Dosimetric Comparison of the Radiotherapeutic Plans between Composite and Synchronous Planning Approaches in Consecutive-VMAT for Prostate Radiotherapy

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OBJECTIVE
The purpose of our study is to compare composite and synchronous planning approaches in prostate radiotherapy in terms of dosimetric and radiobiology.

METHODS
Fifteen prostate patients previously treated at our clinic were used to conduct this study. For each patient, two different types of planning were performed on the Monaco-TPS; a primary plan with an independently planned boost (Synchronous Planning: SP) and a secondary plan with a dependently planned boost (Composite Planning: CP). Dose distributions obtained by two techniques were compared.

RESULTS
Both of the summed plans were achieved according to the original planning goals. At the D_{99} dose (75.76 Gy versus 76.81 Gy; P=0.017), CI (0.91 versus 0.96; p=0.002), HI (0.08 versus 0.05; p=0.001) and MU (1448 versus 719; p=0.001) were found to be significantly better with SP. Better results were obtained in CP at V5, V10 and V20 doses of the body, rectal and bladder doses. When only the boost plans were compared, the results were 11.8% lower at the D_1 dose and 12.01% higher at the D_{99} dose with the SP. In addition, more conformal (CI: 0.96 versus 0.70; p=0.001) and more homogenous (HI: 0.06 versus 0.24; p=0.001) plans were obtained.

CONCLUSION
When the phase1+phase2 total dose distribution was evaluated, better results were obtained with CP. However, if there is a heterogeneous dose distribution in phase1 planning, there may be very low or very high fraction doses within the target volume only in phase2 planning. Even if the defined dose is applied in total, hot or cold dose volumes can directly affect the radiobiological gain and the result of the treatment.

Keywords: Boost planning; composite plan; synchronous plan.

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INTRODUCTION

Intensity modulated or volumetric arc radiation therapy (IMRT/VMAT) treatment for prostate can-cer has gained popularity over the past two decades. Compared to three dimensional conformal radiation therapy (3D-CRT), IMRT/VMAT have been proven to maintain the same level of tumor control probabil-

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ity while decreasing normal tissue toxicity. One important advantage of the IMRT/VMAT techniques is the ability to shape dose distributions, thus avoiding nearby critical structures such as bladder and rectum. [1–3] In addition, with the simultaneous integrated boost (SIB) technique, different doses can be applied to multiple targets simultaneously with high conformity in IMRT/VMAT plans. However, in the SIB technique, the fraction doses in the target and boost volumes may be lower or higher than the normal fractionation, and the critical organ fraction doses may be higher. Therefore, consecutive-IMRT/VMAT may be more appropriate than SIB-IMRT/VMAT when the fraction doses to the critical organs or target volumes are the major concern.[4–6]

Seminal vesicle (PTV56) and Prostate (PTV78) volumes must be irradiated radiobiologically with a dose of 1.8–2.0 Gy per fraction. It has been proven that 1.8–2.0 Gy fraction doses and 76–80 Gy total doses reduce the biochemical failure rates. This is a biologically equivalent dose ($BED_{1.5}$) of 180–200 Gy, assuming an α/β of 1.5.[7–9] Therefore, in case of simultaneous irradiation of PTV56 and PTV78 target volumes with the SIB-IMRT/VMAT technique, the fraction dose of PTV56 volume will be <1.6/1.5 Gy, resulting in a decrease in the biological equivalent dose. It can also cause the doses of critical organs close to the boost regions to increase per fraction.[10] For consecutive radiotherapeutic plans, the normal tissue constrains typically apply to the entire treatment course rather than the individual phase. There were two approaches commonly applied to planning consecutive-VMAT/IMRT in clinics. The first of these is the synchronous planning approach, in which the initial and boost VMAT/IMRT plans are designed and optimized independently. Then, the plans of the two phases are directly summed to obtain the total dose distribution. The second was composite planning approach, in which the boost VMAT/IMRT plan was designed on foundation of the initial VMAT/IMRT plan. The optimization of the boost plan would be adjusted based on dose distributions of the phase1 VMAT/IMRT plan. With these two approaches, different results can be found only in boost plans and total dose distributions.[10]

The purpose of present study was to compare the dosimetric difference and elucidate the dosimetric quality of the radiotherapeutic plans between synchronous and composite planning approaches in consecutive-VMAT for prostate CA. In addition, it was aimed to evaluate the differences in target and critical organ doses of the two approaches in terms of clinical results.

