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CLINICAL INVESTIGATION **Pancreas**

PATTERNS OF RADIOTHERAPY PRACTICE FOR PANCREATIC CANCER IN JAPAN: RESULTS OF THE JAPANESE RADIATION ONCOLOGY STUDY GROUP (JROSG) SURVEY

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Purpose: To determine the patterns of radiotherapy practice for pancreatic cancer in Japan.
Methods and Materials: A questionnaire-based national survey of radiotherapy for pancreatic cancer treated between 2000 and 2006 was conducted by the Japanese Radiation Oncology Study Group (JROSG). Detailed information on 870 patients from 34 radiation oncology institutions was accumulated.
Results: The median age of all patients was 64 years (range, 36–88), and 80.2% of the patients had good performance status. More than 85% of patients had clinical Stage T3-T4 disease, and 68.9% of patients had unresectable disease at diagnosis. Concerning radiotherapy (RT), 49.8% of patients were treated with radical external beam RT (EBRT) (median dose, 50.4 Gy), 44.4% of patients were treated with intraoperative RT (median dose, 25 Gy) with or without EBRT (median dose, 45 Gy), and 5.9% of patients were treated with postoperative radiotherapy (median dose, 50 Gy). The treatment field consisted of the primary tumor (bed) only in 55.6% of the patients. Computed tomography-based treatment planning and conformal RT was used in 93.1% and 83.1% of the patients treated with EBRT, respectively. Chemotherapy was used for 691 patients (79.4%; before RT for 66 patients; during RT for 531; and after RT for 364). Gemcitabine was the most frequently used drug, followed by 5-fluorouracil.
Conclusion: This study describes the general patterns of RT practice for pancreatic cancer in Japan. Most patients had advanced unresectable disease, and radical EBRT, as well as intraoperative RT with or without EBRT, was frequently used. Chemotherapy with gemcitabine was commonly used in conjunction with RT during the survey period. © 2010 Elsevier Inc.

Radiotherapy, pancreatic neoplasm, patterns of radiotherapy, chemotherapy.

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INTRODUCTION

Pancreatic cancer is one of the leading causes of cancer death worldwide. The prognosis of patients with this disease remains extremely poor, with a 5-year survival rate after diagnosis of <5% (1, 2). Most patients present with locally advanced or metastatic disease. The median life expectancy is 3–6 months for those with metastatic disease and 6–10 months for those with nonmetastatic disease (3, 4).

In Japan, the number of patients with pancreatic cancer has been rapidly increasing,, and the number of yearly pancreatic cancer deaths in Japan has increased from approximately 2,000 in 1960 to 20,000 in 2000 (5). Moreover, radiotherapy (RT) has become much more common because a significant number of new methods, as well as technology, for treatment planning has become available (6, 7). Therefore, the optimal management of RT for pancreatic cancer patients has become a major concern in Japan.

Patterns of care studies, initially developed in the United States in the mid-1970s, represent a reliable retrospective study design for establishing the national practice for cancer patients during a specific study period (8–10). A patterns of care study was designed as a national survey to document and analyze the current practice characteristics for cancers in the radiation oncology department. The results of the study could aid in improving healthcare for cancer patients and could also provide data that will allow comparison with other countries. Although several reports have been published on the patterns of RT in Japan for lung, breast, and prostate cancer (11–13), scant information is available on the patterns of RT for pancreatic cancer.

In the present study, the Japanese Radiation Oncology Study Group (JROSG) conducted a nationwide survey of the patterns of RT practice for pancreatic cancer. This study was intended to evaluate the patterns of RT for pancreatic cancer in Japanese radiation oncology centers. To our knowledge, this is the first report to establish how RT is used nationally to treat pancreatic cancer in Japan.

METHODS AND MATERIALS

Between 2008 and 2009, the JROSG conducted a national survey of RT for pancreatic cancer treated between 2000 and 2006 using a questionnaire that requested detailed information regarding patient and treatment characteristics. The following eligibility criteria were used in this survey. The patients were required to have been diagnosed with pancreatic cancer without evidence of distant metastasis; they must have been treated with RT between 2000 and 2006; and they must not have been diagnosed with any other malignancy or have been previously undergone RT. Patients without pathologic verification were diagnosed as having pancreatic cancer according to the clinical and radiographic findings. The clinical findings included serum carbohydrate antigen 19-9 measurements. The radiographic findings included contrast-enhanced computed tomography (CT), ultrasonography, endoscopic ultrasonography, and endoscopic retrograde/magnetic resonance cholangiopancreatography. Of 71 radiation oncology centers in Japan belonging to the JROSG, 34 (48%) agreed to participate in our survey. The other radiation oncology centers did not agree to participate in the present study mostly because too few pancreatic cancer patients were treated with RT between 2000 and 2006. Each center agreeing to participate in the present study provided a database of the patients with pancreatic cancer treated with RT between 2000 and 2006. The study was performed according to the guidelines approved by the institutional review board of each institution whenever necessary.

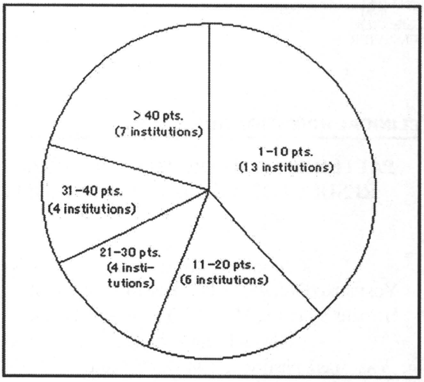

Fig. 1. Distribution of institutions according to number of patients treated between 2000 and 2006. Variations concerning number of patients among institutions.

Statistical analysis was performed using the Statistical Package for Social Sciences, version 11.0 (SPSS, Chicago, IL). The chi-square test and Student's t test were used to investigate the relationship between variables. A probability level of .05 was chosen for statistical significance.

RESULTS

Data registration

Detailed information on 870 patients from 34 radiation oncology institutions (median, 15.5 patients/institution) was accumulated. Figure 1 shows the distribution of the number of institutions according to the number of patients treated during the 7-year period. Variations concerning the number of patients treated during the period were found among the institutions. For example, in 13 (38.2%) of the 34 institutions, 1–10 patients were treated during the 7 years, and in 7 (20.6%), >40 patients were treated during the 7-year period.

Patient and disease characteristics

The patient and disease characteristics of all 870 patients are listed in Table 1. The median patient age was 64 years (range, 36–88), and 42.5% of patients were women. The pretherapeutic evaluations included CT, ultrasonography, and endoscopic retrograde/magnetic resonance cholangiopancreatography for 96.2%, 98.2%, and 61.4% of the patients, respectively. More than 80% of the patients had an Eastern Cooperative Oncology Group performance status of 0-1. Of the 870 patients, 85.2% had Stage T3-T4 disease and 68.9% had unresectable disease. The median maximal tumor

Table 1. Patient and disease characteristics (n = 870)

Characteristic	Patients (n)
Age (median, 64 y)	
<70 y	626 (72.0)
≥70 y	244 (28.0)
Gender	
Female	370 (42.5)
Male	500 (57.5)
Pathologic type verified	
Yes, adenocarcinoma	659 (75.7)
Yes, other	15 (1.8)
No	196 (22.5)
Ultrasonography (before RT)	
Yes	837 (96.2)
No	13 (1.5)
Unknown	20 (2.3)
CT (before RT)	
Yes	854 (98.2)
No	14 (1.6)
Unknown	2 (0.2)
ERCP/MRCP (before RT)	
Yes	534 (61.4)
No	155 (17.8)
Unknown	181 (20.8)
Primary site	
Head	554 (63.7)
Body	277 (31.8)
Tail	33 (3.8)
Unknown	6 (0.7)
Maximal tumor size (median, 4.0 cm)	
<4.0 cm	386 (44.4)
≥4.0 cm	409 (47.0)
Unknown	75 (8.6)
ECOG performance status	
0	166 (19.1)
1	532 (61.1)
2	115 (13.2)
3	10 (1.1)
4	1 (0.2)
Unknown	46 (5.3)
Jaundice	
Yes	276 (31.7)
No	521 (59.9)
Unknown	73 (8.4)
CA19-9 (median, 240 U/mL)	
<1,000 U/mL	565 (64.9)
≥1,000 U/mL	206 (23.7)
Unknown	99 (11.4)
Alcohol consumption	
Yes	253 (29.1)
No	304 (34.9)
Unknown	313 (36.0)
Smoking	
Yes	306 (35.2)
No	314 (36.1)
Unknown	250 (28.7)
Diabetes mellitus	
Yes	237 (27.2)
No	483 (55.6)
Unknown	150 (17.2)
Clinical T stage (UICC 2002)	
Tis	2 (0.2)
T1	30 (3.4)
T2	95 (10.9)
T3	252 (29.0)
T4	488 (56.2)
	(*Continued*)

Table 1. Patient and disease characteristics (n = 870) (*Continued*)

Characteristic	Patients (n)
Unknown	3 (0.3)
Clinical N stage (UICC 2002)	
N0	453 (52.1)
N1	373 (42.9)
Unknown	44 (5.0)
Resectable at diagnosis	
Yes	268 (30.8)
No	599 (68.9)
Unknown	3 (0.3)

Abbreviations: RT = radiotherapy; CT = computed tomography; ERCP/MRCP = endoscopic retrograde cholangiopancreatography/magnetic retrograde cholangiopancreatography; ECOG = Eastern Cooperative Oncology Group; CA19-9 = carbohydrate antigen 19-9; UICC = International Union Against Cancer.

