can now be reduced without compromising therapeutic outcome [18].

Determining whether a patient actually requires concomitant chemotherapy also must be considered [19]. Recently, use of biologically targeted therapy has been shown to improve the outcome without increasing the common toxic effects of radiotherapy plus chemotherapy [20]. These promising approaches combined with robust nutritional support may yield further improvement in the management of non-surgical therapy for head and neck cancers.

Conclusions

The TDRS has the potential to become a useful measure for predicting acute swallowing dysfunction induced by chemoradiotherapy for head and neck cancers. This measure may serve as an index to enable selection of appropriate candidates for prophylactic PEG placement.

Funding

This study was supported by Health and Labour Sciences Research Grants (H19-001), Grants-in-Aid for Cancer Research (20S-5) and Grants-in-Aid for Scientific Research: "Third term comprehensive control research for cancer (H16-039, H19-038)" from the Ministry of Health, Labour and Welfare of Japan.

Conflict of interest statement

The authors report no actual or potential conflicts of interest.

Acknowledgements

The authors are grateful to Mrs. I. Koiwai and Mrs. Y. Ogawa for technical assistance.

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Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1–7, 2010

0360-3016/$–see front matter

ELSEVIER

doi:10.1016/j.ijrobp.2009.07.1751

CLINICAL INVESTIGATION

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR OPERABLE STAGE I NON–SMALL-CELL LUNG CANCER: CAN SBRT BE COMPARABLE TO SURGERY?

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Purpose: To review treatment outcomes for stereotactic body radiotherapy (SBRT) in medically operable patients with Stage I non–small-cell lung cancer (NSCLC), using a Japanese multi-institutional database.

Patients and Methods: Between 1995 and 2004, a total of 87 patients with Stage I NSCLC (median age, 74 years; T1N0M0, $n = 65$; T2N0M0, $n = 22$) who were medically operable but refused surgery were treated using SBRT alone in 14 institutions. Stereotactic three-dimensional treatment was performed using noncoplanar dynamic arcs or multiple static ports. Total dose was 45–72.5 Gy at the isocenter, administered in 3–10 fractions. Median calculated biological effective dose was 116 Gy (range, 100–141 Gy). Data were collected and analyzed retrospectively.

Results: During follow-up (median, 55 months), cumulative local control rates for T1 and T2 tumors at 5 years after SBRT were 92% and 73%, respectively. Pulmonary complications above Grade 2 arose in 1 patient (1.1%). Five-year overall survival rates for Stage IA and IB subgroups were 72% and 62%, respectively. One patient who developed local recurrences safely underwent salvage surgery.

Conclusion: Stereotactic body radiotherapy is safe and promising as a radical treatment for operable Stage I NSCLC. The survival rate for SBRT is potentially comparable to that for surgery. © 2010 Elsevier Inc.

Stereotactic body radiotherapy, Lung cancer, Non–small-cell, Operable, Stage I.

INTRODUCTION

With the popularization of computed tomography (CT) screening, lung cancers are increasingly detected at an early stage. For patients with Stage I (T1 or 2, N0, M0) non–small-cell lung cancer (NSCLC), resection of the set of full lobar and systemic lymph nodes represents standard treatment. Five-year overall survival rates for clinical Stage IA and IB treated surgically are approximately 60–75% and 40–60%, respectively (1–3). However, a proportion of patients who meet the criteria for surgery refuse such intervention for various reasons. Radiotherapy offers a therapeutic alternative in such cases, but the effects of conventional radiotherapy in patients with Stage I NSCLC are unsatisfactory, with local control rates of approximately 50% during a short 5-year survival period in 15–30% of patients (4–7). Survival rates for conventional radiotherapy for a statistically sufficient number of cases of operable Stage I NSCLC have not been reported, because most

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Presented at the 43rd Annual Meeting of the American Society of Clinical Oncology, June 1–7, 2007, Chicago, IL; and the 49th Annual Meeting of the American Society of Therapeutic Radiology and Oncology, October 28–November 1, 2007, Los Angeles, CA.

Supported in part by a Grant-in-Aid from the Ministry of Health, Welfare and Labor of Japan.

Conflict of interest: none.

Acknowledgments—The authors thank the patients and staff who assisted in this study.

Received May 7, 2009, and in revised form July 21, 2009. Accepted for publication July 22, 2009.

patients receiving radiotherapy are inoperable. The poor local control rates with conventional radiotherapy have been attributed to doses of conventional radiotherapy that are too low to control the tumor. Mehta *et al.* (8) provided a detailed theoretical analysis of NSCLC responses to radiotherapy and a rationale for dose escalation. They concluded that higher biologically effective doses (BED) irradiated during a short period must be administered to achieve successful local control of lung cancer. To provide a higher dose to the tumor without increasing adverse effects, three-dimensional conformal radiotherapy techniques have been used, and better local control and survival have recently been reported (9–11). Over the last decade, hypofractionated high-dose stereotactic body radiotherapy (SBRT) has been actively performed for early-stage lung cancer, particularly in Japan (12–17). We have previously reported preliminary results for a Japanese multi-institutional review of 257 patients with Stage I NSCLC treated with SBRT (18). The results showed that local control and survival rates were better with BED $\geq$100 Gy than with <100 Gy, and survival rates were much better for medically operable patients than for medically inoperable patients. These results were encouraging, but the duration of follow-up for the study was somewhat short (median, 38 months), and we have not presented a detailed analysis of medically operable patients as a distinct subgroup. Although the standard therapy for operable Stage I NSCLC remains surgery, the effect of SBRT on medically operable patients is an issue of great concern. We provide herein detailed and matured results of SBRT (BED $\geq$100 Gy) for medically operable patients with Stage I NSCLC, using a retrospectively collected Japanese multi-institutional database.

PATIENTS AND METHODS

Eligibility criteria

All patients who satisfied the following eligibility criteria were retrospectively collected from 14 major Japanese institutions in which SBRT for lung cancer was actively performed: (*1*) identification of T1N0M0 or T2N0M0 primary lung cancer on chest and abdominal CT, bronchoscopy, bone scintigraphy, or brain magnetic resonance imaging; (*2*) histopathologic confirmation of NSCLC; (*3*) medically operable cancer but selection of SBRT after refusal to undergo surgery. Medical operability was discussed within the multidisciplinary tumor board of each institution according to respiratory function, age, and complicating diseases. Basic cutoff values for medical operability were World Health Organization performance status $\leq$2, pressure of arterial oxygen $\geq$65 mm Hg, predicted postoperative forced expiratory volume in 1 s $\geq$800 mL, no heart failure requiring pharmacotherapy, no diabetes requiring insulin, no severe arrhythmia, and no history of cardiac infarction. Positron emission tomography was not essential in the staging procedures.

Patients were informed of the concept, methodology, and rationale of this treatment, which was performed in accordance with the 1983 revision of the Declaration of Helsinki.

Table 1. Patient characteristics

Number (14 institutions)	87
Male	63
Female	24
Age (y), median (range)	74 (43–87)
ECOG performance status	
0	51
1	30
2	6
Histology	
Adenocarcinoma	54
Squamous cell carcinoma	25
Other	8
Stage	
IA	64
IB	23
Tumor diameter (mm), median (range)	25 (7–50)
IA	21
IB	39
Chronic lung disease	
Positive	38
Negative	49

Abbreviation: ECOG = Eastern Cooperative Oncology Group.
Values are number unless otherwise noted.

Patient characteristics

A summary of patient pretreatment characteristics is given in Table 1. From April 1995 to March 2004, a total of 87 medically operable patients with primary NSCLC were treated using hypofractionated high-dose SBRT in 14 major Japanese institutions. Each of these 87 cases was judged medically operable, and surgery was initially recommended, but the patients declined surgery and selected SBRT as a radical treatment. Pathology of all tumors was confirmed as NSCLC by transbronchial or CT-guided percutaneous biopsy. The 14 participating institutions were these: Hokkaido University; Kyoto University; Cancer Institute Hospital; Tokyo Metropolitan Komagome Hospital; Kitasato University; Tohoku University; Hiroshima University; Tokyo Metropolitan Hiroo Hospital; Sapporo Medical University; Institute of Biomedical Research and Innovation; International Medical Center of Japan; Tenri Hospital; Kitami Red Cross Hospital; and Yamanashi University.

Treatment methods

Although the techniques to accomplish stereotactic methods differed among these institutions, all "stereotactic radiotherapy techniques" fulfilled the following five requirements: (*1*) reproducibility of the isocenter (setup error $\leq$5 mm), as confirmed by image guidance for every fraction; (*2*) respiratory motion (internal margin) suppressed using as much as possible, to <5 mm; (*3*) slice thickness on CT $\leq$3 mm for three-dimensional treatment planning; (*4*) irradiation with multiple noncoplanar static ports or dynamic arcs; and (*5*) single high dose $\geq$5 Gy.

Gross target volume (GTV) was delineated on CT images displayed with a lung window level. Clinical target volume (CTV) marginally exceeded GTV by 0–5 mm as judged by the individual radiation oncologist. Internal margin was

calculated and set around the CTV by 2–5 mm according to the individual measurements for respiratory motion of each institution. Internal margin caused by respiratory motion was reduced by gating, tracking, breath-hold technique, or abdominal compression. Planning target volume (PTV) comprised the CTV, a proper internal margin measured in each patient, and a 5-mm safety margin. The total margin between PTV and GTV was thus 7–15 mm. The irradiated port marginally exceeded PTV by 3–5 mm to secure the surface dose of PTV. Dose calculation was performed using the Clarkson algorithm and heterogeneity correction. A total dose of 45–72.5 Gy (mean, 58.7 Gy) at the isocenter in 3–10 fractions with single doses of 6.25–15 Gy was administered with 6-MV X-rays within 20% heterogeneity in the PTV dose. Minimum dose in the PTV corresponded to 85–95% of the prescribed dose in most cases. Typical dose/fractionation schedules were 75 Gy in 10 fractions for 42 patients and 48 Gy in 4 fractions for 38 patients. In principal, patients were treated on consecutive days, but some patients were treated every other day. No chemotherapies were administered before or during radiotherapy.

