J Cancer Sci Clin Ther 2019; 3 (4): 221-228 *DOI: 10.26502/jcsct.5079036*

Research Article

Dosimetric Comparison of Conformal Radiotherapy and Arc-therapy of Ineligible Cervical Cancers for Intracavitary Brachytherapy

Bouchra Amaoui[1*], Dounia Mohssine[2], Malha ait Mohamed Bourhim[2], Nawal Bouih[2], Hicham Tamri[2], Mohamed El Morchid[2], Slimane Semghouli[3]

[1]Regional Center of Oncology, Agadir, Morocco

[2]Al Kindy Treatment Center of Oncology and Diagnosis, Casablanca, Morocco

[3]Higher Institute of Nursing Professions and Health Techniques Agadir, Morocco

[*]Corresponding Author

Bouchra Amaoui, Regional Center of Oncology, Agadir, Morocco, E-mail: bamaoui73@gmail.com

Received: 22 August 2019;

Accepted: 30 September 2019;

Published: 07 October 2019

Citation: Bouchra Amaoui, Dounia Mohssine, Malha ait Mohamed Bourhim, Nawal Bouih, Hicham Tamri, Mohamed El Morchid, Slimane Semghouli. Dosimetric Comparison of Conformal Radiotherapy and Arc-therapy of Ineligible Cervical Cancers for Intracavitary Brachytherapy. Journal of Cancer Science and Clinical Therapeutics 3 (2019): 221-228.

Abstract

Purpose: The purpose of this study was to compare the dosimetric parameters of two radiotherapy techniques for the cervical cancer treatment: three-dimensional conformal radiotherapy and arc-therapy.

Materials and Methods: Twenty patients with locally advanced cervical cancer who had been treated with 50 Gy conformal radiotherapy or arc-therapy, received a further 20 Gy by arc-therapy technique on a Varian treatment planning system. Both techniques were compared on the basis of Dose-Volume Histograms (DVH) for the Planning Target Volume (PTV), Organs At Risk (OAR) as well as homogeneity and conformity indices. Statistical analysis was performed using the SPSS (Statistical Package for the Social Sciences) v23 software (IBM Inc., Chicago, IL).

Results: The results obtained show that there is no significant difference in terms of dose distribution on the planning volumes between these two techniques. For the 50 Gy series, arc-therapy allowed for better OAR savings. V50 was reduced by 85% for the bladder and 89% for the

rectum. For the 70 Gy series, the benefit was also in favor of arc-therapy. Indeed, from V30 to V60 the reduction was 15% to 56% for the bladder and rectum. In the small bowels, the reduction was greater than 61% for volumes beyond V40.

Conclusion: In this study, the arc-therapy compared to the conformational radiotherapy, allows a better coverage of the planning target volume, but also a reduction of the doses received by the organs at risk, which suggests a possible improvement of the therapeutic index. Therefore, arc-therapy may be a suitable technology for the treatment of cervical cancer when brachytherapy is not feasible.