Data in parentheses are percentages.

size was 4.0 cm (range, 0.9–11.0), and the median serum concentration of carbohydrate antigen 19-9 was 240 U/mL. Approximately 30% of patients each drank, smoked, or had diabetes mellitus.

Treatment characteristics

The treatment characteristics for all 870 patients are listed in Table 2. Approximately 20% of the patients were treated with an investigational protocol. The treatment modality used was radical external beam RT (EBRT) for 49.8% of patients (33 of 34 institutions), intraoperative RT (IORT) with or without EBRT for 44.3% of patients (10 of 34 institutions), and postoperative RT (PORT) for 5.9% of patients (14 of 34 institutions). IORT was administered using a 6–18-MeV electron beam. The treatment field consisted of the primary tumor only in 484 (55.6%) of 870 patients and the primary tumor plus regional lymph nodes in 386 (44.4%. CT-based treatment planning and conformal RT was used in >90% and >80% of patients treated with external beam RT, respectively. Chemotherapy was administered to approximately 80% of patients.

Total radiation dose and radiation field

The total radiation dose was analyzed according to the treatment modality. The median dose of the EBRT group, IORT with or without EBRT group, and PORT group was 50.4 Gy (range, 6–60.8), 25 Gy (range, 12–30; IORT) with or without 45 Gy (range, 6–50; EBRT), and 50 Gy (range, 12–60), respectively. For the EBRT group, most of the patients were treated with a total dose of 50–54.9 Gy (Fig. 2). For the PORT group, most of the patients were treated with a total dose of 50–54.9 Gy (Fig. 3). Moreover, the total radiation doses of the EBRT and PORT groups were not significantly different (p = .40). Therefore, almost uniform total doses were used for the EBRT and PORT groups. The median total dose for patients with negative surgical margins and those with positive surgical margins in the PORT group was 50 Gy (range, 12–56) and 50 Gy (range, 39.6–60), respectively (p = .29). However, for the IORT with or without

Table 2. Treatment characteristics (n = 870)

Characteristic	Patients/total (*n*)
Investigational protocol	
Yes	181/870 (20.8)
No	689/870 (79.2)
Treatment modality	
Radical EBRT	434/870 (49.8)
IORT with or without EBRT	385/870 (44.3)
With EBRT	184
Without EBRT	201
PORT	51/870 (5.9)
Radiation field	
Primary only	484/870 (55.6)
Primary plus regional lymph nodes	386/870 (44.4)
Radiation portals	
2 portals	43/669 (6.4)
≥3 portals	626/669 (93.6)
EBRT beam energy (MV)	
<10	39/669 (5.8)
≥10	630/669 (94.2)
EBRT dose/fraction (Gy)	
<1.8	3/669 (4.5)
1.8	266/669 (39.8)
2.0	338/669 (50.5)
>2.0	62/669 (5.2)
EBRT total radiation dose (Gy)	
<40	84/669 (12.6)
≥40	585/669 (87.4)
CT-based treatment planning	
Yes	616/669 (92.1)
No	53/669 (7.9)
Conformal therapy	
Yes	545/669 (81.5)
No	124/669 (18.5)
IORT dose (Gy)	
<25	104/385 (27.0)
≥25	281/385 (73.0)
Chemotherapy	
Yes	691/870 (79.4)
No	179/870 (20.6)

Abbreviations: EBRT = external beam radiotherapy; IORT = intraoperative radiotherapy; PORT = postoperative radiotherapy.
Data in parentheses are percentages.

EBRT group, significant variations in the IORT and EBRT doses were found. For IORT, the dose was 20–35 Gy (Fig. 4a). For EBRT, 79 (42.9%) of 184 patients were treated with EBRT with a dose of 50–54.9 Gy, and 83 (45.1%) received EBRT with a dose of <45 Gy (Fig. 4b). Significant differences were found in the total dose between the EBRT group and the IORT with or without EBRT group (p <.0001) and between the PORT group and the IORT with or without EBRT group (p <.0001).

Table 3 lists the radiation field according to the treatment modality and clinical N stage. Approximately 45% of patients received RT to the primary tumor (bed) only, irrespective of the treatment modality. The radiation field of the patients with Stage N0 was more frequently the primary tumor (bed) only, and for those with Stage N1, it was more frequently the primary tumor (bed) plus the regional lymph nodes. However, some patients with clinical Stage N1 also underwent RT to the primary tumor (bed) only.

Chemotherapy

Chemotherapy was used in combination with RT for 691 patients (79%). Table 4 lists the drugs and timing of chemotherapy for 691 patients treated with chemotherapy. Of the 691 patients, 66 (9.6%) were treated with chemotherapy before RT, 531 (76.8%) during RT, and 364 (52.7%) after RT. Gemcitabine was the most frequently used drug (n = 515, 74.5%), followed by 5-fluorouracil (5-FU) (n = 211, 30.5%), cisplatin (n = 72, 10.4%), a combination of tegafur, 5-chloro-2,4-dihydroxypyridine, and oteracil potassium (TS-1; n = 60, 8.7%), tegafur/uracil (UFT; n = 3, 4.5%), and others (n = 9, 1.3%).

DISCUSSION

Although the results of nationwide surveys of surgical management of pancreatic cancer have been reported (14–18), little information is available regarding the nationwide patterns of RT practice for pancreatic cancer. The National Cancer Database reports and the Surveillance, Epidemiology, and End Results registry have provide data on the proportions of patients treated with RT, but detailed information on RT use has not been described (19, 20). In the present study, we have reported in detail on the patterns of RT practice for pancreatic cancer in Japan between 2000 and 2006. From national surveys of structural characteristics of radiation oncology in Japan, approximately 700 radiation oncology centers were in Japan during the survey period (6, 7). In the present study, although only 34 radiation oncology centers in Japan participated and the patients were not randomly selected, we believe these results, at least roughly, represent the national averages in Japan of the patterns of RT for pancreatic cancer.

Concerning the patient characteristics, our results indicated that >80% of Japanese patients treated with RT had advanced disease, with approximately 70% of patients presenting with unresectable disease, in accordance with previous reports that approximately 80% of patients present with unresectable disease (16, 21). Our results also indicated that the patient performance status was generally good and that >80% of patients were <70 years old. These results indicate that although most of the patients referred for RT had advanced disease, many patients appeared to be good candidates for intensive treatment. In the present study, approximately 30% of patients each were alcohol drinkers, smokers, or had diabetes mellitus. In the United States, 60–81% of patients with pancreatic cancer had diabetes mellitus (22). However, it is not known whether these differences between patients living in Japan and in the United States resulted from differences in access to medical care or biologic differences within the tumors themselves. Additional investigation of the different disease characteristics of the patients in the two countries would be informative.

The present study also showed the treatment characteristics for pancreatic cancer in Japan. No definite treatment guidelines are available for radical and adjuvant RT for pancreatic cancer. Therefore, the National Comprehensive

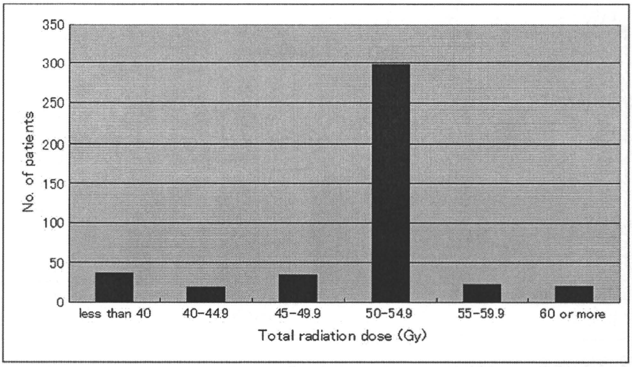

Fig. 2. Distribution of patients treated with radical external beam radiotherapy (EBRT) according to total radiation dose.

