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Physics Contribution

Direction Modulated Brachytherapy for Treatment of Cervical Cancer. II: Comparative Planning Study With Intracavitary and Intracavitary–Interstitial Techniques

Dae Yup Han, PhD,[*,†,‡] Habib Safigholi, PhD,[*,§] Abraam Soliman, PhD,[*,§] Ananth Ravi, PhD,[*,||] Eric Leung, MD,[||,¶] Daniel J. Scanderbeg, PhD,[#] Zhaowei Liu, PhD,[‡] Amir Owrangi, PhD,[*,||] and William Y. Song, PhD[*,§,||]

Department of Medical Physics, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; [†]Department of Radiation Oncology, University of California, San Francisco, San Francisco, California; [‡]Department of Electrical and Computer Engineering, University of California, San Diego, La Jolla, California; [§]Physical Sciences, Sunnybrook Research Institute, Toronto, Ontario, Canada; [||]Department of Radiation Oncology, University of Toronto, Toronto, Ontario, Canada; [¶]Department of Radiation Oncology, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; and [#]Department of Radiation Medicine and Applied Sciences, University of California, San Diego, La Jolla, California

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Summary

A novel DMBT-concept tandem applicator that enables enhanced capacity to sculpt the 3D dose distributions in HDR brachytherapy was proposed in 2014. Subsequently, a comprehensive comparative planning study was performed on 45 cervical cancer patients, enrolled in the EMBRACE trial,

Purpose: To perform a comprehensive comparative planning study evaluating the utility of the proposed direction modulated brachytherapy (DMBT) tandem applicator against standard applicators, in the setting of image guided adaptive brachytherapy of cervical cancer.

Methods and Materials: A detailed conceptual article was published in 2014. The proposed DMBT tandem applicator has 6 peripheral grooves of 1.3-mm width, along a 5.4-mm-thick nonmagnetic tungsten alloy rod of density 18.0 g/cm^3, capable of generating directional dose profiles. We performed a comparative planning study with 45 cervical cancer patients enrolled consecutively in the prospective observational EMBRACE study. In all patients, MRI-based planning was performed while utilizing various tandem-ring (27 patients) and tandem-ring-needles (18 patients) applicators, in accordance with the Groupe Européen de Curiethérapie–European Society for

Reprint requests to: William Y. Song, PhD, Department of Medical Physics, Sunnybrook Health Sciences Centre, 2075 Bayview Ave, Toronto, ON M4N 3M5, Canada. Tel: (416) 480-6100, ext. 87181; E-mail: william.song@sunnybrook.ca

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treated with various intracavitary and intracavitary−interstitial techniques. All cases were replanned with an in-house−developed inverse optimization code. The proposed applicator was found to enhance the plan quality across various clinical scenarios.

Radiotherapy and Oncology recommendations. For unbiased comparisons, all cases were replanned with an in-house−developed inverse optimization code while enforcing a uniform set of constraints that are reflective of the clinical practice. All plans were normalized to the same high-risk clinical target volume D90 values achieved in the original clinical plans.

Results: In general, if the standard tandem was replaced with the DMBT tandem while maintaining all other planning conditions the same, there was consistent improvement in the plan quality. For example, among the 18 tandem-ring-needles cases, the average $D2cm^3$ reductions achieved were $-2.48\% \pm 11.03\%$, $-4.45\% \pm 5.24\%$, and $-5.66\% \pm 6.43\%$ for the bladder, rectum, and sigmoid, respectively. An opportunity may also exist in avoiding use of needles altogether for when the total number of needles required is small (approximately 2 to 3 needles or less), if DMBT tandem is used.

Conclusions: Integrating the novel DMBT tandem onto both intracavitary and intracavitary−interstitial applicator assembly enabled consistent improvement in the sparing of the OARs, over a standard "single-channel" tandem, though individual variations in benefit were considerable. Although at an early stage of development, the DMBT concept design is demonstrated to be useful and pragmatic for potential clinical translation.