Keywords: Cervical cancer; Conformal radiotherapy; Arc-therapy; Dosimetry

1. Introduction

According to the World Health Organization (WHO), cervical cancer is the fourth most common cancer in women worldwide [1]. In 2018, 570000 new cases were estimated with 311000 cases of death. 85% of these cases were in low-income countries. Cervical cancer is the second most common cancer in Moroccan females [2]. The management of locally advanced cervical cancer (Ib2-IVA) is based on concomitant chemoradiotherapy and endocavitary brachytherapy [3]. Adjuvant radiotherapy with or without concomitant chemotherapy is indicated whenever there are anatomo-pathological risk factors in the surgical specimen [4]. When brachytherapy is not feasible (non-catheterizable cervix, large residual tumor, patient's refusal...) an additional 20 to 24 Gy by external radiotherapy is an alternative [5]. Conformational radiotherapy has allowed loco-regional control of the disease at the expense of digestive, bladder and hematopoietic toxicity [6]. Concomitant chemotherapy aggravates acute and late grade III and IV toxicity by 34% and 21%, respectively [7]. In the 2000s, Intensity-Modulated RadioTherapy (IMRT) reduced digestive and hematologic toxicity while maintaining a consistent coverage of the planning target volume [8]. Indeed, the study by Roeske et al. (2000) compared the simulation of three-dimensional radiotherapy (3DRT) treatment with that of IMRT treatment. The latter technique allowed a better conformation of the dose prescribed to the PTV and a reduction of 25% to 13% of the volume of the small bowel which received a dose higher than 45 Gy. Moreover, the IMRT increases the OARs volumes that irradiated by low doses and intermediate doses between 15 Gy and 30 Gy [9]. Another study by Lukovic et al. (2016) compared a simulation of IMRT and 3DRT adjuvant therapy in patients undergoing cervical or endometrial tumor. The results were in favor of IMRT by ensuring better compliance with PTV ($p < 0.001$) and a significant decrease in the dose of the OARs mainly the V_{45Gy} of the small bowel ($p = 0.005$) [10]. Comparison of static and dynamic IMRT by Renard et al. (2012) was significantly in favor of VMAT treatment with better coverage of PTV ($p = 0.01$), better intestinal savings ($p = 0.01$) and a reduction in volume receiving 20 Gy ($p < 0.001$). The VMAT also reduced processing time and monitor units ($p = 0.0001$) [8]. The meta-analysis of Wei et al. (2018) analyzed the results of eight studies comparing the dosimetry of arc-therapy and IMRT in patients with locally advanced tumors between 2008 and 2018. Arc-therapy has resulted in better rectal preservation with a decrease in $V_{40\%}$ (SMD = 0.27, 95% CI = -0.49, -0.05), monitor units (SMD = -9.52, 95% CI = -14.49, -14.35) as well as treatment time (SMD = -10.11, 95% CI = -14.16, -5.96) [11].

The first VMAT treatment in North Africa is carried out at Al Kindy Oncology Center in Casablanca, Morocco, since 2011. The treatment of cervical cancer by arc-therapy is performed when the financial means of the patients allow it. After an MRI evaluation at the end of external radiotherapy and when the brachytherapy is deemed not feasible, an additional 20 Gy by arc-therapy is performed. The objective of this study was to compare 50 Gy dosimetry data between conformal and arc-therapy treatments as well as to evaluate

the contribution of 20 Gy supplemental therapy by arc-therapy on both treatment plans.

2. Materials and Methods

The medical records of 20 patients supported for uterine cancer treated exclusively by concomitant chemoradiotherapy without surgery or brachytherapy were selected. The age of the patients was 37 to 74 years with an average of 59.33 years. According to the FIGO 2018 classification, the tumor was classified: IIA = 2 cases, IIB = 4 cases, IIIA = 4 cases, IIIB = 5 cases, IIIC1 = 4 cases and IVA = 1 case. Twelve of the patients studied had a dose of 70 Gy by arc-therapy, the remaining patients had a dose of 50 Gy 3DRT followed by a supplement of 20 Gy arc-therapy treatment. Patients were in a supine position with their arms on their chest, their feet fixed by a footrest and foam under their knees. The bladder was comfortably full and the rectum was empty (3 days of laxatives). A spiral computed tomography (CT) image acquisition in thin-slice scanning with thicknesses of 2.5 mm. The acquisition of the scout scan is acquired between L2-L3 at the top, and 2 cm below the small trochanter at the bottom.

The delineation of the target volumes and organs at risk OAR was the same for both techniques by following the recommendations of ESTRO and ICRU. Gross Tumor Volume (GTV) is clinically defined and by MRI. It includes cervical, vaginal, uterine, parametrial tumor extensions and macroscopically affected lymphadenopathies. The Clinical Target Volumes (CTV) includes in addition to the GTV the whole uterus, the parameters up to the wall and the vagina according to the stage of its invasion. Ganglion CTV includes internal and external iliac areas, obturators and primitive iliac. Pre-sacral ganglion areas are included in CTV if pelvic lymph nodes or parametres are reached, and inguinal areas are taken in CTV if the vagina is invaded in its 1/3 below. The planning target volume PTV1 includes CTV with a margin of 1.5 cm in 3DRT and 1 cm in VMAT. The PTV2 corresponds to the GTV with a margin of 10 mm. The delineated OARs are the rectum, the bladder in its entirety, the femoral heads. The small bowels with the peritoneal cavity is contoured only for series treated by arc-therapy.

