● 時 論 ●

オーダリングシステム型外来化学療法部の現況と問題点

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Present Situation and Problems of the Ordering System Type Infusion Center: Motoi Kondo, Keiko Tazumi, Keiko Kouji, Natsuko Matsumura, Manabu Takegami, Nobuo Kurokawa, Yuzuru Kanakura, Shinzaburo Noguchi and Masao Mizuki (*Chemotherapy and Oncology Center, Osaka University Hospital*)

Summary

We examined four problems of the ordering system type infusion center. In this system, regimen is made by chief physician and cared by the staff in the infusion center. 1) In securing of the staff, an upbringing of doctors and IV nurses are important. 2) An evidence-based regimen is necessary in order to minimize the differences of regimen made by each doctor. 3) A facility expansion might reduce an incident risk. 4) As the condition of patient suddenly changes, the chief physician of the patient should be contacted. We suggest that it is particularly important to make these problems clarified and solved by the team within the institution. Key words: Chemotherapy, Infusion center (*Received Oct. 2, 2006/Accepted Feb. 6, 2007*)

要旨 外来主治医が抗腫瘍療法のレジメンを決定し，外来化学療法部の専任医師が患者管理を行う“オーダリングシステム型外来化学療法部”の四つの問題点につき検討した。第1の問題点はスタッフの確保である。対策では専門医師とIVナースの育成が早急な課題である。第2の問題点は各科の同疾患におけるレジメンの差異である。対策ではエビデンスに基づいた施設レジメンが必要である。第3の問題点は設備の適正化である。対策では最大利用者数に合わせた設備の拡大が必要であり，インシデントリスクを軽減させる可能性がある。第4の問題点は患者の急変時対応である。対策では主治医対応を原則とすべきである。オーダリングシステム型外来化学療法部の運営では現場の問題点を明確にし，チームで対策を講じ施設の問題とすることが特に重要である。

はじめに

近年，薬剤の進歩により，がん患者における外来化学療法が推奨されている。また，外来化学療法加算は病院経営の観点から重要視されている。しかしながら，外来化学療法が浸透するにつれ，整理，改善すべき問題点も明確となってきた。外来化学療法部（室）の運営は大きく二つの型に分類される。外来化学療法部に専属する医師が抗腫瘍薬剤のレジメンを決定し患者管理を行う主導型外来化学療法部と外来主治医が抗腫瘍薬剤のレジメンを決定し，投薬現場の医師が患者管理を行うオーダリングシステム型（発注型）外来化学療法部である。当院の外来化学療法部では，オーダリングシステム型の運営を採用している。本稿では当院の外来化学療法部における四つの問題点，①スタッフの確保，②各科の同疾患におけるレジメンの差異，③設備の適正化，④患者の急変時対応，について検討した。

Ⅰ．外来化学療法部の運営状況

17診療科（乳腺内分泌外科，消化器外科，泌尿器科，婦人科，消化器内科，呼吸器内科，血液・腫瘍内科，脳外科，呼吸器外科，内分泌・代謝内科，皮膚科，放射線科，整形外科，小児科，神経・精神科，耳鼻咽喉科，眼科）と薬剤部，看護部で外来化学療法部運営委員会を構成し運営委員会を開催している。外来化学療法部運営委員会は，外来化学療法部の運営における協議事項が立案された際に会議を開催し，各部署の意見を統合する。

外来化学療法部の職員は，専任看護師3名（がん看護専門看護師1名），専任医師2名（暫定指導医1名：日本臨床腫瘍学会専門医制度規則に基づき認定される）。木曜

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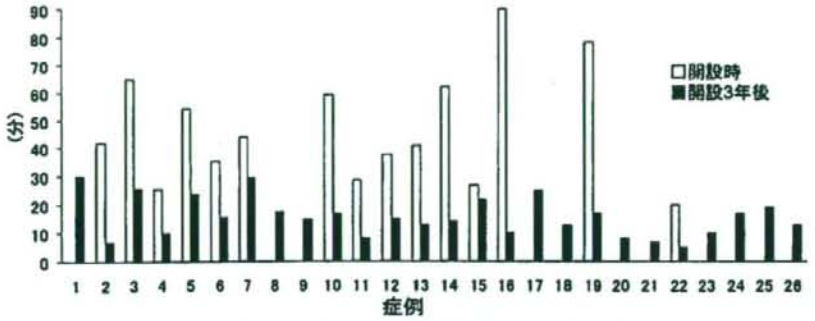


平均待ち時間は，開設時が47.6±17.7分。開設3年後が15.7±6.9分。横軸の各バー1本＝1症例，縦軸＝症例ごとの待ち時間。

図1 各症例における化学療法部受付から薬剤到達までの所要時間

日の全日と月，金曜日の午後は9診療科（乳腺内分泌外科，消化器外科，泌尿器科，婦人科，消化器内科，呼吸器内科，血液・腫瘍内科，脳外科，呼吸器外科）でローテーションを組んで担当医師を派遣している。派遣医師は，当番勤務帯の外来化学療法部利用患者の管理を行っている。

病床数は12床あり，2003年11月の開設から2006年10月までに13,227件の外来化学療法を施行してきた。2005年度の利用患者数は5,138件であった。外来化学療法部では，抗腫瘍薬剤の静注療法と動注療法を対象としている。

II. 投薬手順

外来化学療法部の利用，投薬手順は，①前日11時までに各診療科にて予約を行う。②当日の主治医診察終了後に抗腫瘍薬剤をオーダーし薬剤部にメニューをFAXする。③薬剤師が至適薬剤量の確認を行った後にキャビネット内で薬剤調製し外来化学療法部に運ぶ。④外来化学療法部で薬剤のダブルチェックを行う。⑤バイタルサインを確認する。⑥患者，薬剤確認後に抗腫瘍薬剤を投薬する。

III. 問題点の検討

1．スタッフの確保

現在，外来化学療法部の専任看護師は3名で，がん看護専門看護師の1名に加え，集中治療部，婦人科を経験する看護師1名と乳腺外科を経験する看護師1名で構成されている。今後の病床数増加に加え，専任看護師の増員が協議されている。

専任医師は2名で，日本臨床腫瘍学会の暫定指導医が1名と外科専門医が1名である。専任医師増員のヒアリングも行われている。

2．各科の同疾患におけるレジメン

当院においては主治医によりfirst-lineレジメン内容に多少の差異がある。多くの場合は投薬速度であり，2005年4～6月に実施した2か月間の調査では，約30%に同種点滴速度に差異を認めた[1]。疾患によってはsecond-lineやthird-lineのエビデンスが十分に検証されていない場合も少なくなく，院内の化学療法実施手順標準化ワーキングなどによる標準レジメン，臨床試験のプロトコールの作成が今後の課題と思われる。

3．設備・導線経路とインシデント

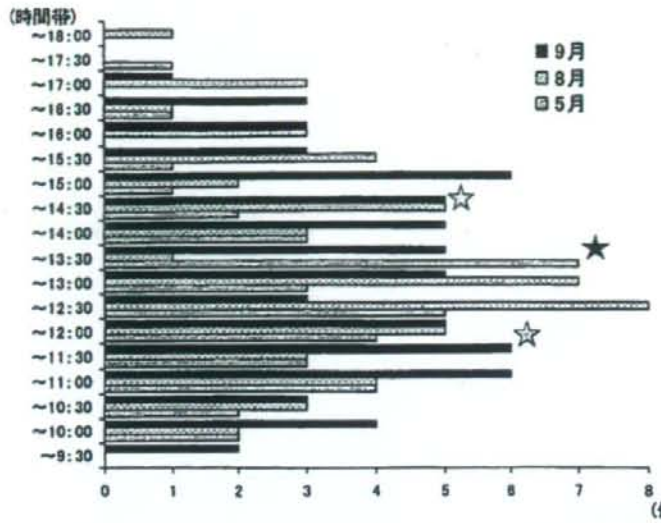
外来化学療法では薬剤オーダーから投薬実施まで極力の導線経路短縮が望まれる。当施設では薬剤オーダーから外来化学療法部への薬剤到達時間が5～30分と比較的長い（図1）。外来化学療法室（後の外来化学療法部）の開設初期には80分を超える待ち時間があったが，調製薬剤師を増員したこと，調製手技に慣れたこと，また調製録出力の自動化により導線経路の短縮が図られている（図1）。また，外来化学療法部利用患者のピークが11～14時にあり，インシデントの発生率がこの時期に重なっている（図2）。

4．急変時の体制

抗腫瘍薬剤にはアレルギー，組織壊死など重篤な合併症を引き起こす薬剤も少なくない。このため外来化学療法時の急変時対策は必須となる。当院では2003年11月の開設から2006年10月までに，3/13,227件（0.00023%）に重篤化の可能性のあるpre-shock（trastuzumab），adverse effect（oxaliplatin），infusion reaction（trastuzumab）を認め，うち2件が緊急入院となった。緊急入院となった2件ではステロイドが投薬され，翌日には臨床症状が安定した。現時点においてはオーダリングシステムでの外来化学療法部運営であり主治医対応を原則とし，不在時には代理を立てることとしている。

IV. 考察

本稿では，オーダリングシステム型の外来化学療法部における四つの問題点，①スタッフの確保，②各科の同疾患におけるレジメンの差異，③設備の適正化，④患者の急変時対応，につき検討した。まず，スタッフの確保



2006年5月，8月，9月の患者利用時間帯における患者対応件数（ルート確保件数と抜針件数の合計件数）とインシデント発生時（☆）の関係。2006年5月の13時～13時30分の間に投薬順序トラブル，8月の14時～14時30分の間に皮下漏出，9月の11時～11時30分の間に動注ルートの破損が発生した。