Introduction

Ever since the introduction of loading radioactive sources via a central uterine tube inserted into the endocervical canal more than 100 years ago, this practice of isotropic dose deposition from the intrauterine tandem applicator combined with vaginal source loading for the treatment of cervical cancer successfully flourished to this modern day (1, 2). Unfortunately, owing to the "single-channel" loading limit, along with a more or less isotropic dose profile of all radioactive brachytherapy sources of the past and present (3-5), the capacity to sculpt the dose distribution from the tandem applicator itself remains largely limited to date. This long dormancy in technological progress of this particular applicator is primarily owed to the success of the point A prescription system, based on 2-dimensional imaging, whereby the generation of the pear-shape dose distribution was faithfully achieved by the conventional design (2). In the past 2 decades, however, the development of incorporating 3-dimensional imaging into the clinical workflow has fast emerged, particularly MRI, known as image guided adaptive brachytherapy (IGABT), with a set of recommendations (6-9). In this scheme the target volume and the organs at risk (OARs) are readily contoured and incorporated into the planning process. This has led to a progressive recognition of, and the need to improve, the limits in the dose sculpting capacity of the standard intracavitary applicators (9-11). In part to overcome this limitation, integrating the intracavitary applicators with interstitial needles, compatible with MRI and CT imaging, was proposed, such as with the Vienna (12) and Utrecht (13) applicators. The clinical applications of these applicators are nicely summarized in a recent review article by Harkenrider et al (14). Some of the recognized challenges of using intracavitary−interstitial applicators relate to the inadequate infrastructure in smaller nonacademic clinics, dependence of the implant quality on the skills and experience of the physicians inserting the needles, and the patient trauma/complications that may arise from needle punctures (15-17). However, despite these challenges, the best treatment option for extended gross diseases remains in using the intracavitary−interstitial techniques for cervical cancer (9-17). Incidentally, Fokdal et al (18) describes a useful strategy in minimizing the procedural burden of the technique using virtual preplanning.

Recognizing an opportunity during a tandem applicator technology assessment, in 2014 we introduced a novel design (19) that conforms to the direction modulated brachytherapy (DMBT) concept (19-22). The main idea is to generate a highly directional dose profile through an intelligently designed shielding (eg, rotating shield brachytherapy exploits a similar concept [23-25]) with a high-density nonmagnetic tungsten alloy that would be closely similar in dimensions to contemporary tandem applicators, thus ensuring compatibility with other complementary applicators (eg, ovoids, rings, needles, and cylinders). In combination with inverse planning optimization, we observed significant improvement in a limited group of 15 patients who were treated with the CT-guided tandem-and-ovoids intracavitary applicators only (19).

As a follow-up to the 2014 concept article (19), here we set out to explore the upper limits of the dose sculpting capacity of the DMBT tandem applicator, via examining a wider range of clinical scenarios, by performing a comprehensive comparative planning study with a group of 45 consecutively treated cervical cancer patients enrolled in the prospective observational EMBRACE study (9, 26), who received various combinations of intracavitary and intracavitary−interstitial techniques, of which the technique selections were guided by direct MRI with applicators in situ (18).

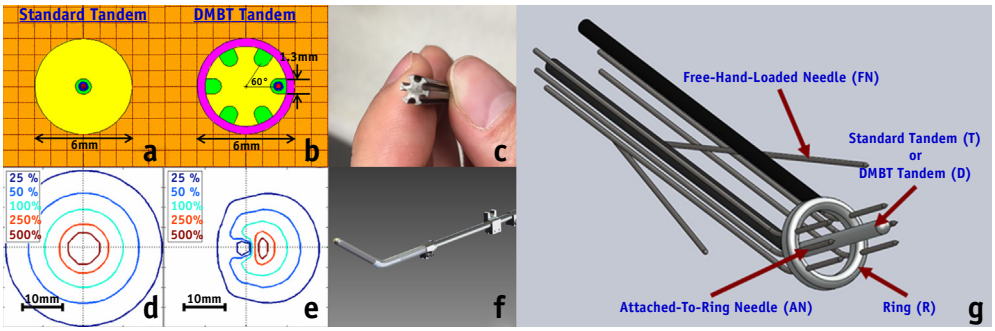

Fig. 1. The proposed direction modulated brachytherapy (DMBT) concept tandem applicator design. (a) Standard plastic tandem and (b) DMBT tandem cross-section with 6 peripheral holes carved out of a nonmagnetic tungsten alloy rod of 5.4-mm diameter, housed by a thin plastic sheath with 0.3-mm wall thickness. (c) A successfully machined-to-specifications tungsten alloy piece to demonstrate the manufacturability of the applicator. The Monte Carlo simulated isodose distributions of an ^{192}Ir source inside (d) a standard tandem and (e) a DMBT tandem. (f) An artistic rendering of the concept applicator in full assembly. (g) Notations for the applicators and needles used in this study.

