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CHOICE OF BEAM ENERGY AND DOSIMETRIC IMPLICATIONS FOR RADIATION TREATMENT IN A SUBPOPULATION OF WOMEN WITH LARGE BREASTS IN THE UNITED STATES AND JAPAN

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Abstract—Radiation complications are often related to the dose inhomogeneity (hot spot) in breast tissue treated with conservative therapy, especially for large patients. The effect of photon energy on radiation dose distribution is analyzed to provide guidelines for the selection of beam energy when tangential fields and limited slices are used to treat women with large breasts. Forty-eight patients with chest wall separation > 22 cm were selected for dosimetric analysis. We compared the maximum dose in the central axis (CAX) plane (2D) using 6-, 10-, and 18-MV photon beams in all patients and 3D data set for 16 patients. Correlation between hot spot dose (HSD), separation, breast cup size, breast volume, and body weight was derived with beam energy. Among the 48 patients in this study, HSD > 10% in the CAX plane was noted in 98%, 46%, and 4% of the population when 2D dosimetry was performed; however, with 3D study, it was in 50%, 19%, and 6% of the patients with 6-MV, 10-MV and 18-MV beams, respectively. The chest wall separation, body weight, and breast volume were correlated with the HSD in both the 2D and 3D plans. Patient's bra size was not correlated with the hot spot. The chest wall separation was found to be the most important parameter to correlate with hot spot in tangential breast treatment. Simple guidelines are provided for dose uniformity in breast with respect to chest wall separation, body weight, bra size, and breast volume with tangential field irradiations. © 2006 American Association of Medical Dosimetrists.

Key Words: **Breast cancer, Radiation dose distribution, Hot spot, Beam energy.**

INTRODUCTION

Radiation dose distribution plays an important role in the outcome analysis of the radiation treatment. However, optimum dose distribution cannot be achieved in the majority of the patients who are treated with breast conservative therapy using three-dimensional (3D) planning with low-energy beams. Traditionally, low-energy beams have been used for breast treatment to provide adequate subcutaneous dose.[1] There is a growing trend of obesity in affluent countries, including the United States, which could impact the breast patient population treated with tangential fields. Often, treatment planning for breast cancer is performed on the central axis (CAX) slice only. However, with the availability of computed tomography (CT) simulation, more patients are being planned with 3D data sets, where hot spots in the entire breast tissue can be readily appreciated and an optimized plan can be used for the treatment. Unfortunately, the hot spot cannot be eliminated with simple wedge pair tangential technique for breast treatment. Various techniques such as field-within-a-field, multisegmented fields, and some form of intensity-modulated beams have been developed to reduce hot spots and to provide a uniform dose to the entire breast.[2–9] Intensity-modulated radiation therapy (IMRT) for breast cancer has also been employed. However, for most clinicians, IMRT for breast is still a debatable issue, due to the lack of suitable standardized optimization software and unavailability of long-term outcome data.

It is a known fact that dose uniformity in breast tissue decreases, especially for large breasts. An analysis of the frequency distributions of patients in the United States from patterns-of-care studies (PCS),[10] Japan, and our institutions (Fig. 1) shows fewer Japanese patients who have large breasts, which might impact the dosimetry of the tangential fields, compared to their United States counterparts. The chest wall separation in the Japanese patient population ranged from 14 to 27.5 cm, with a median value of 18.7 cm (Fig. 1). Among Japanese patients, 14% had large chest wall separation more than 22 cm. On the other hand, the chest wall separation in the United States patients' population ranged from 13 to 35 cm, with a median value of 21 cm.[10] A large subset of the patients (40%) treated in the United States is obese, with a chest wall separation in the range of 22–32 cm. The difference between the PCS and our patient population is significant, which could be attributed to the small pool size and the selection of patients in this study.

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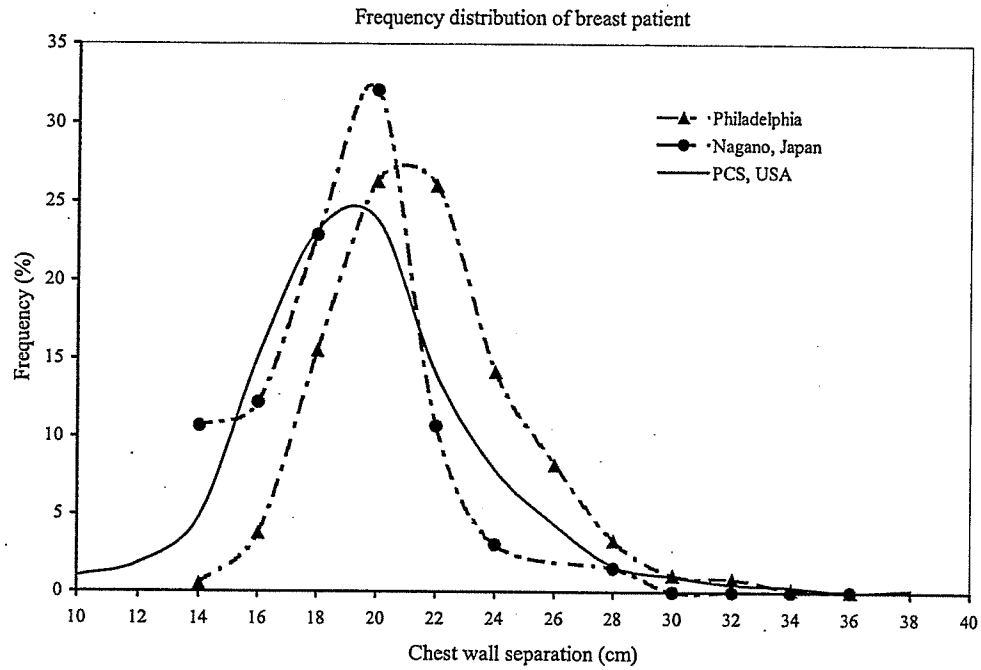

Fig. 1. Frequency distribution of the patient population in our institution, United States, and Japan.

Among the various risk factors associated with poor cosmetic result is breast size, which may indirectly be related to the dose uniformity.[11–20] Most radiation oncologists still favor low-energy photon beams for breast irradiation, although the rationale of such selection for large breasts is not clearly understood. While dose rate and dose uniformity seem to dictate the cosmetic outcome, it is not clear if the underlying issue is related to clinical or physical factors. Das *et al.*[21] reported that chest wall separation is the single most important parameter that is strongly correlated with dose inhomogeneity (hot spot) in tangential breast irradiation. Based on the hot spot criterion,[21] the patients with chest wall separation of more than 22 cm could benefit from treatment using high-energy photon beams degraded with a beam spoiler, to achieve good dose distribution in subcutaneous tissue and to reduce hot spots.[22]

In this study, we investigated the influence of high-energy photon beams on single slice (2D) and multi-slice 3D dose distribution of large-breasted (large chest wall separation) patients who are treated with conservative therapy. Selection of beam energy, in terms of hot spot and various physical parameters, is also presented.

METHODS AND MATERIALS

The chest wall separation was defined as the distance between the midline of the anterior chest wall and the point that was 2 cm below the palpable breast in the CAX plane.[21,23] We reviewed the breast patient population with respect to chest wall separation in Japan and the published data from PCS in the United States[10] for frequency distribution, as shown in Fig. 1. Forty-eight patients with chest wall separation greater than 22 cm in this study were selected from a Unites States population. We measured the chest wall separation in each patient manually or using the CT image in the CAX plane. This data is taken as a sample representation of the population of the breast treatment in Japan and the United States.

This study was performed retrospectively without compromising confidentiality of the patients and hence institutional review board approval was not deemed necessary. All patients were referred for whole breast radiation treatment after breast-conserving surgery. In 32 patients, calculation of dose distribution was performed using the CAX plane alone (2D), and in another 16 patients, calculation of dose distribution was performed using multi-slices (3D) using ROCS treatment planning system (San Diego, CA). Patients were immobilized using Alpha-Cradle and positioned supine with shoulders and elbows flexed and arm overhead. Using a CT simulator, patients were simulated on an inclined board. For 2D patient study, the simulation was performed on a conventional simulator. For 3D study, patients were aligned and positioned to fit through the CT aperture. The chest was carefully palpated to define the borders of the breast, which were marked with thin lead wires. Patients were scanned with 3-mm slice width and 3-mm step size for better digitally-reconstructed radiographs. Each study was transferred to the VoxelQ processor for virtual simulation. A clinical target volume (CTV) was defined on each slice to cover the breast tissue adequately, and the outer contour of CTV was placed on the breast surface. Calculation of breast volume was based on the contours of CTV. Lung volume was also delin-

eated on each slice. The medial border of the radiation field was at the midline of the anterior chest wall, and the lateral border was 2 cm beyond the palpable breast. The upper border was 2 cm beyond the cephalic extent of the palpable breast, and the lower border was 2 cm below the inframammary fold. Medial and lateral tangential fields were set up such that both covered the breast tissue adequately with 2–3 cm of lung tissue.

The posterior beam edge was made coplanar and nondivergent. The reference point of prescribed dose was defined to a point 1.5 cm above the posterior beam edge as described by Das *et al.*[21] Treatment planning was performed to give uniform dose distribution with proper wedge and beam weights for all patients. We compared the maximum dose in the CAX slice using 6-, 10-, and 18-MV photon beams in all 48 patients. ICRU-50[24] has defined hot spot dose (HSD) and maximum dose; however, clinically accepted hot spot[25] area is 2 cm^2, which is used in this study. We analyzed the correlation between hot spot in the CAX plane and such clinical factors as body weight and preoperative bra size, which were gathered from the patient's chart. For the 16 patients with 3D breast planning, we compared the maximum dose in the CAX plane with those in other calculation planes (off-axis +3 cm, +6 cm, +9 cm; cephalus, −3 cm, −6 cm, −9 cm; caudal) with inhomogeneity correction using 6-, 10-, and 18-MV photon beams. We also analyzed the correlation between the maximum dose in multi-slices with various parameters found in the chart such as body weight, preoperative bra size, and breast volume.

