·Intensity-Modulated Radiotherapy Column·

Dosimetric comparison between helical tomotherapy and step-and-shoot intensity modulated radiation therapy for endometrial carcinoma

Rui-Jie Yang,[1] Shou-Ping Xu,[2] Wei-Juan Jiang,[1] Jun-Jie Wang[1] and Chuan-Bin Xie[2]

[1]Department of Radiation Oncology, Cancer Center, Peking University The Third Hospital, Beijing, 100191, P. R. China; [2]Department of Radiation Oncology, General Hospital of The Peoples' Liberation Army, Beijing, 100853, P. R. China

[**Abstract**] **Background and Objective:** Helical tomotherapy (HT) has shown its dosimetric advantages in the radiotherapy for many cancers. To date, no published studies have performed a dosimetric evaluation of whole pelvic radiotherapy (WPRT) using HT for postoperative endometrial cancer. This study was to compare the dosimetric characteristics of HT and step-and-shoot intensity modulated radiation therapy (SaS-IMRT) for endometrial cancer patients undergoing postoperative WPRT, and to explore whether whole pelvic HT for postoperative endometrial cancer has the advantage of dosimetry. **Methods:** Ten patients with endometrial cancer undergoing postoperative WPRT were enrolled in this study. SaS-IMRT and HT Plans were developed for each patient. The dose distributions of the targets, organs at risk and normal tissue were analyzed and compared. **Results:** The mean PTV_{100} were 95.6% and 95.8% (P=0.72) for the SaS-IMRT and HT plans, respectively. The mean homogeneity indexes were 1.10 and 1. 07 (P=0.00). The mean conformity indexes were both 0.87. The mean doses to rectum and bladder for HT were decreased by 1.3 Gy and 3.0 Gy compared with SaS-IMRT, respectively, while the mean dose to pelvic bones was increased by 1.1 Gy. The volumes of small intestine and colon, pelvic bones receiving moderate and low dose also increased. The V_5, V_{10} and V_{20} of normal tissue were increased by 13.0%, 18.0%, and 5.0% (P<0.001). The mean dose to normal tissue was increased by 2.5 Gy (P<0.001). **Conclusions:** Compared with SaS-IMRT, HT resulted in more homogeneous PTV dose distribution, better sparing of rectum and bladder. The volumes of small intestine and colon, pelvic bones and normal tissue receiving moderate and low dose for HT increased. The clinical significance of the dosimetric differences needs further investigations.

Key words: endometrial carcinoma, intensity-modulated radiation therapy, helical tomotherapy, whole pelvic radiotherapy, dosiology

Endometrial cancer is a common gyneco logical malignant tumor in China, and postoperative whole-pelvic radiotherapy has a critical role in the treatment for endometrial cancer.[1, 2] Due to the specific anatomic structures of the pelvic cavity, most pelvic structures, including rectum, bladder and the small intestine that has been pulled into the pelvic cavity in the operation, are subject to radiation at prescribed dosage in routine whole-pelvic conformal radiotherapy,[3] and pelvic bones are also subject to high dosage radiation; therefore, radiotherapy tends to result in substantial acute and chronic toxicity and side effects.[4, 5] Whole pelvic intensity-modulated radiotherapy can reduce the dosage[6-12] and thus the toxicity and side effects[2,10,13-16] in affected organs. Helical tomotherapy (HT), as new intensity-modulated radiotherapy technique, has demonstrated the advantages of homogeneous dosage for the target volume, good conformality and organ protection in varied tumors.[17-24] This study aimed to compare HT and step and shoot intensity-modulated radiotherapy (SaS-IMRT) and to explore whether post-operative whole pelvic helical tomotherapy was dosiologically advantageous in endometrial cancer.

Methods

Case selection and simulation positioning

A total of ten patients with stage Ib–IIb endometrial cancer who received post-operative whole pelvic radiotherapy in our hospital between October 2007 and August 2008 were selected, with a median age of 66 years (range 58–73). All patients had undergone total hysterosalpingo-oophorectomy, together with

Correspondence to: Jun-Jie Wang; Tel: +86-10-62805252; Email: junjiewang47@yahoo.com

This paper was translated into English from its original publication in Chinese by Guangzhou Liheng Medical Translation and Wei Liu on 2009-09-29.