Cancer Network (NCCN) panel has recommended that investigational options should be considered for all stages of disease management (23). In the present study, 20.8% of patients were treated with an investigational protocol. Because many patients have relatively good performance status and are relatively young, investigational protocols should be encouraged for a greater number of patients.

With regard to the treatment modality, not only radical EBRT, but also IORT with or without EBRT, was used frequently in Japan. This high rate of IORT using an electron beam might be a unique characteristic of treatment in Japan, although not many institutions (10 of 34 institutions) had instituted IORT. Routine use of IORT combined with EBRT and/or chemotherapy began in Japanese hospitals in the 1980s (24, 25). The results of the present study have indicated that IORT combined with EBRT has continued to be commonly used into the 21st century. IORT is a specialized RT technique that can increase the radiation dose to the primary tumor volume and has been used to improve local tumor control without increasing normal tissue morbidity. A lower incidence of local failure in most series and improved median survival in some patients have been reported with these techniques when combined with conventional EBRT; however, it is uncertain whether this resulted from superior treatment or case selection (4, 26). Therefore, additional prospective studies are needed to assess the efficacy of IORT.

The results of the present study have indicated that CT-based treatment planning and conformal RT were used for >90% and >80% of patients, respectively. The NCCN guidelines strongly recommend the use of CT-based treatment planning and three-dimensional treatment planning (23). From national surveys of the structural characteristics of

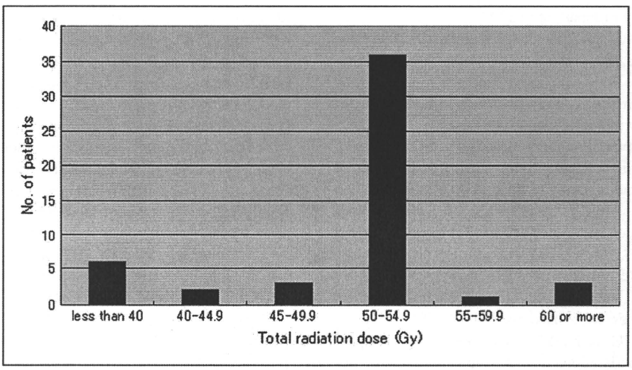

Fig. 3. Distribution of patients treated with postoperative radiotherapy (PORT) according to total radiation dose.

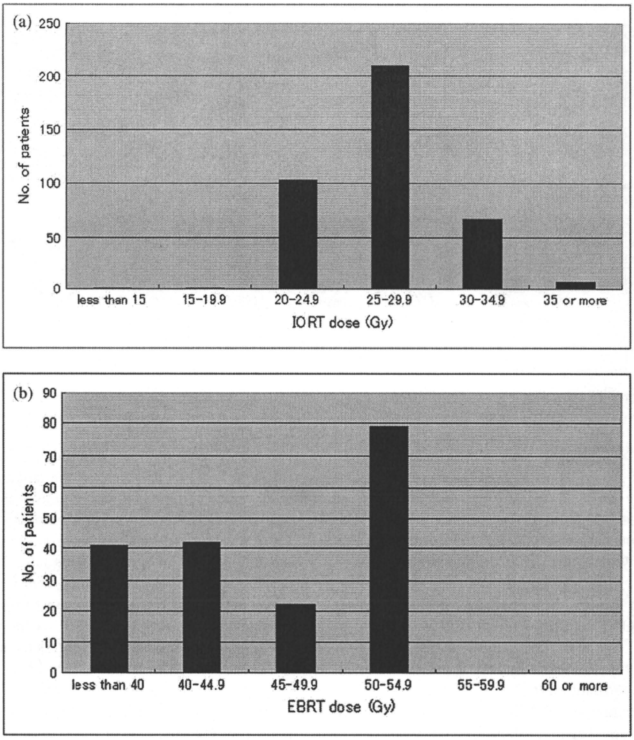

Fig. 4. Distribution of patients treated with (a) intraoperative radiotherapy (IORT) and (b) those treated with IORT plus external beam radiotherapy (EBRT) according to total radiation dose.

radiation oncology in Japan, only 329 (45.3%) of 726 facilities in 2003 and 407 (57.2%) of 712 facilities in 2005 have used CT-based treatment planning (6, 7). These results suggest that patients with pancreatic cancer have undergone RT more often in the facilities with advanced equipment than in facilities without advanced equipment.

Although the optimal radiation dose has yet to be defined, the NCCN guidelines have recommended that for primary definitive chemoradiotherapy, a dose of 50–60 Gy (1.8–2.0 Gy/d) should be administered (23). The NCCN guidelines have also recommended that PORT should be administered at a dose of 45–54 Gy (1.8–2.0 Gy/d). In the present study, most patients were treated with a total dose of 50–54.9 Gy in both the EBRT and the PORT groups. Therefore, almost uniform total doses were used for the EBRT and PORT groups, and the NCCN guideline recommendations appear to have been properly adopted by the Japanese radiation oncology centers. In contrast, for the IORT with or without EBRT group, significant variations in the total doses of IORT and EBRT were found. Concerning IORT, almost all patients were treated with a total dose of 20–35 Gy, and for EBRT, many patients were treated with a total dose of ≤50–54.9 Gy; however, a total dose <45 Gy was also given to some patients. From the previous reports of IORT for pancreatic cancer, the doses have varied among institutions from 10 to 30 Gy (24, 25). These results indicate that the optimal doses of IORT and EBRT have yet to be determined. Additional studies are required to determine the optimal doses when IORT is used.

Concerning the radiation field, our results have indicated that for approximately 45% of patients, the primary tumor (bed) only was treated with RT, irrespective of the treatment modality. Also, for each group analyzed, patients with clinical Stage N0 were more likely to receive treatment covering the primary tumor (bed) only, although some patients with clinical Stage N1 were also treated with the radiation field

Table 3. Radiation field according to treatment modality and clinical N stage

Group	Patients (n)	Radiation field: PT only	Radiation field: PT plus LNs	p
Radical EBRT				<.0001
Total	434	208 (47.9)	226 (52.1)	
N0	263	171	92	
N1	167	33	134	
Unknown	4	4	0	
IORT				<.0001
Total	385	152 (39.5)	233 (60.5)	
N0	162	111	52	
N1	184	36	147	
Unknown	39	5	34	
PORT				.002
Total	51	24 (47.1)	27 (52.9)	
N0	28	16	12	
N1	22	7	15	
Unknown	1	1	0	
Total	870	386 (44.4)	484 (55.6)	

Abbreviations: PT = primary tumor (bed); LNs = regional lymph nodes; other abbreviations as in Table 2.
Data in parentheses are percentages.

Table 4. Drugs used and timing of chemotherapy ($n = 691$)

Variable	Actual patients (n)	Chemotherapy timing* (n): Before RT	During RT	After RT
Actual patients (n)	691 (100)	66 (9.6)	531 (76.8)	364 (52.7)
Drugs				
GEM	515 (74.5)	59	341	283
5-FU	211 (30.5)	2	173	47
Cisplatin	72 (10.4)	5	60	19
T-1	60 (8.7)	5	29	39
UFT	31 (4.5)	2	13	19
Other	9 (1.3)	0	4	2

Abbreviations: RT = radiotherapy; GEM = gemcitabine; FU = fluorouracil; T-1 = combination of tegafur, 5-chloro-2, 4-dihydroxypyridine, and oteracil potassium; UFT = tegafur/uracil.
Data in parentheses are percentages.
* For combination chemotherapy, each drug of combination was counted.

covering the primary tumor (bed) only. Although the optimal radiation field for pancreatic cancer remains to be defined, the NCCN practice guidelines have recommended that when 5-FU–based chemoradiotherapy is used, the treatment volumes should include the primary tumor location and the regional lymph nodes (23). Several reports have indicated that the rate of severe toxicity is greater in patients treated with gemcitabine-based chemoradiotherapy than in those treated with 5-FU–based chemoradiotherapy (27). Additional studies investigating the optimal radiation field when using chemotherapy drugs, such as gemcitabine, should be conducted.

The present study revealed that chemotherapy was routinely administered with RT. In the United States, a trend has occurred from using RT alone to the more frequent use of combined RT and chemotherapy (16). Regarding the drugs used for pancreatic cancer, 5-FU, with or without mitomycin-C, has been frequently used for pancreatic cancer (28, 29). In 1997, Burris *et al.* (30) indicated that single-agent gemcitabine was marginally superior in clinical benefit and survival compared with 5-FU. Therefore, single-agent gemcitabine has become the standard first-line agent for the treatment of pancreatic cancer. In the present study, gemcitabine was commonly used in conjunction with RT during the survey period. These results indicate that the use of gemcitabine combined with RT has been rapidly adopted in Japan.