To compare the effects of various treatment protocols with different fraction sizes and total doses, BED was utilized in a linear-quadratic model (19). Biologically effective dose was here defined as $nd(1 + d/\alpha/\beta)$, with units of Gy, where n is fractionation number, d is daily dose, and α/β is assumed to be 10 for tumors. Biologically effective dose was not corrected with values for tumor doubling time or treatment term. Biologically effective dose was calculated at the isocenter in this study. Median calculated BED was 116 Gy (range, 100–141 Gy).

No restriction was placed on whether the tumor was located peripherally or centrally in the lung, but dose for the spinal cord was limited. Biologically effective dose limitation for spinal cord was 80 Gy (α/β was assumed to be 2 Gy for chronic spinal cord toxicity). Doses for other organs were not restricted.

Evaluation

The objectives of this study were to retrospectively evaluate toxicity, local control rate, and survival rate. Follow-up examinations were performed 4 weeks after treatment first, then patients were seen every 1–3 months. Tumor response was evaluated using the Response Evaluation Criteria in Solid Tumors by CT (20). Chest CT (slice thickness, 2–5 mm) was usually obtained every 2 to 3 months for the first year and repeated every 4–6 months thereafter. Complete response indicated that the tumor had completely disappeared or was judged to have been replaced by fibrotic tissue. Partial response was defined as a ≥30% reduction in maximum cross-sectional diameter. Distinguishing between residual tumor tissue and radiation fibrosis was difficult. Any suspicious residual confusing density after radiotherapy was considered evidence of partial response, so actual complete response rate may have been higher than presented herein. Distinguishing between local recurrence and inflammatory change was also difficult. Here, local recurrence was considered to have occurred only when enlargement of the local tumor continued for >6 months on follow-up CT, obviously positive findings were identified on positron emission tomography, or histologic confirmation was acquired. Findings on CT were interpreted by two radiation oncologists in each case. Absence of local recurrence was defined as locally controlled disease. Lung, esophagus, bone marrow, and skin were evaluated using version 2 of the National Cancer Institute–Common Toxicity Criteria.

Statistical analysis

Cumulative rates of progression-free status at local, regional lymph node, and distant sites and survival were calculated and drawn using Kaplan-Meier algorithms, with day of treatment as the starting point. Subgroups were compared using log–rank statistics. Values of $p < 0.05$ were considered statistically significant. Statistical calculations were conducted using StatView version 5.0 software (SAS Institute, Cary, NC).

RESULTS

All patients completed treatment without obvious complaints. Median durations of observation for all patients and survivors as of final follow-up were 55 and 63 months, respectively.

Local tumor response

Complete response was achieved in 28 patients (32.2%), and partial response was seen in 43 patients (49.4%).

Toxicity

Radiation-induced pulmonary complications of National Cancer Institute–Common Toxicity Criteria (version 2.0) Grade 0, 1, 2, and 3 were noted in 21 (24.1%), 61 (70.1%), 4 (4.6%), and 1 patient (1.1%), respectively. Rib fracture and Grade 3 dermatitis were observed in 4 (4.6%) and 3 patients (3.4%), respectively. All tumors bordered the chest wall. Grade 3 radiation-induced esophagitis was produced in 1 patient, in whom the tumor slightly bordered the esophagus. Maximum esophageal dose in this case was 30 Gy in 5 fractions. No vascular, cardiac, or bone marrow complications had been encountered as of last follow-up. In total, Grade 3 toxicities were identified in 8 patients (9.2%).

No definite second malignancies were found during follow-up, but 1 patient died of acute myelogenous leukemia 3.7 years after completing SBRT.

Recurrence

Local recurrence, lymph node metastases, and distant metastases occurred in 8 (9.2%), 13 (14.9%), and 19 cases (21.8%), respectively.

Cumulative local progression–free rate curves according to stage are shown in Fig. 1. Cumulative local progression–free rate after 5 years was 86.7% (95% confidence interval [CI], 78.3–94.9%) for total cases. Cumulative local progression–free rate at 5 years was 92.0% (95% CI, 83.8–99.6%)

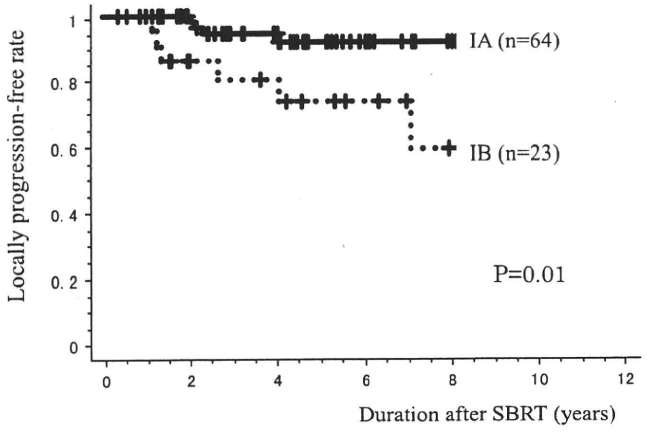

Fig. 1. Cumulative local progression–free rate curves, according to stage. SBRT = stereotactic body radiotherapy.

for the Stage IA subgroup, significantly superior ($p = 0.01$) to that for the Stage IB subgroup (73.0%; 95% CI, 52.2–93.7%). Five-year local progression–free rates were not significantly different between adenocarcinoma (80.9%; 95% CI, 68.7–93.1%) and squamous cell carcinoma (95.5%; 95% CI, 86.7–100.0%). One patient who developed local recurrence underwent surgery and has remained healthy for more than 3 years after operatively. The operation method was upper lobectomy and mediastinal lymphadenectomy, and they were performed safely without any trouble.

Cumulative curves of regional lymph node and distant metastases–free rates according to stage are shown in Figs. 2 and 3, respectively. The 5-year lymph node metastasis–free rate and distant metastasis–free rate for total cases was 85.3% (95% CI, 77.6–93.0%) and 75.1% (95% CI, 64.8–85.4%], respectively. No significant difference was identified between Stage IA and IB subgroups.

In patterns of regional nodal recurrence, 8 patients (61.5%) showed nodal failure alone, 2 patients (15.4%) had nodal failure combined with local failure, and 3 patients (23.1%) showed nodal failure combined with distant metastases.

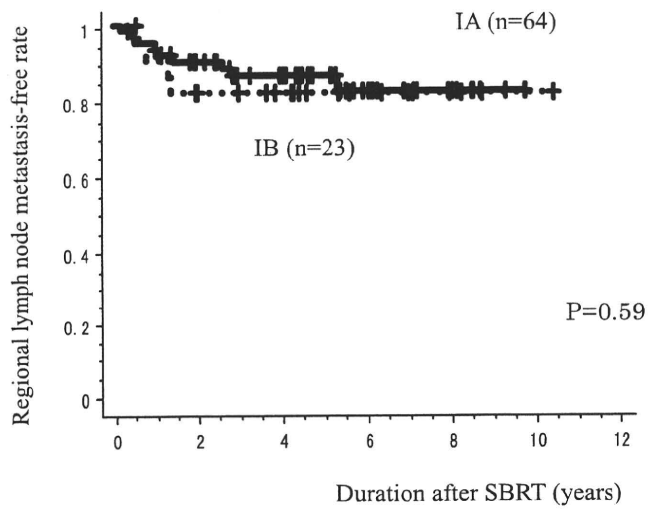

Fig. 2. Cumulative regional lymph node metastasis–free rate curves, according to stage. SBRT = stereotactic body radiotherapy.

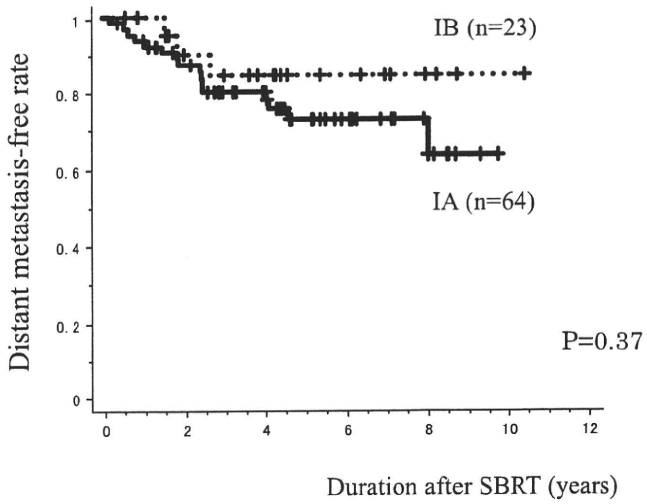

Fig. 3. Cumulative distant metastasis–free rate curves, according to stage. SBRT = stereotactic body radiotherapy.

Survival

Overall and cause-specific 5-year survival rates for total cases were 69.5% (95% CI, 58.8–80.1%) and 76.1% (95% CI, 65.9–86.3%), respectively. Overall and cause-specific survival curves according to stage are shown in Figs. 4 and 5, respectively. Five-year overall survival rate was 72.0% (95% CI, 59.6–84.4%) in Stage IA patients and 63.2% (95% CI, 42.7–83.6%) in Stage IB patients. A marginal but nonsignificant ($p = 0.14$) difference was found between overall survival rates of Stage IA and IB groups. In terms of histology, overall 5-year survival rate was 72.2% (95% CI, 59.2–85.2%) in the adenocarcinoma subgroup and 60.8% (95% CI, 38.4–83.2%) in the squamous cell carcinoma subgroup.

