Hybrid Arc: Combining Forward IMRT and Double arc VMAT in Locally Advanced Rectum Cancer

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ABSTRACT

To investigate the potential of increasing target dose conformity and organ at risk (OAR) sparing of Hybrid Arc approach for patients with locally advanced rectum cancer (LARC) in comparison to VMAT and inverse IMRT. This study consisted of thirteen patients who had LARC, were treated with VMAT in 25 Gy in 5 fractions. Two different new plans for each patient were generated on Pinnacle TPS by inverse IMRT (7 fields) and Hybrid Arc technique (combining forward IMRT (3 fields) with 20% weight and VMAT (double full arcs) with 80% weight). Treatment plans; Hybrid Arc, VMAT and inverse IMRT, were assessed using dose-volume histogram (DVH) parameters of OARs doses for bladder, small bowel, femur heads and penile bulb in male patients' cases. Ad-ditionally, monitor units (MU), conformity index (CI) and homogeneity index (HI) for clinical target volumes (CTV) were compared for all three techniques. Most DVH parameters pertaining to OARs significantly favored Hybrid Arc technique compared to VMAT and inverse IMRT. Hybrid Arc provided significantly improved Bladder DVH parameters in comparison to IMRT & VMAT. The Hybrid technique provided significantly lower small bowel doses in comparison to inverse IMRT and VMAT for all DVH pa-rameters. Mean MU of inverse IMRT was the highest one (MUIMRT= 1803, p= 0.001 vs VMAT; p= 0.023 vs Hybrid Arc). The target dose conformity and homogeneity of VMAT were better than the other two techniques. Hybrid technique combined the advantages of forward IMRT and VMAT for better OAR sparing in comparison to VMAT and inverse IMRT.

Keywords: Rectal cancer, IMRT, VMAT, Hybrid

ÖZET

Lokal İleri Evre Rektum Kanserinde Hibrid Ark

Lokal ileri rektum kanserli (LİRK) olgularda, Hibrit Ark yaklaşımının, VMAT ve IMRT ile karşılaştırılarak, hedef doz konformalitesini ve risk altındaki organ (OAR) korumasını arttırma potansiyelini araştırmaktır. Çalışmamıza, 5 fraksiyonda 25 Gy VMAT ile tedavi edilen 13 LİRK'li olgu dahil edilmiştir. Her hasta için, yeni IMRT ve Hibrit Ark tekniği (forward IMRT (3 alanlar : 275 °, 80 °, 180 °) %20 ağırlık ile ve VMAT (çift tam ark: 182°-178°) %80 ağırlık ile birleştiren) kullanılarak yapılan planlar, Pinnacle TPS'de oluşturuldu. Tedavi planları; Hibrit Ark, VMAT ve IMRT, mesane (V_{25Gy} %, V_{20Gy} %, V_{15Gy} %, V_{10Gy} % ve D_{ort}), ince bağırsak (V_{25Gy} cc, V_{15Gy} cc, V_{10Gy} cc, D_{maks} and D_{ort}), femur başları (V_{25Gy} %, V_{15Gy} %, D_{max} and D_{mean}) ve erkek olgularda penis bulb (D_{max} and D_{mean}) için OAR dozları doz hacim histogramı (DVH) parametreleri kullanılarak değerlendirildi. Ek olarak, klinik hedef hacimleri (CTV) için monitör birimleri (MU), konformalite indeksi (CI) ve homojenite indeksi (HI) her üç teknik için karşılaştırıldı. OAR'larla ilgili DVH parametrelerinin çoğu, VMAT ve IMRT'ye kıyasla önemli ölçüde Hibrit Ark tekniğinden yanaydı. Hibrit Ark yönteminin, IMRT ve VMAT karşılaştırıldığında, Mesane DVH parametrelerini (V_{25Gy} cc, V_{15Gy} cc, V_{10Gy} cc, D_{max} and D_{mean}) azalttığı gösterilmiştir. Hibrit planlama tekniği, ortalama doz dahil olmak üzere listelenen tüm ince bağırsak DVH parametreleri için, IMRT ve VMAT ile karşılaştırıldığında belirgin şekilde daha düşük dozlar sağlamıştır. Hibrit tekniği, VMAT'a kıyasla V_{20Gy}%, V_{15Gy} %'de daha düşük femur başı dozları olduğu saptanmıştır.

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Penis bulbusun, ortalama ve maksimum dozları her üç teknik için benzerdir. IMRT'nin ortalama MU değeri en yüksektir (MUIMRT= 1803, p= 0.001 vs VMAT; p= 0.023 vs Hybrid Arc). VMAT'ın hedef doz konformalitesi ve homojenitesi diğer iki teknikten daha iyiydi. (CI_{VMAT}=1.16 vs CI_{Hybrid}=1.19, p= 0.003; vs CI_{IMRT}= 1.22, p= 0.001 and HI_{VMAT}= 0.33 vs HI_{Hybrid}= 0.36, p= 0.01; vs HI_{IMRT}= 0.37, p= 0.012). Hibrit tekniğinin, VMAT ve IMRT'ye kıyasla, daha iyi OAR koruması için ileri IMRT ve VMAT'ın avantajlarını birleştirmektedir.