図2 インシデント発生時間帯とルート確保件数・抜針件数の関係

であるが，オーダリングシステム型外来化学療法部では十分な専任医師を確保しづらい環境にあるのが現状である。その大きな理由の一つは下請け業務的と周知されるが故である。事実，当院においても専任医師不在の期間が存在し，ローテーション医師のみで対応してきた経緯がある[2]。一方，欧米では外来化学療法部運営の主軸にいわゆるIVナースが存在し，オーダリングシステム型外来化学療法部の専任医師と同様の働きをしている。すなわち，調製薬剤の確認，ルート確保，投薬を行っている[3]。本邦において早々にこのようなシステムを導入することは合併症発生時の対応や医事紛争などの観点から困難と思われるが，今後，IVナースの育成は外来化学療法部運営の重要課題となる可能性がある。

一方，各癌疾患におけるレジメンでは，強いエビデンスに基づく施設（国）レジメンが必要である。無論，患者背景により，いわゆる“さじかげん”療法も考慮される場合もあると考えるが，“さじかげん”療法はエビデンスに基づく療法以上に設定が困難ではないかとわれわれは考えている。患者利益を十分に考慮したレジメンの作成が課題である。

現在，約5,000件/年で外来化学療法部利用患者に対応しているが，ベッドコントロールが限界に近く，5,000件/年以上の外来化学療法部利用患者対応には現状以上(12床)の病床確保や，さらなるベッドコントロールが必要と思われる。当施設では，外来化学療法部利用患者のピークが11～14時にあり，患者の分散がベッドコントロールにおける課題の一つである。ピーク分散には血液検査結果の迅速化，外来主治医診察の迅速化，薬剤調製の迅速化など多方面での調整が必要である。このうち薬剤の調製にはキャビネット台数が1台と少ないことが多少なりとも影響している。また，インシデントの発生時間と利用患者のピークが重なっており，この対策は結果的にインシデント対策に直結する可能性がある。

急変時の患者対応には心肺蘇生術や各種診療科の対応が必要となる場合も想定される。このため当院では抗腫瘍薬剤の投薬を17時までに終了する方向としている。しかしながら，現実的には院内教育の不足から超過する症例もある。施設としてのさらなる取り組みが必要である。

おわりに

オーダリングシステム型外来化学療法部の現況と問題点について述べた。オーダリングシステム型外来化学療法部の運営では，主導型の外来化学療法部（室）運営と異なり現場の問題点への対策が講じにくいが，現場の問題点を明確にし，チームで対策を講じ施設の問題として取り組むことが重要と考えられる。

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CLINICAL INVESTIGATION **Lung**

CHANGES IN PATTERNS OF CARE FOR LIMITED-STAGE SMALL-CELL LUNG CANCER: RESULTS OF THE 99-01 PATTERNS OF CARE STUDY—A NATIONWIDE SURVEY IN JAPAN

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Background: This study was undertaken to analyze the practice process of thoracic radiotherapy (TRT) and evaluate changes in patterns of care for patients with limited-stage small-cell lung cancer (LS-SCLC) in Japan.
Methods and Materials: The Patterns of Care Study (PCS) conducted the second nationwide survey of care process for patients with LS-SCLC treated by using TRT between 1999 and 2001.
Results: The PCS collected data for 139 patients with LS-SCLC (man-woman ratio, 5:1; median age, 69 years; age > 70 years, 43%; Karnofsky Performance Status > 70, 73%; and Stage III, 88%). Median total dose was 50 Gy. Twice-daily TRT was used in 44% of patients. Median field size was 12 × 14 cm. The most commonly used photon energy was 10 MV (77%), whereas obsolete techniques using ^{60}Co or X-ray energy less than 6 MV comprised 12%. Three-dimensional conformal therapy was used with 12% of patients. Computed tomography simulation was performed in 40% of cases. Only 12 patients (8.6%) received prophylactic cranial irradiation (PCI). Concurrent chemotherapy and TRT (CCRT) was used for 94 patients (68%). Only 6 patients (4.4%) entered clinical trials. Compared with the previous PCS 95-97, significant increases in the use of CCRT (34–68%; $p < 0.0001$), twice-daily TRT (15–44%; $p < 0.0001$), and PCI (1.7–8.6%; $p = 0.0045$) were observed, although the absolute number of patients receiving PCI was still extremely low.
Conclusions: Evidence-based CCRT and twice-daily TRT has penetrated into clinical practice. However, PCI is not yet widely accepted in Japan. © **2008 Elsevier Inc.**

Patterns of Care Study, Small-cell lung cancer, Thoracic radiation therapy, Nationwide survey, Practice process.

INTRODUCTION

The Patterns of Care Study (PCS) is a retrospective study designed to investigate the national practice processes for selected malignancies during a specific period (1). In addition to documenting practice processes, the PCS is important in developing and spreading national guidelines for cancer treatment. In Sept 1998, the Japanese PCS conducted the first nationwide survey for patients with lung cancer treated using thoracic radiotherapy (TRT) between 1995 and 1997 (PCS 95-97). The main findings from the PCS 95-97 are summarized as follows. First, the use of TRT for patients with limited-stage small-cell lung cancer (LS-SCLC) in Japan is predominantly influenced by institutional characteristics, rather than age group. Second, patient age significantly influenced the use of chemotherapeutic modality, such as etoposide and cisplatin for patients with LS-SCLC (2, 3).

Because results of several key clinical studies of patients with LS-SCLC were reported between 1997 and 1999, it seems meaningful to evaluate whether practice processes in Japan were changed accordingly. The second PCS for lung cancer investigated patient characteristics, workup studies, the process of TRT, and use of chemotherapy in patients with LS-SCLC treated by using TRT between 1999 and

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2001. The objectives of the present study are as follows. First, compile processes in TRT for patients with LS-SCLC treated between 1999 and 2001, and second, compare patient characteristics and treatment modalities between the PCS 95-97 and PCS 99-01 in Japan.

METHODS AND MATERIALS

Between July 2002 and August 2004, the PCS conducted a second national survey of radiation therapy for patients with lung cancer in Japan. The Japanese PCS developed an original data format for patients with lung cancer. The PCS performed an extramural audit survey for 73 (38 academic and 35 nonacademic institutions) of 556 institutions by using stratified two-stage cluster sampling and collected data for 768 eligible patients with lung cancer. Data collection consisted of two steps of random sampling. Before random sampling, all institutions were classified into one of four groups. Criteria for stratification were described elsewhere (2, 4). Briefly, the PCS stratified Japanese institutions as follows: A1, such academic institutions as university hospitals or national/regional cancer center hospitals treating 430 or more patients per year; A2, academic institutions treating fewer than 430 patients; B1, nonacademic institutions treating 130 or more patients per year; and B2, those treating fewer than 130 patients per year. Cutoff values for numbers of patients treated per year between A1 and A2 institutions and B1 and B2 institutions were increased from those used in the previous PCS because of the increase in number of patients treated using radiation therapy in Japan (4).

Eligible patients included those with 1997 International Union Against Cancer Stages I–III lung cancer treated by using TRT between 1999 and 2001, with Karnofsky Performance Status (KPS) greater than 50 before the start of treatment and no evidence of other malignancies within 5 years. The International Union Against Cancer staging system was used because the PCS comprehensively surveyed patients with non-SCLC and those with SCLC. As mentioned, Stages I–III SCLC do not precisely match the definition of LS-SCLC by Mountain (5). However, no definition of this term has been universally accepted. The PCS survey of TRT charts showed that for patients with SCLC, the tumor could be encompassed within the TRT field. Thus, in the present study, all patients were regarded as having LS-SCLC.

The aims of this study are to provide patterns of practice concerning: (*1*) patient background; (2) workup studies; (*3*) TRT, including photon energies, total dose, spinal cord dose, field arrangements, prescription point, and use of prophylactic cranial irradiation (PCI); and (*4*) chemotherapy, including agents, number of chemotherapy cycles, sequence of chemotherapy, and TRT. Patient background included demographics and medical status, such as KPS, comorbidities, stage, and whether treated on an outpatient basis. In addition, practice patterns of the PCS 99-01 were compared with those of the PCS 95-97.

To validate the quality of collected data, the PCS used the Internet mailing list among all the surveyors. *In situ* real-time check and adjustment of the data input were available between each surveyor and the PCS committee. In tables, "missing" indicates that the item in the data format was left empty, whereas "unknown" means that the item in the format was completed with data unknown. We combined missing and unknown in tables because their meanings were the same in most cases; no valid data were obtained in the given resources. Cases with unknown values were included when both percentage and significance values were calculated. Statistical significance was tested by using chi-square test. A $p < 0.05$ was considered statistically significant. Overall survival, assessed from the first day of radiation therapy, was estimated by using the Kaplan-Meier product-limit method, and differences were evaluated using log-rank test.

RESULTS

Patient backgrounds

There were 141 patients with SCLC, which constituted 18% of all patients with lung cancer surveyed. Of those, 2 patients underwent initial surgical resection and adjuvant postoperative irradiation. Thus, in the present study, the PCS analyzed the remaining 139 patients who did not undergo surgery (Table 1).

There were 116 men and 23 women with an age range of 36–85 years (median, 69 years). Patients older than 70 years constituted 43% of the patient population. For that elderly patient pool, the institutional breakdown was as follows: 31% in A1, 39% in A2, 50% in B1, and 50% in B2 ($p = 0.037$). For comorbidities, the most frequent adverse medical conditions were cardiovascular disease (34%) and diabetes (14%). Seventy-three percent had KPS of 80% or greater. Comparison of four institutional groups failed to show differences in terms of patient background other than patient age and KPS. Patients with KPS of 80 or greater comprised 89% of A1, 55% of A2, 74% of B1, and 65% of B2 strata ($p = 0.0071$). A majority of patients (88%) had Stage III disease. There were no significant differences in distributions of T and N classifications or clinical stages between institutional groups. Only 5% of all patients were treated on an outpatient basis.