DISCUSSION

Exposing a tumor to a higher dose of radiation without increasing adverse effects can be achieved using stereotactic techniques. Stereotactic irradiation is an approach using

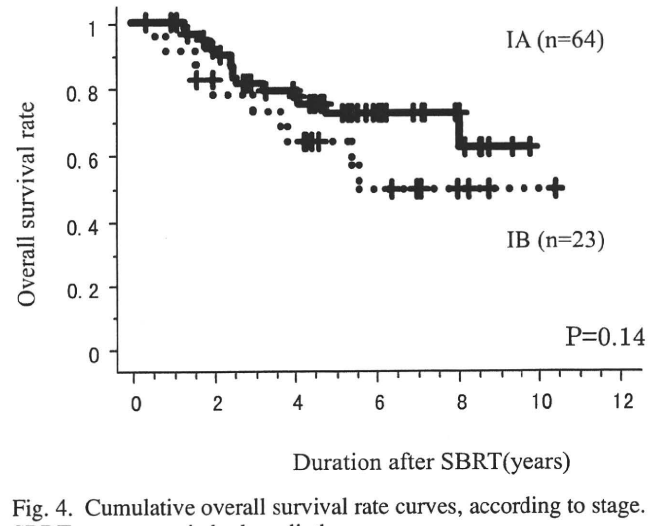

Fig. 4. Cumulative overall survival rate curves, according to stage. SBRT = stereotactic body radiotherapy.

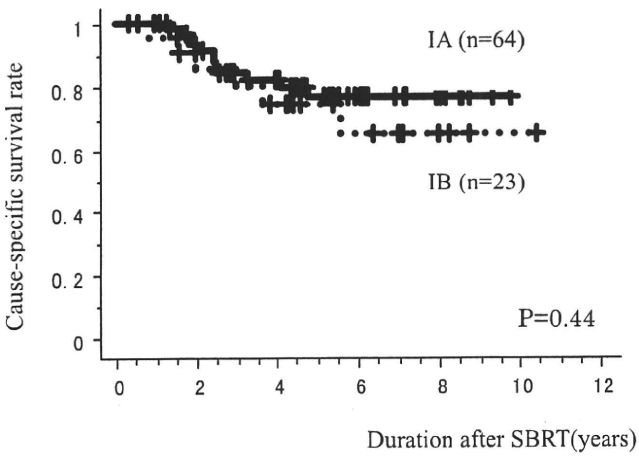

Fig. 5. Cumulative cause-specific survival rate curves, according to stage. SBRT = stereotactic body radiotherapy.

multiple noncoplanar convergent beams, precise localization with a stereotactic coordinate system, rigid immobilization, and single high-dose treatment, maximizing delivery to the tumor and minimizing the exposure of normal tissue. This approach can also substantially reduce overall treatment time from several weeks of conventional radiotherapy schedule to a few days, offering an important advantage to the patient. Stereotactic irradiation techniques are well established for the treatment of intracranial malignancies, but use in extracranial malignancies has been considered problematic because of the issues of fixation and internal motion. In 1994, Blomgren *et al.* (21) described a technique of SBRT using a custom-made body cast and stereotactic coordinates. In 1996, Uematsu *et al.* (22) reported a CT–linear accelerator unit sharing a common couch, enabling image-guided fractionated SBRT without rigid immobilization. Since verification of the effects and safety of SBRT for lung cancer (12), this treatment method has rapidly been adopted in many institutions (Table 2) (12–17, 23, 24). Although various fractionation schedules are undergoing evaluation around the world, a frequently used BED prescribed for tumors with SBRT for Stage I NSCLC in Japan has been set at a little over 100 Gy, as recommended in our previous study (18). However, concerning determination of the truly optimal dose of SBRT for Stage I NSCLC, many problems and controversies remain, such as dose-calculation algorithms (16), inhomogeneity corrections, essential dose for tumor control (24), and dose constraints for organs at risk (25, 26).

Although a number of articles on SBRT for Stage I NSCLC have been published, duration of follow-up in most cases has not been sufficiently long, and almost all treated patients were medically inoperable. The present study thus provides data on two important areas.

One was cumulative local recurrence and metastatic rates with a long duration of follow-up after SBRT. Rates of local control and metastases depend largely on the duration of follow-up and generally deteriorate as the duration of follow-up increases. Furthermore, recurrence rates have been reported in numerous articles, but most of them were crudely calculated rate. We have presented 5-year cumulative local control, regional lymph node recurrence–free and distant metastasis–free rates, calculated using Kaplan-Meier methods. The local progression–free rate in our results was unsatisfactory, particularly for the T2 tumor subgroup. The Japanese Clinical Oncology Group (JCOG) has thus started a multi-institutional dose-escalation study for Stage IB NSCLC patients (JCOG 0702).

Another meaningful result was the overall survival rate with a longer follow-up duration, allowing comparison between SBRT and surgery. Although the survival rate in this study was less than in our previous reports, we consider this information worth reporting, because median duration of follow-up was almost 5 years. Uematsu *et al.* (12) reported a 3-year overall survival rate of 86% in 29 medically operable patients with Stage I NSCLC, but the number of patients was small, and follow-up duration was relatively short. Because the number of medically operable patients treated with SBRT was very small in individual institutions, the present study collated the data of operable patients from multiple institutions. Whether the survival rate of SBRT was lower than that of surgery could not be clarified from our results. Representative 5-year overall survival rates of surgery for clinical

Table 2. Reports of SBRT for Stage I NSCLC

First author (reference)	*N*	Total dose (Gy)	Single dose (Gy)	BED (Gy)	Median follow-up (mo)	Local recurrence (%)	3-y overall survival (%)
Uematsu (12)	50	72	7.2	124	60	6*	6
Nagata (13)	42	48	12	106	52	3*	82
Onimaru (14)	28	48	12	106	27	36†	82 (Stage IA) 32 (Stage IB)
Onishi (15)	26	72	7.2	124	24	8*	75
Takeda (16)	63	50	10	100	31	5†	90 (Stage IA) 63 (Stage IB)
Koto (17)	31	45–60	7.5–15	105–113	32	29*	72
Hof (23)	10	19–26	19–26	55–94	15	40*	37
Fakiris (24)	47	60–66	20–22	180–211	50	12†	43

Abbreviations: SBRT = stereotactic body radiotherapy; NSCLC = non–small-cell lung cancer; BED = biologically effective dose ($\alpha/\beta = 10$).
* Crude data.
† Cumulative data calculated with Kaplan-Meier method.

Table 3. Comparison of 5-y overall survival rate between surgical series and SBRT

Clinical stage	United States (1)	Japanese National Cancer Center (2)	Japanese National Survey (3)	SBRT
IA	61	71	77	76
IB	40	44	60	64

Abbreviation: SBRT = stereotactic body radiotherapy.
Values are percentages.

Stage IA and IB NSCLC are listed in Table 3 (1–3), ranging approximately 60–75% for Stage IA and 40–60% for Stage IB. We cannot conclude that the survival rate for SBRT is equivalent to that for surgery, because the present data for SBRT are based on a retrospective study and small sample size. However, the background of patients treated by SBRT in this study seems likely to have included worse prognostic factors than those in patients treated surgically. Concerning the size and characteristics of tumors, good prognostic factors such as smaller tumor size (27) or lower-density mass (so-called ground-glass opacities) (28) might be more frequently included in patients treated with surgery, because the determination of histological malignancy before SBRT was difficult for such tumors. In addition, median age of patients treated by surgery was approximately 10 years younger in the surgical series (median, 60–65 years) than in the SBRT series (median, 75 years). We therefore believe that survival rates for SBRT in medically operable patients are potentially comparable to those for surgery.

Regarding treatment-related toxicity, the rate of severe (Grade $\geq$3) acute and short-term chronic complications after SBRT was very low and acceptable, despite the high age of those patients (median, 74 years) in our experience. In results for pulmonary lobectomy, Deslauriers *et al.* (29) reported much higher mortality and morbidity rates that increased with aging. In other reports, mortality rates for patients aged >70 years old after pulmonary lobectomy were 7.6% (30). Even though improvements of mortality and morbidity of surgery may have recently been achieved (31), in particular under a technique of video-assisted thoracoscopic lobectomy (32), we consider SBRT as a safer and less invasive treatment modality than surgery, at least for peripherally located lung tumor up to 5 years after treatment. However, reports of SBRT for centrally located lung tumor have shown a comparably high risk (25, 26), and long-term chronic toxicity remains unclear. A longer and larger follow-up of SBRT is needed.

We thus consider that SBRT may offer a useful option for initial radical treatment of at least peripheral Stage IA NSCLC, not only for medically inoperable patients but also for operable patients. However, regarding centrally located or large T2 tumors, surgery must still be recommended as the first choice of treatment until further data can be accumulated. Although we encountered only 1 case in the present study, pulmonary lobectomy and mediastinal lymph node resection were performed without difficulty for a locally recurring tumor after SBRT. Surgery might be an option as salvage therapy for locally recurrent cases after radical SBRT for Stage I NSCLC.

In Japan, the number of patients treated with SBRT has exploded, especially since SBRT for lung cancer has been covered by the national health insurance since 2004. A Phase II multi-institutional study of JCOG researching the efficacy and toxicity of SBRT for both medically operable and inoperable Stage IA NSCLC patients (JCOG 0403) started in 2004, and patient entry was completed in October 2008. A total of 90 medically inoperable and 65 operable patients have been enrolled. In the United States, a Phase II multi-institutional study of SBRT for only medically inoperable Stage I NSCLC patients (Radiation Therapy Oncology Group 0236) has been ongoing.

Even multi-institutional Phase II studies of SBRT for Stage I NSCLC may have inevitable selection bias compared with surgical series. A prospective randomized trial is essential to conclude whether outcomes of SBRT for medically operable patients are truly comparable to those of surgery. A protocol for randomized studies comparing SBRT with surgery for Stage I NSCLC has been initiated (33) but has not progressed. Such a randomized study is likely to prove very difficult to perform, because most patients may hope for more minimally invasive therapy, such as SBRT. Many more experiences for more patients with a longer follow-up duration are thus needed to confirm the safety and effects of SBRT as a radical treatment for operable Stage I NSCLC. If the experience of SBRT for medically operable Stage I NSCLC matures and produces no poor results in future, SBRT will have a marked impact on standard treatment procedures for lung cancer and provide good news for Stage I lung cancer patients, the prevalence of whom is likely to increase.

