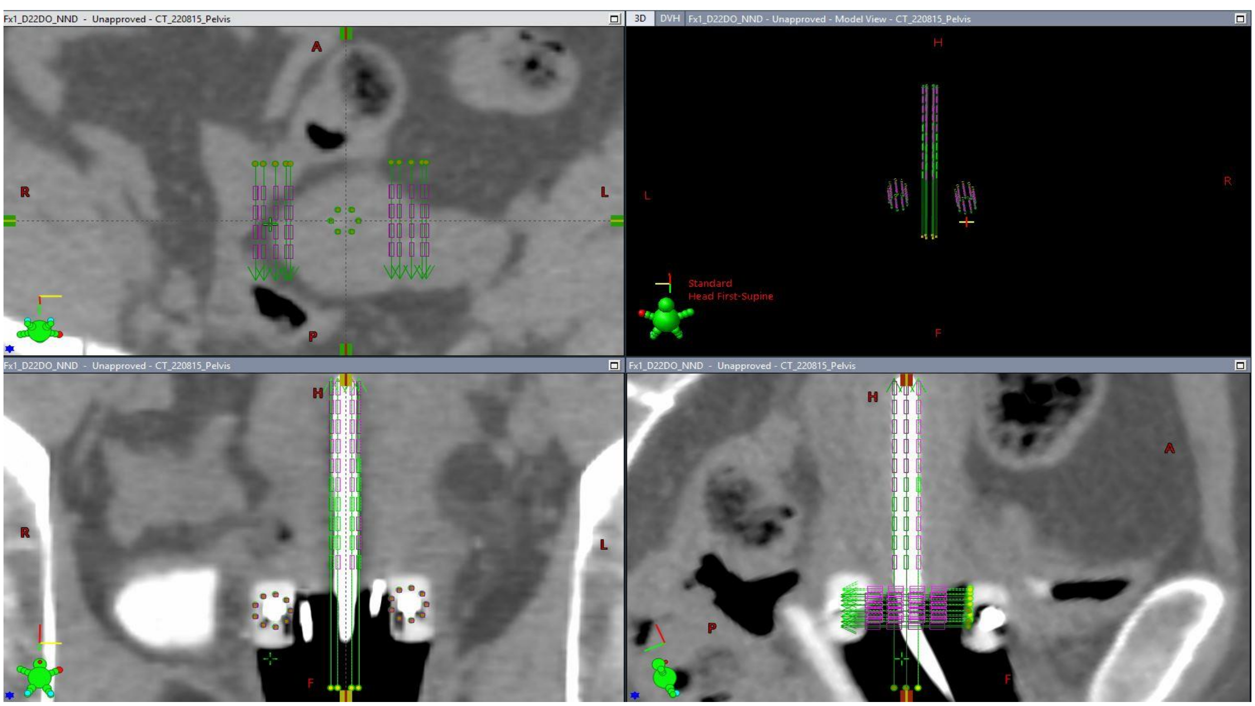

Figure 10: Dwell positions are set to all 6 channels of DMBT tandem and 18 channels of DMBT ovoids after replacing conventional tandem and ring.

3.2. Plan Optimization

Inverse optimization was performed using VEGO Acuros BV Volume Optimization for all 64 plans. Dose calculation was performed through the AcurosBV® model-based dose calculation algorithm. This algorithm also performed the inhomogeneity correction of only tungsten alloy of all DMBT tandem and DMBT ovoids. In this process all other heterogeneities including bone and soft tissues were treated as water.

Artificial contour structures were created to make the DMBT tandem's 100% isodose line same as the pear shaped isodose line of the original plan. To do so, the 100% isodose line of the original plan was converted into a structure named as the "100% dose" structure. Then the Contour application was used to create two optimization structures (PTV and Optimization 2). PTV was created from subtracting areas of overlap between the OARs and the 100% dose structure while overlapping with the HRCTV. Optimization 2 (OPT2) was created to be a 3mm symmetric expansion about the PTV while excluding areas of overlap. Thus, OPT2 was used to confine the regions of high dose from extending into nearby OARs during the optimization step.

To maintain the D90 value to within ± 0.5% of the original plan's D90, upper and lower HRCTV constraints were created. The PTV structure was set such that at least 90% of its volume received at least 90% of the dose and the OPT2 constraint was set to receive no more than 100% of the dose to no more than 1cm3 of its volume to make sure that high dose regions were separated from the regions of OARs. Lastly, higher limit OAR dose constraints were set by the D2cc and D1cc values same as the original plan.

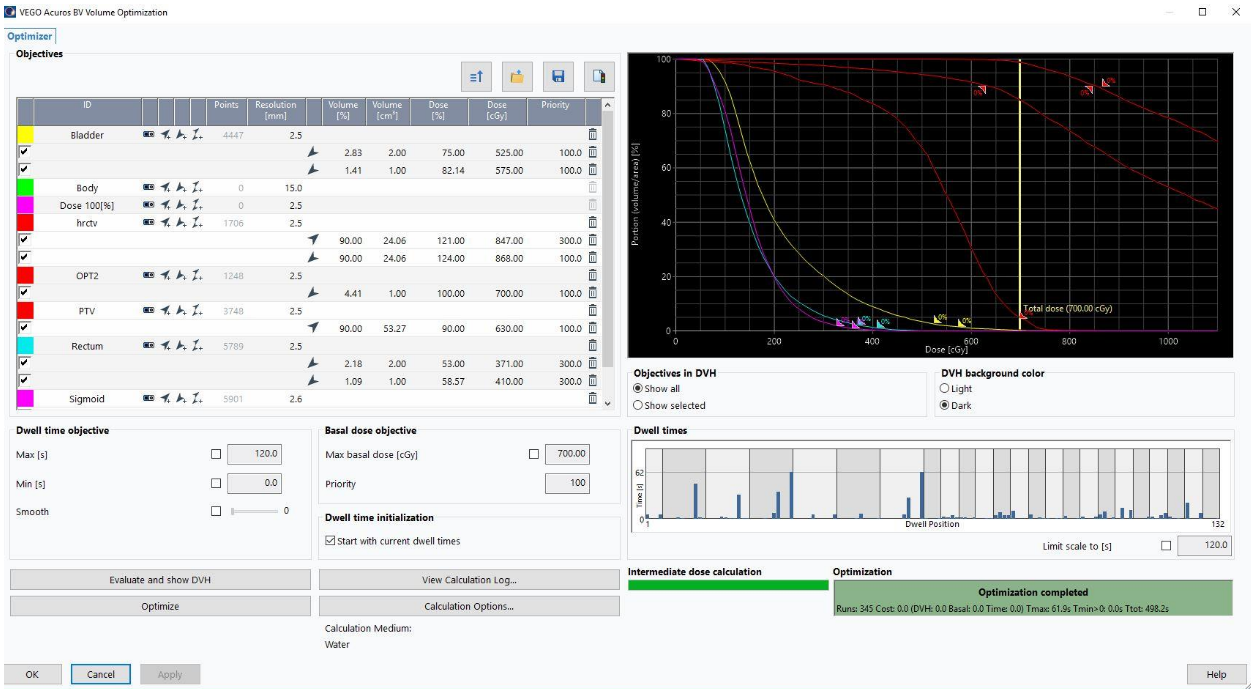

Figure 11: The optimization and calculation step used VEGO Acuros BV Volume optimization.

3.3. Data Analysis:

After completing inverse optimization successfully D90, D98, V100, V150, V200 values of HRCTV, D90 values of PTV and D2cc, D1cc, D0.1cc values of OARs were recorded from DVH of 64 new DMBT tandem-and-ovoid plans. Dose to the RV-RP and all PIBS reference points were also recorded. In addition, treatment time taken by DMBT tandem-and-ovoids were documented. The values of the DMBT tandem and conventional ovoids/ring with no needle plan were then compared to the values of the new DMBT tandem-and-ovoids plan. Deviation of D90 and V100 values of HRCTV and relative and absolute reductions of OAR D2cc, D1cc were documented.

3.4. Dose calculation

To assess the total biological effective dose simple addition of absorbed doses from EBRT and from brachytherapy is not meaningful because of the different biological effectiveness associated with their delivery. The biologically effective dose (BED) is a measure of the true biological dose delivered by a particular combination of dose per fraction and total dose to a particular tissue characterized by a specific α/β ratio [20]. Generally, tumors are assumed to have α/β ratio of 10 Gy and normal tissues have an α/β ratio of 3 Gy. Biologically equivalent doses were calculated in 2 Gy equivalents using the EQD2 equation known as Withers formula [21-23]. EQD2 OAR D2cc values were calculated for all DMBT tandem-and-Ovoids plans and compared to those recommendations set by a 2021 ABS review as shown in Figure 12. The EBRT total dose was assumed to follow a common fractionation scheme of 45 Gy delivered over 25 fractions. The brachytherapy fractionation scheme was determined from the patient information of number of fractions and the prescription dose per fraction.

Target/organs	ABS	EMBRACE trial
Point A	Variable	No recommendation
HR-CTV D90	≥80–90 Gy EQD2	According to institutional practice
IR-CTV D90	No recommendation	According to institutional practice
D_{2cc} bladder	≤90 Gy EQD2	<90 Gy EQD2
D_{2cc} rectum	≤75 Gy EQD2	<70–75 Gy EQD2
D_{2cc} sigmoid	≤75 Gy EQD2	<75 Gy EQD2

Figure 12: Total biologically equivalent dose (EQD2) limits (EBRT+BT) recommendations for the HRCTV and OAR in the treatment of cervical cancer from 2021 review article [24].

4. Results

4.1. Absolute & Relative OAR Dose Differences for 5.4 mm DMBT Tandem and DMBT Ovoids Model

Absolute differences of D2cc and D1cc of bladder, rectum and sigmoid for the plans using 5.4 mm thick DMBT tandem-and-ovoid model with removed needles compared to the original (IC-IS) plans are presented in Table 2. The average absolute reduction in the D2cc using this model for all 12 patients were -41.67 cGy, -43.01 cGy, and -33.57 cGy and the average absolute reduction in the D1cc were -40.85 cGy, -46.90 cGy, and -37.39 cGy for the bladder, rectum, and sigmoid respectively. The maximum absolute D2cc reductions achieved for a particular patient was -106.48 cGy, -115.80 cGy, and -93.02 cGy for the bladder, rectum, and sigmoid respectively.

Relative differences of D2cc and D1cc of bladder, rectum and sigmoid for the same plans using the same model compared to the original (IC-IS) plans are presented in Table 3. In addition, compared to Table 1. The relative variation of V100 and D90 for HRCTV values from original plans are included in Table 2. The average relative reduction in the D2cc using this model for all 12 patients were -10.1%, -16.6%, and -9.2% and the average relative reduction in the D1cc were -9.2%, -16.5%, and -9.2% for the bladder, rectum, and sigmoid respectively. The maximum relative D2cc reductions achieved for a particular patient was -37.6%, -40.7%, and -37.8% for the bladder, rectum, and sigmoid respectively.