RESULTS

2D analysis

Figure 2 shows the hot spot data for a single slice study for 3 energies. Using a 6-MV photon beam, a maximum dose in the CAX plane of more than 10% of the prescribed dose was observed in 98% (47 of 48) of patients. With 10-MV photon beams, it was found in 46% (22 of 48) of patients. When using 18-MV photon beams, it was found only in 4% (2 of 48) of patients. Thus, chest wall separation was strongly correlated with maximum dose in the CAX plane, as shown also by Das *et al.*[21] The HSD was given a functional form with respect to chest wall separation (S).

$$HSD = \alpha S + \beta \quad (1)$$

The α and β are fitted parameters that are shown in Fig. 2 and are noted to be 1.56, 0.99, 0.62, and 78.5%, 84.7%, and 91.4% for the 6-, 10-, and 18-MV beams, respectively. This correlation can be used to predict the HSD in 2D planning. It is shown that ± 5% dose uniformity in breast tissue is hard to achieve with tangential field. The line at the 15% hot spot is drawn to show the choice of energy where such criterion cannot be met.

Body weight of the patient population ranged from 63 to 136 kg, and preoperative bra size ranged from 34B to 41DDD/46D. Body weight was slightly correlated with maximum dose in the CAX plane for all photon energies (Fig. 3). Similar to Eq. (1), HSD can be correlated with body weight with parameters as noted in Fig. 3

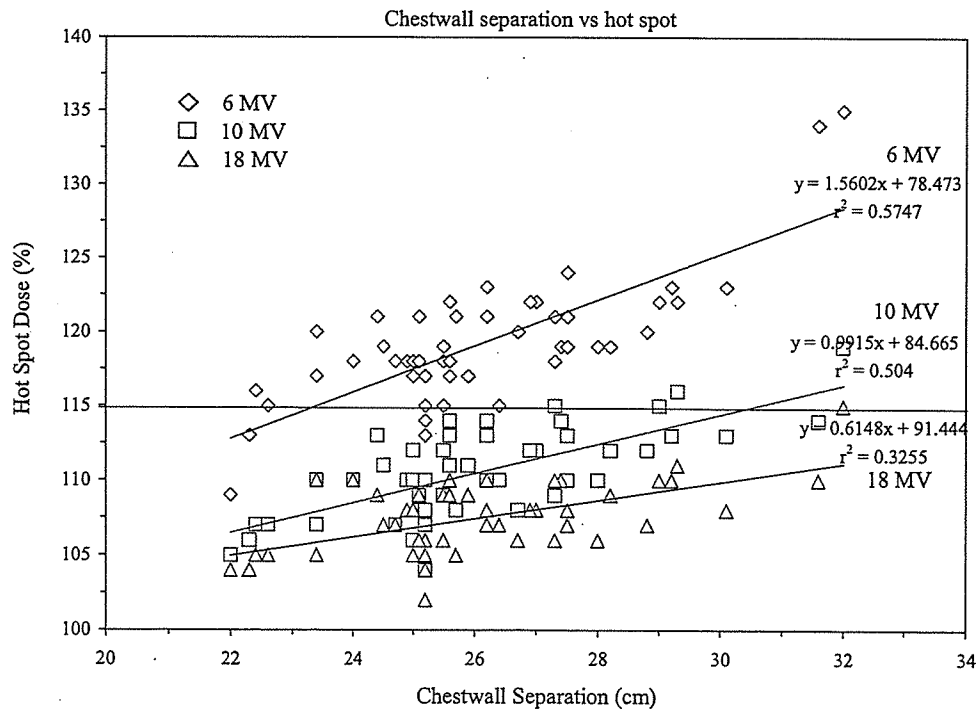

Fig. 2. The maximum HSD (%) at central axis slice vs. chest wall separation with various photon energies. Regression coefficients are also shown.

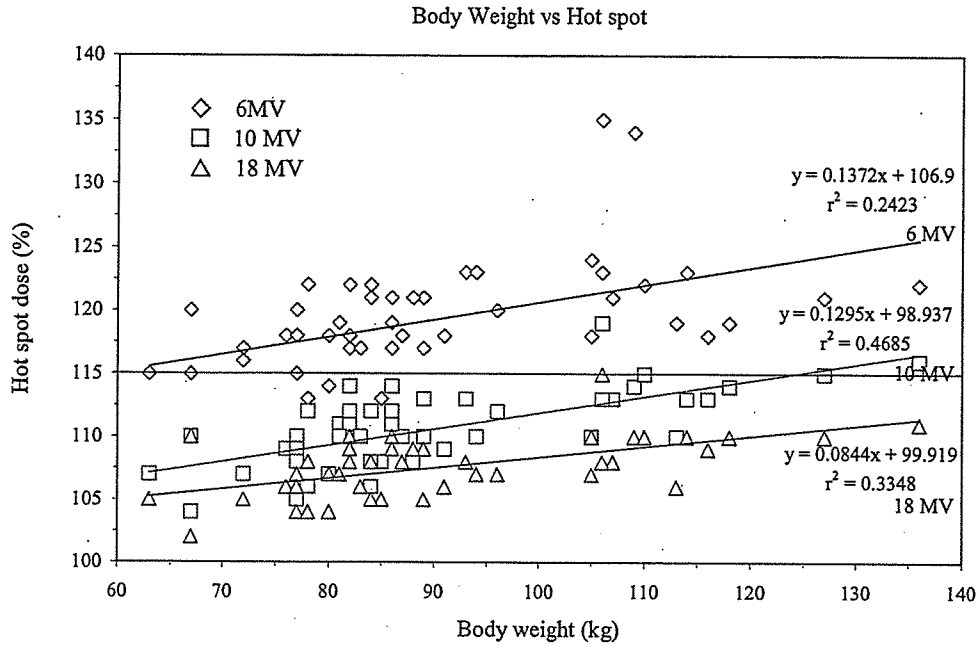

Fig. 3. The correlation between the maximum HSD (%) at central axis slice and body weight. Data with various photon energies and related regressions are shown.

for 6-, 10-, and 18-MV beams, with relatively poor regression coefficient r^2 0.24, 0.47, and 0.33, respectively. These fitted parameters shown in Figs. 2 and 3 are dependent on the accuracy of dose calculation, which varies significantly among various treatment planning systems, as noted by Cheng *et al.*[26] The present data and fitted parameters should be used with caution due to the variability of dose algorithm among the different planning systems. Preoperative bra cup size was not correlated with HSD at the CAX plane using 6-, 10-, or 18-MV photon beams, as shown in Fig. 4, with regression coefficients (r^2) of 0.05, 0.07, and 0.1, for the 6-,

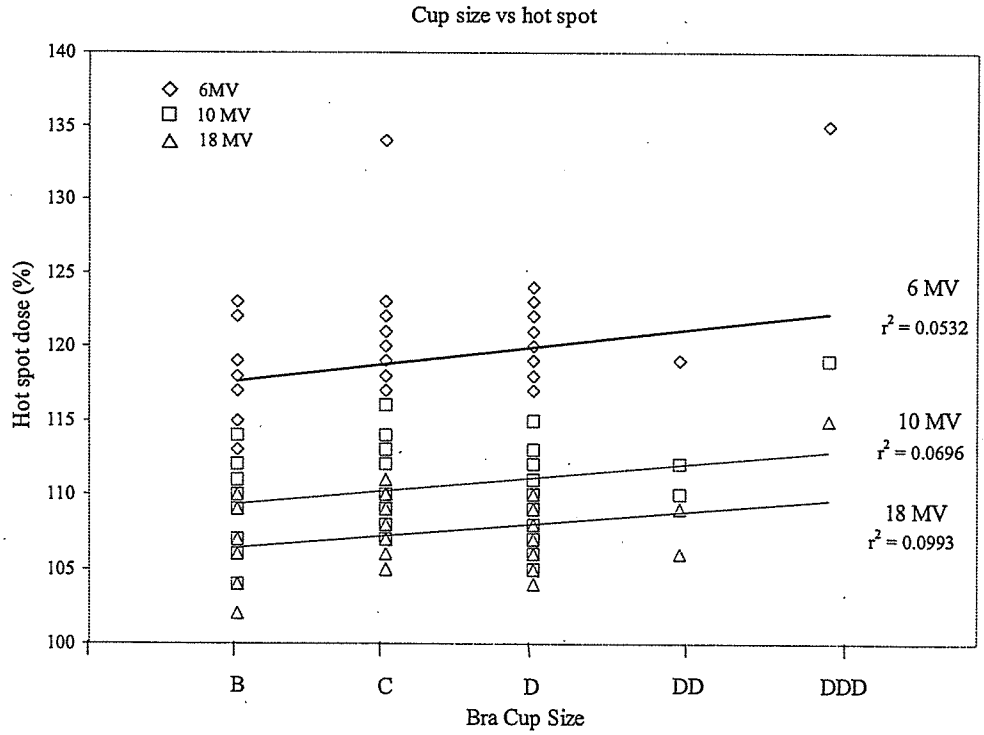

Fig. 4. The maximum HSD (%) at central axis slice plotted against breast cup size and photon energy.