In the present study, the results have shown that chemotherapy was most often administered during RT and next often after RT. These results indicate that chemotherapy during RT (concurrent chemoradiotherapy) has been the more frequent practice in Japan. Many investigators also administer chemoradiotherapy initially and then follow with chemotherapy until disease progression (31–34). Recently, several reports have indicated that a period of chemotherapy followed by consolidated chemoradiotherapy might be preferable to upfront chemoradiotherapy (35, 36). Additional studies investigating the optimal sequencing of RT and chemotherapy should be undertaken.

CONCLUSION

The present report has described the general patterns of RT practice for pancreatic cancer in Japan. Most patients had advanced unresectable disease, and not only radical EBRT, but also IORT with or without EBRT, was frequently used. Concerning chemotherapy, gemcitabine was commonly used in conjunction with RT in Japan. Our study has also shown extensive variation exists with regard to treatment strategies and the patterns of RT. Therefore, patients with pancreatic cancer should continue to be enrolled in prospective studies investigating novel combinations of chemotherapy and/or biologic agents with RT. In the future, repeat surveys and point-by-point comparisons with the results from other countries will demonstrate how RT for pancreatic cancer has been developed and optimized for patients in Japan.

REFERENCES

1. Jemal A, Siegel R, Ward E, *et al.* Cancer statistics, 2008. *CA Cancer J Clin* 2008;58:71–96.
2. Gudjonsson B. Cancer of the pancreas: 50 Years of surgery. *Cancer* 1987;60:2284–2303.

3. Hawes RH, Xiong Q, Waxman I, *et al.* A multispecialty approach to the diagnosis and management of pancreatic cancer. *Am J Gastroenterol* 2000;95:17–31.
4. Willett CG, Czito BG, Bendell JC, *et al.* Locally advanced pancreatic cancer. *J Clin Oncol* 2005;23:4538–4544.
5. National Cancer Center. National Cancer Center Cancer information service. Available from: http://www.ncc.go.jp/. Accessed July 9, 2009.
6. Shibuya H, Tsujii H. The structural characteristics of radiation oncology in Japan in 2003. *Int J Radiat Oncol Biol Phys* 2005;62:1472–1476.
7. Teshima T, Numasaki H, Shibuya H, *et al.* Japanese structure survey of radiation oncology in 2005 based on institutional stratification of patterns of care study. *Int J Radiat Oncol Biol Phys* 2008;72:144–152.
8. Hanks GE, Coia LR, Curry J. Patterns of care studies: past, present and future. *Semin Radiat Oncol* 1997;7:97–100.
9. Owen JB, Sedransk J, Pajak TF. National averages for process and outcome in radiation oncology: Methodology of the patterns of care study. *Semin Radiat Oncol* 1997;7:101–107.
10. Teshima T. Patterns of care study in Japan. *Jpn J Clin Oncol* 2005;35:497–506.
11. Ogawa K, Nakamura K, Onishi H, *et al.* Radical external beam radiotherapy for clinically localized prostate cancer in Japan: Changing trends in the patterns of care process survey between 1996–1998 and 1999–2001. *Anticancer Res* 2005;25:3507–3511.
12. Mitsumori M, Hiraoka M, Negoro Y, *et al.* The patterns of care study for breast-conserving therapy in Japan: Analysis of process survey from 1995 to 1997. *Int J Radiat Oncol Biol Phys* 2005;62:1048–1054.
13. Uno T, Sumi M, Ishihara Y, *et al.* 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. *Int J Radiat Oncol Biol Phys* 2008;71:414–419.
14. Goonetilleke KS, Siriwardena AK. Nationwide questionnaire survey of the contemporary surgical management of pancreatic cancer in the United Kingdom & Ireland. *Int J Surg* 2007;5: 147–151.
15. Makowiec F, Post S, Saeger HD, *et al.* Current practice patterns in pancreatic surgery: Results of a multi-institutional analysis of seven large surgical departments in Germany with 1454 pancreatic head resections, 1999 to 2004 (German Advanced Surgical Treatment study group). *J Gastrointest Surg* 2005;9: 1080–1086.
16. Niederhuber JE, Brennan MF, Menck HR. The National Cancer Data Base report on pancreatic cancer. *Cancer* 1995;76: 1671–1677.
17. Bilimoria KY, Bentrem DJ, Ko CY, *et al.* Multimodality therapy for pancreatic cancer in the U.S.: Utilization, outcomes, and the effect of hospital volume. *Cancer* 2007;110: 1227–1234.
18. Stessin AM, Meyer JE, Sherr DL. Neoadjuvant radiation is associated with improved survival in patients with resectable pancreatic cancer: An analysis of data from the Surveillance, Epidemiology, and End Results (SEER) registry. *Int J Radiat Oncol Biol Phys* 2008;72:1128–1133.
19. Artinyan A, Hellan M, Mojica-Manosa P, *et al.* Improved survival with adjuvant external-beam radiation therapy in lymph node-negative pancreatic cancer: A United States population-based assessment. *Cancer* 2008;112:34–42.
20. Hazard L, Tward JD, Szabo A, *et al.* Radiation therapy is associated with improved survival in patients with pancreatic adenocarcinoma: Results of a study from the Surveillance, Epidemiology, and End Results (SEER) registry data. *Cancer* 2007;110:2191–2201.
21. Li D, Xie K, Wolff R, *et al.* Pancreatic cancer. *Lancet* 2004;363: 1049–1057.
22. DiMagno EP, Reber HA, Tempero MA, for the American Gastroenterological Association. AGA technical review on the epidemiology, diagnosis, and treatment of pancreatic ductal adenocarcinoma. *Gastroenterology* 1999;117:1464–1484.
23. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™: Pancratic adenocarcinoma. V.I. 2008. Available from: http://www.nccn.org/. Accessed July 9, 2009.
24. Ruano-Ravina A, Almazán Ortega R, Guedea F. Intraoperative radiotherapy in pancreatic cancer: A systematic review. *Radiother Oncol* 2008;87:318–325.
25. Hiraoka T, Uchino R, Kanemitsu K, *et al.* Combination of intraoperative radiation with resection of cancer of the pancreas. *Int J Pancreatol* 1990;7:201–207.
26. Roldan GE, Gunderson LL, Nagorney DM, *et al.* External beam versus intraoperative and external beam irradiation for locally advanced pancreatic cancer. *Cancer* 1988;61:1110–1116.
27. Crane CH, Abbruzzese JL, Evans DB, *et al.* Is the therapeutic index better with gemcitabine-based chemoradiation than with 5-fluorouracil–based chemoradiation in locally advanced pancreatic cancer? *Int J Radiat Oncol Biol Phys* 2002;52: 1293–1302.
28. Moertel CG, Reitemeier RJ, Hahn RG. Mitomycin C therapy in advanced gastrointestinal cancer. *JAMA* 1968;204: 1045–1048.
29. Buroker T, Kim PN, Groppe C, *et al.* 5 FU infusion with mitomycin-C vs. 5 FU infusion with methyl-CCNU in the treatment of advanced upper gastrointestinal cancer: A Southwest Oncology Group Study. *Cancer* 1979;44:1215–1221.
30. Burris HA III, Moore MJ, Andersen J, *et al.* Improvements in survival and clinical benefit with gemcitabine as first-line therapy for patients with advanced pancreas cancer: A randomized trial. *J Clin Oncol* 1997;15:2403–2413.
31. Klaassen DJ, MacIntyre JM, Catton GE, *et al.* Treatment of locally unresectable cancer of the stomach and pancreas: A randomized comparison of 5-fluorouracil alone with radiation plus concurrent and maintenance 5-fluorouracil—An Eastern Cooperative Oncology Group study. *J Clin Oncol* 1985;3: 373–378.
32. André T, Balosso J, Louvet C, *et al.* Combined radiotherapy and chemotherapy (cisplatin and 5-fluorouracil) as palliative treatment for localized unresectable or adjuvant treatment for resected pancreatic adenocarcinoma: Results of a feasibility study. *Int J Radiat Oncol Biol Phys* 2000;46:903–911.
33. Ishii H, Okada S, Tokuuye K, *et al.* Protracted 5-fluorouracil infusion with concurrent radiotherapy as a treatment for locally advanced pancreatic carcinoma. *Cancer* 1997;79:1516–1520.
34. Sultana A, Tudur Smith C, Cunningham D, *et al.* Systematic review, including meta-analyses, on the management of locally advanced pancreatic cancer using radiation/combined modality therapy. *Br J Cancer* 2007;96:1183–1190.
35. Huguet F, André T, Hammel P, *et al.* Impact of chemoradiotherapy after disease control with chemotherapy in locally advanced pancreatic adenocarcinoma in GERCOR phase II and III studies. *J Clin Oncol* 2007;25:326–331.
36. Krishnan S, Rana V, Janjan NA, *et al.* Induction chemotherapy selects patients with locally advanced, unresectable pancreatic cancer for optimal benefit from consolidative chemoradiation therapy. *Cancer* 2007;110:47–55.