Patient No	Original HRCTV D90 [cGy]	HRCTV ΔD90 [cGy]	Bladder ΔD2cc [cGy]	Bladder ΔD1cc [cGy]	Rectum ΔD2cc [cGy]	Rectum ΔD1cc [cGy]	Sigmoid ΔD2cc [cGy]	Sigmoid ΔD1cc [cGy]
	619.02	0.98	-10.62	-12.57	-45.03	-43.59	-93.02	-103.84
1	608.21	0.59	-1.15	-5.55	-9.28	-8.98	-24.32	-48.90
2	600.35	4.00	3.54	11.45	-14.03	-6.52	-85.68	-101.24
3	760.31	2.09	-29.99	-31.61	-37.42	-32.29	-26.46	-22.39
	684.18	2.68	-4.03	-3.03	-29.21	-36.16	-36.10	-41.14
4	685.99	4.99	8.80	12.33	-23.66	-29.20	26.55	4.10
	884.10	1.28	-92.76	-107.31	-37.88	-38.22	-46.64	-61.28
	766.00	6.73	-101.88	-123.25	-4.87	5.21	-69.12	-72.60
	871.15	-2.80	-66.99	-63.75	-20.75	-120.02	-39.90	-40.27
5	750.59	10.07	-39.87	-37.09	-34.03	-34.07	-54.38	-56.84
	909.92	1.39	-30.13	-25.63	-77.69	-85.42	-45.94	-47.50
6	975.98	1.77	-32.80	-20.82	-69.68	-75.63	-49.87	-53.00
	879.14	1.92	-25.26	-25.58	-67.24	-74.38	-9.23	-11.32
	860.29	6.69	-76.09	-87.75	-49.68	-54.55	-55.15	-72.66
7	898.40	2.72	-84.10	-79.11	-19.28	-20.45	-5.23	4.17
	691.05	3.15	-31.35	-26.38	-69.66	-68.18	-33.68	-37.37
	733.37	6.03	10.76	8.62	-115.80	-114.68	-13.24	0.36
	718.67	0.33	-0.40	4.95	-43.32	-39.44	0.30	-1.02
8	787.55	5.07	-90.82	-88.36	-71.48	-91.54	-33.34	-39.94
	827.79	5.06	-6.10	8.15	7.90	13.70	-20.10	-19.80
	756.93	7.35	-30.40	-32.80	0.30	9.50	-1.80	2.00
9	695.73	0.74	-49.51	-47.11	-65.85	-71.96	-10.58	-7.61
	811.89	5.41	-90.63	-102.43	-39.69	-43.97	-44.81	-51.19
	779.00	2.00	-106.48	-102.83	-57.38	-58.18	-31.57	-29.57
10	765.50	0.60	-44.00	-34.40	-34.40	-33.50	-17.00	-21.20
	755.00	6.10	-5.30	-6.20	-50.10	-45.90	-15.90	-23.80
	771.75	3.95	-72.28	-77.77	-74.08	-79.93	-47.28	-48.82
	769.08	6.92	-59.40	-53.70	-73.40	-78.80	-25.70	-29.20
11	753.46	6.84	-42.70	-33.50	-23.40	-20.80	-21.00	-27.20
	744.74	3.52	-48.50	-49.00	-48.60	-47.50	-50.80	-43.60
	740.93	5.76	-24.90	-15.53	-39.55	-43.73	-37.60	-37.93
12	720.48	2.37	-58.03	-59.59	-38.03	-31.73	-55.53	-55.74
Average	768.02	3.63	-41.67	-40.85	-43.01	-46.90	-33.57	-37.39
SD	88.02	2.74	34.69	38.70	26.78	33.00	25.01	27.62
MAX	975.98	10.07	10.76	12.33	7.90	13.70	26.55	4.17
MIN	600.35	-2.80	-106.48	-123.25	-115.80	-120.02	-93.02	-103.84

Table 2: Absolute differences of D90 for HRCTV and D2cc and D1cc for bladder, rectum and sigmoid respectively for the plans using DMBT tandem model 5.4mm thick and DMBT ovoids compared to the original (IC-IS) plan when needles are removed from all 32 (IC-IS) plans.

Patient No	HRCTV ΔV100 [%]	HRCTV ΔD90 [%]	Bladder ΔD2cc [%]	Bladder ΔD1cc [%]	Rectum ΔD2cc [%]	Rectum ΔD1cc [%]	Sigmoid ΔD2cc [%]	Sigmoid ΔD1cc [%]
1	-0.16	0.13	-3.3%	-3.5%	-13.3%	-12.0%	-36.3%	-34.6%
	0.02	0.13	-0.3%	-1.4%	-3.8%	-3.5%	-8.1%	-14.2%
2	0.40	0.67	1.2%	3.7%	-4.0%	-1.7%	-37.8%	-37.9%
3	0.73	0.26	-6.6%	-6.3%	-10.7%	-8.6%	-6.2%	-4.9%
4	0.33	0.38	-1.0%	-0.7%	-8.6%	-9.7%	-8.5%	-8.8%
	0.72	0.71	1.9%	2.4%	-12.1%	-12.8%	6.0%	0.8%
	-0.37	0.18	-29.7%	-30.2%	-14.0%	-13.1%	-10.3%	-12.1%
5	0.85	0.96	-37.6%	-39.9%	-2.3%	2.1%	-14.3%	-13.7%
	-0.34	-0.40	-13.0%	-11.4%	-7.7%	-30.7%	-10.8%	-9.9%
	0.53	1.43	-10.0%	-8.7%	-13.0%	-11.4%	-15.2%	-14.2%
6	-0.67	0.17	-5.5%	-4.3%	-30.1%	-30.5%	-10.0%	-9.5%
	0.63	0.22	-5.9%	-3.4%	-34.4%	-34.6%	-10.4%	-10.2%
	0.58	0.24	-4.7%	-4.3%	-38.3%	-38.8%	-2.1%	-2.3%
7	0.17	0.83	-21.1%	-22.1%	-28.7%	-28.2%	-11.7%	-13.6%
	-2.01	0.34	-16.7%	-14.4%	-12.3%	-11.9%	-1.3%	0.9%
	0.15	0.45	-7.3%	-5.7%	-24.4%	-22.1%	-7.2%	-7.3%
8	0.55	0.86	2.3%	1.6%	-32.9%	-30.0%	-2.5%	0.1%
	0.04	0.03	-0.1%	0.8%	-14.9%	-12.3%	0.1%	-0.2%
	0.47	0.72	-17.9%	-16.1%	-30.4%	-34.0%	-6.6%	-7.3%
	0.09	0.73	-1.2%	1.4%	2.1%	3.4%	-5.9%	-5.3%
9	0.87	1.05	-5.8%	-5.7%	0.1%	3.2%	-0.6%	0.6%
	-0.08	0.11	-8.8%	-7.6%	-28.8%	-28.7%	-2.5%	-1.7%
	-1.26	0.77	-25.2%	-25.8%	-10.5%	-10.7%	-19.2%	-19.5%
10	-0.02	0.23	-23.7%	-21.3%	-23.0%	-21.9%	-6.6%	-5.6%
	0.90	0.05	-10.6%	-7.5%	-14.2%	-13.1%	-8.2%	-8.9%
	59.71	0.92	-0.9%	-1.0%	-12.6%	-10.6%	-3.2%	-4.4%
11	0.67	0.57	-25.1%	-24.7%	-40.7%	-41.1%	-12.5%	-11.8%
	1.35	0.98	-13.6%	-11.0%	-31.2%	-30.9%	-6.8%	-7.2%
	0.50	0.97	-10.0%	-7.3%	-7.9%	-6.6%	-4.9%	-5.4%
	0.88	0.50	-8.5%	-8.2%	-12.4%	-11.6%	-11.1%	-9.0%
12	0.08	0.82	-4.9%	-2.9%	-7.7%	-8.0%	-9.4%	-8.6%
	0.74	0.34	-9.9%	-9.7%	-8.3%	-6.5%	-10.6%	-10.1%
Average	2.10	0.51	-10.1%	-9.2%	-16.6%	-16.5%	-9.2%	-9.2%
SD	10.53	0.39	10.0%	10.4%	11.8%	12.7%	8.9%	8.7%
MAX	59.71	1.43	2.3%	3.7%	2.1%	3.4%	6.0%	0.9%
MIN	-2.01	-0.40	-37.6%	-39.9%	-40.7%	-41.1%	-37.8%	-37.9%

Table 3: Relative differences of V100 [%] and D90 [%] for HRCTV and D2cc [%] and D1cc [%] of bladder, rectum and sigmoid respectively for the plans using DMBT tandem model 5.4mm thick and DMBT ovoids compared to the original (IC-IS) plans when needles are removed from all plans.

Also, the absolute and relative deviations of D90 for HRCTV are presented in Table 2 and Table 3 respectively where the average relative deviation of D90 for HRCTV for this model is 0.51% indicating nearly identical HRCTV coverage. Note that the absolute D2cc reduction for the smallest target (HRCTV =9.8 cm3) using 5.4mm DMBT tandem model were -84.10 cGy, -19.28 cGy, and -5.23 cGy for the bladder, rectum, and sigmoid respectively. This corresponds to a relative D2cc reduction of -16.7%, -12.3%, and -1.3% for the bladder, rectum, and sigmoid respectively for the single fraction with a prescription dose of 800 cGy. The absolute D2cc reductions for the largest target (HRCTV = 69.58 cm3) using 5.4mm thick DMBT tandem model were -5.3 cGy, -50.10 cGy, and -15.90 cGy for the bladder, rectum, and sigmoid respectively. This corresponded to relative D2cc reductions of -0.9%, -12.6%, and -3.2% for the bladder, rectum, and sigmoid respectively for a single fraction with a prescription dose of 700 cGy.

4.1.1. Target size vs Absolute OAR Dose Differences for 5.4mm DMBT Tandem and DMBT Ovoids Model

The absolute D2cc differences (cGy) for all plans were compared for model 5.4 mm thick DMBT tandem and DMBT ovoid to 5.4 mm DMBT tandem and conventional ovoid/ring model with removed needles from all 32 (IC-IS) plans as shown in Figure 13. We have noticed that among 32 plans of 5.4mm DMBT tandem and DMBT ovoids model we were not able to achieve D2cc reduction only for 7 cases (3 bladder, 2 rectum, and 2 sigmoid) but we were able to achieve that in case of 8.0mm model which is presented later in Table 5 and Figure 16. Although the correlation of D2cc reduction with respect to HRCTV size is not significant but using the combination of DMBT tandem and DMBT ovoids made a big difference in case of the D2cc reduction compared to the plans when there were no DMBT ovoids. We performed a statistical analysis which was a type 2, two tailed T-test. The average dose reduction (ΔD2cc for the bladder, rectum and sigmoid were 41.67 cGy (P=0.05), -43.01 cGy (P=0.02), and -33.57 cGy (P=0.07) respectively compared to original plan where the value of dose reduction in case of rectum is statistically significant for this model.

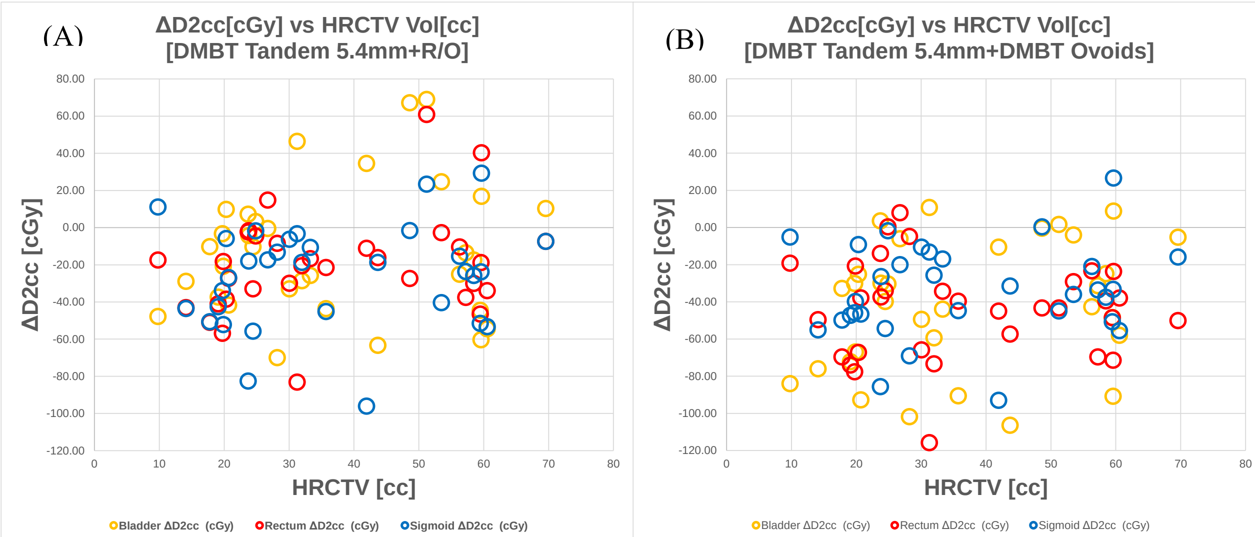

Figure 13: The absolute differences in the D2cc of the bladder, rectum, and sigmoid compared to original plans. (A) 5.4 mm thick DMBT model and conventional ovoids/ring with removed needles from 32 (IC-IS) plans to (B) 5.4 mm DMBT tandem and DMBT ovoids.

4.1.2. Number of Needles vs. Absolute OAR Dose Deviations for 5.4mm DMBT Tandem and DMBT Ovoids Model

Again, absolute D2cc differences for bladder, rectum and sigmoid are compared between the models of 5.4mm DMBT tandem with conventional Ovoids/Ring and 5.4mm DMBT tandem with DMBT ovoids. Although the correlation of the D2cc reduction with respect to the number of needles is not significant but from the diagram it is noticeable that reduction of D2cc in most of the plans are higher in case of DMBT ovoids than the plans when there was no DMBT ovoids.