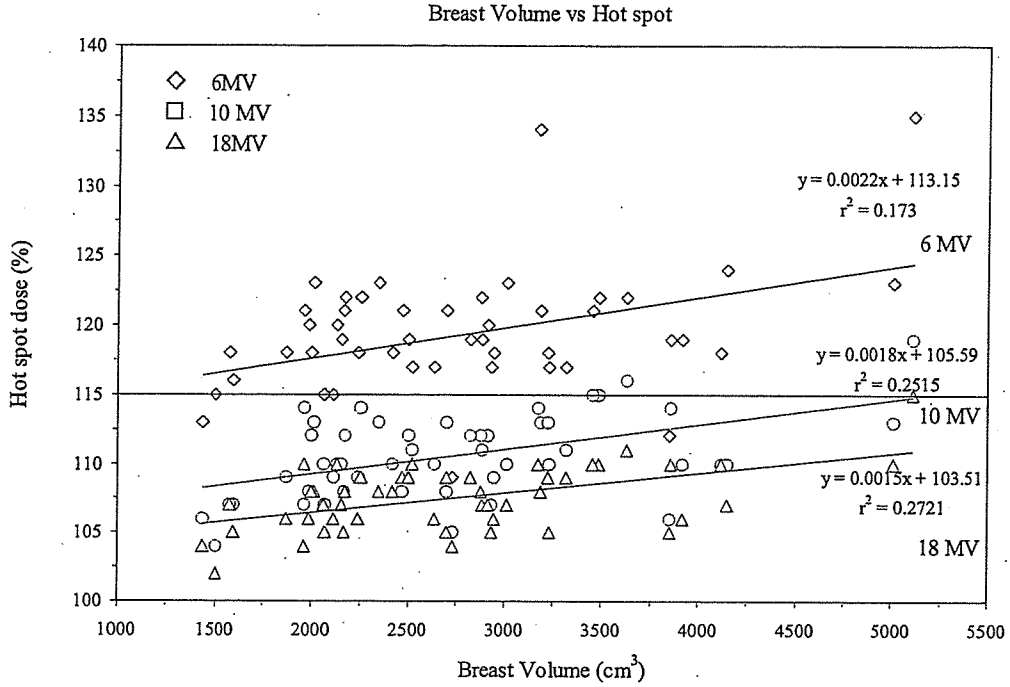

Fig. 5. The maximum HSD (%) vs. breast volume when 3D dose distribution is performed. Note that hot spot reduces with beam energy but increases linearly with breast volume.

10-, and 18-MV x-ray beams, respectively. It is obvious that bra size is a poor measure of the breast parameter and should not be used for quantitative dosimetry and outcome analysis. Although breast volume (breast size) is independent of the chest wall separation, a good correlation was observed in this study. The breast volume was also correlated with the HSD, as shown in Fig. 5, but with relatively weaker r^2.

3D analysis

Evaluation of dose distribution using 3D data set was accomplished in a limited set (16) of patients. The calculated breast volume ranged from 793 cm^3 to 3221 cm^3, and the median volume was 1423 cm^3 in the 3D study, as shown in Table 1. Even though a limited set of slices could provide a general dose distribution, as suggested by Cheng et al,[27] full CT data was used in this study to evaluate the global hot spot with proper inhomogeneity correction.

The correlation between the maximum HSD in 3D between chest wall, body weight, and breast volume was similar to the 2D results, except that the magnitude of the hot spots was higher. This is shown in Fig. 6 with respect to the chest wall separation. The error bar represents the

Table 1. Characteristics of patients for 3D dose calculation

Chest Wall Separation (cm)	Body Weight (kg)	Bra Cup Size	Breast Volume (cm^3)	Difference in HSD in 3D Breast to CAX (%)		
				6 MV	10 MV	18 MV
32.0	106	DDD	3050	6	4	3
24.0	105	DD	3221	3	3	2
24.4	89	DD	1706	10	7	7
27.5	107	D	1454	9	8	7
22.4	72	D	970	4	7	5
24.7	80	B	835	9	8	4
23.4	72	D	1511	10	9	7
22.6	63	D	1113	10	7	6
24.5	81	D	1450	7	6	7
22.0	77	D	1423	14	10	7
25.0	84	D	1685	10	8	7
23.4	67	D	793	9	8	5
24.9	87	D	1490	12	11	10
22.3	78	B	793	17	9	7
25.1	88	D	1174	11	12	8
25.5	91	D	1184	5	1	1

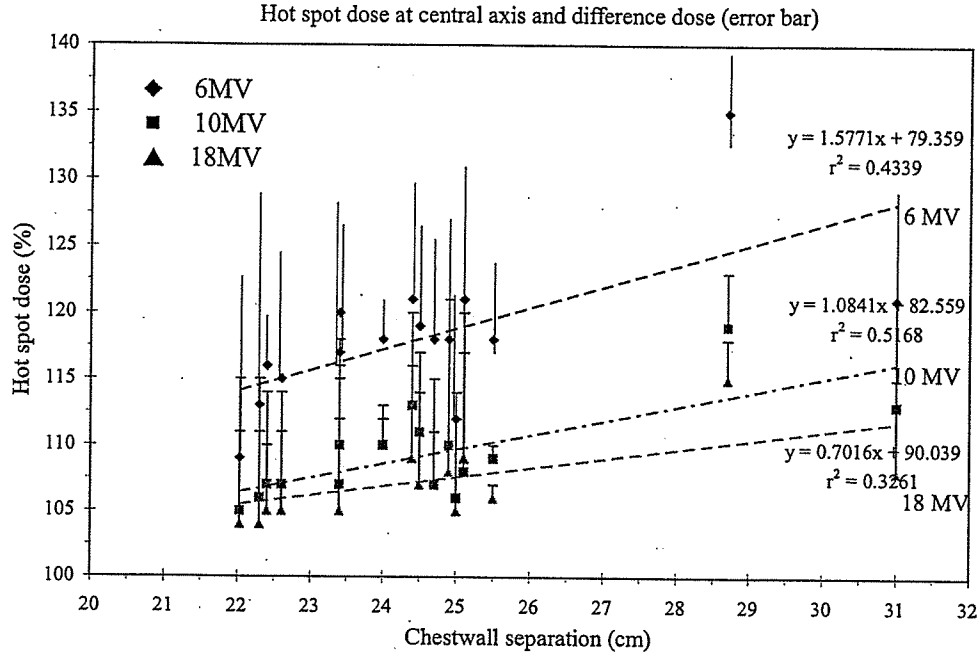

Fig. 6. Plot of HSD vs. chest wall separation when 3D (multi-slice) dose calculation is performed. The error bar indicates the differences in global hot spots to the central axis hot spot for various energies. The fitted parameters and regression coefficients are also noted.

difference in the global hot spot for 3D calculation. Using 6-MV photon beams, the maximum dose (> 10%) in multi-slice calculation was noted in 50% of the patients (Table 1). However, using 10- and 18-MV beams, HSD > 10% was found in only in 19% (3 patients) and 6%, (1 patient), respectively, when 3D multi-slice planning was used. The difference between the maximum dose in the multi-slice planning and that in the 2D planning calculation was not dependent on the chest wall separation, body weight, and preoperative bra cup size and breast volume as shown in Table 1. When 3D data was used, the dose inhomogeneity for 6-MV beam was much greater than that for the 10- and 18-MV photon beams, as noted in Fig. 6. Using 6-MV beams, the maximum dose was seen in the −9 cm or −6 cm plane cranial to the central in 81% (13 of 16) patients. However, with 10- and 18-MV beams, the HSD were seen in the −9-cm or −6-cm plane in 15 patients.

DISCUSSION

Dose uniformity in the target volume is greatly desired within ± 5%. However, with low-energy beams and wide separation of chest wall, often variation up to 15% is clinically tolerated in breast treatment. Dose inhomogeneity in breast tissue has been attributed to the lung correction, size of the breast, and beam energy.[18,21,28] Neal *et al.*[29] reported the positive correlation for breast dose inhomogeneity vs. bra cup size, breast area, and chest wall separation. Incidentally, when women with large breasts are planned and treated, high-energy beam is needed (Figs. 2–4). In our experience, bra cup size was not correlated with hot spots. On the other hand, body weight and breast volume had a weak correlation with dose inhomogeneity, given that we selected patients with large breasts who had chest wall separation of more than 22 cm in this study. The chest wall separation, which is easily acquired for treatment planning, was found to be the most important factor for estimation of dose uniformity in breast treatment.

At some institutions, patients with large breasts are treated with high-energy photon beams to achieve good dose distribution. However, high-energy photon beams reduce the subcutaneous dose because of the buildup phenomenon. Using 3D planning with varying photon energies, Solin *et al.*[30] demonstrated that the use of Cobalt-60 (^{60}Co) was associated with an increase in the magnitude and volume of hot spots, and high-energy photons, such as 10- and 15-MV, were associated with less acceptable target coverage at shallow depths. A Lucite beam spoiler or bolus can overcome the effects of skin sparing of high-energy photon beam.[22,31] Wertheim *et al.*[32] evaluated 1000 mastectomy specimens histologically, and reported that the incidence of skin involvement was uncommon in patients with early breast cancer. Also, Monson *et al.*[1] reported that machine energy less than 8 MV did not significantly affect treatment outcome, such as skin and breast recurrences, without bolus and beam spoiler. They reported skin failures represented less than 1% of failures in each energy, which included 4-, 6-, and 8-MV photon beams. In our institution, high-

energy photon beam with beam spoiler does not seem to lead to high frequency of local recurrence after breast conservative therapy.

