Matsuo Y, Onishi H, Nakagawa, Nakamura M,Ariji T, Kumazaki Y, Shinbo M, Tohyama, Nishio T, Okumura M, Shirato H and Hiraoka M.	Guidelines for respiratory motion management in radiation therapy.	Journal of Radiation Research	13	1-8	2012

Stereotactic Body Radiation Therapy for Stage I Non-small Cell Lung Cancer Patients with Chronic Respiratory Insufficiency Requiring Domiciliary Oxygen Therapy

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Abstract. *Background: The efficacy of stereotactic body radiation therapy (SBRT) for patients treated with domiciliary oxygen therapy is not well-known. Patients and Methods: We collected the clinical records of 15 patients with chronic respiratory insufficiency requiring domiciliary oxygen therapy at 1-3 l/min who were treated with SBRT for stage I non-small cell lung cancer. All patients were fixed with a thermoplastic body cast system. SBRT was given in 7-8 fields with an isocenter dose of 40-60 Gy in 4-10 fractions (median, 48 Gy in 4 fractions). Results: The overall 2-year and 5-year survival rates for all patients were 67.4% and 34.7%, while the disease-specific 2-year and 5-year survival rates were 90.0% and 72.0%, respectively. Pulmonary adverse effects were mild in the majority of the patients, although two patients had grade 2 radiation pneumonitis. The oxygen flow required increased slightly at follow-up periods greater than one year, but was still at an acceptable level. Conclusion: SBRT was feasible for patients requiring domiciliary oxygen therapy.*

Although surgical resection remains the present standard-of-care for early-stage non-small cell lung cancer (NSCLC), stereotactic body radiation therapy (SBRT) is a worthwhile alternative. In particular, SBRT for NSLC is considered for patients who are medically inoperable because of pulmonary co-morbidities or other medical conditions (1-6). If a patient has severe lung function impairment, observation is a viable

non-surgical option (7) because possible radiation-induced pneumonitis or fibrosis may be critical for such patients. However, medically inoperable patients with untreated early-stage lung cancer have a poor prognosis, with >50% of patients dying of lung cancer (7). Although it has been recently shown that poor pulmonary function does not predict reduced survival or pulmonary function after SBRT (8, 9), the efficacy of SBRT for patients treated with domiciliary oxygen therapy is not been well-known.

In this retrospective study, we investigated the feasibility of using SBRT to treat patients with stage I NSCLC with chronic respiratory insufficiency requiring domiciliary oxygen therapy, particularly in focusing on changes in oxygen flow rate.

Patients and Methods

Patients. From April 2004 to April 2010, 259 patients with early-stage lung cancer were treated with SBRT at the Department of Radiology of Kyushu University Hospital. Out of these, we retrospectively collected the clinical records of 15 patients (5.8%) with chronic respiratory insufficiency, requiring domiciliary oxygen therapy before SBRT. These patients had been treated with 1-3 l/min of oxygen to maintain an oxygen saturation of ≥88%, as measured by pulse oximetry.

Patients' characteristics are presented in Table I. Pulmonary function tests were performed before treatment, and results are shown in Table II.

Treatment. The SBRT technique has been previously described (10). Briefly, the patients were fixed with a body cast system composed of a thermoplastic body cast, a vacuum pillow, arm and leg support, and a carbon plate (Engineering Systems Co., Matsumoto, Japan). The body cast restricted the chest and abdominal wall movement in order to immobilize the patients during planning and treatment. Respiratory movement was evaluated with an X-ray simulator for the diaphragm and the tumor. CT scans were performed at 2-mm intervals on the day of planning and the first treatment day for verification. CT volume data were transferred to a three-dimensional radiotherapy treatment planning (3D-RTP) system (Eclipse; Varian Medical Systems, Inc., Palo Alto, CA, USA). Seven to eight multi-leaf collimator-shaped static ports of 4- or 6-MV X-rays were selected. To maintain the

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4041

Table I. *Patients characteristics (n=15).*

	Number
Gender	
Male:female	10:5
Age	
Median, range (years)	75 (60-83)
Performance status	
0	0
1	3
2	8
3	3
4	1
Underlying disease	
COPD	12
Post-operative respiratory failure	1
Chronic pulmonary tuberculosis	1
Chronic heart failure	1
Histology	
Squamous cell carcinoma	8
Adenocarcinoma	1
Unknown	6
Clinical stage	
T1aN0M0	7
T1bN0M0	5
T2aN0M0	8
Tumor size	
Median, range (mm)	20 (8-48)

COPD, Chronic obstructive pulmonary disease.

Table II. *Pulmonary function test values before stereotactic body radiotherapy.*

Test	Median, range
FEV_1 (l)	0.74 (0.38-1.85)
FEV_1 (%)	43.1 (21.1-77.7)
FVC (l)	1.81 (0.87-3.58)
FVC (%)	63.3 (43.3-116.2)

FEV, Forced expiratory volume in 1 second; FVC, forced vital capacity.

isocenter setup accuracy, a comparison of the anterior, posterior (AP) and lateral digital portal images with the planning AP and lateral digitally reconstructed radiographs was performed daily. The dose was 48 Gy in four fractions to the isocenter for 13 of the tumors, 60 Gy in 10 fractions for one tumor, and 40 Gy in 4 fractions for 1 tumor. The linear accelerator used was a Clinac-21Ex (Varian Medical Systems, Inc.). The median percentage of total lung receiving more than 20 Gy (V20) was 4.8% (range 2.2-8.7%).

Follow up. In principle, patients were assessed after completion of SBRT every four weeks for the first six months, every three months for the next 36 months, and every six months thereafter. Toxicity was graded according to the Common Terminology Criteria Adverse Events version 3 (CTCAE v3.0) (11), and chest CT or x-ray was performed at every follow-up. Oxygen therapy continued after SBRT. Oxygen flow was moderated to achieve target oxygen saturation levels of ≥88%, based on pulse oximetry.

The overall and disease-specific survival rates were calculated using the Kaplan Meier method. The median follow-up was 23 months (range 6-69 months).

Results

Survival and patterns of failure. The overall 2-year and 5-year survival rates for all patients were 67.4% and 34.7%, while the disease-specific rates were 90.0% and 72.0%, respectively (Figure 1).

Six patients (40%) had disease recurrence. Three patients (20%) had a local recurrence, and one had a pleural dissemination. Two patients experienced disease relapse in the hilar lymph nodes. No patient developed distant metastases. During the observation time, three patients died of lung cancer; five patients died of concurrent disease (chronic obstructive pulmonary disease (COPD) in four patients, cardiovascular disease in one patient).

Adverse effects. Pulmonary adverse effects were mild in the majority of the patients. Although two patients had grade 2 radiation pneumonitis, medical management including steroid administration improved their symptoms. There were no severe complications for the remaining 13 patients.

Oxygen flow before and after treatment, used to maintain oxygen saturation levels of ≥88% are shown in Figure 2. No patient exhibited reduced oxygen flow levels after SBRT. Out of five patients whose oxygen flow levels were evaluated at an interval less than one year after SBRT, only one patient exhibited an increase in the oxygen flow required. In contrast, the necessary oxygen flow increased slightly with follow-up periods of more than one year.

Discussion

To our knowledge, this is the first report of the feasibility of SBRT for patients with stage I NSCLC with chronic respiratory insufficiency requiring domiciliary oxygen therapy. Although the sample size was small, the treatment was well-tolerated and the tumor control rate was high.