The original Chinese version of this paper is published in *Chinese Journal of Cancer* 28(11); http://www.cjcsysu.cn/cn/article.asp?id=16028.

Submitted: 2009-03-19; Revised: 2009-05-10

pelvic lymph node dissection/sampling. Written informed consent was obtained before the therapy. The patients were immobilized with thermoplastic sheet and underwent CT scanning for simulation and positioning, with seven patients in supine position and three in prone position; porose cystosepiment was used to assist positioning. Before the positioning scanning, all patients were given vaginal suppository, oral and intravenously injected contrast agent, and were given 1500 mL water at one hour before the scanning. At the end of the scanning, images from these patients were submitted to the Pinnacle treatment planning system for delineation of target volume and affected organs and designing of SaS IMRT scheme.

Definitions of target volume and affected organs

Clinical target volume (CTV) was delineated in accordance with the Consensus Guidelines for Delineation of Clinical Target Volume for Intensity-modulated Pelvic Radiotherapy in Post-operative Treatment of Endometrial and Cervical Cancer[25] co-recommended by organizations including Radiation Therapy Oncology Group (RTOG, US). CTV included pelvic lymph nodes (including common, external and internal iliac lymph nodes), proximal end of vaginas (3 cm) and paravaginal tissue. For patients with invasion in cervical muscular layer, CTV also included anterior sacral lymph nodes. Planning target volume (PTV) was obtained by extending 1 cm from CTV. Small intestine and colon (collectively known as bowel hereunder), bladder, rectum, pelvic bone, and body profile and normal tissue were delineated within PTV on all horizontal slices and in a vertical scope obtained by extending the margin of PTV 2 cm upward and downward, respectively. Normal tissue was defined as the tissue volume obtained by subtracting PTV from the internal volume of the entire body profile within this scope. Pelvic bone included ilium, lower pelvic bone, and lumbar and sacral vertebrae.[26]

Treatment planning

Pinnacle treatment planning system was used to design SaS-IMRT scheme for each patient. Based on the results of previous studies[7, 12, 26] and our pilot study, nine homogeneously distributed coplanar fields were used in the SaS IMRT scheme, with an initial field angle of 0 degree. Dosage-volume restriction was placed on the SaS IMRT scheme according to conformal radiotherapy scheme and the results from our pilot study (Table 1).

Table 1 Dose-volume constraints on targets and organs at risk used in step and shoot intensty-modulated radiation therapy (SaS-IMRT) plans

Structures	Dose volume constraints
PTV	Minimal dose, 47.5 Gy; maximal dose 55 Gy; ⩾95% of PTV receiving 50 Gy
Bowel	⩽35% of bowel receiving ⩾35 Gy
Bladder	⩽40% of bladder receiving ⩾40 Gy
Rectum	⩽60% of bladder receiving ⩾40 Gy
Normal tissue	EUD, 18 Gy
Ring[a]	EUD, 38 Gy

PTV, plan target volume; EUD, equivalent uniform dose.

[a]Dose shaping structure between PTV plus 0.5 cm and PTV plus 1.5 cm.

When target volume and affected organs were delineated by Pinnacle planning system for each patient, their CT imaging data and the profile information in Digital Imaging and Communication in Medicine RT protocol (DICOM) format were submitted to helical tomotherapy planning workstation (Hi-Art Tomotherapy 2.2.4.1, TomoTherapy, Madison, WI), where HT scheme was designed for each patient. Based on SaS IMRT scheme and the results from our pilot study, dosage-volume restriction and optimization parameters, including weighting factor and punishment factor, were set for the HT scheme. Iterative modification was made on these optimization parameters, until the schemes were compliant to the dosage-volume restriction that had been set. The field width, pitch and beam intensity modulation factor in the HT scheme were 2.5, 0.3 and 3.0 cm, respectively.