MATERIALS AND METHODS

CT Scanning and Target Volume Delineation
Tomography scans of 15 prostate patients in 3 mm slice thickness were performed with Siemens® Biograph mCT (Knoxville, TN, USA) device. The patients were scanned in the supine position and with a full bladder. In Prosoma 4.1 (Medcom, Darmstadt, Germany) contouring program, the target and normal tissues (bladder, rectum, femoral heads, and small bowel) were contoured. PTV56 volume was obtained by giving the prostate and the seminal vesicle a margin of 3 mm in the posterior direction and 5 mm in the other directions. PTV78 volume was obtained by giving only to prostate a margin of 3 mm in the posterior direction and 5 mm in other directions.

The Prescribed Dose and Treatment Planning
In the Monaco 5.11 (Elekta CMS, Maryland Heights, MO, USA) treatment planning system (TPS), plans were created using 10 MV energized VMAT fields. In the plans, double arcs VMAT technique was used. Dose calculations in plans were done in Monte Carlo dose calculation algorithm, dose to medium mode, grid space 3 mm, and statistical uncertainty at 1%. The phase1 plan was prescribed to 56 Gy in 28 fractions to the PTV56 which includes prostate and seminal vesicle, while the boost phases were prescribed to 22 Gy in 11 fractions to the PTV78 that targets only the prostate. The basal plan made in phase1 was defined and only boost plans were made in synchronous and composite approaches. The basis of the composite approach was based on the dose distribution obtained in phase 1, and the planning was made by optimizing the total target volume doses and critical organ dose constraints. This was referred to as the composite approach, as a total dose distribution was constructed based on the dose distribution in phase 1 in boost planning. In the synchronous approach, the boost plan is prepared completely independently of the phase1 plan. Then, the dose distribution obtained in phase 1 and the dose distribution obtained from the boost plan was physically summed to obtain the total dose distribution.

The most important point in composite planning, optimization, is trying to construct the total prescribed dose homogeneously in PTV78, taking into account the hot and cold dose points in the phase1 dose distribution. And also, PTV56 creates total dose distributions by adjusting target volume doses and critical organ dose constraints according to the doses that they receive in phase 1 (Fig. 1).
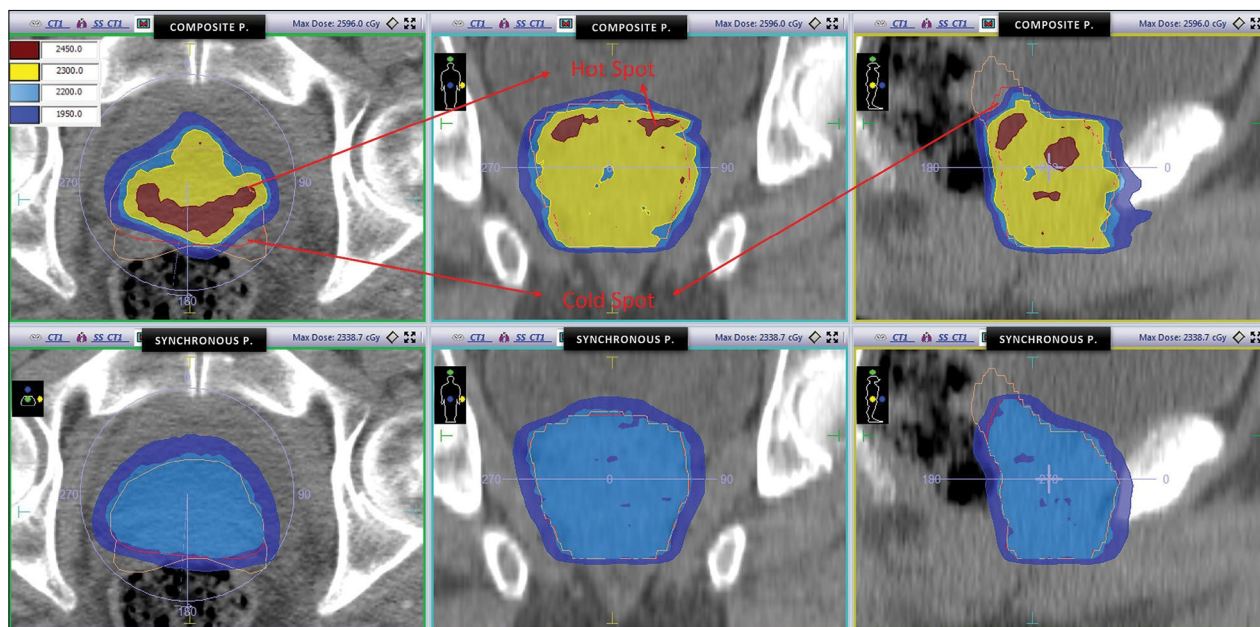
Fig. 1. Dose distributions and hot dose points of composite and synchronous planning.