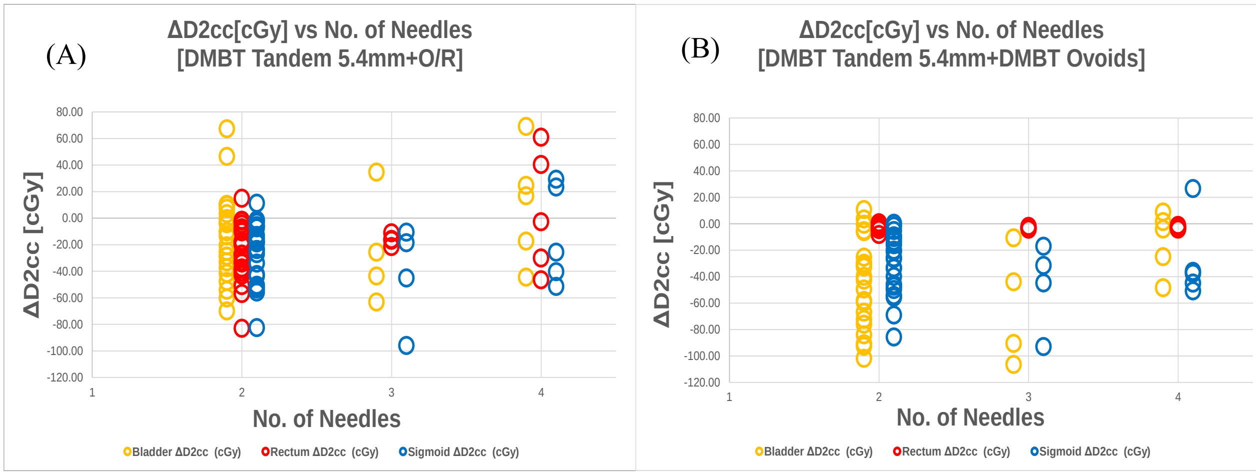

Figure 14: The absolute differences in the D2cc of the bladder, rectum, and sigmoid compared to original plans (A) 5.4 mm thick DMBT model and conventional ovoids/ring with removed needles from 32 (IC-IS) plans to (B) 5.4 mm DMBT tandem and DMBT ovoids model.

4.1.3. Total OAR Dose (EQD2) Differences for 5.4mm DMBT Tandem and DMBT ovoids Model

The differences of EQD2 D2cc values for each OAR and for each plan using 5.4mm thick DMBT tandem and DMBT ovoids from original plans are presented in Table 4. The average absolute EQD2 D2cc reductions over all plans for 5.4mm DMBT tandem and DMBT ovoids model were -3.48 Gy, -2.67 Gy, -2.74 Gy for the bladder, rectum, and sigmoid respectively. The corresponding relative EQD2 D2cc reductions were -5.1%, -4.6% and -4.2% respectively. The maximum relative EQD2 D2cc reductions achieved for a particular patient was -9.29%, -8.22%, and -6.69% for the bladder, rectum, and sigmoid respectively.

In addition, differences of OAR EQD2 D2cc were compared between the 5.4mm thick DMBT tandem and conventional ovoids/ring model and 5.4mm thick DMBT tandem and DMBT ovoids model when needles are removed in each case as shown in Figure 15. Although the correlation of EQD2 D2cc differences with respect to HRCTV size is not significant but the purpose of using the combination of DMBT tandem and DMBT ovoids model that increased the D2cc reduction compared to the plans when there were no DMBT ovoids in Figure 15.

Patient No	HRCTV Volume [cc]	Bladder EQD2 ΔD2cc [Gy]	Bladder EQD2 ΔD2cc [%]	Rectum EQD2 ΔD2cc [Gy]	Rectum EQD2 ΔD2cc [%]	Sigmoid EQD2 ΔD2cc [Gy]	Sigmoid EQD2 ΔD2cc [%]
1	41.95	-1.00	-1.6%	-4.20	-6.5%	-6.69	-11.6%
	51.22	-0.12	-0.2%	-0.72	-1.3%	-2.13	-3.5%
2	23.71	0.31	0.5%	-1.38	-2.1%	-5.72	-10.4%
3	23.8	-2.12	-3.3%	-2.16	-3.8%	-1.79	-2.9%
4	53.49	-0.37	-0.5%	-2.23	-3.7%	-3.22	-4.7%
	59.66	0.88	1.2%	-1.26	-2.5%	2.58	3.7%
	20.69	-6.17	-10.5%	-2.43	-4.4%	-4.31	-6.1%
5	28.2	-6.04	-10.9%	-0.28	-0.5%	-6.64	-9.0%
	19.87	-6.76	-8.8%	-1.36	-2.4%	-3.18	-5.1%
	24.46	-3.38	-5.2%	-2.15	-3.9%	-4.19	-6.7%
6	19.75	-2.47	-3.5%	-3.45	-6.6%	-3.23	-5.0%
	17.79	-2.71	-3.8%	-2.66	-5.4%	-3.62	-5.5%
	20.32	-2.06	-2.9%	-2.36	-4.9%	-0.65	-1.0%
7	14.11	-4.31	-7.5%	-1.78	-3.7%	-3.94	-6.0%
	9.8	-6.17	-9.1%	-0.69	-1.4%	-0.35	-0.6%
	57.25	-2.83	-4.1%	-4.46	-7.9%	-3.25	-4.5%
8	31.26	1.08	1.5%	-8.22	-13.4%	-1.43	-1.8%
	48.62	-0.05	-0.1%	-2.90	-5.1%	0.03	0.0%
	59.59	-8.90	-11.7%	-3.99	-7.5%	-3.42	-4.5%
	26.73	-0.66	-0.8%	0.66	1.0%	-1.55	-2.6%
9	24.88	-3.22	-4.1%	0.02	0.0%	-0.13	-0.2%
	30.06	-5.46	-6.6%	-3.64	-6.9%	-0.95	-1.4%
	35.72	-6.73	-10.8%	-3.23	-5.1%	-2.59	-4.9%
10	43.7	-9.29	-13.3%	-3.41	-6.3%	-3.11	-4.2%
	33.3	-3.83	-5.7%	-2.06	-3.8%	-0.95	-1.8%
	69.58	-0.60	-0.7%	-4.18	-6.4%	-1.62	-2.2%
11	19.09	-4.65	-8.2%	-3.50	-7.0%	-3.81	-6.0%
	31.99	-5.30	-7.7%	-4.10	-7.7%	-2.11	-3.3%
	56.3	-3.80	-5.6%	-1.62	-2.8%	-1.91	-2.8%
	59.48	-5.39	-6.5%	-4.02	-6.2%	-4.75	-6.7%
12	58.48	-2.58	-3.4%	-4.06	-5.3%	-3.21	-4.9%
	60.55	-6.54	-7.7%	-3.57	-5.0%	-5.72	-7.4%
Average	36.73	-3.48	-5.1%	-2.67	-4.6%	-2.74	-4.2%
SD	17.15	2.81	4.1%	1.71	2.8%	2.03	3.1%
MAX	69.58	1.08	1.5%	0.66	1.0%	2.58	3.7%
MIN	9.80	-9.29	-13.3%	-8.22	-13.4%	-6.69	-11.6%

Table 4: Absolute and relative differences of EQD2 D2cc values of bladder, rectum and sigmoid respectively for the plans using DMBT tandem model 5.4mm thick and DMBT ovoids without needles compared to the 32 original (IC-IS) plans.

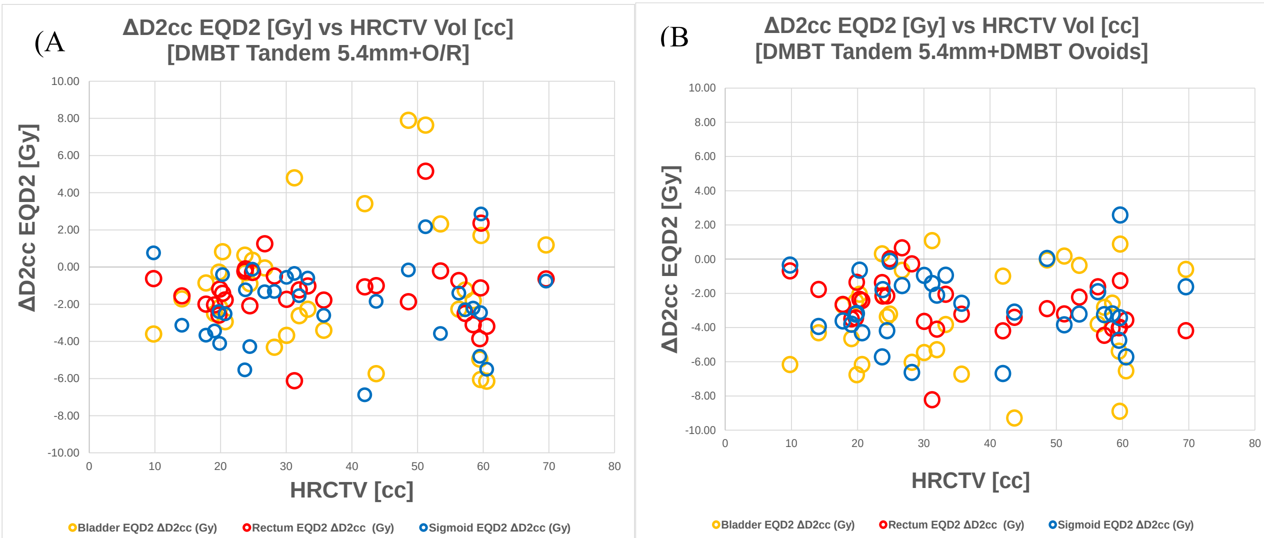

Figure 15: The absolute differences in EQD2 D2cc of the bladder, rectum, and sigmoid compared to original plans (A) 5.4 mm thick DMBT model and conventional ovoids/ring with removed needles (B) 5.4 mm DMBT tandem and DMBT ovoids model with removed needles.

4.2. Absolute & Relative OAR Dose Reduction for 8.0mm DMBT Tandem and DMBT Ovoids Model

Absolute reductions of D2cc and D1cc of bladder, rectum and sigmoid for the plans using DMBT tandem model 8.0mm thick and DMBT ovoid model with removed needles compared to the original (IC-IS) plans are presented in Table 5. The average absolute reduction in the D2cc using this model for all 12 patients were -48.62 cGy, -44.32 cGy, and -41.73 cGy and the average absolute reduction in the D1cc were -50.67 cGy, -48.83 cGy, and -46.72 cGy for the bladder, rectum, and sigmoid respectively. The maximum absolute D2cc reductions achieved for a particular patient was -111.73 cGy, -111.60 cGy, and -109.77 cGy for the bladder, rectum, and sigmoid respectively.

Relative reductions of D2cc and D1cc of bladder, rectum and sigmoid for the plans using DMBT tandem model 8.0mm thick and DMBT ovoid model with removed needles compared to the original (IC-IS) plan are presented in Table 6. The average relative reduction in the D2cc using this model for all 12 patients were -11.5%, -16.9%, and -11.2% and the average relative reduction in the D1cc were -11.1%, -16.9%, and -11.3% for the bladder, rectum, and sigmoid respectively. The maximum relative D2cc reductions achieved for a particular patient was -35.6%, -39.3%, and -42.8% for the bladder, rectum, and sigmoid respectively.

