A comparative planning study of step-and-shoot IMRT versus helical tomotherapy for whole-pelvis irradiation in cervical cancer

Imjai Chitapanarux1*, Ekkasit Tharavichitkul1, Wannapa Nobnop1, Somsak Wanwilairat1, Roy Vongtama2 and Patrinee Traisathit3

1Division of Therapeutic Radiology and Oncology, Department of Radiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand
2St Teresa Comprehensive Cancer Center, Stockton, CA, USA
3Department of Statistics, Faculty of Science, Chiang Mai University, Chiang Mai, Thailand

*Corresponding author. Division of Therapeutic Radiology and Oncology, Faculty of Medicine, Chiang Mai University, 110 Intavarorose Rode, Chiang Mai, 50200, Thailand. Tel: 66 53 945456; Fax: +66-5394-5491; Email: imjai@hotmail.com or imjai.chitapanarux@cmu.ac.th

Received July 6, 2014; Revised January 9, 2015; Accepted January 14, 2015

ABSTRACT

The aim of this study was to compare the dosimetric parameters of whole-pelvis radiotherapy (WPRT) for cervical cancer between step-and-shoot IMRT (SaS-IMRT) and Helical Tomotherapy™ (HT). Retrospective analysis was performed on 20 cervical cancer patients who received WPRT in our center between January 2011 and January 2014. SaS-IMRT and HT treatment plans were generated for each patient. The dosimetric values for target coverage and organ-at-risk (OAR) sparing were compared according to the criteria of the International Commission on Radiation Units and Measurements 83 (ICRU 83) guidelines. Differences in beam-on time (BOT) were also compared. All the PTV dosimetric parameters (D5%, D50% and D95%) for the HT plan were (statistically significantly) of better quality than those for the SaS-IMRT plan (P-value < 0.001 in all respects). HT was also significantly more accurate than SaS-IMRT with respect to the D98% and Dmean of the CTV (P-values of 0.008 and <0.001, respectively). The median Conformity Index (CI) did not differ between the two plans (P-value = 0.057). However, the Uniformity Index for HT was significantly better than that for SaS-IMRT (P-value < 0.001). The median of D50% for the bladder, rectum and small bowel were significantly lower in HT planning than SaS-IMRT (P-value < 0.001). For D2%, we found that HT provided better sparing to the rectum and bladder (P-value < 0.001). However, the median of D2% for the small bowel was comparable for both plans. The median of Dmax of the head of the left femur was significantly lower in the HT plan, but this did not apply for the head of the right femur. BOT for HT was significantly shorter than for SaS-IMRT (P-value < 0.001). HT provided highly accurate plans, with more homogeneous PTV coverage and superior sparing of OARs than SaS-IMRT. In addition, HT enabled a shorter delivery time than SaS-IMRT.

KEYWORDS: IMRT, step-and-shoot, tomotherapy, cervical cancer

INTRODUCTION

Cervical cancer is the second most common cancer among women in Thailand; 9999 new cases were diagnosed in 2008 [1]. A significant survival benefit has been demonstrated for the combined approach of concurrent chemoradiotherapy (CCRT) [2–4]. The radiation therapy component consists of external beam irradiation to the primary tumor and regional lymph nodes, followed by a brachytherapy boost to the gross tumor in the cervix. However, acute Grade 3 or 4 hematological and gastrointestinal toxicities were found to be significantly higher in the CCRT group than in the radiotherapy (RT) alone group. Tan et al. [5] also demonstrated increased late toxicity after CCRT for locally advanced cervical cancer.

To combat this increase in toxicity, whole-pelvic intensity-modulated radiotherapy (WP-IMRT) has been applied to gynecologic malignancies with excellent planning target volume (PTV) coverage and this has been associated with less acute gastrointestinal sequelae than conventional whole-pelvic radiotherapy (WPRT), as reported by Mundt et al. [6]. It has been demonstrated that, with the same...
target coverage, IMRT is superior to conventional techniques in normal tissue sparing for the treatment of cervical cancer, with lower gastrointestinal, genitourinary, and bone marrow toxicity [7–11]. Whole-pelvic step-and-shoot (SaS) IMRT for cervical cancer patients has been used in our center since 2007. A newer technique for delivering IMRT, helical tomotherapy™ (HT) (using a continuously rotating beam), can provide highly conformal dose distributions and simultaneous critical organ-sparing ability [12, 13]. It is being studied for use in gynecologic malignancies and thus far has provided promising results with respect to reliable set-up accuracy and a reduction in planning margin [14]. In our center, SaS-IMRT started in the year 2007, and HT (TomoTherapy Hi-Art) with treatment planning system (TPS) Hi-Art version 4.2.1) commenced in 2012. We use both techniques in our practice. This is the first dosimetric comparison study of the two techniques in WPRT for locally advanced cervical cancer in our country.