In conclusion, treatment results of SBRT reviewed from a Japanese multi-institutional database showed that SBRT is safe and promising as a radical treatment for operable Stage I NSCLC. The survival rate of SBRT is potentially comparable to that of surgery.

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A Simple Respiratory Indicator for Irradiation during Voluntary Breath Holding: A One-Touch Device without Electronic Materials[1]

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Purpose: To evaluate the use, structural principles, operation, and acquired reproducibility of a respiratory monitoring device to be used for voluntary patient breath holding.

Materials and Methods: Evaluation was performed of a respiratory monitoring device that enables determination of the respiratory level in a patient by measuring the movement of two contacts on the abdomen and chest wall. Neither metallic nor electronic materials are used in the mechanics for this device. The initial study group comprised 21 consecutive patients (15 men, six women; mean age, 75 years; range, 56–92 years) with lung or abdominal tumors who underwent examination with the device and computed tomography (CT) for three-dimensional reproducibility of lung base position during voluntary breath holding with or without use of the device.

Results: One patient with mild dementia was excluded; in most of the remaining 20 patients, high reproducibility of the breath-holding position was achieved in a short time with the device. In these 20 patients who were able to adapt to use of the device, three-dimensional mean maximum differences in lung base position during three random voluntary breath holds were 2.0 mm along the cranial-caudal axis, 1.5 mm along the anterior-posterior axis, and 1.2 mm along the right-left axis. The differences in all axes were significantly smaller with use of the respiratory monitoring device than without the device.

Conclusion: The device demonstrates satisfactory reproducibility of voluntary patient breath holding easily and inexpensively and may offer a convenient device for easy use during irradiation with voluntary breath-holding conditions that require a small internal margin.

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Received June 20, 2009; revision requested August 19; revision received October 30; accepted November 9; final version accepted January 7, 2010. Supported in part by a grant-in-aid from the Ministry of Health, Welfare, & Labor, Japan. **Address correspondence to** H.O. (e-mail: *honishi@yamanashi.ac.jp*).

During radiation therapy to the abdominal and thoracic organs, minimizing the size of the radiation field while allowing for organ motion is important to reduce normal tissue toxicity and improve therapeutic effectiveness. Although image-guided radiation therapy systems are effective for reducing interfractional setup margins, intrafractional internal motion caused by patient respiration cannot be controlled. Interest in techniques designed to control respiratory movements has been growing since the mid-1990s, with the development of approaches including breath holding (1–3), respiratory gating (4,5), and beam tracking (6). Of all these techniques, we consider breath holding to be the most obvious and simplest solution to reduce uncertainties related to movements induced by breathing and to increase the reproducibility of treatment. Two approaches can be used for breath holding: active breathing control (1) and voluntary breath holding (2,3). Although these methods initially appear similar, the former is relatively invasive in nature for patients, since breathing is controlled forcibly by a valve in the spirometer. Voluntary breath holding thus appears preferable for patients with lung cancer in whom pulmonary function is apt to be poor. Though some teams have tried nonmonitored voluntary breath holding with a certain degree of success (7–10), these techniques have been considered uncertain, and various respiratory monitoring apparatuses have been introduced to improve the reproducibility of breath holding. However, as most existing apparatuses are complex, costly, or inaccurate (11), voluntary breath-holding techniques that use such devices are again unsuitable for small and intermediate-sized medical facilities with inexperienced staff.

We therefore aimed to develop a method of self–breath holding that can be performed as simply, nonelectronically, noninvasively, and inexpensively as possible. The purpose of our study was to evaluate the use, structural principles, operation, and acquired reproducibility of a newly developed simple respiratory monitoring device that has two contacts on the abdominal and chest wall of the patient.

Advances in Knowledge

- We developed a respiratory indicator that is simpler and less expensive than other conventional indicators.
- This device enables determination of the respiratory level in a patient by measuring movement of two contacts on the abdomen and chest wall without needing electronic materials.
- Our preliminary experiences show that this device is easily used during irradiation with voluntary breath-holding conditions that require a small internal margin.

Materials and Methods

All study protocols were approved by the institutional review board, and all patients provided written informed consent prior to participating in the study.

Technical aspects of the device including the structural principles, materials used, and the indicator rotation setting in relation to the contact movement were partially suggested by the coauthor (H.K.) who is an investigator at Apex Medical (Tokyo, Japan). The company provided no other material or financial support and had no control or other involvement in the study.

Implications for Patient Care

- The device uses a simple method to achieve good reproducibility for voluntary patient breath holding during irradiation.
- The device can minimize intrafractional respiratory organ motion nonelectronically, noninvasively, and inexpensively.
- The device may offer substantial benefits to facilities that lack highly trained staff and resources.

Structure and Operation of the Device

Figure 1 shows the main body of the device, which consists of thoracic and abdominal contacts, a stand, a mechanical unit, and a respiratory level indicator panel. The framework of the device is hollow and made of carbon. As a result, the effect of radiation absorption by the device on dose distribution of the irradiation field is negligible.

The device is normally used by placing the one contact each on the chest and abdomen of the patient, who lies in a supine position (Fig 2). The equipment used for the study in conjunction with the device included a whole-body computed tomography (CT) scanner (Hi-Speed DX/I; GE Yokogawa Medical Systems, Tokyo, Japan), and an x-ray simulator (SAT-20; Shimadzu, Kyoto, Japan).

Vertical motions of the chest and abdomen associated with breathing are detected by the thoracic and abdominal contacts, and movements of the contacts are added and converted to a rotational angle of a needle in the level meter. The contacts are designed such that a 1-cm movement on the body surface results in a rotation of 23° on the level meter. When both contacts move 1 cm in the same direction as a result of breathing by the patient, the indicator rotates by as much as 46°. The patient can thus control his or her breathing by watching the indicator.

The level indicator panel has two markers, red and yellow, that define the levels of full exhalation and full inhalation and one blue marker that defines

Published online
10.1148/radiol.10090890

Radiology 2010; 255:917–923

Author contributions:
Guarantors of integrity of entire study, H.O., H.K., T.K., K.K., M.A., R.S.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; literature research, H.O., K.K., R.S.; clinical studies, H.O., H.K., K.M., K.K., M.A., R.S., S.A.; experimental studies, H.O., H.K., T.K., M.A., R.S.; statistical analysis, H.O., R.S.; and manuscript editing, H.O., R.S., T.A.

See Materials and Methods for pertinent disclosures.

Figure 1

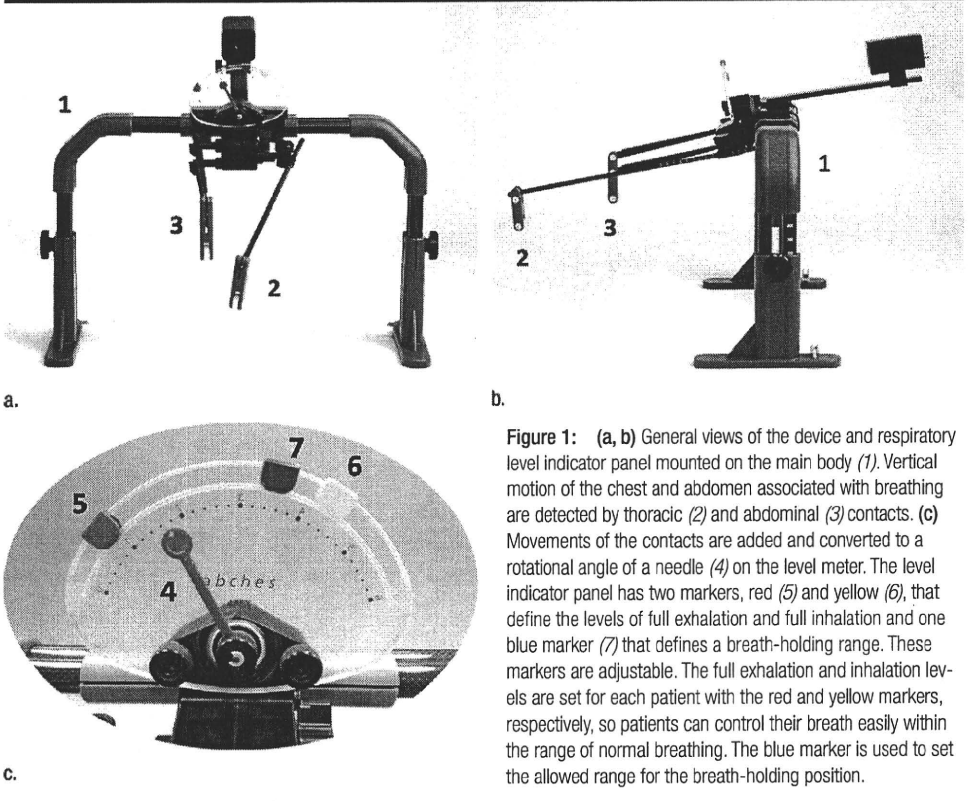

Figure 1: **(a, b)** General views of the device and respiratory level indicator panel mounted on the main body *(1)*. Vertical motion of the chest and abdomen associated with breathing are detected by thoracic *(2)* and abdominal *(3)* contacts. **(c)** Movements of the contacts are added and converted to a rotational angle of a needle *(4)* on the level meter. The level indicator panel has two markers, red *(5)* and yellow *(6)*, that define the levels of full exhalation and full inhalation and one blue marker *(7)* that defines a breath-holding range. These markers are adjustable. The full exhalation and inhalation levels are set for each patient with the red and yellow markers, respectively, so patients can control their breath easily within the range of normal breathing. The blue marker is used to set the allowed range for the breath-holding position.

a breath-holding range (Fig 1). The patient holds his or her breath to bring the indicator to the blue marker. In this way, CT scanning and irradiation can be performed accurately for the duration of patient-controlled breath holding.

The device has auxiliary components that include a mirror and a switch for the patient (Fig 2). The mirror allows the patient in the supine position to easily watch the level indicator. The switch is used by the patient to inform the radiotherapist of the breath-holding state, so that the radiotherapist can then perform treatment in collaboration with the patient.