Patient No	Original HRCTV D90 [cGy]	HRCTV ΔD90 [cGy]	Bladder ΔD2cc [cGy]	Bladder ΔD1cc [cGy]	Rectum ΔD2cc [cGy]	Rectum ΔD1cc [cGy]	Sigmoid ΔD2cc [cGy]	Sigmoid ΔD1cc [cGy]
1	619.02	10.36	-20.58	-22.66	-56.46	-58.39	-109.77	-118.45
	608.21	-0.81	-2.15	-7.05	-4.78	-3.78	-20.92	-43.10
2	600.35	0.82	-0.97	3.51	-23.03	-19.32	-90.47	-107.00
3	760.31	12.62	-43.13	-48.59	-36.63	-33.67	-43.60	-43.08
4	684.18	2.19	-17.79	-18.03	-30.32	-38.37	-62.96	-75.65
	685.99	5.17	-2.98	0.57	-12.29	-14.53	-40.83	-72.76
5	884.10	2.35	-88.10	-102.89	-42.18	-42.25	-40.84	-57.67
	766.00	-0.23	-96.66	-118.77	-5.44	5.93	-81.78	-85.91
	871.15	4.16	-70.83	-69.93	-19.78	-119.55	-36.75	-37.54
	750.59	6.02	-49.67	-49.72	-38.18	-39.06	-55.69	-58.61
6	909.92	5.09	-43.90	-46.52	-62.23	-68.72	-54.27	-56.82
	975.98	1.85	-55.40	-49.98	-66.01	-72.52	-50.39	-53.04
7	879.14	3.66	-33.39	-37.40	-43.04	-47.97	-34.45	-37.77
	860.29	5.10	-64.61	-75.65	-54.86	-62.99	-65.08	-83.22
	898.40	6.02	-46.61	-39.40	-40.09	-43.81	-42.29	-38.24
8	691.05	5.75	-45.95	-41.48	-87.96	-90.08	-42.38	-48.37
	733.37	4.72	-25.54	-42.38	-111.60	-111.88	-20.44	-11.94
	718.67	6.63	-11.10	-11.55	-51.32	-42.34	-0.80	-3.12
	787.55	3.76	-88.77	-86.36	-88.13	-109.44	-36.48	-41.34
9	827.79	2.51	-12.10	2.85	-9.80	-8.20	-6.60	-3.60
	756.93	6.46	-21.00	-25.00	-13.60	-7.60	-14.70	-13.10
	695.73	6.59	-54.01	-57.41	-62.35	-68.86	-22.88	-21.62
10	811.89	-0.09	-111.73	-124.93	-28.19	-31.27	-49.01	-55.69
	779.00	6.30	-82.68	-83.43	-43.68	-43.48	-29.77	-33.87
	765.50	4.80	-60.90	-55.30	-34.30	-33.80	-15.40	-19.50
11	755.00	0.50	-38.80	-43.60	-64.00	-61.10	-14.50	-17.40
	771.75	2.75	-59.48	-65.57	-71.58	-76.43	-49.28	-51.92
	769.08	2.42	-71.10	-67.20	-63.30	-67.80	-31.50	-35.60
	753.46	4.94	-60.10	-58.20	-16.00	-15.50	-13.50	-14.60
12	744.74	5.52	-55.00	-59.50	-64.90	-65.40	-68.70	-67.80
	740.93	6.26	-46.20	-41.03	-28.95	-31.43	-41.20	-41.23
	720.48	3.27	-74.73	-78.69	-43.43	-39.03	-48.23	-45.54
Average	768.02	4.30	-48.62	-50.67	-44.32	-48.83	-41.73	-46.72
SD	88.02	2.89	28.83	32.47	25.84	31.41	24.35	27.88
MAX	975.98	12.62	-0.97	3.51	-4.78	5.93	-0.80	-3.12
MIN	600.35	-0.81	-111.73	-124.93	-111.60	-119.55	-109.77	-118.45

Table 5: Absolute differences of D90 for HRCTV and absolute reductions of D2cc and D1cc for bladder, rectum and sigmoid respectively for the plans using DMBT tandem model 8.0mm thick and DMBT ovoids compared to the original (IC-IS) plans when needles are removed.

Patient No	HRCTV ΔV100 [%]	HRCTV ΔD90 [%]	Bladder ΔD2cc [%]	Bladder ΔD1cc [%]	Rectum ΔD2cc [%]	Rectum ΔD1cc [%]	Sigmoid ΔD2cc [%]	Sigmoid ΔD1cc [%]
1	0.62	1.72	-6.3%	-6.3%	-16.6%	-16.0%	-42.8%	-39.5%
	-0.08	-0.17	-0.6%	-1.8%	-2.0%	-1.5%	-7.0%	-12.5%
2	0.09	0.13	-0.3%	1.1%	-6.6%	-5.0%	-39.9%	-40.0%
3	1.77	1.58	-9.5%	-9.7%	-10.4%	-9.0%	-10.2%	-9.4%
4	0.34	0.31	-4.2%	-4.0%	-8.9%	-10.3%	-14.8%	-16.2%
	0.69	0.73	-0.6%	0.1%	-6.3%	-6.4%	-9.2%	-14.1%
5	-0.23	0.34	-28.2%	-29.0%	-15.6%	-14.5%	-9.1%	-11.4%
	0.17	-0.03	-35.6%	-38.5%	-2.6%	2.4%	-16.9%	-16.2%
	-0.70	0.59	-13.8%	-12.5%	-7.4%	-30.5%	-10.0%	-9.2%
	0.06	0.85	-12.4%	-11.6%	-14.5%	-13.1%	-15.5%	-14.6%
6	-0.77	0.64	-8.0%	-7.9%	-24.1%	-24.6%	-11.8%	-11.4%
	0.61	0.23	-10.0%	-8.1%	-32.6%	-33.2%	-10.5%	-10.2%
7	0.33	0.46	-6.2%	-6.3%	-24.5%	-25.0%	-7.8%	-7.7%
	-0.26	0.63	-18.0%	-19.0%	-31.7%	-32.5%	-13.8%	-15.6%
	-0.70	0.75	-9.3%	-7.2%	-25.5%	-25.5%	-10.3%	-8.6%
8	0.35	0.82	-10.7%	-9.0%	-30.8%	-29.2%	-9.0%	-9.4%
	0.55	0.67	-5.4%	-8.1%	-31.7%	-29.2%	-3.8%	-2.1%
	0.44	0.93	-2.0%	-1.9%	-17.7%	-13.3%	-0.2%	-0.6%
	0.87	0.54	-17.5%	-15.7%	-37.5%	-40.7%	-7.2%	-7.5%
9	-0.31	0.34	-2.3%	0.5%	-2.7%	-2.0%	-1.9%	-1.0%
	0.77	0.92	-4.0%	-4.3%	-5.2%	-2.6%	-4.6%	-3.6%
	0.82	0.94	-9.6%	-9.2%	-27.3%	-27.4%	-5.5%	-4.8%
10	-0.76	-0.01	-31.1%	-31.4%	-7.5%	-7.6%	-21.0%	-21.2%
	0.08	0.84	-18.4%	-17.3%	-17.5%	-16.4%	-6.2%	-6.4%
	0.90	0.65	-14.6%	-12.1%	-14.2%	-13.2%	-7.4%	-8.2%
11	0.55	0.12	-6.9%	-7.3%	-16.1%	-14.1%	-2.9%	-3.2%
	0.37	0.39	-20.6%	-20.8%	-39.3%	-39.3%	-13.1%	-12.6%
	0.65	0.35	-16.3%	-13.7%	-26.9%	-26.6%	-8.4%	-8.8%
	0.00	0.70	-14.0%	-12.6%	-5.4%	-4.9%	-3.1%	-2.9%
12	0.88	0.78	-9.7%	-9.9%	-16.6%	-16.0%	-15.0%	-14.0%
	-0.42	0.89	-9.1%	-7.6%	-5.7%	-5.8%	-10.3%	-9.4%
	0.94	0.47	-12.8%	-12.8%	-9.5%	-8.0%	-9.2%	-8.2%
Average	0.27	0.60	-11.5%	-11.1%	-16.9%	-16.9%	-11.2%	-11.3%
SD	0.59	0.41	8.6%	9.0%	11.1%	11.9%	9.1%	8.9%
MAX	1.77	1.72	-0.3%	1.1%	-2.0%	2.4%	-0.2%	-0.6%
MIN	-0.77	-0.17	-35.6%	-38.5%	-39.3%	-40.7%	-42.8%	-40.0%

Table 6: Relative differences of V100 [%] and D90 [%] for HRCTV and relative reductions of D2cc [%] and D1cc [%] of bladder, rectum and sigmoid respectively for the plans using DMBT tandem model 8.0mm thick and DMBT ovoids compared to the original (IC-IS) plan when needles are removed from all plans

Also, the absolute and relative deviations of D90 for HRCTV are presented in Table 5 and Table 6 respectively where the average relative deviation of D90 HRCTV for this model is 0.6% indicating nearly identical HRCTV coverage. Note that the absolute D2cc reduction for the smallest target (HRCTV =9.8 cm3) using 8.0mm DMBT tandem model were -46.61 cGy, -40.09 cGy, and -2.29 cGy for the bladder, rectum, and sigmoid respectively. This corresponds to a relative D2cc reduction of -9.3%, -25.5%, and -10.3% for the bladder, rectum, and sigmoid respectively for the single fraction with a prescription dose of 800 cGy. The absolute D2cc reductions for the largest target (HRCTV = 69.58 cm3) using 8.0mm thick DMBT tandem model were -38.80 cGy, -64.0 cGy, and -14.50 cGy for the bladder, rectum, and sigmoid respectively. This corresponded to relative D2cc reductions of -6.9%, -16.1%, and -2.9% for the bladder, rectum, and sigmoid respectively for a single fraction with a prescription dose of 700 cGy.

4.2.1. Target Size vs. Absolute OAR Dose Reduction for 8.0mm DMBT Tandem and DMBT ovoids Model

The absolute D2cc reduction (cGy) for all plans is compared for model 8.0mm thick DMBT tandem and DMBT ovoid to 8.0mm DMBT tandem and conventional ovoid/ring model with removed needles from all 32 (IC-IS) plans as shown in Figure 16.

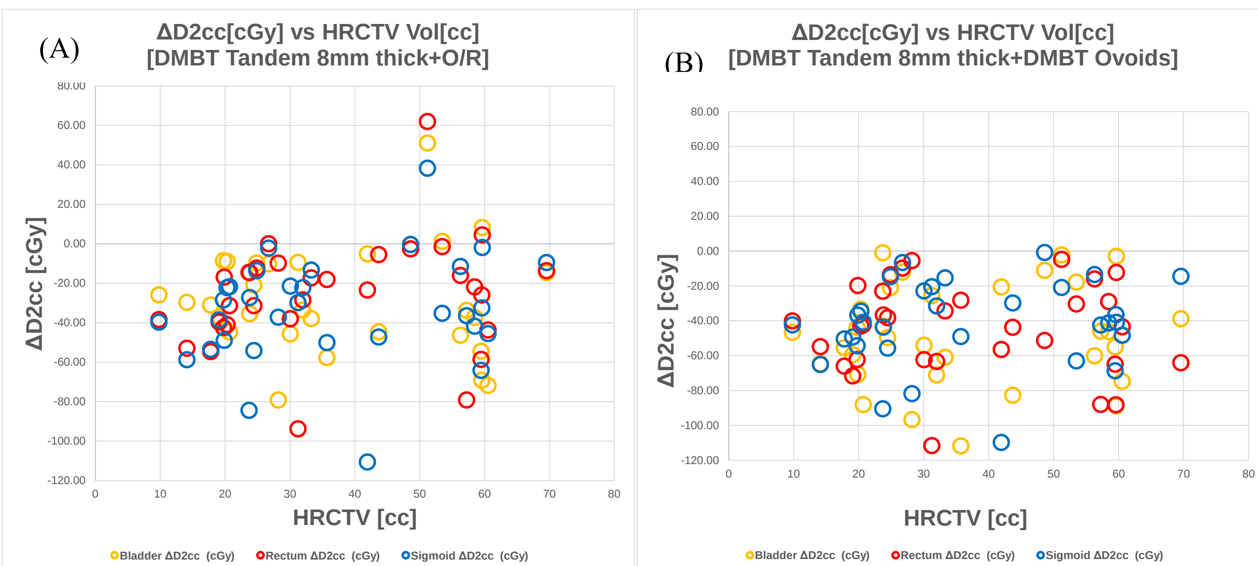

Figure 16: The absolute reduction in the D2cc of the bladder, rectum, and sigmoid with respect to HRCTV size (cc). Comparing (A) 8.0mm thick DMBT model and conventional ovoids/ring with removed needles from 32 (IC-IS) plans to (B) 8.0mm DMBT tandem and DMBT ovoid model.

Although the correlation of D2cc reduction with respect to HRCTV size is not significant but using the combination of DMBT tandem and DMBT ovoids made a big difference in case of the D2cc reduction compared to the plans when there were no DMBT ovoids. We performed a statistical analysis which was a type 2, two tailed T-test. The average dose reduction (ΔD2cc for the bladder, rectum and sigmoid were -48.62 cGy (P=0.02), -44.32 cGy (P=0.02), and -41.73 cGy (P=0.03) respectively compared to original plan that means all D2cc reductions are statistically significant for this model.