**MATERIALS AND METHODS**

A total of 20 cervical cancer patients who received whole-pelvis irradiation with the SaS-IMRT technique at the Division of Therapeutic Radiology and Oncology, Chiang Mai University, between January 2011 and January 2014 were retrospectively identified.

For IMRT planning, a computed tomography (CT) simulation was performed. VAC-Loc was used to immobilize patients in position. To prepare the bladder, patients were advised to urinate 20 min before scanning and to drink 200 ml of water after voiding. Patients were then set up in CT. For rectal preparation, a laxative was administered in case of rectal dilatation. This protocol was used during irradiation to maintain bladder and rectal volume. With the patients in supine treatment position and legs relaxed on the table, the pelvic region from the L1–L2 interspace and covering the whole vagina was scanned without intravenous contrast to obtain appropriate images. The CT slice thickness was 5 mm (no interslice gap). In our center, we have only one 12-year-old CT-simulator unit, which has a single slice thickness for IMRT planning (Toshiba: Asteion). To preserve the machine, a 5-mm slice thickness was selected (for a large volume region such as for pelvic irradiation).

After imaging was completed, image data was sent for contouring (Oncentra Masterplan®, Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) and planning (KonRad treatment planning software®, Siemens, Concord, CA, USA).

The RTOG/JCOG recommendations were used in combination as a guide for contouring the clinical target volume (CTV) [15–18]. The CTV was composed of the cervix, uterus, adnexae, upper half of the vagina, and pelvic lymph nodes (common iliac lymph nodes (LNs), external iliac LNs, internal iliac LNs, obturator LNs and presacral LNs). The PTV was defined as the CTV plus a 0.7-cm margin (for the pelvic lymph nodes) and a 1–1.5-cm margin (for the primary cervical tumor). The bladder, rectum, sigmoid colon, small bowel and heads of femurs were contoured as organs at risk (OARs). For the PTV, the dose of 1.8–2 Gy per fraction at five fractions per week was prescribed (i.e. a total dose of 45–46 Gy). The D95 (dose to 95% of the volume) of the PTV was calculated. Additional to the doses to 5% of the bladder, rectum and small bowel, the maximal doses to the heads of the femurs were also evaluated. As described earlier, patients were advised to prepare the bladder and rectum for treatment as for the CT simulation. An electronic portal imaging device (EPID) was used weekly to evaluate and make corrections to positioning.

An SaS-IMRT plan was generated for each patient using KonRad, Siemens TPS, with seven coplanar step-and-shoot beams at fixed gantry angles G1 to G7. The G1 to G7 for most cases were 0, 40, 80, 125, 235, 280 and 320 degrees, respectively. For only six of the patients, G4 and G5 were 5-degrees modified to 120 and 240 degrees, respectively. All patients received SaS-IMRT whole-pelvis irradiation with our Siemens Primus.

A HT plan was then created using the Tomotherapy treatment-planning system (HiArt, Tomotherapy, Tomotherapy Inc., Madison, WI) for every patient (by the same medical physicist who planned the SaS-IMRT). The optimization parameters of dose constraint and overlap priority were given the same consideration in both the SaS-IMRT plan and the HT plan.