The treatment goal for summed plan in the entire treatment course was that the prescribed dose would cover 95% of the PTV volume, cover 100% of the clinical target volume (CTV), and the maximum dose would not exceed 110%. For critical organs, volumes receiving 40 Gy and 65 Gy in the rectum and bladder, and dose absorbed by 10% volume in the femurs, limitations were taken into account. In addition, the dose to other normal tissues was minimized within a reasonable range without affecting the target coverage.

Plan Quality Assurance

Verification of synchronous and composite plans has been done with Iba MatriXX Evolution (IBA Dosimetry, Germany) dosimeter system. In the MatriXX measurements, the holder attached to the head of the linear accelerator was placed 5 cm RW3 phantom and MatriXX was placed under it. The MatriXX measurements, the SSD was set at 71.2 cm. The gamma index method was developed by Low et al. (1997) to compare the planning system and measurement results. In 2003, Low and Dempsy developed the current version of the gamma index method, enabling it to enter routine use in clinics. The Gamma index method is a program that compares the measured dose fluence map with the dose fluence map obtained from TPS. The program compares the dose difference (DD%) and the distance to agreement (DTA) of these maps at any point.[11,12] In our study, 2% DD-2 mm DTA, 3% DD-3 mm DTA, and 4% DD-4 mm DTA values were compared.

Plan evaluation

The evaluation of treatment plans was performed by means of standard dose-volume histograms (DVHs). Data were analyzed for PTV56 and PTV78. The main comparing parameters were minimum and maximum doses as defined by the values of D_{99} and D_1 (dose received by the 99%, and 1% of the volume), mean dose, and D95 (volume of PTV receiving 95% prescribed dose). $CI_{Paddick}=(TV_{PIV})^2/TV \times PIV$; where TV_{PIV}: Target volume covered by the reference isodose, TV: Target volume, and PIV: Prescription isodose volume. The higher CI is, the more conformal the plan is.[13] The homogeneity index (HI) for the plans was defined as follows: $HI=(D_{2\%}-D_{98\%})/D_{50\%}$. $D_{2\%}-D_{98\%}$ is the dose of difference between the dose covering 2% and 98% of the PTV. $D_{50\%}$ is the dose covering 50% of the PTV. A higher HI indicates poorer homogeneity.[14] In addition, the MUs were also investigated.

In the critical organs, the volume of the rectum and bladder receiving V65 (volume of the rectums or bladders receiving 65 Gy) and the volume receiving V40 (volume of the rectums or bladders receiving 40 Gy) was compared. Doses received by 10% of femurs were compared. Finally, 5 Gy, 10 Gy, and 20 Gy volumes of the whole body were compared.