4.2.2. Number of Needles vs. Absolute OAR Dose Reduction for 8.0mm DMBT Tandem and DMBT Ovoids Model

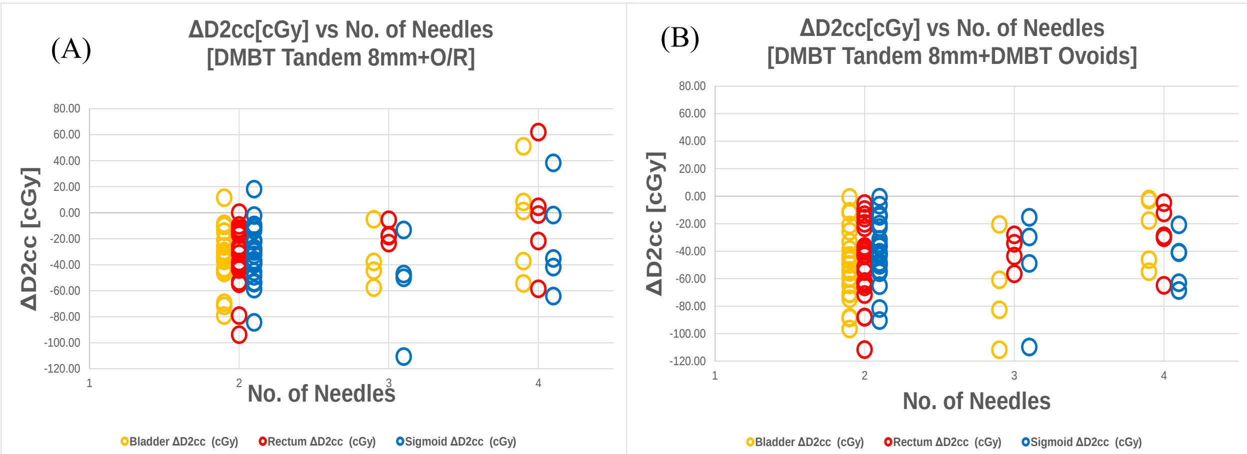

Figure 17: The absolute reduction in the D2cc of the bladder, rectum, and sigmoid with respect to the number of needles. Comparing (A) 8.0mm thick DMBT model and conventional ovoids/ring with removed needles from 32 (IC-IS) plans to (B) 8.0mm DMBT tandem and DMBT ovoids model.

Absolute D2cc reductions for bladder, rectum and sigmoid are compared between the models of 8.0mm DMBT tandem with conventional Ovoids/Ring and 8.0mm DMBT tandem with DMBT ovoids. Although the correlation of the D2cc reduction with respect to the number of needles is not significant but from the diagram it is noticeable that reduction of D2cc is higher in case of DMBT ovoids model than the model when there was no DMBT ovoids

4.2.3. Total OAR Dose (EQD2) Reduction for 8.0mm DMBT Tandem and DMBT ovoids Model

The reduction of EQD2 D2cc values for each OAR and for each plan using 8.0mm thick DMBT tandem and DMBT ovoids from original plans are presented in Table 7. The average absolute EQD2 D2cc reductions over all plans for 8.0mm DMBT tandem and DMBT ovoids model were -4.18 Gy, -2.79 Gy, -3.38 Gy for the bladder, rectum, and sigmoid respectively. The corresponding relative EQD2 D2cc reductions were -6.0%, -4.8% and -5.1% respectively. The maximum relative EQD2 D2cc reductions achieved for a particular patient was -13%, -12.9%, and -13.4% for the bladder, rectum, and sigmoid respectively.

Patient No	HRCTV Volume [cc]	Bladder EQD2 ΔD2cc [Gy]	Bladder EQD2 ΔD2cc [%]	Rectum EQD2 ΔD2cc [Gy]	Rectum EQD2 ΔD2cc [%]	Sigmoid EQD2 ΔD2cc [Gy]	Sigmoid EQD2 ΔD2cc [%]
1	41.95	-1.92	-3.0%	-5.21	-8.0%	-7.72	-13.4%
	51.22	-0.22	-0.3%	-0.37	-0.7%	-1.84	-3.0%
2	23.71	-0.08	-0.1%	-2.24	-3.4%	-6.00	-10.9%
3	23.8	-3.01	-4.7%	-2.12	-3.7%	-2.91	-4.7%
4	53.49	-1.61	-2.4%	-2.31	-3.8%	-5.48	-8.1%
	59.66	-0.29	-0.4%	-0.67	-1.3%	-3.74	-5.4%
5	20.69	-5.89	-10.1%	-2.69	-4.8%	-3.79	-5.4%
	28.2	-5.77	-10.4%	-0.31	-0.6%	-7.77	-10.6%
	19.87	-7.13	-9.3%	-1.29	-2.3%	-2.94	-4.7%
	24.46	-4.17	-6.4%	-2.40	-4.4%	-4.28	-6.9%
6	19.75	-3.56	-5.0%	-2.82	-5.4%	-3.79	-5.9%
	17.79	-4.50	-6.3%	-2.53	-5.1%	-3.65	-5.6%
7	20.32	-2.71	-3.8%	-1.57	-3.3%	-2.37	-3.8%
	14.11	-3.70	-6.4%	-1.95	-4.0%	-4.61	-7.1%
	9.8	-3.52	-5.2%	-1.38	-2.9%	-2.74	-4.5%
8	57.25	-4.09	-6.0%	-5.51	-9.7%	-4.06	-5.6%
	31.26	-2.49	-3.4%	-7.96	-12.9%	-2.20	-2.8%
	48.62	-1.23	-1.5%	-3.41	-6.0%	-0.08	-0.1%
	59.59	-8.72	-11.5%	-4.80	-9.0%	-3.74	-4.9%
9	26.73	-1.30	-1.7%	-0.81	-1.3%	-0.52	-0.8%
	24.88	-2.24	-2.9%	-0.88	-1.6%	-1.08	-1.8%
	30.06	-5.94	-7.2%	-3.47	-6.6%	-2.04	-3.0%
10	35.72	-8.11	-13.0%	-2.32	-3.6%	-2.81	-5.3%
	43.7	-7.37	-10.5%	-2.64	-4.9%	-2.93	-4.0%
	33.3	-5.22	-7.8%	-2.05	-3.8%	-0.86	-1.7%
11	69.58	-4.32	-5.2%	-5.27	-8.1%	-1.48	-2.0%
	19.09	-3.89	-6.8%	-3.39	-6.8%	-3.96	-6.2%
	31.99	-6.28	-9.1%	-3.58	-6.7%	-2.57	-4.0%
	56.3	-5.27	-7.7%	-1.12	-2.0%	-1.24	-1.8%
12	59.48	-6.08	-7.4%	-5.29	-8.2%	-6.32	-8.9%
	58.48	-4.71	-6.2%	-3.00	-3.9%	-3.50	-5.3%
	60.55	-8.32	-9.9%	-4.06	-5.7%	-5.00	-6.4%
Average	36.73	-4.18	-6.0%	-2.79	-4.8%	-3.38	-5.1%
SD	17.15	2.40	3.4%	1.75	2.8%	1.90	3.0%
MAX	69.58	-0.08	-0.1%	-0.31	-0.6%	-0.08	-0.1%
MIN	9.80	-8.72	-13.0%	-7.96	-12.9%	-7.77	-13.4%

Table 7: Absolute and relative reductions of EQD2 D2cc and EQD2 D1cc values for bladder, rectum and sigmoid respectively for the plans using DMBT tandem model 8.0 mm thick and DMBT ovoids compared to the original (IC-IS) plan when needles are removed from all 32 plans.

Reduction of OAR EQD2 D2cc were compared between the 8.0mm thick DMBT tandem and conventional ovoids/ring model and 8.0mm thick DMBT tandem and DMBT ovoids model when needles are removed in each case as shown in Figure 18.

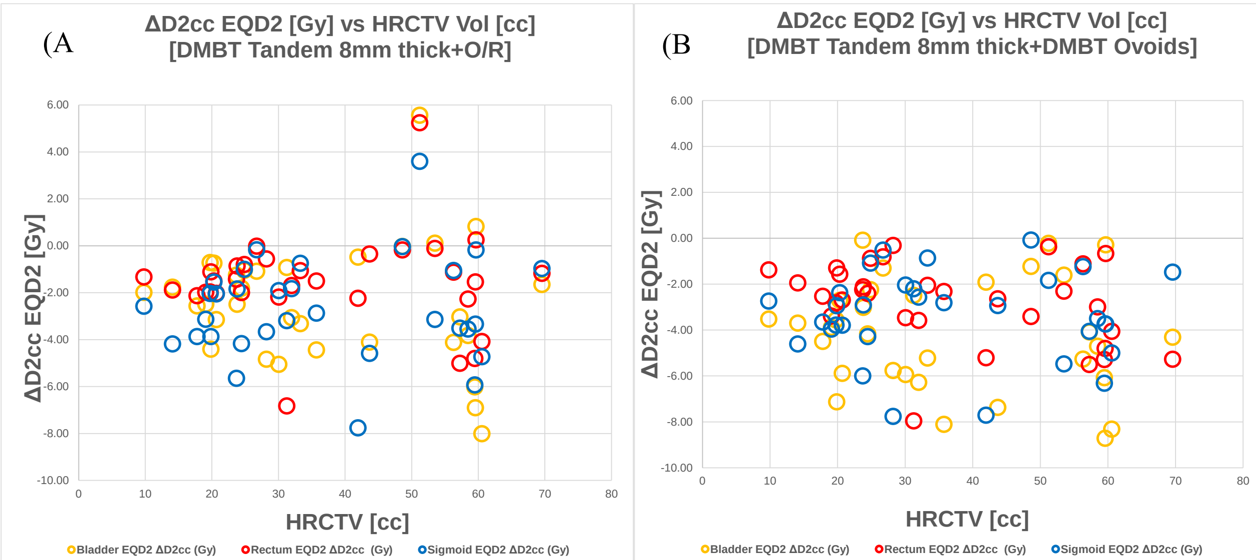

Figure 18: The absolute reduction in EQD2 D2cc of the bladder, rectum, and sigmoid with respect to HRCTV size (cc). Comparing (A) 8.0mm thick DMBT model and conventional ovoids/ring with removed needles from 32 (IC-IS) plans to (B) 8.0mm DMBT tandem and DMBT ovoid model.

4.3. Relative RV-RP & PIBS Dose Reductions for 8.0mm DMBT Tandem and DMBT Ovoids Model

The average relative reduction for 32 plans by DMBT tandem 8.0mm and DMBT ovoids model was -26.65%, -25.14%, -26.34%, -25.43%, -24.91% and -24.24% for the RV-RP, PIBS+2, PIBS+1, PIBS, PIBS-1, and PIBS-2 respectively as shown in Table 8. The maximum relative reductions came from a plan that belongs to patient 1 were -15.64%, -49.16%, -49.17%, -47.79%, -46.28% and -44.99% for the RV-RP, PIBS+2, PIBS+1, PIBS, PIBS-1, and PIBS-2 respectively.

Patient No	ΔRecto-Vaginal point (%)	ΔPIBS+2cm (%)	ΔPIBS+1 cm (%)	ΔPIBS (%)	ΔPIBS-1cm (%)	ΔPIBS-2cm (%)
1	-15.64%	-49.16%	-49.17%	-47.79%	-46.28%	-44.99%
	-4.03%	-34.76%	-26.86%	-23.29%	-19.20%	-14.37%
2	-9.86%	-24.35%	-21.74%	-20.83%	-20.17%	-18.68%
3	-6.87%	106.43%	-6.00%	-22.65%	-26.74%	-27.45%
4	-13.30%	-52.68%	-45.73%	-44.41%	-42.84%	-42.06%
	-4.41%	-18.36%	-48.15%	-33.91%	-29.44%	-29.05%
5	-17.18%	-15.55%	-15.03%	-15.32%	-16.96%	-17.86%
	-15.51%	-17.89%	-35.58%	-34.22%	-19.54%	-20.55%
	0.70%	-2.42%	-4.90%	-6.09%	-9.17%	-10.87%
6	-7.48%	-15.67%	-17.83%	-18.41%	-18.34%	-20.61%
	-19.95%	-5.89%	-8.70%	-9.92%	-10.83%	-10.47%
	-30.16%	-24.32%	-22.78%	-21.00%	-19.64%	-18.27%
7	-20.91%	-25.42%	-26.07%	-26.22%	-25.34%	-23.96%
	-28.30%	-10.69%	-12.68%	-14.18%	-14.61%	-14.17%
	-25.33%	-17.97%	-19.18%	-19.94%	-20.66%	-20.05%
8	-40.77%	-23.41%	-22.53%	-21.52%	-22.00%	-22.31%
	-31.47%	-10.71%	-14.50%	-18.19%	-19.43%	-19.92%
	-48.42%	-10.96%	-11.13%	-12.48%	-14.45%	-15.11%
	-28.54%	-35.26%	-36.97%	-37.68%	-38.36%	-38.54%
9	-13.52%	-18.41%	-19.30%	-19.71%	-20.37%	-20.12%
	-18.11%	-11.33%	-10.49%	-11.23%	-11.62%	-12.87%
	-19.20%	-17.42%	-16.76%	-19.41%	-20.72%	-21.37%
10	-14.79%	-14.20%	-15.68%	-17.96%	-18.90%	-19.55%
	-17.47%	-34.90%	-35.71%	-36.51%	-36.81%	-36.12%
	-18.59%	-12.29%	-15.55%	-16.52%	-17.92%	-19.77%
11	-20.89%	-14.98%	-13.24%	-14.85%	-17.48%	-19.43%
	-33.60%	-21.83%	-22.62%	-24.50%	-26.62%	-28.16%
	-26.96%	-22.30%	-25.11%	-27.46%	-28.39%	-29.19%
	-14.10%	-35.94%	-34.45%	-33.44%	-31.95%	-30.17%
12	-28.63%	-6.43%	-7.64%	-7.41%	-6.16%	-4.11%
	-3.10%	-7.11%	-8.53%	-9.70%	-10.09%	-9.33%
	-37.66%	-1.11%	-3.52%	-3.06%	-3.54%	-3.50%
Average	-26.65%	-25.14%	-26.34%	-25.43%	-24.91%	-24.24%
SD	0.16	0.34	0.32	0.32	0.30	0.29
MAX	-15.64%	-1.11%	-3.52%	-3.06%	-3.54%	-3.50%
MIN	-37.66%	-49.16%	-49.17%	-47.79%	-46.28%	-44.99%

Table 8: The relative reduction in the dose to the RV-RP (%) and PIBS points (%) for all 32 plans using DMBT tandem 8.0mm and DMBT ovoids model.