We used the same contouring as for SaS-IMRT for plan generation. Both plans were required to use identical planning objectives with respect to optimal PTV coverage and OAR sparing. Plans were designed using a field width of 5 cm, a pitch of 0.287 and modulation factor of 2.2 to 2.8. The mean setting and actual modulation factor were 2.235 and 2.032, respectively.

| No. | Age | Stage | Dose prescription |
|-----|-----|-------|-------------------|
| 1   | 51  | IIB   | 45 Gy/25 Fx       |
| 2   | 51  | IIB   | 45 Gy/25 Fx       |
| 3   | 62  | IIB   | 45 Gy/25 Fx       |
| 4   | 63  | IIB   | 45 Gy/25 Fx       |
| 5   | 53  | IIB   | 45 Gy/25 Fx       |
| 6   | 46  | IIB   | 45 Gy/25 Fx       |
| 7   | 52  | IIB   | 45 Gy/25 Fx       |
| 8   | 57  | IIB   | 45 Gy/25 Fx       |
| 9   | 52  | IIB   | 45 Gy/25 Fx       |
| 10  | 54  | IIB   | 45 Gy/25 Fx       |
| 11  | 52  | IIB   | 45 Gy/25 Fx       |
| 12  | 53  | IIIB  | 45 Gy/25 Fx       |
| 13  | 61  | IIB   | 45 Gy/25 Fx       |
| 14  | 57  | IIB   | 45 Gy/25 Fx       |
| 15  | 63  | IIB   | 45 Gy/25 Fx       |
| 16  | 73  | IIB   | 46 Gy/23 Fx       |
| 17  | 70  | IIB   | 46 Gy/23 Fx       |
| 18  | 67  | IIIB  | 46 Gy/23 Fx       |
| 19  | 53  | IIB   | 46 Gy/23 Fx       |
| 20  | 72  | IIB   | 46 Gy/23 Fx       |
Dosimetric parameters were analyzed for each technique. D50%, D95% and D5% of the PTV were selected. The priorities were prescribed as follows: PTV, bladder, rectum, sigmoid colon, small bowel, and head of femur. For organs-at-risk, D50% and D2% to the small bowel, rectum and bladder were considered. The Dmax of the bilateral heads of the femurs were also analyzed. To assess the uniformity of dose distribution in the PTV, we calculated a uniformity index (UI) from the formula UI = D5/D95, where D5 and D95 were the minimum doses delivered to 5% and 95% of the PTVs. The ideal value is 1, and it increases as the plan becomes less homogeneous.

We also calculated the quality of coverage, with a conformity index (CI) that was defined as the ratio between the target volume and the target volume that was covered by the reference isodose. A CI = 1 corresponds to ideal conformation. A CI > 1 indicates that the irradiated volume is greater than the target volume. A CI < 1 indicates that the target volume is only partially irradiated.

A direct comparison of the dosimetric parameters between SaS-IMRT and HT was also performed (using the Wilcoxon's matched pairs test) to determine if there was a significant difference for any of the parameters examined. Differences were considered statistically significant at P < 0.05. Additionally, beam-on times (BOTs) (defined as the time from first beam on until the last beam was turned off) of the two delivery systems were also evaluated and compared. The study was approved by our Institutional Review Board. All analyses were performed using SPSS version 17.

**RESULTS**

**Patient characteristics**

A total of 20 women were included, with a median age of 55.5 years (IQR, 52–63 years). All patients belonged to FIGO Stage IIB and IIIB and received concurrent chemoradiotherapy with weekly cisplatin at 40 mg/m². All of the patients were treated with WP SaS-IMRT followed by brachytherapy or external beam radiotherapy according to the tumor status after WPRT. Baseline patient characteristics were shown in Table 1. The dosimetric data for SaS-IMRT and HT are shown in Tables 2 and 3, respectively.