Workup studies

Workup studies are listed in Table 2. Pretreatment workup included chest computed tomography (CT) in 96%, bronchoscopy in 93%, brain CT or magnetic resonance imaging in 86%, and bone scan in 79% of surveyed patients. Chest/abdominal CT and bone scan were used for a majority of patients, whereas positron emission tomography (PET) was used for an extremely small number of patients. Comparison of four institutional groups failed to show differences in terms of workup studies.

Practice process of TRT

Thoracic radiotherapy methods are listed in Table 3. Median total dose of TRT was 50 Gy, and median field size was 12 × 14 cm. Median dose to the spinal cord was 42 Gy. A CT simulator was used for planning in 40% of patients. Three-dimensional conformal therapy was used in 12%. The planning target volume included the ipsilateral hilus in 96%, ipsilateral mediastinum in 96%, contralateral mediastinum in 84%, contralateral hilus in 17%, ipsilateral supraclavicular region in 25%, and contralateral supraclavicular region in 15%. Field reduction during the course of TRT was done for 61%. Twice-daily radiotherapy was used for 44%. Photon energy generally was 10 MV (77%), whereas obsolete techniques using ^{60}Co or X-ray energy less than 6 MV were used for 12%. Only 12 patients (8.6%) received PCI. Median dose of PCI was 25 Gy. Only 6 patients (4.4%) entered clinical trials.

Table 1. Patient and tumor characteristics

Characteristics	Stratification of institutions					*p*-value
	A1	A2	B1	B2	Total	
No. of patients	36	23	54	26	139	
Age (y)						0.037
Range	44–85	36–81	40–81	54–85	36–85	
Median	69	68	71	71	69	
>70 (%)	31	39	50	50	43	
Sex						0.780
Men	30	18	47	21	116	
Women	6	5	7	5	23	
Karnofsky performance status ≥80 (%)	89	55	74	65	73	0.013
Clinical stage/UICC 1997						0.475
I	0	1	2	2	5	
IIA, IIB	3	3	4	1	11	
IIIA	10	6	19	10	45	
IIIB	23	13	28	13	77	
Unknown/missing	0	0	1	0	1	
T classification						0.569
T1–2	14	11	25	14	64	
T3–4	22	12	28	12	74	
Unknown/missing	0	0	1	0	1	
N classification						0.551
N0–1	7	4	9	6	26	
N2–3	29	19	44	20	112	
Unknown/missing	0	0	1	0	1	

Abbreviation: UICC = International Union Against Cancer.

Institutional stratification influenced several radiotherapeutic parameters (Table 4). Photon energy of 6 MV or greater was used for 97% of patients in A1, 96% in A2, 87% in B1, and 69% in B2 institutions ($p = 0.0006$). The ^{60}Co machines were not used in any A1 to B1 institutions. Twice-daily radiotherapy was used for 57 of 113 patients in A1 to B1 institutions, but only 4 of 26 patients in B2 institutions were treated in that manner ($p = 0.0012$). The PCI was used for 7 of 36 patients (19%) in A1 institutions, but only 5 patients (4.9%) in the remaining institutions ($p = 0.0073$). Use of a CT simulator was more frequent in A1 (52%) and A2 (65%) compared with B1 (34%) and B2 (17%) institutions ($p = 0.011$).

One hundred twenty-nine patients (93%) received systemic chemotherapy. Of those, platinum-based chemotherapy constituted 98%. Concurrent chemotherapy and TRT (CCRT) was used for 68% (73% of patients who received systemic chemotherapy). Median number of chemotherapy cycles was four. Median times from the first day of systemic chemotherapy to the first date and last date of TRT were 3 and 44 days, respectively. Proportions of patients who received chemotherapy were 97% in A1, 96% in A2, 91% in B1, and 89% in B2 institutions ($p = 0.49$).

Comparison between two PCS studies

Patient backgrounds and practice patterns in PCS 99-01 were compared with those in PCS 95-97. Differences between the two studies are listed in Table 5. Based on two-stage cluster sampling, the ratios of academic to nonacademic institutions were almost equal in the two surveys. Although median age in PCS 99-01 was slightly older than that in PCS 95-97, patients' backgrounds were similar in the studies. Use of obsolete treatment equipment (photon energy < 6 MV and ^{60}Co) decreased from 20% in PCS 95-97 to 12% in PCS 99-01 ($p = 0.06$). The greatest differences were seen in the use of twice-daily TRT and CCRT. Twice-daily TRT increased from 15% in PCS 95-97 to 44% in PCS 99-01 ($p < 0.0001$). Use of CCRT in PCS 99-01 was twice as high as in PCS 95-97 (68% vs. 34%; $p < 0.0001$). Although a significant increase in the use of PCI was observed (1.7–8.6%; p = 0.0045), the rate was still extremely low in Japanese practice.

Table 2. Percentage of patients examined by using each diagnostic technique in the course of staging

Chest CT	96%
Chest MRI	7%
Bronchoscope	93%
Bone scan	79%
Abdominal CT	88%
Positron emission tomography	2%
Brain CT or MRI	86%

Abbreviations: CT = computed tomography; MRI = magnetic resonance imaging.

Table 3. Process of thoracic radiation therapy for patients with limited-stage small-cell lung cancer

Median total dose (Gy)	50
Median spinal cord dose (Gy)	42
Use of CT simulator (%)	40
Three-dimensional conformal therapy (%)	12
Beam energy (%)	
^{60}Co	1.4
<6 MV	10.8
≥6 MV	88
Median field size (cm)	12 × 14
Field reduction during treatment (%)	61
IRB-approved protocol treatment (%)	4.4
Twice-daily radiotherapy (%)	44
Prophylactic cranial irradiation (%)	8.6
Area included in planning target volume (%)	
Ipsilateral hilus	96
Ipsilateral mediastinum	96
Contralateral mediastinum	84
Contralateral hilus	17
Ipsilateral supraclavicula	25
Contralateral supraclavicula	15
Systemic chemotherapy (%)	93
Concurrent chemotherapy and thoracic radiotherapy (%)	68

Abbreviations: CT = computed tomography; IRB = institutional review board.

Comparison of preliminary outcomes between studies

There are known limitations in survival analyses in this type of retrospective survey study. Still, preliminary outcome data in the two studies could be compared. Overall survival rates of the entire patient pool in each study are shown in Fig. 1. Two-year survival rates in PCS 95-97 and PCS 99-01 were 34% and 45%, with a median follow-up of only 11 months in both studies, respectively. Median survival times of the patient pools in PCS 95-97 and PCS 99-01 were 14 and 17 months, respectively. These differences did not reach a statistically significant level.

Table 4. Process of thoracic radiation therapy influenced by institutional stratification

	Stratification of institutions					
Characteristics	A1	A2	B1	B2	Total	*p*-value
Photon energy						0.0006
^{60}Co	0	0	0	2	2	
<6 MV	1	1	7	6	15	
≥6 MV	35	22	47	18	122	
Twice-daily fractionation used						0.0012
Yes	18	11	28	4	61	
No	18	12	26	22	78	
Treatment planning						0.011
Use of CT simulator (%)	52	65	34	17	40	
Prophylactic cranial irradiation used						0.0002*
Yes	7	2	3	0	12	
No	29	17	48	24	118	
Unknown/missing	0	4	3	2	9	

Abbreviation: CT = computed tomography.
* A1 vs. A2–B2: $p = 0.0073$.

Table 5. Comparison of treatment modalities between two studies

Background and treatment process	PCS 95-97 (n = 174)	PCS 99-01 (n = 139)
SCLC/all lung cancer (%)	16	18
Median age (y)	65	69
KPS > 70 (%)	70	73
Stage III (%)	87	88
Median total dose (Gy)	50	50
Photon energy <6 MV or ^{60}Co (%)	20	12
Use of CT-simulator (%)	NA	40
Twice-daily thoracic radiotherapy (%)*	15	44
Chemotherapy used (%)	92	93
Concurrent chemoradiation (%)†	34	68
Prophylactic cranial irradiation (%)‡	1.9	8.6
Survival at 2-years (%)	34	45

Abbreviations: PCS = Patterns of Care Study; SCLC = small-cell lung cancer; KPS = Karnofsky Performance Status; CT = computed tomography; NA = not available.
* $p < 0.0001$ by chi-square test.
† $p < 0.0001$ by chi-square test.
‡ $p = 0.0045$ by chi-square test.

DISCUSSION

Results of the present PCS reflect national treatment trends for TRT for patients with LS-SCLC in Japan between 1999 and 2001. Through this second nationwide audit survey and data analysis, PCS established the general patterns of care for patients with LS-SCLC in Japan. Results also show the influence of the structure of radiation oncology on the process of TRT and how state-of-the-art cancer care supported by clinical trial results has penetrated into the national practice process during the study period.

During the study period, TRT for LS-SCLC constituted less than one fifth of all radiation therapy for patients with lung cancer. This result was similar to data from the United States (6). Use of such staging studies as chest CT, bone scan, and PET scan for patients with SCLC was in line with guidelines (7) and very similar to the report from the United States (6). A PET scan in clinical use was still scarce. Only a small fraction of patients participated in clinical trials similar to those observed in the United States. In Japan, twice-daily TRT was used more frequently and PCI was used less frequently compared with the United States. However, it should be noted that subjects of the PCS in the United States were treated between 1998 and 1999, preceding the results of key studies that supported the use of twice-daily radiation therapy and PCI.