The Treatment Planning System (TPS) used for all the treatment plans is Eclipse version 13.5 of Varian Medical System. VMAT arc-therapy consisting of two coplanar arcs from 180.1° to 179.9° and from 179.9° to 180.1° with clockwise and counterclockwise rotation, respectively. Collimator angle was selected between 30 and 45 degrees to cover the entire PTV with photon beam energy of 6MV. The 3DRT planning consisted of the four-field box.

The prescribed dose was 50Gy (25 fractions of 2 Gy) to PTV1 given by 3DRT or by arc-therapy. A supplement of 20 Gy is added to PTV2 by arc-therapy. The primary objective of the constraints was a good coverage of the planning target volumes by 95% reference isodose. Dose constraints for OARs are summarized in Table 1.

OAR	Dose Contraints
Rectum	V_{50} <50%
	V_{60} <15%
Bladder	V_{40} <50%
	V_{65} <50%
Small Bowel	V_{50} <5%
Femoral head	V_{40} <50%

Table 1: OARs dose constraints.

From Dose-Volume Histograms (DVH), we noted for the PTV the $D_{98\%}$, $D_{95\%}$, $D_{50\%}$, $D_{5\%}$, $D_{2\%}$ the $V_{99\%}$ and V_{total}. For the rectum, bladder and small bowel we collected the V_{10Gy}, V_{20Gy}, V_{30Gy}, V_{40Gy}, V_{50Gy}, V_{60Gy} and D_{max}. The femoral heads will be evaluated on V_{15Gy} and D_{max}. The dosimetric values of both techniques were exploited by the IBM SPSS Statistics 25 system.

2.1 Monitoring and toxicity

During radiotherapy, a weekly consultation was conducted to evaluate the toxicity and acute complications of the treatment. Then, at the end of the first series, a clinical examination and an MRI were done. Once the brachytherapy was considered not feasible the 2nd series of radiotherapy was performed. A follow-up consultation was conducted every three months in the first two years and then every six months for five years. An MRI of control was requested at the first consultation then annually.

3. Results

3.1 For the 50 Gy series

The coverage of the planning target volume by 3DRT and VMAT is summarized in Table 2. These results show that there is no difference between these two techniques. For, the homogeneity index was close to 0 (0.068 for 3DRT vs 0.090 for VMAT). As for the conformity index, it tended to 1 (0.99 for 3DRT vs. 0.98 for VMAT) with a slightly significant p = 0.039. For organs at risk, Arc-therapy had reduced the bladder irradiated volumes by doses greater than 50 Gy (p = 0.01). It allowed a better rectal saving concerning volumes V_{30}, V_{40} and V_{50} significantly (Table 3). When with femoral heads, there is no significant difference between conformal radiotherapy and arc-therapy.

PTV Coverage (%)	**RT3D**	**VMAT**	**P Value**
$D_{2\%}$	51,83 ± 0,49	52,42 ± 1,04	0,173
$D_{5\%}$	51,75 ± 0,52	52,16 ± 1,06	0,336
$D_{50\%}$	51,63 ± 3,19	50,44 ± 0,92	0,325
$D_{95\%}$	48,83 ± 0,94	48,31 ± 1,08	0,429
$D_{98\%}$	48,34 ± 0,75	47,40 ± 1,23	0,097
IC	0,990 ± 0,0055	0,98 ± 0,009	0,039
IH	0,068 ± 0,0223	0,09 ± 0,012	0,031

Table 2: Dosimetric comparison of RT3D and VMAT treatment plans of 50 Gy for PTV.

Organs a Risks	**Volume Coverage**	**RT3D-50Gy**	**50 Gy VMAT**	**P Value**
Bladder	**V_{20}**	93,875 ± 17,32	82,85 ± 11,78	0,249
	V_{30}	93,875 ± 17,32	68,378 ± 12,24	0,027
	V_{40}	91,00 ± 17,26	55,725 ± 11,82	0,060
	V_{50}	61,88 ± 29,90	9,33 ± 10,62	0,010
	V_{60}	51,38 ± 2,02	2 ± 0,89	0,845
	D_{max}	93,72 ± 17,27	87,97 ± 6,97	0,587
Rectum	**V_{20}**	94,78 ± 13,79	69,56 ± 11,57	0,021

	V_{30}	86,15 ± 20,56	54,57 ± 13,58	0,018
	V_{40}	45,84 ± 21,03	4,99 ± 6,27	0,020
	V_{50}	50,56 ± 1,49	50,42 ± 1,32	0,915
	V_{60}	16,01 ± 4,51	39,25 ± 12,35	0,217
	D_{max}	50,66 ± 0,39	47,00 ± 5,32	0,636
Femur	V_{15}	93,875 ± 17,32	82,85 ± 11,78	0,249
	D_{max}	93,875 ± 17,32	68,378 ± 12,24	0,027

Table 3: Dosimetric comparison of RT3D and VMAT treatment plans of 50 Gy for OARs.