| Table 2. The data for SaS-IMRT |
|--------------------------------|
| No. | Bladder | Rectum | Head of femur | Bowel | CTV | PTV |
|-----|---------|--------|---------------|-------|-----|-----|
|     | D50 (Gy) | D2 (Gy) | D50 (Gy) | D2 (Gy) | Dmax Lt (Gy) | Dmax Rt (Gy) | D50 (Gy) | D2 (Gy) | Dmean (Gy) | D98 (Gy) | CI | UI |
| 1   | 41.2     | 48.5   | 37.2        | 49.2   | 46.9          | 45.1          | 28.5       | 46.2   | 48.0        | 45.2        | 0.981 | 1.103 |
| 2   | 44.9     | 47.5   | 41.3        | 47.5   | 45.2          | 45.4          | 30.5       | 44.8   | 47.8        | 45.4        | 0.986 | 1.084 |
| 3   | 41.4     | 48.2   | 38.3        | 49.0   | 47.4          | 43.6          | 21.9       | 37.6   | 47.8        | 45.1        | 0.981 | 1.107 |
| 4   | 42.9     | 48.9   | 37.0        | 48.8   | 44.8          | 41.9          | 28.9       | 41.5   | 48.5        | 45.9        | 0.989 | 1.084 |
| 5   | 40.5     | 48.0   | 36.6        | 48.6   | 38.3          | 39.0          | 26.3       | 40.0   | 48.1        | 45.8        | 0.986 | 1.094 |
| 6   | 41.1     | 48.8   | 43.5        | 50.3   | 42.3          | 40.9          | 31.2       | 46.5   | 48.7        | 46.2        | 0.994 | 1.108 |
| 7   | 41.3     | 50.3   | 35.9        | 52.0   | 47.4          | 47.7          | 28.6       | 41.8   | 49.8        | 47.0        | 0.999 | 1.105 |
| 8   | 40.2     | 51.0   | 40.6        | 50.8   | 48.0          | 48.0          | 24.9       | 41.8   | 49.5        | 46.2        | 0.998 | 1.110 |
| 9   | 48.0     | 50.8   | 34.6        | 52.0   | 45.9          | 45.3          | 27.4       | 41.0   | 49.7        | 47.2        | 0.999 | 1.096 |
| 10  | 40.5     | 49.5   | 37.9        | 48.8   | 47.3          | 47.1          | 25.2       | 39.6   | 49.2        | 46.7        | 0.996 | 1.101 |
| 11  | 37.5     | 49.9   | 40.4        | 50.0   | 48.8          | 46.5          | 28.2       | 41.8   | 49.7        | 46.8        | 0.994 | 1.101 |
| 12  | 38.1     | 48.9   | 36.2        | 46.4   | 45.5          | 43.7          | 26.2       | 40.8   | 49.9        | 47.0        | 0.998 | 1.100 |
| 13  | 40.4     | 50.8   | 36.7        | 50.9   | 44.2          | 41.1          | 29.7       | 40.5   | 49.3        | 46.2        | 0.992 | 1.113 |
| 14  | 37.1     | 49.7   | 40.2        | 49.8   | 44.3          | 43.8          | 28.0       | 39.2   | 49.3        | 46.5        | 0.996 | 1.102 |
| 15  | 38.5     | 50.4   | 35.9        | 50.8   | 46.1          | 43.9          | 23.5       | 38.9   | 49.9        | 47.0        | 1.000 | 1.095 |
| 16  | 41.9     | 52.8   | 41.1        | 50.7   | 44.4          | 43.0          | 29.6       | 49.0   | 50.7        | 48.0        | 0.994 | 1.100 |
| 17  | 42.4     | 51.1   | 44.2        | 52.2   | 42.0          | 41.8          | 31.1       | 49.2   | 49.0        | 46.3        | 0.982 | 1.111 |
| 18  | 39.7     | 50.1   | 42.0        | 49.2   | 38.8          | 41.0          | 22.1       | 47.5   | 48.9        | 45.8        | 0.976 | 1.099 |
| 19  | 44.4     | 49.9   | 41.3        | 48.8   | 42.3          | 42.6          | 22.9       | 48.6   | 49.0        | 45.2        | 0.967 | 1.113 |
| 20  | 42.2     | 50.3   | 37.9        | 48.8   | 44.1          | 42.0          | 29.4       | 49.2   | 48.9        | 46.5        | 0.982 | 1.093 |
The dosimetric parameters for the HT and IMRT plans were analyzed (Table 4). Dose distribution in all SaS-IMRT and HT plans for all 20 patients satisfied clinical requirements. The dose distributions for SaS-IMRT and HT planned for one patient are shown in Fig 1. HT planning demonstrated a Dmean and D98% closer to the prescription dose than SaS-IMRT planning, with a P-value of < 0.001 and 0.008, respectively. All the PTV dosimetric parameters (D5%, D50% and D95%) of the HT plan were of significantly better quality than for the IMRT plan. The dose conformity and the CI did not differ between the plans, but the target dose UI of the HT plan was significantly better than that of the SaS-IMRT plan.

