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Validation of Nomogram-based Prediction of Survival Probability after Salvage Re-irradiation of Head and Neck Cancer

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Objective: Treatment outcomes after salvage re-irradiation in patients with recurrent head and neck cancer vary widely due to heterogeneous patient characteristics, and it is difficult to evaluate optimal re-irradiation schedules. This study aimed to validate a nomogram, originally developed by Tanvetyanon et al., used to predict the survival probability of patients with recurrent head and neck cancer after re-irradiation.

Methods: Twenty-eight patients with recurrent head and neck cancer who underwent salvage re-irradiation between June 2007 and November 2011 were evaluated. The median total dose used for initial radiotherapy was 60 Gy (range, 22–72). Re-irradiation sites included the nasopharynx or Rouviere's node ($n = 14$), external ear ($n = 4$), neck lymph node ($n = 3$) and other sites ($n = 7$). Overall survival after re-irradiation was calculated using the Kaplan–Meier method, and the 2-year survival probability was estimated using Tanvetyanon's nomogram.

Results: Twenty-two patients were treated with stereotactic body radiotherapy using a median total dose of 30 Gy (range, 15–40) in 1–7 fractions and six patients were treated with conventional external beam radiotherapy using 45 Gy (range, 23.4–60) in 10–30 fractions. The 2-year overall survival was 21.7% (95% confidence interval: 9.3–41.3), and the 2-year survival probability was 16.8% (95% confidence interval: 9.9–23.6). The 2-year overall survival in 20 patients with unfavorable prognosis (median 2-year survival probability, 5.5%) and in 8 patients with favorable prognosis (median 2-year survival probability, 45%) were 11.0 and 45.7%, respectively ($P = 0.05$).

Conclusions: Our findings show that Tanvetyanon's nomogram accurately estimates the survival probability in patients with recurrent head and neck cancer after re-irradiation.

Key words: salvage re-irradiation – head and neck cancer – nomogram – stereotactic body radiotherapy

INTRODUCTION

About 500 000 patients with head and neck cancer (HNC) are diagnosed each year worldwide (1). Despite comprehensive treatment strategies including surgery, radiotherapy and chemotherapy, approximately half of the patients with HNC die due to locoregional failure, distant metastases and second

primary neoplasms (2). Recurrent HNC (rHNC) and second primary neoplasms in the previously irradiated area represent a clinical challenge, and are normally treated with salvage surgical resection as this method offers the greatest probability for long-term survival (3–4). However, the population of candidates for curative salvage surgery is relatively small, and some patients require chemotherapy or re-irradiation in addition to surgery. The survival time after salvage chemotherapy has been estimated to be ~6 months (5). Re-irradiation using a full dose is associated with severe toxicities including tissue necrosis, bleeding and infection, and treatment-related deaths due to carotid hemorrhage (6–8). Recent studies using intensity modulated radiotherapy (IMRT), stereotactic body radiotherapy (SBRT), twice-daily radiotherapy and concurrent chemotherapy reported the feasibility and effectiveness of re-irradiation in patients with rHNC (2,7,9). These studies also reported locoregional control rates after re-irradiation ranging from 19 to 64%, and median survival times (MST) ranging from 8.5 to 28 months (1,8,10–12). Treatment outcomes vary widely due to heterogeneous patient characteristics and diverse treatment schedules. Moreover, an optimal salvage re-irradiation schedule has not yet been established (1,8). Optimal sub-classification according to a confidential prognostic index is essential to rigorously compare treatment outcomes. Tanvetyanon et al. (13) developed a nomogram to predict 2-year survival probability in patients with rHNC after salvage re-irradiation. The nomogram includes the following: the presence of comorbidities, organ dysfunction, presence or absence of isolated neck recurrence, tumor bulk and time interval between the previous radiotherapy and start of re-irradiation. The overall goal of the present study was to validate this nomogram in patients with rHNC who were mainly treated with SBRT.

PATIENTS AND METHODS

Twenty-eight consecutive patients with local rHNC who underwent salvage re-irradiation between June 2007 and November 2011 were evaluated. The male-to-female ratio was 20:8, with a median age of 65 years (range, 43–90). Patients were treated for nasopharyngeal cancer ($n = 8$), external ear cancer ($n = 4$), hypopharyngeal cancer ($n = 3$) and other cancers ($n = 13$). Patient characteristics are shown in Table 1. Initial radiotherapy included treatment with definitive radiotherapy ($n = 22$), postoperative radiotherapy ($n = 5$) and salvage radiotherapy ($n = 1$) for recurrent disease after surgery. Twenty-three patients were treated with conventional three-dimensional external beam radiotherapy using Clinac iX or Trilogy (Varian Medical Systems, Inc., Palo Alto, CA) with a photon energy of 4 or 6 MV. Treatment plans included lateral opposed field, wedged pair field or multiple-field techniques. The radiation field covered the primary site, surrounding the lymph node area, and/or the prophylactic regional lymph node area. The prescribed dose was calculated at the center of the radiation field or from the planning target volume (PTV). The median total

Table 1. Patient characteristics

	Patient number	Median	Range
Age (years)		67	43–90
Gender			
Male	20		
Female	8		
Performance status			
0	20		
1	4		
2–4	4		
Initial diagnosis			
Nasopharyngeal cancer	8		
External ear cancer	4		
Hypopharyngeal cancer	3		
Tongue cancer	2		
Paranasal cavity cancer	2		
Others	9		
Pathology			
Squamous cell carcinoma	24		
Leiomyosarcoma	1		
Neuroblastoma	1		
Round cell sarcoma	1		
Salivary duct carcinoma	1		
Initial radiotherapy			
Total dose (Gy)		60	22–72
Fraction size (Gy)		2	1.8–22
Site of re-irradiation			
Nasopharynx or Rouviere's node	14		
External ear	4		
Neck lymph node	3		
Oropharynx	2		
Paranasal cavity	2		
Others	3		
Maximum diameter of recurrent disease			
Stereotactic radiotherapy (cm)		2.9	1.0–6.0
Conventional radiotherapy (cm)		3.8	2.5–10.0
Interval between initial treatment and salvage re-irradiation			
1–6 (months)	10		
Over 6 (months)	18		
Re-irradiation			
Stereotactic radiotherapy	22		
Total dose (Gy)		30	15–40
Fraction size (Gy)		8	5–23
Conventional radiotherapy	6		
Total dose (Gy)		45	23.4–60
Fraction size (Gy)		2	1.8–3

dose was 60 Gy (range, 48–72) in 24–36 fractions over a 5- to 7-week period. Five patients were treated with using robotic image-guided radiotherapy (Cyberknife Robotic Radiosurgery System; Accuracy, Inc., Sunnyvale, CA) with a median total dose of 38 Gy (range, 22–39) in one to six fractions over a 1- to 6-day period. The prescribed dose for SBRT was defined as the dose covering at least 80% of the PTV. Sixteen patients received systemic chemotherapy concurrently or sequentially, which included platinum-based or 5-fluorouracil (5-FU) regimens (Table 2).

The median interval from initial radiotherapy to salvage re-irradiation was 9 months (range, 3–40). Twenty-two patients had comorbidities and nine had organ dysfunction (e.g. tracheostomy and dysphagia) at the start of salvage re-irradiation. The median maximum diameter of recurrent disease was 3.4 cm (range, 1–10). Re-irradiation sites included the nasopharynx or Rouviere's node ($n = 14$), external ear ($n = 4$), neck lymph node ($n = 3$) and other sites ($n = 7$). Twenty-two patients were treated with SBRT and six were treated with conventional external beam radiotherapy. The median total dose administered during salvage re-irradiation using SBRT was 30 Gy (range, 15–40) in one to seven fractions over a 1- to 9-day period. The median total dose of salvage re-irradiation using conventional external beam radiotherapy was 45 Gy (range, 23.4–60) in 10–30 fractions over a 2- to 6-week period. Both re-irradiation techniques adopted narrow field margins without prophylactic regional lymph node irradiation. Three patients who were treated with conventional external beam radiotherapy received chemotherapy (i.e. platinum-based or 5-FU regimens) concurrently with radiotherapy.