4.4. Treatment Time

Total treatment times were recorded from the brief report window of the TPS for each plan. The DMBT tandem and DMBT ovoids treatment time were calculated by adding dwell time at each channel and recorded as well. The differences of treatment times in case of 8mm DMBT tandem and DMBT ovoids model compared to original plans are presented in Table 9. The average increase in total treatment time of all 32 DMBT plans was 248.54 seconds where average increase of treatment time by DMBT tandem and DMBT ovoids were 194.84 seconds and 120.45 seconds respectively.

Patient No	ΔTotal Treatment Time (10 Ci) (s)	ΔTandem Treament Time (10 Ci) (s)	ΔOvoids Treament Time (10 Ci) (s)	ΔNeedles Treament Time (10 Ci) (s)
1	187.64	195.86	85.54	-93.75
	474.24	243.14	376.47	-145.37
2	184.67	153.49	58.51	-27.32
3	219.64	200.71	64.98	-46.05
4	222.78	247.44	55.15	-79.81
	303.40	301.33	136.20	-134.13
5	186.27	28.24	175.83	-17.80
	170.61	111.69	74.25	-15.33
	194.02	120.83	111.35	-38.17
6	184.17	97.63	115.81	-29.26
	245.90	153.42	146.27	-53.80
	221.98	114.06	118.47	-10.54
7	183.18	78.26	135.65	-30.74
	193.72	99.59	116.65	-22.52
	158.21	103.67	85.18	-30.64
8	269.93	353.01	88.66	-171.75
	192.64	188.91	54.89	-51.16
	264.61	232.62	104.79	-72.80
	267.95	218.27	238.82	-189.14
9	206.49	184.46	64.61	-42.59
	188.17	167.20	47.74	-26.77
	217.49	180.63	105.20	-68.34
10	350.05	166.29	209.80	-26.05
	293.70	303.24	94.91	-104.45
	200.21	132.52	105.12	-37.43
11	321.14	207.17	231.76	-117.80
	196.15	69.33	135.86	-9.04
	231.21	151.83	171.88	-92.49
	271.94	267.50	35.20	-30.76
12	371.22	486.15	64.58	-179.51
	383.69	322.14	163.48	-101.93
	396.21	354.81	80.85	-39.45
Average	248.54	194.86	120.45	-66.77
SD	77.40	98.58	69.98	51.98
MAX	474.24	486.15	376.47	-9.04
MIN	158.21	28.24	35.20	-189.14

Table 9: The increase in total treatment time, DMBT tandem treatment time and DMBT ovoids treatment time of 32 plans.

5. Discussion

It is apparent from the results presented in Table (2,3,5,6) that when needles are removed DMBT tandem (both 5.4mm and 8.0mm thick) and DMBT ovoids model can significantly reduce the dose to bladder, rectum and sigmoid when maintaining the similar ΔD90 HRCTV coverage as original plan. Comparing the DMBT tandem and conventional Ovoids/Ring model to the DMBT tandem-and-ovoids model as shown in Figure (13-18). It is also apparent that using DMBT ovoids could lower the dose to bladder, rectum and sigmoid even more than conventional Ovoids/Ring could do. For example, in case of 5.4mm DMBT tandem and DMBT ovoids the average dose reduction (ΔD2cc) for the bladder, rectum and sigmoid were -41.67 cGy, -43.01 cGy, and -33.57 cGy respectively where in case of 5.4mm DMBT tandem and conventional ovoids/ring the average dose reduction (ΔD2cc) for the bladder, rectum and sigmoid were -12.34 cGy, -20.02 cGy, and -25.37 cGy respectively. Also, in case of 8.0mm DMBT tandem and DMBT ovoids the average dose reduction (ΔD2cc) for the bladder, rectum and sigmoid were -48.62 cGy, -44.32 cGy, and -41.73 cGy respectively where in case of 8.0mm DMBT tandem and conventional ovoids/ring the average dose reduction (ΔD2cc) for the bladder, rectum and sigmoid were -28.14 cGy, -25.67 cGy, and -33.33 cGy respectively. The reduction of EQD2 dose to OARs was calculated and presented in Table 4 and Table 6. It was shown that lower EQD2 dose to OARs were achievable by using DMBT tandem (both 5.4mm and 8.0mm thick) and DMBT ovoids model. Figure 15. and Figure 18. are evident that more reduction of EQD2 dose to OARs are achievable by DMBT ovoids model compared to conventional Ovoids/Ring model. It is noticeable that the reduction of dose to OARs was decreased with the increased size of HRCTV as shown in Figure 13. and Figure 16. This is because the dose modulation decreased with the increased distance from DMBT tandem and DMBT ovoids. An additional consideration was the number of needles. It is observed that the reduction of dose to OARs were decreased with the increased number of needles as shown in Figure 14 and Figure 17. This is because an increased number of needles were used in case of increased size of HRCTV, specially in the case of larger tumors which extend into the parametrium and/or paravaginal tissues and it is usually difficult to maintain a good coverage to larger HRCTV by minimizing dose to OARs. The shape of target might have contributed to the need of more needles which needs more study to confirm. Significant reductions in doses to the recto-vaginal and vaginal reference points were achieved by using DMBT tandem and DMBT ovoids model as presented in Table 8. The thicker DMBT tandem model performed better than the thinner one. Comparing DMBT tandem and DMBT ovoids models that are only varying by tandem thickness, it is observed that 8.0mm thick DMBT tandem model could provide more conformal and lower dose to OARs than 5.4mm thick DMBT tandem as shown in Figure 19-21.

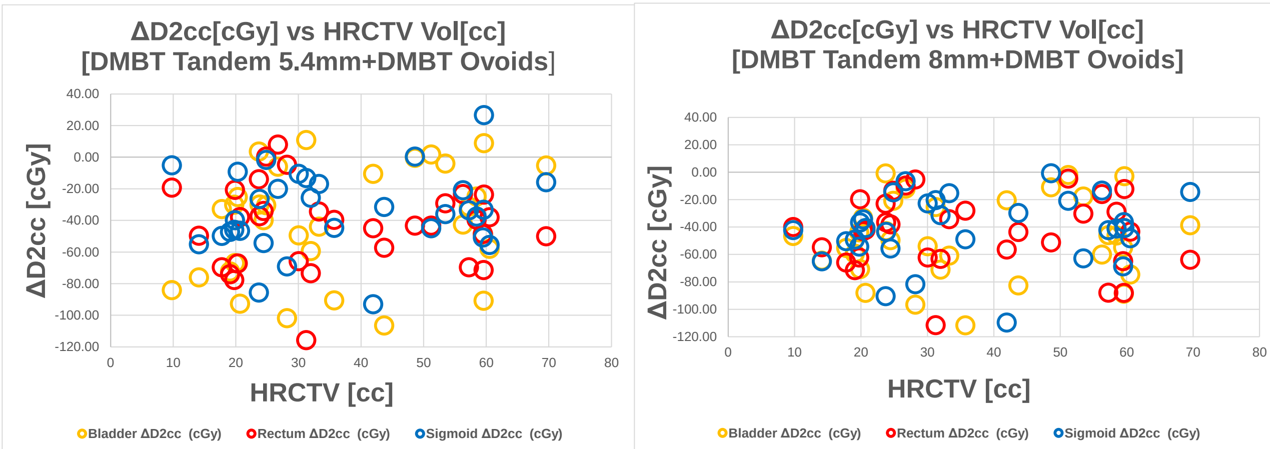

Figure 19: The absolute reduction in the D2cc of the bladder, rectum, and sigmoid with respect to HRCTV size (cc). Comparing (Left) 5.4mm thick DMBT tandem and DMBT ovoids model with removed needles from 32 (IC-IS) plans to (Right) 8.0mm DMBT tandem and DMBT ovoids.

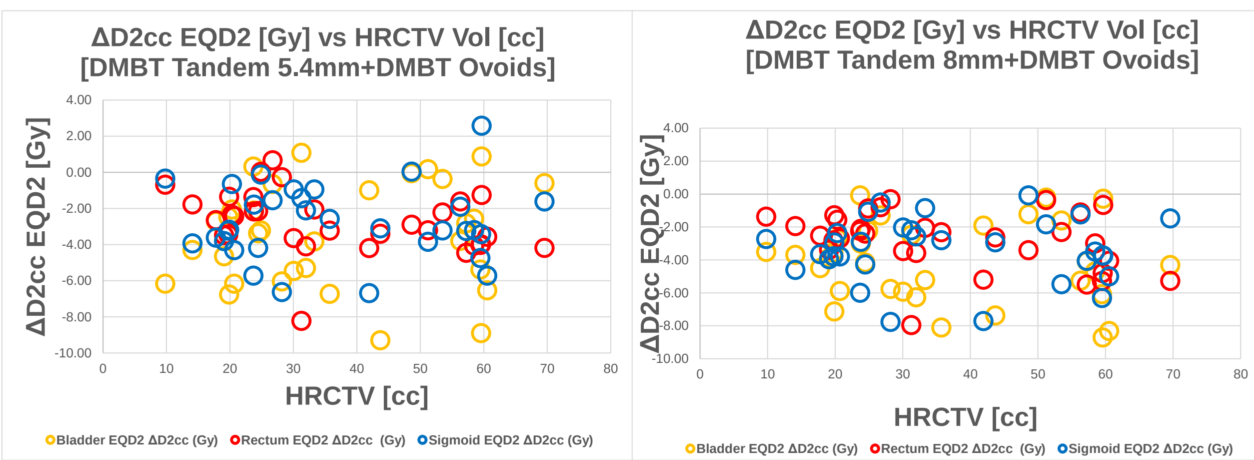

Figure 20: The absolute EQD2 reduction in the D2cc of the bladder, rectum, and sigmoid with respect to HRCTV size (cc). Comparing (Left) 5.4mm thick DMBT tandem and DMBT ovoids model with removed needles from 32 (IC-IS) plans to (Right) 8.0mm DMBT tandem and DMBT ovoid model.

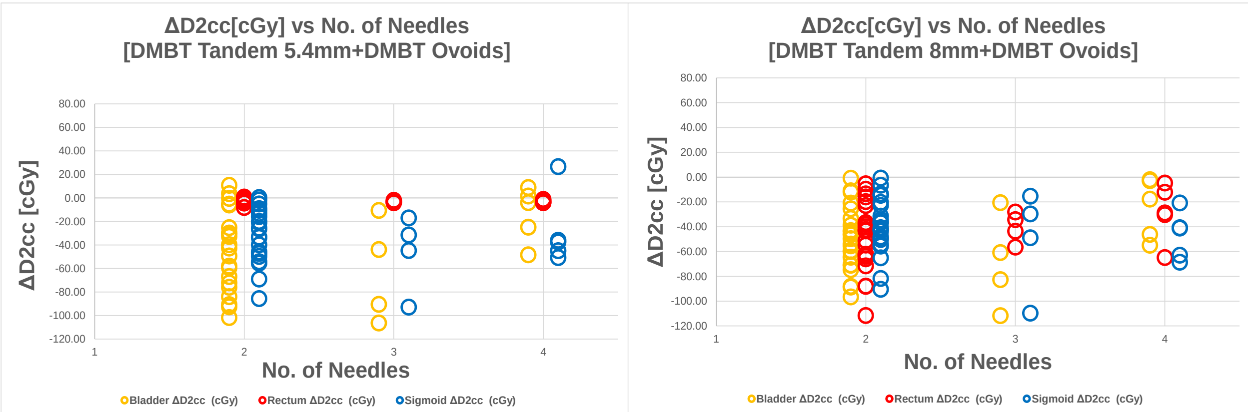

Figure 21: The absolute reduction in the D2cc of the bladder, rectum, and sigmoid with respect to number of needles. Comparing (Left) 5.4mm thick DMBT tandem and DMBT ovoids model with removed needles from 32 (IC-IS) plans to (Right) 8.0mm DMBT tandem and DMBT ovoid model.