Statistical Analysis

The SPSS version 16.0 software (SPSS Inc., Chicago, USA) was applied for statistical analysis. The paired Wilcoxon signed-rank test was used to analyze the

Table 1   PTV78 doses and plan quality indexes, 95% dose of PTV56 and MU values of the plans in composite and synchronous planning approaches

	PTV78						PTV56	MU
	D_1 (Gy)	D_{99} (Gy)	D_{mean} (Gy)	D_{95} (Gy)	HI	CI	D_{95} (Gy)	Phase 2
Composite planning	83.84±166	75.76±114	81.70±132	79.19±56	0.08±0.02	0.91±0.04	63.65±581	1448±322
Synchronous planning	82.14±100	76.81±40	80.25±77	78.37±21	0.05±0.01	0.96±0.03	66.22±725	719±147
p	0.001	0.017	0.001	0.001	0.001	0.002	0.011	0.001

PTV: Planning target volume; MU: Monitor Unit; HI: Homogeneity index; CI: Conformity index; Gy: Gray

Table 2   Dose values of rectum, bladder, femurs and body in composite and synchronous planning approaches

	Rectum		Bladder		R femur	L femur	Body		
	V65 (%)	V40 (%)	V65 (%)	V40 (%)	10% (Gy)	10% (Gy)	V5 (%)	V10 (%)	V20 (%)
Composite planning	4.64±1.92	24.44±7.35	7.87±4.27	18.37±8.01	26.16±367	25.36±373	19.72±5.85	15.14±4.78	5.86±2.28
Synchronous planning	4.76±1.1	24.69±6.26	9.07±3.6	022.23±8.11	25.19±292	24.01±241	21.03±6.23	16.32±5.06	6.10±2.53
p	0.28	0.191	0.887	0.01	0.041	0.026	0.62	0.9	0.02

differences between the synchronous and composite planning approaches. The two-sided p<0.05 was considered to be statistical significance for all tests.

RESULTS

Phase1 plans for target volume PTV56 that is the same in both approaches; CI: 0.98±0.02, HI: 0.07±0.02, and MU: 874±127. Synchronous and composite planning approaches could also be implemented according to prescription planning goals in all 15 patients. In our study, PTV78 was found to be significantly higher with composite planning at the rate of 2.07% at the D_1 dose (83.84 Gy versus 82.14 Gy; p=0.001), 1.81% at the D_{mean} dose (81.70 Gy versus 80.25 Gy; p=0.001), and 1.05% at the D_{95} dose (79.19 Gy versus 78.37 Gy; p=0.001). It was found to be significantly lower in composite planning at a rate of 1.39% the D_{99} dose (75.76 Gy vs. 76.81 Gy; p=0.017), which defines the maximum dose in PTV78 volume. However, CI (0.91 versus 0.96; p=0.002), HI (0.08 versus 0.05; p=0.001), and MU (1448 versus 719; p=0.001) were found to be significantly better with synchronous planning (Table 1).

Lower results were obtained with the composite planning approach in the rectum and bladder. With composite planning in the rectum, lower results were found for the V65 dose 4.64% versus 4.76% (p=0.28), and the V40 dose 24.44% versus 24.69% (p=0.191). In

the bladder, lower results were found for the V65 dose 7.87% versus 9.07% (p=0.887), and the V40 dose by 22.23% (p=0.01) versus 18.37%.

In synchronous planning approach, significantly lower results were obtained with a difference of 3.71% (25.19 Gy vs. 26.16 Gy; p=0.041) for 10% of the right femur and 5.32% (24.01 Gy vs. 26.35 Gy; p=0.026) for 10% of the left femur. V5, V10, and V20 doses of the body were obtained with the lower results with the composite planning (Table 2).