3.2 For the 70 Gy series

The addition of a 20 Gy complement dose by arc-therapy after 50 Gy by 3DRT allowed PTV2 coverage to be similar to that achieved by arc-therapy alone (Table 4). In addition, this supplement did not bring any significant benefit to the organs at risk. Indeed, the Arc-therapy allowed a better bladder, rectal and small bowels savings with clearly significant p (Table 5).

PTV Coverage (%)	3DRT	VMAT	P Value
$D_{2\%}$	72,84 ± 1,60	72,54 ± 1,35	0,655
$D_{5\%}$	72,52 ± 1,39	72,22 ± 1,36	0,642
$D_{50\%}$	68,92 ± 5,28	70,76 ± 1,18	0,429
$D_{95\%}$	66,37 ± 7,24	68,04 ± 1,33	0,919
$D_{98\%}$	65,63 ± 7,02	67,04 ± 1,80	0,522
IC	0,99 ± 0,005	0,97 ± 0,03	0,134
IH	0,11 ± 0,12	0,07 ± 0,005	0,453

Table 4: Dosimetric comparison of RT3D and VMAT treatment plans of 70 Gy for PTV.

Organs a Risks	Volume Coverage	RT3D-50Gy and VMAT- 20 Gy	70 Gy VMAT	P Value
Bladder	V_{20}	100,00 ± 0,00	99,00 ± 1,41	0,189
	V_{30}	100,00 ± 0,00	85,81 ± 7,30	0,012
	V_{40}	99,85 ± 0,26	73,78 ± 7,9	0,020
	V_{50}	83,82 ± 19,58	62,50 ± 8,80	0,040
	V_{60}	56,52 ± 15,51	30,20 ± 28,63	0,048
	D_{max}	71,84 ± 0,59	70,92 ± 1,40	0,336
Rectum	V_{20}	99,85 ± 0,37	94,78 ± 6,32	0,139
	V_{30}	99,68 ± 0,83	84,95 ± 6,80	0,008
	V_{40}	99,17 ± 1,94	68,58 ± 6,77	0,001
	V_{50}	92,17 ± 7,40	54,16 ± 7,80	0,001

	V_{60}	55,40 ± 9,10	22,50 ± 21,43	0,043
	D_{max}	71,59 ± 0,74	70,34 ± 1,34	0,207
Small Bowel	V_{20}	100,00 ± 0, 00	80,04 ± 15,29	0,043
	V_{30}	100,00 ± 0,00	58,74 ± 15,17	0,004
	V_{40}	98,50 ± 0,10	38,09 ± 11,40	0,001
	V_{50}	78,90 ± 11,02	19,04 ± 8,78	0,009
	V_{60}	11,50 ± 4,90	2,60 ± 4,18	0,038
	D_{max}	62,23 ± 14,7	66,03 ± 5,47	0,175
Femur	V_{15}	30,65 ± 27,9	35,49 ± 19,55	0,754
	D_{max}	61,15 ± 4,25	61,48 ± 5,96	0,818

Table 5: Dosimetric comparison of RT3D and VMAT treatment plans of 70 Gy for OARs.

3.3 Evolutions and toxicities

All patients completed their radiotherapy protocol. No acute complications of grade III or IV were recorded during the first series. A case of cystitis and neutropenia grade III has been reported after 50 Gy in a patient's FIGO stage IVA. The median follow-up after the end of radiotherapy was 45 months. The progression was marked by a locoregional recurrence rate of 30% (25% in the Arc-therapy arm vs 37% in the 3DRT arm) and by a metastasis of 8.33% in the arc-therapy arm. Locoregional and metastatic relapses were more frequent in stage III compared to stage II (46.15% vs 33.33%). A case of chronic grade III cystitis was reported in a patient's FIGO stage IVA. We also recorded a death rate of 30% (25% in the Arc-therapy arm vs 37% in 3DRT arm).