**OARs**
HT showed better OAR dose sparing than SaS-IMRT. For the radiation dose to the bladder and rectum, the D50% and D2% of HT planning were both significantly less than for the SaS-IMRT plan (P-value < 0.001). Regarding the dose to the small bowel, D50% for the HT plan was also statistically less than for the SaS-IMRT plan (P-value < 0.001). However, we did not find a statistically significant difference in D2% for the small bowel when comparing the two techniques. The Dmax of the head of the left femur was (statistically significantly) lower in the HT plan, whereas there was no difference for the head of the right femur between the two techniques. The dose statistics of the OARs are also listed in Table 4.

**Beam-on time**
The median BOT was significantly shorter in HT delivery (230.6 s) than in SaS-IMRT delivery (900.0 s), with a P-value of < 0.001.

**DISCUSSION**
For the treatment of cervical cancer, WPRT has been used for more than five decades. The conventional two- or four-field box techniques were applied to the target, which was composed of the primary site and the pelvic LNs. Although this simple technique yielded good treatment results and acceptable toxicity, the OARs still received...
significant dosages, even with good blocking. With new techniques of imaging (CT or MRI) and planning, the possibility of keeping the target dose high and reducing the dose to the OARs has become a reality. After the first publication concerning the use of IMRT in gynecological cancers by Portelance et al. [7], the use of high-technology radiation therapy soon became more prevalent. Most studies have reported the benefits of IMRT in reducing the dose to OARs in radical and postoperative settings. [6, 7, 19–22].

Moreover, the supported study from Cancer Care Ontario reported comparative clinical outcomes for three dimension conformal radiotherapy (3DCRT) and IMRT. This report supported the use of IMRT in the treatment of gynecologic cancers in order to reduce the toxicity of the treatment. However, this group warned that clinicians should be aware of the uncertainties involved and be judicious in the use of gynecologic IMRT with the primary goal of reducing toxicity [23]. The development of intensity-modulated arc therapy (IMAT) was the next area of advancement in technique. The new variation of dynamic-IMRT allowed 360° treatment. HT, volumetric-modulated arc therapy (VMAT™) and RAPID arc™ are all IMAT technologies that were developed to improve treatment quality compared with conventional IMRT [24–26].

Table 4. Wilcoxon matched pairs test between the two treatment plans

| Structure             | DVH criteria | Tomotherapy median (IQR) | SaS-IMRT median (IQR) | P-value |
|-----------------------|--------------|--------------------------|-----------------------|---------|
| Age                   |              | 55.50 (52.00–63.00)      |                       |         |
| Bladder D50           | 38.15 (35.80–38.75) | 41.15 (39.95–42.30)     | <0.001                |
| Bladder D2            | 46.80 (46.45–47.10) | 49.90 (48.85–50.60)     | <0.001                |
| Rectum D50            | 35.65 (33.85–38.70) | 38.10 (36.65–41.20)     | <0.001                |
| Rectum D2             | 46.65 (46.25–47.40) | 49.50 (48.80–50.80)     | <0.001                |
| Small bowel D50       | 25.10 (23.20–26.60) | 28.10 (25.05–29.50)     | <0.001                |
| Small bowel D2        | 42.10 (41.00–45.75) | 41.80 (40.25–47.00)     | 0.823                |
| Head of femur Dmax Left | 43.70 (42.00–44.60) | 45.00 (42.75–47.20)     | 0.021                |
| Head of femur Dmax Right | 43.35 (42.15–44.05) | 43.65 (41.82–45.38)     | 0.225                |
| CTV Dmean             | 46.45 (46.30–46.95) | 49.10 (48.60–49.70)     | <0.001                |
| CTV D95               | 46.60 (45.40–46.00) | 46.25 (45.80–46.90)     | 0.008                |
| CTV CI                | 0.99 (0.99–1.00)   | 0.99 (0.98–1.00)        | 0.057                |
| CTV UI                | 1.03 (1.03–1.05)   | 1.10 (1.09–1.10)        | <0.001                |
| PTV D5                | 47.0 (46.8–47.75)  | 51.25 (50.35–51.88)     | <0.001                |
| PTV D50               | 46.30 (46.20–46.90) | 48.70 (48.15–49.40)     | <0.001                |
| PTV D95               | 44.90 (44.90–45.55) | 44.90 (44.53–45.00)     | <0.001                |
| PTV CI                | 0.95 (0.94–0.95)   | 0.94 (0.94–0.95)        | 0.093                |
| PTV UI                | 1.05 (1.04–1.05)   | 1.14 (1.13–1.15)        | <0.001                |
| Beam-on time          | 230.6 (217.4–240.1) | 900.0 (840.0–904.0)     | <0.001                |