Das *et al.*[21] reported that the HSD ranged between 115% and 125% depending on the treatment protocol and breast size, and only 57% of the patient population had hot spots of less than 10% on the central axis plane using 6-MV photon beam. Buchholz *et al.*[33] studied the dose inhomogeneity of off-axis planes for breast cancer, and suggested that in women with large breasts, a significant volume of breast tissue receives both a daily fractionated dose and a total dose of 10% or greater than the prescription dose. It was also noted that the greatest dose inhomogeneity occurred in the lower anatomical quadrants of the breast. Incidentally, our data showed that the greatest dose inhomogeneity was observed in the upper anatomical quadrants, where separation could be significant. The patients in our study were selectively chosen to have large breasts (S > 22 cm), which might have contributed to this difference. With the availability of 3D data sets from CT simulation, such issues are insignificant, because off-axis dose inhomogeneity should be considered in the planning of tumor bed with proper lung correction. Although this study does not provide clinical data for cosmesis or outcome, hot spots play an important role and should be avoided. The radiation outcome could also be dependent on the difference normalization points (dosimetry), fraction size, duration of treatment, the boost technique, surgical techniques, and chemotherapy.

Various studies[27,34] have analyzed the number of CT slices for breast planning; however, a 3D study provides a comprehensive data set to allow determination of global maximum and accurate inhomogeneity correction, as noted by Chin *et al.*[28] The role of 3D treatment planning for breast cancer has become important with the availability of CT data. A single slice (2D) approach for breast planning does not provide adequate knowledge of hot and cold spots, even though limited slices analysis has been suggested.[27] The data presented here could be used to estimate the expected HSD in a central axis slice with various parameters, which may lead to better decision making, either by changing the technique, as suggested by various groups, from supine to prone treatment,[35–38] or by increasing the beam energy. More refined treatment techniques such as the use of proton beams, IMRT, and segmented therapy with low energy have been proposed.[2,3,6–8,39–45] However, for most clinics, such options are not available, and the simple 2D technique is still prevalent.

CONCLUSIONS

A correlation between chest wall separation and HSD (dose heterogeneity) is presented for various photon energies in simple tangential breast treatment (Fig. 2). This correlation provides an easy estimate in selecting beam energy where high-energy photon beams may be useful to achieve good 2D and 3D dose distribution in patients with large breasts. For an acceptable hot spot of 15% in breast tissue, a chest wall separation > 22 cm may require energy higher than 6 MV and for chest wall separation > 28 cm, beam energy higher than 10 MV is needed (Figs. 2 and 3). For the Japanese population, our results show that low-energy beam could still be used for the majority of the patients. Body weight could be a surrogate for the breast size and chest wall separation, which is correlated with the hot spot and beam energy (Fig. 3). Bra size is not correlated with the hot spot and beam energy. A direct relationship is also provided when breast volume is available and maximum dose in breast with respect to beam energy is needed (Fig. 5). To appreciate the magnitude of the hot spot in the entire breast, single-slice approach should be avoided and a 3D dose distribution should be performed to appreciate the dose to the tumor bed and the degree of dose inhomogeneity.

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胃悪性リンパ腫における照射方法の検討

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RADIATION TREATMENT PLANNING FOR GASTRIC LYMPHOMA

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Abstract: Purpose: To examine the methods of radiation treatment planning for gastric lymphoma.
Materials and Methods: Twenty-six patients who underwent radiotherapy for gastric lymphoma between February 2000 and April 2005 were included in the study. Radiation doses were 30–40.5 Gy (median: 30) with a daily fraction size of 1.5 Gy. We considered that the volume irradiated with 20 Gy or more in the bilateral kidneys (K-V20) may be reduced to 50% or less. Anterior-posterior/posterior-anterior parallel-opposed fields (AP/PA) were compared retrospectively with the 4-field technique in 12 patients whose simulation data could be reconstructed in the radiation treatment planning system.
Results: Twenty-four patients were treated with AP/PA, one patient with 4-field and one patient with 3-field. The predefined rules in margin-setting were not observed in 7 patients (27%) to reduce the irradiated volume of the kidney. Twenty-two patients achieved complete remission, and the overall 2-year survival rate was 95%. No late adverse events were seen. Our retrospective comparison of AP/PA with the 4-field technique in the radiation planning system indicated that K-V20 became more than 50% in 4 patients treated with AP/PA, but in none of those treated with the 4-field technique. In all 8 patients with K-V20 of less than 50% with AP/PA, the caudal side of the stomach was located above the mid-slice of the left kidney on abdominal CT.
Conclusion: The outcome of gastric lymphoma after radiotherapy is excellent. When the position of the stomach is low relative to that of the left kidney, the 3D-based 4-field technique may allow realization of optimal radiation therapy ensuring sufficient margins of the target and increased safety for the kidney.

Key words: Gastric Lymphoma, Radiation therapy, Toxicity

はじめに

胃悪性リンパ腫は，消化管原発悪性リンパ腫の中で最も発生頻度が高い．組織型の多くは，いわゆるMALT（mucosa associated lymphoid tissue）リンパ腫，もしくはdiffuse large B-cell lymphoma（DLBCL）であり，過去の報告における両者の発生頻度は，ほぼ同等である[1)-2)]．低悪性度リンパ腫であるMALTリンパ腫と中・高悪性度リンパ腫であるDLBCLでは，異なった治療戦略がとられる．一般に限局期悪性リンパ腫に対する治療においては，化学療法と放射線治療が中心的な役割を担っているが[3)]，限局期胃原発MALTリンパ腫においては，局所療法として手術が行われてきた[4)]．しかし，Helicobacter pyloriの除菌により60～90%の症例で完全寛解を得られることが報告され[5)]，感染例には第一に除菌療法が行われるようになった．また，放射線治療による高い治療効果と安全性が報告され[6)]，除菌無効例，もしくは非感染例においては，放射線治療が有効な治療選択肢の1つとなっている．DLBCLに対しても，化学療法と放射線治療による保存的治療が多く試みられており，良好な成績が報告されている[7)-8)]．胃悪性リンパ腫に対する照射では，現在のところ，胃癌の放射線治療を参考にした照射方法が広く行われており[7)-9)]，X線シミュレータを用いて治療計画を行う前後対向2門照射法が主として用いられてきた．この際，胃の位置が日々異なることや，呼吸性移動などを考慮すると，確実に胃全体を照射野内に収めるためには十分な照射野マージンをつけることが必要であるが，腎臓への線量を考慮すると，十分な照射野マージンをとることが困難であることをしばしば経験する．今回われわれは，過去に行った胃悪性リンパ腫に対する根治的放射線治療における治療成績を検討するとともに，マージンの取り方やリスク臓器との関係を中心に照射野を再検討した．

対象と方法

当院において，2000年2月から2005年4月までに限局期胃原発悪性リンパ腫に対し放射線治療を行った26例を対象とした（Table 1）．Lugano staging system for gastrointestinal lymphomas[10)] に基づいて病期分類を行った．7例には，前治療としてCHOP療法（cyclophosphamide, doxorubicin, vincristine, predonisone）を3～6サイクル（中央値：6）行った．放射線治療は10 MVの超高圧X線を用い，1回線

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Table 1 Patients background

Age		45-80 (median: 69)
Gender		
male		16
Female		10
Stage		
I		21
II_1		5
Histology		
	MALT lymphoma	20
	DLBCL	3
	MALT with DLBCL	3
Chemotherapy		
	CHOP	7

MALT: mucosa associated lymphoid tissue
DLBCL: diffuse large B-cell lymphoma
CHOP: cyclophosphamide, doxorubicin, vincristine, prednisone

量1.5 Gyで総線量30～40.5 Gy（中央値 30）を週 5 回の通常分割法にて投与した．MALTリンパ腫では30 Gyまで，DLBCLでは30 Gyを照射した後，照射野を縮小して総線量40.5 Gyまで投与した．照射野設定においては，空腹の状態で200W／V％の濃度のバリウムを50 ml程度内服し，透視下にて描出された胃全体，および腫大したリンパ節を照射開始時のCTV（clinical target volume）とし，呼吸性移動を加味したITV（internal target volume）に，さらに 2 cmのマージンを付加したものをPTV（planning target volume）とした．縮小照射野においては，化学療法前のgross tumor volumeに呼吸性移動を加味したITVに更に2 cm程度のマージンを付加したものをPTVとした．線量評価点は，中心軸上の体厚中心点，もしくは中心軸上の各ビームの交点とした．両側腎において，20 Gy以上照射される体積の割合（K-V20）が50％を超えないようにし，肝においては，20 Gy以上が照射される体積の割合（L-V20），30 Gy以上が照射される体積の割合（L-V30）がそれぞれ67％，50％を超えないように配慮した[7),11),12)]．各症例において安静吸気ー呼気間の胃角部大弯側，および胃底部の移動距離を調査し，より大きい値をその症例の呼吸性移動とした．空腹の状態で照射するため，朝食前あるいは昼食前に治療を行うようにした．放射線治療開始日を観察開始日とし，あらゆる原因による死亡をイベントとした全生存率をKaplan-Meier法を用いて算出した．算出にはStatView version 5.0（SAS Institute Inc., 米国）を用いた．完全寛解が得られた症例のうち，再び胃病変が出現したもの，および非完全寛解例においては残存病変が再増大したものを局所の再燃と定義した．

次に 3 次元治療計画が行われた12例において，前後対向 1 門照射法と前後左右 4 門照射法をCT治療計画装置上でシミュレーションし，両者の比較を行った．この際CTVはCT画像上の胃全体とし，CTVに 2 cmのマージンを付加し，さらに呼吸性移動として頭尾方向に 1 cmを付加したものをPTVとした．前後対向 2 門照射法，前後左右 4 門照射法，いずれにおいても各ビームの線量配分は均等とした．照射線量は30 Gy / 20回とし，K-V20およびL-V20，L-V30を算出した．CTはスライス厚 2 mmあるいは 5 mmを用いて非呼吸停止下に撮影した．治療計画装置はCadplan version 6.4.7（Varian Medical Systems, 米国）およびEclipse version 6.5（Varian Medical Systems, 米国）を用いた．前後対向二門照射法，前後左右四門照射法におけるK-V20，L-V20，L-V30を算出し比較した．統計学的検定にはStatView version 5.0（SAS institute Inc., 米国）にてStudentのt検定を用いた．