Methods and Materials

DMBT tandem applicator

Figure 1 illustrates the concept design as outlined in our previous work (19). The DMBT tandem has 6 peripheral grooves of 1.3-mm width, along a 5.4-mm-thick nonmagnetic tungsten alloy rod of density 18.0 g/cm^3, housed by a thin plastic sheath with 0.3-mm wall thickness, with total overall diameter not exceeding 6 mm (Fig. 1b). This set of dimensions was deliberately chosen to be closely similar to the standard plastic CT/MR-compatible intrauterine tandem applicators used in clinic (Fig. 1a; Elekta Brachytherapy, Veenendaal, The Netherlands) (27). Because of the high density of the tungsten alloy, with the holes spaced 60° apart, we can achieve directional dose profiles along 6 angular directions (Fig. 1e), compared with the standard isotropic dose profile we have long been accustomed to (Fig. 1d). A successfully machined-to-specifications tungsten alloy piece is pictured in Figure 1c, demonstrating the manufacturability of the applicator; and an artistic rendering of the final-assembled concept applicator is illustrated in Figure 1f. Figure 1g illustrates the notations used in this work.

Patient data

The first fraction plan of each of 45 consecutively treated cervical cancer patients, using pulsed dose rate (PDR) brachytherapy, enrolled in the prospective observational EMBRACE study (26), was evaluated. All patients were treated at the Department of Oncology, Aarhus University Hospital, Denmark. The high-risk clinical target volumes (CTV_{HR}s) and all OARs were delineated on T2-weighted MR images and subsequently planned. All plans had at least the CTV_{HR}, bladder, rectum, and sigmoid contoured. International Federation of Gynecology and Obstetrics stages ranged between IB and IVB (median IIB, with 1 IVB patient). All patients received combined external beam radiation therapy of either 1.67 Gy × 30 fractions or 1.80 Gy × 25 fractions to the whole pelvis, followed by IGABT of either 15.0 Gy × 2 fractions or 17.5 Gy × 2 fractions, respectively. Of the 45 cases, 27 used standard tandem and ring (T&R) applicators only, 9 used T&R with attached-to-ring needles (ANs), and the remaining 9 used T&R with both ANs and free-hand-loaded needles (FNs) (with 2 cases receiving T&R with FNs only but included in the ANs-and-FNs group for analysis). Figure 1g provides definitions of the notations. The CTV_{HR} volumes ranged from 34.5 ± 19.4 cm^3 (range, 12.2-93.3 cm^3), 28.6 ± 14.6 cm^3 (range, 12.2-81.1 cm^3), 32.9 ± 10.3 cm^3 (range, 18.3-51.0 cm^3), and 53.6 ± 27.3 cm^3 (range, 21.0-93.3 cm^3) for all 45 cases, 27 T&R cases, 9 T&R+AN cases, and 9 T&R+AN+FN cases, respectively.

Treatment planning

All plans were reoptimized and normalized to receive the same CTV_{HR} D90 coverage as achieved in the original

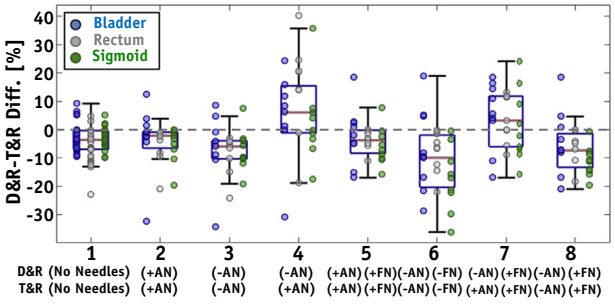

Fig. 2. Box and whisker plot of the percentage difference in the organ at risk D2cm^3 values between the direction modulated brachytherapy and standard tandem plans (eg, Diff. [%] = (D&R-T&R)/T&R) for the 27 cases that did not have any interstitial needles (column 1), 9 cases that had ANs only (columns 2-4), and the remaining 9 cases that had ANs+FNs (columns 5-8) in the original plans. See Fig. 1g for definitions of abbreviations.

Table 1 Percentage difference in the organ at risk D2cm^3 values between the direction modulated brachytherapy (DMBT) and standard tandem plans for the 9 cases that had attached-to-ring needles (ANs) only (eg, Diff. [%] = (D&R − T&R)/T&R)