Recently, several reports have been published regarding pulmonary function after SBRT for patients with early-stage NSCLC. Henderson *et al.* reported that poor baseline pulmonary function did not predict reduced survival or pulmonary function after SBRT for patients with stage I NSCLC treated with a dose of 60–66 Gy in three fractions (9). Bishawi *et al.* reviewed collected data of stage I-II lung cancer prospectively, and demonstrated that SBRT did not have an effect on forced expiratory volume in 1 second (FEV1) or forced vital capacity (FVC) at a mean follow-up time of four months (8). In our study, the oxygen flow
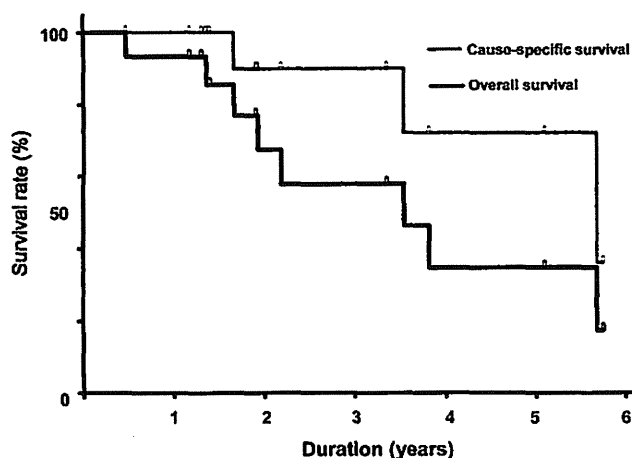
Figure 1. *Overall and disease-specific survival rates for 15 patients treated with stereotactic body radiation therapy for stage I non-small cell lung cancer.*

Figure 2. *Oxygen flow before and after stereotactic body radiation therapy (SBRT) to maintain oxygen saturation levels of ≥88%. In one patient, chronic respiratory failure acutely worsened; the oxygen flow levels necessary for this acute-on-chronic form of respiratory failure were excluded. The plots are divided into three categories according to the period between SBRT and the follow-up evaluation of oxygen flow (<1 year, 1-3 years, >3 years). The median follow-up period was 1.2 years (range 0.1-5.7 years).*

required to maintain oxygen saturation levels of ≥88% increased slightly in most cases with follow-up periods of more than one year, but was still at acceptable levels.

In this study, we used a median total dose of 48 Gy with four fractions, which is the most frequently used schedule of SBRT for primary lung cancer in Japan (12), although it is smaller than the doses used in the United States (5). We were able to achieve very low V20 values for the lungs, but three patients (20%) had a local recurrence. Multi-institutional phase II trials of SBRT are currently underway in Japan (13), and patient enrollment for these trials has already closed. The results will hopefully validate the efficacy of this schedule of SBRT for NSCLC.

Patients with chronic respiratory insufficiency requiring domiciliary oxygen therapy have a poor prognosis. Crockett *et al.* examined the prognosis of patients treated with domiciliary oxygen therapy for COPD, and demonstrated that the overall crude survival was 75.1%, 51.3%, and 18.9% at 1, 2, and 5 years respectively (14). Therefore, observation alone may be a non-surgical option for patients with severe lung function impairment (7). In our study, five patients (26.7%) died of concurrent diseases, and the overall 2-year and 5-year survival rates for all patients were 67.4% and 34.7%, respectively. However, McGarry *et al.* reported that medically inoperable patients with untreated stage I-II NSCLC have a poor prognosis, with >50% of patients dying of lung cancer; the median survival time for such patients with no treatment was 14.2 months (7). Therefore, based on the fact that poor pulmonary function does not predict reduced survival or pulmonary function after SBRT (8, 9), SBRT may be a treatment option for patients already requiring domiciliary oxygen therapy.
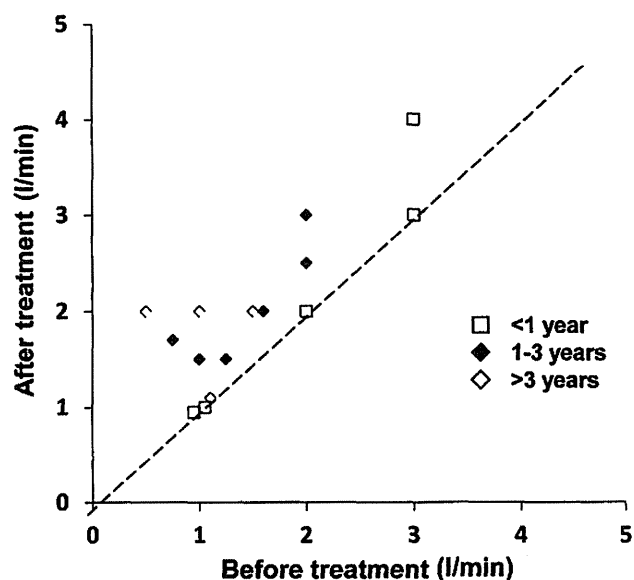
In this retrospective study, SBRT proved feasible for patients requiring domiciliary oxygen therapy. However, the number of patients was small, and this finding is in contrast to the situation after conventionally fractionated radiotherapy, where COPD and reduced FEV1 were associated with severe acute radiation pneumonitis (15). The exact benefit of SBRT for patients with domiciliary oxygen therapy may be elucidated by larger prospective observational studies.

Acknowledgements

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Clinical Investigation: Normal Tissue

Radiation-Induced Rib Fractures After Hypofractionated Stereotactic Body Radiation Therapy: Risk Factors and Dose—Volume Relationship

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Summary

Radiation-induced rib fracture (RIRF) is one of the late adverse effects after hypofractionated stereotactic body radiation therapy (SBRT) for lung tumors. However, the incidence and risk factors have not been determined, to our knowledge. We performed this study to assess the clinical features, risk factors, and dose—volume relationship of RIRF after hypofractionated SBRT. The incidence of RIRF after hypofractionated SBRT is relatively high. The

Purpose: The purpose of this study was to clarify the incidence, the clinical risk factors, and the dose—volume relationship of radiation-induced rib fracture (RIRF) after hypofractionated stereotactic body radiation therapy (SBRT).

Methods and Materials: One hundred sixteen patients treated with SBRT for primary or metastatic lung cancer at our institution, with at least 6 months of follow-up and no previous overlapping radiation exposure, were included in this study. To determine the clinical risk factors associated with RIRF, correlations between the incidence of RIRF and the variables, including age, sex, diagnosis, gross tumor volume diameter, rib—tumor distance, and use of steroid administration, were analyzed. Dose—volume histogram analysis was also conducted. Regarding the maximum dose, V10, V20, V30, and V40 of the rib, and the incidences of RIRF were compared between the two groups divided by the cutoff value determined by the receiver operating characteristic curves.

Results: One hundred sixteen patients and 374 ribs met the inclusion criteria. Among the 116 patients, 28 patients (46 ribs) experienced RIRF. The estimated incidence of rib fracture was 37.7% at 3 years. Limited distance from the rib to the tumor (<2.0 cm) was the only significant risk factor for RIRF ($p = 0.0001$). Among the dosimetric parameters used for receiver operating characteristic analysis, the maximum dose showed the highest area under the curve. The 3-year estimated risk of RIRF and the determined cutoff value were 45.8% vs. 1.4% (maximum dose, $\geq$42.4 Gy or less), 51.6% vs. 2.0% (V40, $\geq$0.29 cm^3 or less), 45.8% vs. 2.2% (V30, $\geq$1.35 cm^3 or less), 42.0% vs. 8.5% (V20, $\geq$3.62 cm^3 or less), or 25.9% vs. 10.5% (V10, $\geq$5.03 cm^3 or less).

maximum dose and high-dose volume are strongly correlated with RIRF.

Conclusions: The incidence of RIRF after hypofractionated SBRT is relatively high. The maximum dose and high-dose volume are strongly correlated with RIRF. © 2012 Elsevier Inc.

Keywords: Stereotactic body radiation therapy, Rib fracture, Dose—volume histogram analysis

Introduction

Stereotactic body radiation therapy (SBRT) allows escalation of the fractional dose, which is important to improve the local control rate of tumors and overall survival. In general, therefore, SBRT is performed by using a large volume per fraction in fewer (from one to five) treatment sessions, a modality called hypofractionated SBRT. Because of its excellent local control and survival rates, hypofractionated SBRT is accepted as one of the best alternative treatments for medically inoperable patients with early-stage non-small-cell lung cancer (1). Recently, indications for SBRT have been extended to so-called oligometastases, with good potential for improved survival in patients with them (2).

Radiation-induced rib fracture (RIRF) is known to be a rare late adverse effect after conventional radiotherapy for thoracic lesions. Its incidence has been reported as 6% and 0.3% to 1.8% after mastectomy and breast-conservation surgery followed by chest wall irradiation (3—5). Recently, we have also observed patients who experienced RIRF after hypofractionated SBRT for lung tumors. Generally, in hypofractionated SBRT, the normal tissue adjacent to the planning target volume receives not only a high dose overall but also a high dose per fraction. Therefore, it is assumed that the predictive risk of normal tissue toxicity after hypofractionated SBRT is different from that after three-dimensional conformal radiotherapy with conventional fractionation. Our aim in this study was to assess the incidence, clinical features, risk factors, and dose—volume relationship of RIRF after hypofractionated SBRT for lung tumors.