When the dose distributions obtained only from the boost plans for the two approaches are compared; significantly better results were obtained with synchronous planning at the PTV78 volume, 11.8% at the D_1 dose (23.09 Gy vs. 26.19 Gy; p=0.001), and 12.01% at the D_{99} dose (21.55 Gy vs. 18.96 Gy; p=0.016). With synchronous planning approaches, more conformal (0.96 vs. 0.70; p=0.001) and more homogenous (0.06 vs. 0.24; p=0.001) plans were obtained in the PTV78 target volume (Table 3).

When all plans prepared with these two approaches were evaluated according to gamma index analysis, they have been found to be suitable for treatment. Especially, according to 3% DD-3 mm DTA criteria, all plans have pass values over 95%. According to 3% DD-3 mm DTA and 2% DD-2 mm DTA criteria, more feasible dose distributions were obtained from the plans prepared with composite planning (p=0.477 and p=0.09) (Table 4).

Table 3 Dose and quality index values of PTV78 obtained in phase 2 planning with composite and synchronous approaches

	D_1 (Gy)	D_{99} (Gy)	HI	CI
Composite planning	26.19±1.3	18.96±2.7	0.24±0.07	0.70±0.07
Synchronous planning	23.09±3.0	21.55±2.0	0.06±0.02	0.96±0.03
p	0.001	0.016	0.001	0.001

PTV: Planning target volume; HI: Homogeneity index; CI: Conformity index

DISCUSSION

In our study, the dosimetric differences of radio-therapeutic plans between synchronous and composite planning approaches in consecutive-VMAT were compared for prostate radiotherapy. Initially, the prostate and seminal vesicles were planned to have 56 Gy in 28 fractions in phase 1. In phase 2, the prostate was planned to have 22 Gy in 11 fractions in boost plan. Synchronous planning is relatively difficult. Because critical organ doses are obtained after completing and summing the maximum and minimum dose values in target volumes both of phase 1 and phase 2 plans. If

Table 4 Gamma index analysis results

	4%–4mm	3%–3mm	2%–2mm
Composite planning	99.4±1.5	98.5±2.5	95.2±5.9
Synchronous planning	100±0	97.8±2.3	90.6±6.1
p	0.109	0.477	0.096

the targeted dose distribution cannot be achieved, it should be summed up and evaluated after re-planning. The challenge in planning and optimization is determining the appropriate distribution of the normal tissue tolerance dose between the treatment phases.[15] To overcome these difficulties, instead of synchronous planning approach, a composite planning approach can be preferred to develop a plan with better dose distribution in phase 1+phase 2 overall.

