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ORIGINAL ARTICLE

Normal Tissue Objective Tool in Radiotherapy Planning for Endometrial Cancer: A Dosimetric Study

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OBJECTIVE

This dosimetric study investigated the influence of the normal tissue objective (NTO) tool in the Eclipse™ radiotherapy (RT) planning system on intensity-modulated RT (IMRT) for adjuvant RT planning in endometrial cancer.

METHODS

Twenty patients, diagnosed with stage-2 endometrial cancer according to the International Federation of Gynecology and Obstetrics, were enrolled from our Radiation Oncology department. For each patient, three IMRT plans were devised: Without NTO (NTO-OFF), with manually configured NTO (NTO-MAN), and with automatically configured NTO (NTO-AUTO). The plans were compared using parameters derived from dose-volume histogram analysis, including planning target volume and organs at risk (OARs).

RESULTS

The mean conformality index was superior with NTO-MAN (0.76±0.05) compared to NTO-AUTO (0.72±0.03, p=0.001) and NTO-OFF (0.62±0.02, p=0.000). IMRT with NTO-MAN provided enhanced OAR protection, particularly for the bladder (V45=32.84±2.03 vs. 37.03±1.55, p=0.000) and rectum (V30=56.18±2.05 vs. 60.50±3.86, p=0.000), compared to NTO-AUTO. The dose constraints for the bladder and rectum were not exceeded in any patient treated with NTO-MAN but exceeded in 19 (95%) and 9 (45%) patients, respectively, with NTO-AUTO.

CONCLUSION

The manual NTO tool resulted in greater conformality and OAR protection. Therefore, we recommend the use of manual NTO in adjuvant IMRT planning for endometrial cancer patients.

Keywords: Endometrial cancer; intensity modulated radiotherapy; normal tissue objective tool.

INTRODUCTION

Endometrial carcinoma is the most common gynecological malignancy in both developed countries and in Türkiye.[1] The primary approach to treatment involves surgery, with adjuvant measures typically involving systemic therapy and/or radiotherapy (RT).[2] The International Federation of Gynecology and Obstetrics (FIGO) surgical staging/histological grading system and the presence of adverse risk factors, such as advanced age, lymphovascular invasion, and p53 mutation, guide the administration of adjuvant treatment.[3,4]

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Adjuvant RT involves the application of vaginal brachytherapy (BRA) and/or external beam RT (EBRT). Among the contemporary EBRT techniques, intensity-modulated RT (IMRT) allows optimal dose distributions and a sharper dose fall-off at the planning target volume (PTV) edge.[5] The increased conformality reduces the exposure of organs at risk (OARs) to ionizing radiation and maximizes radiation exposure to the PTV, resulting in a greater therapeutic ratio, improved cancer control, and reduced toxicity.[6] Maximizing this ratio is fundamental to RT, and can be achieved by optimization through RT planning systems.[7]

Various RT planning systems, including Eclipse™ (Varian Medical Systems, Palo Alto, CA, USA), have been developed globally. Eclipse™, particularly versions 10 and above, incorporates the normal tissue objective (NTO) tool for optimization. The NTO tool uses exponential decay of the dose based on distance during inverse planning optimization. It penalizes high dose levels to mitigate hot spots, promoting a rapid dose fall-off in OARs.[8] Thus, the tool affects dose homogeneity and conformality in PTV.[9] The tool has three settings: Without NTO (NTO-OFF), with manually configured NTO (NTO-MAN), and with automatically configured NTO (NTO-AUTO). According to the manufacturer, its use is not mandatory, leaving it to the discretion of the radiation oncology physicist during optimization.[8,10–12] Although the evidence about the effects of NTO in RT planning is limited and conflicting, many radiation oncology physicists prefer to plan RT without NTO or with NTO-AUTO for ease and speed.[8,10]

Based on results from the Radiation Therapy Oncology Group (RTOG) 0418 and RTOG 1203 trials, IMRT has gained acceptance as the standard EBRT technique for the treatment of endometrial cancer.[13,14] However, the literature lacks studies on the influence of the NTO tool in Eclipse™ on IMRT techniques during adjuvant RT planning for endometrial cancer. The present dosimetric study was conducted to address this gap.