Methods and Materials

Patient eligibility

We retrospectively reviewed all cases treated with SBRT for primary lung cancer or metastatic lesions to the lung (including histologically unproven lesions) at Kyusyu University between April 2003 and May 2007. The indications for SBRT at our institution are as follows: (1) early-stage (cT1 or T2N0M0) primary lung cancer or small (<5 cm, in principle) oligometastatic lesions in the lung; (2) medical inoperability, generally due to complications and age, or refusal of operation; and (3) lesions not adjacent to the hilar area. Inclusion criteria for this study were as follows: (1) prescribed dose of 48 Gy in four fractions for the isocenter; (2) availability of follow-up computed tomography (CT) images at least 6 months after SBRT; (3) no previous overlapping radiation exposure; and (4) no overlapping surgical procedures. The patients who received radiation therapy with overlap to initial treatment site after SBRT were handled as censored cases at the time the radiation therapy started. Surgical procedures are known to be a risk factor for osteoradionecrosis (ORN), and we therefore excluded patients with overlapping surgical procedures within the radiation fields. After these adjustments, a total of 116 patients met our criteria. A summary of

patient and tumor characteristics is shown in Table 1. No patients were receiving steroid therapy in our series.

Treatment

All patients were immobilized in a stereotactic body frame (Engineering System Co., Matsumoto, Japan), which uses a rigid frame, vacuum pillow, and thermoplastic body shell (6). No respiratory gating techniques were used, and all patients were under shallow breathing during simulation and treatment. Tumors and adjacent structures were screened with fluoroscopy on the anterior—posterior view and the lateral view to measure respiratory tumor motion. Treatment planning was performed with multidetector (four-row) CT with a slice thickness of 2 mm with the patient under free breathing. Treatment planning was conducted using an Eclipse system, ver. 6.5 (Varian Medical Services, Palo Alto, CA). The gross tumor volume (GTV) was contoured on each axial CT slice with the use of a pulmonary window setting (window level, -700 HU; window width, 2000 HU). The clinical target volume was defined as being the same volume as the GTV. The internal target volume, including the internal margin, was defined on the basis of three-dimensional tumor motion measured on fluoroscopy. The planning target volume, including the setup margin, was created by adding 5 mm to the internal target volume in all directions. The beam arrangement consisted of six to eight coplanar and noncoplanar photon beams accelerated to 4 to 10 MV. In all cases, the prescribed dose was 48 Gy in four fractions for the isocenter. In this study, the pencil beam convolution algorithm with Batho Power Law for tissue heterogeneity was used for dose calculation.

Follow-up and clinical assessment

To evaluate the clinical features of RIRF, we assessed the crude and estimated cumulative incidence, the time to onset, and the symptoms. We adopted follow-up chest CT scans after SBRT to identify RIRFs. The follow-up CT was initially performed 1 or 2 months after the completion of SBRT and then every 3 months during the first 2 years and every 4 to 6 months thereafter. All

Table 1   Patient, tumor, and radiotherapy characteristics

Characteristic	No. of patients (range)
Age, y (median)	36—92 (75)
Sex	
M	66
F	50
Diagnosis	
Primary lung cancer	97
Metastatic lung tumor	19
Tumor size, cm (median)	1.0—5.1 (2.4)
Rib—tumor distance, cm (median)	0.3—6.2 (2.0)

follow-up chest CT images were re-evaluated by one of the authors (A.K.) to determine the exact number and location of the rib fractures. The diagnosis of rib fracture was made by the findings of cortical discontinuity or linear sclerotic change across the rib. We defined an RIRF as a newly appearing fracture located within the irradiated volume of SBRT and with no obvious history of trauma. Clinical symptoms associated with rib fracture were estimated by reviewing the clinical records and were graded using the National Cancer Institute Common Toxicity Criteria version 3.0. To clarify the predictive factor of RIRF, we assessed the following clinical factors: age, sex, diagnosis, tumor size, and rib—tumor distance. Tumor size was defined as the maximum diameter of GTV measured on the axial plane. We defined the rib—tumor distance as the minimum distance from the radiation isocenter to the rib on the three orthogonal planes.

Dose—volume relationship analysis

All ribs receiving doses of 20 Gy or more, even to a small area, were subject to the dose—volume relationship analysis. This threshold was chosen because there were no fractures in the ribs that received a maximum dose of less than 20 Gy. After examination of the isodose distribution in all 116 cases, 374 ribs met our criteria. We contoured just on the rim of the ribs but did not include the cartilage, under the bone window setting (window level, 400; window width, 2000), on the radiation treatment planning system, and calculated the irradiated dose (Fig. 1). The following dosimetric parameters were calculated for each rib: maximum dose (Dmax) and the absolute volume receiving ≥ 10 Gy (V10), ≥ 20 Gy (V20), ≥ 30 Gy (V30), and ≥ 40 Gy (V40).

Statistics

The cumulative incidence of rib fracture was estimated by the Kaplan-Meier method. For the risk factor analysis, each factor (age, sex, diameter of GTV, and chest wall—tumor distance) was divided into two groups by using the median value as a cutoff, and the statistical significance was calculated with the log-rank test for univariate analysis. The irradiated doses to the ribs were compared between fractured ribs and unfractured ribs, and the statistical

significance of the differences was evaluated by Student's t test. The receiver operating characteristic (ROC) curve was also generated to assess the predictability of dosimetric parameters related to rib fracture and to determine the optimal cutoff value for each dosimetric parameter. The curve was defined as the plot of the sensitivity vs. the false-positive rate (1-specificity). Each dosimetric parameter was divided into two groups by using the optimal cutoff value obtained from ROC analysis, and the estimated incidence of rib fractures was compared between the two groups with the log-rank test. Statistical significance was defined as a p value <0.05. Analyses were performed with the JMP8.0 software (SAS Institute, Inc., Cary, NC).

Results

Incidence of rib fracture and clinical risk factors

Among the 116 cases included in this study, RIRF developed in 28 patients (24.1%). Twenty-four patients had primary lung cancer, and 4 patients had oligometastatic lesions. The median time to onset of RIRF was 22 months (range, 9—42 months) after the completion of SBRT. The estimated cumulative incidence of RIRF was 37.7% at 3 years (Fig. 2). Among the 28 cases of fracture, 12 cases (42.9%) were symptomatic. The symptoms associated with rib fracture were localized pain (12 cases) and neurologic pain (2 cases). The symptomatic severity was grade 1 in 4 patients, grade 2 in 7 patients, and grade 3 in 1 patient. In most of the cases, the duration of symptoms was short (only a few months). However, 1 patient with grade 3 pain required oral administration of a narcotic agent for 9 months. As for radiologic findings of RIRF at the point of diagnosis, 15 cases showed cortical discontinuity (7 cases were symptomatic), 8 cases showed linear sclerotic change (4 cases were symptomatic) and 5 cases showed boss findings (2 cases were symptomatic).

In univariate analysis to estimate the clinical risk factors related to RIRF, shortness of rib—tumor distance was the only significant factor: the 3-year cumulative incidence of RIRF was 58.1% in those with a distance of <2.0 cm and 24.4% in those with a distance of ≥ 2.0 cm ($p = 0.0001$). All other clinical factors, including age (≥ 75 years vs. <75 years), sex, diagnosis,
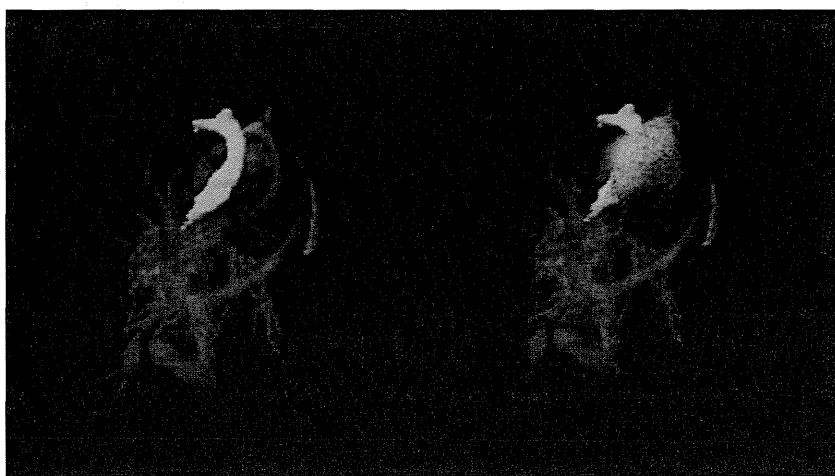

Fig. 1.   Delineation of ribs for dose—volume histogram analysis. (Left) All parts of the rib that received more than 20 Gy, even in a small region, were delineated. (Right) Overlap image of delineated ribs and dose—volume more than 20 Gy.
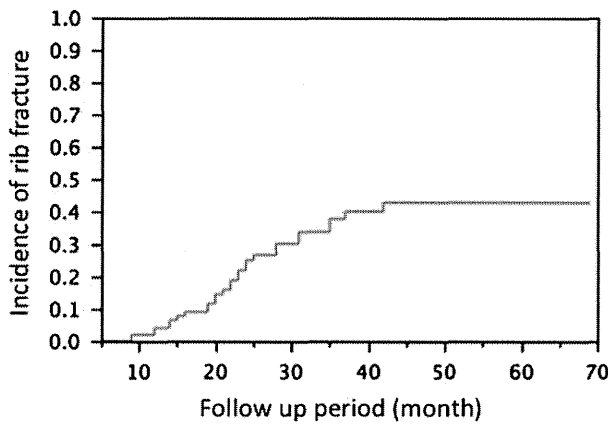
Fig. 2.   Cumulative incidence of radiation-induced rib fracture.

and GTV diameter ($\geq$2.4 cm vs. <2.4 cm) were not significantly correlated with the RIRF (Table 2).