		D&R(+AN) − T&R(+AN) Diff. [%]			D&R(−AN) − T&R(−AN) Diff. [%]			D&R(−AN) − T&R(+AN) Diff. [%]		
Patient no.	No. of AN used	Bladder D2cm^3	Rectum D2cm^3	Sigmoid D2cm^3	Bladder D2cm^3	Rectum D2cm^3	Sigmoid D2cm^3	Bladder D2cm^3	Rectum D2cm^3	Sigmoid D2cm^3
1	1	−2.14	−1.27	−3.31	−4.10	−3.05	−5.66	−0.14	−1.13	−3.31
2	1	−32.41*	−20.98*	−19.70*	−34.25*	−24.18*	−19.11*	−30.75*	−18.84*	−17.44*
3	3	−2.70	−1.16	−0.14	−8.81	−10.19	7.44	11.74	−1.02	−0.28
4	3	12.51	−3.69	−0.88	8.52	−5.47	−9.76	15.84	24.54	−1.24
5	3	3.83	−1.85	−7.00	−0.78	−4.24	−3.34	8.36	20.39	4.05
6	4	−4.35	−8.15	−10.40	−4.03	−10.24	−11.81	−0.08	14.11	−6.64
7	4	−1.02	−1.14	−0.11	−10.51	−14.90	−10.28	1.22	20.61	7.62
8	6	−0.70	−2.38	−5.05	−5.93	−4.12	−3.95	6.26	14.01	6.08
9	7	1.50	−9.48	−2.07	4.75	−6.45	−10.16	24.23	40.23	35.69
Average		−2.83	−5.57	−5.41	−6.13	−9.20	−7.40	4.08	12.55	2.73
Standard deviation		12.17	6.56	6.36	12.18	6.79	7.33	15.34	17.31	14.49
Minimum		−32.41	−20.98	−19.70	−34.25	−24.18	−19.11	−30.75	−18.84	−17.44
Maximum		12.51	−1.14	−0.11	8.52	−3.05	7.44	24.23	40.23	35.69
Paired *t* test		.52240	.03201*	.04494*	.23893	.00274*	.01048*	.57081	.04749*	.76903

Abbreviations are defined in Fig. 1g.

Three clinical scenarios were compared, in which: (*1*) ANs were included in all plans: D&R(+AN) − T&R(+AN); (*2*) ANs were excluded in all plans: D&R(−AN) − T&R(−AN); and (*3*) ANs were excluded only in the DMBT plans: D&R(−AN) − T&R(+AN). Negative (green) and positive (red) values represent lower and higher D2cm^3 values achieved by the D&R plans, respectively. (A color version of this table is available at www.redjournal.org.)

*Statistically significant differences ($P<.05$) in absolute D2cm^3 doses and largest individual reductions.

clinical plans, using the in-house coded gradient projection convex optimization algorithm (19-22), with a normalized source strength of 1 Ci (standard for ^{192}Ir PDR source). Using a simple quadratic objective function with weights assigned to each volume of interest, various ranges of weights were repeatedly tested to find a combination of weights that seemingly generated the most optimal plans. During optimization, multiple constraints were enforced, including non-negativity in dwell times, individual dwell times to not exceed 800 and 100 seconds inside tandems and needles, respectively, and total dwell times to not exceed 3000 seconds inside the ring as well as to fall between 50% and 100% of that compared with the total dwell times in the tandem. This is to ensure close emulation of the planning practice in clinic, as well as to preserve the original pear-shaped dose distribution. No graphic optimization (ie, manually dragging isodose lines) by an expert clinician followed, however, primarily owing to the limitations of the in-house software, but this limitation also made the plans free from potential bias and ensured consistency in capturing the dose sculpting capacity of the applicators. Some clinically relevant parameters, such as D2cm^3 for the OARs and D90 for the CTV_{HR}, were calculated. Total equivalent dose in 2 Gy per fraction (EQD2) doses were calculated assuming the first fraction plans were reused in the second fractions and summing with the external beam radiation therapy doses.

To simplify the naming convention, the following are used for the 18 cases with the needles. Plans that included or excluded the needles during the optimization have (+) or (−) next to the name, respectively. For example, for a plan that utilized the dwell positions inside the DMBT tandem, the ring, the ANs, but not the FNs during the optimization will have the notation: D&R(+AN)(−FN).

Results

Figure 2 displays the box and whisker plot of the percentage differences in the OAR D2cm^3 values between various DMBT tandem and ring (D&R) and T&R plans generated. As can be seen, when the planning conditions are identical between the D&R and T&R plans (ie, with/without needles—columns 1, 2, 3, 5, 6, and 8), the vast majority of data points sit on the negative side, indicative of the positive impact of having DMBT tandem over a standard tandem on plan quality. For the 27 intracavitary cases (column 1), the average D2cm^3 reductions were −2.61% ± 5.37%, −6.30% ± 5.91%, and −2.65% ± 3.44% for the bladder, rectum, and sigmoid, respectively. For the 9 T&R with ANs only (columns 2-4) and 9 T&R with ANs+FNs (columns 5-8) cases, Tables 1 and 2 list all percentage differences, respectively. For when all needles were permitted use (first case in the tables), the D&R plans were able to improve D2cm^3 for all 3 OARs simultaneously in 6 of 9 (66.7%) and 4 of 9 (44.4%) cases, respectively. Interestingly, and perhaps expectedly, the D&R advantage improves further when all needles were prohibited from use