The study shows that more suitable photon energies were used in TRT at academic institutions. Thirty-one percent of patients in B2 institutions were treated with a linear accelerator with less than 6 MV or a ^{60}Co machine that did not meet the standard of care for equipment to treat patients with lung

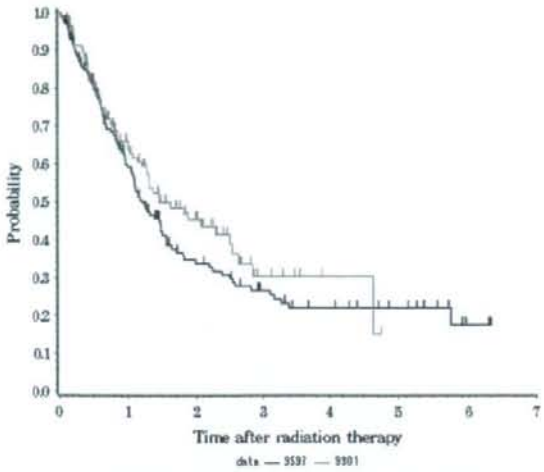

Fig. 1. Kaplan-Meier estimate of overall survival of patients with Stages I–III small-cell lung cancer surveyed in the 1995–1997 (dark line) and 1999–2001 (bright line) Patterns of Care Studies in Japan.

cancer, although this rate decreased from PCS 95-97 (>40% in B2) and was somewhat favorable compared with postoperative radiation therapy for patients with lung cancer in the same period (8). The availability of CT simulators was greater than 50% in academic institutions, but only one third in B1 and even lower in B2 institutions. In modern radiation therapy, CT-based treatment planning is essential for TRT to achieve optimal target coverage while reducing the dose to normal tissue. Twice-daily TRT was used more frequently for patients in A1 to B1 institutions than patients in B2 institutions. The PCI was used for 19% of patients in A1 institutions, but only 4.9% of patients in the remaining institutions. Although the general quality of radiation oncology improved from PCS 95-97, results of the present study show that institutional stratification still influences the structure and process of radiotherapy, such as availability of CT simulators, the flexibility of external beam energy selection, and use of evidence-based cancer care in Japan.

During the past 20 years, survival prolongation in patients with LS-SCLC was attained mainly by clinical trials that studied some aspect of radiation therapy, such as integration of TRT (9, 10), optimization of timing and fractionation of TRT (11), and introduction of PCI (12). The TRT is an essential component of the standard management of patients with LS-SCLC. Two meta-analyses showing the advantage of the addition of TRT to systemic chemotherapy, published in 1992 (9, 10), preceded our first national survey (PCS 95-97). In PCS 99-01, although 43% of all surveyed patients were older than 70 years and 23% of all patients had KPS of 70% or less, 93% of all patients received chemotherapy. This percentage is very similar to that in PCS 95-97 (2, 3).

When interpreting our data, it is important to note that they are limited to patients who received TRT as part of their overall treatment regimen. However, these two surveys showed that use of systemic chemotherapy was reasonably high in Japanese practice. Based on several studies published during the past 10 years, CCRT up front has emerged as a standard of care generating the highest survival rates (11, 13, 14). A landmark study supporting twice-daily TRT was published in 1999 after the previous PCS 95-97 (11). In that study, Turrisi *et al.* (11) showed a significant benefit in 5-year survival rate with the use of twice-daily TRT (45 Gy in 1.5 Gy fractions twice daily) concurrent with chemotherapy compared with once-daily TRT (45 Gy in 1.8 Gy fractions every day). Use of CCRT in PCS 99-01 (68%) was twice as high as in PCS 95-97 (34%). Similarly, there was a notable increase in the use of twice-daily TRT after PCS 95-97. In the present study, 44% of patients received twice-daily TRT, nearly three times as high as in PCS 95-97. Although it is still unclear whether twice-daily TRT to 45 Gy in 3 weeks is superior to a higher total dose of 60–70 Gy delivered by using more standard fractionation, it seems that diffusion of twice-daily TRT to Japanese practitioners was rapid. It seems likely that the marked increase in use of twice-daily TRT with concurrent chemotherapy in Japan contributed to the widespread use (95%) of inpatient treatment in PCS 99-01. In general, once-daily treatment is better accepted for outpatient care, whereas twice-daily scheduling is convenient for the care of inpatients, but at greater cost. Marked increases in the use of CCRT and twice-daily TRT indicates greater acceptance of these treatment modalities by radiation oncologists across Japan.

However, PCI has yet to be systematically adopted in Japanese practice. Despite the 1999 publication of another landmark trial that showed the survival advantage of PCI for complete responders (12), only 8.6% of all patients received this intervention. At the time of PCS 95-97, the role of PCI had not been established and it was used for only 1.9% of all patients (2). Before the present survey, it was expected that the percentage of patients who received PCI would be greater on the basis of the meta-analysis. Although a slight increase in use of PCI was observed, the rate was still extremely low in Japan. Information about the number of complete responders was outside the audit. However, a complete response rate of at least 50% is expected for study subjects (15). Whether this is caused by the small number of radiation oncologists in Japan or the small number of patients who received radiation therapy for cancer treatment is unknown. We reported previously that the number of full-time radiation oncologists is low, especially in nonacademic institutions in Japan (2). According to cancer statistics in Japan, radiation therapy was used for only 11.3% of all patients with cancer in 1999 compared with medical (27.5%) and surgical treatment (69.9%) (16). It is not clear why evidence-based PCI has not yet been widely accepted in Japan as opposed to the rapid diffusion of CCRT and twice-daily TRT in clinical practice. It appears that physicians in Japan hesitate to use PCI, and their patients are reluctant to receive PCI even if it is beneficial. Results of the ongoing third national survey in Japan will be particularly interesting in this regard.

Nonsignificant survival improvement in patient outcome was observed between PCS 95-97 and PCS 99-01. The current PCS has limitations in terms of outcome analysis because of a short follow-up period, significant variations in follow-up information according to institutional stratification (4, 17), and difficulties in outcome survey. One of the ultimate goals of the PCS is to determine how structure and processes of radiation therapy affect patient outcomes, including local control, survival, and quality of life. However, since 2006, personal information is strictly protected by law and outcome surveys are difficult to perform in Japan, even for patients with cancer. Cancer is not yet a reportable disease in Japan. Currently, limitations in data accumulation concerning patient outcomes in this type of survey encouraged us to develop new health care data collection systems and linkages among systems that make systematic recording and analysis of structure/process and outcome data part of routine quality monitoring (Japanese National Cancer Database, funded by the Ministry of Health, Labor, and Welfare Japan).

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CLINICAL INVESTIGATION **Cervix**

PATTERNS OF RADIOTHERAPY PRACTICE FOR PATIENTS WITH CERVICAL CANCER (1999–2001): PATTERNS OF CARE STUDY IN JAPAN

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Purpose: To describe the patterns of definitive radiotherapy practice for patients with uterine cervical cancer from 1999 to 2001 in Japan.

Methods and Materials: The Japanese Patterns of Care Study (JPCS) working group conducted a third extramural audit survey of 68 institutions and collected specific information on 324 cervical cancer patients treated with definitive radiotherapy.

Results: Almost all patients (96%) were treated with whole pelvic radiotherapy using opposing anteroposterior fields (87%). A midline block was used in 70% of the patients. Intracavitary brachytherapy (ICBT) was applied in 82% of cases. Most patients (89%) were treated with high-dose rate (HDR) ICBT. Calculation of doses to organs at risk (ICRU 38) was performed for rectum in 25% of cases and for bladder in 18% of cases. Only 3% of patients were given intravenous conscious sedation during ICBT applicator insertions. The median total biologically effective dose at point A (EBRT+ICBT) was 74 Gy_{10} in cases treated with HDR-ICBT. There was no significant difference in total biologically effective dose between stages. The median overall treatment time was 47 days. Concurrent chemoradiation was applied in 17% of patients.

Conclusions: This study describes the general patterns of radiotherapy practice for uterine cervical cancer in Japan. Although methods of external radiotherapy seemed to be appropriate, there was room for improvement in ICBT practice, such as pretreatment. A substantial difference in total radiotherapy dose between Japan and the United States was observed. © **2008 Elsevier Inc.**

Patterns of care study, Cervix, Radiotherapy.

INTRODUCTION

Several randomized controlled trials (RCTs) conducted in the 1990s have demonstrated that concurrent chemoradiotherapy (CCRT) reduced the mortality risk in uterine cervical cancer patients by 30%–50% compared with radiotherapy alone (1–3). Another RCT demonstrated no difference in the survival rates between definitive radiotherapy and surgery for early-stage cancer patients with Stages IB and IIA (4). Consequently, radiation therapy has become the more appropriate option in the treatment of cervical cancer. In the United States, the American Brachytherapy Society (ABS) issued the radiotherapy guidelines for uterine cervical cancer (5, 6), and in Japan, the General Rules for Clinical and Pathological Study of Uterine Cervical Cancer provide treatment guidelines, including the standard treatment schedule of radiotherapy (7). Currently, organizations such as the Gynecologic Cancer Intergroup (GCIG) are trying to set up international clinical trials of radiotherapy for uterine cervical cancer (8). Although international standardization of radiotherapy is an important issue, some between-country differences in the clinical practice of radiotherapy can be expected.