The OS was calculated using the Kaplan–Meier method, and the median 2-year survival probability was estimated using the nomogram developed by Tanvetyanon et al. (13) The OS was measured from the start of re-irradiation and calculated using death due to any cause as an event. Tumor responses were classified as complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD) according to the revised Response Evaluation Criteria in Solid Tumors (revised RECIST guideline version 1.1) (14). In-field recurrence was defined as an increase in the tumor size or appearance of new lesions in the re-irradiation area from diagnostic images, and out-field recurrence was defined as an increase in the tumor size or appearance of new lesions in the non-irradiated head and neck area. Distant metastases were defined as the appearance of new lesions beyond the head and neck area. Toxicity was assessed using the Common Terminology Criteria Adverse Event (CTCAE version 4.0). Statistical analyses were performed using JMP version 5.1J (SAS Institute, Inc.).

Table 2. Patient characteristics in the favorable and unfavorable groups

	Favorable group	Unfavorable group
Age (years)	59.0 (44–72)	69.5 (43–90)
Gender		
Male	7	13
Female	1	7
Performance status		
0	8	12
1	0	4
2–4	0	4
Pathology		
Squamous cell carcinoma	8	16
Others	0	4
Initial radiotherapy		
Total dose (Gy)	60	57
Fraction size (Gy)	2	2
Site of re-irradiation		
Nasopharynx or Rouviere's node	5	9
External ear	1	3
Neck lymph node	1	2
Oropharynx	1	1
Paranasal cavity	0	2
Others	0	3
Maximum diameter of recurrent disease		
Stereotactic radiotherapy (cm)	1.6	3.6
Conventional radiotherapy (cm)	N/A	3.8
Interval between initial treatment and salvage re-irradiation		
1–6 (months)	3	7
Over 6 (months)	8	10
Organ dysfunction		
No	7	11
Yes	1	9
Re-irradiation		
Stereotactic radiotherapy	8	14
Total dose (Gy)	26	30
Fraction size (Gy)	9.4	8
Conventional radiotherapy	0	6
Total dose (Gy)	N/A	45
Fraction size (Gy)	N/A	2

RESULTS

The median follow-up time in the present study was 7.3 months (range, 1.7–25.3). After re-irradiation, 5 patients (18%) achieved CR, 8 (28%) achieved PR and 15 (54%) showed SD or PD. In addition, two patients achieving PR received salvage surgery and one patient achieving PR and three showing SD received systemic chemotherapy (i.e. Tegafur Gimeracil Oteracil Potassium, S-1). The other patients were carefully monitored and received supportive

care. The median progression-free survival time after re-irradiation was 5.5 months [95% confidential interval (CI), 3.3−7.2]. Among the patients with re-progressive disease after re-irradiation, 15 (83%) developed in-field recurrence with or without out-field recurrence and/or distant metastases, two (11%) developed distant metastases alone and one (6%) developed recurrence in the field margin. However, no patients developed regional recurrence alone. The sites of distant metastases included the lung and mediastinal lymph nodes. Thirteen patients (46%) achieved a relative response (RR), which included CR and PR, and had a median maximum tumor diameter of 2.7 cm (range, 1.0−6.0). In patients who did not achieve RR, the median maximum tumor diameter was 3.7 cm (range, 1.5−10.0; $P = 0.03$). MST after re-irradiation of patients who achieved RR was 13.3 months (95% CI, 6.0–N/A) and 7.3 months for those who did not achieve RR (95% CI, 3.8–14.9; $P = 0.03$).

Univariate analyses revealed that MST and 2-year OS of 19 patients with small recurrent disease <4 cm were 13.0 months (95% CI, 6.0–N/A) and 26.6%, and those of 9 patients with large recurrent disease 4 cm or larger were 7.3 months (95% CI, 1.7–N/A) and not applicable, respectively ($P = 0.39$). MST and 2-year OS of 8 patients who developed recurrence within 6 months from the initial treatment were 7.9 months (95% CI, 1.7–N/A) and 20.2%, and those of 18 patients who developed it beyond 6 months were 8.6 months (95% CI, 7.3–18.9) and not applicable, respectively ($P = 0.62$). MST and 2-year OS of 24 patients with good performance status (PS = 0–1) were 13.3 months (95% CI, 7.3–N/A) and 24.9%, and those of 4 patients with poor PS (PS = 2–4) were 3.9 months (95% CI, 1.7–N/A) and 0%, respectively ($P = 0.02$).

The 2-year OS estimated using the Kaplan–Meier method was 21.7% (95% CI, 9.3–41.3), and the MST was 8.6 months (95% CI, 6.0–14.9; Fig. 1). The median 2-year survival probability estimated by Tanvetyanon's nomogram was 16.8% (95% CI, 9.9–23.6). The 2-year OS in 20 patients with unfavorable prognosis whose 2-year survival probability was <15% (median, 5.5; range, 1−11) and the 2-year OS in eight patients with favorable prognosis whose 2-year survival probability was >15% (median, 45; range, 15−55) was 11.0 and 45.7%, respectively ($P = 0.05$; Fig. 2).

Two patients (7.1%) developed adverse events (Grades 2−3), which included tumor bleeding (Grade 2) and oral bleeding (Grade 3). In addition, three patients (10.7%) developed severe adverse events (Grade 5). All three patients developed local progression after re-irradiation, with two of them developing local infection and soft tissue necrosis in the submandibular area and paranasal cavity. These two patients died due to tumor progression and infection. The third patient was initially treated with whole neck conventional radiotherapy (60 Gy in 30 fractions) followed by adjuvant chemotherapy, and also received salvage SBRT (25.6 Gy in 5 fractions) to treat left-neck lymph node recurrence. Despite these treatments, the patient developed in-field recurrence 6 months later, which was treated with re-salvage SBRT (24 Gy in two fractions); however, recurrence was not controlled and the patient died eight months later due to a carotid artery rupture. Four patients who developed severe adverse events (Grades 3−5) were treated with

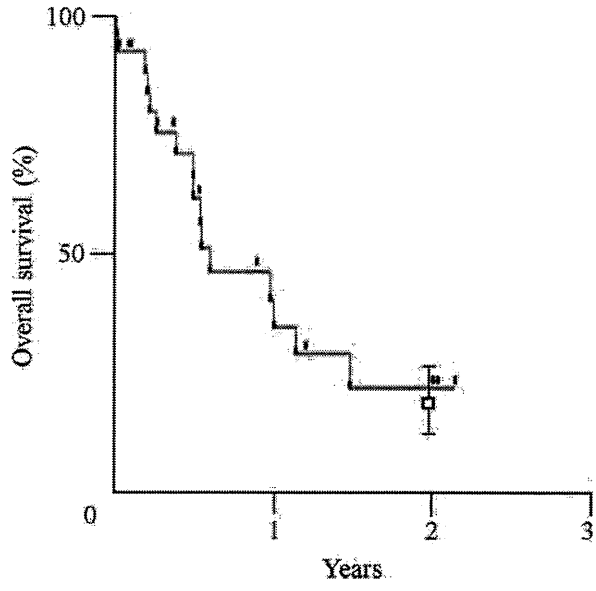

Figure 1. The overall survival curve (OS) of 28 patients with recurrent head and neck cancer (rHNC) was estimated using the Kaplan–Meier method. The white box shows the 2-year survival probability (16.8%) estimated using Tanvetyanon's nomogram. The vertical line indicates the 95% confidence interval of the 2-year OS rate (95% CI, 9.9–23.6%). This figure shows approximate values for the 2-year OS calculated by the Kaplan–Meier method and the 2-year survival probability estimated by Tanvetyanon's nomogram.