4. Discussions

In a Japanese study, Roeske et al. (2003) compared arc-therapy with 3DRT. This study did not report any significant difference in terms of coverage of the PTV ($D_{95\%}$ = 94.5% vs 95.1% and $D_{98\%}$ = 102.1% vs 102%). For the complement by arc-therapy on the high-risk CTV, it recommended a PTV greater than one centimeter considering the important mobility of the uterus in intra and inter-fractions [12]. Several other studies have confirmed these results [13, 14, 15]. In our series the complement by arc-therapy after 50Gy was done with a 1 cm PTV2 around the high risk CTV. The results found are similar in both arms. They allow a homogeneous coverage and a good conformation of the target volumes.

In our series the complement by external radiotherapy was decided after the end of the 50Gy and consequently it was not possible to deliver on the tumor volume at high risk that 70 Gy in 35 sessions of 2 Gy. This approach does not allow to reach the recommended high-risk CTV doses of 80 to 90 Gy. Indeed, in a purely theoretical approach Guerrerro et al. were able to deliver doses equivalent to 60, 70 and 80 Gy in the tumor with fractions 2.4, 2.8 and 3.2 Gy in 25 sessions taking into account the biological equivalent dose on OARs [16]. Currently, in arc-therapy the Simultaneous Integrated Boost (SIB) is promising that the sequential boost in terms of dose distribution on the target volume ($p < 0.05$) [17].

In a comparative study of the adjuvant treatment of gynecologic cancers by 3D radiotherapy and IMRT (45 to 50.4 Gy), Lukovic et al. (2016) showed that IMRT significantly reduces the volume of all organs at risk [18]. Indeed, the V_{45} was reduced by 77% for the bladder and 63.7% for the rectum. In our study the arc-therapy reduced the V_{50} of the bladder by 85%. For the rectum the contribution of the arc-therapy was largely significant on the DVH by reducing V_{30} by 26.6%, V_{40} by 36.6% and V_{50} by

89%.The results of our study show that after 50 Gy of 3D radiotherapy a 20 Gy supplement by arc-therapy is not as beneficial as the exclusive arc-therapy at 70 Gy. Indeed, the arc-therapy has minimized considerably irradiation of organs at risk. For the small bowel, it reduced toxicity by reducing V_{40} by 61.4%, V_{50} by 75% and V_{60} by 77%. For the bladder and rectum the arc-therapy also reduced the V_{50} and V_{60} by 25 to 46%. Similar results have been published by Portelance et al. [19] regarding the reduction of 30-70% doses to OARs by IMRT compared to conventional radiotherapy.

Grade III gastrointestinal acute toxicity and grade III and IV hematologic toxicities [20] were reported by Dang et al. (2018). It represented respectively 8.1%, 39% and 5.4%. In our series we recorded 5% grade III acute hematologic toxicities. According to published studies, late gastrointestinal toxicity was 3% to 4%. For cystitis grade III, it ranged from 2% to 5.6%. Whereas, for grade III proctitis, it was around 11%. In our study, we recorded only 5% grade III cystitis [21, 22, 23].

5. Conclusion

This work aims to compare dosimetry treatment plans by conformal radiotherapy and arc-therapy for cervical cancer. The results obtained show that the arc-therapy allows a better conformity, coverage and homogeneity of the PTV. It also allows better preservation of organs at risk such as the rectum; bladder and small bowel thus reducing the acute and late toxicities of treatment. Arc-therapy would be a better therapeutic alternative when brachytherapy is not feasible. It could improve the patient's life quality.

Conflicts of Interest

All authors declare no conflict of interest.

Acknowledgements

We would like to thank all the staff of the Oncology and Diagnostic Treatment Center Al Kindy in Casablanca who helped us to realize this Study.