The technician also can observe the device indicator needle remotely by means of a charge-coupled device monitor mounted on the patient table, and when the technician notices that the breath is not being held appropriately, the technician will assist the patient to improve control.

Setting of the Device and Instruction on Breath Holding

Initially, 21 patients who had been introduced consecutively to our department to undergo radiation therapy for lung or abdominal tumors were included as subjects, but one patient (92-year-old female) was excluded from the study because she was unable to understand the breath-hold technique owing to mild dementia. As a result, 20 patients were enrolled in the study. The background and clinical characteristics of the 20 patients are shown in Table 1. Nine patients had chronic pulmonary disease, and respiratory function parameters were below normal limits in seven of 20 patients.

The body of the patient was fixed with a vacuum pillow, and use of the device was explained to patients by showing them a fluoroscopic image of the diaphragm in respiratory motion. Using the device, subjects were taught to keep a regular respiratory rhythm within a uniform range on the indicator of the device. Signal waveforms of respiratory volume were acquired by using a spirometer (HI-801; Central Sports, Tokyo, Japan) during free respiration with and without use of the device. Subjects were then instructed to hold their breath during inspiration so as to maintain an identical position through voluntary breath holding.

Measurement of Reproducibility of Lung Base Position during Repeated Breath Holds

After patients fully understood and mastered voluntary breath holding with and without the use of the device, a set of three CT scans was obtained with the device and another set was obtained without the device (ie, six CT scans total), to obtain randomly timed images of 2 mm thickness in the vicinity of the lung base. The CT scanning interval

Figure 2

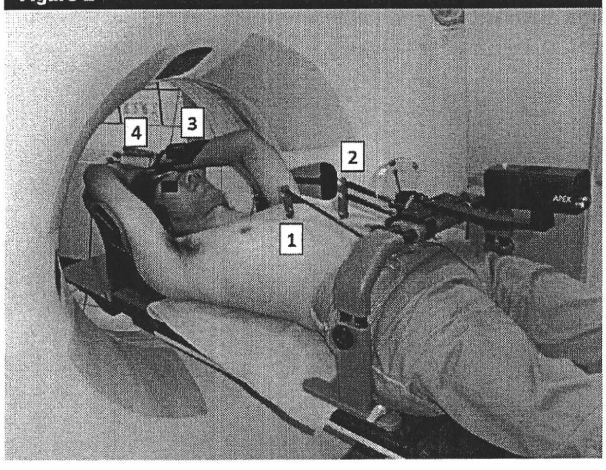

Figure 2: View of the main body of the device in use on a patient. Two contacts are placed on the chest *(1)* and abdomen *(2)* of a patient lying in a supine position. Auxiliary components on the device include a mirror *(3)* and a switch *(4)* for the patient. The height of the device is adjusted to the body size of each patient to ensure that the two contacts touch the abdomen and thorax.

Table 1

Patient Characteristics

Characteristic	Finding
Total no. of patients	20
Men	15
Women	5
Age (y)	56–86 (74)
Men	56–84 (72)
Women	72–86 (77)
Smoking index*†	
0–200	6
200–600	10
>600	4
Tumor site†	
Thoracic	16
Abdominal	4
ECOG performance status	0–2 (1)
$FEV_{1.0}$ (mL)	650–2350 (1520)
SaO_2 (mmHg)	65–90 (76)

Note.—Unless otherwise indicated, data are ranges, and numbers in parentheses are medians. ECOG = Eastern Cooperative Oncology Group, $FEV_{1.0}$ = forced expiratory volume in the first second, SaO_2 = arterial oxygen saturation.

*Average daily number of cigarettes multiplied by years.

† Data are numbers of patients.

was approximately 5 minutes. The first three scans were obtained during breath holding by using the device; the next three scans were obtained without the device. On the 2-mm-thick images in the vicinity of the lung base, an arbitrary point for measuring reproducibility of repeated breath holds was set on a clear peripheral vascular structure, and the maximum difference in measurement point for the three CT scans was calculated along three axes: cranial-caudal, anterior-posterior, and right-left. The detailed method for measuring reproducibility has been described previously (7).

Statistical Analysis

The statistical significance of disparities in maximum differences of lung base position in all patients with and without the device was determined by using a paired *t* test. All probabilities were two-tailed, with $P < .05$ considered to indicate a statistically significant difference. Statistical calculations were performed by using statistical software (StatView, version 5; SAS Institute, Cary, NC).

Results

Effect of the Device on Breathing

Figure 3 shows examples of respiratory volume curves measured with the spirometer obtained during free breathing without the device and under an instruction to breathe within a uniform range using the device. The respiratory volume curve obtained by using the device was more regular than that without the device.

Reproducibility of Breath Holding

All 20 patients practiced self-controlled breath holding by using the respiratory monitoring device. The mean time necessary for each of the 20 patients to be instructed on the use of the device and to master voluntary breath holding with and without the device was 20 minutes (range, 15–30 minutes). Mean duration of each breath hold was 18 seconds (range, 10–40 seconds).

Among the 20 patients who understood the breath-holding method, reproducibility of the measurement point during breath holds obtained by using the device was compared with that obtained without the device. The results are shown in Table 2. For the 20 patients, mean maximum differences in the measurement points obtained with and without the device, respectively, were 2.0 and 4.2 mm along the cranial-caudal axis, 1.5 and 2.8 mm along the anterior-posterior axis, and 1.2 and 2.0 mm along the right-left axis. Differences in all axes were significantly smaller ($P < .05$) with the device than without the device.

Case

An electronic portal imaging device was used to evaluate the reproducibility of tumor position during each radiation therapy session. Real-time electronic portal imaging was performed five to 10 times during each fraction. Examples of CT images and intrafractional electronic portal images in the vicinity of the tumor during voluntary breath holding with the device obtained before and during radiation therapy are shown in Figure 4 and 5, respectively.

Discussion

A widely used voluntary breath-holding technique is performed with a spirometer connected to a screen or video glasses

Figure 3

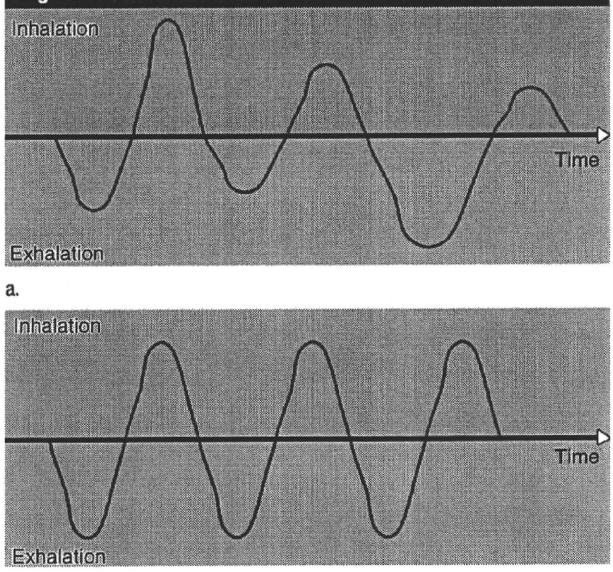

Figure 3: Examples of respiratory volume curves measured by using spirometry (HI-801; Central Sports, Tokyo, Japan) obtained during **(a)** free-breathing and **(b)** an instruction to breathe within a uniform range with the device.

Table 2

Reproducibility of Breath-holding Position of the Lung Base with and without the Device

Axis	With Device (mm)	Without Device (mm)
Craniocaudal direction		
Mean ± standard deviation*	2.0 ± 1.3	4.2 ± 2.2
Range	0–4	0–10
Anteroposterior direction		
Mean ± standard deviation*	1.5 ± 1.2	2.8 ± 1.8
Range	0–3.6	0.3–4.0
Left-right direction		
Mean ± standard deviation*	1.2 ± 1.1	2.0 ± 1.5
Range	0.0–3.0	0.3–3.8

*Differences in all axes were significantly smaller ($P < .05$) with this system than without it.

and indicates in real time, for the technicians and/or patient, the desired and actually achieved levels of breath hold (2,3). Hanley et al (2) used a voluntary deep-inspiration breath-hold system with a spirometer for patients with non–small cell lung cancer, and reported an intra–breath-hold reproducibility of 1.0 mm ± 0.9 and an inter–breath-hold reproducibility of 2.5 mm ± 1.6. In regard to intrafraction reproducibility of breath-holding positions, our technique using the device was not inferior to these other breath-hold techniques and devices.

The method performed with the present device has some merits for voluntary breath-holding technique. The greatest merit of the device is the simplicity of the mechanism and structure and convenience for patients and radiation therapy staff. To our knowledge, no other devices have been described that do not use electronic materials. Setting of other existing systems is regarded to be relatively more complicated than that of the present device. This device is also easy to install and is inexpensive. While most small and intermediate-sized medical facilities do not have equipment to compensate for respiratory motion, because such facilities have insufficient time, manpower, and/or money to introduce complicated irradiation schemes, our device appears highly effective for solving the above-mentioned problems.

In addition, existing commercially available respiratory monitoring systems, such as the Real-time Position Management system (Varian, San Francisco, Calif) and the Anzai motion-monitoring system (AZ-773V; Anzai Medical, Tokyo, Japan), have only one detection point for respiratory monitoring and may not be able to capture precise breathing phases, which are affected in a complex fashion by the respiratory motions of the thorax and abdomen. While Mageras et al (12) and Vedam et al (13) reported a good phase relationship between abdominal and diaphragm motions, Nakamura et al (14) and Ahn et al (15) reported some differences between lung tumor and abdominal motions. A hysteresis curve was also observed. In contrast, with the present device, two detection points can be set arbitrarily on the chest and abdomen. This may allow synthesis of the movements measured at two sites, and we have been investigating whether the device can achieve more precise monitoring than other devices using one detection point.

Moreover, the device is versatile and enables a therapeutic procedure that normally requires high precision. The range of stabilized respiration was better with our device than without it (Fig 3). The device is also helpful for regulating breathing levels in a steady range and thus may be useful for gated or tracking radiation therapy.