Table 2 Percentage difference in the organ at risk D2cm^3 values between the direction modulated brachytherapy (DMBT) and standard tandem plans for the 9 cases that had both ANs and FNs (eg, Diff. [%] = (D&R − T&R)/T&R)

Patient no.	No. of AN used	No. of FN used	D&R(+AN)(+FN) − T&R(+AN)(+FN) Diff. [%]			D&R(−AN)(−FN) − T&R(−AN)(−FN) Diff. [%]			D&R(−AN)(+FN) − T&R(+AN)(+FN) Diff. [%]			D&R(−AN)(+FN) − T&R(−AN)(+FN) Diff. [%]		
			Bladder D2cm^3	Rectum D2cm^3	Sigmoid D2cm^3	Bladder D2cm^3	Rectum D2cm^3	Sigmoid D2cm^3	Bladder D2cm^3	Rectum D2cm^3	Sigmoid D2cm^3	Bladder D2cm^3	Rectum D2cm^3	Sigmoid D2cm^3
1	0	2	18.52	−0.29	−15.78*	19.00	−0.56	−15.72	18.52	−0.29	−15.78*	18.52	−0.29	−15.78
2	3	2	−15.12	−3.76	−10.23	−28.74*	−14.55	−29.69	−11.03	0.00	−6.90	−20.97*	−6.99	−19.53*
3	6	2	−4.68	−0.25	−0.54	−8.19	−1.48	−36.16*	4.01	3.22	8.94	−3.49	−0.08	−13.92
4	6	2	2.29	−3.06	−5.45	4.71	−6.24	−3.41	14.43	13.14	16.34	4.64	−6.93	−11.30
5	8	2	−5.06	−5.51	7.79	−16.73	−4.58	−21.36	16.44	11.44	24.12	−7.94	−4.20	−7.66
6	0	3	−16.92*	−0.08	−8.64	−21.60	−0.14	−11.15	−16.92*	−0.08	−8.64	−16.92	−0.08	−8.64
7	6	3	2.77	−1.32	−2.39	−9.45	−12.36	−0.50	11.08	11.88	2.05	−7.33	−10.81	−0.75
8	7	3	−1.90	−11.00*	−10.66	−9.93	−22.02*	−22.16	5.60	−8.91*	−2.26	−7.22	−18.40*	−14.55
9	2	4	1.02	−4.68	−7.23	5.15	−6.65	−17.08	3.28	−5.58	−6.08	0.86	−4.72	−10.81
Average			−1.15	−3.31	−5.98	−7.31	−7.62	−17.47	5.05	2.76	1.31	−3.80	−5.61	−11.75
Standard deviation			10.64	3.54	6.80	14.82	7.36	11.54	12.15	7.88	12.90	11.91	6.25	5.67
Minimum			−16.92	−11.00	−15.78	−28.74	−22.02	−36.16	−16.92	−8.91	−15.78	−20.97	−18.40	−19.53
Maximum			18.52	−0.08	7.79	19.00	−0.14	−0.50	18.52	13.14	24.12	18.52	−0.08	−0.75
Paired *t* test			.32823	.04307*	.03915*	.08348	.03307*	.01511*	.53053	.39255	.77695	.14114	.03700*	.00265*

Abbreviations are defined in Fig. 1g.

Four clinical scenarios were compared, in which: (*1*) ANs and FNs were included in all plans: D&R(+AN)(+FN) − T&R(+AN)(+FN); (*2*) ANs and FNs were both excluded in all plans: D&R(−AN)(−FN) − T&R(−AN)(−FN); (*3*) ANs were excluded only in the DMBT plans: D&R(−AN)(+FN) − T&R(+AN)(+FN); and (*4*) ANs only were excluded in all plans: D&R(−AN)(+FN) − T&R(−AN)(+FN). Note, however, that 2 of the 9 cases did not have ANs (patients 1 and 2). Negative (green) and positive (red) values represent lower and higher D2cm^3 values achieved by the D&R plans, respectively. (A color version of this table is available at www.redjournal.org.)

* Statistically significant differences ($P<.05$) in absolute D2cm^3 doses and largest individual reductions.