MATERIALS AND METHODS

Ethics Statement

This dosimetric study was approved by the local ethics committee (acceptance number: 2023/493). Written informed consent was obtained from all patients prior to participation in the study.

Patients

We included 20 patients diagnosed with stage-2 endometrial cancer according to the International Federation of Gynecology and Obstetrics (FIGO 2017; 8th edition) who sought adjuvant RT at our radiation oncology department.

The sample size for this study was determined by a power analysis based on data from a previous study with a cohort of 15 patients,[12] where power was established at 89% (effect size: 0.4) regarding the conformality index (CI), and alpha (α) set at 0.05. To enhance the study strength, we designed our study with a cohort of 20 patients.

Simulation

The patients were immobilized in the supine position with both arms raised above their heads, maintaining a comfortably full bladder, an empty rectum, and breathing freely. Subsequently, each patient underwent computed tomography (CT) twice with a slice thickness of 3 mm, using a CT simulator (Aquilion LB; Toshiba Medical Systems, Otawara, Japan). The first non-contrast scan was done for RT planning purposes, while the second was used to visualize blood vessels.[15] Then the acquired datasets were transferred to the RT planning system (Eclipse™ 17.0; Varian Medical Systems, Palo Alto, CA, USA) through a digital imaging and communications in medicine (DICOM) network.

Target Volume and Organs at Risk Determination

The delineation of clinical target volume (CTV), PTV, and OARs was based on the RTOG Consensus Guidelines[15] and the Target Volume Delineation and Field Setup guidance.[16] CTV-1 included the vaginal cuff, while CTV-2 included paravaginal/parametrial tissues. CTV-3 included the common iliac, external iliac, internal iliac, and presacral nodal regions, with the exclusion of bone and muscles from CTV. PTV-1, PTV-2, and PTV-3 were defined 15 mm beyond CTV-1, 10 mm beyond CTV-2, and 7 mm beyond CTV-3, respectively. PTV-total was obtained by combining these PTVs.[15,16]

OARs consisted of the bone marrow, bladder, rectum, bowel, and femoral heads.[16] Bone marrow delineation spanned from the L4 vertebral body to the ischial tuberosities.[17] The bladder was delineated from its base to the dome, encompassing the outer bladder wall. The rectum was defined as the outer rectal wall, extending from the level of the sigmoid flexure to the anus. The term "bowel" collectively referred to both the small and large intestines, delineated from 2 cm cranial of the PTV to the most caudal point in the pelvis, encompassing the entire peritoneal cavity. Femoral head was defined as the entire femoral head excluding the femoral neck.[16] Tissues within the RT field, excluding the PTV, were categorized as normal tissue (NT).

Fig. 1. View of the normal tissue objective tool in the Eclipse radiotherapy planning system.
CTV: Clinical target volume; PTV: Planning target volume.

External Beam Radiotherapy Planning

Contrast and non-contrast CT scans were merged for delineation, but RT planning was based on non-contrast CT scans.[15] The treatment planning phase utilized Eclipse™ (version 17.0) for delivery via a linear accelerator (Varian Truebeam SN-2934 version 2.7), equipped with a 120 Millennium multileaf collimator (the central 20 cm of the field employed leaves 0.5 cm wide, while the outer field used leaves 1 cm wide). Three distinct plans, with NTO-OFF, NTO-MAN, and NTO-AUTO settings, were generated for each patient.