Anahtar Kelimeler: Rektal kanser, IMRT, VMAT, Hibrid

INTRODUCTION

3D conformal radiotherapy (3D-CRT) technique has been widely used as a standard treatment technique for the treatment of locally advanced rectum cancer (LARC), where organs at risk (OAR) such as small bowel, bladder and femur heads are tried to be spared during shaping the treatment volumes. Many studies pointed out a strong relationship between the amount of small bowel receiving low-to-intermediate-doses of radiation and the rates of acute grade 3 small bowel toxicity, including diarrhea.[1-6] The modern radiotherapy techniques such as intensity modulated radiotherapy (IMRT) have promised to reduce the treatment volume of small bowel, bladder and femur heads in radiation.[7] Arc-based IMRT technique with rotational beam directions, named as volumetric modulated arc therapy (VMAT) or Tomotherapy, are also available for the best possible optimization of large treatment volumes in LARC.[8-10] VMAT and IMRT could ensure similar sparing for OAR, as VMAT plans have been proved to provide higher efficiency than IMRT plans on whole pelvic radiation therapy (WPRT).[11,12] In the transition period from IMRT to VMAT, using the combination of IMRT fixed angles and dynamic conformal arc technique (DCA) have been studied as an alternative planning approach.[13] DCA and 5-field IMRT techniques in different arc numbers were combined[14] and revealed that the rectum dose could be lowered via this new hybrid technique in comparison to DCA alone, as similar goals reached by IMRT in prostate cancer radiotherapy. Similarly, the same hybrid approach in radiotherapy of esophageal cancer has been shown to be superior to other standard treatment plans.[15] The Hybrid Arc technique, combining of DCA and IMRT delivery, has been developed and made commercially available.[16,17] The Hybrid Arc technique described by Jeong et. al.[17] consists flexible weights of arcs and beams to a planner, while lacking the intensity modulation in comparison to another arc technique (e.g. VMAT). Another type of hybrid approach, tested dosimetrically with the combination of double arc VMAT technique and three-dimensional conformal fields, was shown to be promised in non-small cell lung cancer treatment planning.[18] We have also recently tested a hybrid technique, formed by combining 2 half-arc VMAT technique with the static artificial IMRT fields. Then, we have documented a statistically significant dosimetric improvement in comparison to separate IMRT and VMAT plans in radiotherapy of locally advanced lung cancer patients.[19]

As IMRT has been promising to decrease the gastrointestinal acute toxicity in comparison to 3D-CRT[20,21], combination of fixed beams and arc techniques sounds encouraging to achieve better dosimetry on OAR. Therefore, we have investigated whether or not hybrid volumetric arc therapy, as a combination of forward IMRT and VMAT (double full arc), offers a superior dose distribution over forward IMRT and VMAT separately in terms of dose conformity and OAR sparing.

MATERIALS AND METHODS

Patients Selection and Simulation:

Our study cohort comprised of thirteen patients who had LARC, treated with a short course (25 Gy) radiotherapy in our department. Seven of these patients were males and all were N1 with T3 or T4 stage. The patients in the cohort (the first quality assurance patients in the transition was from IMRT to VMAT techniques for LARC treatment between 2011 and 2012) were treated with using VMAT technique after reaching our clinical quality assurance satisfaction and justification based on organ at risks constrains matching at least to the previous IMRT plans. The CT simulation was

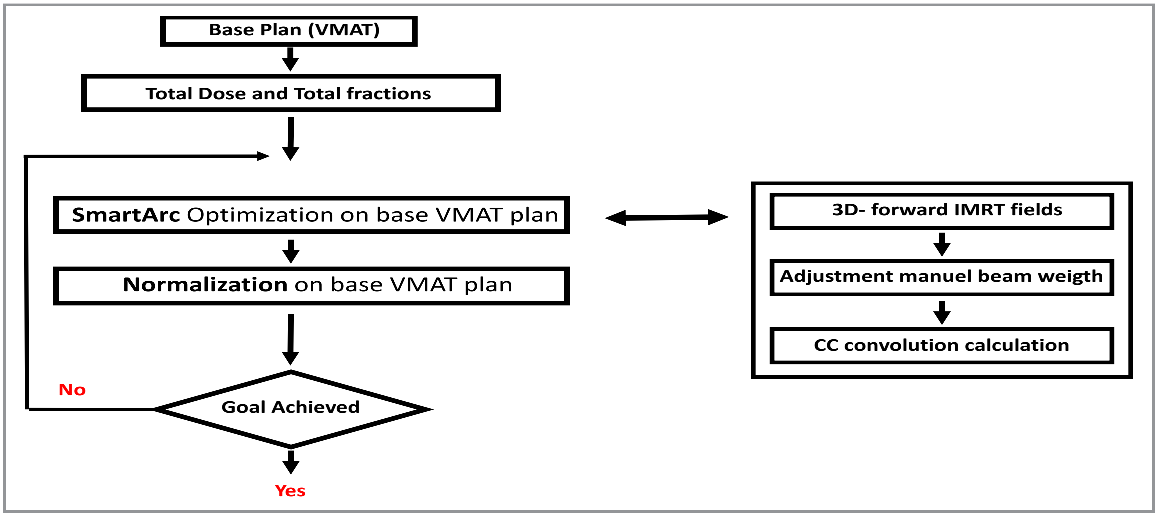

Figure 1. A study strategy of a hybrid arc optimization

performed in the supine position with full bladder in A-bar and knee-foot stopper immobilization (CIVCO, Kalona, Iowa). Computed tomography (CT) scans with a 3 mm slice thickness from the umbilicus to the medium femur bone were obtained with a Philips Brilliance Big Bore 16 slice CT scanner (Philips Medical Systems Inc, Cleveland, OH). Reproducibility in bladder filling throughout the CT simulation, and fraction per day were assured by a daily pretreatment bladder scan device (Bladder Scan BVI 6400 bladder volume instrument, Verathon Healthcare, USA) , as well as on board cone beam CT match.

Volume Definition:

Clinical target volume (CTV) was delineated and peer reviewed by radiation oncologists according to the published consensus guidelines on 3 mm CT image.[22] Planning target volume (PTV) was defined by adding 0.7 cm to all directions of CTV. Small bowel, bladder and femoral heads were defined as organs at risk. The small bowel border was contoured as a bowel bag starting 5 cm above PTV. The bladder and femur heads were fully delineated.

Treatment Planning:

All patients were treated with double arc VMAT respect to standard approach of our clinic with a prescription dose of 25 Gy in five fractions given in one week. Hybrid Arc, IMRT and VMAT plans were designed for each patient on the Philips Pinnacle Treatment Planning System 9.0 (Philips Medical Systems Inc., Cleveland, OH) in which the planning system consisted of collapse cone convolution (CCC) algorithm. The treatment plans were generated on Varian Trilogy (Varian Medical Systems, Palo Alto, CA) by utilizing 120 leafs millennium multileaf collimator (MLC) delivery system with 6 MV photon energy and delivering with a maximum dose rate of 600 MU/min. A grid size of 0.3 x 0.3 x 0.3 cm^3 was applied for all calculations.