The only limitation that is observed in the case of DMBT tandem and DMBT ovoids model is increase of total treatment time. As the source is travelling through six channels of tandem and 18 channels of ovoids it is apparent that total treatment time will increase compared to original plan's treatment time. Also increased thickness of DMBT tandem and ovoids are playing a role to increase the total treatment time as shown in Figure 22.

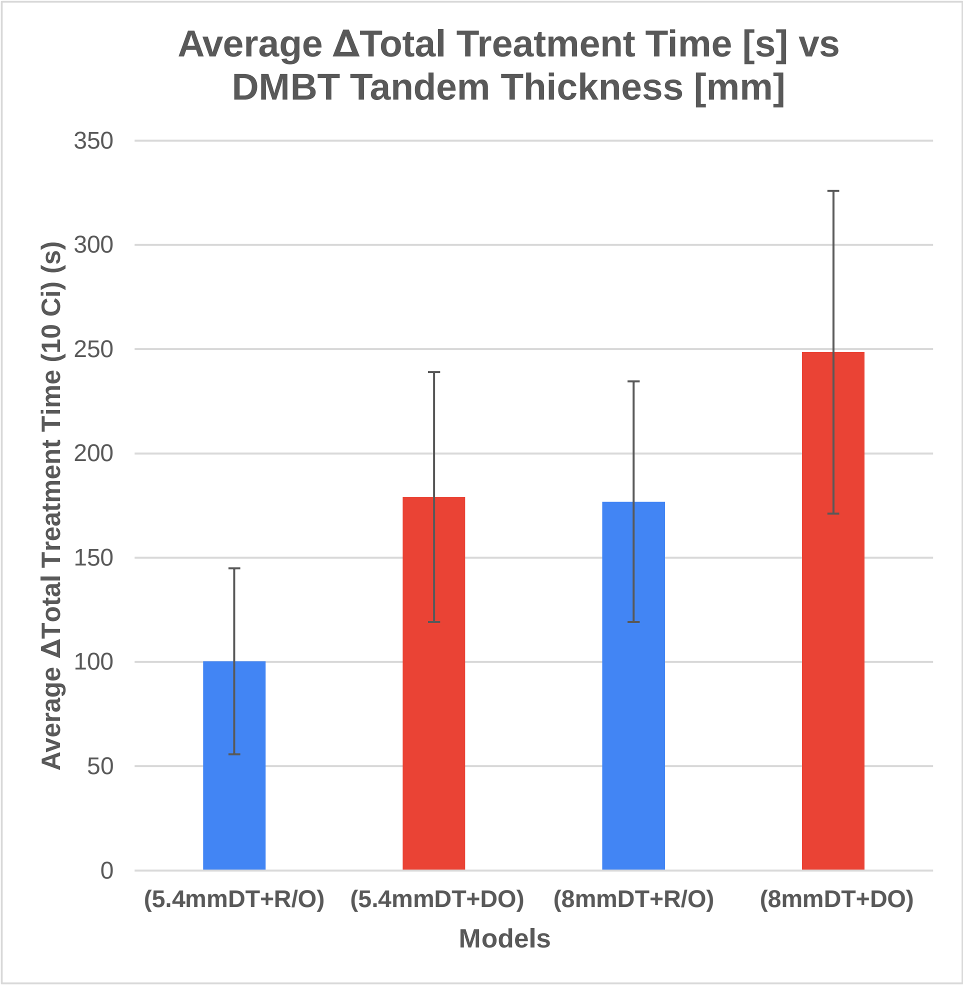

Figure 22: Comparing increase of average total treatment time between 5.4mm thick and 8.0mm thick DMBT tandem models. Red represents DMBT tandem and DMBT ovoids model and blue represents DMBT tandem and conventional O/R model.

The following Figures 23-30 show the spatial dose distribution for various plans using DMBT tandem-and-ovoids model where the areas of improved dose sparing are visible.

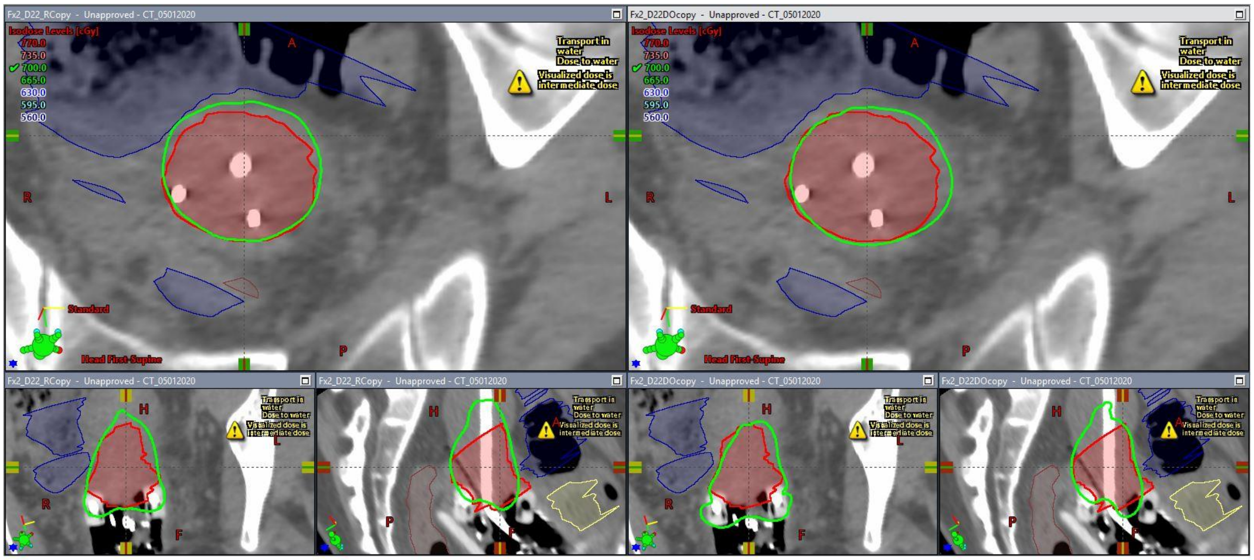

Figure 23: The spatial dose distribution of the DMBT tandem plan (left) and the DMBT tandem and DMBT ovoids plan (right). This fraction belonged to patient 5 which had a HRCTV of 28.2 cm3 with a prescription dose of 700 cGy.

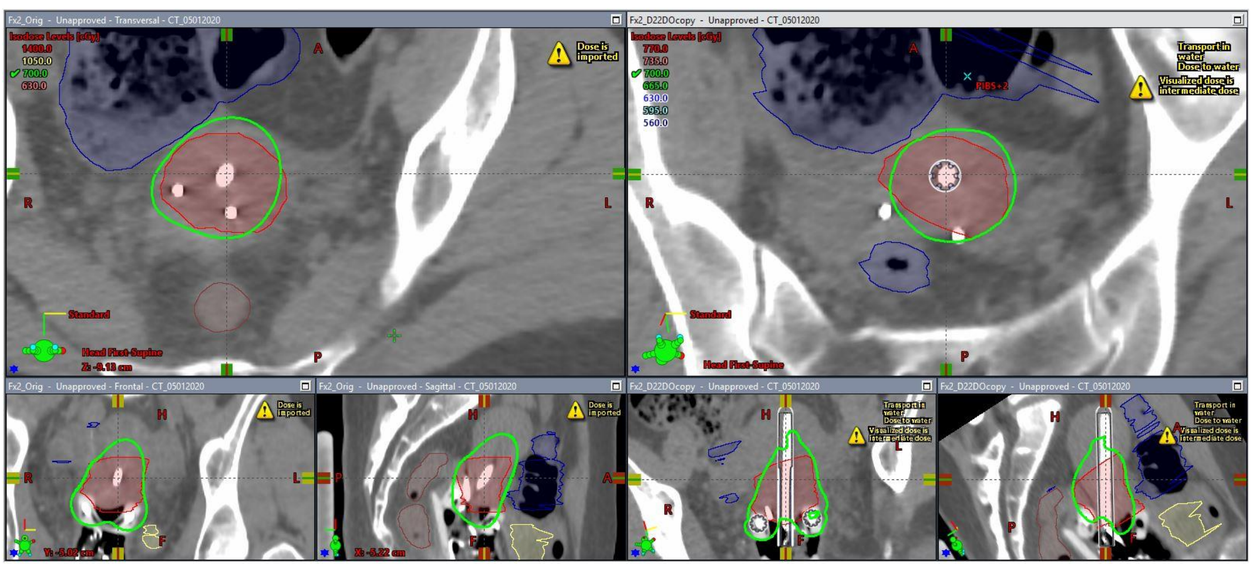

Figure 24: The spatial dose distribution of the original plan (left) and the DMBT tandem and DMBT ovoids plan (right) of patient 5.

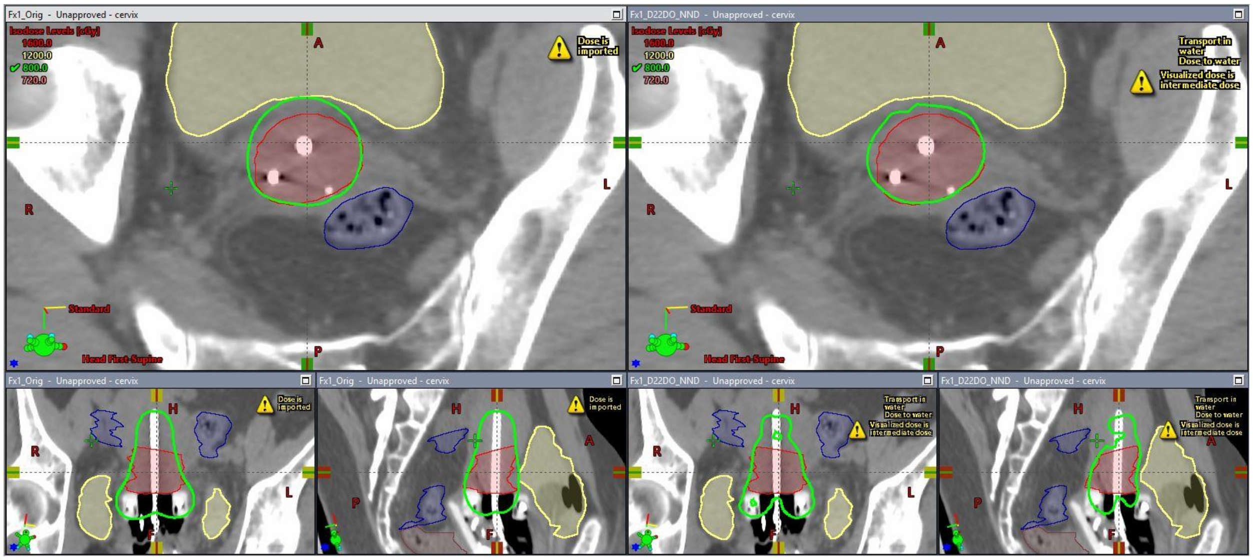

Figure 25: The spatial dose distribution of the original plan (left) and the DMBT tandem and DMBT ovoids plan (right) of patient 7.