Dose—volume relationship

Among the 374 ribs, RIRF was observed in 46 ribs. Table 3 lists the values of the Dmax and V40, V30, V20, and V10 doses for the ribs with or without rib fracture. The Dmax, V40, V30, and V20 were significantly higher in fractured ribs than in unfractured ribs. Among the fractured ribs, the minimum value of Dmax was 34.1 Gy. The approximate AUC results from the ROC plots for Dmax, V40, V30, V20, and V10 were 0.83, 0.82, 0.81, 0.71, and 0.56, respectively. This result revealed that the best predictor of rib fracture was Dmax, and the high dose irradiated volume was more strongly correlated with rib fracture than the low dose irradiated volume. As shown in Table 4, the 3-year estimated risk of RIRF when a division was made into two groups with the cutoff value determined by ROC analysis was 45.8% vs. 1.4% (Dmax, $\geq$42.4 Gy or less), 51.6% vs.

Table 3   Comparison of dosimetric factors between fractured and unfractured ribs

Parameter	Fractured	Unfractured	p value
Dmax (Gy)	47.02 ± 2.77	36.31 ± 9.42	<0.0001
V40 (cm^3)	1.81 ± 1.19	0.67 ± 1.35	<0.0001
V30 (cm^3)	3.10 ± 1.30	1.3 ± 2.01	<0.0001
V20 (cm^3)	4.48 ± 1.53	3.31 ± 3.57	0.0283
V10 (cm^3)	6.74 ± 2.35	6.51 ± 3.45	0.6573

2.0% (V40, $\geq$0.29 cm^3 or less), 45.8% vs. 2.2% (V30, $\geq$1.35 cm^3 or less), 42.0% vs. 8.5% (V20, $\geq$3.62 cm^3 or less), or 25.9% vs. 10.5% (V10, $\geq$5.03 cm^3 or less). In each parameter, the difference in the incidence of RIRF between the two groups was statistically significant. However, the difference was greater for Dmax, V40, and V30 than for V20 and V10.

Discussion

Adverse effects to the chest wall after hypofractionated SBRT have been known to include chest wall pain, fibrosis of soft tissue, and rib fracture (7). RIRF is often found as a result of pain, but it is sometimes asymptomatic and is found incidentally. In several previous reports, dosimetric analysis was performed to determine the radiation dose to the chest wall or ribs to predict the risk of RIRF after SBRT (8—12). However, in most of these studies, the radiation dose to the chest wall was the object of the analysis, because chest wall toxicity, including both chest wall pain and rib fracture, was the main interest. In this study, we focused on dose to the ribs to clarify the precise dose—volume relationship with respect to RIRF. In previous studies focusing on the rib dose, Voroney et al. (10) and Andolino et al. (12) analyzed the maximum dose to the rib fracture sites in patients treated with SBRT for liver and lung lesions. Pettersson et al. performed a dose—volume relationship analysis for 81 ribs of 33 patients who received SBRT for non-small-cell lung cancer (8). Our dosimetric study included 374 ribs (113 cases), making it the largest study in this field so far, to our knowledge.

Adverse effects on mature bone after radiotherapy include radiation osteitis, ORN, pathologic fracture, and, in rare cases,

Table 2   Univariate analysis of clinical factors

Parameter	Fractured	Unfractured	Cumulative 3-year incidence, %	p value
Age, y				
$\geq$75	12	46	38.3	0.94
<75	16	42	37.2	
Sex				
M	13	54	31.7	0.2
F	15	34	46.5	
Diagnosis				
Primary lung tumor	24	73	38.3	0.62
Oligometastasis	4	15	34.0	
Tumor size (cm)				
$\geq$2.4	15	44	49.3	0.72
<2.4	13	44	27.8	
Rib—tumor distance (cm)				
$\geq$2.0	9	50	24.4	0.0001
<2.0	19	38	58.1	

Table 4   Comparison of the provability of radiation-induced rib fracture (RIRF) for each dosimetric parameter

Parameter	Cutoff value	3-year cumulative incidence of RIRF (%)	p value
Dmax	$\geq$42.4 Gy	45.8	<0.0001
	<42.4 Gy	1.43	
V40	$\geq$0.29 cm^3	51.6	<0.0001
	<0.29 cm^3	2.01	
V30	$\geq$1.35 cm^3	45.8	<0.0001
	<1.35 cm^3	2.16	
V20	$\geq$3.62 cm^3	42.0	<0.0001
	<3.62 cm^3	8.53	
V10	$\geq$5.03 cm^3	25.9	0.03
	<5.03 cm^3	10.5	

radiation-induced neoplasm. Radiation-induced fractures have been considered to occur in a bone structurally weakened by irradiation and are characterized by high rates of nonunion or delayed union. The biologic effect of ionizing radiation on bone has been considered to be a combination of direct cell injury and radiation-induced vascular injury that can lead to radiation osteitis, atrophy, osteopenia, ORN, and resultant bone fragility (13).

In conventional radiotherapy, the known risk factors of osteoradionecrosis are previous surgery, abuse of alcohol and tobacco, and no use of steroids (14). In the present study, the only risk factor significantly correlated with rib fracture was a short rib–tumor distance. When the rib–tumor distance was less than 2.0 cm, the predictive risk of rib fracture was about 60% over 3 years. However, the distance of the rib to the tumor has been strongly correlated with the dosimetric distribution to the ribs, so the relationship between the fracture rate and the rib–tumor distance must change with the prescribed dose and number of fractions. Considering that there were no significant correlative clinical factors except for the rib–tumor distance, it may rather be assumed that the fracture rate was more strongly influenced by the dosimetric distribution than by the patients' clinical factors in hypofractionated SBRT because of its higher biologically effective dose.

In conventional radiotherapy, it is known that biologic changes are dose dependent. The threshold for radiation-induced changes in bone has been reported to be 30 Gy, with cell death and devascularization of bone occurring at doses over 50 Gy (15). Another report described that ORN occurs after conventionally fractionated radiotherapy up to a total target dose of 66 Gy and higher (16). According to these previous studies, the threshold dose of radiation-induced fracture is considered to be 50 to 60 Gy in conventional radiotherapy.

The dose distributions of hypofractionated SBRT are steeper and more complex than those of conventional radiotherapy because the lower-dose region tends to become large and irregular, whereas the higher-dose region can be concentrated uniformly around the tumor. In addition, less is known about the dose–volume relationship of normal tissue toxicity when a large dose per fraction is used. Fenner et al. reported that histologic changes attributed to ORN could be reproducibly obtained in rat mandibular bones by stereotactic irradiation with a total dose of 60 Gy in four fractions at 6 weeks after the completion of irradiation (17). The metabolic rates in rodents have been known to be four to six times higher than those in humans. Therefore, it is possible that ORN develops 6 to 9 months after the completion of irradiation in humans. In fact, the earliest case of rib fracture was found 9 months after SBRT in the present study.