Comparisons of the dosages

To compare these two schemes, they were both normalized based on the prescribed dosage of 50 Gy in 95% PTV. Dosage distribution in target volume, affected organs and normal tissue was compared between SaS-IMRT and HT schemes. In target volume, percentages of tissue receiving 95%, 100%, 105% and 110% prescribed dosage (PTV_{95}, PTV_{100}, PTV_{105} and PTV_{110}), mean dosage in PTV (D_{mean}) and homogeneity and conformality of dosage distribution were compared. Homogeneity and conformality of dosage distribution were reflected by homogeneity index (HI) and conformality index (CI), respectively. HI was defined as D_5/D_{95} (minimum dosage in the 5% PTV receiving high dosage radiation/minimum dosage in the 95% PTV receiving high dosage radiation). A smaller HI (approximate to 1) indicated more homogeneous dosage. Since prescribed dosage would not cover the entire PTV, CI was calculated by this formula: CI = CF (cover factor) × SF (spill factor). CF was defined as the ratio of the volume receiving prescribed dosage within PTV to the PTV volume, while SF was defined as the ratio of the volume receiving prescribed dosage within PTV to the entire volume receiving prescribed dosage. A CI more approximate to 1 indicated better conformality of dosage distribution. In affected organs and normal tissue, percentages of volumes (V_5, V_{10}, V_{20}, V_{30}, V_{40} and V_{50}) receiving varied dosage levels (5 Gy, 10 Gy, 20 Gy, 30 Gy, 40 Gy and 50 Gy) and mean dosage were compared.

Statistical processing

A self-control design was used for the study. Statistical tests were conducted on the differences in varied parameters between two schemes using two-tailed paired t test (Student's t test). $P<0.05$ indicated statistically significant difference. Statistical software SPSS13.0 was used in the analysis.

Results

Dosage distributions in target volume

Table 2 showed the dosage distributions in PTV in SaS-IMRT scheme and HT scheme. PTV coverage was comparable in two schemes; mean PTV_{95} were 100.0% in SaS IMRT scheme and

99.8% in HT scheme (P=0.37), while PTV_{100} were 95.6% in SaS-IMRT scheme and 95.8% in HT scheme (P=0.72). Mean dosage in target volume was slightly lower in HT scheme: the PTV D_{mean} of the two schemes were 52.6 Gy and 51.5 Gy, respectively ($P<0.001$). Dosage distribution conformality was also comparable between the two schemes, with a conformality index of 0.87 in both schemes (P=0.27). However, when compared with SaS-IMRT scheme, HT scheme had more homogeneous dosage in target volume: for these two schemes, mean PTV_{105} were 48.8% and 15.6%, respectively; and PTV_{110} were 7.6% and 0.6%, respectively; homogeneity index (HI) were 1.10 and 1.07, respectively (all $P<0.001$).

Table 2 Summary of PTV coverage data for SaS-IMRT and HT plans ($\bar{x}\pm s$)

	PTV_{95}(%)	PTV_{100}(%)	PTV_{105}(%)	PTV_{110}(%)	D_{mean}(Gy)	CI	HI
SaS-IMRT	100.0±0.0	95.6±0.2	48.8±10.2	7.6±5.0	52.6±0.4	0.87±0.02	1.10±0.01
HT	99.8±0.0	95.8±0.1	15.6±3.6	0.6±0.3	51.5±0.2	0.87±0.02	1.07±0.01
t	0.94	−0.37	7.50	4.23	8.03	1.17	6.77
P	0.37	0.72	0.00	0.00	0.00	0.27	0.00

HT, helical tomotherapy; CI, conformity index; HI, homogeneity index. Other footnotes as Table 1.

Dosage distributions in affected organs

Table 3 showed the dosage distributions in small intestine and colon, rectum, bladder and pelvic bone. When compared with SaS IMRT scheme, HT scheme reduced V_{30}, V_{40} and V_{50} in rectum by 8.0%, 6.0% and 3.0%, respectively; mean dosage was reduced by 1.3 Gy. In bladder, V_{30}, V_{40} and V_{50} were reduced by 17.0%, 9.0% and 3.0%, respectively, and mean dosage by 3.0 Gy. However, V_5 and V_{10} in small intestine and colon were increased by 5.0% and 7.0%, respectively; V_5, V_{10} and V_{20} in pelvic bone increased by 5.0%, 7.0% and 4.0%, respectively; and mean dosage increased by 1.1 Gy.