Inverse IMRT:

The treatment plans of the 13 patients were made with inverse IMRT (7 step-and-shoot fix fields technique using 7 coplanar beams of 30^0, 80^0, 130^0, 180^0, 230^0, 280^0 and 330^0 gantry angles). Multiple segments (140 numbers), at least 20 segments for each gantry angle, were created by using the direct machine parameter optimization (DMPO) algorithm in Pinnacle.[23]

VMAT:

VMAT treatment plans were generated according to the standard approach of our clinical practice using two full arcs with the same isocenter rotating clockwise and counter clockwise starting from

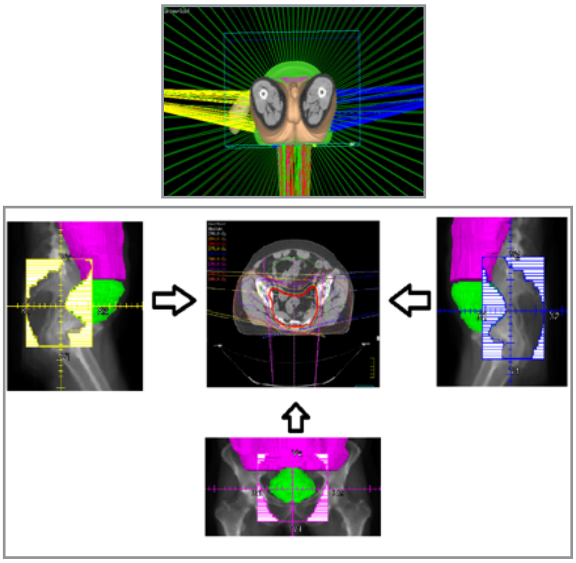

Figure 2. (a) 3D image reconstruction of the hybrid technique on a body, and **(b)** the concept of the hybrid arc with BEV of forward IMRT beams (275°, 85° and 180°) on center-axial slice of an example patient. The pink color shows small bowel structure and the green color shows bladder structure.

182^0 and 178^0 with a 15^0 collimator angle. The collimator angle was fixed to $15^0/345^0$ so to minimize the effects of interleaf leakage and tongue-and-groove. The same dose objectives and weightings were applied for both the fixed fields of IMRT and VMAT plans.

Hybrid Arc (HA: Forward IMRT and VMAT Combination):

A Hybrid Arc technique was also created by combining forward IMRT (included 6 MV or 18 MV energy) and VMAT (double full arc) techniques, without fusion, in this investigation. Figure 1 depicts our hybrid arc optimization strategy as a treatment planning flow. Our hybrid arc optimization strategy is composed of three steps once the standard double full arcs VMAT treatment plan has been established:

(i) a geometrical arrangement of forward IMRT with the static gantry fields was first defined, and the relative weight of forward IMRT dose relative to VMAT was then adjusted. The hybrid strategy offers unlimited field types and weight ratios to planners. Our initial priority was sparing OARs such as bladder and intestines with dedicated constraints. Following various trials of different numbers and angles of fields, the two lateral fields with a high energy photon, and one posterior field with a low energy photon sounded to provide the best OARs sparing. Here directly opposed fields were avoided in forward IMRT, while left-right oblique and posterior fields gave the best geometry (275^0, 85^0, and 180°). Different weights of forward IMRT (Wimrt) as a part of this hybrid arc were tested on the total treatment dose. Wimrt was calculated as 100% - Wvmat, where Wimrt was found to be satisfactory as 20% in the total treatment dose to compensate reducing the OAR doses in balance with VMAT part of hybrid arc. Particularly, adding forward IMRT fields provided more control points with fixed gantry to VMAT technique, and it was possible to optimize the advantages of the static gantry fields. The 18 MV lateral fields of IMRT were used to form the hybrid plan that covered the vast majority of PTV while minimizing the irradiated OAR (intestine and bladder) volume. All lateral fields weight was 40% of weight on IMRT part while posterior field weight was 20% of weight on IMRT part.

(ii) The second step was about optimization of the VMAT arcs and forward IMRT fields. No current TPS supports the calculation of the optimization of different treatment techniques together at the same time. Therefore, optimizations of the forward IMRT and the VMAT were done separately in this hybrid strategy. CC convolution in pinnacle TPS and optimization of the Smart arc for VMAT were completed using total dose constraints. A hybrid plan provided a balance between forward IMRT and VMAT to reach the desired goals of target, bladder and small intestine constraints, similar to simultaneous integrated treatment techniques. Overall, the advantages of static fields and arcs in combination by this hybrid strategy have been used via optimization on the total dose. The same normalization volume was chosen to achieve the same coverage volume for both techniques.

(iii) The third step was about the treatment plan optimizations. Final dose calculation was performed in Pinnacle TPS after the goal was achieved. If the optimal plan with a better dose volume histogram within OAR dose constraints does not achieve, the

Table 1. Dosimetric comparison of PTV for IMRT, VMAT and Hybrid Arc plans, including MU, CI, and HI values

	VMAT	IMRT	HYBRID	p value VMAT vs IMRT	p value VMAT vs Hybrid	p value IMRT vs Hybrid
PTV Dmax (Gy)	27.45	27.82	27.25	0.173	0.382	0.016
PTV Dmean (Gy)	25.96	25.92	25.88	0.507	0.172	0.600
MU	1263.62	1803.85	1494.77	0.001	0.001	0.023
CI	1.16	1.22	1.19	0.001	0.003	0.012
HI	0.33	0.37	0.36	0.012	0.010	0.127

strategic plan should trigger the first step (when it is applied). The possible hybrid ratio solution seems to be a composite plan with contributions of 80% VMAT with double arcs and 20% forward IMRT with the 3 angles in this hybrid strategic plan.