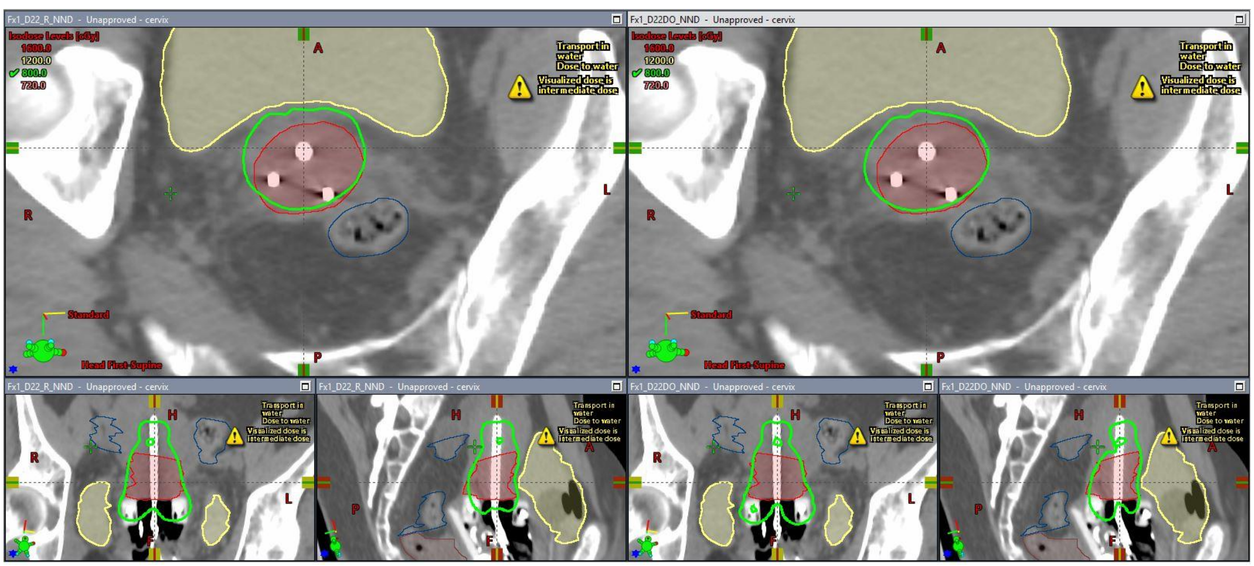

Figure 26: The spatial dose distribution of the DMBT tandem plan (left) and the DMBT tandem and DMBT ovoids plan (right). This fraction belonged to patient 7 which had a HRCTV of 20.32 cm3 with a prescription dose of 800 cGy.

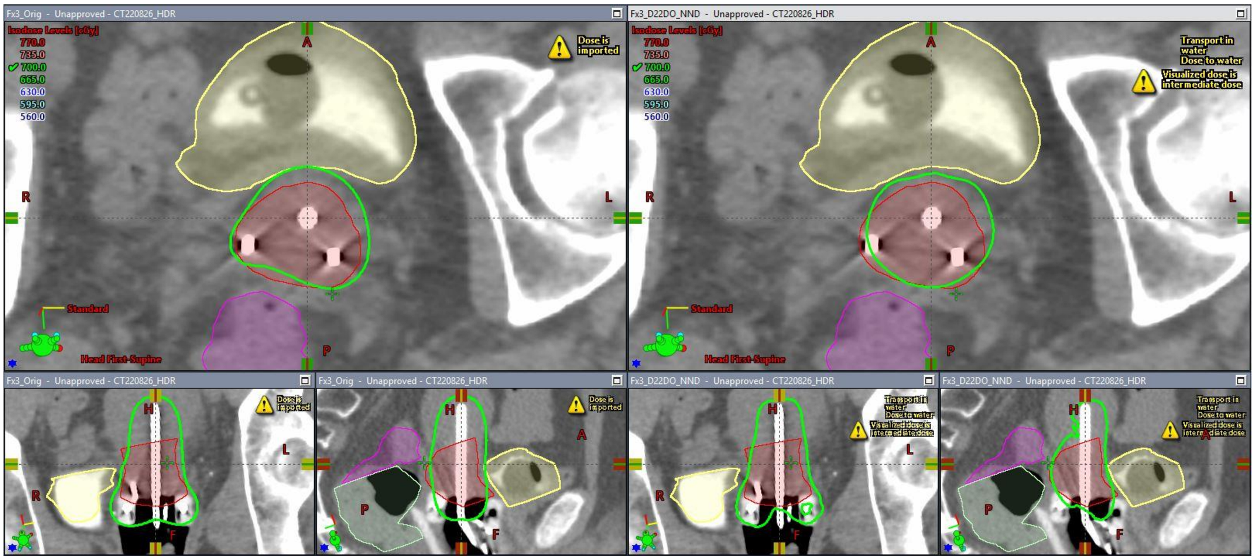

Figure 27: The spatial dose distribution of the original plan (left) and the DMBT tandem and DMBT ovoids plan (right) of patient 9.

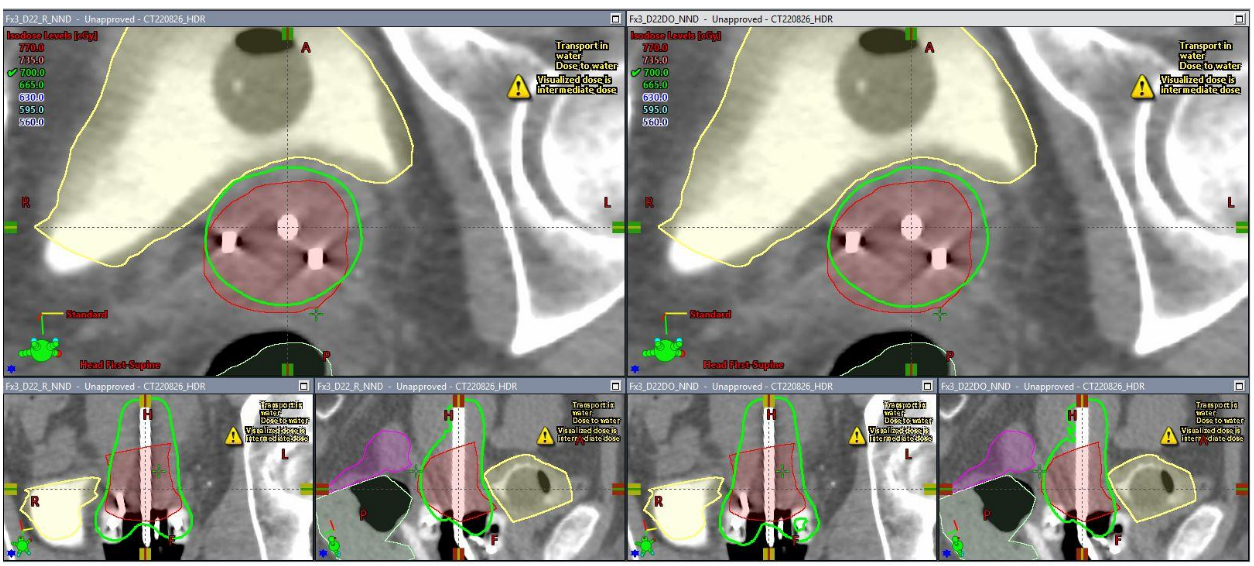

Figure 28: The spatial dose distribution of the DMBT tandem plan (left) and the DMBT tandem and DMBT ovoids plan (right). This fraction belonged to patient 9 which had a HRCTV of 24.88 cm3 with a prescription dose of 800 cGy.

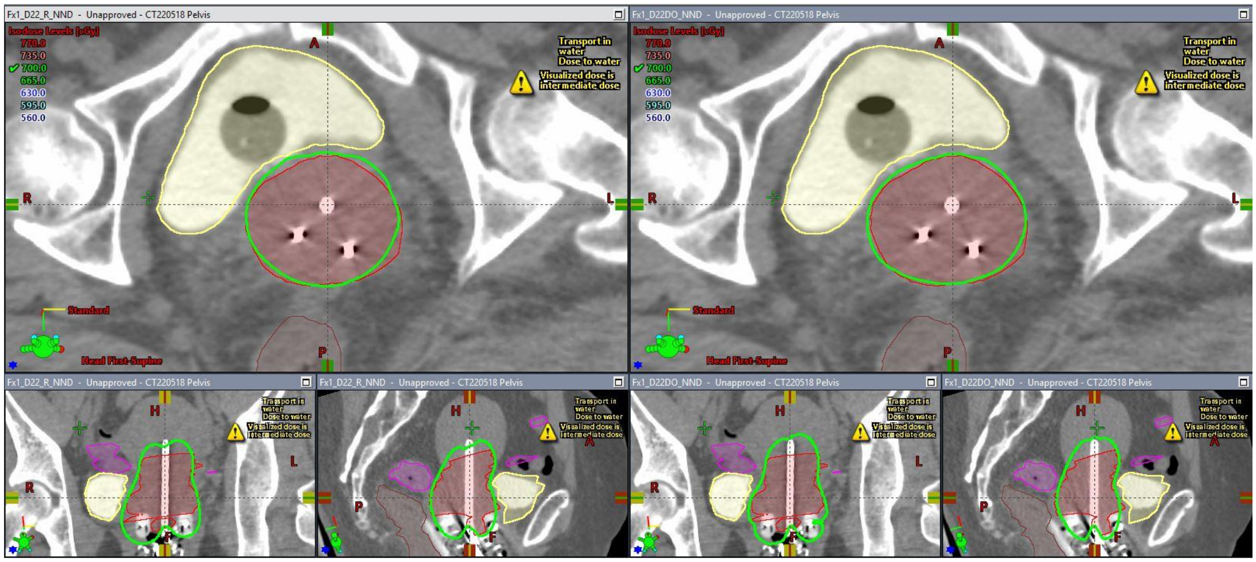

Figure 29: The spatial dose distribution of the DMBT tandem plan (left) and the DMBT tandem and DMBT ovoids plan (right). This fraction belonged to patient 11 which had a HRCTV of 69.58 cm3 with a prescription dose of 700 cGy.

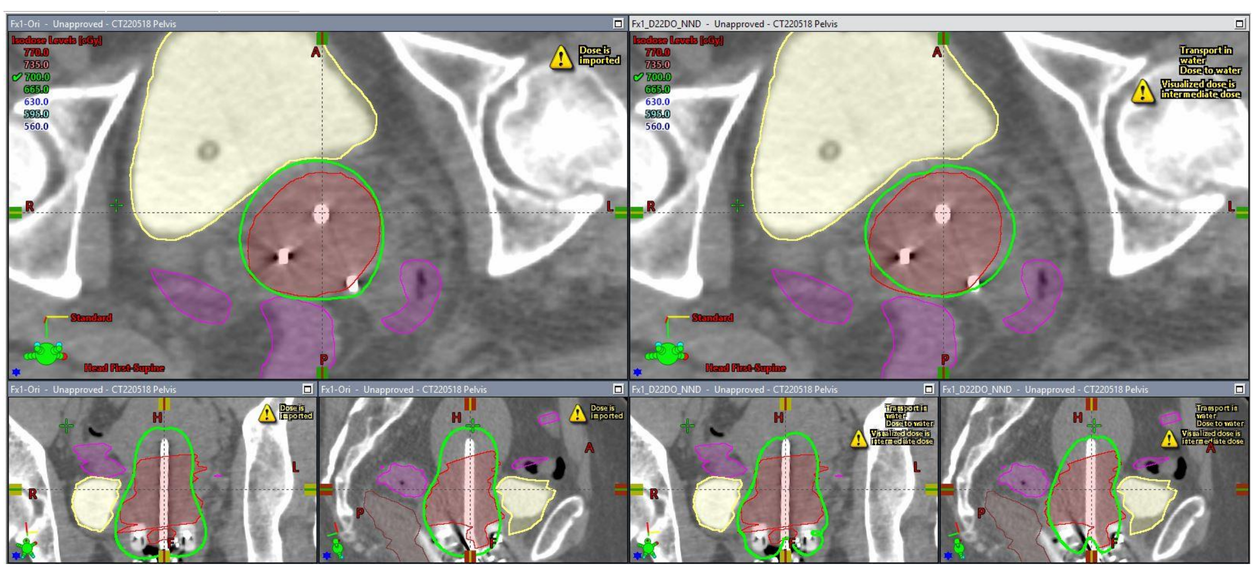

Figure 30: The spatial dose distribution of the original plan (left) and the DMBT tandem and DMBT ovoids plan (right) of patient 11.

6. Conclusions

Two DMBT tandems and one ovoids model are successfully incorporated into a commercial TPS and re-planned 32 cases, to a total of 64 plans. Both DMBT tandem-and-ovoid models exhibited the ability to significantly lower OAR doses compared to conventional plans while maintaining equivalent target coverage. The DMBT ovoids performed better than the conventional ovoids or ring due to its multichannel source capability and tungsten-alloy material and the thicker DMBT tandem model performed better than the thinner model. Plans with a smaller number of needles showed better dose conformity by using DMBT tandem-and-ovoids. According to the results, it is clinically feasible to replace the conventional IC-IS cases, with 2-4 freehand-loaded needles, with the DMBT tandem-and-ovoids models, effectively avoiding the need for IS needles.

7. References

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