In a previous study using a normal tissue complication probability model, Pettersson et al. evaluated the dose administered to 81 ribs and reported a fracture rate of 50% and 5% for patients when the D_{2cc} was above 50 Gy and 27 Gy in three fractions, respectively (8). In our study, we determined optimal cutoff value using ROC curves for dosimetric parameters including Dmax, V40, V30, V20, and V10 of the ribs. The results showed that the highest AUC was in Dmax, and the AUC for V10 to V40 was higher in the order V40 to V10. In addition, the estimated fracture rate in 3 years was approximately 50% when Dmax, V40, or V30 was higher than the respective cutoff value. Our results are consistent with the results of Pettersson et al. in that a high dose in a small volume was more important to predict the risk of rib fracture than a lower dose in a larger volume in hypofractionated SBRT (8). In addition, our results suggested that the rib volume

receiving $\geq$30 Gy (V30) or $\geq$40 Gy (V40) may also be important in predicting the risk of rib fractures. Dunlap et al. evaluated the dose to the chest wall in 60 patients after SBRT and reported that the chest wall volume receiving $\geq$30 Gy (V30) best predicted the risk of severe chest wall pain and/or rib fracture, among V20, V30, V40, V50, and V60 (9). Welsh et al. also reported that the risks of both skin changes and chest wall pain were correlated with the volume of the chest wall receiving $\geq$30 Gy (18). Therefore, when we predict the risk of chest wall toxicity, including chest wall pain, rib fracture, and skin toxicity, V30 and V40 may be a better parameter to use than Dmax.

It is known that RIRF is often painless and is discovered incidentally, unlike traumatic fracture (3). In our study, approximately half of the patients with fracture experienced pain that was transient and not severe, a finding compatible with previous reports. By contrast, Welsh et al. also reported that 67 of 265 patients (25.3%) experienced chest wall pain after hypofractionated SBRT (18). Among the patients with chest wall pain, only 8 patients had rib fractures. They found that body mass index and diabetes were strong predictors for the development of chest pain (18). At our institution, only a few patients described having chest wall pain after SBRT. The low obesity rate in Japan might be a cause of the difference in symptom presentation between the two nationalities.

There is a limitation to our study. In this study, we use a pencil beam convolution algorithm to calculate dose, which is known to be suboptimal for dose calculation for SBRT.

In conclusion, RIRF was a not uncommon but relatively tolerable late adverse effect after hypofractionated SBRT. A high dose volume was more strongly correlated with rib fractures than a low dose volume. To reduce the risk of RIRF, a restriction of the high dose volume of the rib should be considered, provided that coverage of the tumor will not be compromised.

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Ⅱ 前立腺癌 －外部照射法－

1 放射線療法の意義と適応

　前立腺癌の放射線治療は大きな進歩を遂げ，前立腺に線量を集中し，その周囲への被曝を低減する種々の技術が開発された。わが国でも，強度変調放射線治療（IMRT），画像誘導放射線治療（IGRT），粒子線治療等の最新技術が普及しつつあり，合併症を少なく，安全に，そしてより効果的に治療できるようになっている。

　放射線治療の利点は，手術と比較して，男性機能，尿路系機能に対する治療後の QOL が高いことである。一方，主な有害事象は直腸障害である。

　前立腺癌の放射線治療を行うにあたり，前立腺癌の予後は他の悪性腫瘍と比較して良好であり，原則的に期待余命が十分見込まれる場合に根治的治療法が検討される。また，治療効果の主な指標に用いられる生化学的再燃は前立腺癌死と直接関係しているかどうかはっきり証明されておらず，治療後の患者の QOL がより重要になることを念頭に置いて，治療方針を決定すべきである。

　前立腺癌の予後因子には，臨床病期，治療前 PSA（prostate specific antigen），Gleason 分類などがあり，被膜外浸潤，精嚢浸潤，リンパ節転移のリスクが推定できる[1]。前立腺癌の放射線治療は，単に病期分類のみならず，これらのリスク因子を考慮に入れた治療戦略を立てる必要がある。NCCN ガイドラインでは，低リスク群（T1-2a かつ Gleason スコア 2～6 かつ PSA＜10 ng/mL），中リスク群（T2b-2c または Gleason スコア 7 または PSA 10～20 ng/mL），高リスク群（T3a または Gleason スコア 8～10 または PSA＞20 ng/mL），超高リスク群（T3b-4）にて，治療方針の決定を行っている[2]。骨盤リンパ節転移陽性の場合には，内分泌療法単独または外部照射との併用が行われる。期待余命が見込まれる場合には，積極的に外部照射との併用を行うべきとの意見もある。

　以下に，臨床的にリンパ節転移のない前立腺癌に対する治療計画を中心に記載する。

2 放射線治療

1）標的体積・リスク臓器

GTV：前立腺（T3 以上の場合には，浸潤部分も含む）とする。

CTV：GTV±精嚢基部～全体とするのが一般的である。低リスクは GTV，中リスクは GTV＋精嚢基部 1 cm 程度，高リスクは GTV＋精嚢基部 2 cm～精嚢全体とする場合が多い。T3b 以外で精嚢全体を CTV に含む場合は 50～60 Gy 以降は GTV に限局した照射野に縮小することが勧められる。

　　CTV については，リスクに応じて，直腸側以外の前立腺周囲に 5 mm 程度のマージンを設定するとの考え方もある[3]。

PTV：前立腺は直腸や膀胱の状態により位置が変動することが知られており，一般的には CTV＋0.8～1.0 cm 程度とするが，直腸側をさらに小さくすることが多い。マージンは各施設のセットアップの精度などに依存する。

リスク臓器：直腸，膀胱，尿道。

2）放射線治療計画

　前立腺の解剖をよく表すのは CT よりも MRI であり，治療計画 CT 上にて前立腺を囲む場合，

MRI を参照することが望ましい。

　治療計画 CT では，膀胱および直腸が過度に拡張していないように注意する。場合によっては，浣腸などで直腸内容を排泄させることも必要である。

　予後因子にて十分にリスク評価を行い[1,2]，リンパ節転移，精嚢浸潤，被膜外浸潤などの可能性を考慮して，照射範囲を決定する。骨盤リンパ節への転移のリスクの高い群については，骨盤照射と内分泌療法を併用することにより，生化学的非再燃率が低下することが知られているが[4]，実際に骨盤照射を行うべきかは明らかでなく，現在のところ治療医の判断にゆだねられている。

3) エネルギー・照射法

　6〜10 MV 以上の高エネルギー X 線を用いる。治療体位による再現性は両論があり腹臥位，背臥位はいずれでもよい。3 次元治療計画では，4 門以上の固定多門照射，両側方向 80〜120 度程度の振り子照射，回転原体照射（直腸線量を減少させるために，回転角を前方 240〜300 度程度にする）等が行われる。IMRT では，5 門以上や回転照射（volumetric modulated arc therapy の場合）が用いられる。

　高線量を投与する場合には，日々の IGRT が推奨される。

　骨盤領域を照射する場合には 4 門照射または IMRT で行う。前立腺癌の所属リンパ節は総腸骨動脈の分岐部以下の骨盤リンパ節であり，上縁を第 5 腰椎〜第 1 仙椎間，下縁を坐骨結節下縁とする。側方からの照射野の後縁は，第 3 仙椎以上の骨盤，仙骨前面のリンパ節領域を含み，第 2 仙椎以下では直腸後壁をはずすようにする。前縁は恥骨結合前縁より 0.5〜1.0 cm 後方とする。図 1 に照射野の例を示す。

4) 線量分割

　1 回線量 2 Gy の通常分割照射法が標準である。3DCRT または IMRT にて照射する。総線量は，3DCRT の場合 70〜72 Gy，IMRT の場合には 74〜78 Gy が用いられることが多い。線量処方は，3DCRT の場合にはアイソセンタにて処方される場合が多いが，IMRT では，PTV の D_{95}（体積の 95 ％をカバーする線量）や D_{50}（体積の 50 ％をカバーする線量）等，施設によりさまざまである。また，1 回線量を 2 Gy より大きくした少（寡）分割照射については，未だ臨床試験の段階である。

　骨盤部を照射する場合には，1 回 1.8〜2.0 Gy，総線量 45〜50 Gy を骨盤領域に投与した後，前立腺部に縮小する。

5) 併用療法

　前立腺癌はアンドロゲン依存性であることが多く，内分泌療法が有効であり，しばしば放射線治療と併用される。特に高リスク群では，2〜3 年の長期の内分泌療法が推奨されている[5]。一方，内分泌療法には，性機能障害の他に，筋力低下，ホットフラッシュ，女性化乳房，肥満，耐糖能低下，気力低下，心血管障害，骨粗鬆症等の有害事象が知られており，低リスク群への併用は十分慎重にすべきである。