Dosage distributions in normal tissue

Table 4 showed the dosage distributions in normal tissue in the two schemes. As compared with SaS-IMRT scheme, HT scheme increased V_5, V_{10} and V_{20} in normal tissue by 13.0%, 18.0% and 5.0%, respectively (all P=0.00); mean dosage was increased by 2.5 Gy ($P<0.001$).

Discussion

With the widespread implementation and continuing improvement of helical tomotherapy, its advantages including homogeneous dosage distribution in target volume, excellent conformality and protection for affected organs have been

Table 3 Summary of dose distribution to organs at risk for SaS-IMRT and HT plans ($\bar{x}\pm s$)

Structures	V_5(%)	V_{10}(%)	V_{20}(%)	V_{30}(%)	V_{40}(%)	V_{50}(%)	D_{mean}(Gy)
Bowel							
SaS-IMRT	93.2±5.1	85.2±6.4	63.2±6.1	38.2±9.3	20.1±3.3	8.9±3.1	26.0±7.2
HT	98.3±1.2	91.3±7.2	64.3±8.2	33.2±12.1	19.3±7.2	8.2±3.8	26.3±7.0
t	−5.09	−7.32	−0.34	2.68	1.67	0.92	−0.80
P	<0.01	<0.01	0.74	0.03	0.13	0.38	0.45
Rectum							
SaS-IMRT	99.3±0.6	98.2±1.2	96.7±2.5	92.9±6.3	63.8±15.2	27.1±12.3	42.6±5.6
HT	100.0±0.0	100.0±0.0	97.5±2.2	85.2±10.1	57.2±7.3	25.2±5.3	41.3±6.3
t	−1.16	−1.61	−1.29	3.23	3.06	2.37	3.04
P	0.28	0.14	0.23	0.01	0.01	0.04	0.01
Bladder							
SaS-IMRT	100.0±0.0	99.2±0.5	89.1±3.2	68.2±6.4	38.3±15.1	17.3±8.9	35.8±6.2
HT	100.0±0.0	100.0±0.0	86.2±4.9	51.2±16.7	28.9±7.3	14.0±4.4	32.8±6.6
t	0.18	−1.73	0.85	4.87	5.77	1.98	6.90
P	0.68	0.11	0.42	<0.01	<0.01	0.08	<0.01
Pelvic bones							
SaS-IMRT	92.2±4.7	84.2±7.3	65.2±9.3	45.3±5.9	24.3±5.1	9.3±5.6	27.3±0.9
HT	97.3±2.3	91.4±3.2	69.2 5.2	43.8±3.1	24.1±3.8	9.2±2.3	28.4±1.1
t	−6.00	−6.73	−2.45	1.40	0.42	−1.64	−3.75
P	<0.01	<0.01	0.04	0.19	0.68	0.14	0.01

Footnotes as Table 2.

Table 4 Summary of normal tissue dose distribution for SaS-IMRT and HT plans ($\bar{x}\pm s$)

	V_5(%)	V_{10}(%)	V_{20}(%)	V_{30}(%)	V_{40}(%)	V_0(%)	D_{mean}(Gy)
SaS-IMRT	79.3±5.2	63.1±6.0	37.0±4.8	18.3±3.4	7.2±1.4	1.2±0.1	18.1±3.1
HT	92.4±2.1	81.4±3.2	42.1±5.2	17.1±2.3	6.3±2.2	1.0±0.2	20.6±5.2
t	−8.36	−11.13	−4.95	0.99	0.89	−0.69	−11.15
P	0.00	0.00	0.00	0.32	0.40	0.23	0.00

Footnotes as Table 2.

recognized in the treatment for nasopharyngeal cancer and other head-and-neck tumors,[17-21] intracranial tumors, [22] prostatic cancer[23], and lung cancer.[24] Di Cui et al.[17] compared the dosiology of step-and-shoot intensity modulated radiotherapy (SaS-IMRT) and helical tomotherapy (HT) in nasopharyngeal cancer, and revealed that HT improved the conformality of dosage distribution and the dosage homogeneity in target volume, and was better at protecting affected organs, such as parotid gland. Similar conclusion was reached in the study by Lee et al.[18] Cattaneo et al.[24] found that HT significantly improved the dosage homogeneity in target volume in treating lung cancer, and could better protect the lung, esophagus and heart. However, the postoperative whole pelvic radiotherapy for endometrial cancer, when compared with the radiotherapy for the cancers mentioned above, has completely different features with regard to size and geometric distribution of target volume and affected organs, dosage-volume prescription and tolerability of affected organs. Currently, no published literature has reported dosiological study on postoperative whole pelvic helical tomotherapy for endometrial cancer. By comparing HT to SaS-IMRT and examining whether postoperative whole pelvic HT was dosiologically advantageous for endometrial cancer, as well as analyzing and comparing the dosage distribution in target volume, affected organs and normal tissue, our study set out to reveal the dosiological features of HT and provide quantitative data for technique modification and clinical study, as well as guidance for designing clinical treatment plan.