Table 2 Fields and 2-cm margin observation

Applied fields	Observed	Not observed	Total
AP/PA	18	6	24
4 fields	0	1	1
3 fields	1	0	1
Total	19	7	26

AP/PA: anterior-posterior/posterior-anterior parallel-opposed fields

結　果

1．全26例の治療成績

26例中24例で，対向 2 門照射が行われた．また 1 例が 3 門照射，1 例が 4 門照射であった．全症例中 7 例（27％）において 2 cmのマージンを付加できなかった（Table 2）．この 7 例中 5 例において，左腎が右腎よりも照射野に入る容積が多かった．胃の呼吸性移動は4.0～0.7 cm（中央値：2）であった．K-V20が50％を明らかに超えていたと思われる症例は，1 例のみであった．26例中22例（85％）に，照射終了時の判定で完全寛解が得られた．2 例が部分寛解，2 例が治療効果判定不能であった．全症例において，経過観察期間中に重篤な有害事象は見られなかった．2 年全生存率は95％（95％信頼区間：85～100）であった，経過中 2 例に局所の再燃を認め，2 例とも手術が行われた，うち 1 例はその後の経過が不明，もう 1 例は 1 年後に不明死した．

2．前後対向 2 門照射法と前後左右 4 門照射法の比較

前後対向 2 門照射法，前後左右 4 門照射法（Fig. 1）におけるK-V20は，それぞれ13～92％（平均値±SD：40.9±27.0），1～24％（平均値±SD：7.7±6.7）であり，前後左右 4 門照射法において有意に低下した（<0.001）．前後対向 2 門照射法においては，12例中 4 例でK-V20が50％以上となったが，前後左右 4 門照射法においては，全例でK-V20が50％未満となった．前後対向 2 門照射法，前後左右 4 門照射法におけるL-V20は，それぞれ11～47％（平均値±SD：22.2±9.9），6～52％（平均値±SD：26.5±11.9）で

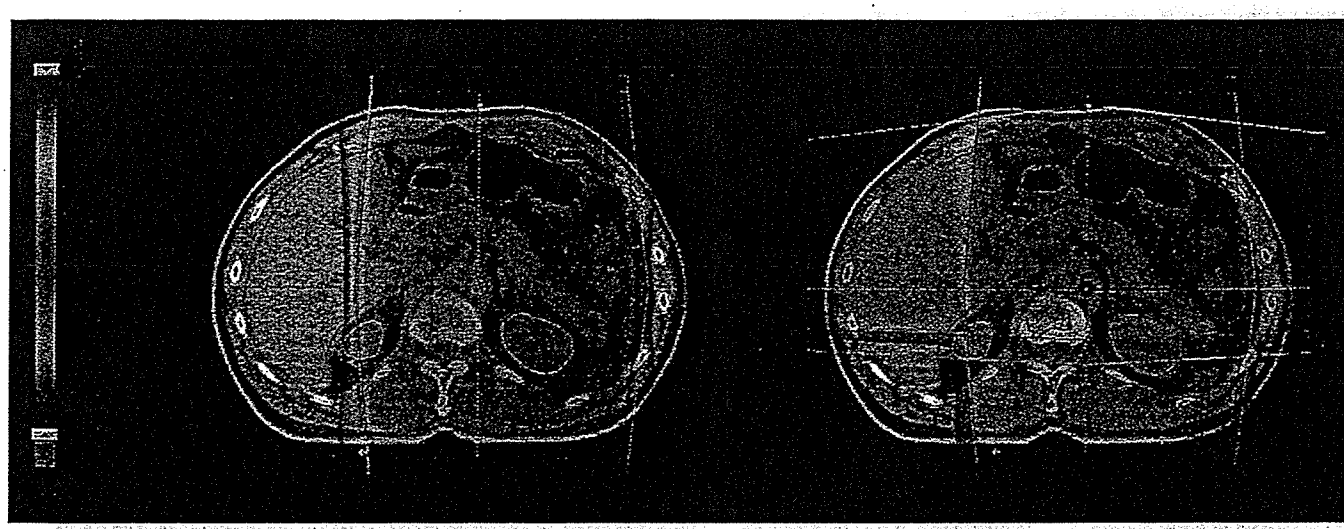

Fig. 1 An example of the dose distributions.
A: Anterior-posterior/posterior-anterior parallel-opposed fields.
B: Anterior-posterior/posterior-anterior/left-right/right-left fields.

あり，前後左右 4 門照射法において有意に上昇した（p=0.03）が，前後左右 4 門照射法におけるL-V20の中で67％を超えるものは見られなかった．前後対向 2 門照射法，前後左右 4 門照射法におけるL-V30は，それぞれ 0～12％（平均値±SD：5.7±3.4），3～17％（平均値±SD：9.3±4.4）であり，前後左右 4 門照射法において有意に上昇した（p=0.002）が，前後左右 4 門照射法におけるL-V20の中で，50％を超えるものは見られなかった（Table 3）．前後対向 2 門照射法にてK-V20が50％未満であった 8 例は，治療計画CTにおける胃の最尾側のスライス位置がいずれも左腎の中央より頭側であったが，K-V20が50％以上であった 4 例中 3 例は尾側に位置していた（Fig. 2）．

考　察

限局期胃原発悪性リンパ腫に対する放射線治療は，良好な治療成績が報告されており，われわれの結果も諸家の報告と同様に良好であった[6),8)]．また，観察期間中に重篤な合併症は生じていなかった．

この治療では，次の二つの条件を満たすことが重要である．それは標的臓器である胃全体に十分な線量を投与すること，リスク臓器への線量が耐容線量を超えないようにすることである．Ishikuraらは，胃原発DLBCLに対する化学放射線療法に関する第 2 相試験において前後対向 2 門照射法を採用しているが，この試験において，腎への線量をプロトコル規定値以下に抑制するため，39％の症例で，標的臓器に付加する照射野マージンに関して規定が遵守されなかったと報告している[7)]．われわれの検討でも，安全性を確保するため予定したマージンを十分付加できなかった症例が少なからず見受けられた．こうした問題に対応するため，3 次元治療計画に基づいた多門照射法が模索されている．Biancaらは，前後対向 2 門照射法におけるPTV内に腎が入る場合，前後左右 4 門照射法を用いることで，胃への十分な線量を保ちながら腎への線量を軽減できると報告している[2)]．われわれが治療計画装置上で行ったretrospectiveな検討においても，前後対向 2 門照射法では1/3 の症例でK-V20が50％以上となったが，前後左右 4 門照射法では，全例でK-V20が50％未満となっており，腎への線量を軽減する手段として，前後左右 4 門照射法は有用であると考える．

しかしながら，前後左右 4 門照射法では照射される肝の体積が増大するという欠点がある．胃原発のMALTリンパ

Table 3 Retrospective comparison of AP/PA and 4 fields in 12 patients on the radiation treatment planning system

Case	AP/PA			4 fields		
	K-V20	L-V20	L-V30	K-V20	L-V20	L-V30
1	15	27	4	7	33	7
2	37	28	12	14	36	17
3	57	17	6	12	21	9
4	13	28	6	7	33	12
5	48	17	5	24	25	13
6	86	11	1	5	15	4
7	34	19	9	1	6	14
8	20	11	3	4	15	6
9	22	47	7	1	52	3
10	52	24	9	5	29	13
11	92	23	0	11	28	7
12	15	15	6	1	25	7

AP/PA: anterior-posterior/posterior-anterior parallel-opposed fields
4—fields: anterior-posterior/posterior-anterior/left-right/right-left fields
K-V20: rate of volume irradiated with 20 Gy or more in the kidneys (%)
L-V20: rate of volume irradiated with 20 Gy or more in the liver (%)
L-V30: rate of volume irradiated with 30 Gy or more in the liver(%)