This hybrid arc strategy has the same isocenter of VMAT (double full arcs with 182^0-178^0 clockwise and counter clockwise with a 15^0- 345^0collimator angles) and forward IMRT (two lateral 18 MV fields with 85^0 and 275^0 gantry angles, and posterior 6 MV field with 180^0 gantry angle). 3D image reconstruction and schematic diagram of the concept of hybrid arc with static gantry beams 275^0, 85^0 and 180^0 BEV on axial slice of a patient are shown in Figure 2.

Dosimetric Comparison:

In clinical practice, normal tissue dose limits were set as follows: Small bowel as D_{max}< 27 Gy, V25 Gy< 2 cc, V15> 60 cc, Femurs: V20< 35%, V15 < 50%, Bladder: V20< 35%, V15< 50%. Dosimetric comparison between the three treatment plans (VMAT, inverse IMRT, and Hybrid Arc) was performed for OARs doses of bladder (V25Gy %, V_{20Gy} %, V_{15Gy} %, V_{10Gy} %, D_{mean}), small bowel (V_{25Gy} cc, V_{15Gy} cc, V_{10Gy} cc, Dmax, Dmean), femur heads (V_{25Gy} %, V_{15Gy} %, Dmax, Dmean) and penile bulb (D_{mean}, D_{max}) in male patients' cases. Conformity index (CI) and homogeneity index (HI) for clinical target volumes (CTV) were compared for the three techniques. The conformity index CI95 was calculated as the ratio of the volume enclosed by the 95% isodose volume to the part of the target volume receiving more than 95% (i.e., $CI_{95}= V_{95\%} / TV_{95\%}$). The 95% isodose was chosen according to ICRU-62 report to provide 95% target volume coverage.[24] Homogeneity index was also calculated as $HI= D_{2\%} - D_{98\%}/D_{50\%}$, according to the ICRU-83 report.[24] Furthermore, total treated monitor units (MU: sum of delivery of all fractions) were also compared. These three different techniques were dosimetrically compared by two-tailed pair wise Wilcoxon signed-ranked test.[25] A value of $p< 0.05$ was considered to indicate statistically significant differences.

RESULTS

Target Coverage:

Maximum dose (D_{max}) of PTV was quite similar to in both VMAT and Hybrid Arc techniques ($D_{max\ VMAT}$= 27.45 Gy vs $D_{max\ Hybrid}$= 27.25 Gy, $p> 0.05$), as Hybrid Arc D_{max} of PTV was different from D_{max} of PTV from inverse IMRT ($D_{max\ IMRT}$= 27.82 Gy, $D_{max\ Hybrid}$= 27.25 Gy, $p= 0.016$). Mean doses of PTV were similar to in all three techniques ($D_{mean\ VMAT}$= 25.96 Gy, $D_{mean\ IMRT}$= 25.92 Gy, $D_{mean\ Hybrid}$= 25.88 Gy, $p> 0.05$, $p> 0.05$, $p> 0.05$, respectively). The target dose conformity and the homogeneity of VMAT were better than the other two techniques (CI_{VMAT}= 1.16 vs CI_{Hybrid}= 1.19, $p= 0.003$; vs CI_{IMRT}= 1.22, $p= 0.001$ and HI_{VMAT}= 0.33 vs HI_{Hybrid}= 0.36, $p= 0.01$; vs HI_{IMRT}= 0.37, $p= 0.012$). Also, the conformity index of the Hybrid in comparison to inverse IMRT was found to be statistically significant ($p= 0.012$) while the

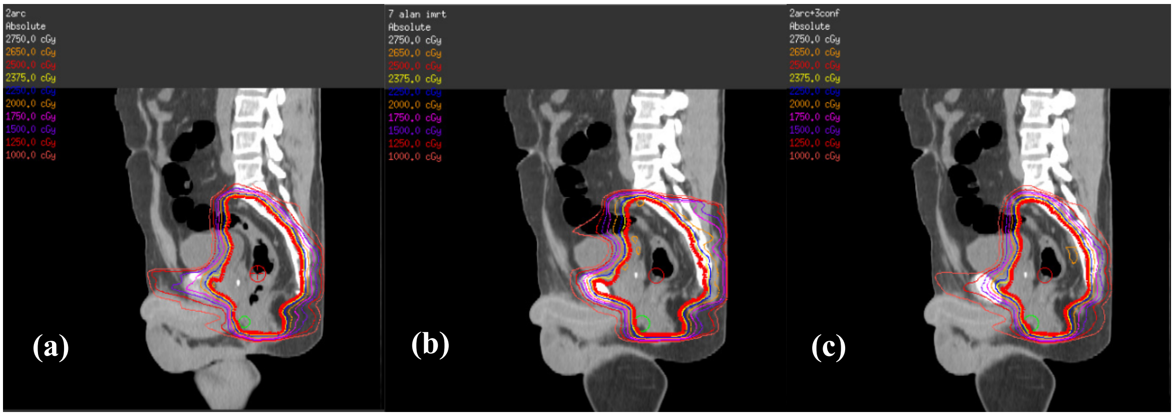

Figure 3. Sagittal view of isodose distribution of **(a)** VMAT, **(b)** IMRT, **(c)** Hybrid Arc

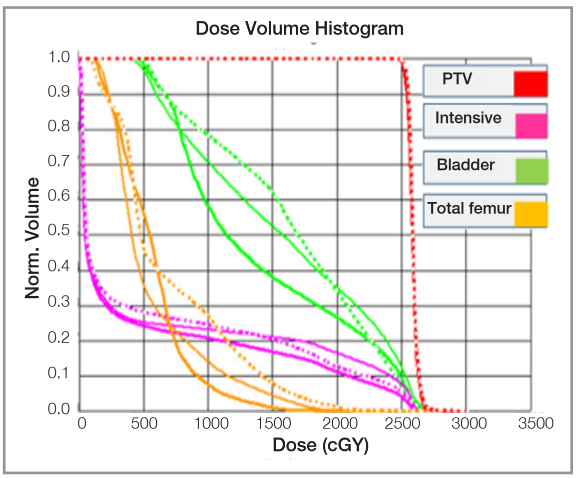

Figure 4. DVH for Hybrid Arc (solid-thick line), VMAT (solid-thin line) and IMRT (dash line), for the same patient

homogeneity index was not different between Hybrid and inverse IMRT (p> 0.05). As detailed in Table 1, statistically significant differences in these analyses are not clinically significant because the maximum dose difference between the techniques, without statistical comparison, is 0.57 Gy.