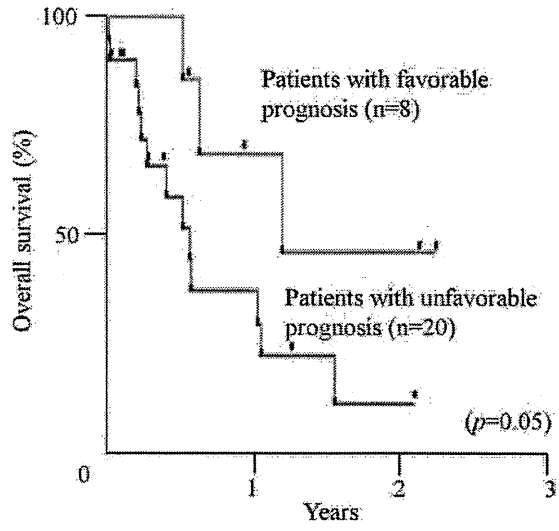

Figure 2. OS curves of patients with rHNC with favorable and unfavorable prognoses. The 2-year OS in 20 patients with unfavorable prognosis whose 2-year survival probability was <15% and the 2-year OS in eight patients with favorable prognosis whose 2-year survival probability was >15% were 11.0 and 45.7%, respectively ($P = 0.05$).

re-irradiation using SBRT; however, there was no difference between re-irradiation modalities ($P = 0.25$).

DISCUSSION

The American College of Radiology (ACR) Expert Panel on Head and Neck Cancer reviewed relevant literature on re-irradiation after definitive radiotherapy and evaluated its appropriateness, including radiation technique, treatment volume, doses and treatment schedule (3). The ACR Expert Panel emphasized the importance of patient selection and recommended careful evaluation and treatment by a comprehensive cancer team. Furthermore, they recommended considering re-irradiation with and without chemotherapy in patients with favorable prognosis and with relatively long estimated survival times. They also recommended performing a computed tomography (CT) scan of the chest and positron emission tomography/CT to determine the presence of metastatic disease, and evaluating patient conditions such as comorbidities, performance status, speech and swallowing function, and nutritional status. Moreover, a multi-disciplinary cancer care team should decide on the appropriate treatment strategy (e.g. salvage surgery, intensive re-irradiation with or without chemotherapy, chemotherapy alone and palliative care). The total absolute radiation dose to critical organs such as the spinal cord, carotid artery and optic pathways should be estimated using previous radiation dosimetry and latest patient images (8). Another important consideration is the interval between previous radiotherapy and start of salvage re-irradiation. One study showed that a longer interval was associated with a lower probability of severe adverse events due to re-irradiation and lower occurrence rates of distant metastases (15). In Tanvetyanon's nomogram, the interval is an important component used to estimate 2-year survival probabilities after re-irradiation (13). Previously published clinical trials have used intervals of >6 months to determine the eligibility for re-irradiation (6,7). Hoebers et al. (15) reported that an interval of over 3 years was associated with a favorable OS. However, the appropriate interval between previous radiotherapy and re-irradiation remains unknown.

The Fox Chase Cancer Center conducted a phase I study (FCCC 96-006) combining twice-daily radiotherapy (1.5 Gy per fraction bid; 5 days every other week; four cycles) with concurrent cisplatin and paclitaxel administration during salvage therapy (16). The MST was 9.5 months, and the 1- and 2-year OS were 41 and 27%, respectively. Hematologic toxicities were feasible, and grade 3 mucositis occurred in only 6% of patients. Given these encouraging results, the Radiation Therapy Oncology Group (RTOG) conducted a phase II study (RTOG 9911) to evaluate the efficacy and toxicity of twice-daily radiotherapy (1.5 Gy per fraction bid; 5 days every other week; four cycles) with concurrent cisplatin and paclitaxel administration (6). One-hundred and five patients were enrolled into the study, and 1- and 2-year OS were 50.2 and 25.9%, respectively. These findings suggest that this strategy is a promising treatment option; however, eight treatment-related deaths (8%), including acute neutropenic sepsis and late carotid hemorrhage, were noted. Spencer et al. (17) conducted a phase I study on previously irradiated patients with rHNC who received hydroxyurea and 5-FU in combination with daily radiotherapy (2 Gy per fraction) during a 2-week period followed by a 1-week break. These patients then received hyperfractionated radiotherapy on weeks 4 and 5 (total dose 50 Gy). The 1- and 2-year OS were 41 and 15%, respectively, and one patient died 3 weeks after the study due to pneumonia. Furthermore, two patients acquired soft tissue ulcers, and one developed trismus and a non-healing clavicular fracture. Therefore, concurrent chemoradiotherapy using twice-daily regimens are not considered ideal strategies for re-irradiation (18).

Hoebers et al. (15) evaluated 58 patients who had received re-irradiation at a median cumulative dose of 119 Gy (range, 76 – 140) with or without chemotherapy. The group reported a 2-year OS of 42%, and that higher re-irradiation doses and concurrent chemoradiation were associated with severe adverse events. They also reported that re-irradiation alone (compared with concurrent chemo-re-irradiation), a longer interval between initial radiotherapy and salvage re-irradiation, and a lower cumulative radiation dose were associated with better local control rates. Lee et al. (4) reported a study of 105 patients with rHNC who received re-irradiation with or without chemotherapy. The multivariate analyses revealed that non-nasopharynx and non-IMRT were associated with an increased risk of locoregional failure. Administration of chemotherapy could not be used to predict improved locoregional control rates and OS. The role of concurrent or sequential chemotherapy remains uncertain for re-irradiation in patients with rHNC. In the present study, 83% of patients with progressive disease after re-irradiation developed in-field recurrence with or without distant metastases. Lee et al. (4) reported the occurrence of locoregional failure with or without distant metastases in 65% of patients who developed progressive disease after re-irradiation. They also emphasized that future efforts for maximizing tumor control in a recurrent setting, including dose escalation with IMRT and effective chemotherapy, were warranted. The median re-irradiation dose of 45 Gy in our conventional radiotherapy is low compared with previously published doses. We could not use IMRT then for head and neck cancers in our institute, and thus relatively low re-irradiation doses were used to avoid the risk of high radiation exposure of organs. As it is now possible to use IMRT, more aggressive radiation therapy should be tried in the salvage setting.

Stereotactic radiotherapy, such as single fraction stereotactic radiosurgery (SRS) and fractionated SBRT using concave dose distributions, is useful since it protects critical organs (e.g. carotid artery, spinal cord, brain stem and optic pathway). The University of Pittsburgh conducted a phase I dose-escalation study in patients with rHNC. The results revealed that 44 Gy in five fractions over a 2-week period was

well tolerated (2). Vargo et al. (1) reported a retrospective study which included 34 patients with rHNC who received SBRT at a median dose of 40 Gy in five fractions (range, 30–44) as a strategy for salvage therapy. The report showed that local control was significantly improved for small tumors (i.e. <25 cc), and that late grade 3 adverse events occurred only in 6% of patients. Lee et al. (4) reported that IMRT was better suited to predict locoregional tumor control. New technologies such as stereotactic radiotherapy (SRT), SBRT and IMRT might be useful tools to increase the prescribed dose without incrementing the exposure to critical organs. In our study, 79% of patients received SRT/SBRT and the majority developed minor recurrent disease. The most frequent recurrence after re-irradiation occurred within the re-irradiation field. However, our findings did not highlight the superiority of SRT/SBRT, and it did not clarify what the appropriate modality and radiation schedule should be. Unger et al. (19) reported a study on 65 patients who received a median initial radiotherapy of 67 Gy and a median re-irradiation SBRT dose of 30 Gy (range, 21−35) in two to five fractions. They reported that the 2-year OS and locoregional control rates were 41 and 30%, respectively. In addition, they showed by multivariate analysis that a higher total dose, surgical resection and naopharynx site were significantly associated with an improved locoregional control rate. Surgical resection and non-squamous histology were also associated with an improved OS (19). However, 11% of patients in that study experienced severe toxicities due to re-irradiation. Lee et al. (4) reported that a nasopharyngeal site and IMRT technique were associated with a good locoregional progression-free survival (LRPFS) in patients with rHNC who received re-irradiation. Finally, they concluded that achieving locoregional control was crucial to improve OS and that radiation doses >50 Gy were associated with better LRPFS and OS.