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The Patterns of Care Study (PCS) initially surveyed radiotherapy practice in the United States. The subjects of the survey were selected by the two-staged cluster sampling method (medical institutions and patients) from institutions providing radiotherapy throughout the United States. The national averages for radiotherapy practice can be demonstrated using this method (9). In the United States, PCSs have been conducted for more than 30 years, and the structure, process, and outcome of radiotherapy, as well as various problems in clinical practice, have been identified for uterine cervical cancer (10–13). In Japan, the Japanese Patterns of Care Study (JPCS) began in 1996 and used the same methods (14). We previously reported the PCS results for radiotherapy practice in uterine cervical cancer patients treated in 1992–1994 and 1995–1997 (15, 16). We report here the corresponding results for 1999–2001. We compared the data from this study with those of the preceding JPCS (1995–1997) and the U.S. PCS. The changes over the years in radiotherapy practice were examined for cervical cancer in Japan, and the differences between Japan and the United States were also examined.

METHODS AND MATERIALS

Between July 2002 and June 2004, the JPCS conducted a third national survey of patients with uterine cervical cancer treated with radiotherapy. Eligibility criteria for the survey were as follows: (*1*) carcinoma, (*2*) treated between January 1999 and December 2001, (*3*) no distant metastases, (*4*) no prior or concurrent malignancy, (*5*) no gross para-aortic lymph node metastases, and (*6*) no previous pelvic radiotherapy. Sixty-eight of 640 institutions were selected for the survey using a stratified two-staged cluster sampling method. Before the random sampling, all institutions were classified into four groups. Institutions were classified by type and number of patient treated with radiotherapy. The criteria for stratification have been detailed elsewhere (14). In brief, the JPCS stratified Japanese institutions as follows: A1, academic institutions treating ≥430 patients annually; A2, <430 patients; B1, nonacademic institutions treating ≥130 patients annually; B2, <130 patients. Academic institutions included cancer center hospitals and university hospitals. Nonacademic institutions consisted of other facilities, such as national, prefectural, municipal, and private hospitals.

The JPCS surveyors performed on-site chart review at each participating facility using an originally developed database format for uterine cervical cancer. Data collection included patient characteristics (e.g., patient's history, age, performance status, laboratory data, pathology, and stage), details of pretreatment workup, therapeutic information (e.g., radiotherapy, chemotherapy, and surgery), and treatment outcome. The JPCS collected clinical data on 631 patients with uterine cervical cancer who were treated with radiotherapy from 68 institutions. In this study, 324 patients treated by radiotherapy without planned surgery were analyzed. These included 115 patients from A1 institutions, 70 patients from A2 institutions, 104 patients from B1 institutions, and 35 patients from B2 institutions.

Statistical significance was tested using the chi-square test. Unknown and missing data were combined in the tables because these were the same in most cases: no valid data were found in the given resources (17). Ratios were calculated using unknown or missing data, but continuous variables did not include these data (17), as seen in a U.S. PCS report (18).

RESULTS

Table 1 shows the characteristics of the 324 patients in our survey. In total, 276 patients (85%) were hospitalized for treatment. Of these, 190 patients (59%) were hospitalized during both external beam radiotherapy (EBRT) and brachytherapy, 78 (24%) were hospitalized only during EBRT, and 8 (2%) only during brachytherapy.

External beam radiotherapy

External beam radiotherapy (EBRT) was performed in 320 patients (99%). Twenty-two patients (7%) received EBRT at another facility. In 142 cases (44%), multileaf collimators (MLC) were used to shape the portals. For 308 patients (96%), the planning target volume (PTV) included the whole pelvic region. The upper border of the pelvic field was at the L4 to L5 interspace in 238 of the 308 patients (77%). Only 10 patients (3%) received extended field radiotherapy including the para-aortic region. Treatment parameters of pelvic EBRT are shown in Table 2. The most frequently used beam energy was 10-14 MV X-rays. Pelvic EBRT was most often given using an opposing anteroposterior (AP-PA) technique. The median isocenter depth of the AP-PA portals was 9 cm (range, 6.5–12.9 cm). A midline block was used in 70% of the patients. A single-daily fraction dose of 1.8 or 2.0 Gy was used for most patients.

Brachytherapy

No patient surveyed received interstitial brachytherapy. Table 3 shows the details of intracavitary brachytherapy (ICBT). ICBT was applied in more than 80% of cases. The ICBT application rate by Fédération Internationale de

Table 1. Patient and tumor characteristics of 324 patients with uterine cervical cancer treated with radiotherapy.

Characteristics	No. of patients	(%)
Total no.	324	
Age (yrs)		
Range	26-100	
Median	71	
KPS		
<=70	64	20
80	103	32
90	114	35
100	21	6
Unknown/missing	22	7
Histology		
Squamous cell carcinoma	300	93
Adenocarcinoma	14	4
Adenosquamous cell carcinoma	4	1
Other	2	1
Unknown/missing	4	1
FIGO stage		
I	43	13
II	102	31
III	122	38
IVA	35	11
Unknown/missing	22	7

Table 2. Treatment parameters of pelvic external beam radiotherapy

Parameters	*n*	%
Beam energy		
Co-60	2	1
3–5 MV	30	10
6–9 MV	45	15
10–14 MV	220	71
15 MV	9	3
other	0	0
Unknown/missing	2	—
Technique		
AP-PA	269	87
Four-field box	21	7
Other	17	6
Unknown/missing	1	—
Midline block		
Yes	215	70
No	72	23
Unknown/missing	21	7
Daily fraction size (Gy)		
<1.8	25	8
1.8	135	44
1.8–2	2	1
2	137	45
>2	6	2
Missing	3	—

Gynécologie Obstétrique (FIGO) stages was 88% for Stage I, 88% for Stage II, 89% for Stage III, and 51% for Stage IVA. Its application was significantly less frequent in stage IVA patients (p <0.0001). Sixty-four patients (25%) received ICBT at another facility. Approximately 90% of the patients were treated with high-dose rate (HDR) ICBT. The most frequent radionuclide for ICBT source was cobalt-60 (Co-60), followed by iridium-192 (Ir-192). A rigid-type applicator was used for about 60% of the patients. In vivo rectal dosimetry was performed in approximately one quarter of the patients, whereas bladder dosimetry was rarely performed. ICRU 38 reference doses at the rectum and bladder were calculated in one quarter or less of the patients. Supportive medication before or during the applicator insertion was almost never given; when it was administered, it seemed to be inadequate. The dose calculation was performed for every HDR-ICBT fraction for more than three quarters of the patients. In most patients, all HDR-ICBT procedures (applicator insertion, radiograph generation and treatment) were performed in the same room.

Radiation dose and overall treatment time

Table 4 shows radiotherapy dose as a function of the FIGO stage. Total EBRT dose to the central pelvis (point A dose) significantly increased with increasing FIGO stage. Although a significant difference was also observed in total dose to the lateral pelvis (point B dose), median dose was almost the same at all stages. Median ICBT fraction size at point A was 524 cGy for HDR and 1740 cGy for LDR. The most frequent HDR-ICBT dose per fraction at point A was 500–599 Gy (79/215, 37%), followed by 600–699 cGy (48/215, 22%),

Table 3. Details of intracavitary brachytherapy

Parameters	*n*	%
ICBT given		
Yes	265	82
No	58	18
Unknown/missing	1	0
Dose rate		
HDR	215	89
LDR	27	11
HDR+LDR	0	0
Other	0	0
Unknown/missing	23	-
Source		
Co-60	112	46
Ir-192	102	42
Cs-137	21	9
Ra-226	7	3
Unknown/missing	23	-
Method of ICBT		
Tandem + vaginal applicator	202	83
Tandem only	26	11
Vaginal applicator	16	6
Unknown/missing	21	-
Applicator		
Rigid	166	63
Nonrigid	66	25
Unknown/missing	33	12
In vivo dosimetry: bladder		
Yes	8	3
No	207	78
Unknown/missing	50	19
In vivo dosimetry: rectum		
Yes	71	27
No	145	55
Unknown/missing	49	18
ICRU38: bladder		
Yes	48	18
No	146	55
Unknown/missing	71	27
ICRU38: rectum		
Yes	65	25
No	128	48
Unknown/missing	72	27
Preparation		
None	90	54
NSAIDs; orally/rectally	68	41
IV continous sedation	5	3
other	3	2
Unknown/missing	99	-
All procedures in same room*		
Yes	167	78
No	11	5
Unknown/missing	37	17
Each fraction planned*		
Yes	159	74
No	49	23
Unknown/missing	7	3

Abbreviations: HDR = high dose rate; ICBT = intracavitary brachytherapy; ICRU = International Commission on Radiation Units and Measurements; LDR = low dose rate, NSAIDs = nonsteroidal anti-inflammatory drugs.

* 215 patients treated with HDR-ICBT.

Table 4. Radiotherapy dose according to Fédération Internationale de Gynécologie Obstétrique stage

Dose (Gy)	Missing (n)	Stage I	Stage II	Stage III	Stage IVA	Total
EBRT						
Total point A dose						$p<0.001$
0–20	1	6 (18%)	5 (5%)	0	2 (6%)	13 (5%)
20–30	6	8 (24%)	19 (19%)	10 (8%)	3 (9%)	40 (14%)
30–40	3	10 (30%)	38 (38%)	65 (54%)	8 (24%)	121 (42%)
40–50	7	4 (12%)	19 (19%)	32 (27%)	7 (21%)	62 (22%)
50–60	2	5 (15%)	18 (18%)	12 (10%)	11 (34%)	46 (16%)
>60	0	0	0	1 (1%)	2 (6%)	3 (1%)
Missing	3	10	3	2	2	39
Median		30	30.6	34.9	41.1	32.4
Total point B dose						$p=0.0003$
0–20	0	2 (5%)	0	0	2 (6%)	4 (2%)
20–30	2	2 (5%)	1 (1%)	3 (3%)	2 (6%)	8 (3%)
30–40	1	3 (8%)	2 (2%)	5 (4%)	3 (9%)	13 (4%)
40–50	11	15 (38%)	35 (35%)	38 (31%)	7 (21%)	95 (32%)
50–60	5	17 (44%)	60 (60%)	72 (59%)	16 (49%)	165 (56%)
>60	0	0	2 (2%)	3 (3%)	3 (9%)	8 (3%)
Missing	3	4	4	1	2	31
Median		46.0	50.0	50.0	50.0	50.0
HDR-ICBT						
Total point A dose						$p=0.025$
0–10	0	0	2 (3%)	2 (2%)	1 (7%)	5 (2%)
10–20	3	5 (17%)	14 (18%)	34 (40%)	5 (36%)	58 (28%)
20–30	3	18 (62%)	49 (64%)	40 (47%)	6 (43%)	113 (54%)
30–40	0	2 (7%)	5 (6%)	1 (1%)	0	8 (4%)
>40	0	1 (3%)	0	0	0	1
Missing	4	3 (11%)	7 (9%)	8 (10%)	2 (14%)	24 (11%)
Median		23.1	22.0	20.0	20.0	20.3

Abbreviations: EBRT= external beam radiotherapy; HDR-ICBT= high dose rate intracavitary brachytherapy.