　NCCN ガイドラインでは，低リスク群では，外部照射単独または小線源療法が推奨されている。中リスク群では，外部照射 ±4〜6 カ月程度の内分泌療法 ±小線源療法，高リスク群および超高リスク群では，外部照射 +2〜3 年の内分泌療法または外部照射併用小線源療法 ±4〜6 カ月程度の内分泌療法が推奨されている[2]。
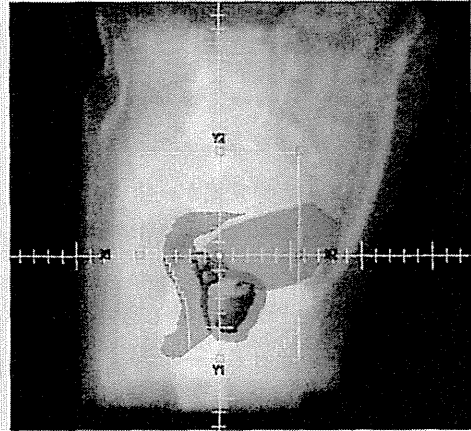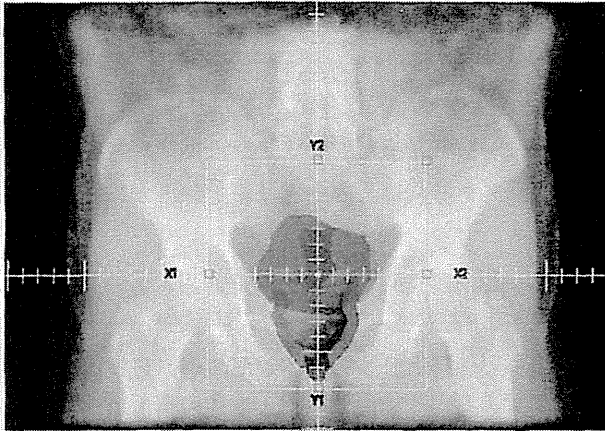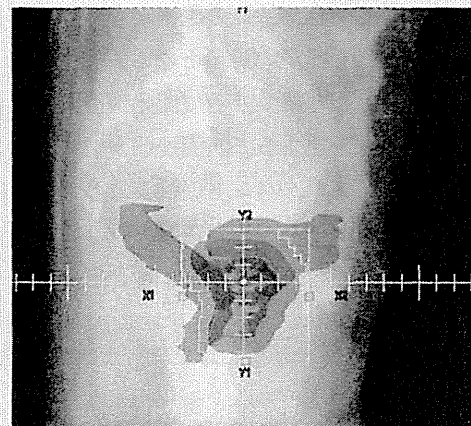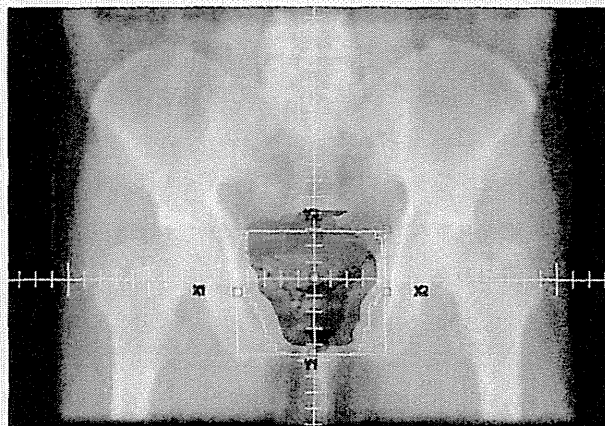
a. 全骨盤への照射野の一例
黄：前立腺および精嚢，紫：膀胱，青：直腸
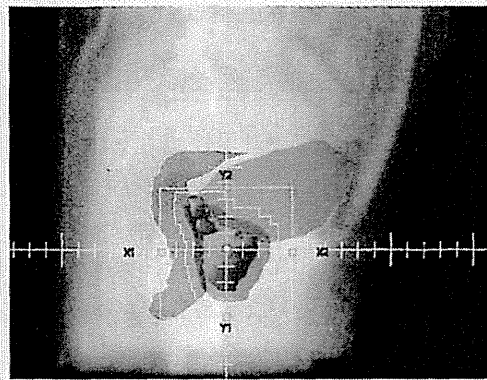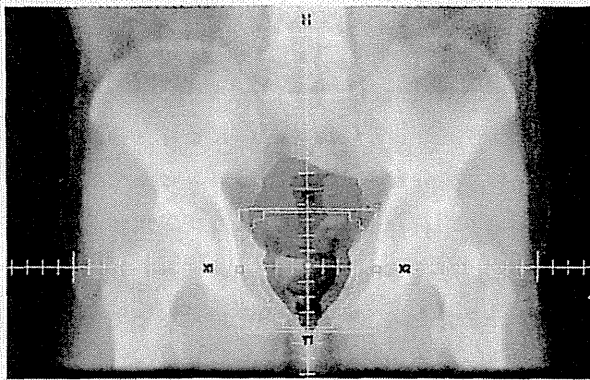
b. 前立腺への照射野の一例
黄：前立腺および精嚢，赤：前立腺および精嚢の一部を CTV とした場合の PTV，紫：膀胱，青：直腸

c. 術後照射野の一例
黄：腫瘍床，赤：腫瘍床を CTV とした場合の PTV，紫：膀胱，青：直腸

図1 前立腺癌に対する代表的照射野

3 | 標準的な治療成績

70 Gy までの放射線治療単独での 10 年生化学的非再燃率は，低リスク群で約 80%，中リスク群で約 50%，高リスク群で約 30% とされている[6]。しかし，高精度放射線治療により高線量を投与することにより治療成績が向上する。また，中，高リスク群には，内分泌療法を併用することによっても生化学的非再燃率や全生存率の向上が見込める。

4 | 合併症

急性の有害事象として，下痢，肛門周囲の皮膚炎，直腸出血，頻尿等があるが，可逆的である。晩期有害事象として最も問題となるものは直腸出血である。手術を要するような出血や閉塞をきたす頻度は 1% 以下であるが，輸血を含めた内科的な処置の必要な出血の起こる頻度は数%～20%程度にみられるとされている[7]。その他，長期的には，放射線性膀胱炎による出血，尿道狭窄等がある。手術に比べ頻度は低いものの，性機能障害も発生する。

5 | 前立腺全摘除術後の放射線治療

全摘除術にて断端陽性であった場合，アジュバント療法として外部照射などを行うことがあるが，PSA の上昇を確認してから何らかの救済治療を行う場合もあり，一定のコンセンサスは得られていない[8]。pT3 など病理的に高リスクであった場合，外部照射を加えたほうが生化学的再燃率は低いと考えられている。一部には生存率の改善があったとの報告もあるが[9]，無転移発生率，生存率には影響がないとする報告が多い。アジュバント療法としての放射線治療においては，60～64 Gy 程度の線量を照射する。照射開始時期としては，尿失禁などの有害事象を避けるため，十分尿禁制を保つことができるようになってから治療を開始する。

術後に PSA が上昇した場合には救済療法として外部照射を考慮する必要がある。PSA の上昇時，尿道吻合部付近の生検がなされても必ずしも病理学的に再発が証明されるわけではないが，この場合にも照射の対象となる。治療開始の目安となる PSA カットオフ値は 0.4～1.0 ng/mL 程度とされ，早い時期での治療開始が予後を改善するとされている。膀胱尿道吻合部を十分含めた前立腺床を照射野とする。精嚢浸潤が認められた場合には，精嚢床を含める。ASTRO コンセンサスパネルでは，アジュバント療法より多めの 64 Gy 以上の線量が推奨されている[10]。通常 4 門照射で行われることが多いが，高線量を投与する場合には，直腸出血を避けるため，照射法を工夫する。有害事象として，尿道狭窄などの合併症が 1～3% に認められる。

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CLINICAL INVESTIGATION   **Education and Training**

NATIONAL MEDICAL CARE SYSTEM MAY IMPEDE FOSTERING OF TRUE SPECIALIZATION OF RADIATION ONCOLOGISTS: STUDY BASED ON STRUCTURE SURVEY IN JAPAN

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Purpose: To evaluate the actual work environment of radiation oncologists (ROs) in Japan in terms of working
pattern, patient load, and quality of cancer care based on the relative time spent on patient care.
Methods and Materials: In 2008, the Japanese Society of Therapeutic Radiology and Oncology produced a questionnaire for a national structure survey of radiation oncology in 2007. Data for full-time ROs were crosschecked
with data for part-time ROs by using their identification data. Data of 954 ROs were analyzed. The relative practice index for patients was calculated as the relative value of care time per patient on the basis of Japanese Blue
Book guidelines (200 patients per RO).
Results: The working patterns of RO varied widely among facility categories. ROs working mainly at university
hospitals treated 189.2 patients per year on average, with those working in university hospitals and their affiliated
facilities treating 249.1 and those working in university hospitals only treating 144.0 patients per year on average.
The corresponding data were 256.6 for cancer centers and 176.6 for other facilities. Geographically, the mean annual number of patients per RO per quarter was significantly associated with population size, varying from 143.1
to 203.4 ($p < 0.0001$). There were also significant differences in the average practice index for patients by ROs working mainly in university hospitals between those in main and affiliated facilities (1.07 vs 0.71: $p < 0.0001$).
Conclusions: ROs working in university hospitals and their affiliated facilities treated more patients than the other
ROs. In terms of patient care time only, the quality of cancer care in affiliated facilities might be worse than that in
university hospitals. Under the current national medical system, working patterns of ROs of academic facilities in
Japan appear to be problematic for fostering true specialization of radiation oncologists.   © 2012 Elsevier Inc.