Dynamic IMRT planning was performed using seven noncoplanar fields and 6 MV photon beams. The isocenter was positioned at the midpoint of the PTVs. Gantry angles were set at 75°, 110°, 145°, 180°, 215°, 250°, and 285° for all plans. The collimator angle was 0° for gantry angles of 75°, 145°, and 250°, and 90° for gantry angles of 110°, 180°, 215°, and 285° across all plans. Photon dose calculation was performed using the anisotropic analytical algorithm, with heterogeneity corrections activated throughout dose calculations. The maximum dose rate was established at 300 monitor units (MU)/min, and the dose calculation grid was set to 2.5 mm. Manual NTO settings were configured with a priority of 100, a distance from the target border (PTV margin=x_{start}) of 0.15 cm, an initial dose (f_0=start dose) of 98%, a final dose (f_∞=end dose) of 60%, and a fall-off (k) of 0.25 (Fig. 1).

Dose prescriptions were based on the recommendations of the International Commission on Radiation Units and Measurements 83 report, with a prescribed dose of 50.4 Gy administered in 28 fractions.[18] Normalization ensured that 95% and 100% of the PTV and CTV received the prescribed dose, respectively. Strict measures were taken to ensure that the maximum dose did not surpass 110% of the prescribed dose.

Dose Constraints of Organs at Risk

Specific dose constraints for OARs were established as follows: Bone marrow, volume receiving 40 Gy (V40) limited to <37%; bladder, volume receiving 45 Gy (V45) limited to <35%; rectum, volume receiving 30 Gy (V30) limited to <60%; bowel, volume receiving 40 Gy (V40) limited to <30%; and femoral heads, volume receiving 30 Gy (V30) limited to <15%.[13,19]

Evaluation of Radiotherapy Planning

The cumulative dose-volume histogram parameters included the volume of the PTV receiving >107% of the prescribed dose (V>107%), dose received by 2% of the PTV ($D_{2\%}$), dose received by 98% of the PTV ($D_{98\%}$), dose received by 50% of the PTV ($D_{50\%}$), mean dose

Turk J Oncol 2024;39(2):167–175
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Table 1 Dosimetric parameters for planning target volumes in each technique

	Mean±SD (minimum–maximum)			Global p
	NTO-OFF	NTO-MAN	NTO-AUTO	
V>107 (%)	0.03±0.08[a] (0.00–0.37)	0.20±0.29[b] (0.00–0.81)	0.08±0.12[c] (0.00–0.37)	0.007*
$D_{2\%}$ (cGy)	5259±40[a] (5170–5329)	5323±52[b] (5192–5436)	5277±41[c] (5186–5341)	0.000*
$D_{98\%}$ (cGy)	4964±47[a] (4878–5080)	4905±42[b] (4819–4962)	4949±47[c] (4869–5056)	0.000*
$D_{50\%}$ (cGy)	5164±38[a] (5106–5219)	5219±28[b] (5171–5266)	5179±40[c] (5117–5231)	0.000*
D_{mean} (cGy)	5157±33[a] (5102–5199)	5207±31[b] (5157–5293)	5168±34[c] (5114–5214)	0.000*
HI	0.05±0.01[a] (0.03–0.08)	0.08±0.01[b] (0.05–0.12)	0.06±0.01[c] (0.04–0.08)	0.000*
CI	0.62±0.02[a] (0.58–0.68)	0.76±0.05[b] (0.68–0.86)	0.72±0.03[c] (0.68–0.80)	0.000*
MU	1408±108[a] (1283–1648)	1249±149[b] (1048–1558)	1340±122[c] (1145–1614)	0.000*

[a,b,c:] In the comparison between two groups, if the groups have the same letter, there is no statistically significant difference, but if the same letter is not found, there is a statistically significant difference; *: Means statistically significant=p<0.05; V>107 (%)=volume receiving >107% but <110% of the prescribed dose. SD: Standard deviation; NTO-OFF: Treatment planning without normal tissue objective tool; NTO-MAN: Treatment planning with manually configured normal tissue objective tool; NTO-AUTO: Treatment planning with automatically configured normal tissue objective tool; $D_{2\%}$: Dose received by 2% of the target volume; $D_{98\%}$: Dose received by 98% of the target volume; $D_{50\%}$: Dose received by 50% of the target volume; HI: Homogeneity index; CI: Conformality index; MU: Monitor units