The present study has a few limitations worth noting. First, this study is a retrospective review of patients from a single institution, and thus selection- and physician-based biases may exist. In addition, it is important to note that the results are based on a small number of patients who underwent diverse radiotherapy schedules. Secondly, a minority of patients received conventional external beam re-irradiation, whereas no patients received IMRT. Finally, the median follow-up time in the study was only 7.3 months (range, 1.7−25.3). Longer follow-up periods are needed to clarify the long-term complications associated with re-irradiation.

CONCLUSION

Our results suggest that Tanvetyanon's nomogram accurately estimates survival probability after salvage re-irradiation in patients with rHNC. This nomogram is a practical tool for optimal sub-classification of patients with rHNC to evaluate treatment outcomes. Future prospective studies using this nomogram should be performed to establish the appropriate re-irradiation schedule for these patients.

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Conflict of interest statement

None declared.

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A Newly Introduced Comprehensive Consultation Fee in the National Health Insurance System in Japan: A Promotive Effect of Multidisciplinary Medical Care in the Field of Radiation Oncology—Results from a Questionnaire Survey

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Objective: The consultation fee for outpatient radiotherapy was newly introduced in the national health insurance system in Japan in April 2012. We conducted a survey on the use of this consultation fee and its effect on clinical practices.
Methods: The health insurance committee of the Japanese Society of Therapeutic Radiology and Oncology conducted a questionnaire survey. The questionnaire form was mailed to 160 councilors of the Society, the target questionees. A total of 94 answers (58% of the target questionees) sent back were used for analyses.
Results: The analyses revealed that 75% of the hospitals charged most of the patients who receive radiotherapy in an outpatient setting a consultation fee. The introduction of the consultation fee led to some changes in radiation oncology clinics, as evidenced by the response of 'more careful observations by medical staff' in 37% of questionees and a 12% increase in the number of full-time radiation oncology nurses. It was also shown that the vast majority (92%) of radiation oncologists expected a positive influence of the consultation fee on radiation oncology clinics in Japan.
Conclusions: Our questionnaire survey revealed the present status of the use of a newly introduced consultation fee for outpatient radiotherapy, and the results suggested its possible effect on promoting a multidisciplinary medical care system in radiation oncology departments in Japan.

Key words: consultation fee – outpatient radiotherapy – multidisciplinary medical care – questionnaire survey

INTRODUCTION

Under the Japanese national health insurance system, patients are generally charged a constant basic consultation fee for every hospital visit. This is because all medical interventions must be based on doctors' examinations and decisions on the day of the patient's hospital visit under the Japanese Medical

Practitioners' Act (1). But radiation oncologists have long been examining the patients once a week during the course of daily radiotherapy in Japanese hospitals since several decades ago, as is the case with other countries. Patients are irradiated by radiotherapy technologists five times per week according to the physician's comprehensive direction, which is provided on the day of the physician's weekly examination. The Ministry of Health, Labor and Welfare (MLHW) of Japan has long assumed that such a situation in Japanese radiation oncology clinics is illegal. In other words, four out of five irradiations per week are treatments that are not based on the physician's examination, according to the ministry's interpretation.

Because there was a big gap between the law and the real situations in radiation oncology clinics, the Japanese MLHW newly introduced a medical service fee, called a consultation fee for outpatient radiotherapy, in the Japanese national health insurance system in April 2012 (2). Under the rules of the new consultation fee, the situation of Japanese radiation oncology clinics described above is remedied if the hospital fulfills certain requirements of the structure of a multidisciplinary medical care team in the radiation oncology department (Table 1) and notifies the Regional Bureau of Health and Welfare. The patients are charged a new consultation fee once a week on the same day of the doctor's examination, instead of a daily basic consultation fee. Thus, the requirement of the Japanese Medical Practitioners' Act has changed to permit daily radiotherapy with once-a-week physician's examination in the Japanese health insurance system. This means that the introduction of this weekly comprehensive consultation system was a milestone change not only for Japanese radiation oncology clinics, but also for the Japanese medical community, because the Japanese Medical Practitioners' Act approved medical cares and treatments without a physician's examination for the first time in Japanese medical history.

A weekly comprehensive consultation system had long been sought in Japan because of the problem of workforce shortages of radiation oncologists to resolve 'illegal' situations in Japan. We report here the results of the questionnaire survey, as well as the present status of the consultation fee and its problems.

Table 1. Structural requirements of radiation oncology centers in charging a consultation fee for outpatient radiotherapy in Japan

1. At least one radiation oncologist with $\geq$5 years of experience in clinical radiation oncology is attending in the department when the patients receive radiotherapy.

2. At least one full-time radiation oncology nurse and one full-time radiotherapy technologist is in the department.

3. At least one medical physicist is attending in the department who is regularly in charge of quality assurance and control for radiotherapy machines.

4. There is an organization of communicating with radiation oncologists who can deal with the morbidities of the patients promptly, in case of an emergency.

The hospitals that fulfill the four requirements listed above can charge the outpatient who is receiving radiotherapy for this consultation fee after notifying the regional Bureau of Health and Welfare.

MATERIALS AND METHODS

The health insurance committee of the Japanese Society for Therapeutic Radiology and Oncology (JASTRO) carried out a questionnaire survey on the operations and the problems of a consultation fee for outpatient radiotherapy. The questionnaire consisted of 15 questions on the present status of the questionee's affiliation, changes in the clinics after introduction of this new consultation fee system and opinions on the rules of the cost accrual of the consultation fee (refer to the Supplementary data). The questionnaire form was mailed to the councilors of JASTRO on 5 September 2012. The questionees were asked to sign the form. As of 30 November 2012, 94 out of 160 councilors (59%) returned the form, including three anonymous questionees. Responses from all 94 questionees were used for the analyses.

RESULTS

Charging Status of the Consultation Fee for Outpatient Radiotherapy

We asked about the fulfillment of the requirements at the questionees' affiliated hospitals. Of the 94 questionees, 86 (91%) answered that their affiliated hospitals fulfilled all the requirements. Among these 86 questionees, 73 (85%) answered that their affiliated hospitals had notified the regional bureau about charging for the consultation fee. Of the 73 questionees whose affiliated hospitals had notified the bureau, 55 (75%) responded that the hospitals had charged almost all their patients a consultation fee for outpatient radiotherapy (Fig. 1).

Changes at the Clinics After Introduction of the Consultation fee

The 73 questionees whose affiliated hospitals had notified the bureau were asked about the effects of introduction of the consultation fee for outpatient radiotherapy. Selecting from multiple options, the most frequent answer was 'more careful observations by medical staff' (34 answers, 47%) (Fig. 2A). In addition, 15% (11 out of 73 questionees whose affiliated hospitals had notified the bureau) reported institutional decisions to increase the number of full-time radiation oncology nurses. This is presumably because a significant portion of hospitals intended to meet the requirements for the cost accrual of the consultation fee to avoid an 'illegal' status. In contrast, there were no reports of increased numbers of radiation oncology physicians, radiotherapy technologists or medical physicists after introduction of the consultation fee (Fig. 2A).