Finally, the device has the great merit of requiring active patient involvement in switching and voluntary breath holding. When using the device, it is most important that the patient understands the purpose and nature of the method. A report of Task Group 76 of the American Association of Physics in Medicine (16) stressed that breath control requires active participation of the patient. This device contributes to such participation in treatment.

Carlson et al (17) reported good breath-hold reproducibility by using a bellows-based breath-hold monitoring

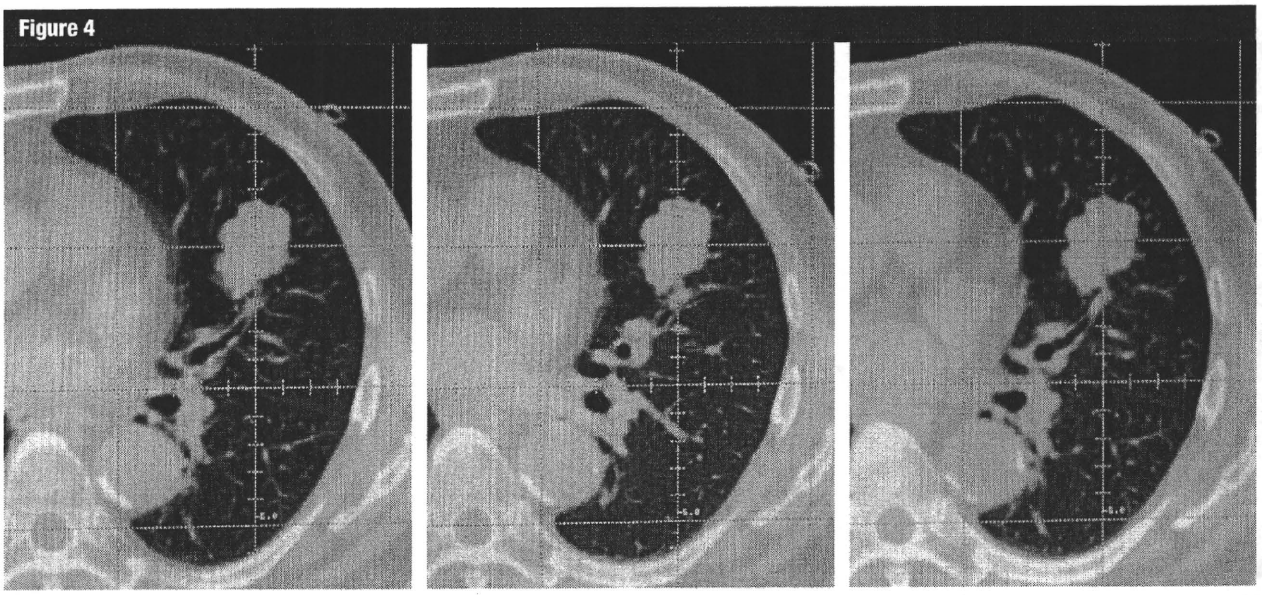

Figure 4: CT images obtained during voluntary breath holding with the device. Before every session of radiation therapy, a set of three CT scans is performed to obtain randomly timed images of 2 mm thickness in the vicinity of the tumor. **(a–c)** Images obtained with the first, second, and third scan, respectively. The scanning interval was approximately 5 minutes. Maximum differences in tumor position in craniocaudal, anteroposterior, and right-left directions on three CT studies were 1, 0.7, and 0.5 mm, respectively.

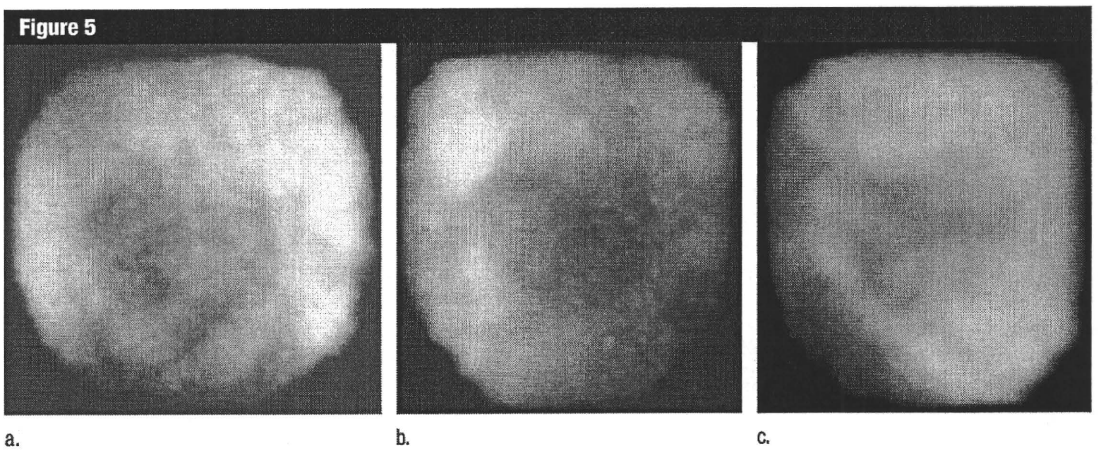

Figure 5: Example of intrafractional electronic portal images obtained during radiation therapy during voluntary breath holding with the device. Radiation therapy was performed with 10 noncoplanar static ports. **(a–c)** Three of the 10 portal images show that the tumor shadow lay appropriately on the planned position in each port.

and feedback system for CT-guided biopsy of the lung and upper abdomen. The basic components of the system are a Velcro belt with expandable bellows, a light-emitting diode monitor for patient feedback, and a system control unit. Variation in the length of the bellows causes a pressure change within the tubing, which is measured with a pressure-sensitive transducer. Although no detailed reproducibility of breath hold using this system was described in the report, the patient feedback system resembles our own. The device used in our study may also contribute to such operations of interventional radiology requiring good breath-hold reproducibility.

Applicability of the device must be established for each patient during preliminary practice sessions. Moreover, some key points should be noticed when patients are instructed on how to hold their breath. We routinely instruct patients to maintain smooth and regular breathing before breath holding. It is also important to educate patients

not to use abdominal muscles to adjust the indicator. If a patient deviates from these instructions, a large error can be produced that exceeds the estimated error. Sufficient instruction and practice are essential to achieving good reproducibility with the device.

In summary, we developed a simple and accurate respiratory monitoring indicator for irradiation during self-controlled voluntary breath holding that will offer substantial benefits to all facilities even if they lack highly trained staff and resources.

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J. Radiat. Res., 51, 543–552 (2010) Regular Paper

What is the Optimum Minimum Segment Size Used in Step and Shoot IMRT for Prostate Cancer?

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Step and shoot IMRT/Minimum segment size/Prostate cancer.

Although the use of small segments in step and shoot IMRT provides better dose distribution, extremely small segments decrease treatment accuracy. The purpose of this study was to determine the optimum minimum segment size (MSS) in two-step optimization in prostate step and shoot IMRT with regard to both planning quality and dosimetric accuracy. The XiO treatment planning system and Oncor Impression Plus were used. Results showed that the difference in homogeneity index (HI), defined as the ratio of maximum to minimum doses for planning target volume, between the MSS 1.0 cm and 1.5 cm plans, and 2.0 cm plans, was 0.1%, and 9.6%, respectively. With regard to V107 of PTV, the volume receiving 107% of the prescribed dose of the PTV, the difference between MSS 1.0 cm and 1.5 cm was 2%. However, the value of the MSS 2.0 cm or greater plans was more than 2.5-fold that of the MSS 1.0 cm plan. With regard to maximum rectal dose, a significant difference was seen between the MSS 1.5 cm and 2.0 cm plans, whereas no significant difference was seen between the MSS 1.0 cm and 1.5 cm plans. Composite plan verification revealed a greater than 5% dose difference between planned and measured dose in many regions with the MSS 1.0 cm plan, but in only limited regions in the MSS 1.5 cm plan. Our data suggest that the MSS should be determined with regard to both planning quality and dosimetric accuracy.

INTRODUCTION

Intensity-modulated radiation therapy (IMRT) has been used to provide highly conformal dose distribution to irregular targets. A major and unique characteristic of IMRT is that each field is composed of many subfields or segments which are delivered in sequence, enabling dose distribution to be concentrated on the planning target volume (PTV) while sparing surrounding normal tissues.

The complex segments are calculated using inverse planning. Various commercial treatment planning systems with different optimization methods in inverse planning are available.[1–6] One optimization method is direct aperture optimization.[2–6] In this technique, a set of deliverable apertures is included in the optimization, wherein the optimization parameters include aperture shapes, weights, or both. In two-step IMRT optimization, in contrast, each field is divided into a grid of beamlets, the weights of which are then optimized.[1] The optimization provides an ideal intensity map, and the ideal beamlet intensities are then segmented into segments deliverable by the multileaf collimator (MLC). This information is then used to calculate final dose. Therefore the use of small segments increases the deliverable MLC patterns, which potentially improves the final dose distribution. With regard to direct machine parameter optimization (DMPO) available within the Pinnacle[3] treatment planning system, Worthy *et al.* reported that a minimum segment area of 8 cm^2 is optimal.[6] Regarding two-step optimization, however, no quantitative analysis of the effects of minimum segment size on planning quality, including PTV coverage and hot spots in organs at risk, has not been reported.

Although the use of small segments might improve dose distribution in the treatment planning system, it become difficult to assure the accuracy of beam delivery.[7–12] In addition, as the number of small segments increases, monitor unit (MU) increases, which could result in longer treatment times and subsequently to intrafractional patient movement.

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doi:10.1269/jrr.10018

Here, we investigated the optimum minimum segment size (MSS) in two-step optimization with regard to planning quality. Further, we also conducted composite verifications by various MSS plans to evaluate dosimetric accuracy.