Monitor Units:

Mean MUs of the hybrid plan was significantly higher than mean MU values of VMAT (MU_{Hybrid}= 1495 vs MUVMAT= 1264, p= 0.001). However, mean MU of the inverse IMRT plan was the highest one (MU_{IMRT}= 1803, p= 0.001 vs VMAT; p= 0.023 vs Hybrid Arc), as given in Table 1.

Dose distribution in the target volumes was similar to in all three techniques, as given in Table 1. However, the sagittal views reflected the dose distribution of the three technical differences better, as shown in Fıgure 3.

Dose volume histograms (DVH) were obtained for all critical organs of the patients to compare the three treatment techniques. Hence, Figure 4 shows the dose volume histogram (DVH) for all critical organs. Hybrid plan for OARs was shown to be better than the other two techniques without changing the target coverage on the sample DVH.

Organ at Risk:

Using the three planning techniques, the dosimetric comparison including p values for OARs (small bowel, bladder, femoral heads, and penile bulb) were made, and listed in Table 2 and Table 3, respectively. The outcomes were briefly explained, as following.

Small Bowel:

As given in Table 2, small bowel parameters were not significantly different from the outcomes of VMAT and inverse IMRT, except V_{10Gy} cc (V_{25Gy} VMAT= 1.40 cc vs V_{25Gy} IMRT= 1.46 cc, p> 0.05; V_{15Gy} VMAT= 45.82 cc vs V_{15Gy} IMRT= 46.95 cc, p> 0.05; D_{max} VMAT= 25.23 Gy vs D_{max} IMRT= 24.81 Gy, p> 0.05; D_{mean} VMAT= 7.22 Gy vs D_{mean} IMRT= 7.28 Gy, p> 0.05). VMAT revealed significantly low V_{10Gy} cc in comparison to inverse

Table 2. Average dosimetric results for small bowel using IMRT, VMAT and Hybrid Arc

	VMAT	IMRT	HYBRID	p value VMAT vs IMRT	p value VMAT vs Hybrid	p value IMRT vs Hybrid
V25Gy (cc)	1.40	1.46	0.12	0.575	0.003	0.002
V15Gy (cc)	45.82	46.95	23.22	0.929	0.002	0.002
V10Gy (cc)	115.67	133.01	63.62	0.007	0.001	0.002
Dmax (Gy)	25.23	24.81	23.43	0.221	0.001	0.002
Dmean (Gy)	7.22	7.28	5.25	0.650	0.001	0.002

IMRT (V_{10Gy} VMAT= 115.67 cc vs V_{10Gy} IMRT= 133.01 cc, p= 0.007). The hybrid arc provided significantly improved V_{25Gy} cc, V_{15Gy} cc, V_{10Gy} cc, D_{max} and D_{mean} in comparison to inverse IMRT & VMAT results (V_{25Gy} Hybrid= 0.12 cc vs V_{25Gy} VMAT, p= 0.003; vs V_{25Gy} IMRT, p= 0.002; V_{15Gy} Hybrid= 23.22 cc vs V_{15Gy} VMAT, p= 0.002; vs V_{15Gy} IMRT, p= 0.002; V_{10Gy} Hybrid= 63.62 cc vs V_{10Gy} VMAT, p= 0.001; vs V_{10Gy} IMRT, p= 0.002; D_{max} Hybrid= 23.43 Gy vs D_{max} VMAT, p= 0.001; vs D_{max} IMRT, p= 0.002; D_{mean} Hybrid= 5.25 Gy vs D_{mean} VMAT, p= 0.001; vs Dmean IMRT, p= 0.002). The volumes (cc) of small bowel doses (V_{25Gy}, V_{15Gy} and V_{10Gy}) in Hybrid Arc is approximately half of the other two techniques. Especially, the volume of prescribing dose in the small bowel (V_{25Gy} Hybrid= 0.12 cc) was be found nearly zero for Hybrid Arc technique. More details of the small bowel data were given in Table 2.

Bladder:

Again, the statistically outcomes of VMAT and inverse IMRT were not significantly different from all parameters (V_{20Gy} VMAT= % 34.53 vs V_{20Gy} IMRT= % 34.33, p> 0.05; V_{15Gy} VMAT= % 50.07 vs V_{15Gy} IMRT= % 51.03, p> 0.05; D_{mean} VMAT= 17.86 Gy vs D_{mean} IMRT= 17.93 Gy, p> 0.05) except percent in volumes of high and lower doses. However, for two parameters; the V_{25Gy} % value of inverse IMRT was statistically different comparison to VMAT, whereas the V_{10Gy} % value of VMAT was found statistically different comparison to inverse IMRT (V_{25Gy} VMAT= % 23.07 vs V_{25Gy} IMRT= % 20.74, p= 0.004; V_{10Gy} VMAT= % 81.49 vs V_{10Gy} IMRT= % 84.58, p= 0.012). The hybrid technique provided significantly lower doses in comparison to inverse IMRT and VMAT for all parameters including the mean dose (V_{25Gy} Hybrid= % 15.30 vs V_{25Gy} VMAT, p= 0.001; vs V_{25Gy} IMRT, p= 0.002; V_{20Gy} Hybrid= % 26.86 vs V_{20Gy} VMAT, p= 0.001; vs V_{20Gy} IMRT, p= 0.001; V_{15Gy} Hybrid= % 39.73 vs V_{15Gy} VMAT, p= 0.001; vs V_{15Gy} IMRT, p= 0.001; V_{10Gy} Hybrid= % 67.92 vs V_{10Gy} VMAT, p= 0.001; vs V_{10Gy} IMRT, p= 0.001; D_{mean} Hybrid= 15.66 Gy vs D_{mean} VMAT, p= 0.001; vs D_{mean} IMRT, p= 0.001). More details of the bladder data were given in Table 3.