0–499 cGy (43/215, 20%), and 700–799 cGy (15/215, 7%). A single dose to point A over 8 Gy was applied only in two patients. The median number of HDR-ICBT insertions was 4 (range, 1–8). The median total dose of ICBT at point A was 20.3 Gy for HDR and 40.1 Gy for LDR. In cases of HDR-ICBT, total dose to point A decreased significantly with increasing stages. Median total dose of HDR-ICBT at point A was 23.1 Gy for Stage I, 22.0 Gy for Stage II, 20.0 Gy for Stage III, and 19.9 Gy for Stage IVA ($p = 0.025$). For calculation of total dose of EBRT and HDR-ICBT, biologically effective doses (BED) for tumor effect were calculated on the basis of $\alpha/\beta = 10$. The median total BED at point A was 74 Gy_{10} in cases treated with HDR-ICBT. There was no significant difference in total BED among the stages. Median total point A BED was 72 Gy_{10} for Stage I, 75 Gy_{10} for Stage II, 72 Gy_{10} for Stage III, and 77 Gy_{10} for Stage IVA ($p = 0.47$).

The median overall treatment time (OTT) was 47 days. OTT exceeded 8 weeks in 88 patients (28%).

Chemotherapy

Chemotherapy was applied in 104 patients (32%). Fifty-six patients (17%) were treated with concurrent chemoradiation (CCRT). Use of CCRT significantly varied according to FIGO stage ($p = 0.0039$). Chemotherapy was administered to 3 patients (7%) in Stage I, 12 patients (12%) in Stage II, 34 patients (28%) in Stage III, and 5 patients (14%) in Stage IVA. Neoadjuvant chemotherapy (NAC) before radiation therapy was given in 52 patients (16%).

DISCUSSION

This study describes the general patterns of radiotherapy practice for uterine cervical cancer from 1999 to 2001 in Japan. We examined the changes within Japan over the years and the differences in practice between Japan and the United States (Table 5).

External beam radiotherapy

For the radiation field (planning target volume [PTV]), almost all patients were treated with whole pelvic radiotherapy. Only a small number of patients received radiotherapy with an extended field including the para-aortic region. These results did not change over the years when comparisons were made with the previous JPCS (16). The U.S. PCS reported that only 11% of patients received extended field radiotherapy (12). Despite the positive results of the Radiation Therapy Oncology Group trial 79-20 (19), the standard PTV for EBRT in clinical practice in both Japan and the United States remained the whole pelvic region without para-aortic irradiation.

Table 5. Comparison of patterns of radiotherapy in cervical cancer patients between Japan and the United States

Parameters	Japan PCS 1995–1997*	Japan PCS 1999–2001	US PCS
External beam			
PTV			
Extended field	1%	3%	11%†
Beam energy			
Co60–9 MV	30%	26%	17%†
10–14 MV	57%	71%	19%†
15 MV≤	8%	3%	62%†
Technique			
Anteroposterior	95%	87%	19%†
Four-field box	2%	7%	80%†
Midline block			
Yes	69%	70%	6%†
Intracavitary brachytherapy			
Performed			
Yes	77%	82%	93%‡
Dose-rate			
LDR	8%	11%	78%‡
HDR	85%	89%	13%‡
Total dose to central tumor§ (median BED)	—	74 Gy_{10}	103 Gy_{10}†
Overall treatment time (median)	49 days	47 days	57 days‡

Abbreviations: BED = biologically effective dose; LDR = low dose rate; HDR = high dose rate; PTV = planning target volume.

* Recalculated % including missing values.

§ point A dose (EBRT+HDR-ICBT).

† 1992–1994.

‡ 1996–1999.

As for beam energy, use of 9 MV or less decreased, and use of 10–14 MV increased (16). In the United States, the percentage of patients receiving 15 MV was largest (9, 12). The four-field technique was applied slightly more frequently in the present JPCS than the preceding JPCS (16). However, most patients were treated with the opposing AP-PA technique. In contrast, the four-field technique was applied in 80% of the patients in the United States (12). In the present survey, median isocenter depth of the AP-PA portals was 9 cm, indicating that the body thickness of females in Japan is small. Although there are no data, the body thickness is presumed to be larger in American patients compared with Japanese patients. Therefore, after taking body thickness into account, we thought that the beam energy and method of external beam radiotherapy used in Japan is appropriate. Even in Japanese patients whose body thickness is smaller than that of American patients, multiple field radiotherapy (*e.g.*, four-field) should be selected when a low-energy beam is used.

In this survey, a midline block was used in most patients, and no change in this practice was observed over the years (16). In contrast, the midline block was rarely used in the United States (12). The widespread use of the midline block was considered the result of following schedules specified in Japanese guidelines (7). One reason for less frequent use of the midline block in the United States may be the use of the four-field technique. Mell *et al.* (20) reported use of intensity-modulated radiation therapy (IMRT) in 27% of patients with gynecologic cancer in the United States. Because the use of IMRT could increase in Japan as well, it will be necessary to reexamine the advantages of using the midline block.

Intracavitary brachytherapy

The application rate of ICBT slightly increased compared with the previous PCS (16). However, the application rate was less in Japan than in the United States (12, 13). Intracavitary brachytherapy should be applied more routinely for patients treated by definitive radiotherapy in Japan. One fourth of the patients had received ICBT at another medical institution. In contrast, the percentage of such patients was reported as 8.5% in the United States (21).

HDR was used in approximately 90% of the patients, which was almost the same rate as that of the previous JPCS (16). In the United States, this rate was lower than that of Japan: 24% according to the ABS survey (1995) (22) and 16% according to the U.S. PCS survey (1996–1999) (21). We consider that the difference in the dose rate is one of the major differences between Japan and the United States. In the present study, the ICBT sources Co-60 and Ir-192 were used in roughly the same number of cases. The use of Ir-192 increased compared with the previous JPCS (16). In the early 2000s, the Japanese Society for Therapeutic Radiology and Oncology recommended the discontinuation of Co-60 as a remote afterloading brachytherapy source in Japan. The increase in the use of Ir-192 could be the result of compliance with this recommendation. Further increase in the use of Ir-192 and decrease in the use of Co-60 are expected in the next survey.

The ABS made a number of recommendations regarding HDR-ICBT techniques (5). The present study showed that analysis of the dose to organs at risk was performed in only a small percentage of patients. The doses were more often determined by using a dosimeter than the ICRU 38 reference point calculation. Sakata *et al.* indicated that the measured rectal dose significantly correlated with the incidence of rectal complications (23). In the United States, the practice of using a dosimeter for dosimetry has been called into question. The ABS recommended the use of the ICRU 38 reference point calculation (5). Many studies showed that late rectal complications can be predicted by the calculated doses at the ICRU 38 reference points (24, 25). According to the ABS survey, rectal/bladder doses are evaluated in 80% or more of patients at U.S institutions where HDR is performed (22).

The ABS also recommends conscious sedation for HDR-ICBT applicator insertions (5). However, it was surprising to discover that many patients in both the present and previous JPCS (16) received no pretreatment for HDR-ICBT applicator insertion. Intracavitary brachytherapy plays an important role in the radiotherapy of uterine cervical cancer. Accurate insertion can hardly be achieved if patients

Table 6. Standard radiotherapy schedule for uterine cervical cancer in Japan

FIGO stage	Central pelvic dose of EBRT (Gy)	Point A dose of HDR-ICBT (Gy/fc.)	Total BED at point A (Gy_{10})
I	0	29/5	46
II small	0	29/5	46
II large	20	23/4	60
III (small-medium)	20–30	23/4	60–72
III (large)	30–40	15/3–20/4	71–78
IVA	30–50	15/3–20/4	71–83

Abbreviations: BED = biologically effective dose; EBRT = external beam radiotherapy; FIGO = Fédération Internationale de Gynécologie Obstétrique; HDR-ICBT: high dose rate intracavitary brachytherapy.

experience discomfort. Therefore, we consider that pretreatment, such as conscious sedation, should be used for HDR-ICBT applicator insertion.

The single, total dose of HDR-ICBT was lower in the present study than the previous JPCS (16). The reason is unknown, but it might be related to an increase in the use of concurrent chemoradiotherapy (CCRT), which will is discussed subsequently.

Radiation dose

Table 6 shows the radiotherapy schedules indicated in the aforementioned general rules (7) and their biologically effective doses (BED) by stages. It also shows that the dose for the cervical tumor—namely, the total dose of EBRT and HDR-ICBT (point A dose)—increases with stage progression. In this present study, BED ranged from 72 to 77 Gy_{10} among the stages, indicating that differences among the stages were small. The schedules advocate the use of the midline block starting at 0–20 Gy of EBRT for Stages I and II. However, only 20% of patients followed the rule in this present study. Many other patients received EBRT exceeding these doses without the midline block. As a result, the total dose (EBRT+HDR-ICBT) to the central pelvis in early FIGO stages was higher than estimated. In contrast, treatment of patients in Stage III and IVA followed the schedules indicated in the general rules.