Among 11 questionees who reported an increase in the number of full-time radiation oncology nurses, 8 (73%) also reported 'more careful observations by medical staff' (Fig. 2B), whereas only 26 answers of 'more careful observations by medical staff' were reported among the remaining 62

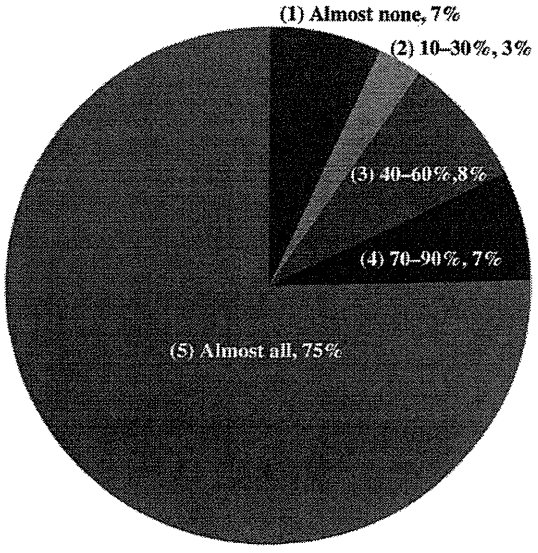

Figure 1. Proportion of the patients who are charged with the consultation fee for outpatient radiotherapy. Each questionee was asked to select from one of five options on the proportion of the patients who were charged with this consultation fee in his or her affiliated hospital: (1) almost none, (2) 10–30% of all outpatients, (3) 40–60% of all outpatients, (4) 70–90% of all outpatients and (5) almost all outpatients.

questionees whose affiliations had no increase in the number of full-time radiation oncology nurses (42%). The proportion of such answers appears to be higher among those who reported an increase in the number of full-time radiation oncology nurses than among other questionees, although the difference was marginally significant by a χ^2 test (73 vs. 42%, $P = 0.059$, Fig. 2B). In addition, the frequency of weekly examinations by radiation oncologists might has been slightly different between institutions with and without an increase in the number of full-time radiation oncology nurses. In the institutions with an increase in the number of nurses, the frequency of examinations by radiation oncologists was generally lower (Fig. 2B). In contrast, a considerable portion of the institutions reported an increase in the frequency of examinations (16%), which was greater than the response of less frequency of examinations among the whole questionees (Fig. 2A).

Perspective on the Consultation Fee

The questionees were asked whether introduction of the consultation fee for outpatient radiotherapy was presumed to contribute to the development of radiation oncology clinics in Japan. Among all the questionees, 35 had no distinct opinion.

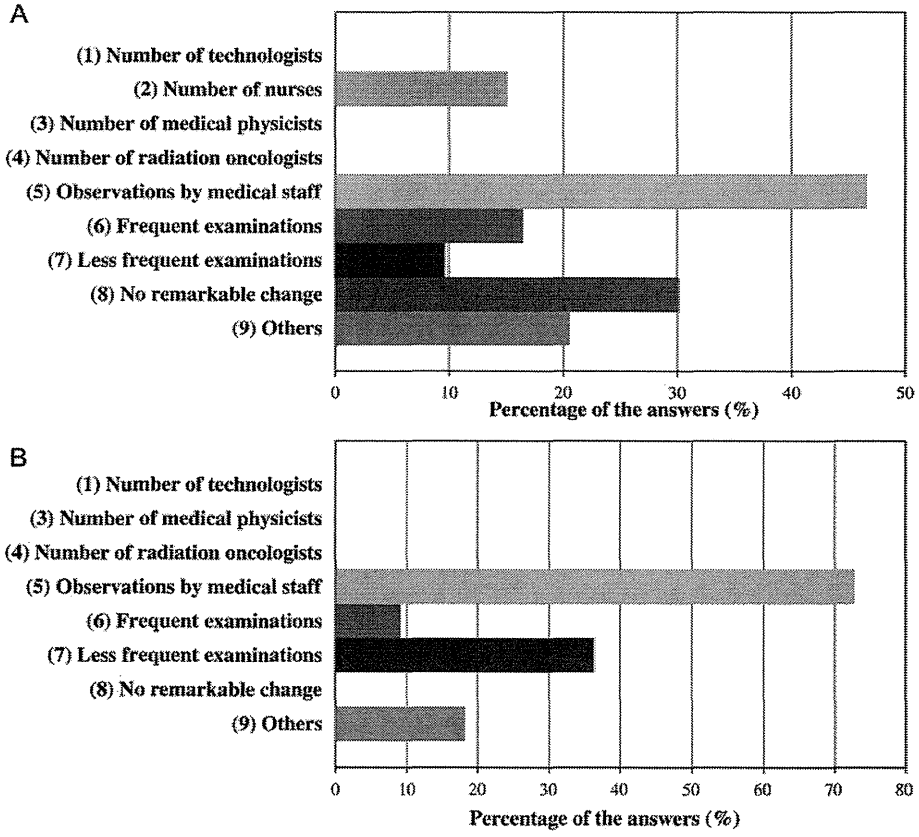

Figure 2. Changes after introduction of the consultation fee. The questionees were asked to select from nine options: (1) an increase in the number of radiotherapy technologists, (2) an increase in the number of full-time radiation oncology nurses, (3) an increase in the number of medical physicists, (4) an increase in the number of radiation oncologists, (5) more careful observations by medical staff, (6) more frequent examinations by radiation oncologists, (7) less frequent examinations by radiation oncologists, (8) no remarkable change and (9) others. Multiple selections were allowed. (A) Answers from all 73 questionees in whose affiliated hospitals the consultation fee can be charged from the outpatients. No increase in the numbers of radiotherapy technologists, medical physicists or radiation oncologists was reported. (B) Answers from 11 questionees who reported an increase in the number of full-time radiation oncology nurses.

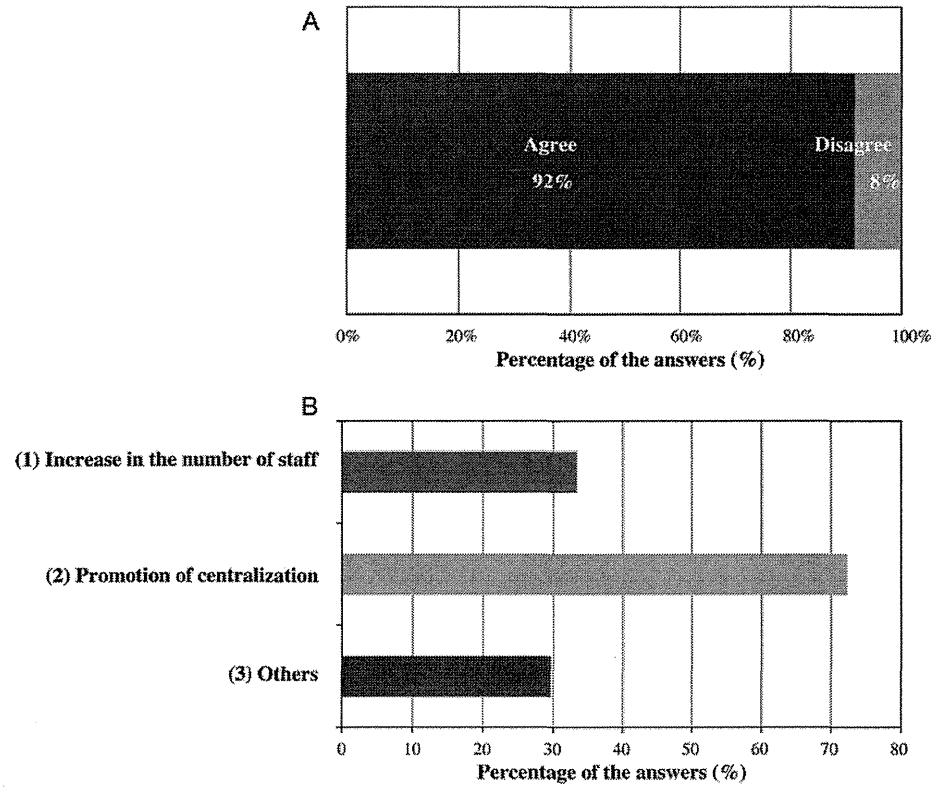

Figure 3. The influence of the consultation fee for outpatient radiotherapy on radiation oncology clinics in Japan. (A) The questionees were asked whether introduction of this consultation fee is expected to contribute to the future development of radiation oncology clinics in Japan. (B) Those who answered 'agree' in the above question were asked to select the reasons for their assumption from the following options: (1) compelling force to increase the number of staff in the radiation oncology department, (2) promotion of centralization of resources and staff in radiation oncology and (3) others. Multiple selections were allowed.