Table 3. Average dosimetric results for bladder using IMRT, VMAT and Hybrid Arc

	VMAT	IMRT	HYBRID	p value VMAT vs IMRT	p value VMAT vs Hybrid	p value IMRT vs Hybrid
V25Gy (%)	23.07	20.74	15.30	0.004	0.001	0.002
V20Gy (%)	34.53	34.33	26.86	0.386	0.001	0.001
V15Gy (%)	50.07	51.03	39.73	0.306	0.001	0.001
V10Gy (%)	81.49	84.58	67.92	0.012	0.001	0.001
Dmean (Gy)	17.86	17.93	15.66	0.753	0.001	0.001

Table 4. Average dosimetric results for femur heads using IMRT, VMAT and Hybrid Arc						
	VMAT	**IMRT**	**HYBRID**	**p value VMAT vs IMRT**	**p value VMAT vs Hybrid**	**p value IMRT vs Hybrid**
Dmax (Gy)	22.60	23.21	20.60	0.422	0.002	0.002
Dmean (Gy)	8.09	8.04	7.79	0.382	0.196	0.345
V20Gy (%)	4.15	2.36	1.92	0.019	0.008	0.515
V15Gy (%)	15.06	12.22	10.51	0.116	0.002	0.625

Femoral Heads:

Again, the statistically outcomes of VMAT and inverse IMRT in femur heads were not significantly different from all parameters except V_{20Gy} % ($D_{max\ VMAT}$= 22.60 Gy vs $D_{max\ IMRT}$= 23.21 Gy, p> 0.05; $D_{mean\ VMAT}$= 8.09 Gy vs $D_{mean\ IMRT}$= 8.04 Gy, p> 0.05; $V_{15Gy\ VMAT}$= % 15.06 vs V15Gy IMRT= % 12.22, p> 0.05). IMRT revealed significantly low V_{20Gy} % in comparison to VMAT ($V_{20Gy\ VMAT}$= % 4.15 vs $V_{20Gy\ IMRT}$= % 2.36, p= 0.019). The hybrid technique provided statistically significantly lower doses in comparison VMAT for all parameters except mean dose for femur heads ($D_{max\ Hybrid}$= 20.60 Gy vs $D_{max\ VMAT}$, p= 0.002; $V_{15Gy\ Hybrid}$= % 10.51 vs $V_{15Gy\ VMAT}$, p= 0.002; $D_{mean\ Hybrid}$= 7.79 Gy vs $D_{mean\ VMAT}$, p> 0.05). Also, the hybrid technique yielded lower doses for all parameters in comparison to inverse IMRT besides maximum dose was statistically different between the two techniques ($D_{max\ Hybrid}$ vs $D_{max\ IMRT}$, p= 0.002). More details of the femoral heads data were given in Table 4.

Penile Bulb:

The mean and maximum doses of the penile bulb were found to be similar for the three techniques. The hybrid technique yielded lower doses for all parameters in comparison to inverse IMRT and VMAT, while there were not statistically different for all comparisons ($D_{max\ VMAT}$= 20.24 Gy vs $D_{max\ IMRT}$= 18.86 Gy vs $D_{max\ Hybrid}$= 16.43 Gy; $D_{mean\ VMAT}$= 10.68 Gy vs $D_{mean\ IMRT}$= 10.42 Gy vs $D_{max\ Hybrid}$= 8.43 Gy; for all comparisons p> 0.05). More details of the penile bulb data were given in Table 5.

DISCUSSION

A major clinical problem in pre-conformal era radiotherapy of patients with LARC was acute toxicity that is caused by wide radiation fields, decreasing treatment tolerability of the patients.[1] Therefore, besides other clinical treatment techniques, inverse IMRT and VMAT have increasingly been preferred for LARC treatment in recent years.[8] Though IMRT and VMAT have evolved radiotherapy in great extent, they still have some limitations in terms of OAR sparing, such as low dose bath or long treatment duration. This study, being a planning study, has investigated a new treatment strategy, combining forward IMRT and VMAT, and offers a progressing planning technique for especially rectum and bladder sparing. The dosimetric comparisons revealed statistically significant, but OARs high dose region gains, which could be considered important due to as low as reasonably achievable (ALARA) principle for a long term quality of life.

Table 5. Average dosimetric results for penile bulb using IMRT, VMAT and Hybrid Arc.						
	VMAT	**IMRT**	**HYBRID**	**p value VMAT vs IMRT**	**p value VMAT vs Hybrid**	**p value IMRT vs Hybrid**
Dmax (Gy)	20.24	18.86	16.43	0.068	0.068	0.068
Dmean (Gy)	10.68	10.42	8.43	0.465	0.068	0.273

In theory, hybrid arc technique, minimizing the disadvantages of each technique, could evolve as an optimal treatment technique as compared to VMAT, DCA (conformal arc therapy), 3D-CRT, and IMRT.[14,26-30] Generally, a combination of two different plans, which had been already calculated to whole course prescription, were generated, and thereafter these selected plans were fused in a single TPS with an effective weight of each planning.[14] This method could have resulted in more effective organ at risk sparing with increasing maximum dose points. A part from the hybrid strategy of the recent articles[14,19,26,27,29], we tried to implement a clinically practical and implementable combination of VMAT and forward IMRT with a new planning strategy to lower hot points while keeping the advantageous of better sparing of OARs. Our planning strategy mimics the approach of simultaneous integrated boost planning using the two different planning modalities. We chose VMAT plan as primary base plan so to decrease a low dose bath and to get the strength dose delivery with IMRT fields with a combination of 80% to 20%, respectively. The combination of directly changing dose distribution for the forward IMRT as a part of hybrid, as well as a choice of beam geometry, allows a planner to better control where dose falls. This planning system has been performed in Pinnacle TPS and could be restricted to the hybrid planning system, which is out of this manuscripts aim.