Our study revealed comparable conformality of dosage distribution for SaS IMRT scheme and HT scheme, but HT scheme had more homogeneous dosage and lower mean dosage in target volume. In addition, HT scheme reduced the dosage in rectum and bladder. In particular, volume receiving moderate to high dosage radiation was decreased, and mean dosage was significantly reduced as well. However, volume receiving low to moderate dosage radiation in small intestine and colon, pelvic bone and normal tissue was increased with HT scheme, and mean dosage in pelvic bone and normal tissue increased as well. The helically delivered intensity-modulated radiation by a binary collimator, which is characterized in HT, allows for a full range of intensity modulation and helps achieve highly homogeneous dosage in target volume as well as protect the high dosage area in affected organs around target volume. However, due to this helically delivered treatment (helical radiation on 51 field angles within 360 degree), more volume in affected organs and normal tissue that are far away from target volume is thus receiving low dosage radiation. For a lesion with a larger target volume, such as endometrial cancer, this issue will be more prominent. Of course, we can place dosage-volume restriction accordingly for normal tissue and affected organs when optimizing the plan, and thereby modulate or even change the dosage distribution in target volume, affected organs and normal tissue to a certain extent. For example, volume receiving low to moderate dosage radiation in small intestine and colon, pelvic bone and normal tissue was reduced in our study, but as a result, its advantages including the protection for rectum and bladder and the dosage homogeneity in target volume were also compromised. Since the objective of our study was to compare the dosiological features of SaS-IMRT and HT, we tried to reveal the features of these techniques by using proper design to the extent possible and reducing the impact of the understanding about the systems and the use and design of dosage-volume restriction and optimization parameters on the results. However, due to the different optimization algorithms used in these schemes, the same optimization parameters (such as punishment factor and weighting factor) did not necessarily produce the same results. Therefore, we tried to incorporate current clinical practice, SaS-IMRT scheme and the results from our pilot study, and designed the same dosage-volume restriction and optimization parameters such as punishment factor and weighting factor for these two schemes and made iterative modification on these optimization parameters, so as to ensure that these schemes were compliant to the dosage-volume restrictions that had been designed. In addition, dosage prescription was normalized by the same method.

Likewise, we also incorporated domestic and foreign published literatures,[6-8, 12, 26] clinical practice and the routine in our hospital when designing the gap between CTV and PTV. A population-based gap with non-online position correction of 1 cm was selected. In previous study report, the positioning error in patients with gynecological tumors was about 0.3 cm.[12] The study subjects in our study were postoperative patients with endometrial cancer, where the clinical target volume was hardly affected by organ movement and the main influential factor for target volume position was rectum and bladder filling. HT scheme required slightly longer treatment time as compared with SaS-IMRT, the positioning was therefore more likely to be affected by organ movement. In both SaS-IMRT and HT, the gap between CTV and PTV could be reduced and thus affected organs could be better protected if imageological guidance and adaptive radiotherapy were used, particularly in patients receiving radical radiotherapy or pre-operative radiotherapy.