It was reconfirmed that the dose to uterine cervical tumors was lower in Japan than in the United States (25–27). The biologically effective dose (BED) of the schedules recommended by the ABS is approximately 100 Gy_{10} (5). In the United States PCS, the mean value of the linear quadratic equivalent dose was 85.5 Gy for patients treated using HDR-ICBT in 1996–1999 (21). When converted to BED, this value was 103 Gy_{10}. The difference in dose between Japan and the United States may be attributed to the difference in the standard schedules recommended in each country. The issue of dose range will need to be resolved before an international collaborative study can be initiated (8). The validity of each dose needs to be evaluated by outcome analysis.

Overall treatment time

Overall treatment time (OTT) is considered an important factor that affects the outcome of radiotherapy for uterine cervical cancer (28, 29). The ABS proposed that the OTT should be limited to within 8 weeks (5). The median OTT was shorter in this study (47 days) than in the previous JPCS (16). However, the OTT exceeded 8 weeks in almost 30% of patients. More effort to avoid treatment interruption to limit OTT within 8 weeks should be made. In the United States, the median OTT was reported to be 57 days (21). This difference between Japan and the United States may be due to differences in treatment schedules. In Japan, a midline block is inserted and ICBT starts in the middle of the EBRT treatment period.

Chemotherapy

In the present study, 32% of the patients received chemotherapy, indicating an increase from the previous JPCS (16). In particular, the rate of CCRT increased from 5% to 17% (16). The increase could be due to adoption of practices shown effective by RCTs published in 1999 (1–3). In the U.S. PCS (1996–1999), the percentage of patients who received chemotherapy was reported to be 19% in 1996, 28% in 1997, and 26% in 1998. However, it dramatically increased to 63% in 1999 (13). Further increase in the use of CCRT is expected in both Japan and the United States, and the monitoring of such changes should be continued.

Whereas several RCTs revealed negative therapeutic value of neoadjuvant chemotherapy (NAC) before radiotherapy in the mid-1990s, 16% of the patients were still treated with this strategy during this surveyed period. Surprisingly, the application rate was almost the same as that reported in the 1995–1997 JPCS survey (14%) (16). The usage of this strategy should be further monitored closely as well as CCRT.

Conclusions

We describe the status of definitive radiotherapy for uterine cervical cancer in Japan from 1999 to 2001. As in the previous survey (1995–1997), the EBRT conditions, such as the beam energy and technique of EBRT, were different between Japan and the United States. However, conditions of EBRT in Japan were becoming more standardized. For ICBT, aspects of the technique, such as dosimetry of organs at risk and supportive medication (*i.e.*, conscious sedation), can be improved. The total BED (EBRT + HDR-ICBT) delivered to the primary lesion in Japan was approximately 70% of that in the United States. The median OTT in Japan was approximately 80% of that in the United States. Compared with the previous JPCS, our study found that the use of CCRT has increased. This increase is considered to be due to the adoption of practices shown effective by RCT results published in 1999.

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CLINICAL INVESTIGATION **Radiation Oncology Practice**

JAPANESE STRUCTURE SURVEY OF RADIATION ONCOLOGY IN 2005 BASED ON INSTITUTIONAL STRATIFICATION OF PATTERNS OF CARE STUDY

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Purpose: To evaluate the structure of radiation oncology in Japan in terms of equipment, personnel, patient load, and geographic distribution to identify and improve any deficiencies.

Methods and Materials: A questionnaire-based national structure survey was conducted between March 2006 and February 2007 by the Japanese Society of Therapeutic Radiology and Oncology. These data were analyzed in terms of the institutional stratification of the Patterns of Care Study.

Results: The total numbers of new cancer patients and total cancer patients (new and repeat) treated with radiotherapy in 2005 were estimated at approximately 162,000 and 198,000, respectively. In actual use were 765 linear accelerators, 11 telecobalt machines, 48 GammaKnife machines, 64 ^{60}Co remote-controlled after-loading systems, and 119 ^{192}Ir remote-controlled after-loading systems. The linear accelerator systems used dual-energy function in 498 systems (65%), three-dimensional conformal radiotherapy in 462 (60%), and intensity-modulated radiotherapy in 170 (22%). There were 426 Japanese Society of Therapeutic Radiology and Oncology-certified radiation oncologists, 774 full-time equivalent radiation oncologists, 117 medical physicists, and 1,635 radiation therapists. Geographically, a significant variation was found in the use of radiotherapy, from 0.9 to 2.1 patients/1,000 population. The annual patient load/FTE radiation oncologist was 247, exceeding the Blue Book guidelines level. Patterns of Care Study stratification can clearly discriminate the maturity of structures according to their academic nature and caseload.

Conclusions: The Japanese structure has clearly improved during the past 15 years in terms of equipment and its use, although the shortage of manpower and variations in maturity disclosed by this Patterns of Care Study stratification remain problematic. These constitute the targets for nationwide improvement in quality assurance and quality control. © **2008 Elsevier Inc.**

Structure survey, Radiotherapy facility, Radiotherapy personnel, Radiotherapy equipment, Caseload.

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INTRODUCTION

The medical care systems of the United States and Japan have very different backgrounds. In 1990, the Patterns of Care Study (PCS) conducted a survey of the 1989 structure of radiation oncology facilities for the entire census of facilities in the United States. The results of the survey, together with trends in the structure of specialization since 1974, were reported in detail by Owen *et al.* (1). In 1991, the Japanese Society of Therapeutic Radiation Oncology (JASTRO) conducted the first national survey of the structure of radiotherapy (RT) facilities in Japan based on their status in 1990, with the results reported by Tsunemoto (2). The first comparison of these two national structure surveys to illustrate the similarities and differences present in 1989–1990 was conducted by Teshima *et al.* (3) and reported in 1995. The resultant international exchange of information proved valuable for both countries, because each could improve their own structure of radiation oncology using those data.

The Japanese structure of radiation oncology has improved in terms of the greater number of cancer patients who are treated with RT, as well as the public awareness of the importance of RT, although problems still exist that should be solved. The JASTRO has conducted national structure surveys every 2 years since 1990 (4). In Japan, an anticancer law was enacted in 2006 in response to patients' urgent petitions to the government. This law strongly advocates the promotion of RT and increasing the number of radiation oncologists (ROs) and medical physicists. The findings of the international comparisons and the consecutive structural data gathered and published by the JASTRO have been useful in convincing the Japanese bureaucracy of the importance of RT. In this report, the recent structure of radiation oncology in Japan is presented, with reference to data obtained from previous international comparisons.

METHODS AND MATERIALS

Between March 2006 and February 2007, the JASTRO conducted a questionnaire using a national structure survey of radiation oncology in 2005. The questionnaire included the number of treatment machines by type, number of personnel by category, and number of patients by type, site, and treatment modality. For variables measured over a period, data were requested for the calendar year 2005. The response rate was 712 (96.9%) of 735 of active facilities. The data from 511 institutions (69.5%) were registered in the International Directory of Radiotherapy Centres in Vienna, Austria in April 2007.

The PCS was introduced in Japan in 1996 (5–11). The PCS in the United States used structural stratification to analyze the national averages for the data in each survey item using two-stage cluster sampling. The Japanese PCS used similar methods. We stratified the RT facilities nationwide into four categories for the regular structure surveys. This stratification was based on academic conditions and the annual number of patients treated with RT in each institution, because the academic institutions require, and have access to, more resources for education and training and the annual caseload also constitutes essential information related to structure. For the present study, the following institutional stratification was used: A1, university hospitals/cancer centers treating ≥440 patients/y; A2, the same type of institutions treating ≤439 patients/y; B1, other national/public hospitals treating ≥130 patients/y; and B2, other national hospital/public hospitals treating ≤129 patients/y.

The Statistical Analysis Systems, version 8.02 (SAS Institute, Cary, NC), software program (12) was used for statistical analyses, and statistical significance was tested using the chi-square test, Student *t* test, or analysis of variance.

RESULTS

Current situation of radiation oncology in Japan

Table 1 shows that the numbers of new patients and total patients (new plus repeat) requiring RT in 2005 were estimated at approximately 162,000 and 198,000, respectively. According to the PCS stratification of institutions, almost 40% of the patients were treated at academic institutions (categories A1 and A2), even though these academic institutions constituted only 18% of the 732 RT facilities nationwide.

The cancer incidence in Japan in 2005 was estimated at 660,578 (13) with approximately 25% of all newly diagnosed patients treated with RT. The number has increased steadily during the past 10 years and is predicted to increase further (4).

Facility and equipment patterns

Table 2 lists the RT equipment and related function. In actual use were 767 linear accelerators, 11 telecobalt machines, 48 Gamma Knife machines, 65 ^{60}Co remote-controlled afterloading systems (RALSs), and 119 ^{192}Ir RALSs. The linear accelerator system used dual-energy function in 498 systems

Table 1. PCS stratification of radiotherapy facilities in Japan

Institution Category	Description	Facilities (*n*)	New patients (*n*)	Average new patients/facility* (*n*)	Total patients (new + repeat) (*n*)	Average total patients/facility* (*n*)
A1	UH and CC (≥440 patients/y)	66	45,866	694.9	54,885	831.6
A2	UH and CC (<440 patients/y)	67	17,161	256.1	21,415	319.6
B1	Other (≥130 patients/y)	290	71,627	247.0	88,757	306.1
B2	Other (<130 patients/y)	289	21,664	75.0	26,116	90.4
Total		712	156,318†	219.5	191,173†	268.5

Abbreviations: PCS = Patterns of Care Study; UH = university hospital; CC = cancer center hospital; Other = other national, city, or public hospital.