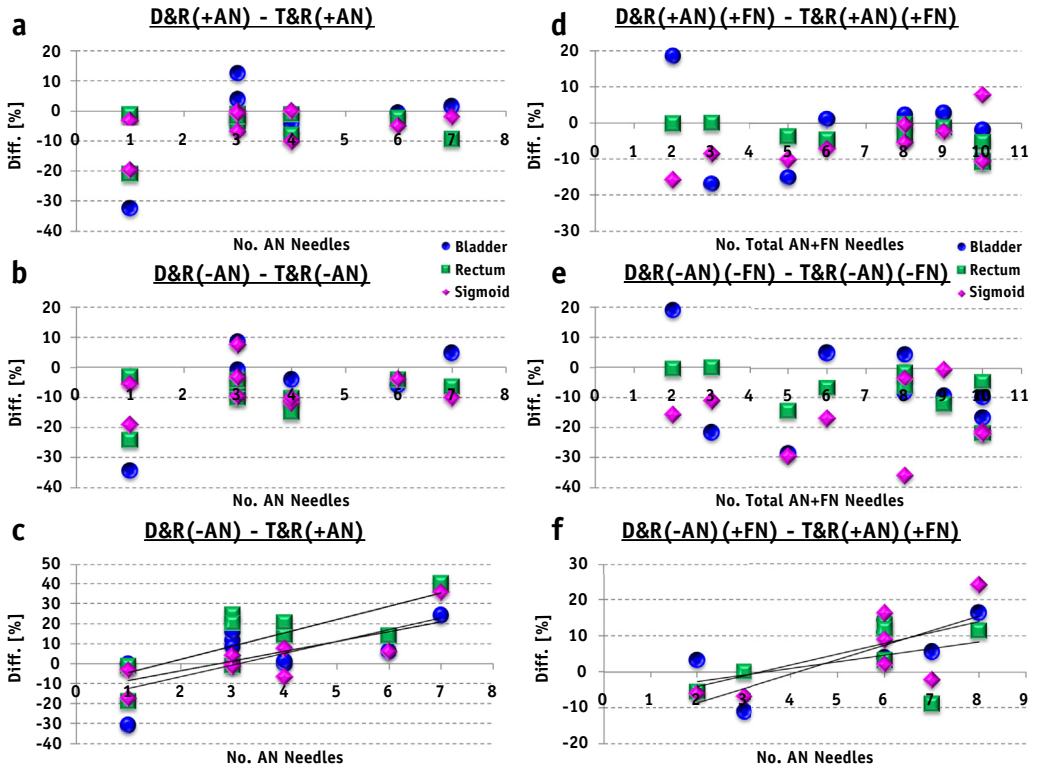

Fig. 3. A consolidated plot of the percentage differences listed in Tables 1 and 2. Data in (a-f) are also in Fig. 2 columns 2-7, respectively. See Fig. 1g for definitions of abbreviations.

(second case in the tables). Additionally, not all D&R plans achieved lower D2cm^3 for all 3 OARs simultaneously; when such occurred, however, this happened to no more than 1 OAR out of the 3, and they remained below the recommended EQD2 limits (28), for all 45 cases.

Figure 3 is a consolidated plot of the data listed in Tables 1 and 2, for easier trend visualization. As can be seen, when the planning conditions are the same (ie, Figs. 2a, 2b, 2d, and 2e), most data points are at near or below zero, suggesting the prudence of using the DMBT tandem whenever possible, if given the option. No obvious trends or dependence on the total number of needles, and disease stage, were observed. On the other hand, when ANs are excluded only in the D&R planning, Figure 3c suggests a trend of increasing dependence on the ANs that cannot be substituted by the DMBT tandem's intensity modulation capacity alone because the 3 linear regression lines intersect zero at approximately 2 to 3 ANs. This means, for cases generally requiring up to 1 to 2 ANs, it could then be possible to avoid the use of ANs altogether via the use of the DMBT tandem applicator. In the same manner, Figure 3f (which purposely excluded the 2 cases with zero ANs from analysis) exhibits a similar trend, whereby the lines intersect at approximately 3 to 4 ANs, whereas the FNs are permitted usage in the planning. Therefore, though not exhaustive, Figures 3c and 3f combine to indicate possible upper limits of the DBMT tandem's clinical utility in its current design form.

Figure 4 shows 3 representative anatomies chosen to further illustrate the capacity of the DMBT tandem to sculpt dose. The first case (Figs. 4a, 4d, and 4g) used an intracavitary technique with no needles, therefore (d) and (g) are identical. As can be seen, because of the location of the tandem, it is unavoidable to irradiate part of the sigmoid with the standard T&R applicator if the CTV_{HR} coverage is to be ensured. The DMBT tandem was able to pull the isodose away from the sigmoid without compromising the overall CTV_{HR} coverage. The second case (Figs. 4b, 4e, and 4h) required 3 ANs owing to the nonideal anteriorly shifted tandem position inside the CTV_{HR}, forcing the T&R plans in (e) and (h) to irradiate larger areas than the target volume. This is especially accentuated when needles are not permitted in (h). Fortunately, however, the OARs were sufficiently distanced away from the target to be of clinical concern. Nonetheless, the DMBT tandem was able to pull and push the isodose in desired directions to create more conformal dose distributions, for example more lateral coverage and less posterior spill in Figure 4e and more posterior coverage and less anterior spill in Figure 4h. The third case (Figs. 4c, 4f, and 4i) required both ANs and FNs (ie, 3 and 2, respectively), owing to the bulging target volume on the left side. When all needles are permitted for planning in (Fig. 4f), the DMBT tandem plan is able to create more conformal dose distribution around the CTV_{HR}. However, owing to the excessive size of the bulging mass, a compromise in target coverage was needed to be made to