Of the remaining 59 questionees, 92% (54 out of 59) assumed that there was a positive influence of the consultation fee on radiation oncology clinics in Japan (Fig. 3A). The principal reason for this positive opinion was the compelling force to increase the numbers of staffs in the radiation oncology department (Fig. 3B).

DISCUSSION

In Japan, the consultation fee for outpatient radiotherapy was newly introduced in the national health insurance system in April 2012 (1). We assessed the effect of introduction of this consultation fee on radiation oncology clinics through a questionnaire survey. The results revealed that this consultation fee has prevailed in Japan, and most patients who receive radiotherapy in an outpatient setting in Japan are charged for this consultation fee (Fig. 1). The questionees of this survey were the councilors of JASTRO, whose affiliated hospitals were, in general, larger than those of average Japanese radiation oncology centers. Accordingly, the proportion of the patients who were charged a consultation fee might be overestimated in this survey.

Overall, an increased number of full-time radiation oncology nurses after introduction of the consultation fee for outpatient radiotherapy were reported by 15% of the questionees (Fig. 2A). A multidisciplinary medical care system was not common in Japan before the 1990s, but the Japanese MLHW introduced a multidisciplinary palliative care fee and a multidisciplinary nutrition support fee in 2002 and 2006, respectively, in the national health insurance system in Japan (3,4). These medical fees promoted multidisciplinary medical care teams for palliative care or nutrition support in Japan (4,5). A similar effect of promoting multidisciplinary radiation oncology teams is expected by introduction of the consultation fee for outpatient radiotherapy. In fact, more frequent observations of patients by medical staff were reported even from institutions where there was no increase in the number of medical staff for radiation oncology clinics.

JASTRO carries out national structure surveys in Japan every year, which include the number of personnel in each radiation oncology facility (6–8). The number of personnel is based on the answers from about 700 Japanese radiation oncology facilities (>90% of facilities at work in Japan), and these answers were provided by radiation oncologists at an administrative position of each facility. Compared with the JASTRO's national structure surveys, the targets for this questionnaire were a limited number of radiation oncologists, since there are about 1000 radiation oncologists in Japan (9). In addition, the data presented here were not based on the

administrative data of the hospital, but on the reports from the questionees. This was a major limitation of the study. However, because it was a small survey for a specific topic, our questionnaire could promptly detect a change in the number of personnel engaged in radiation oncology clinics in relation to this new consultation fee, compared with the JASTRO's national structure survey.

In conclusion, our questionnaire survey revealed that one reason for the workforce shortage in radiation oncology clinics might be attributable to poor reimbursement from the health insurance system in Japan, where there have long been smaller numbers of medical staff engaged in radiation oncology clinics than in the USA and European countries (10,11). A large proportion of the questionees were also expecting positive results on the development of radiation oncology clinics in Japan due to introduction of the consultation fee (Fig. 3A). The authors also assume that this consultation fee compels the development of radiation oncology clinics in Japan through an increase in the number of full-time radiation oncologists and other medical staff, and the prevalence of multidisciplinary medical care teams in radiation oncology.

Supplementary data

Supplementary data are available at http://www.jjco.oxfordjournals.org.

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Conflict of interest statement

None declared.

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High-dose-rate interstitial brachytherapy for gynecologic malignancies—dosimetric changes during treatment period

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Abstract

Go to:

To overcome cranio-caudal needle displacement in pelvic high-dose-rate interstitial brachytherapy (HDRIB), we have been utilizing a fullystretched elastic tape to thrust the template into the perineum. The purpose of the current study was to evaluate dosimetric changes during the treatment period using this thrusting method, and to explore reproducible planning methods based on the results of the dosimetric changes. Twenty-nine patients with gynecologic malignancies were treated with HDRIB at the Cancer Institute Hospital. Pre-treatment and post-treatment computed tomography (CT) scans were acquired and a virtual plan for post-treatment CT was produced by applying the dwell positions/times of the original plan. For the post-treatment plan, D90 for the clinical target volume (CTV) and D2cc for the rectum and bladder were assessed and compared with that for the original plan. Cranio-caudal needle displacement relative to CTV during treatment period was only 0.7 ± 1.9 mm. The mean D90 values for the CTV in the pre- and post-treatment plans were stable (6.8 Gy vs. 6.8 Gy) and the post-treatment/pre-treatment D90 ratio was 1.00 ± 0.08. The post-/pre-treatment D2cc ratio was 1.14 ± 0.22 and the mean D2cc for the rectum increased for the post-treatment plan (5.4 Gy vs. 6.1 Gy), especially when parametrial infiltration was present. The mean D2cc for the bladder was stable (6.3 Gy vs. 6.6 Gy) and the ratio was 1.06 ± 0.20. Our thrusting method achieved a stable D90 for the CTV, in contrast to previous prostate HDRIB reports displaying reductions of 35–40% for D90 during the treatment period.

Keywords: interstitial brachytherapy, needle displacement, gynecologic malignancy, dose–volume histogram

INTRODUCTION

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For gynecologic tumors unsuitable for standard intracavitary brachytherapy, such as recurrent tumors or tumors with excessive invasion to the vagina/parametrium, interstitial brachytherapy has been used to achieve better tumor coverage [1–3]. Contemporary planning software for high-dose-rate interstitial brachytherapy (HDRIB) using pre-treatment computed tomography (CT) images enables a conformal dose

distribution to a target, while minimizing doses to organs at risk (OARs). To reproduce the plan in actual irradiation, relative locations of applicator needles to the clinical target volume (CTV) and OARs should also be reproduced exactly at each treatment session. However, in the literature on prostate HDRIB, needle displacements as high as 18–42 mm in the cranio-caudal direction have been reported, resulting in decreases of 35–40% in CTV coverage [4–7]. Displacements in other directions have never been explored. The needle-template unit in these studies was not sufficiently stabilized to a target. To overcome the caudal force exerted by perineal edema, we have been utilizing cranial force from fully stretched elastic tapes thrusting the template into the perineum. The purpose of the current study was to explore dosimetric changes caused by these dimensional (3D) displacements and organ mobility or deformation, to ensure safe delivery of the HDRIB treatment. To the best of our knowledge, this is the first study to report dose–volume histogram (DVH) changes during the treatment period for gynecologic HDRIB.

MATERIAL AND METHODS

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Patients

Between March 2006 and October 2008, 29 patients with gynecologic cancer (cervix 21, corpus 7, vulva 1) were treated at the Cancer Institute Hospital using HDRIB in combination with/without external beam radiotherapy. Patient characteristics are summarized in Table 1. Fourteen patients displayed non-recurrent disease, and 15 patients displayed recurrent disease following surgery (n = 12), radiation (n = 1) or both (n = 2).