Fig. 1. Dose distribution for SAS-IMRT (left) and HT (right) plan.
This study provides a dosimetric analysis of SaS-IMRT and HT to assess optimal treatment planning for pelvic irradiation in locally advanced cervical cancer. We performed the comparative planning studies by independently optimizing planning in the same patient. Our results indicate that HT had better conformal CTV and PTV coverage and sparing of OARs than did SaS-IMRT, as shown in Table 4. HT demonstrated a 3 Gy lower median dose at D2% of the bladder and rectum with statistically significant differences. HT did demonstrate a 1 Gy higher dose difference of the small bowel, which was concerning, although it was not significant statistically. HT was of clear benefit in lowering the cumulative bladder and rectal dose when compared with brachytherapy. All the PTV dosimetric parameters (D5%, D50% and D95%) for the HT plan were of significantly better quality than for the IMRT plan. Although the D98 of the CTV had a 1-Gy difference (45.6 versus 46.27; \( P = 0.008 \)), the UI of HT was significantly closer to 1 than SaS-IMRT (\( P < 0.001 \)) with the same CI (0.99). This demonstrates a lower overdose region for treatment by HT. After much discussion between radiation oncologists and medical physicists in our center, we have just this year changed the plan evaluation from D95 to D50 of the PTV, as per ICRU 83. So, D95 of the PTV was the main evaluation for the target, but we evaluated additional parameters as per ICRU 83 [27] recommendations. Although the median dose at D95 of the PTV had statistical significance, all plans achieved the target dose to D95 of the PTV, and HT planning showed better UI and less data deviation than SaS-IMRT. Moreover, our findings suggest that using HT will have a favorable impact on BOT.

Another limitation in using pelvic SaS-IMRT for cervical cancer is organ motion, which is not evaluated prior to treatment delivery. This would be another advantage of using HT: using megavoltage CT before each treatment session, thus allowing the plan to have an impact on BOT.

**CONCLUSION**

When treating cervical cancer with IMRT, HT provided a distinct advantage compared with SaS-IMRT with respect to target coverage and OARs. Moreover, it had shorter delivery treatment time.

**ACKNOWLEDGEMENTS**

The authors offer many thanks to the staff of the NRU–CMU in the Gynecologic Oncology Cluster and the Division of Therapeutic Radiology and Oncology, Faculty of Medicine, Chiang Mai University, for supporting this study.

**CONFLICT OF INTEREST**

The authors have declared that there are no conflicts of interest.

**FUNDING**

Funding by Faculty of Medicine, Chiang Mai University. Funding to pay the Open Access publication charges for this article was provided by Faculty of Medicine, Chiang Mai University.