In our study, there were differences between composite and synchronous planning approaches in terms of critical organ doses and dose distributions. With synchronous planning lower MU values, more homogeneous and conformal plans were obtained. On the other hand, with composite planning, rectum and bladder protection was better provided and especially in PTV56 volume, the seminal vesicle dose was kept at lower levels (Fig. 2). In addition, V5, V10, and V20
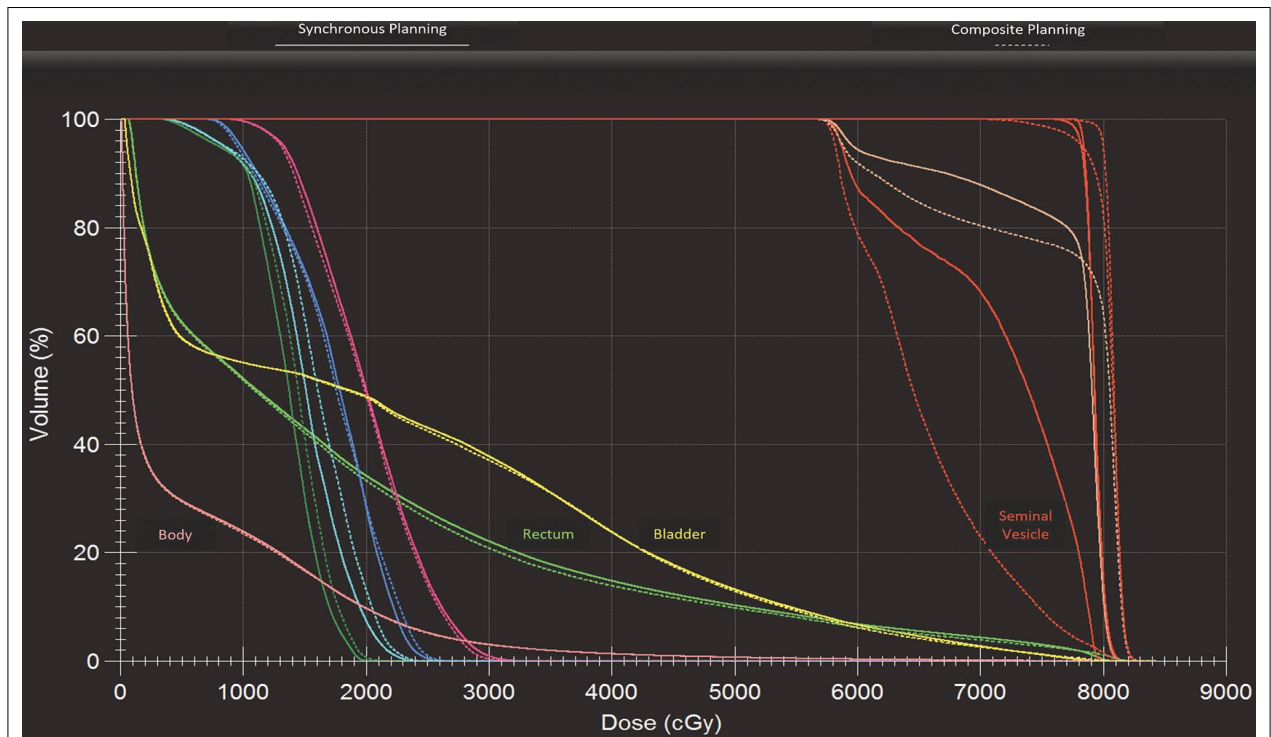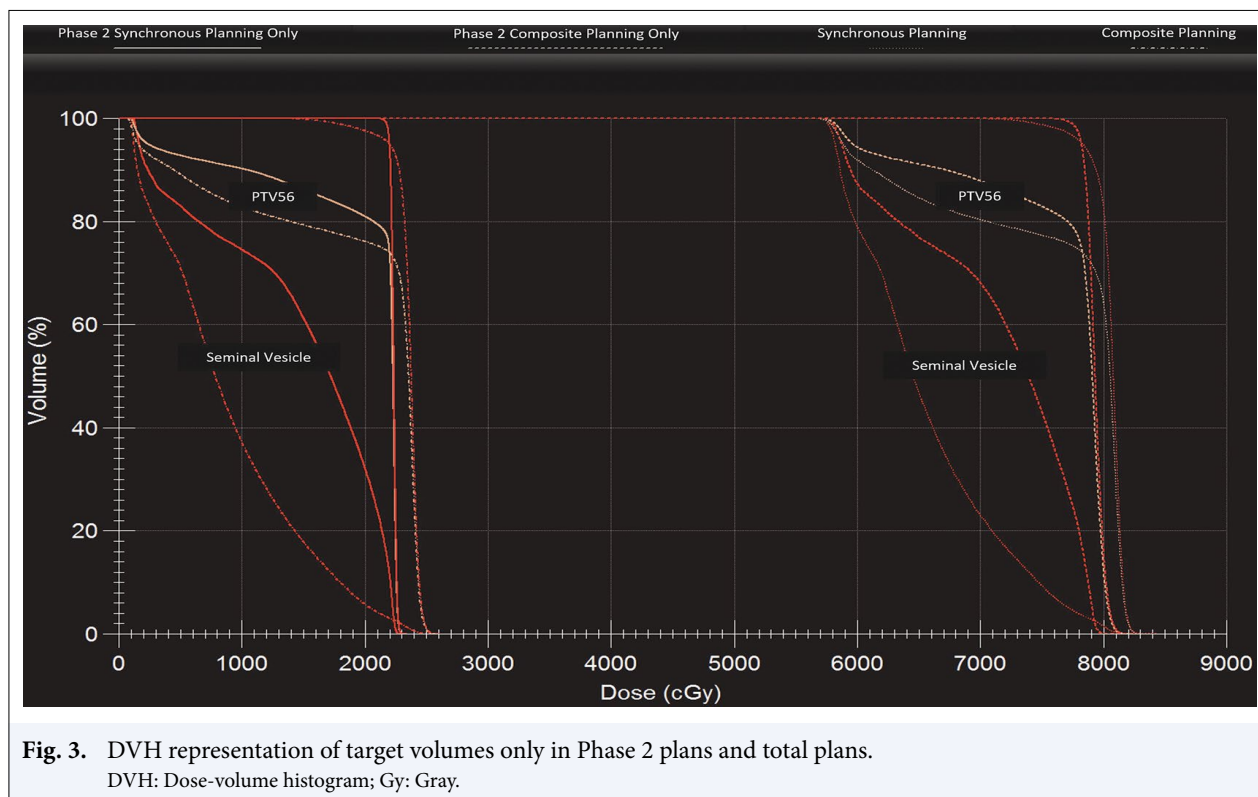