放射線治療最近の進歩と島根県の現状

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放射線治療最近の進歩と島根県の現状

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がん診療連携拠点病院

要　旨

がんの放射線治療の歴史は100年余であるが，最近はコンピュータ技術の進歩に伴い照射技術が格段に向上した。これにより，副作用が少なく局所制御率の良好な高精度放射線治療が可能となりつつある。島根大学病院も1981年の開院直後より放射線治療を開始し，経験と症例を重ねてきた。その間，装置の更新と最新治療の導入に加え，放射線治療を専門とする診療科の開設など，より良い放射線治療を提供する体制を整えてきた。前立腺がんのヨウ素シード永久挿入療法，定位放射線治療や強度変調放射線治療（IMRT）の開始，特殊なアイソトープ治療などである。一方で島根県で放射線治療の専門的医療者は不足しており，県内の地域格差も大きい。本稿では放射線治療の概略と島根大学病院および島根県での現状と課題を紹介する。

はじめに

1895年，レントゲン博士が放射線（X線）を発見したが，翌年には放射線をがん治療に応用する試みがなされたとされる。それ以来がんの放射線治療は100余年の歴史を刻んでいる。

現在では，放射線治療は，手術，薬物療法と並ぶ「がん治療の3本柱」であると称されている。日本ではがん患者のうち放射線治療を受ける人の割合は20％程度とされているが，これは欧米の50－60％の半分以下である。その理由として日本人に胃がんなど放射線治療が適応となりにくい種類のがんが多かったこと，放射線治療装置の整備の遅れ，放射線治療医や技術者が欧米に比べ極端に少ないこと，放射線被曝に対する国民の恐怖感状などが考えられている。

今後，人口のさらなる高齢化，放射線治療が適したがん（肺がん，前立腺がん，乳がんなど）の増加，医療情報の普及などにより，日本でも放射線治療の適応が広まると予測されている。放射線治療は近い将来特殊な治療ではなくなると考えら

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れ，より多くの医療従事者が放射線治療に関する基礎知識を持つことが必要である。

本稿では放射線治療の概略と当院で最近開始した新しい放射線治療法を紹介し，島根県における放射線治療の現状と課題についても触れる。

放射線治療とは

がん治療には局所療法と全身療法があるが，放射線治療は手術と並ぶ局所治療である。このため，効果も有害事象（副作用）も治療した部位に出現する。

1．作用機序

放射線治療の作用機序は，主に細胞中のDNAを損傷させて分裂死を起こすことによる。正常細胞も同時に照射されるとDNA損傷を受けるが，腫瘍細胞に比べて損傷からの回復力が大きいため，結果的に腫瘍のみが縮小していく。

2．放射線治療の特徴

1）腫瘍の発生した臓器を切除しないため，機能と形態を温存した治療が可能である。
2）低侵襲な治療であり，高齢者や合併症を有し手術困難な場合でも施行可能である。
3）組織型により効果が異なる。
4）腫瘍周囲の正常組織にも放射線が照射されるため，正常組織の放射線障害の可能性の多寡により治療が制限される。

などが放射線治療の特徴として挙げられる。

3．放射線治療の方法

大きく分けて，1）外部照射，2）小線源治療，3）アイソトープ治療（内用療法）がある。

1）外部照射

リニアックなどの治療装置で発生させたX線や電子線を体外から病巣に照射する（**図1**）。粒子線治療も外部照射の一種であるが，大規模な施設を必要とする。

2）小線源治療

腫瘍病巣に直接小線源を挿入して直接照射をおこなう。病巣の部位や大きさにより適用が限定されるが，病巣局所に効率的に放射線を照射することができ，非常に有用である。外部照射と小線源治療を併用することも多い。

3）アイソトープ治療（内用療法）

アイソトープ（放射線同位元素）を注射や内服で体内に投与し，体内から照射をおこなう。アイソトープが腫瘍部分に特異的に集積し，そ

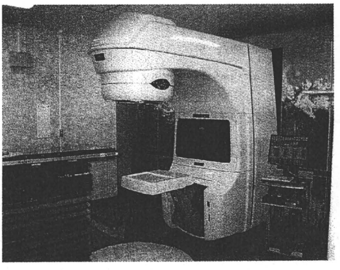

図1－a　外部放射線治療装置（リニアック）

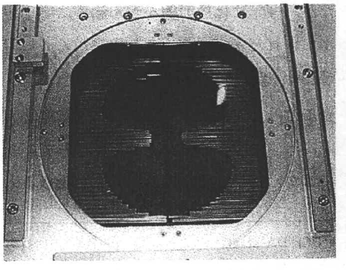

図1－b　マルチリーフコリメータ

こから数 mm しか到達しない放射線を出すため，腫瘍に限局した治療が可能である。現在，甲状腺疾患（バセドウ病，甲状腺癌），骨転移，悪性リンパ腫などで施行可能である。

4．放射線治療の適応疾患（図2）

殆どのがん腫が放射線治療の適応となりうるが，組織型により放射線への反応性が異なる。

1）放射線治療単独で根治が望める

1期の舌がん，喉頭がんなどを代表とする頭頸部腫瘍，食道がん，非小細胞肺がん，前立腺がん，子宮がんなどいずれも病巣が限局期であるもの

2）化学療法と併用で根治が望める

局所進行期（おおむね臨床病期2－3期）の多くのがん，1－2期のリンパ腫など

3）手術と放射線，あるいは抗がん剤も組み合わせておこなうのが標準治療

局所進行期（おおむね臨床病期2－3期）の多くのがん。

4）がんの進行に伴う症状緩和目的で適応となる

骨転移，脳転移，神経圧迫症状，腫瘍による出血や狭窄症状

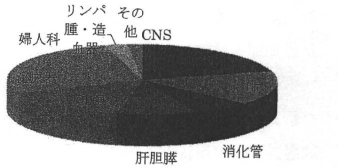

図2　島根大学病院放射線治療患者の原発病巣別割合（2008年度 363名）

島根大学病院における放射線治療

島根大学病院では1981年の開院直後より放射線治療を開始し，経験と症例を重ねてきた。その間，装置の更新と最新治療の導入に加え，放射線治療科の開設など，より良い放射線治療を提供する体制を整えてきた。通常の外部照射の他に高精度放射線治療，小線源治療，アイソトープ治療の全てが可能である。

1．チーム医療

現在，島根大学病院放射線治療科では5名の放射線治療の専門医が適応の決定，治療計画，治療経過のチェックなどの診療にあたっている。放射線治療は医師だけでは施行困難であり，放射線治療装置を操作して実際の照射をおこなう診療放射線技師，看護師，がん相談員など多職種が関わるチーム医療である。近年放射線治療は非常に高精度化しており，医療機器の安全管理や治療の精度管理の専門家の役割が大きくなっている。当院では医学物理士や放射線治療品質管理士の資格を有する者がこれらの業務にあたっている。

2．新しい放射線治療技術

外部照射装置（リニアック）2台と小線源治療装置2台，放射線治療専用 CT 1台を保有する。

1）高精度放射線治療

従来は，外部照射装置から出る放射線ビームは矩形のみの形状であった。現在では，ビームの出口のところで，左右から対になった5 mm 幅の鉛の遮蔽物（マルチリーフコリメータ）をコンピュータ制御で出し入れすることにより，腫瘍の形状にあった照射野を作ることができる（図1）。このなかで特殊な高精度治療として（a）定位放射線治療，（b）強度放射線治療がある。