References

1. Organisation mondiale de la sante accélérer l'élimination du cancer du col uterin. OMS (2018).
2. Benider A. Registre du cancer de la région du grand Casablanca pour la période 2008-2012. (2016): 204.
3. Green JA, Kirwan JM, Tierney JF, et al. Survival and concurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix; a systematic review and meta-analysis.The lancet 358 (2000): 781-786.
4. Mancuso S, Smaniotto D, Benedetti Panici P, et al. Phase I-II trial of preoperative chemoradiation in locally advanced cervical carcinoma. Gynecol Oncol 78 (2000): 324-328.
5. Mazeron R, Glimore J, KhodariW, et al. Complement d'irradiation dans le cancer du col de l'uterus localement évolué: curiethérapie utérovaginale ou radiotherapie conformationnelle avec modulation d'intensite? Cancer radiotherapie 15 (2011): 477-483.
6. Key HA, Baidy BN, Stehman FB, et al. Cisplatin radiation and adjuvant hesterectomy compared with radiation and adjuvant hysterectomy for bulky stade IB cervical cancer. N Eng J Med 340 (1999): 1154-1161.
7. Klopp AH, Moughan J, Portance L, et al. Hematologic toxicity in RTOG 0418: a phase 2 study of post operative IMRT for gynecologic cancer. Int J Radiat Oncol Biol Phys 86 (2013): 83-90.
8. Renard OS, Brunaud C, Huger S, et al. Comparaison dosimétrique des radiothérapies comformationnalles avec modulation d'intensité par faisceaux statiques et rapid Arc des cancers du col. Cancer- radiothérapie 16 (2012): 209-214.
9. Roske JC, Lujan A, Rotmmensh J, et al. Intensity modulated whole pelvic radiation therapy in patients

with gynaecologic malignancies. Int J Radiat Oncol Biol Ohys 48 (2000): 1613-1621.

10. Wei B, Kou C, Yu W, et al. Dosimetric comparison of volumetric modulated Arc therapy in patients with cervical cancer: a meta-analysis Onco targets and therapy11 (2018): 7179-7186.
11. Roeske JC, Bonla D, Mell JK, et al. A dosimetric analysis of acuite gastro intestinal toxicite in women receving intensity modulated whole pelvic radiation therapy. Radiother oncol 69 (2003): 201-207.
12. Jadon R, Rombroke CA, Hanna CL, et al. A systematic review of organ motion and image-guided strategies in external beam radiotherapy for cervical cancer. Clin oncol (R Coll Radiol) 26 (2014): 135-196.
13. Chan P, Dinniwell R, Haider MA, et al. Inter and intra fractionnal tumor and organ movement in patients with cervical cancer undergoing radiotherapy: a cinematic-MRI point of interest study. Int J Radiation Oncol Biol Phys 70 (2008): 1507-1515.
14. Lim K, Kelly V, Stewart J, et al. Pelvic radiotherapy for cancer of the cervix. Is what you plan actually what you deliver? Int J Radiation Oncol Biol Phys 74 (2009): 304-312.
15. Guerrero M, Li XA, Ma I, et al. Simultaneous integrated intensity-medulated radiotherapy boost for locally advanced gynaecological cancer: radiobiological and dosimetric considerations. Int J Radiation Oncol Biol Phys 62 (2005): 933-939.
16. Wali L, Helal A, Douwesh R, et al. A dosimetric comparison of Volumetric Modulated Arc Therapy (VMAT) and High Dose Rate (HDR) brachytherapy in localized cervical cancer radiotherapy. J Xray Sci Technol 27 (2019): 473-483.
17. Lukovic J, Patil N, D'souza D, et al. Intensity modulated radiation therapy versus 3D conformal radiotherapy for post-operative gynaecologic cancer: are the coverning the same planning target volume? Cureus 25 janvier 8 (2016): e467.
18. 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 51 (2001): 261-266.
19. Dang MYZ, Li P, Li JP, et al. Efficacy and Toxicity of IMRT-Based Simultaneous Integrated Boost for the Definitive Management of Positive Lymph Nodes in Patients with Cervical Cancer. Journal of Cancer 10 (2019): 1103-1109.
20. Zolciaksiwinska A, Gruszczynska E, Bijok M, et al. Computed Tomography -planned high-dose-rate brachytherapy for treating uterine cervical cancer. Int J Radiat Oncol Biol Phys 96 (2016): 87-92.
21. Koh V, Choo BA, Lee KM, et al. Feasibility study of toxicity outcomes using GEC-ESTRO contouring guidelines on CT based instead of MRI-based planning in locally advanced cervical cancer patients. Brachytherapy 16 (2017): 126-132.
22. Chen CC, Wang L, Lin JC, et al. The prognostic factors for locally advanced cervical cancer patients treated by intensity-modulated radiation therapy with concurrent chemotherapy. J Formos Med Assoc 114 (2015): 231-237.