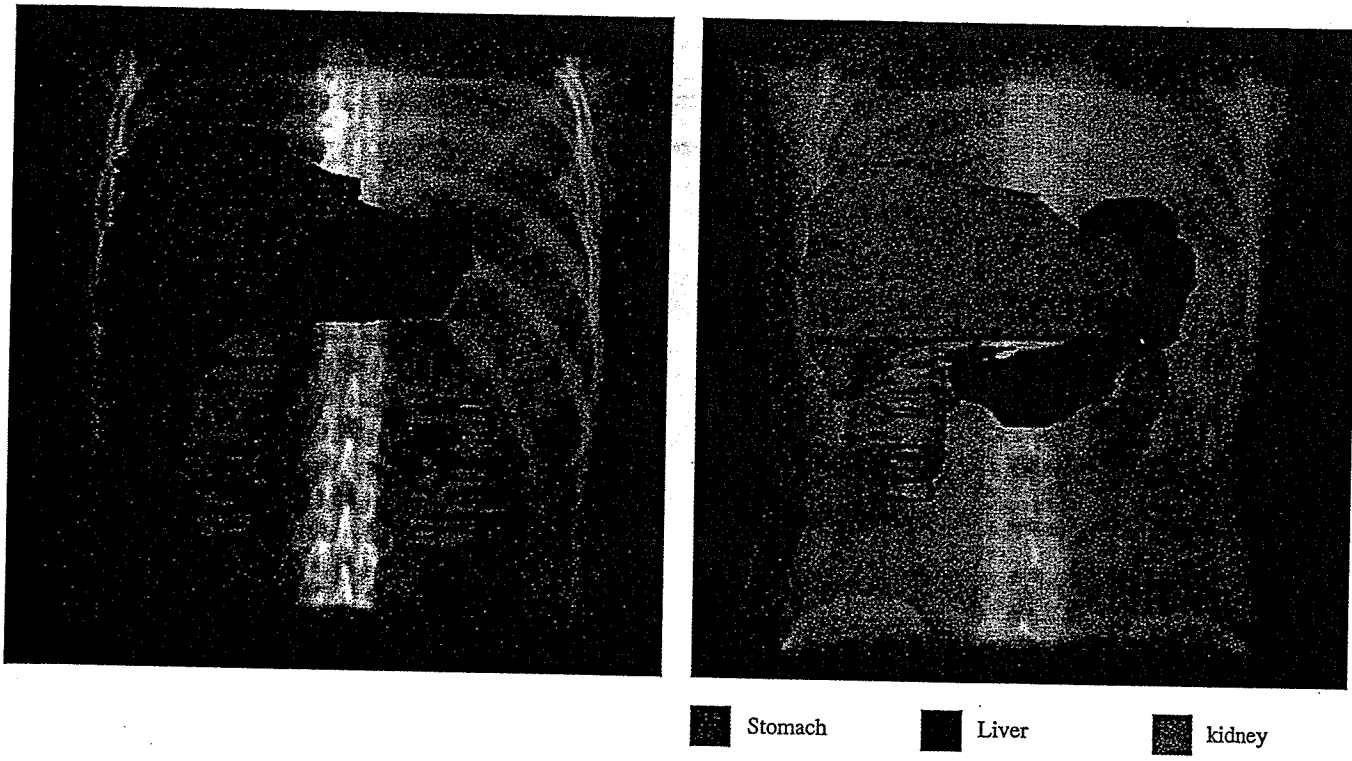

Fig. 2 Examples of the positions of the stomach and the risk organs.
A: The caudal side of the stomach was located above the mid-slice of the left kidney.
B: The caudal side of the stomach was located below the mid-slice of the left kidney.

腫に対する照射線量としては，30 Gy程度が一般的であり[4),12)-14)]，DLBCLの場合は，胃全体に30 Gy程度の照射を行った後に10 Gy程度のboost照射が加えられる[7),8)]．我々の結果からは，前後左右4門照射法を用いて胃全体へ30 Gy程度の照射を行っても，肝への照射線量が耐容線量を超える可能性は低いと考えられた[11)]．

Biancia ら[2)]は，胃と腎の位置関係が照射法を選択するうえにおいて重要であると述べている[2)]．彼らは，胃と腎が前後方向で重ならない場合は前後対向2門照射法を使用し，それ以外の場合は前後左右四門照射法を採用すべきであるとしている[2)]．この場合，前後対向2門照射法で治療される症例はごく一部に限られることになる．われわれの検討結果からは，CT上の胃の最尾側のスライス位置が左腎の中央よりも頭側に存在すれば，前後対向2門照射法でも安全に治療が行える可能性があり，前後対向2門照射法の適応は必ずしも胃と腎が前後方向で重ならない場合に限る必要はないと思われる．現在われわれの施設では，すべての患者で前後対向2門照射法，および前後左右4門照射法の3次元治療計画を作成し，双方のK-V20，L-V20，L-V30を比較して，実際行う照射方法を決定している．

胃に対する照射方法は他にも，さまざまな方法が考案されている．Tsang ら[2)]は，胃の頭側を前後対向2門照射法で，尾側を左右対向2門照射法で照射する方法を提唱しており，これによりリスク臓器である肝および腎への照射線量を低減できるとしている[12)]．

現在のところ，胃悪性リンパ腫に対する最適な照射方法は確立していない．しかし，3次元治療計画装置の発達により，さまざまな方法が実行可能となっている．今後，更なる研究により，胃悪性リンパ腫に対する放射線治療の最適化が望まれる．

結　論

胃悪性リンパ腫における放射線治療後の成績は良好であった．多くの症例では，前後対向2門照射法による対応が可能であったが，腎臓への線量を考慮し，約1/3の症例で照射野マージンの変更や多門照射法などの工夫が必要であった．胃の位置が左腎に対し相対的に低く，前後対向二門照射法が困難である場合，3次元治療計画に基づいた前後左右4門照射法を用いることで，十分なマージンを保ちつつ，腎への合併症を増加させない治療を行える可能性が示唆された．

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要旨：【目的】胃悪性リンパ腫に対する放射線治療後の治療成績を解析するとともに、照射方法を検討する。
【対象と方法】2000年2月から2005年4月までに限局期胃原発悪性リンパ腫にて放射線治療を行った26例を対象とした。放射線治療は一回線量1.5 Gyにて30～40.5 Gy(中央値30)が投与された。両側腎に20 Gy以上が照射される体積の割合(腎V20)が50%以下となるように配慮した。また、3次元治療計画が行われた12例では前後対向2門照射法と前後左右4門照射法を用いた仮想の治療計画を立て、両照射法の腎V20の比較を行った。
【結果】26例中24例に前後対向2門照射、1例に前後左右4門照射、1例に3門照射が行われた。腎への線量を軽減するため、規定した照射野マージンを立てできなかった症例が7例(27%)見られた。照射後観察時に22例が完全寛解し、全症例の2年全生存率は95%であった。臨床的に問題となる晩期有害事象はなかった。3次元治療計画で比較が可能であった12例のうち、前後対向2門法では4例において腎V20が50%以上となったが、前後左右4門法においては全例で腎V20が50%未満となった。また、前後対向2門法で腎V20が50%未満であった8例は、治療計画CTにおける胃の尾側の大彎の位置がいずれも左腎の中央よりも頭側であった。
【結論】放射線治療後の成績は良好であった。胃の位置が左腎の位置に対し相対的に低い場合、前後左右4門法を用いることで十分な照射野マージンを保ちつつ、腎への線量を軽減した治療が可能と考えられた。

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Initial Experience with the Quality Assurance Program of Radiation Therapy on behalf of Japan Radiation Oncology Group (JAROG)

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Background: We evaluated the efficacy of our quality assurance (QA) program of radiation therapy (RT) in a prospective phase II study. This is the first description of the experience of the Japan Radiation Oncology Group (JAROG) with this program.
Methods: Clinical records, all diagnostic radiological films or color photos that depicted the extent of disease of 37 patients with stage IEA extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) were collected for review. Radiation therapy charts, simulation films or digitally reconstructed radiographs, portal films and isodose distributions at the central axis plan were also reviewed. All documents were digitally processed, mounted on Microsoft PowerPoint, and for security returned from researchers by mail in CD-ROM format. The QA committee members reviewed all documents centrally, utilizing the slide show functionality.
Results: All patients were prescribed their specified dose to the dose specification point in accordance with the protocol. Three patients were regarded as deviations, because of a smaller margin than that specified in the protocol ($n = 2$) or a prolonged overall treatment time ($n = 1$). No violations were observed in this study.
Conclusions: This is the first report with regard to the QA program in MALT lymphoma. We demonstrated that our QA program was simple and inexpensive. We also confirmed that the radiation oncologists in Japan adhered closely to the protocol guidelines.

Key words: MALT lymphoma – quality assurance – QA program – radiation therapy

INTRODUCTION

It has been estimated that about 170 thousand cancer patients will be treated with radiation therapy (RT) either as part of their primary treatment or in connection with recurrences or palliation in 2005 in Japan (1). It is anticipated that RT will play an increasingly important role because of the improvements of early detection of and screening for cancer. Furthermore, other factors will also prompt the use of RT: the trend toward less drastic organ-conserving surgery combined with adjuvant RT; the improvement in identification of patients with high risk of developing loco-regional recurrences following surgery; and the aging population of Japan. It is undeniable that the deleterious consequences of poor quality treatment contribute not only to the rise of complications but also to deterioration of outcomes. They also lead to both an increase in health care costs and a decrease in the

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quality of life. Thus, it has long been recognized that quality assurance (QA) in RT is vital to guarantee provision of safe and effective treatments (2–12).

The Radiation Therapy Oncology Group (RTOG) and European Organisation for Research and Treatment of Cancer (EORTC) are the two largest working organizations presenting the models for the application of valid QA procedures in radiation oncology trials. Both organizations have funding for centralized data collection, inter-institutional dosimetry programs and regular site visits, utilizing medical, dosimetric and physics staff. For the data to be useful with regard to RT, a rigorous review process must be implemented to document the radiation used, volume irradiated, fraction size and dose delivered to comply with the designated therapeutic protocol. This is the most accurate way to confirm the uniformity of the treatment and usefulness of the outcome data.

The Japan Radiation Oncology Group (JAROG) conducted a QA program to guarantee the treatment quality of RT in a phase II study. This study evaluated the efficacy and toxicity of moderate dose RT for patients with extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma). In pursuing the project, the JAROG were faced with a difficult situation in order to ensure that the clinical and technical compliance to the specified protocol was satisfactory, without having the financial, structural or personnel resources to conduct a comprehensive clinical QA program. Thus, we developed a simple and less expensive computer based method to easily execute our QA program.

Our QA program was based on a central radiation oncological review of all patients' diagnostic imaging, color photographs and clinical findings. Additionally, an individual RT prescription for every patient was provided. All of these documents were digitally processed, and were mailed to researchers in CD-ROM format. The purpose of the present study was to assess the feasibility of such a procedure in multicenter trials and its impact on the definition of the extent of disease and patients' treatment among Japanese radiation oncologists. This is the first report describing the QA program in MALT lymphoma.