of the PTV (D_{mean}), homogeneity index (HI), CI, MU, V40 for bone marrow, V45 for the bladder, V30 for the rectum, V40 for the bowel, and V30 for femoral heads. HI was calculated using the formula: $HI=(PTV_{D2\%} - PTV_{D98\%})/PTV_{D50\%}$. HI values ranged from 0 to 1, with a decrease indicating increased homogeneity. CI was determined using the formula: $CI=(TV_{ref}/TV)\times(TV_{ref}/V_{ref})$, where TV_{ref} is the target volume (cm^3) covered by the reference isodose, TV is the target volume (cm^3), and V_{ref} is the volume (cm^3) covered by the reference isodose. CI values ranged from 0 to 1, with an increase indicating improved conformality. HI and CI were defined in accordance with the International Commission on Radiation Units and Measurements reports 83 and 62, respectively.[20]

Statistical Analysis

The values for the dosimetric parameters in each RT planning method were documented and compared. Dosimetric variances between two and three RT plans were analyzed using the paired two-tailed Wilcoxon's signed-rank and Friedman tests, respectively. OAR overdose rates were examined using a more-than-two-group ratio test. Statistical analyses were performed using SPSS software (version 22.0; IBM Corp., Armonk, NY, USA). A significance level of p<0.05 was considered statistically significant.

RESULTS

Dosimetric Parameters for Planning Target Volume

The dosimetric parameters for the PTV in each planning method are shown in Table 1. The mean V>107% and mean $D_{2\%}$ values were higher in NTO-MAN compared to NTO-OFF (p=0.013 and p=0.001) or NTO-AUTO (p=0.048 and p=0.001), primarily due to the elevated maximum point doses. Homogeneity exhibited a favorable outcome with NTO-OFF surpassing both NTO-MAN (p=0.04) and NTO-AUTO (p=0.000), with NTO-AUTO demonstrating a better homogeneity than NTO-MAN (p=0.006). When the planning system aimed to safeguard NTs surrounding the target volume using NTO, there was an associated increase in the maximum point dose within the PTV, leading to reduced homogeneity. The least homogeneity was achieved with NTO-MAN. Conformality was better

Table 2 Dosimetric parameters for organs at risk with each planning technique

	Mean±SD (minimum–maximum)			Global p
	NTO-OFF	NTO-MAN	NTO-AUTO	
Bone marrow V40 (%)	55.30±5.28[a] (44.35-64.22)	47.79±7.53[b] (33.90–58.12)	48.33±3.31[b] (42.51-56.65)	0.000*
Bladder V45 (%)	41.70±6.07[a] (33.16-61.18)	32.84±2.03[b] (28.62–34.88)	37.03±1.55[c] (34.05-39.96)	0.000*
Rectum V30 (%)	64.92±5.83[a] (52.98-74.64)	56.18±2.05[b] (52.16–59.77)	60.50±3.86[c] (53.26-68.56)	0.000*
Bowel V40 (%)	30.48±8.39[a] (12.11-41.78)	25.76±8.56[b] (10.11–39.46)	25.46±9.03[b] (6.94-38.93)	0.000*
Right femoral head V30 (%)	13.24±1.81 (10.36-18.56)	12.19±1.34 (10.33–14.87)	12.82±1.34 (11.04-15.19)	0.247
Left femoral head V30 (%)	13.85±1.12 (12.33-16.27)	12.58±1.48 (9.29–14.85)	13.48±1.67 (11.24-19.24)	0.212
Normal tissue (cGy)	2123±409[a] (968-2596)	1966±416[b] (855–2509)	2009±392[b] (900-2504)	0.000*

[a,b,c]: In the comparison between two groups, if the groups have the same letter, there is no statistically significant difference, but if the same letter is not found, there is a statistically significant difference; *: Means statistically significant=p<0.05. V40: Volume receiving ≥40 Gy of the prescribed dose; V45: Volume receiving ≥45 Gy of the prescribed dose; V30: Volume receiving ≥30 Gy of the prescribed dose