* $p < 0.0001$.

† Number of radiotherapy institutions was 735 in 2005, and number of new patients was estimated at approximately 162,000; corresponding number of total patients (new plus repeat) was 198, 000.

Table 2. Equipment, its function and patient load per equipment by PCS institutional stratification

RT equipment and function	A1 (n = 66)		A2 (n = 67)		B1 (n = 290)		B2 (n = 289)			Total (n = 712)	
	n	%	n	%	n	%	n	%	p	n	%
Linear accelerator	133		85		283		264		—	765	
With dual energy function	97	72.9*	62	72.9*	197	69.6*	142	53.8*	<0.0001	498	65.1*
With 3D-CRT function (MLC width ≤1.0 cm)	109	82.0*	59	69.4*	176	62.2*	118	44.7*	<0.0001	462	60.4*
With IMRT function	65	48.9*	25	29.4*	55	19.4*	25	9.5*	<0.0001	170	22.2*
Annual patients/linear accelerator	412.7†		243.8†		279.9†		93.4†		<0.0001	234.6†	
Particle	5		0		1		1		—	7	
Tomotherapy	0		0		0		1		—	1	
Microtron	8		3		9		4		—	24	
Telecobalt (actual use)	7 (5)		6 (1)		7 (1)		14 (4)		—	34 (11)	
Gamma Knife	6		3		32		7		0.0004	48	
^{60}Co RALS (actual use)	8 (8)	12.1‡ (12.1)	13 (12)	19.4‡ (17.9)	41 (36)	14.1‡ (12.4)	12 (8)	4.2‡ (2.8)	<0.0001	74 (64)	10.4‡ (9.0)
^{192}Ir RALS (actual use)	53 (52)	80.3‡ (78.8)	27 (24)	38.8‡ (34.3)	35 (35)	12.1‡ (12.1)	8 (8)	2.8‡ (2.8)	<0.0001	123 (119)	17.1‡ (16.6)
^{137}Cs RALS (actual use)	0 (0)		0 (0)		2 (2)		0 (0)		—	2 (2)	

Abbreviations: PCS = Patterns of Care Study; RT = radiotherapy; 3D-CRT = three-dimensional conformal radiotherapy; MLC = multileaf collimator; IMRT = intensity-modulated radiotherapy; RALS = remote-controlled after-loading system.

* Percentage calculated from number of systems using this function and total number of linear accelerator systems.

† Percentage calculated from number patients and number of institutions with linear accelerators; institutions without linear accelerators excluded from calculation.

‡ Percentage of institutions that have this equipment (≥2 pieces of equipment per institution).

(65%), three-dimensional conformal RT in 462 (60%), and intensity-modulated RT (IMRT) in 170 (22%). These functions were installed more frequently in the equipment of academic institutions than in that of nonacademic institutions ($p < 0.0001$). The annual numbers of patients/linear accelerator were 413 for A1, 244 for A2, 280 for B1, and 93 for B2 institutions. The number of institutions with telecobalt machines in actual use showed a major decrease to 11. The Gamma-Knife machine was installed more frequently in B1 institutions. A significant replacement of ^{60}Co RALS by ^{192}Ir RALS was observed, especially in academic institutions. We had seven particle machines, three with carbon beam and five with proton beam RT. The total number of patients treated at the seven institutions was estimated at approximately 1,600 (1% of all new patients in Japan). Eleven advanced institutions were included in the A1 category and treated >800 patients annually. They were equipped with linear accelerators with dual-energy function (71% of the institutions), three-dimensional conformal RT function (89%) and IMRT function (70%), as well as with ^{192}Ir-RALS (90%) and a computed tomography (CT) simulator (100%).

Table 3 lists the RT planning and other equipment. X-ray simulators were installed in 70% of all institutions, and CT simulators in 55%. A significant difference was found in the rate of CT simulator installation by institutional stratification, from 91% in A1 to 45% in B2 institutions ($p < 0.0001$). Only a very few institutions used magnetic resonance imaging for RT, although computer use for RT recording was pervasive.

Staffing patterns and patient loads

Table 4 lists the staffing patterns and patients loads by institutional stratification. The total number of full-time equivalent (FTE) ROs in Japan was 774. The average number of FTE ROs was 4.41 for A1, 1.43 for A2, 0.89 for B1, and 0.45 for B2 institutions ($p < 0.0001$). The patient load/FTE RO in Japan was 247, and the number for A1, A2, B1, and B2 institutions was 189, 224, 343, and 202, respectively ($p < 0.0001$), with the patient load for B1 institutions by far the greatest. In Japan, 40% of the institutions providing RT had their own designated beds, and ROs must also take care of their inpatients. The percentage of distribution of institutions by patient load/FTE RO is shown in Fig. 1 and indicates that the largest number of facilities featured a patient/FTE staff level of 101–150, with 151–200 the second largest number. More than 60% of the institutions (438 of 712) had <1 FTE RO, as shown by the gray areas of the bars.

A similar trend for radiation technologists and their patient load by stratification of institutions was observed ($p < 0.0001$). The percentage of distribution of institutions by patient load/radiation technologist is also shown in Fig. 2. The largest number of facilities had a patient/RT technologist level in the 81–100 range, with 101–120 the second largest number. There were 117 full-time (and 30 part-time) medical physicists and 257 full-time (and 13 part-time) RT quality assurance staff. In this survey, duplication reporting of these personnel numbers could not be checked because of a lack of

Table 3. Radiotherapy planning and other equipments by PCS institutional stratification

RT planning and other equipment	A1 ($n = 66$)		A2 ($n = 67$)		B1 ($n = 290$)		B2 ($n = 289$)			Total ($n = 712$)	
	n	%	n	%	n	%	n	%	p	n	%
X-ray stimulator	58	84.8*	53	76.1*	201	68.6*	190	65.7*	0.0130	502	69.7*
CT stimulator	66	90.9*	48	68.7*	163	54.8*	130	44.6*	<0.0001	407	55.3*
RTP computer (≥2)	209 (190)	100* (71.2)	114 (82)	94.0* (46.3)	336 (101)	95.9 (14.8)	281 (50)	88.6* (8.7)	0.0005 (<0.0001)	940 (146)	93.1* (20.5)
MRI (≥2)	164 (153)	95.5* (78.8)	134 (124)	94.0* (79.1)	470 (351)	96.9 (55.9)	344 (148)	92.4* (24.6)	0.1136 (<0.0001)	1,112 (338)	94.7* (47.5)
For RT only	3	3.0*	1	1.5*	5	1.7*	3	0.7*		12	1.4*
Computer use for RT recording	63	95.5*	62	92.5*	263	90.7*	238	82.4*	0.0015	626	87.9*

Abbreviations: CT = computed tomography; RTP = radiotherapy planning; MRI = magnetic resonance imaging; other abbreviations as in Table 2.
* Percentage of institutions that have equipment (≥2 pieces of equipment per institution).

individual identification on staffing data. Finally, there were 907 nurses and clerks.

Distributions of primary sites, specific treatment and palliative treatment

Table 5 lists the distribution of primary sites by institutional stratification. The most common disease site was the breast, followed by lung/bronchus/mediastinum and genitourinary. In Japan, the number of patients with prostate cancer undergoing RT was approximately 13,200 in 2005, but the number has been increasing most rapidly. The stratification of institutions indicated that more patients with lung cancer were treated at the nonacademic institutions (B1 and B2), and more patients with head-and-neck cancer were treated at academic institutions (A1 and A2; $p < 0.0001$).

Table 6 lists the distribution of use of specific treatment and the number of patients treated with these modalities by the PCS stratification of institutions. Brachytherapy, such as intracavitary RT, interstitial RT, and radioactive iodine therapy, for prostate cancer was used more frequently in academic institutions than in nonacademic institutions ($p < 0.0001$). Similar trends were observed for other specific treatments such as total body RT, intraoperative RT, stereotactic brain RT, stereotactic body RT, IMRT, thermoradiotherapy, and RT of the pterygium by ^{90}Sr. In 2005, 4.6% of patients ($n = 755$) were treated with IMRT at 33 institutions. This percentage was significantly lower than that of institutions using linear accelerators with IMRT function (22%; Table 2).

Table 7 lists the number of patients with any type of brain metastasis or bone metastasis treated with RT according to the same institutional stratification. B1 institutions treated more patients with brain metastasis (11% of all patients) than other types of institutions ($p < 0.0001$), and the use of RT for bone metastasis ranged from 11% for A1 to 19% for B2 ($p < 0.0001$). Overall, more patients were treated with RT at nonacademic type B2 institutions than at A1 or A2 institutions.

Geographic patterns

Figure 3 shows the geographic distributions of the annual number of patients (new plus repeat) per 1,000 population by 47 prefectures arranged in order of increasing number of JASTRO-certified physicians per 1,000,000 population (14). Significant differences were found in the use of RT, from 0.9 patients/1,000 population (Saitama and Okinawa) to 2.1 (Hokkaido). The average number of patients/1,000 population per quarter ranged from 1.37 to 1.57 ($p = 0.2796$). A tendency was found for a greater number of JASTRO-certified physicians to be accompanied by an increased use of RT for cancer patients, although the correlation was not statistically significant. The use rate of RT in a given prefecture was not necessarily related to its population density in 2005, just as we observed in the 1990 data (3).

DISCUSSION

In 1990, fewer facilities for RT were available and fewer patients were treated with RT in Japan than in the United States. However, the numbers for Japan improved