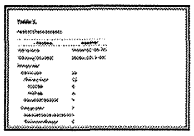

Table 1.
Patient characteristics

Methods

Implantation and CT acquisition Thirteen patients were treated with tandem and needles and 16 patients with needle alone. Mean number of needles used was 18 ± 4 (range 9–28). All needles and the template were unified with stopper screws and the template was sutured to the perineum using six silk stitches. To overcome the caudal movement resulting from perineal edema, the needle-template unit was thrust into the perineum using two fully stretched elastic tapes of about 30 cm in length (ELASTIKON®; Johnson & Johnson, New Brunswick, NJ) attached from the ventral skin near the umbilicus through both sides of the template to the dorsal skin at the umbilical level.

About 3 h after implantation, pre-treatment CT for planning was performed. A post-treatment CT was taken prior to removal of the implant after the last treatment session. Both CT scans were performed with the bladder filled with about 200 ml saline. The interval between the two CTs was 3.4 ± 0.8 days (range 2–6 days).

Treatment planning Planning was performed using pre-treatment CT data transferred to a planning computer (PLATO BPS® ver. 14.3.5; Nucletron, Veenendaal, the Netherlands). A central plane and the basal dose points were determined according to the extrapolated Paris system. Geometrical optimization with manual adjustments was used to achieve CTV coverage, and to keep doses for OARs below ceiling doses, and to keep hyperdose sleeves within 8–10 mm. When these three conditions (CTV coverage, OAR doses, hyperdose sleeve) could not be achieved simultaneously, the plan was clinically compromised. The selected isodose surface (85.4 ± 2.4% basal dose isodose surface (BDIS)) covering CTV was essentially chosen for dose prescription. The prescribed dose was 6.0 Gy per fraction to this isodose surface.

Organ delineation For each set of CT images, the CTV, rectum, bladder and the urethra were delineated by a single radiation oncologist (T.O.) and reviewed by another who is certified (T.N.) to eliminate inter-observer variation. The CTV, including all the areas of gross and potentially microscopic disease which consisted of the vagina, the parametrial tissues and the uterus, was delineated on each slice using clinical information,

CT/magnetic resonance imaging (MRI) and the implanted markers. For OARs, only the outer surface of the rectum, bladder and urethra were contoured and all of the volume inside the outer surface was utilized for the indices following GEC-ESTRO recommendations [8]. The rectum was delineated from the sigmoid colon curvature to the caudal level of ischial tuberosity. For the urethra, the outer surface of the Foley catheter was contoured from the bladder base to the external urethral meatus.

Dosimetric analysis A virtual plan for post-treatment CT was produced by duplicating the air kerma strength for the Ir-192 source, the dwell times and positions of the original plan. Dosimetric analysis was performed using the GEC-ESTRO recommendations [8]. To evaluate the coverage of the target, the dose received by 90% of the CTV (=D90) was generated. For OARs, the minimum doses to the most irradiated 2 cm^3 portions (=D2cc) for the rectum and bladder were generated. The dose to 50% of the urethra (=D50) was evaluated according to a study by Akimoto [9]. For each index, %BDIS and the ratio of post-treatment value to pre-treatment value was generated. All statistical analyses were performed using Dr.SPSS II (SPSS, Chicago, IL, USA). The Wilcoxon signed-rank test was used to compare DVH parameters between pre-treatment and post-treatment plans.

RESULTS

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Needle displacement relative to CTV centroid

Needle displacement relative to CTV centroid during treatment period was 0.5 ± 2.1 mm in the lateral direction (minus (right)–plus (left)), 1.6 ± 3.9 mm in the dorso-ventral direction (minus (dorsal)–plus (ventral)) and–0.7 ± 1.9 mm in the cranio-caudal direction (minus (caudal)–plus (cranial)).

Volumetric and dosimetric results of the CTV and OARs

The volumetric and dosimetric results of CTV and OAR for the rectum, bladder and urethra are presented in Table 2. The CTV volumes showed a slight decrease during treatment (77.7 ± 45.5 cm^3 vs. 73.8 ± 41.1 cm^3), but the CTV doses were stable for both D90 values (6.8 ± 0.7 Gy vs. 6.8 ± 0.9 Gy). No difference was seen in the volumes for OARs between the pre- and post-treatment plans, but dosimetric results varied among the organs. For the rectum, the mean D2cc increased from 5.4 Gy ± 1.1 Gy to 6.1 Gy ± 1.5 Gy ($P < 0.01$). For the bladder, the mean D2cc tended to increase from 6.3 ± 1.8 Gy to 6.6 ± 2.1 Gy ($P = 0.16$). The mean D50 values for the urethra in the pre- and post-treatment plans were 3.7 ± 1.1 Gy vs. 3.6 ± 1.0 Gy ($P = 0.22$).

Table 2.
Volumetric results in CTV and OARs (rectum, bladder, urethra and sigmoid colon)

Dosimetric analysis for the CTV and OARs

The post-/pre-treatment D90 ratio for the CTV was 1.00 ± 0.08 (range 0.83–1.26). For 72.4% (=21/29) of the patients, the difference between pre- and post-treatment D90 for the CTV was within ±5%. The post-/pre-treatment D90 ratio was poorly correlated with cranio-caudal needle displacement: 0.95 ± 0.09 with displacement ≥ 3.0 mm ($n = 4$) vs. 1.01 ± 0.07 with displacement <3.0 mm ($n = 25$). Volume changes for the CTV also had little influence on the post-/pre-treatment D90 ratios, which were 1.01 ± 0.08 in cases with volume increase ($n = 9$) vs. 0.97 ± 0.05 in cases with volume reductions ($n = 20$).

The post-/pre-treatment D2cc ratios for the rectum and bladder were 1.14 ± 0.22 (range 0.71–1.63) and 1.06 ± 0.20 (range 0.67–1.48), respectively. The post-/pre-treatment D2cc ratio for the rectum was significantly higher when parametrial infiltration was present (1.22 ± 0.11, $n = 17$) than when absent (1.02 ± 0.15, $n = 12$). The post-/pre-treatment D2cc ratio for the bladder was significantly higher when tandem use was present (1.13 ± 0.17) than when absent (1.01 ± 0.21), and also higher when cranio-caudal displacement was <3.0 mm (1.09 ± 0.20), compared with displacement >3.0 mm (0.90 ± 0.10). Lower vaginal infiltration and post-hysterectomy status showed little impact on dosimetry for the CTV and OARs (Table 3).

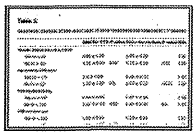

Table 3.
Dosimetric analysis of the dose ratio of post-treatment/pre-treatment CT planning according to locations

Figure 1 shows the frequency distributions of the post-/pre-treatment D90 ratios for the CTV and OARs. The distribution for the D90 ratio shows a narrow range with a large peak at around 1.00, whereas the distribution for D2cc ratios for the rectum and bladder displayed a relatively wide distribution. The urethra D50, however, showed a narrow range with a peak at around 1.00 similar to the distribution for the D90 ratio for the CTV.

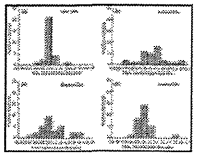

Fig. 1.
Frequency distribution chart for post-/pre-treatment ratios of CTV and OARs. (**a**) Abscissa: post-/pre-treatment ratios of D90 for CTV. Ordinate: number of patients. Distribution approximates Gaussian and has steep peak, with a mean ratio of 1.00 ± ...

Dosimetric analysis (%BDIS)

For %BDIS of mean dose at pre-treament planning, the CTV mean was the highest (140.1 ± 30.3%) followed by that of the urethra (52.5 ± 15.1%), rectum (36.3 ± 9.8%) and bladder (24.1 ± 7.7%). The pre-treatment %BDIS of rectal D2cc was higher when parametrial infiltration was present (85.2 ± 9.1%) than when absent (73.5 ± 18.1%) (P = 0.05). To assess the relationships between relative locations of CTV for each OAR and applicator, a scattergram was generated comparing the post-/pre-treatment dose ratios and %BDIS at pre-treatment planning (Fig. 2a and b). For CTV D90 and urethra D50, the ratios were distributed around 1.00 regardless of the pre-treatment %BDIS of the mean dose. The post-/pre-treatment ratios for D2cc for the rectum in cases with %BDIS of D2cc at pre-treatment planning ≤ 90% and >90% were 1.20 ± 0.19 and 0.91 ± 0.19 (P = 0.03). The corresponding ratios for bladder D2cc were 1.10 ± 0.21 and 1.03 ± 0.18 (P = 0.31).