Several studies have shown a strong dose-volume relationship between the irradiated small bowel volume and the severity of diarrheal toxicity at different dose levels.[1,2] Additionally, as well as previous studies, the latest studies have proved that a strong dose-volume correlation existed between the irradiated small bowel volume and acute diarrhea at all dose levels and they constructed a predictive model for acute toxicity.[5,10,11] Similar studies have shown the importance of intermediate dose levels V_{15Gy}, V_{20Gy} and V_{25Gy} with regard to severe diarrhea.[4,5] In our analyses, the hybrid technique reduced dose on all parameters of small bowel and bladder compared to inverse IMRT and VMAT separately.

A few studies have also investigated different treatment techniques, such as 3D-CRT, IMRT, VMAT and tomotherapy for rectal cancer.[5,10,31] IMRT and VMAT were all significantly superior to 3D-CRT in most of the relevant values evaluated of target response, OARs and normal tissue sparing [9]; besides comparable dosimetric parameters of all techniques for target volume, Zhao et al noted IMRT to be a better technique to spare OARs.[9] While keeping the subjectivity of physics planner dependency in mind, Lin et al recently documented tomotherapy to be superior to IMRT and VMAT in most clinically evaluated endpoints for values of OARs except in the small bowel [10]; additionally, Lin et al also claimed that, neither prone nor supine positions were different from modern radiation techniques for OARs.[10] Richetti et al published their technical and clinical experience of 25 patients with LARC treated with VMAT and a planning comparison with a matched cohort of patients who underwent conventional conformal radiotherapy.[31] Although PTV coverage was similar, single arc VMAT achieved significantly superior dose conformity with a trend to improvement in homogeneity and improved OAR sparing (small bowel, femora and healthy tissue).[31] Furthermore, VMAT treatment in preoperative CRT for LARC showed the potential of substantially decreasing high-grade acute and late toxicity.[8] Depending on these studies, we also preferred VMAT technique, which is the standard treatment for LARC in our clinic, as a basic plan of hybrid arc in our study. As the dose flexibility potential of a treatment plan is related with the number of control points taken into account (if it allows), our hybrid arc plan was combining forward IMRT and VMAT, including approximately 218 (40 + 178) control points to assure better dose modulation and control of dose fall off around the PTV.

With respect to efficiency of treatment delivery, necessary MUs per unit dose is very important in regard to the effect of leakage dose received by patients.[32] The forward IMRT part of the hybrid arc significantly increases total MUs due to additional MLC sequences. The recent literature already reported that hybrid techniques require more MU and delivery time compared to VMAT technique[18,29]; and our hybrid plan would be expected to increase the delivery time in comparison to VMAT, because of containing more MUs and three fixed fields. A typical VMAT treatment, with double arc in our routine clinic for a patient with LARC, has a beam on time of approximately 3 minutes per fraction; however, approximately 7 minutes for inverse IMRT would be required to be completed per fraction. Therefore, the hybrid technique per fraction would probably last between 2 and 7 minutes. Longer delivery time might bring the increase in intra-fraction organ motion on board, while such a potential disadvantage in the hybrid therapy technique could be reduced via modern IGRT methods (e.g. surface tracking, the fluoroscopic image during treatment, etc.).

This investigation has limitations, such as being a dosimetric study and consisting only limited number of patients. On the other hand, this dosimetric study might trigger comparable hybrid planning strategies both in LARC and in other tumor sites for possible future daily clinical practice implementation. The major advantages of our approach are simultaneous processing of the planning and lowering the maximum dose points.

Conclusion

The hybrid arc planning strategy was designed to increase sparing of OARs with balanced switching of static gantry fields and arcs. Our results highlighted a possibility of an achievable more conformal plan with a balanced OAR sparing and homogenous dose distribution via the addition of static fields with segmentation, sufficiently applied to the baseline VMAT plan. Our hybrid arc approach was similar to inverse IMRT and VMAT for target coverage, while achieving lower OARs doses with acceptable MUs. Therefore, this hybrid planning strategy could be encouraged for larger irradiation fields including OARs with low radiation tolerance doses.

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REFERENCES

1. Baglan KL, Frazier RC, Yan D, et al. The dose-volume relationship of acute small bowel toxicity from concurrent 5-FU-based chemotherapy and radiation therapy for rectal cancer. Int J Radiat Oncol Biol Phys 52: 176-183, 2002..
2. Tho LM, Glegg M, Paterson J, et al. Acute small bowel toxicity and preoperative chemoradiotherapy for rectal cancer: investigating dose-volume relationships and role for inverse planning. Int J Radiat Oncol Biol Phys 66: 505-513, 2006.
3. Abbas AS, Moseley D, Kassam Z, et al. Volumetric-modulated arc therapy for the treatment of a large planning target volume in thoracic esophageal cancer. J Appl Clin Med Phys 14: 4269, 2013.
4. Wolff HA, Wagner DM, Conradi LC, et al. Irradiation with protons for the individualized treatment of patients with locally advanced rectal cancer: a planning study with clinical implications. Radiother Oncol 102: 30-37, 2012.
5. Robertson JM, Lockman D, Yan D, Wallace M. The dose-volume relationship of small bowel irradiation and acute grade 3 diarrhea during chemoradiotherapy for rectal cancer. Int J Radiat Oncol Biol Phys 70: 413-418, 2008.
6. Meyer JL, Sharpe M, Brock K, et al. Advanced technologies in the radiotherapy clinic: system fundamentals. Front Radiat Ther Oncol 43: 29-59, 2011.
7. Urbano MTG, Henrys AJ, Adams EJ, et al. Intensity-modulated radiotherapy in patients with locally advanced rectal cancer reduces volume of bowel treated to high dose levels. Int J Radiat Oncol Biol Phys 65: 907-916, 2006.
8. Droge LH, Weber HE, Guhlich M, et al. Reduced toxicity in the treatment of locally advanced rectal cancer: a comparison of volumetric modulated arc therapy and 3D conformal radiotherapy. BMC Cancer 15: 750, 2015.
9. Zhao J, Hu W, Cai G, et al. Dosimetric comparisons of VMAT, IMRT and 3DCRT for locally advanced rectal cancer with simultaneous integrated boost. Oncotarget 7: 6345-6351, 2016.
10. Lin JC, Tsai JT, Chen LJ, et al. Compared planning dosimetry of TOMO, VMAT and IMRT in rectal cancer with different simulated positions. Oncotarget 8: 42020-42029, 2017.
11. Cilla S, Caravatta L, Picardi V, et al. Volumetric modulated arc therapy with simultaneous integrated boost for locally advanced rectal cancer. Clin Oncol (R Coll Radiol) 24: 261-268, 2012.
12. Riou O, Regnault de la Mothe P, Azria D, et al. Simultaneous integrated boost plan comparison of volumetric-modulated arc therapy and sliding window intensity-modulated radiotherapy for whole pelvis irradiation of locally advanced prostate cancer. J Appl Clin Med Phys 14: 4094, 2013.
13. Otto K. Volumetric modulated arc therapy: IMRT in a single gantry arc. Med Phys 35: 310-317, 2008.