Table 3 Overdose rates (greater than dose constraints) for organs at risk in each planning technique

	NTO-OFF		NTO-MAN		NTO-AUTO		Global p
	n	%	n	%	n	%	
Bone marrow V40 (%)	20	100[a]	16	80[b]	20	100[a]	0.014*
Bladder V45 (%)	19	95[a]	0	0[b]	19	95[a]	0.000*
Rectum V30 (%)	17	85[a]	0	0[b]	9	45[c]	0.000*
Bowel V40 (%)	11	55	5	25	7	35	0.139
Right femoral head V30 (%)	2	10	0	0	1	5	0.349
Left femoral head V30 (%)	3	15	0	0	2	10	0.217

[a,b,c]: In the comparison between two groups, if the groups have the same letter, there is no statistically significant difference, but if the same letter is not found, there is a statistically significant difference; *: Means statistically significant=p<0.05

with NTO-MAN compared to NTO-AUTO (p=0.001) and NTO-OFF (p=0.000), while NTO-AUTO demonstrated superior conformality compared to NTO-OFF (p=0.000). Treatment was quicker with NTO-MAN (mean MU=1249±149) than with NTO-AUTO (mean MU=1340±122; p=0.000) or NTO-OFF (mean MU=1408±108; p=0.000), and NTO-AUTO exhibited quicker treatment compared to NTO-OFF (p=0.000).

Dosimetric Parameters for Organs At Risk

Tables 2 and 3 provide the dosimetric parameters and overdose rates (exceeding dose constraints) for OARs in each planning method. Bone marrow protection was worse with NTO-OFF compared to NTO-MAN (p=0.003) and NTO-AUTO (p=0.000), while NTO-MAN and NTO-AUTO demonstrated comparable bone marrow protection (p=0.765). The bone marrow dose constraint was surpassed in 100% (n=20), 80% (n=16), and 100% (n=20) of the patients with NTO-OFF, NTO-MAN, and NTO-AUTO, respectively. The bladder exhibited superior protection with NTO-MAN compared to NTO-OFF (p=0.000) and NTO-AUTO (p=0.000), while NTO-AUTO provided better

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bladder protection than NTO-OFF (p=0.000). While the bladder dose constraint was not exceeded in any patients with NTO-MAN, it was surpassed in 19 patients (95%) with both NTO-OFF and NTO-AUTO. For the rectum, NTO-MAN demonstrated better protection than NTO-OFF (p=0.000) and NTO-AUTO (p=0.000), while NTO-AUTO provided superior rectum protection compared to NTO-OFF (p=0.001). Although the rectum dose constraint was not exceeded in any patients with NTO-MAN, it was surpassed in 17 patients (85%) with NTO-OFF and 9 patients (45%) with NTO-AUTO. In terms of bowel protection, NTO-OFF was less effective than NTO-MAN (p=0.000) and NTO-AUTO (p=0.000), while NTO-MAN and NTO-AUTO showed similar bowel protection levels (p=0.940). The bowel dose constraint was exceeded in 11 (55%), 7 (35%), and 5 (25%) patients with NTO-OFF, NTO-AUTO and NTO-MAN, respectively. The three planning methods exhibited similar protection (p=0.247 for right and p=0.212 for left) for femoral heads. NT received a higher radiation dose with NTO-OFF compared to NTO-AUTO (p=0.000) and NTO-MAN (p=0.000), with comparable doses between NTO-MAN and NTO-AUTO (p=0.433).