Structure survey, Working pattern, Patient load, Quality of cancer care, Medical care system.

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INTRODUCTION

The medical care systems of the United States and Japan are very different, which influences the personnel cost of medical staff. In radiation oncology, too, there is thus a major difference in personnel distribution between the United States and Japan. Most radiotherapy facilities in the United States are supported by full-time radiation oncologists (ROs), whereas the majority of radiotherapy facilities in Japan still rely on part-time ROs. Radiotherapy facilities with less than one full-time equivalent (FTE) RO on their staff still account for 56% nationwide (1). The Cancer Control Act was implemented in Japan in 2007 in response to patients' urgent petitions to the government (2). This act strongly advocates the promotion of radiotherapy (RT) and an increase in the number of ROs and medical physicists. However, a shortage of ROs still remains a major concern in Japan and will remain so for the foreseeable future.

The Japanese Society of Therapeutic Radiology and Oncology (JASTRO) has conducted national structure surveys of RT facilities in Japan every 2 years since 1990 (1, 3). The structure of radiation oncology in Japan has improved in terms of equipment and its functions in response to the increasing number of cancer patients who require RT.

In this study, we used the data of the JASTRO structure survey of 2007 to evaluate the actual work environment of radiation oncologists in Japan in terms of working pattern, patient load, and the quality of cancer care based on the relative time spent on patient care.

MATERIALS AND METHODS

Between March and December 2008, JASTRO carried out a national structure survey of radiation oncology in the form of a questionnaire in 2007 (1). The questionnaire consisted of questions about the number of treatment machines and modality by type, the number of personnel by job category, the number of patients by type, and the site. The response rate was 721 of 765 (94.2%) from all actual RT facilities in Japan.

Table 1 shows the overview of radiation oncology in Japan. University hospitals accounted for 15.8% of all RT facilities and had 40.0% of the total full-time ROs and treated 29.5% of all patients. The corresponding data were 4.0%, 7.8%, and 10.2% for cancer centers, and 80.2%, 52.2%, and 60.3% for other RT hospitals, respectively. "Full-time/part-time" indicates the employment pattern of RO. In Japan, even full-time ROs must work part-time in smaller facilities such as other RT hospitals. We considered these numbers to be inappropriate for accurate assessment of personnel. For this survey, we therefore collected FTE (40 h/week for radiation

oncology services only) data depending on hours worked in clinical RT of each RO. For example, if an RO works 3 days at a university hospital and 2 days at an affiliated hospital each week, FTE of the RO at the university hospital is 0.6 and at an affiliated hospital it is 0.4. The FTE of a facility that has three ROs with 0.8, 0.4, and 0.6 is calculated as 1.8 in total.

This survey collected the work situation data of a total of 1,007 full-time ROs and 534 part-time ROs. The data of full-time ROs were crosschecked with those of part-time ROs by using their identification data. Table 2 shows the result of crosschecking between data of full-time ROs and data of part-time ROs. In this study, data of 954 ROs were analyzed. Table 3 shows an overview of the analyzed data. In ROs working mainly in university hospitals, there are two ROs who worked at a maximum of six facilities (main facilities and five affiliated facilities) SAS 8.02 (SAS Institute Inc., Cary, NC) (4) was used for the statistical analysis, and the statistical significance was tested by means of the Student's t-test or analysis of variance.

The Japanese Blue Book guidelines (5, 6) for structure of radiation oncology in Japan based on Patterns of Care Study (PCS) data were used as the standard for comparison with the results of this study. PCS in Japan have been used since 1996 and have disclosed significant differences in the quality of RT by the type of facilities and their caseloads (7, 8). The standard guidelines for annual patient load per FTE RO have been set at 200 (warning level 300).

To evaluate quality of cancer care provided by ROs, the relative practice index for patients was calculated by the following expression.

$$\frac{\sum_{k=1}^{n} f_k}{\sum_{k=1}^{n} a_k} \times 200$$

in which n is the number of facilities that the RO works in (n = 1, 2, 3, ..., k), f_k is the FTE of the RO in facility k, and a_k is the annual number of patients per RO in facility k

Calculation method of coefficient "200:"

1) Number of weeks per year = (365–15)/7 = 50 weeks
   ※ Japan has 15 national holidays a year
2) 1.0 FTE = 40 h/week
3) Annual working hours of FTE 1.0 = 50 × 40 h = 2,000 h
4) Relative practice index for patients was normalized using the Blue Book guideline of 200 patients/FTE RO. For this guideline, care time per patient was set at 10 hours (2,000 h/200 patients).
5) Coefficient was 200 (2000/10).

RESULTS

Working patterns

Figure 1 shows working patterns of ROs working mainly in (a) university hospitals, (b) cancer centers, and (c) other

Table 1. Categorization of radiotherapy facilities in Japan

Facility category	Number of facilities	New patients	Total patients (new + repeat)	Full-time ROs		Part-time ROs	
				n	FTE	n	FTE
University hospital	114	50,351	60,555	403	293.0	70	21.6
Cancer center	29	16,794	20,968	78	73.7	14	2.5
Other radiotherapy hospital	578	103,084	123,564	526	351.8	450	83.7
Total	721	170,229	205,087	1,007	718.5	534	107.8

Abbreviations: RO = radiation oncologist; FTE = full-time equivalent (40 hours per week for radiation oncology services only).

Table 2. Connection between full-time and part-time
RO data

Data of full-time ROs	
Total number	1,007
Number of full-time ROs excluded from this analysis*	53
Number of full-time ROs analyzed	954
Breakdown	
Number of ROs who worked as full-time staff at main facilities and as part-time staff at affiliated facilities	199
Number of ROs who conducted only radiotherapy-related work as full-time staff at individual facilities (FTE of the RO was 1.0)	275
Number of ROs who conducted radiotherapy-related and other work as full-time staff at individual facilities (FTE of the RO was less than 1.0)	480
Data of part-time ROs including duplicate ROs	
Total number	534
Number of ROs who worked as full-time staff at main facilities and as part-time staff at affiliated facilities (number of part-time ROs analyzed)	280
Number of ROs who worked as only part-time staff at the facilities (Number of part-time ROs excluded from this analysis)	254

Abbreviations: RO = radiation oncologist; FTE = full-time equivalent (40 hours per week for radiation oncology service only).
  * Data of full-time ROs who worked at facilities with few patients were excluded, as were duplicated data of full-time ROs.

RT hospitals. The percentages of white parts in Figures 1 (a-c) were 17.4%, 5.0%, and 32.0%.

In university hospitals, the mean FTE RO for main facilities was 0.73 and for affiliated facilities it was 0.10. The corresponding figures were 0.94 and 0.01 for cancer centers, and 0.67 and 0.01 for other RT hospitals. For university hospitals, the ratio of ROs working only in main facilities was 16.4%, and the corresponding figures for cancer centers and other RT hospitals were 79.5% and 31.7%, respectively. The ratio of ROs working mainly in university hospitals and part-time in affiliated facilities was 44.5%. The corresponding data were 6.5% of ROs working primarily in cancer centers and 7.5% of ROs working mainly in other RT hospitals.

Patient loads

Figure 2(a) shows the patient load per RO working mainly in university hospitals, cancer centers, and other RT hospitals. Of ROs working primarily in university hospitals, 40.1% treated more than 200 patients per year. The corresponding ratios were 74.4% of ROs working primarily in cancer centers and 36.5% of those working mainly in other RT hospitals. The average number of patients treated by ROs working primarily in university hospitals was 189.2, with the corresponding figures being 256.6 patients in cancer centers and 176.6 in other RT hospitals. Figure 2(b) shows the patient load per RO working primarily in university hospitals. Of ROs working in university hospitals and affiliated facilities, 65.9% treated more than 200 patients per year, and the percentage was 19.3% of ROs working only in university hospitals. The former treated an average of 249.1 patients and the latter 144.0 patients per year.