14. Robar JL, Thomas C. HybridArc: a novel radiation therapy technique combining optimized dynamic arcs and intensity modulation. Med Dosim 37: 358-368, 2012.
15. Martin S, Chen JZ, Rashid Dar A, Yartsev S. Dosimetric comparison of helical tomotherapy, RapidArc, and a novel IMRT & Arc technique for esophageal carcinoma. Radiother Oncol 101: 431-437, 2011.
16. Zhang GG, Ku L, Michael Yu HH, et al. Dosimetric analysis of modulated and hybrid arcs in stereotactic radiosurgery. J Radiosurg SBRT 1: 177-182, 2011.
17. Jeong K, Basavatia A, Mynampati D, et al. SU-F-T-589: HybridArc Planning Criteria for Brain SRS. Medical Physics 43: 3599-3599, 2016.
18. Chan OS, Lee MC, Hung AW, et al. The superiority of hybrid-volumetric arc therapy (VMAT) technique over double arcs VMAT and 3D-conformal technique in the treatment of locally advanced non-small cell lung cancer--a planning study. Radiother Oncol 101: 298-302, 2011.
19. Saglam Y, Bolukbasi Y, Alpan V, et al. Hybrid Arc Could Combine the Benefits of IMRT and VMAT to Deliver a Fast, Conformal, Homogeneous Treatment in Non-Small Cell Lung Cancer Without Limitations of Low Dose Bath: A Planning Study. UHOD 27: 161-170, 2017.
20. Hong TS, Moughan J, Garofalo MC, et al. NRG Oncology Radiation Therapy Oncology Group 0822: A Phase 2 Study of Preoperative Chemoradiation Therapy Using Intensity Modulated Radiation Therapy in Combination With Capecitabine and Oxaliplatin for Patients With Locally Advanced Rectal Cancer. Int J Radiat Oncol Biol Phys 93: 29-36, 2015.
21. Samuelian JM, Callister MD, Ashman JB, et al. Reduced acute bowel toxicity in patients treated with intensity-modulated radiotherapy for rectal cancer. Int J Radiat Oncol Biol Phys 82: 1981-1987, 2012.
22. Mok H, Crane CH, Palmer MB, et al. Intensity modulated radiation therapy (IMRT): differences in target volumes and improvement in clinically relevant doses to small bowel in rectal carcinoma. Radiat Oncol 6: 63, 2011.
23. Bergman AM, Bush K, Milette MP, et al. Direct aperture optimization for IMRT using Monte Carlo generated beamlets. Med Phys 33: 3666-3679, 2006.
24. 3. Special considerations regarding absorbed-dose and dose-volume prescribing and reporting in IMRT". In Journal of the ICRU. 27-40, 2010.
25. Nahm FS. Nonparametric statistical tests for the continuous data: the basic concept and the practical use. Korean Journal of Anesthesiology 69: 8-14, 2016.
26. Zhao N, Yang R, Wang J, et al. An IMRT/VMAT Technique for Nonsmall Cell Lung Cancer. Biomed Res Int 2015: 613060, 2015.
27. Matuszak MM, Steers JM, Long T, et al. FusionArc optimization: a hybrid volumetric modulated arc therapy (VMAT) and intensity modulated radiation therapy (IMRT) planning strategy. Med Phys 40: 071713, 2013.
28. Bedford JL, Smyth G, Hanson IM, et al. Quality of treatment plans and accuracy of in vivo portal dosimetry in hybrid intensity-modulated radiation therapy and volumetric modulated arc therapy for prostate cancer. Radiother Oncol 120: 320-326, 2016.
29. Zhao N, Yang R, Jiang Y, et al. A hybrid IMRT/VMAT technique for the treatment of nasopharyngeal cancer. Biomed Res Int 2015; 2015: 940102, 2015.
30. Kopp RW, Duff M, Catalfamo F, et al. VMAT vs. 7-field-IMRT: assessing the dosimetric parameters of prostate cancer treatment with a 292-patient sample. Med Dosim 36: 365-372, 2011.
31. Richetti A, Fogliata A, Clivio A et al. Neo-adjuvant chemo-radiation of rectal cancer with volumetric modulated arc therapy: summary of technical and dosimetric features and early clinical experience. Radiat Oncol 5: 14, 2010.
32. Zhang SX, Xu HR, Lin SQ, Li WH. Comparison of the irradiation doses for IMRT and conventional radiotherapy in nasopharyngeal carcinoma patients. Di Yi Jun Yi Da Xue Xue Bao 24: 937-939, 2004.

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