DISCUSSION

Endometrial cancer is the fourth most common cancer among women, with an incidence on the rise because of obesity and the aging population.[1] It predominantly affects postmenopausal women, particularly those over the age of 65 years, often accompanied by comorbidities common in both the obese and elderly population.[21,22] Aging results in unfavorable changes in various organs, with a significant impact on bone marrow, an important hematopoietic organ.[21,23] It significantly reduces bone marrow reserves, with the primary production area being concentrated in the pelvis. Bone marrow is highly sensitive to RT.[24,25] The primary treatment for endometrial cancer is surgery, applicable to more than 90% of patients.[26] However, after surgery, the sigmoid colon, rectum and small intestines are displaced towards the RT target area and the incidence of bladder dysfunction is increasing. [6,14,27] Based on the FIGO stage, histological grade, and adverse risk factors, adjuvant treatments may involve combinations of systemic therapy, EBRT, and vaginal BRA. Pelvic surgery followed by RT increases the risk of both short- and long-term adverse events in the gastrointestinal and lower genitourinary systems. Patients ineligible for BRA and those with metastatic lymph nodes may require higher irradiation doses with an EBRT boost. The risk for adverse events is significantly greater with EBRT than with BRA.[28] Advances in cancer diagnosis and treatment techniques are anticipated to extend the lifespan of endometrial cancer patients, leading to increased rates of relapse, re-irradiation, and RT-related adverse events.[29]

Various unfavorable factors, categorized as patient- and treatment-related factors, contribute to RT-related adverse events. Patient-related factors include female sex, advanced age, obesity, comorbid diseases, radiosensitivity, malnutrition, low body mass index, alcohol consumption, and tobacco use. Treatment-related factors include pelvic surgery, high ionizing radiation dose, re-irradiation, use of multiple treatment modalities, and non-modern irradiation techniques.[30] While some factors (e.g., age) cannot be controlled, others (e.g., the irradiation technique) can be modified or controlled. One of the controllable factors in RT planning involves inverse planning dose optimization for IMRT within the RT planning system, leading to an improved therapeutic ratio.

Inverse planning dose optimization is a standard procedure in IMRT that allows the radiation intensity to be modulated. The optimization algorithm, photon optimizer (version 17.0), in the Eclipse™ RT planning system contains several optimization tools for this purpose that are licensed and available for a fee. One of these tools is NTO. NTO-AUTO is a formula defined by the manufacturer and set automatically by the system, while NTO-MAN contains five parameters that can be manually controlled by a medical physicist. These parameters include priority, distance from target border [PTV margin (cm)=x_{start}], initial dose [f_0 (%)=start dose], final dose [f_∞ (%)=end dose], and fall off [k]. Priority represents the weight attributed against other optimization parameters. If priority is equal to zero, NTO is turned off. "x_{start}" indicates the distance from the PTV border. "f_0" and "f_∞" represent the maximum and minimum accepted doses outside the PTV, respectively, while "k" represents the strength of the dose fall off. NTO is a collection of parameters that define how the dose should fall off outside the PTV. Determining the optimal NTO setting can be challenging because of the multitude of possible combinations.[10,12] Bell et al.[10] investigated the effect of NTO (version 13.6) on the stereotactic body RT (SBRT) technique in lung cancer patients (n=10). SBRT plans using NTO-MAN, with different priorities (1–999) and fall off val-