The advantages of HT scheme by providing homogeneous dosage in target volume and reducing dosage in rectum and bladder were expected to decrease acute and chronic toxicity in

rectum and bladder to a certain extent. But the clinical implication of increased volume receiving low to moderate dosage radiation in small intestine and colon, pelvic bone and normal tissue had to be further observed. Extensive radiation at low to moderate dosage in pelvic bone might increase the risk for hematological toxicity[27] and bone fracture,[28] particularly in patients who needed local boost radiation and concomitant/sequential chemotherapy. Studies had already demonstrated that concomitant chemotherapy significantly increased the acute toxicity and side effects, mostly hematological and gastrointestinal reactions, as compared with radiotherapy alone.[29] The possibility that low dosage radiation in normal tissue might induce a second primary cancer should also be further evaluated, especially in young patients who had longer expected lifespan.[30]

In conclusion, when compared with step and shoot intensity-modulated radiotherapy, helical tomotherapy provides more homogeneous dosage in target volume and is better at protecting bladder and rectum. The clinical implication of increased volume receiving low to moderate dosage radiation in small intestine and colon, pelvic bone and normal tissue has yet to be further investigated.

References

[1] Greven K, Winter K, Underhill K, et al. Preliminary analysis of RTOG 9708: Adjuvant postoperative radiotherapy combined with cisplatin/paclitaxel chemotherapy after surgery for patients with high-risk endometrial cancer [J]. Int J Radiat Oncol Biol Phys, 2004,59(1):168-173.

[2] Beriwal S, Jain SK, Heron DE, et al. Clinical outcome with adjuvant treatment of endometrial carcinoma using intensity-modulated radiation therapy [J]. Gynecol Oncol, 2006,102(2):195-199.

[3] Ahamad A, D'Souza W, Salehpour M, et al. Intensity-modulated radiation therapy after hysterectomy: comparison with conventional treatment and sensitivity of the normal-tissue-sparing effect to margin size [J]. Int J Radiat Oncol Biol Phys, 2005,62(4):1117-1124.

[4] Roeske JC, Mundt AJ, Haplern H, et al. Late rectal sequelae following definitive radiation therapy for carcinoma of the uterine cervix: a dosimetric analysis [J]. Int J Radiat Oncol Biol Phys, 1997,37(2):351-358.

[5] Perez CA, Grigsby PW, Lockett MA, et al. Radiation therapy morbidity in carcinoma of the uterine cervix: dosimetric and clinical correlation [J]. Int J Radiat Oncol Biol Phys, 1999, 44(4):855-866.

[6] Lin Y,Zhou LJ,Xu ZY,et al.Technical and dosimetric study of three-dimensional conformal and intensity-modulated pelvic radiotherapy for post-hysterectomy cervical carcinoma[J].Chin J Radiat Oncol,2008,17(3):372-376. [in Chinese]

[7] Li B,An JS,Wu LY , et al.A comparative dosimetric study of conventional conformal and intensity-modulated radiotherapy in postoperative pelvic irradiation of cervical cancer[J].Chin J Radiat Oncol,2008,17(3):211-215. [in Chinese]

[8] Lujan AE, Mundt AJ, Yamada SD, et al. Intensity-modulated radiotherapy as a means of reducing dose to bone marrow in gynecologic patients receiving whole pelvic radiotherapy [J]. Int J Radiat Oncol Biol Phys, 2003,57(2):516-521.

[9] Mundt AJ, Lujan AE, Rotmensch J, et al. Intensity-modulated whole pelvic radiotherapy in women with gynecologic malignancies [J]. Int J Radiat Oncol Biol Phys, 2002,52(5):1330-1337.

[10] Portelance L, Chao KS, Grigsby PW, et al. Intensity-modulated radiation therapy (IMRT) reduces small bowel, rectum, and bladder doses in patients with cervical cancer receiving pelvic and para-aortic irradiation [J]. Int J Radiat Oncol Biol Phys, 2001,51(1):261-266.

[11] Heron DE, Gerszten K, Selvaraj RN, et al. Conventional 3D conformal versus intensity-modulated radiation therapy for the adjuvant treatment of gynecologic m alignancies: A comparative dosimetric study of dose volume histograms [J]. Gynecol Oncol, 2003,91(1):39-45.

[12] Roeske JC, Lujan A, Rotmensch J, et al. Intensity-modulated whole pelvis radiation therapy in patients with gynecologic malignancies [J]. Int J Radiat Oncol Biol Phys, 2000,48(5):1613-1621.

[13] Mundt AJ, Mell LK, Roeske JC. Preliminary analysis of chronic gastrointestinal toxicity in gynecologic patients treated with intensity-modulated whole pelvic radiation therapy [J]. Int J Radiat Oncol Biol Phys, 2003,56(5):1354-1360.