**REFERENCES**

1. Ferlay J, Shin H, Bray F, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010;127:2893–917.
2. Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med 1999;340:1144–53.
3. Whitney CW, Sause W, Bundy BN, et al. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IB–IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. J Clin Oncol 1999;17:1339–48.
4. John M, Flam M, Caplan R, et al. Final results of a phase II chemoradiation protocol for locally advanced cervical cancer: RTOG 85–15. Gynecol Oncol 1996;61:221–6.
5. Tan LT, Zahra M. Long-term survival and late toxicity after chemoradiation for cervical cancer—the Addenbrooke’s experience. Clin Oncol 2008;20:358–64.
6. Mundt AJ, Lujan AE, Rotmensch J, et al. Intensity-modulated whole pelvic radiotherapy in women with gynecologic malignancies. Int J Radiat Oncol Biol Phys 2002;52:1330–7.
7. 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. Int J Radiat Oncol Biol Phys 2001;51:261–6.
8. Brixey CJ, Roesske JC, Lujan AE, et al. Impact of intensity-modulated radiotherapy on acute hematologic toxicity in women with gynecologic malignancies. Int J Radiat Oncol Biol Phys 2002;54:1388–96.
9. 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. Int J Radiat Oncol Biol Phys 2003;57:516–21.
10. Ahmed RS, Kim RY, Duan J, et al. IMRT dose escalation for positive para-aortic lymph nodes in patients with locally advanced cervical cancer while reducing dose to bone marrow and other organs at risk. Int J Radiat Oncol Biol Phys 2004;60:505–12.
11. Bunt L, Heide UA, Ketelaars M, et al. Conventional, conformal, and intensity-modulated radiation therapy treatment planning of external beam radiotherapy for cervical cancer: the impact of tumor regression. Int J Radiat Oncol Biol Phys 2006;64:189–96.
12. Shueng PW, Wu LJ, Chen SY, et al. Concurrent chemoradiation therapy with helical tomotherapy for oropharyngeal cancer – a preliminary result. Int J Radiat Oncol Biol Phys 2010;77:175–21.
13. Shueng PW, Lin SC, Chong NS, et al. Total marrow irradiation with helical tomotherapy for bone marrow transplantation of multiple myeloma: first experience in Asia. Technol Cancer Res Treat 2009;8:29–38.
14. Hsieh CH, Wei MC, Lee HY, et al. Whole pelvic helical tomotherapy for locally advanced cervical cancer: technical implementation of IMRT with helical tomotherapy. Radiat Oncol 2009;4:62.
15. Lim K, Small W Jr, Portelance L, et al. Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy for the definitive treatment of cervix cancer. Int J Radiat Oncol Biol Phys 2011;79:348–55.
16. Taylor A, Rockall AG, Reznik RH, et al. Mapping pelvic lymph nodes: guidelines for delineation in intensity-modulated radiotherapy. Int J Radiat Oncol Biol Phys 2005;63:1604–12.
17. Toita T, Ohno T, Kaneyasu Y, et al. A consensus-based guide-line defining the clinical target volume for pelvic lymph nodes in...
external beam radiotherapy for uterine cervical cancer. *Jpn J Clin Oncol* 2010;40:456–63.

18. Toita T, Ohno T, Kaneyasu Y, et al. A consensus-based guideline defining clinical target volume for primary disease in external beam radiotherapy for intact uterine cervical cancer. *Jpn J Clin Oncol* 2011;41:1119–26.

19. Chen MF, Tseng CJ, Tseng CC, et al. Clinical outcome in posthysterectomy cervical cancer patients treated with concurrent Cisplatin and intensity-modulated pelvic radiotherapy: comparison with conventional radiotherapy. *Int J Radiat Oncol Biol Phys* 2007;67:1438–44.

20. Beriwal S, Heron DE, Kim H, et al. Intensity-modulated radiotherapy for the treatment of vulvar carcinoma: a comparative dosimetric study with early clinical outcome. *Int J Radiat Oncol Biol Phys* 2006;64:1395–400.

21. Loiselle C, Koh WJ. The emerging use of IMRT for treatment of cervical cancer. *J Natl Compr Canc Netw* 2010;8:1425–34.

22. Hasselle MD, Rose BS, Kochanski JD, et al. Clinical outcomes of intensity-modulated pelvic radiation therapy for carcinoma of the cervix. *Int J Radiat Oncol Biol Phys* 2011;80:1436–45.

23. D’Souza DP, Rumble RB, Fyles A, et al. Intensity-modulated radiotherapy in the treatment of gynaecological cancers. *Clin Oncol* 2012;24:499–507.

24. Poon DM, Kam M, Leung CM, et al. Dosimetric advantages and superior treatment delivery efficiency of RapidArc over conventional intensity-modulated radiotherapy in high-risk prostate cancer involving seminal vesicles and pelvic nodes. *Clin Oncol* 2013;25:706–12.

25. Hall WA, Fox TH, Jiang X, et al. Treatment efficiency of volumetric modulated arc therapy in comparison with intensity-modulated radiotherapy in the treatment of prostate cancer. *J Am Coll Radiol* 2013;10:128–34.

26. Lee TF, Chao PJ, Ting HM, et al. Comparative analysis of Smart Arc-based dual arc volumetric-modulated arc radiotherapy (VMAT) versus intensity-modulated radiotherapy (IMRT) for nasopharyngeal carcinoma. *J Appl Clin Med Phys* 2011;12:3587.

27. Gregoire V, Mackie TR, et al. State of the art on dose prescription, reporting and recording in Intensity-Modulated Radiation Therapy (ICRU report No. 83). *Cancer Radiother* 2011;15:555–9.