MATERIALS AND METHODS

We analyzed five consecutive prostate cancer patients who received step and shoot IMRT in our hospital. The XiO ver. 4.33.2 (CMS, St Louis, MO) treatment planning system was used in this study. For beam delivery, an Oncor Impression Plus (Siemens Medical Solutions, Erlangen, Germany) equipped with an Optifocus MLC (41 pairs of leaves, with the central leaves having a width of 1.0 cm) were used with a dose rate of 300 MU/min.

Beam setup in treatment planning and delivery

The clinical target volume (CTV) was generated for the prostate and a part of the seminal vesicle by adding a 10-mm margin to the anterior, superior, inferior, left, and right directions of the prostate and 6-mm margin to the posterior direction. The overlapping region of the CTV and rectum was then subtracted, and the resulting volume was defined as the PTV. A 5-field coplanar treatment plan with beam angles of 45°, 105°, 180°, 255°, 315° was generated with a 10 MV photon beam for each patient.

IMRT optimization and plan evaluation

The XiO IMRT treatment planning system uses two-step optimization. The optimization process can be divided into two stages. During the first stage, the optimizer uses inverse planning objectives, anatomy contours, and beamlets to produce ideal intensity maps and ideal doses. By "ideal", it is meant beamlet intensities and doses that might be delivered if the realities of treatment delivery could be ignored. In the second stage, ideal beamlet intensities are converted to a deliverable form; that is, field segments for MLC delivery. This step allows the setting of constraints for generating MLC segments, including minimum segment size. New beam deliverable doses are recalculated and the dose is then reoptimized using the same objectives as in the first stage by modulating the beam weights. Finally, dose is calculated.

Figure 1 shows the overall methodology of the study. IMRT optimization was done with constraints for the PTV, rectum, and bladder. Table 1 shows the set of objective function parameters used for all MSS plans for each patient in this study. After optimization, deliverable MLC segments were calculated to achieve the ideal beamlet fluence. In this step, the MSS setting was changed by 1.0 cm, 1.5 cm, 2.0 cm, 2.2 cm, 2.5 cm, and 3.0 cm. The final dose was then calculated by a Fast Fourier Transform (FFT) convolution algorithm with a 2.0 mm grid size. The prescription dose for this study was selected as 70 Gy with the D95 prescription for the PTV. Analysis included the total number of segments and total MU; PTV homogeneity index (HI), defined as the ratio of PTV maximum dose to PTV minimum dose; V107 of PTV, the volume receiving 107% of the prescribed dose; and maximum rectal and bladder dose in various MSS plans. In addition, the relative proportion of subsegment areas was evaluated, with 'subsegment area' defined as follows: if there was one aperture in one segment, as in Fig. 2 (a), we counted one set of 1-cm^2 subsegments; if there were five aper-

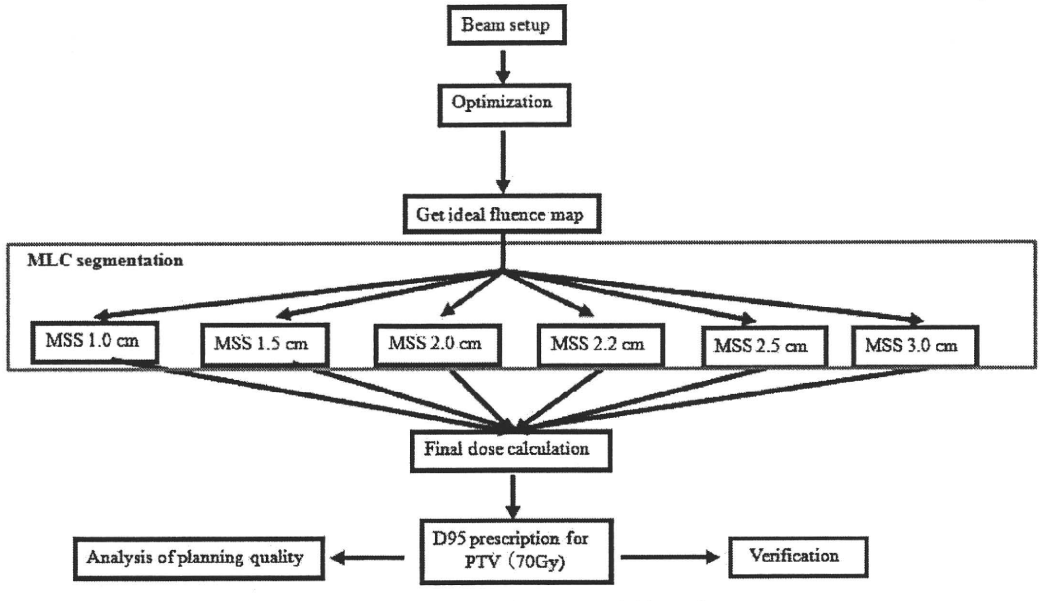

Fig. 1. Overall methodology of this study.

tures in one segment, as in Fig. 2 (b), we counted one set of 14-cm^2 subsegments and four sets of 1-cm^2 subsegments.

Table 2 shows patient characteristics, with column 5 showing the number of total segments in the MSS 1.0 cm plan. In patient 1, who had an extremely large PTV, the IMRT beams contained 85 segments, while the number of total segments for the other patients ranged from 68 to 75. Column 6 of Table 1 shows the proportion of 1.0-cm^2 subsegments in the MSS 1.0 cm plan. In patient 1, about 18% of subsegments were 1.0 cm^2.

Composite plan verification

Composite IMRT plan verification was performed using GafChromic-type EBT film (International Specialty Products, Wayne, NJ) and the I'mRT phantom (IBA Dosimetry GmbH, Schwarzenbruck, Germany). The verification plan of patient 1 was chosen because this had the highest proportion of 1.0 × 1.0 cm^2 subsegments with the MSS 1.0 cm plan (Table 2), which is the most severe condition to assure dosimetric accuracy. Films were loaded into the phantom in the isocenter plane perpendicular to the beam axis. Composite fields with the MSS 1.0 cm, 1.5 cm, 2.0 cm, and 2.5 cm plans were irradiated.

A flatbed scanner (Epson Seiko Corporation, Nagano, Japan) was used to analyze films. Due to post-exposure density growth in films, many reports recommend that films be scanned at least 6 hours after irradiation.[13–15] We therefore scanned all irradiated films at least 12 hours after the completion of irradiation. Further, because flatbed scanners require correction for scanning light intensity in the lateral scan direction,[16,17] we corrected these effects in software developed in-house. Calibration curves were obtained just before the composite plan verification at a 25 cGy increment. Dose distributions of XiO and the films were read into the software and compared by analyzing dose differences and DTA.

Table 1. Set of objective function parameters that were used for all plans for each patient.

Structure	Type	Dose (Gy)	Volume (%)	Rank	Weight
Rectum	Maximum dose	70	0	1	80
	Dose volume	60	13		80
	Dose volume	40	35		40
Bladder	Maximum dose	72	0	3	50
	Dose volume	60	25		50
	Dose volume	40	50		50
PTV	Maximum dose	71	0	2	100
	Minimum dose	70	100		90

Abbreviation: PTV = planning target volume

RESULTS

Effects of MSS on IMRT beam parameters

Table 3 shows changes in the number of total segments and MU according to various MSS plans. As the MSS increased, the number of segments significantly decreased with those of the MSS 1.5 cm, 2.0 cm, 2.2 cm, 2.5 cm, and 3.0 cm plans being 7%, 14%, 20%, 30%, and 40% lower than that of the MSS 1.0 cm plan, respectively. As MSS increased,

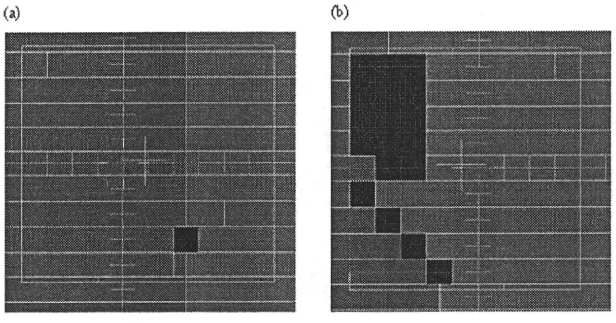

Fig. 2. Examples of segment shapes. In the present study, the definition of subsegment in (a) was one set of 1-cm^2 subsegment, and in (b) was one set of 14-cm^2 and four sets of 1-cm^2 subsegments.

Table 2. Patient characteristics.

	GTV (cc)	CTV (cc)	PTV (cc)	Seminal vesicle volume (cc)	Total segment at MSS 1.0 cm plan	Proportion of 1 × 1 cm^2 subsegments with the MSS 1.0 cm plan (%)
Pt 1.	51.7	184.9	176.8	12.3	82	18.3
Pt 2.	19.2	99.0	94.7	11.5	79	14.0
Pt 3.	33.2	128.3	123.3	9.8	77	14.3
Pt 4.	15.2	81.4	79.8	4.8	71	12.6
Pt 5.	22.2	92.2	91	2.1	49	6.1

Abbreviations: Pt = patient; GTV = gross tumor volume; CTV = clinical target volume; PTV = planning target volume; MSS = minimum segment size

Table 3. Number of total segment and MU by MSS. All differences were significant with $p < 0.01$.

MSS (cm)	1.0	1.5	2.0	2.2	2.5	3.0
Total number of segment	72 ± 14	67 ± 13	61 ± 11	57 ± 10	50 ± 10	42 ± 8
Total MU	714 ± 160	654 ± 147	600 ± 127	570 ± 118	55 ± 140	534 ± 125

Abbreviation: MSS = minimum segment size

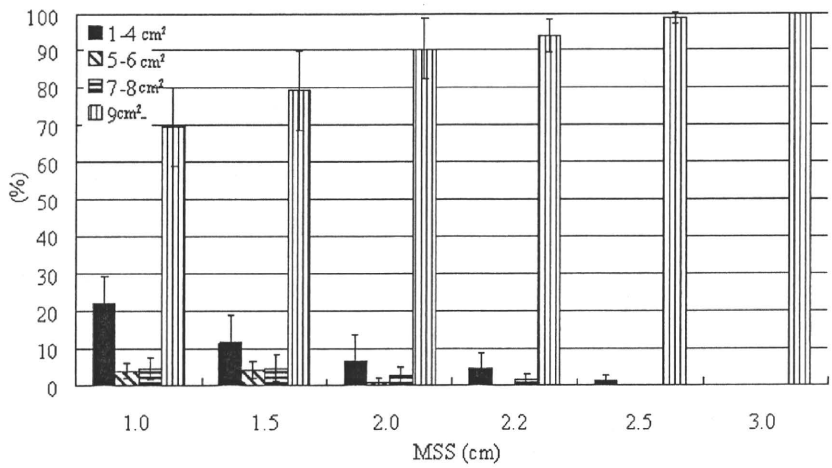

Fig. 3. Relative proportion of subsegment area by MSS setting.