Fig. 2. DVH representation of dose distributions obtained in synchronous and composite planning.
DVH: Dose-volume histogram; Gy: Gray.

Fig. 3. DVH representation of target volumes only in Phase 2 plans and total plans.
DVH: Dose-volume histogram; Gy: Gray.

doses of the body could be reduced with the composite planning.[16] Although lower results were obtained in critical organ doses with composite planning, it was observed that hot and cold dose volumes were higher in boost plans. This could lead to radiation related complications including rectal bleeding, gastrointestinal complication, and irritative urinary symptoms.[17,18] Although a homogeneous and conformal dose distribution was obtained when the total dose distribution was examined in the composite planning approach, it was found that it was very heterogeneous and less conformal when only the boost plans were evaluated compared to the synchronous planning. Compared to synchronous planning, there is a very heterogeneous dose distribution in composite planning, since the D_1 dose is 11.8% lower and the D_{99} dose is 12.01% higher (Fig. 3). As a result, volumes that are 1.8–2 Gy below or above the fraction doses may occur in boost plans. These hot and cold dose volumes may cause different BED values within the target and may lead to radiobiological failures.[7,9] Narayanasamy et al.[19] both physical and radiobiological criteria were used in evaluation of a multi-phased treatment plan with a dependent or an independent boost. In radiobiological evaluation, they suggested that the advantages of dependent boost planning are not significant unless a near perfect composite

plan is achieved. They determined that if an optimal primary plan is achieved, a dependent boost phase planning should not be necessary.

The approach in composite planning is based on the dose distribution in the phase 1 plan, on which phase 2 dose distribution is planned. If there are cold or hot volumes in phase 1 plan, since the composite approach will focus on the total dose, either a lower or higher dose will be applied to these volumes in phase 2. As a result, phase 2 fraction doses can cause very low or very high fraction doses compared to normal fractionation. This may be clinically significant (Fig. 1). If the fractionated dose is less than 1.8 Gy or more than 2 Gy at those cold/hot spots, the BED value will change. As a result, it directly affects the probability of tumor control.[10,20] The most important issue to be considered in the composite approach is that there are very heterogeneous dose distributions that may occur in phase1 planning, which may cause the fraction doses to be very different in these heterogeneous volumes in phase 2. Moreover, even if the prescribed prescribed dose is reached in the sum of this treatment, the differences in the fraction doses of these heterogeneous dose volumes in the target volume will directly affect the therapeutic gain and consequently may directly affect the outcome of the treatment.

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