ues (0.01–5.00) but constant x_{start} (0.10 cm), f_0 (100%), and f_∞ (10%) values were compared between SBRT plans using NTO-AUTO and without NTO (i.e., ring structure-based planning). NTO-MAN demonstrated a lower ratio of the 50% prescription isodose volume to PTV ($R_{50\%}$; 4.00 vs. 4.35, p=0.002), a lower volume receiving ≥ 20 Gy of the prescribed dose for lungs (V20; 1.22 vs. 1.32, p=0.006), and a higher maximum PTV dose (PTV_{max}; 138% vs. 122%, p=0.002) compared to planning without NTO. Furthermore, the higher priority and fall-off values in NTO-MAN resulted in greater conformality, improved OAR protection, and decreased homogeneity and MU values. Additionally, NTO-AUTO was found to be inadequate in preventing dose scatter compared to the other two techniques, supporting the use of NTO-MAN in lung cancer SBRT. Caldeira et al.[8] investigated the effect of NTO (version 11.8) on the volumetric modulated arc therapy (VMAT) technique in prostate cancer patients (n=25) and found no statistically significant difference between VMAT planning with and without NTO in terms of CI, HI, radiation planning index, and treatment duration. They concluded that the lack of benefit of NTO may be related to the anatomical location of the prostate or the version of the software. Gerdán et al.[11] investigated the optimum values of NTO parameters for SBRT in lung cancer patients (n=10), and recommended using NTO with a "k" value of 0.15 and a priority value of 500 for SBRT in lung cancer. Paluszyńska et al.[31] investigated the effect of NTO (version 16.1) on VMAT with simultaneous integrated boost (SIB) technique in prostate cancer patients, and found no statistically significant difference between VMAT-SIB planning with and without NTO in terms of CI, gradient index, and OAR doses. They also concluded that the lack of benefit of NTO may be related to the anatomical location of the prostate. Investigating the effect of NTO (version 13.7) on dynamic IMRT technique in brain tumor patients (n=15), Indrayani et al.[12] compared NTO-MAN, having different priorities (1–500) and fall-off values (0.05–5.00) but constant x_{start} (0.10 cm), f_0 (105%), and f_∞ (60%) values, with NTO-AUTO and NTO-OFF. The authors reported better conformality and OAR protection with NTO-MAN (CI=0.96±0.03) compared to NTO-AUTO (CI= 0.92±0.09, p=0.035) and NTO-OFF (CI=0.77±0.16, p=0.002), and recommended using NTO-MAN with a "k" value of 0.5 and a priority value of 100 for IMRT in brain tumors.

Our dosimetric study adhered to the prescribed doses for the PTV and dose constraints for OARs recommended in the RTOG 0418 trial. All dynamic IMRT planning parameters were kept consistent, except for the NTO settings, facilitating a comprehensive comparison among the RT plans. We observed higher mean $D_{2\%}$ and V>107% values with NTO-MAN in the PTV compared to the other two techniques, resulting in the most non-homogeneous plans with NTO-MAN. Nevertheless, the maximum detected dose in all plans remained below 110%, consistent with the methods of the RTOG 0418 study. NTO-MAN resulted in higher conformality and lower MU values, indicating a more rapid irradiation process that enhanced patient compliance to immobilization. This in turn allows a reduction in the PTV margin and facilitated the application of image-guided RT. Additionally, we found that NT and OARs, with the exception of femoral heads, received better protection with NTO than without NTO. Following, the bladder and rectum exhibited superior protection with NTO-MAN compared to NTO-AUTO. In contrast to the RTOG 0418 trial, where different gantry angles were used for IMRT plans and there were no specified dose constraints for the bone marrow (bladder, rectum, bowel, and femoral head dose constraints were exceeded in 66.7%, 76.2%, 16.7%, and 33.3% of the patients, respectively), we used similar gantry angles and NTO-MAN parameters for comparability between groups. With NTO-MAN, while the dose constraints for bone marrow in 80% of the patients and for bowel in 25% of the patients were exceeded, the dose constraints for the bladder, rectum, and femoral heads were not exceeded in any of the patients. We believe that further optimization, particularly for bone marrow and bowel protection, can be achieved by using different gantry angles and optimal NTO-MAN parameters.

CONCLUSION

Literature regarding the use of the NTO tool in IMRT planning is limited and controversial. IMRT planning is the gold standard for endometrial cancer. To the best of our knowledge, this is the first study to investigate the effect of NTO on adjuvant IMRT planning in endometrial cancer patients. The manual NTO tool resulted in greater conformality and OAR protection. Therefore, we recommend the use of manual NTO in adjuvant IMRT planning for endometrial cancer patients. Further studies investigating the NTO tool in different IMRT techniques (e.g., VMAT), RT machines (e.g., Ring-mounted Linac), cancer sites, and versions are needed.

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