（a）定位放射線治療（図3）

細い放射線ビームを病変の形状に正確に一致

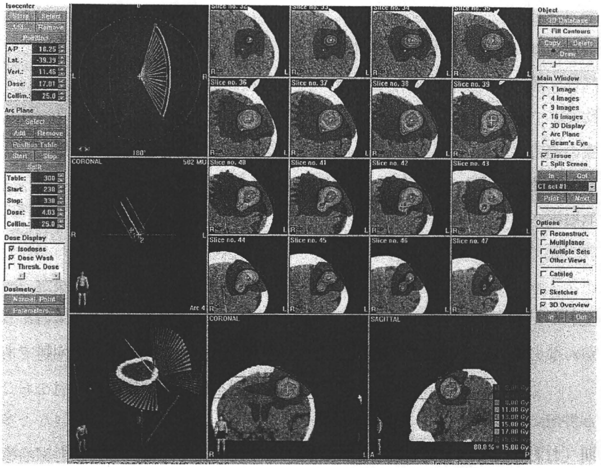

図3　転移性脳腫瘍に対する定位照射の1例

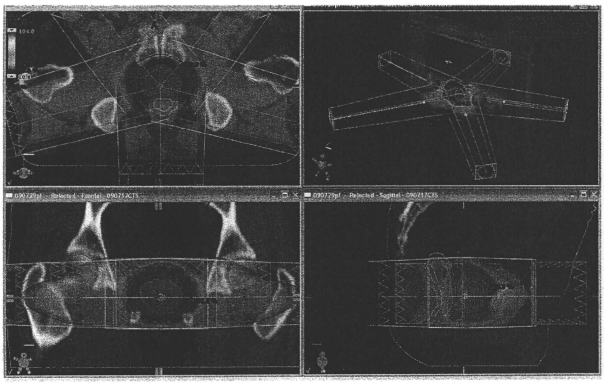

図4　前立腺がんの強度放射線治療（IMRT）の1例

させて多方向からピンポイント的に集中照射する方法である。ガンマナイフは定位放射線治療の代表であるが，外部照射装置のX線でガンマナイフと同じように脳腫瘍を治療できるほか，小さな肺がんや肝臓がんにも適応がある。特に1－2期の非小細胞肺がんは国内多施設研究で手術と遜色ない良好な治療成績を得ている。

（b）強度放射線治療（IMRT）（図4）

コンピュータで放射線ビームに複雑な強弱をつけ，病巣の形に適した照射をおこなう。コンピュータが何千・何万通りの照射法の中から最適な方法を算出して治療計画（インバースプラン）をおこなう。そしてマルチリーフコリメータをコンピュータ制御することにより計算結果どおりの照射をおこなうことができる。周囲正常組織への照射を減らすことができるため副作用が減り，結果として，より多くの放射線を腫瘍に照射することが可能となり，治療成績の向上が望める。2008年4月より，中枢神経，頭頸部，前立腺の原発性腫瘍に対するIMRTが保険適応となった。放射線治療専門医の人数や経験，品質管理を担当する技術者（医学物理士等）と治療専任の診療放射線技師や測定器が必要など治療施設の認定基準が定められている。

2）小線源治療

（a）後充填式遠隔操作法（ラルス）

放射線同位元素が封入された小線源が入る器具（アプリケーター）を，あらかじめ腫瘍内あるいは体腔内に挿入しておき，遠隔操作で中に小線源を送り込み一定時間留置する治療法である。主に舌がんなどの口腔内腫瘍や子宮がん，食道がんなどが適応となる。特に子宮頸がんは良い適応で，骨盤部全体への外部照射と小線源治療を併用することにより治療効果が高い。

（b）前立腺がんのヨウ素シード永久挿入療法

転移や浸潤のない前立腺がんに対して，小線源（長さ：約4.5 mm，直径：約0.8 mm，シード）を50～100個ほど前立腺内に永久的に挿入して直接放射線を照射する（**図5**）。手術と同等の治療効果が得られるうえ，副作用は少なく入院期間も3日間である。当院では2005年11月山陰地方で初めて導入し，既に150例以上の治療実績があり，良好な成績を収めている。

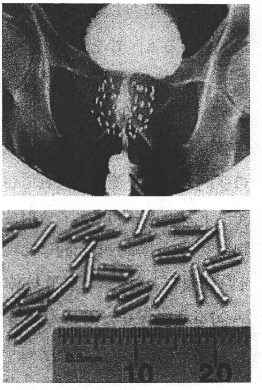

図5　前立腺がんのヨウ素シード永久挿入療法の1例
経会陰的に前立腺内に小線源（シード）を約50個挿入留置している。挿入直後の膀胱造影写真と小線源（日本メジフィジックス社提供資料）

3）アイソトープ治療（内用療法）

当科では，甲状腺疾患に対するヨウ素－131内服療法，骨転移の疼痛治療に対する塩化ストロンチウム－89（メタストロン®）治療，そして特殊な悪性リンパ腫に対するイットリウム－90（ゼヴァリン®）による放射性免疫療法が可能である。1回の注射やカプセルの内服で投与するので，患者負担も少ない。いずれも保険適応で，適切な管理指導のもとでおこなえば侵襲が低く有効な治療である。

（a）ヨウ素－131

主に甲状腺がんの肺や骨への多発転移の状態が主な適応で，内服後約3日間の放射線治療室への入室が必要である。甲状腺機能亢進症（バセドウ病）のコントロールにも有効で，この場合は外来でも治療可能である。

（b）塩化ストロンチウム－89

がんの骨転移の場合の疼痛治療に用いる。がんが骨に転移すると，骨を溶かしてカルシウム代謝が活発になる。カルシウムの同族体であるストロンチウム－89を注射すると，骨転移部に集積して微弱な放射線を出す。臨床試験では70％程度の症例で疼痛改善が得られている。

（c）イットリウム－90による放射性免疫療法

B細胞性リンパ腫細胞の表面に発現しているCD20抗原を標的として，CD20抗体にイットリウム－90を標識させたものを注射投与するターゲット療法である。化学療法やリツキサンが有効でなかった症例の約80％に効果があり，約60％で治癒が期待できると報告されている。2009年4月から山陰地方では初めて当院で治療可能となった。

島根県の放射線治療の現状と課題

コンピュータ技術の発展に伴い急速に進歩してきた放射線治療であるが，専門医や専門的技術者の不足が大きな問題である。島根県は人口の高齢化率が高く，侵襲の低い放射線治療の重要が今後増していくと考えられる。現在当院を含め6施設で放射線治療が可能であるが，県東部には5か所6台の外部放射線照射装置があるのに比べ，中西部には1か所1台であり地域格差が大きい。がん診療連携拠点病院が県内の放射線治療の大部分を担っているが，病院間での連携と役割分担を進めることが必要である。専門的医療従事者の育成が急務であることももちろんである。

結　　語

放射線治療は臓器と機能の温存が可能ながんの局所治療で，比較的低侵襲である。コンピュータ技術の発展の恩恵を受けて急速に進歩しており，今後治療患者数の増加が予測されている。島根県内でも専門的人材の育成や治療技術の向上とともに治療施設間の連携強化などを進めていく必要がある。

参 考 文 献

1）高橋和久　編集：講義録　腫瘍学　メジカルビュー社　2009年
2）Edward C Halperin et al., ed.: Perez and Brady's Principles and Practice of Radiation Oncology (5th ed), Lippincott Williams & Wilkins, (2007)
3）Eric J Hall et al., ed.: Radiobiology for the Radiologist (6th ed.), Lippincott Williams & Wilkins, (2005)
関連URL
日本放射線腫瘍学会　http://www.jastro.jp/

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CLINICAL INVESTIGATION **Radiation Oncology Practice**

JAPANESE STRUCTURE SURVEY OF RADIATION ONCOLOGY IN 2007 BASED ON INSTITUTIONAL STRATIFICATION OF PATTERNS OF CARE STUDY

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Purpose: To evaluate the ongoing 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 from March to December 2008 by the Japanese Society of Therapeutic Radiology and Oncology (JASTRO). 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 radiation in 2007 were estimated at 181,000 and 218,000, respectively. There were 807 linear accelerator, 15 telecobalt, 46 Gamma Knife, 45 ^{60}Co remote-controlled after-loading, and 123 ^{192}Ir remote-controlled after-loading systems in actual use. The linear accelerator systems used dual-energy function in 539 units (66.8%), three-dimensional conformal radiation therapy in 555 (68.8%), and intensity-modulated radiation therapy in 235 (29.1%). There were 477 JASTRO-certified radiation oncologists, 826.3 full-time equivalent (FTE) radiation oncologists, 68.4 FTE medical physicists, and 1,634 FTE radiation therapists. The number of interstitial radiotherapy (RT) administrations for prostate, stereotactic body radiotherapy, and intensity-modulated radiation therapy increased significantly. Patterns of Care Study stratification can clearly identify the maturity of structures based on their academic nature and caseload. Geographically, the more JASTRO-certified physicians there were in a given area, the more RT tended to be used for cancer patients.
Conclusions: The Japanese structure has clearly improved during the past 17 years in terms of equipment and its use, although a shortage of personnel and variations in maturity disclosed by Patterns of Care Study stratification were still problematic in 2007. © 2010 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 structure of radiation oncology facilities in 1989 for the entire census of facilities in the United States (1). In 1991 the Japanese Society of Therapeutic Radiology and 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 and identify similarities and differences in 1989–1990 was conducted by Teshima *et al.* (3) and reported in 1996. The resultant international exchange of information proved especially valuable for Japan, because we could improve our own structure of radiation oncology based on those data.