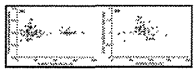

Fig. 2.
(**a**) Correlation between the dose ratio (ordinate: post-/pre-treatment dose ratio) and the relative locations at pre-treatment planning (abscissa: %BDIS (6 Gy = 100%) of mean dose at pre-treatment planning) for CTV and OARs. Red = CTV mean, brown = rectum ...

DISCUSSION

Go to:

Recent planning software for HDRIB enables conformal dose distribution to a target, while minimizing doses to OARs. According to the ICRU 58, PTV is identical to CTV since the applicators move with the CTV [10] and relative locations of brachytherapy needles should be identified at each treatment session to reproduce the plan in actual irradiation. In previous reports for prostate HDRIB, however, only cranio-caudal needle displacements have been explored and have been reported to peak as high as 18–42 mm, which caused a reduction in the D90 for the prostate of 30–40% [4–7]. In our study, cranio-caudal displacement was only 0.7 ± 1.9 mm, obtained by using our fixation method with fully stretched elastic tapes. Displacements were also shown in other directions, 0.5 ± 2.1 mm in the lateral and 1.6 ± 3.9 mm in the dorso-ventral directions. In pelvic HDRIB, this is the first study to investigate DVH changes of CTV and OARs by these 3D displacements and also to demonstrate DVH changes during gynecologic HDRIB treatment.

In contrast to previous prostate HDRIB reports, D90 for the CTV showed no change between pre-treatment (6.8 ± 0.7 Gy) and post-treatment (6.8 ± 0.9 Gy) and the deviation of the post-/pre-treatment D90 ratio was also small (1.00 ± 0.08). Using our simple fixation method, cranio-caudal needle displacement relative to CTV was nearly negligible and good CTV coverage was obtained during HDRIB treatment. Lateral and dorso-ventral displacements were also small enough that D90 did not change for the CTV.

The resultant CTV coverage and small deviation of the post-/pre-treatment D90 ratio for CTV in the current

study are similar to results of our previous *in vivo* dosimetry study on pelvic HDRIB for 66 patients in which the same fixation method was used [11]. The compatibility ratio of the measured/calculated doses for the target (vaginal wall) was excellent (91 ± 8%). Moreover, a 9% negative shift was considered to be attributed to the lack of inhomogeneity correction in the software for the vaginal cylinder, which has a density of 1.24. The small deviation of the compatibility ratio was largely attributable to our fixation method with fully stretched tape and synchronization in movement and deformation between the CTV and the applicator. The CTV was always deformed slightly due to the surrounding organs, but when the applicators were implanted into the target, a 'CTV–template-needle complex' was formed. The target always moved or deformed synchronously with the applicator, and applicator movement in the dorso-ventral or lateral directions had little influence on CTV coverage. Consequently, CTV coverage was not changed between pre-treatment and post-treatment CT.

We found that a large deviation was seen in post-/pre-treatment D2cc for both the rectum and bladder, which was also similar to the results of our *in vivo* dosimetry study. The rectum and bladder were independently deformed and inflated regardless of applicator movement. As a result, the distance from the applicator was varied during treatment. When the distance from the applicator was reduced, the doses increased. In this study, rectal dose increased from 5.4 Gy to 6.1 Gy and the deviation of post-/pre-treatment D2cc ratio was large (1.14 ± 0.22), and bladder dose tended to increase from 6.3 Gy to 6.6 Gy and the deviation was also large (1.06 ± 0.20). Furthermore, great variability was seen in the post-/pre-treatment volume ratios for both the rectum (1.18 ± 0.68) and bladder (1.03 ± 0.33). The patient must stay in bed during implantation because applicators protrude from the perineum, thus defecation or degassing by her own efforts is quite difficult. Similarly, a predetermined amount of injection into the bladder was sometimes difficult because of severe irritation.

There is not enough space between the rectum and the applicators, so the rectum gets covered by higher dose areas (=6.0 Gy iso-dose line) when expanded. The result of this study indicates that the rectal dose was more easily increased in patients with parametrial infiltration and/or in cases of %BDIS of D2cc for rectum >90% at pre-treatment planning. When parametrial infiltration existed, it was necessary to implant needles in the parametrium, the lateral to the rectum. This method made the rectum expansion restricted, which results the rectal dose being easily increased (Fig. 3a and b). The %BDIS =90% region was nearly equivalent to the region of the peripheral area of the CTV. In cases of %BDIS of D2cc at pre-treatment planning ≤ 90%, the organ had inflatable space for applicators while little space was available in cases of %BDIS of D2cc >90%. In order to avoid unexpected higher rectal doses, a degassing method should be considered when rectal inflation is observed with fluoroscopy or CT.

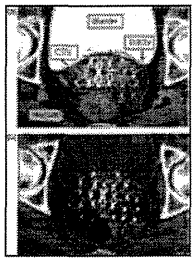

Fig. 3.
Transverse CT image of dose distribution of HDRIB planning at the time of (**a**) the pre-treatment planning and (**b**) the post-treatment planning. D (reference isodose (6 Gy)) = green, CTV = red, rectum = brown, bladder = blue, urethra = purple. CTV–template-needle ...

On the other hand, the bladder has enough space to distend ventrally or cranially as well as posteriorly. Therefore, the distance from applicator changes little with changes in bladder volume. In this study, 200 ml saline was injected in each treatment session in order to fill the bladder. In gynecologic brachytherapy, the full bladder technique has been recommended to reduce the dose to the small intestine and sigmoid colon. In some reports for gynecologic intracavitary brachytherapy with CT-based 3D planning, bladder-filling control can lead to a significant reduction in the dose to the small bowel without exceeding the bladder dose [12–13].

In contrast, the post-/pre-treatment D50 ratio for the urethra was 1.00 ± 0.12, showing a similar deviation to D90 for CTV. The scattergram pattern in the urethra also displayed similar characteristics to the CTV D90. The urethra was a less deformed or inflated organ, and applicators were implanted in parallel in the dorsal and lateral spaces of the urethra, urethral movement was synchronized with the applicators and urethral

coverage was stable during HDRIB treatment.

To successfully achieve the treatment goal of HDRIB treatment for gynecological malignancies, the first consideration has to be the reproduction of the CTV and the needle-template unit position for each treatment. With our simple fixation method, cranio-caudal needle displacement is small and a highly reproducible CTV coverage is expected during HDRIB treatment. To control bladder and rectal volume at each treatment session is also important but is difficult. This requirement can be met by use of the recent image-guided methods, which are capable of providing volume images of soft-tissue organs. If large cranio-caudal displacements are confirmed, an increased margin around the CTV or a dose increment for the prescription dose is required as a safety margin. However, these increases need to be evaluated with clinical judgement because D2cc for the rectum and bladder will also rise as a result.

Finally, we used HDRIB with metal applicators in this study. However, metal applicators cause artifacts on CT images, making it difficult to draw organ contours. Some groups are performing image-based brachytherapy by using plastic/titanium applicators compatible with MRI [14–15]. We also plan to start MRI-based image-guided HDRIB.

In conclusion, with our simple method of fixing the needle-template unit using elastic tapes, needle displacement relative to the CTV was nearly negligible and excellent CTV coverage was achieved at the final treatment session. The difference between pre- and post-treatment D90 for the CTV was within ±5% for 72.4% (21 of 29) of the patients in most cases.

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Go to:

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