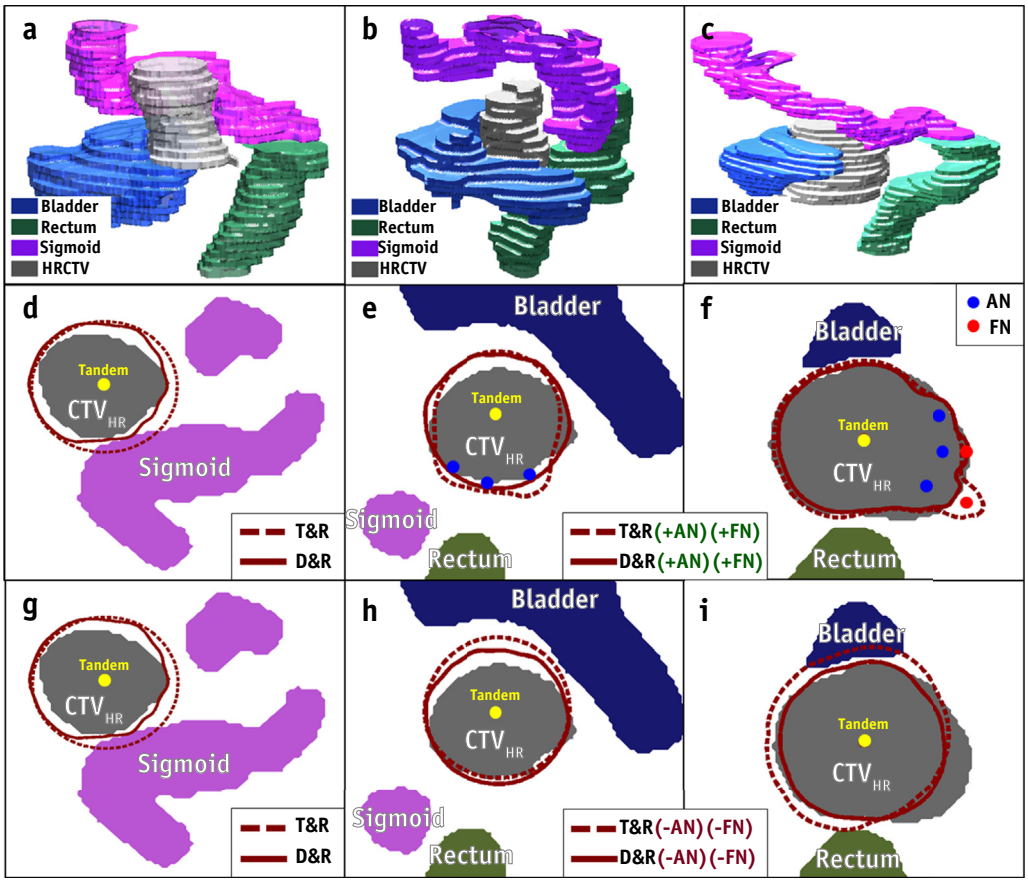

Fig. 4. Three uniquely challenging anatomies are shown: (a, d, g) an intracavitary case; (b, e, h) an ANs only case; and (c, f, i) an ANs+FNs case. (a-c) Three-dimensional volume rendering of the volumes of interest. (d-i) Dotted and solid dark red lines are the prescription isodose lines generated by the T&R and D&R plans overlaid on the anatomy, respectively. The tandem position is marked as a yellow dot. See Fig. 1g for definitions of abbreviations.

spare the bladder and rectum when needles are prohibited in Figure 4i, indicating a limit in the DMBT tandem's dose sculpting capacity. For the same target coverage, however, the D&R plan is shown to be superior to the T&R plan in the sparing of both the bladder and rectum.

In terms of the total dwell times summed up for the DMBT and the standard tandem plans, when everything else was kept the same (ie, rings and with/without needles) there were consistent increases ranging between 20% and 30% for the DMBT plans over all 45 cases. Thus, this can be attributed to the directional modulation activities of the DMBT tandem.