The geographic patterns

Figure 3 shows the geographic distribution for 47 prefectures of the mean annual number of patients (new plus repeat) per RO arranged in order of increasing population by all prefectures in Japan (9). The average annual number of patients per RO per quarter ranged from 143.1 to 203.4, with significant differences among quarters ($p < 0.0001$). Figure 4 shows the top 10 prefectures with ROs who treated more than 200 patients per year in descending order: Tokyo, Osaka, Kanagawa, Hokkaido, Chiba, Aichi, Fukuoka, Hyogo, Miyagi, and Hiroshima.

Relative practice index for patients of ROs

` Figure 5(a) shows the average relative practice index for patients of ROs in university hospitals and affiliated facilities (ROs working mainly in university hospitals). The average practice index of RO for patients was 1.07 at university hospitals and 0.71 at affiliated facilities for a statistically significant difference ($p < 0.0001$). Figure 5(b) shows the average relative practice index for patients of ROs working only in university hospitals, only in cancer centers, and only in other RT hospitals. The respective indices for the three categories were 1.26, 1.02, and 1.01. There were significant differences in the indices between university hospitals and cancer centers ($p = 0.0278$) and between university hospitals and other RT hospitals ($p < 0.0001$). The difference between cancer

Table 3. Overview of analyzed data

Main facility category	Number of full-time ROs working at main facilities	Number of part-time ROs working at affiliated facilities					
		First*	Second*	Third*	Fourth*	Fifth*	Subtotal
University hospital	372	160	59	14	4	2	239
Cancer center	78	5	0	0	0	0	5
Other radiotherapy hospital	504	34	2	0	0	0	36
Total	954	199	61	14	4	2	280

Abbreviation: RO = radiation oncologist.
  * First: first affiliated facilities; second: second affiliated facilities; third: third affiliated facilities; fourth: fourth affiliated facilities; fifth: fifth affiliated facilities.
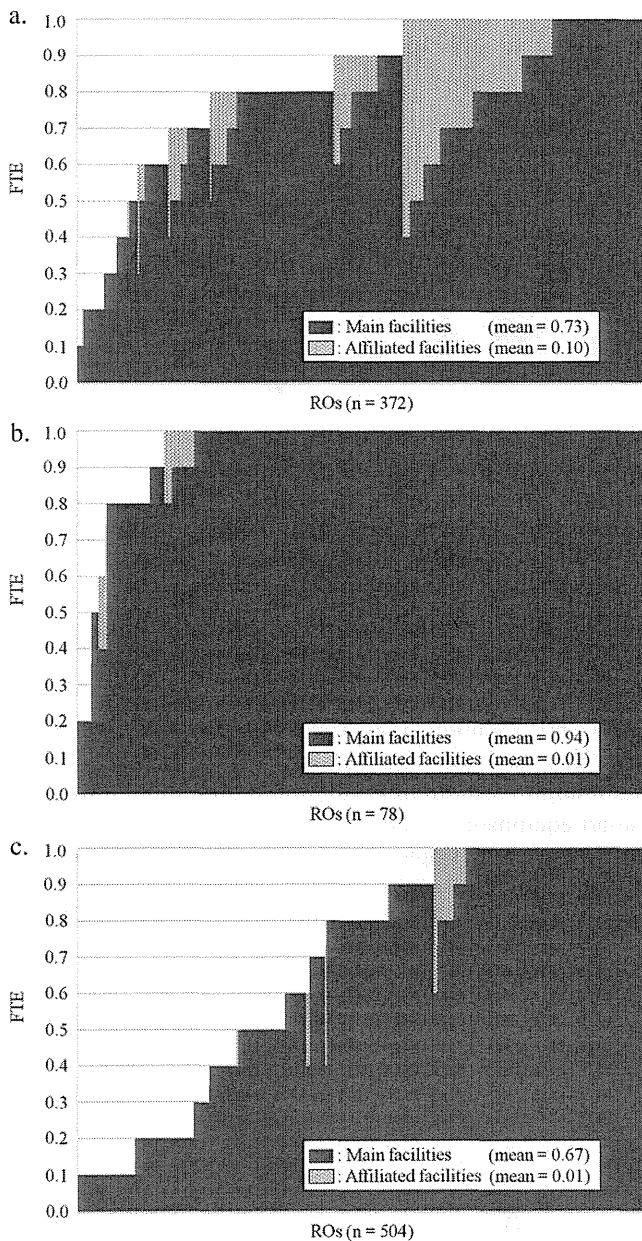
Fig. 1. Working patterns of ROs working mainly at (a) university hospitals, (b) cancer centers, and (c) other radiotherapy hospitals. Distribution of FTE ratio between main and affiliated facilities on each RO. Horizontal axis represents ROs in ascending order of own total FTE. *Abbreviations:* RO = radiation oncologist; FTE = full-time equivalent (40 hours per week for radiation oncology services only).
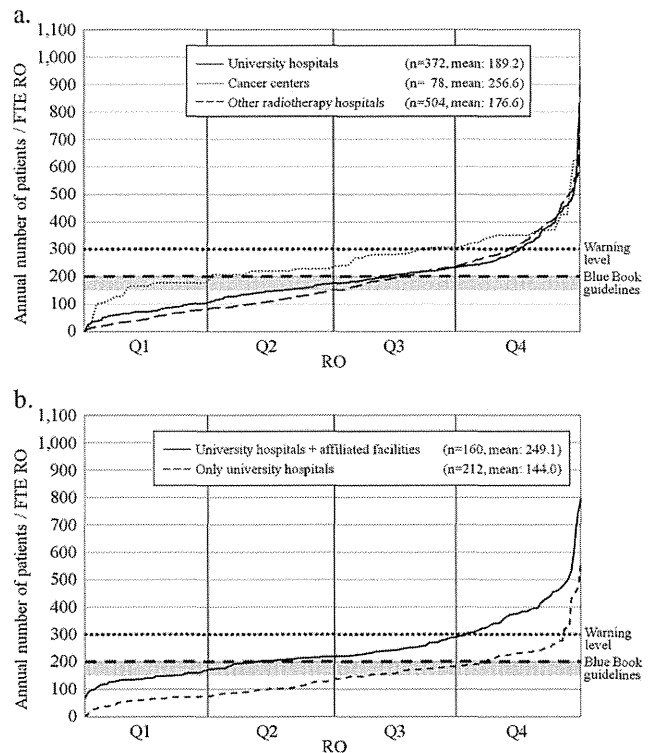

Fig. 2. Distribution of annual patient load/RO. (a) RO working mainly in university hospitals, cancer centers, and other radiotherapy hospitals. (b) RO working mainly in university hospitals. Horizontal axis represents ROs in ascending order of annual numbers of patients/RO. Q1: 0–25%, Q2: 26–50%, Q3: 51–75%, Q4: 76–100%. *Abbreviations:* RO = radiation oncologist; FTE = full-time equivalent (40 hours per week for radiation oncology services only).

centers and other RT hospitals was not significant ($p = 0.9459$).

DISCUSSION

In the United States, most RT facilities are supported by full-time ROs, with an FTE of 1.0 for most ROs working at their own facilities. In Japan, on the other hand, more than a half of the facilities still rely on part-time ROs. The main reason of this discrepancy is a shortage of ROs. Between 2005 and 2007, the increase in the number of cancer

patients requiring RT (7.3%) was higher than that in the number of FTE ROs (6.7%) (1). To make up for the shortage of ROs, most ROs in university hospitals must work part-time at affiliated hospitals, as is evident from the date shown in Figure 1. White parts of Figure 1 (a: 17.4%, b: 5.0% c: 32.0%) represent three types of data: (a) FTE data of ROs who were not provided in the survey questionnaire; (b) FTE data of part-time ROs whose identification data could not connect to those of full-time ROs; (c) FTE data of ROs working in nonradiation oncology services. In this survey, the data of type (a) and (b) were missing data and the data of type (c) were not collected. In other RT hospitals, the FTE of most ROs working in their own facilities is low and these ROs do not work part-time at other hospitals. There are two reasons for this. First, diagnosticians partly provide RT as ROs in their own hospitals and, second, other specialists (such as brain surgeons using gamma knife) partly function as ROs to provide RT. Because those facilities have few cancer patients, their patient load is less than that of university hospitals and cancer centers. These findings are evident from Figure 2(a). There was a major difference in the working patterns of ROs between university hospitals and cancer centers. FTE at their own facilities of most ROs working in university hospitals is less than 1.0, whereas that of most ROs working in cancer centers is 1.0,