METHODS

Study Design

From April 2002 to November 2004, 37 eligible patients with stage IEA MALT lymphoma received RT. The protocol specified three different total doses of RT, which were dependent on the tumor location and its maximum diameter. Patients with orbital disease or those who had minimal residual disease after surgical removal received 30.6 Gy. Patients with tumors that were less than 6 cm received RT with 36 Gy, and those with $\geq$ 6 cm of disease were treated with 39.6 Gy. A fraction size was 1.8 Gy in every setting. The clinical target volume (CTV) was defined as an entire involved organ (orbit, thyroid, salivary gland, breast) or gross tumor volume (GTV) with a margin of at least 20 mm. We did not intend to treat the adjacent first echelon lymph node region. A lens shield was placed to prevent this except where the block compromised tumor coverage. Radiation doses were specified according to the report of ICRU 50. In electron beam therapy, doses were specified at the peak dose on the beam axis reached.

Procedure of Quality Assurance Program

Clinical records, all diagnostic radiological films or color photos that depicted the extent of disease of all patients were collected for review. Radiation therapy charts, simulation films or digitally reconstructed radiographs, and portal films were reviewed. In cases of patients who received electron beam RT, color photos demonstrating the treatment position in the treatment room were assessed. The isodose distributions at the central axis were also submitted for review. In addition to the evaluation of adherence of the protocol, an evaluation of the response assessment was examined by reviewing the clinical records, diagnostic radiological films and color photos. All documents were digitally processed, and mounted using Microsoft PowerPoint. Each researcher de-identified all materials before submission. Afterwards, each researcher returned the data via a CD-ROM, and the QA committee member reviewed it using the slide show functionality. The patient data was not delivered via the internet for reasons of security. Figure 1 shows an example of the PowerPoint template.

Our QA programs included evaluation of the fraction size, the elapsed days, the prescribed dose to the reference point, the relationship between GTV, CTV and radiation field, and the difference between simulation film and portal film. The isodose distributions were also examined as reference data.

Definition of Protocol Violations and Protocol Deviations

Protocol violations were defined as a fractional dose less than 1.5 Gy, a total dose to the reference point either $<$90% or $>$110% of the dose prescribed in the protocol, the incomplete coverage of GTV, and more than 1 cm of difference between simulation film and portal film. In addition, protocol deviations were defined as an overall treatment time either $<$three weeks or $\geq$six weeks, the difference between simulation film and portal film $>$5 mm, the field border $<$20 mm away from CTV, and a dose to the reference point either $<$95% or $>$105% of the dose prescribed in the protocol.

RESULTS

We held the QA committee meeting on 19 March 2005. There were no missing data for any patients, and all documents were of adequate quality for review. Table 1 shows the relationship between the RT technique and primary site.

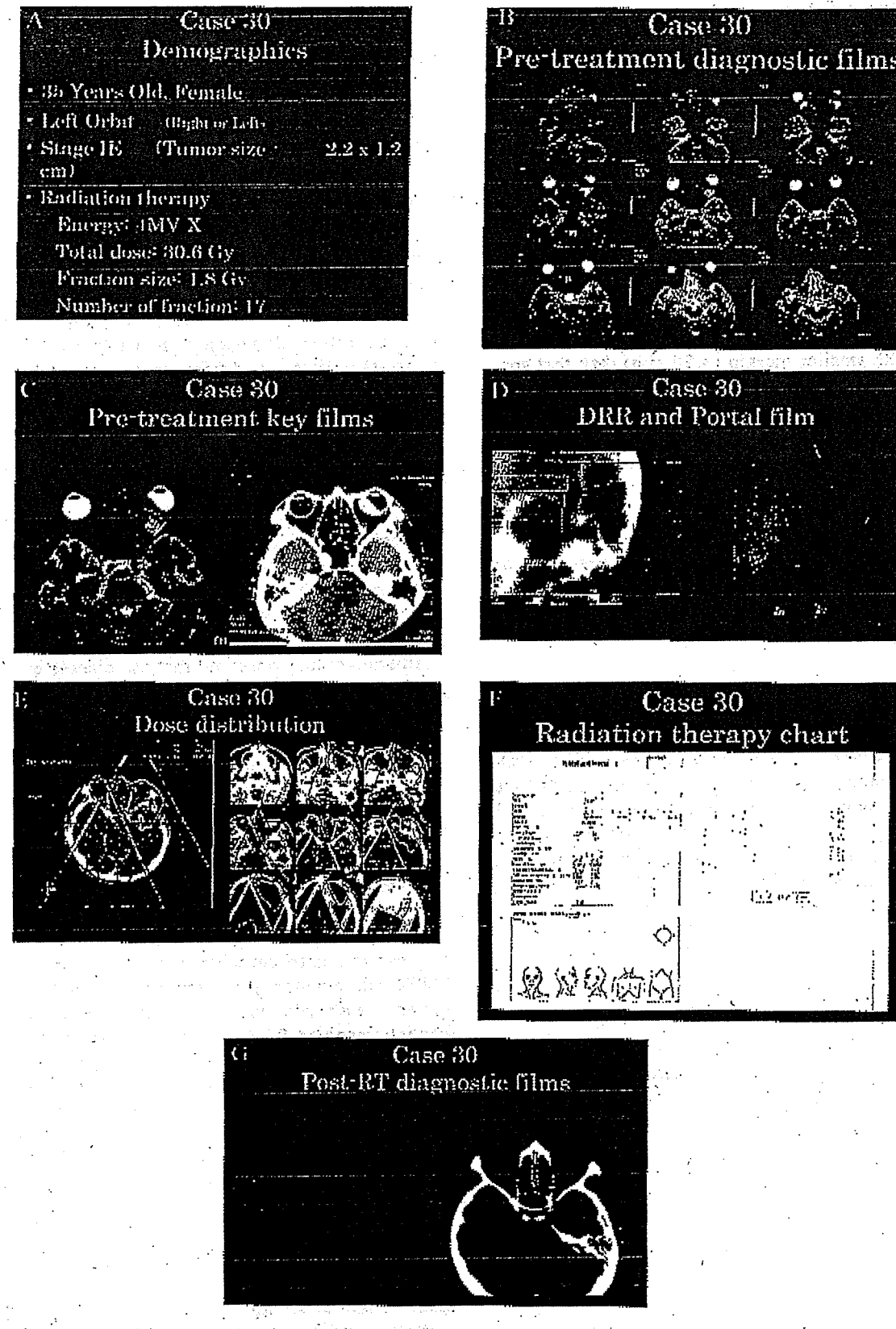

Figure 1. Examples are shown of the types of data that were used in this template. (A) a patient demographics, (B) pretreatment diagnostic films, (C) pretreatment key films, (D) digitally reconstructed radiograph (DRR) and portal film, (E) dose object, (F) radiation therapy chart, and (G) post treatment diagnostic films. The original documentation was written in Japanese. (Please note that a colour version of this figure is available as supplementary data at http://www.ijco.oxfordjournals.org).

The most common field arrangement was a single anterior–posterior field (41% of patients), and two oblique fields follow (30%). Two anterior–posterior or lateral opposing field techniques were employed in nine patients (24%). No patient received RT with a 3D conformal technique or intensity modulated radiation therapy (IMRT). All patients were prescribed their specified dose to the dose specification point in accordance with the protocol. No patients received RT with a fraction size other than 1.8 Gy. Only one patient required an overall treatment time more than 6 weeks, which was defined as deviation. The cause of this prolonged treatment time was merely personal. Adequate tumor coverage was achieved in 95% of the patients. Although CTV was covered enough in the treatment volume, the field border was placed with smaller margin (<20 mm) than that specified in the protocol in the remaining two patients. These two cases were defined as deviations. The isodose distributions at the central axis plan were acceptable in all patients. Overall, deviations were observed in three patients and the QA committee concluded that 92% of patients received RT as specified by the protocol. No protocol violations were observed in this study.

Because all documents were digitally processed in this study, the cost per patient, including CD-ROM and postage, was about ¥150 (i.e. about US$1.30). It took about an hour to prepare each patient data for review.

DISCUSSION

This report described our initial experience with a QA program in a multi-institutional prospective study. Our program is very simple and inexpensive. Ishikura et al. (13) investigated the quality of RT in a Japanese clinical trial and found that 60% of patients received less satisfactory RT in 2001. They extended their research to 2005 and demonstrated that protocol violation decreased dramatically to less than 5%. The early RTOG study also showed that the frequency of major and minor deviation was as high as between 60 and 70%. They reported that the appropriateness rate rose over time, because the participating radiation oncologists became familiar with the protocol (2). The Trans-Tasman Radiation Oncology Group (TROG) also demonstrated an improvement in QA over time (14). Our observation that 92% of patients received RT per protocol specification was very promising for the initial QA experience. In addition to the decrease of protocol violation over time, Halperin et al. (15) reported that institutional experiences affected the incidence of major deviations. RTOG also found that the QA performance was significantly better at principal centers compared with satellites. We were not able to assess institutional difference, because only three patients were judged as being a violation of protocol guidelines.

It has long been realized that the quality of treatment seriously affects the outcome of clinical trials. Several groups have evaluated the relationship between violation and staging, treatment strategies, and outcome. The German Hodgkin's Study Group (GHSG) evaluated the quality of RT for early stage HL (Hodgkin's lymphoma) and found that freedom from treatment failure (FFTF) was significantly influenced by the quality of RT. Those who received RT as per protocol obtained 82% of FFTF, and those with violation demonstrated only 70% of FFTF after five years (16). Furthermore, they observed that the disease extent recorded on the case report forms was significantly different from that shown on diagnostic CT, which resulted in a change of disease stage, treatment group allocations, and treatment volume (17,18). As these misinterpretations lead to protocol violations, they recommended an early central prospective review. Dieckmann and colleagues (19) also concluded that an up-front centralized review of patient data and consecutive set-up and delivery of individualized treatment proposals for every patient are feasible within a large multicenter trial involving pediatric HL.