[14] Randall ME, Ibbott GS. Intensity-modulated radiation therapy for gynecologic cancers: Pitfalls, hazards, and cautions to be considered [J]. Semin Radiat Oncol, 2006,16(3):138-143.

[15] Brixey CJ, Roeske JC, Lujan AE, et al. Impact of intensity-modulated radiation therapy on acute hematologic toxicity in women with gynecologic malignancies [J]. Int J Radiat Oncol Biol Phys, 2002,54(5):1388-1396.

[16] Jhingran A. Potential advantages of intensity-modulated radiation therapy in gynecologic malignancies [J]. Semin Radiat Oncol, 2006,16(3):144-151.

[17] Cui D,Dai XK,Ma L,et al.A dosimetric comparision between helical tomotherapy and linear accelerator-based intensity modulated radiation therapy for nasopharyngeal carcinoma [J].Chin J Radiat Oncol,2008,17(3):169-173. [in Chinese]

[18] Lee TF, Fang FM, Chao PJ, et al. Dosimetric comparisons of helical tomotherapy and step-and-shoot intensity-modulated radiotherapy in nasopharyngeal carcinoma [J]. Radiother Oncol, 2008, 89(1):89-96.

[19] Van Vulpen M, Field C, Raaijmakers CP, et al. Comparing step-and-shoot IMRT with dynamic helical tomotherapy IMRT plans for head-and-neck cancer [J]. Int J Radiat Oncol Biol Phys, 2005,62(5):1535-1539.

[20] Sheng K, Molloy JA, Read PW. Intensity-modulated radiation therapy (IMRT) dosimetry of the head and neck: a comparison of treatment plans using linear accelerator-based IMRT and helical tomotherapy [J]. Int J Radiat Oncol Biol Phys, 2006,65(3):917-923.

[21] Sheng K, Molloy JA, Larnera JM, et al. A dosimetric comparison of non-coplanar IMRT versus Helical Tomotherapy for nasal cavity and paranasal sinus cancer [J]. Radiother Oncol, 2007,82(2):174-178.

[22] Han C, Liu A, Schultheiss TE, et al. Dosimetric comparisons of helical tomotherapy treatment plans and step-and-shoot intensity-modulated radiosurgery treatment plans in intracranial stereotactic radiosurgery [J]. Int J Radiat Oncol Biol Phys, 2006,65(2):608-616.

[23] Aoyama H, Westerly DC, Mackie TR, et al. Integral radiation dose to normal structures with conformal external beam radiation [J]. Int J Radiat Oncol Biol Phys, 2006,64(3):962-967.

[24] Cattaneo GM, Dell'oca I, Broggi S, et al. Treatment planning comparison between conformal radiotherapy and helical tomotherapy in the case of locally advanced-stage NSCLC [J]. Radiother Oncol, 2008,88(3):310-318.

[25] Small W Jr, Mell LK, Anderson P, et al. Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy in postoperative treatment of endometrial and cervical cancer [J]. Int J Radiat Oncol Biol Phys, 2008,71(2):428-434.

[26] Mell LK, Tiryaki H, Ahn KH et al. Dosimetric comparison of bone marrow-sparing intensity-modulated radiotherapy versus conventional techniques for treatment of cervical cancer [J]. Int J Radiat Oncol Biol Phys, 2008,71(5):1504-1510.

[27] Sood BM, Gorla GR, Garg M, et al. Extended-field radiotherapy and high-dose-rate brachytherapy in carcinoma of the uterine cervix: Clinical experience with and without concomitant chemotherapy [J]. Cancer, 2003,97(7):1781-1788.

[28] Baxter NN, Habermann EB, Tepper JE, et al. Risk of pelvic fractures in older women following pelvic irradiation [J]. JAMA, 2005,294(20):2587-2593.

[29] Zeng SY, Li LY, Shu KY, et al. Concurrent chemoradiotherapy versus radiotherapy in advanced cervical carcinoma [J]. Chin J Cancer, 2008,27(9): 942-946.

[30] Hall EJ, Wuu CS. Radiation-induced second cancers: the impact of 3D-CRT and IMRT [J]. Int J Radiat Oncol Biol Phys, 2003,56(1):83-88.