Discussion

The design in Figure 1 is proposed because of several meritorious characteristics. First, the close similarity in its dimensions to contemporary tandem applicators guarantees compatibility with complementary applicators such as ovoids, rings, needles, and cylinders (27). Second, because of the selection of the weakly paramagnetic tungsten alloy as the shielding material (eg, for comparison, >2.5× less magnetic susceptibility than titanium) (19), it exhibits minimal artifacts in MRI (29, 30), as well as being CT compatible when used with commercial metal artifact reduction algorithms (31). Third, with the recent advent of the model-based dose calculation algorithms (5), all major commercial treatment planning systems are now capable of integrating high-density metal alloys into the dose calculations and inverse planning processes (32, 33). Fourth, the width of the grooves in the tungsten alloy rod is wide enough for all commercial HDR and PDR ^{192}Ir sources to travel through. This has been clinically validated (19). Fifth, the addition of 6 channels from the 6 grooves is well below the total number of channels typically available in modern day afterloaders (ranging from 20 to 40). Thus, expensive and cumbersome hardware modifications are not necessary. Sixth, and finally, the increase of 20% to 30% in the total dwell times is acceptable in most, if not all, clinics because this adds only few minutes to the total treatment time for HDR and is an irrelevant issue for PDR due to the much lengthier treatments.

The next logical step is to model the DMBT tandem applicator into the applicator library of one of the commercial treatment planning systems, develop a complete

prototype applicator, map out a planning process, and carry out a prospective clinical study with expert clinical users. One of the limitations of the present study is that we used rather simple in-house developed software for planning, coded in MATLAB (The MathWorks, Natick, MA), where typical interactive fine-tuning by a clinician was not possible, nor did we have the full disease characteristics and patient history available at the time of replanning as a guide. Therefore, given the advantages in percent $D2cm^3$ reductions demonstrated in this study, this is a sufficient motivation to test the applicator in a controlled clinical setting as a next step.

We envision the clinical workflow with the DMBT tandem applicator to be no different than a current IGABT. To ensure the channels properly construct inside the DMBT tandem, one should accurately register the 3-dimensional applicator model to CT/MR images. Once registered, treatment planning ensues, incorporating inverse planning and manual graphical optimizations. Many well-resourced centers around the world are installing CT/MRI systems directly integrated onto the brachytherapy suite, where the treatment can be performed on the imaging couch, drastically minimizing the possibility of applicator shift between imaging and treatment sessions (34). Otherwise, just before treatment, a quick check of the integrity of the internal orientation of the applicators with respect to anatomy can be done with transabdominal ultrasound (35).

Although recognizing the limitations of the study, as well as being cognizant of the early developmental stage of the applicator, the results presented here nonetheless provide an insightful reference to the capabilities and limits of the dose sculpting capacity and the clinical contributions that the DMBT tandem applicator can make during IGABT of cervical cancer under various clinical scenarios involving intracavitary and intracavitary−interstitial techniques. Consistent improvements in OAR sparing were observed across various clinical scenarios, as seen in Figure 2 and Tables 1 and 2, especially when a standard tandem is replaced with the DMBT tandem as the only change in the planning conditions. Therefore, if the DMBT tandem is available in clinic, one could simply use the DMBT tandem for immediate gain in OAR sparing, without having to change the clinical practice at all; for example, if needles are used, continue using the needles. An opportunity may also exist in avoiding use of (AN) needles altogether for when the total number of needles required are small (ie, approximately 2-3 needles or fewer), because the DMBT tandem is seemingly able to compensate for the differences, as seen in Figures 3c and 3f. A clinically common hybrid approach consists of delivering the first brachytherapy fraction with an intracavitary technique, followed by analysis and determination of optimal intracavitary−interstitial implant geometry at subsequent fractions (36). Use of the DMBT tandem as part of the intracavitary technique could minimize (or entirely avoid) the plan quality insufficiencies that may otherwise arise in the first fraction (and also thereafter). Yet another opportunity is, because cervical cancer local control demonstrates dose dependence (37-41), especially for bulkier CTV_{HR} (37, 41), one could escalate the dose while ensuring the recommended OAR sparing levels are not exceeded (23-25, 28). All in all, with future clinical implementations, and with the anticipated know-how to be gained, will undoubtedly help in defining the best-suited treatment strategies for the technology. For this to happen, the community embrace of the technology is necessary—the prospect of which is exciting because the long-successful "single-channel" tandem design may finally get an upgrade.

Conclusions

Integrating the novel DMBT tandem onto both intracavitary and intracavitary−interstitial applicator assembly enabled consistent improvement in the sparing of the OARs, over a standard "single-channel" tandem, though individual variations in benefit were considerable. An opportunity may also exist in avoiding use of needles altogether for when the total number of needles required is small (approximately 2-3 needles or fewer), if DMBT tandem is used. Although at an early stage of development, the DMBT concept design is demonstrated to be useful and pragmatic for potential clinical translation.

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