However, two groups have concluded that violation did not lead to a detrimental treatment outcome. The EORTC 20884 trial evaluating the efficacy of involved field RT in patients with advanced HL demonstrated that 47% of patients received RT with major violation (20). However, their conclusion was that the outcome was not influenced by violation of the radiotherapy protocol. In another multicenter trial involving pediatric medulloblastoma, 57% of the fully evaluable patients had one or more major deviations in their treatment schedule (21). Major deviations regarding the treatment site were also found in more than 40% of patients. Despite these high major deviation rates, underdosage or geographical misses were not associated with a worse outcome. Although these two groups did not demonstrate a relationship between violation and treatment outcome, it is assumed that these high violation rates make it difficult to correctly understand the true message of clinical trials. With respect to violation rates, our present trial was satisfactory and the outcome data are robust.

Table 1. Primary site and RT technique

Primary site	RT technique			
	AP	Oblique	Opposing field	Others
Orbit	15	6	3	0
Thyroid	0	3	1	0
Salivary gland	0	2	2	0
Waldeyer's ring	0	0	2	0
Prostate	0	0	0	1
Lung	0	0	0	1
Cecum	0	0	1	0
Total	15	11	9	2

RT, radiation therapy; AP, single anterior-posterior field; Opposing field, two anterior-posterior or lateral opposing field techniques.

Advances in imaging and other technology have enhanced our ability to create complete anatomic and functional 3D data for each patient that facilitates the use of advanced technology RT delivery tools, including 3D conformal RT, intensity modulated RT, stereotactic RT and radiosurgery, and image-guided RT. Implementing these advanced technologies safely in clinical practice will require innovative and efficient methodologies for clinical QA. For example, Palta et al. (22) introduced the new web-based QA program to allow the rapid peer review of radiotherapy data through a simple personal computer-based web browser. RTOG has already developed a web-based QA program, and EORTC will also adopt a similar system to facilitate their QA program.

This is the first report that evaluates the QA program in MALT lymphoma. The technical deviation rate, technical data quality and completeness of this phase II trial were acceptable, and in addition our QA procedures were inexpensive and not time consuming. Furthermore, in multi-institutional studies, this analysis continues to lend credence to efforts related to QA for RT.

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Conflict of interest statement

None declared.

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CLINICAL INVESTIGATION **Cervix**

MULTI-INSTITUTIONAL STUDY OF RADIATION THERAPY FOR ISOLATED PARA-AORTIC LYMPH NODE RECURRENCE IN UTERINE CERVICAL CARCINOMA: 84 SUBJECTS OF A POPULATION OF MORE THAN 5,000

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Purpose: Most patients who had any recurrent sites of cancer have been considered to be in their last stage of life. However, recent advances of clinical research reveal some patients achieve long-term survival even in recurrence. Furthermore, for patients who had only one recurrent region, radiation therapy could play an important role. As for uterine cervical carcinoma, the most common recurrent site other than the pelvis is the para-aortic lymph nodes. Thus we conducted the current study.

Patients and Methods: Between 1994 and 2003, more than 5,000 uterine cervical carcinoma patients were treated with curative intended treatments at 13 Japanese hospitals. Of these patients, 84 developed para-aortic lymph node recurrence as the only site of initial tumor progression. These patients were treated with external beam radiation therapy. Radiation therapy protocol was as follows: 1.7–2.0 Gy per fraction, 5 fractions per week, and the mean total dose was 50.8 Gy (25–60 Gy).

Results: Three- and 5-year overall survival rates of all patients were 49.5% and 31.3%, respectively. Stratified by symptom sign, 3-year overall survival rate of symptom positive was 27.6% and those of the negative was 56.1% ($p = 0.018$). Three-year overall survival rates of the total dose ≥51 Gy and that of ≤50 Gy were 58.0% and 42.8%, respectively ($p = 0.07$). As for morbidity, no patients received Grade 3 or greater late toxicity.

Conclusions: The current study suggested that radiation therapy for isolated para-aortic lymph node recurrence in uterine cervical carcinoma could have a significant impact on survival. © 2006 Elsevier Inc.

Uterine cervical carcinoma, Isolated para-aortic lymph node recurrence, Radiation therapy, Oligo-recurrence.

INTRODUCTION

Most patients who have any recurrent sites of cancer are considered to be in their last stage of life. However, recent advances of clinical research reveal some patients achieve long-term survival even with recurrent cancers, a term we first defined as oligo-recurrence in our previous study (1). Furthermore, for patients who have only one recurrent region, radiation therapy could play an important role.

As for uterine cervical carcinoma, the most common

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recurrent site other than pelvis is the para-aortic lymph nodes. Furthermore, improvement of diagnostic imaging enables us to detect more frequently isolated para-aortic lymph node recurrence. In Japan, the largest population-based study of the frequency of isolated para-aortic lymph node recurrence in patients with uterine cervical carcinoma has been recently reported (1). Sixty-seven patients of 3,137 uterine cervical carcinoma (Stage Ia-IVa) treated with curative treatment have recurred in isolated para-aortic lymph node regions (2.1%). Moreover, Singh *et al.* recently reported that isolated para-aortic lymph node recurrence in uterine cervical carcinoma treated with concurrent chemoradiotherapy achieved 100% of 5-year survival according to Kaplan-Meier method, although this study consisted of only 7 patients, and only 1 patient achieved actual 5-year survival (2). Regions in Asia have the highest incidence of uterine cervical carcinoma. Kim *et al.* in Korea recently reported that 3-year overall survival rate of isolated para-aortic lymph node recurrence in uterine cervical carcinoma patients treated with hyperfractionated radiation therapy totaling 60 Gy combined with concurrent chemotherapy was 19% (3). Chou *et al.* in Taiwan reported that the 5-year survival rate for isolated para-aortic lymph node recurrence treated with concurrent chemoradiotherapy was 51.2% (4). Hong *et al.* in Taiwan reported 34% of 5-year survival (5). In Japan, 38% of 5-year survival was reported for these patients treated by radiation therapy or radiation therapy combined with chemotherapy (6).

However, no studies such as these have been performed on a large population. Thus we conducted a multi-institutional study for isolated para-aortic lymph node recurrence in uterine cervical carcinoma of a population of more than 5,000.

Table 1. Patient characteristics

Mean age	
at the initial treatment	54.8 years (25–80 years)
at the recurrence	56.4 years (26–81 years)
Histopathology	
SCC	74
Adenocarcinoma	5
Adenosquamous cell carcinoma	5
Clinical stage at the initial treatment	
Ia	0
Ib	16
IIa	3
IIb	15
IIIa	1
IIIb	42
IVa	7
The mean serum SCC level	
at the initial treatment	17.8 ng/dL (0.5–100 ng/dL)
at the recurrence	7.0 ng/dL (0.4–92.8 ng/dL)
Symptom	
None	66
Lumbago	12
Edema of lower extremities	4
Pain of lower extremities	2

Abbreviation: SCC = squamous cell carcinoma.

Table 2. Treatment characteristics

Initial treatment	
Radiation therapy alone (combination of external beam radiation therapy with intracavitary irradiation)	42
Chemoradiotherapy (radiation therapy as above)	16
Surgery with radiation therapy	11
Surgery with chemoradiotherapy	6
Surgery alone	9
Mean total dose for isolated PAN	50.8 Gy (25–61 Gy)
Chemotherapy regimens	
BOMP	8
UFT	8
CDDP	5
Others	11

Abbreviations: PAN = para-aortic lymph node recurrence; BOMP = bleomycin, Oncovin, mitomycin C, cisplatin; UFT = uracil-tegafur; CDDP = cisplatin.

PATIENTS AND METHODS

More than 5,000 uterine cervical carcinoma patients (Ia-Iva) were treated with curative treatment such as surgery, radiation therapy, or a combination of these treatments in 13 major Japanese hospitals. Of these, 84 patients, who recurred in isolated para-aortic lymph node, were treated with radiation therapy for para-aortic regions between 1994 and 2003. These patients are analyzed in the current study. Patient characteristics are listed in Table 1. The mean age at the initial treatment (pelvis) was 54.8 years (range, 25–80 years). On the other hand, the mean age at the isolated para-aortic recurrence was 56.4 years (range, 26–81 years). The mean duration time was 22.0 months (range, 1–103 months). The clinical stage at the initial treatment was as follows: 0 were Stage Ia, 16 were Stage Ib, 3 were Stage IIa, 15 were Stage IIb, 1 was Stage IIIa, 42 were Stage IIIb, and 7 were Stage IVa. The mean serum squamous cell carcinoma (SCC) antigen level at

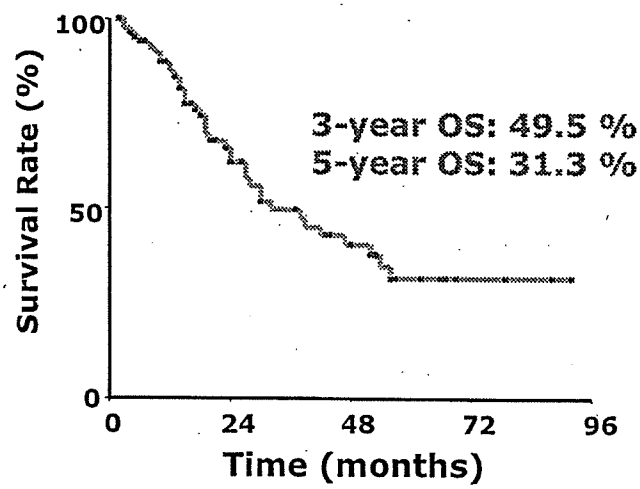

Fig. 1. Overall survival (OS) curve of all patients is demonstrated. Five-year overall survival of all patients was 31.3%.