The Japanese structure has gradually improved in terms of a greater number of cancer patients who are treated with radiation as well as public awareness of the importance of RT. The Japanese Society of Therapeutic Radiology and Oncology has conducted national structure surveys every 2 years since 1990 (4), and in 2006 an anticancer law was enacted in Japan, which strongly advocates the promotion of RT and an increase in the number of radiation oncologists (ROs) and medical physicists. The Japanese Ministry of Education, Sciences, and Sports is supporting the education of these specialists at university medical hospitals. Findings of international comparisons and the consecutive structural data gathered and published by JASTRO have been useful for an understanding of our current position and future direction (4, 5). In this report the recent structure of radiation oncology in Japan is analyzed and compared with the data of 2005 (5).

METHODS AND MATERIALS

From March to December 2008, JASTRO conducted a questionnaire based on the national structure survey of radiation oncology in 2007. The questionnaire dealt with the number of treatment machines by type, number of personnel by category, and number of patients by type, site, and treatment modality. To measure variables over a longer period of time, data for the calendar year 2007 were also requested. The response rate was 721 of 765 active facilities (94.2%). The data from 573 institutions (79.5%) were registered in the International Directory of Radiotherapy Centres in Vienna, Austria, in October 2008.

The PCS was introduced in Japan in 1996 (6–15). The Japanese PCS used methods similar to those of the American version, which used structural stratification to analyze national averages for the data in each survey item by means of two-stage cluster sampling. We stratified RT facilities throughout the country into four categories for the regular structure surveys. This stratification was based on academic conditions and the annual number of patients treated with radiation at each institution, because academic institutions require and have access to more resources for education and training whereas the annual caseload also constitutes essential information related to structure. For the study reported here, the following institutional stratification was used: A1, university hospitals/cancer centers treating 440 patients or more per year; A2, university hospitals/cancer centers treating 439 patients or fewer per year; B1, other national/public hospitals treating 140 patients or more per year; and B2, other national hospital/public hospitals treating 139 patients or fewer per year.

We used SAS 8.02 (SAS Institute, Cary, NC) (16) for statistical analyses, and statistical significance was tested by means of 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) undergoing radiation in 2007 were estimated at 181,000 and 218,000, respectively, showing a 7.3% increase over 2005 (5). According to the PCS stratification of institutions, 40.1% of the patients were treated at academic institutions (Categories A1 and A2), even though these academic institutions constituted only 18.6% of the 765 RT facilities nationwide.

Table 1. Patterns of Care Study stratification of radiotherapy facilities in Japan

Institution category	Description	Facilities (*n*)	New patients (*n*)	Average new patients/ facility* (*n*)	Total patients (new + repeat) (*n*)	Comparison with data of 2005† (%)	Average total patients/ facility* (*n*)	Comparison with data of 2005† (%)
A1	UH and CC (≥440 patients/y)	71	49,866	702.3	60,398	10.0	850.7	2.3
A2	UH and CC (<440 patients/y)	71	17,974	253.2	21,867	2.1	308.0	−3.6
B1	Other (≥140 patients/y)	288	78,154	271.4	94,188	6.1	327.0	6.8
B2	Other (<140 patients/y)	291	24,235	83.3	28,634	9.6	98.4	8.8
Total		721	170,229‡	236.1	205,087‡	7.3	284.4	5.9

Abbreviations: UH = university hospital; CC = cancer center hospital; Other = other national, city, or public hospital.

* $p < 0.0001$.

† Rate of increase compared with data of 2005. The calculating formula was as follows: $\frac{data\ of\ 2007\ (n) - data\ of\ 2005\ (n)}{data\ of\ 2005\ (n)} \times 100\ (\%)$.

‡ The number of radiotherapy institutions was 765 in 2007, and the number of new patients was estimated at approximately 181,000; the corresponding number of total patients (new plus repeat) was 218,000.

The cancer incidence in Japan in 2007 was estimated at 692,502 (17), with approximately 26.1% of all newly diagnosed patients treated with radiation. This number has increased steadily during the last 17 years and is expected to increase further (12). In 1990 the rate was estimated to be approximately 15% (3). The corresponding rates were 16%, 17%, 20%, 22%, 23.3% (4), 24.5% (5), and 26.1% in 1995, 1997, 1999, 2001, 2003, 2005, and 2007, respectively.

Facility and equipment patterns

Table 2 shows an overview of RT equipment and related functions. There were 807 linear accelerator (linac) systems, 15 telecobalt systems, 46 Gamma Knife systems, 45 ^{60}Co remote-controlled after-loading systems (RALSs), and 123 ^{192}Ir RALSs in actual use. The linac system used dual-energy function in 539 units (66.8%), three-dimensional (3D) conformal radiation therapy (CRT) in 555 (68.8%), and intensity-modulated radiation therapy (IMRT) in 235 (29.1%). The IMRT function was used more frequently in the equipment of academic institutions (A1, 61.6%; A2, 31.9%) than that of nonacademic institutions (B1, 26.4%; B2, 13.0%). However, 3D CRT functions were disseminated widely in both academic and nonacademic institutions, with more than 50% even in B2 institutions. Image-guided radiation therapy functions have been gradually spreading from A1 institutions (28.5%) to the other types of institutions (8.2% to 11.1%), although the rate of expansion has remained low. The annual numbers of patients per linac were 400 for A1 institutions, 238.6 for A2, 296.2 for B1, and 98.4 for B2. The number of institutions with telecobalt in actual use showed a major decrease to 15, and Gamma Knife was installed more frequently in B1 and B2 institutions. A significant replacement of ^{60}Co RALSs with ^{192}Ir RALSs was observed especially in academic institutions, whereas the number of new-type ^{60}Co RALSs in use did not increase. Six particle machines were registered in this survey, two with carbon beam and five with proton beam irradiation. One machine at Hyogo is delivering either carbon or proton. Although Heavy Ion Medical Accelerator in Chiba (HIMAC) at Chiba has two synchrotrons, it was registered as one machine in the 2007 survey. The total number of new cancer patients treated at these six institutions was estimated at 1,643 (0.9% of all new patients in Japan). Twenty-one advanced institutions were included in the A1 Category and treated more than 800 patients per year. They were equipped with linac with dual-energy function (77.6% of the institutions), 3D CRT function (91.4%), and IMRT function (65.5%), as well as with ^{192}Ir RALS (85.7%) and a computed tomography (CT) simulator (95.2%).

Table 3 shows an overview of RT planning and other equipment. X-ray simulators were installed in 60.9% of all institutions and CT simulators in 65.6%, with the latter exceeding the former for the first time in 2007. There was a significant difference in the rate of CT simulators installed by institutional stratification, from 93% in A1 institutions to 52.6% in B2 institutions. Very few institutions used magnetic resonance imaging for RT only, whereas computer use for RT recording was pervasive.

Staffing patterns and patient loads

Table 4 shows the staffing patterns and patient loads by institutional stratification. "Full time or part time" indicates the style of employment. Even full-time ROs must share the diagnosis in a week in smaller institutions like B2 institutions. We considered that these numbers were not sufficient for accurate evaluation of personnel. Therefore full-time equivalent (FTE) (40 hours/week only for radiation oncology service) data were surveyed depending on clinical working hours for RT of each person. For example, FTE of a person who has 4 days working is 0.8 and that of 1 day is 0.2. The FTE of an institution that has 3 persons with 0.8, 0.2, and 0.4 is calculated as 1.4 in total. This is a measure to represent actual personnel at each institution. The total number of FTE ROs in Japan was 826.3, whereas the average numbers were 4.3 for A1 institutions, 1.4 for A2, 1.0 for B1, and 0.5 for B2. The number in B1 institutions improved by 12.1% compared with 2005 (5). The overall patient load per FTE RO in Japan was 248.2, and the numbers for A1, A2, B1, and B2 institutions were 200.1, 218.2, 327.3, and 209.9, respectively, with the patient load for B1 institutions being by far the highest. The increase in the rate of FTE ROs was 6.7% over 2005 (5). In Japan 39% of the institutions providing RT have their own designated beds, where ROs must also take care of their inpatients. The percentage distribution of institutions by patient load per FTE RO is shown in Fig. 1, indicating that the largest number of facilities featured a patient/FTE staff level in the 101 to 150 range and the second largest number was in the 151 to 200 range. The blue areas of the bars show that 56% of the institutions (405 of 721) had fewer than 1 FTE RO. Compared with the data of 2005 (5), the patient load is shifting to a larger volume.