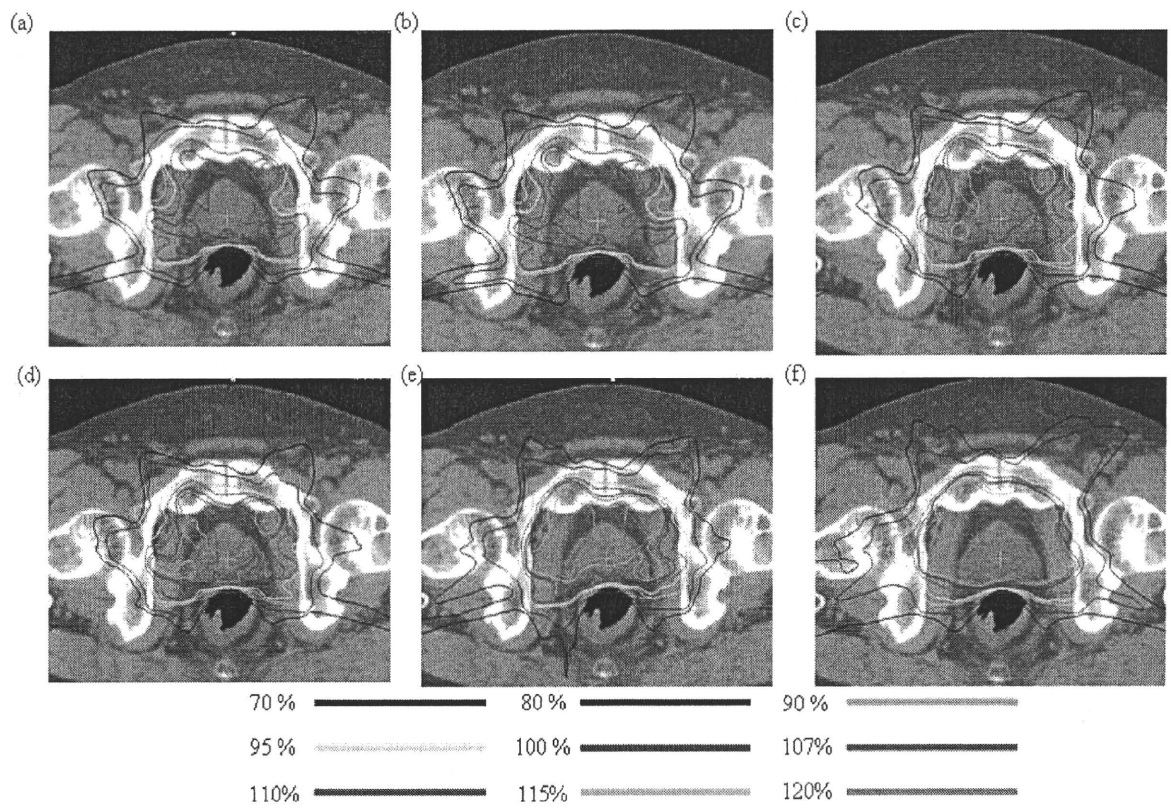

Fig. 4. Effect of MSS setting on dose distribution for patient 1. (a) MSS 1.0 cm, (b) 1.5 cm, (c) 2.0 cm, (d) 2.2 cm, (e) 2.5 cm, and (f) 3.0 cm.

total MU significantly decreased, with those at an MSS of 1.5 cm, 2.0 cm, and 3.0 cm being 8%, 15%, 20%, 22%, and 25% less than that of the MSS 1.0 cm plan, respectively.

Figure 3 shows the relative proportion of subsegment area according to various MSS plans. As MSS increased, the percentage of smaller segments in which segment area was below 7 cm^2 decreased. On the other hand, the percentage of larger segments with an area greater than 9 cm^2 increased. The percentage of subsegments less than or equal to 4 cm^2 at an MSS of 1.0 cm, 1.5 cm, 2.0 cm, 2.2 cm, 2.5 cm, and 3.0 cm was 22%, 12%, 6%, 5%, 1%, and 0%, respectively. In plans with an MSS of 2.0 cm or greater, more than 90% of subsegments were greater than 9 cm^2.

Effects of MSS on planning quality

Figure 4 (a)–(f) shows the example of axial dose distribution in various MMS plans of patient 1. The PTV was covered by a 95% isodose line (yellow line) in all plans because D95 prescription for PTV was performed. Although a slight difference between the MSS 1.0 cm and 1.5 cm plans was observed, large area of high dose was observed as MSS increased. The area enclosed by the 115% isodose line was greater with the MSS 2.0 cm than with the MSS 1.5 cm plan.

High-dose areas of more than 115% (orange) and 120% (dark yellow) of the prescribed dose were observed with the MSS 2.0 cm and 2.2 cm plans, and the 2.5 cm and 3.0 cm plans, respectively.

Figure 5 shows the example of DVHs of various MSS plans in patient 1. Little difference was observed between the MSS 1.0 cm and 1.5 cm plans in PTV (Fig. 5 (a)). However, the DVHs were degraded as MSS increased. With regard to the DVH of the rectum, low dose volume increased as the MSS decreased, whereas high dose volume increased as MSS increased (Fig. 5 (b)). With regard to the DVH of the bladder, little difference was observed between the MSS 1.0 cm and 1.5 cm plans, as was also seen with the DVH of

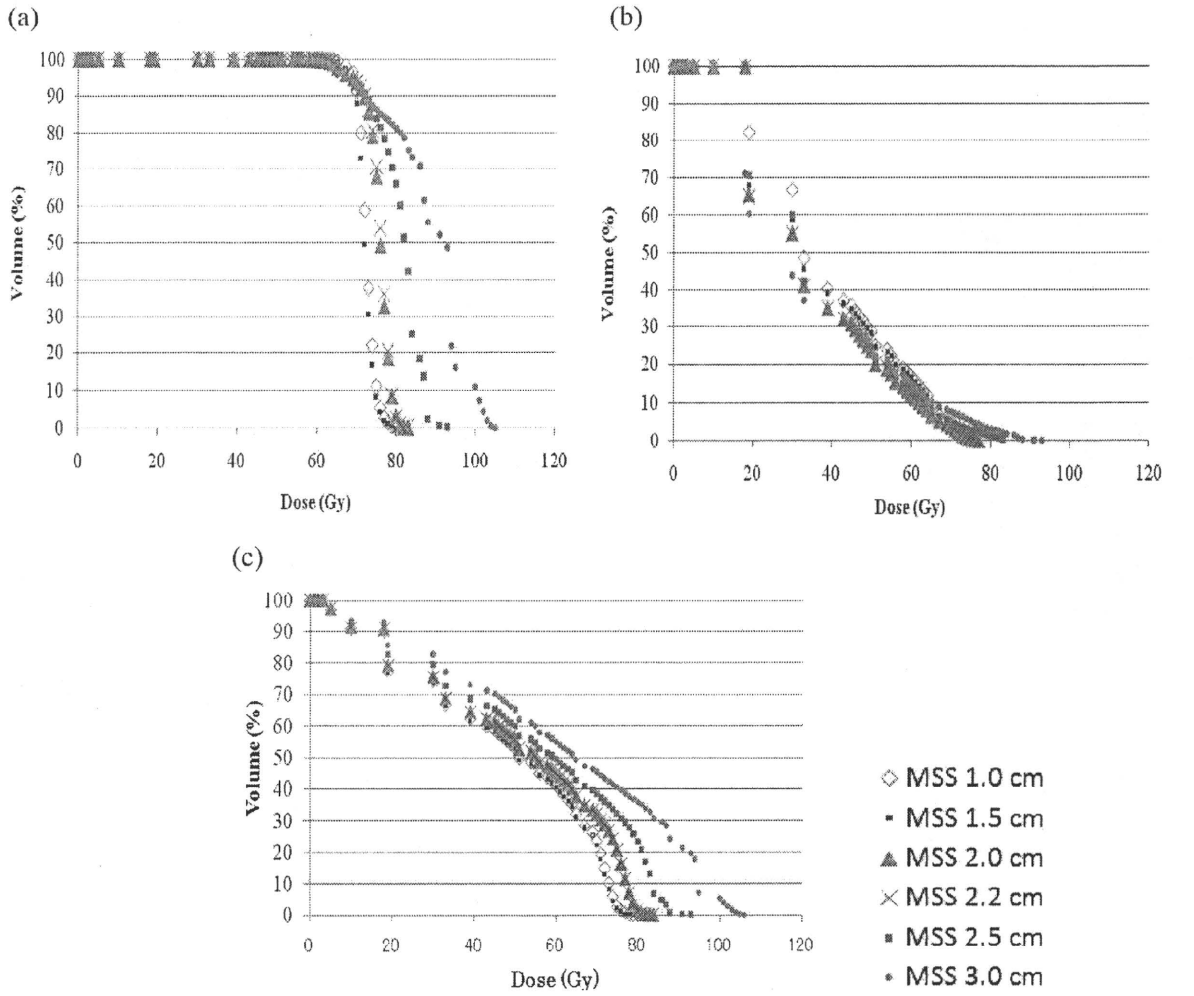

Fig. 5. Effect of MSS setting on DVHs of (a) PTV (b) rectum, and (c) bladder for patient 1.