A similar trend was observed for RT technologists and their patient load by institutional stratification. The percentage distribution of institutions by patient load per radiation technologist is shown in Fig. 2. The largest number of facilities had a patient–per–RT technologist level in the 101 to 120 range, with the second largest number showing a range of 61 to 80 and the third largest showing a range of 121 to 140. There were 68.4 FTE medical physicists and 106.6 RT quality assurance (QA) staff. For this survey, personnel numbers were checked for duplicate reporting by individual identification on staffing data, and these data will be analyzed in detail in another report. Finally, there were 494.4 FTE nurses.

Distribution of primary sites, specific treatment, and palliative treatment

Table 5 shows the distribution of primary sites by institutional stratification. The most common disease site was breast, followed by lung/bronchus/mediastinum and genitourinary sites. In Japan the number of patients with prostate cancer undergoing RT was 16,225 in 2007, an increase of 22.7% over 2005 (5). By disease site, the rate of increase

Table 2. Equipment and its function and patient load per equipment type by Patterns of Care Study institutional stratification

Radiotherapy equipment and its function	A1 (n = 71)		A2 (n = 71)		B1 (n = 288)		B2 (n = 291)		Total (n = 721)		Comparison with data of 2005 (%)
	n	%	n	%	n	%	n	%	n	%	
Linear accelerator	151		91		296		269		807		5.5*
With dual-energy function	116	76.8†	64	70.3†	216	73.0†	143	53.2†	539	66.8†	1.7‡
With 3D CRT function (MLC width ≤1.0 cm)	136	90.1†	63	69.2†	214	72.3†	142	52.8†	555	68.8†	8.4‡
With IMRT function	93	61.6†	29	31.9†	78	26.4†	35	13.0†	235	29.1†	6.9‡
With IGRT function	43	28.5†	10	11.0†	33	11.1†	22	8.2†	108	13.4†	
With CT on rail	7	4.6†	6	6.6†	17	5.7†	17	6.3†	47	5.8†	
With treatment position verification system	42	27.8†	18	19.8†	36	12.2†	14	5.2†	110	13.6†	
Annual No. patients/linac	400.0§		238.6§		296.2*		98.4§		243.2§		3.7*
Particle	4		0		1		1		6		
Betatron	0		0		0		0		0		
Microtoron	4		2		4		3		13		
Telecobalt (actual use)	6 (4)		2 (0)		7 (2)		13 (9)		28 (15)		
Gamma Knife	3		2		31		10		46		
Other accelerator	1		1		2		5		9		
Other external irradiation device	1		2		2		1		6		
New-type ^{60}Co RALS (actual use)	3 (3)	4.2‖ (4.2)	1 (1)	1.4‖ (1.4)	10 (10)	3.5‖ (3.5)	2 (2)	0.7‖ (0.7)	16 (16)	2.2‖ (2.2)	
Old-type ^{60}Co RALS (actual use)	6 (5)	8.5‖ (7.0)	5 (2)	7.0‖ (2.8)	24 (20)	8.3‖ (6.9)	4 (2)	1.4‖ (0.7)	39 (29)	5.4‖ (4.0)	
^{192}Ir RALS (actual use)	56 (55)	78.9‖ (77.5)	31 (29)	43.7‖ (40.8)	35 (35)	12.2‖ (12.2)	5 (4)	1.7‖ (1.4)	127 (123)	17.6‖ (17.1)	
^{137}Cs RALS (actual use)	1 (1)		1 (1)		2 (1)		0 (0)		4 (3)		

Abbreviations: A1 = university hospitals/cancer centers treating 440 patients or more per year; A2 = university hospitals/cancer centers treating 439 patients or fewer per year; B1 = other national/public hospitals treating 140 patients or more per year; B2 = other national hospital/public hospitals treating 139 patients or fewer per year; 3D CRT = three-dimensional conformal radiotherapy; MLC = multileaf collimator; IMRT = intensity-modulated radiotherapy; IGRT = image-guided radiation therapy; CT = computed tomography; linac = linear accelerator; RALS = remote-controlled after-loading system.

* Rate of increase compared with data of 2005. The calculating formula was as follows: $\frac{\text{data of 2007 } (n) - \text{data of 2005 } (n)}{\text{data of 2005 } (n)} \times 100$ (%).

† Percentage calculated from number of systems by use of this function and the total number of linear accelerator systems.

‡ Comparison with data of 2005. The calculating formula was as follows: Data of 2007 (%) − Data of 2005 (%).

§ Number of patients over number of linear accelerators; institutions without linear accelerators excluded from calculation.

‖ Rate of institutions that have this equipment (Ratio of institutions that have two or more equipment).

Table 3. Radiotherapy planning and other equipments by Patterns of Care Study institutional stratification

RT planning and other equipment	A1 (n = 71)		A2 (n = 71)		B1 (n = 288)		B2 (n = 291)		Total (n = 721)		Comparison with data of 2005† (%)
	n	%*	n	%*	n	%*	n	%*	n	%*	
X-ray simulator	55	76.1	52	69.0	165	56.6	173	59.5	445	60.9	−8.8
CT simulator	74	93.0	58	77.5	210	69.1	155	52.6	497	65.6	10.3
RTP computer (≥2)	277 (60)	100 (84.5)	117 (26)	100 (36.6)	370 (57)	97.2 (19.8)	306 (25)	91.1 (8.6)	1070 (168)	95.3 (23.3)	2.2 (2.8)
MRI (≥2)	201 (60)	95.8 (84.5)	137 (54)	93.0 (76.1)	502 (185)	97.2 (64.2)	349 (71)	95.2 (24.4)	1189 (370)	95.8 (51.3)	1.1 (3.8)
For RT only	1	1.4	3	4.2	7	2.4	0	0	13	1.5	—
Computer use for RT recording	63	88.7	64	90.1	268	93.1	245	84.2	640	88.8	0.9

Abbreviations: A1 = university hospitals/cancer centers treating 440 patients or more per year; A2 = university hospitals/cancer centers treating 439 patients or fewer per year; B1 = other national/public hospitals treating 140 patients or more per year; B2 = other national hospital/public hospitals treating 139 patients or fewer per year; RT = radiotherapy; CT = computed tomography; RTP = radiotherapy planning; MRI = magnetic resonance imaging.

* Ratio of institutions that have equipment (Ratio of institutions that have two or more equipment).

† Comparison with data of 2005. The calculating formula was as follows: data of 2007 (%) − data of 2005 (%).

was the highest for prostate cancer, at 22.7%; the second highest was for breast cancer, at 20.1%; and the third highest was for lung cancer, at 14.9%. Stratification of institutions indicates that the rate of increase was notable for lung at A1, B1, and B2 and the corresponding rates for prostate cancer were high at A1, A2, and B1, from 24.7% to 26.2%. On the other hand, the corresponding rate for breast was the lowest (15.6%) at A1, whereas those at A2, B1, and B2 ranged from 20.7% to 22.5%.

Table 6 shows the distribution of usage of specific treatments and the number of patients treated with these modalities by PCS stratification of institutions. Use of interstitial irradiation, radioactive iodine therapy for prostate cancer, stereotactic body RT, and IMRT increased significantly by 19.0%, 52.4%, 50.2%, and 270.7%, respectively, over 2005 (5). On the other hand, the use of intraoperative RT decreased significantly by 35.1% and that of hyperthermia decreased by 41.5%. Institutional stratification shows that there was a dramatic increase of 623.6% in the use of IMRT in B1 (5). In 2007, 58 institutions (8%) actually used IMRT. This percentage was significantly lower than 235 linac systems with IMRT function (29.1%) as shown in Table 2.

Table 7 shows the number of patients with brain or bone metastasis treated with radiation according to the same institutional stratification. The B1 institutions treated more patients with brain metastasis (13.9% of all patients) than other types of institutions, whereas usage of radiation for bone metastasis ranged from 11.4% for A1 to 17.4% for B2. Overall, more patients with bone metastasis were treated with radiation at nonacademic than at academic institutions. Compared with the data of 2005 (5), the number of patients with brain metastasis increased by 38.6%.

Geographic patterns

Figure 3 shows the geographic distributions for 47 prefectures of the annual number of patients (new plus repeat) per 1,000 population arranged in order of increasing number of JASTRO-certified ROs per 1,000,000 population (18). There were significant differences in the use of RT, from 0.9 patients per 1,000 population (Saitama and Okinawa) to 2.1 (Miyagi). The average number of patients per 1,000 population per quarter ranged from 1.42 to 1.69 (p = 0.0996). The more JASTRO-certified physicians there were in a given area, the more RT tended to be used for cancer patients, although the correlation was of borderline significance. A similar trend was observed in 2005 (5). The utilization rate of RT in every prefecture increased in 2007 compared with 2005. However, the rate in 2007 was not related to a prefecture's population density, as we also observed in the data for 1990 (3).

DISCUSSION

In 1990 there were fewer facilities for radiation treatment and patients treated with radiation in Japan than in the