Table 1. PCS stratification of radiotherapy facilities in Japan

Institution category	Description	Facilities (*n*)	New patients (*n*)	Average new patients/facility[a] (*n*)	Total patients (new + repeat) (*n*)	Comparison with data of 2007[b] (%)	Average total patients/facility[a] (*n*)	Comparison with data of 2007[b] (%)
A1	UH and CC (≥462 patients/y)	70	52 078	744.0	62 124	2.9	887.5	4.3
A2	UH and CC (<462 patients/y)	70	18 842	269.2	22 717	3.9	324.5	5.4
B1	Other (≥158 patients/y)	280	84 938	303.4	101 730	8.0	363.3	11.1
B2	Other (<158 patients/y)	280	26,532	94.8	31 258	9.2	111.6	13.5
Total		700	182 390[c]	260.6	217 829[c]	6.2	311.2	9.4
						7.3		5.9

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

[a] $P < 0.0001$.

[b] Rate of increase compared with the data of 2007. Calculating formula: $\frac{data\ of\ 2009\ (n) - data\ of\ 2007(n)}{data\ of\ 2007(n)} \times 100\ (\%)$

[c] Number of radiotherapy institutions was 770 in 2009, and the number of new patients was estimated at approximately 201 000; the corresponding number of total patients (new plus repeat) was 240 000.

therapy (IGRT) has been steadily expanding from A1 institutions (30.4% to 33.5%) to the other types of institutions (14.0% to 35.5%). The annual numbers of patients/Linac were 393.2 for A1, 244.3 for A2, 339.1 for B1 and 118 for B2 institutions and showed a 9.8 % increase compared with the data from 2007. The number of institutions with telecobalt in actual use showed a major decrease to 9 and became stable compared with 2007. Gamma Knife was installed more frequently in B1 and B2 institutions. A significant replacement of ^{60}Co RALS with ^{192}Ir RALS was observed especially in academic institutions, while the number of new ^{60}Co RALS-type systems 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 in Hyogo Prefecture can deliver either carbon or proton beams. Although the HIMAC in Chiba Prefecture has two synchrotrons, it was registered as one machine in the 2009 survey. The total number of new cancer patients treated at these six institutions was estimated at 2038 (1.19% of all new patients in Japan). Twenty-seven advanced institutions were included in the A1 category and treated more than 800 patients per year. They were equipped with Linacs with dual energy (75.3% of the institutions), 3DCRT (97.2%) and IMRT function (82.2%), as well as with ^{192}Ir RALS (92.6%) and a computed tomography (CT) simulator (96.3%).

Table 3 shows an overview of RT planning and other equipment. X-ray simulators were installed in 51.6% of all institutions, and CT simulators in 82.1%, 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 95.7% in A1 to 69.3% in B2 institutions. Very few institutions (16 institutions) used magnetic resonance imaging (MRI) for RT only, while computers were widely used for RT recording.

Staffing patterns and patient loads

Table 4 shows the staffing patterns and patient loads by institutional stratification. 'Full-time or part-time' refers to the style of employment. Since even full-time ROs must share the diagnosis in a week at smaller institutions such as found in the B2 category, we felt that these numbers were not adequate for an accurate evaluation of man power. Therefore, data for full-time equivalent (FTE: 40 h/week for radiation oncology service only) were assessed in terms of the clinical working hours in RT of each individual. This is thus a method to determine actual man power at each institution. The total number of FTE ROs in Japan stood at 939.4, while the average numbers were 4.6 for A1, 1.6 for A2, 1.3 for B1 and 0.6 for B2 institutions. The number in B1 improved by 30% compared with 2007 [6]. The overall patient load per FTE RO in Japan was 231.9, and for A1, A2, B1 and B2 institutions the loads were 193.5, 205.2, 290.6 and 198.4, respectively, with the patient load for B1 institutions being by far the highest. The increase in the overall patient load per

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

Radiotherapy equipment and its function	A1 ($n = 70$)		A2 ($n = 70$)		B1 ($n = 280$)		B2 ($n = 280$)		Total ($n = 700$)		Comparison with data of 2007 (%)
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	
Linear accelerator	158		93		300		265		816		1.1[a]
with dual energy function	122	*77.2*[b]	70	*75.3*[b]	235	*78.3*[b]	159	*60.0*[b]	586	*71.8*[b]	5.0[c]
with 3DCRT function (MLC width ≥1.0 cm)	150	*94.9*[b]	81	*87.1*[b]	247	*82.3*[b]	185	*69.8*[b]	663	*81.3*[b]	12.5[c]
with IMRT function	116	*73.4*[b]	46	*49.5*[b]	127	*42.3*[b]	48	*18.1*[b]	337	*41.3*[b]	12.2[c]
with cone beam CT or CT on rail	48	*30.4*[b]	33	*35.5*[b]	73	*24.3*[b]	41	*15.5*[b]	195	*23.9*[b]	
with treatment position verification system (X-ray perspective image)	51	*32.3*[b]	31	*33.3*[b]	85	*28.3*[b]	37	*14.0*[b]	204	*25.0*[b]	
with treatment position verification system (other than those above)	53	*33.5*[b]	18	*19.4*[b]	77	*25.7*[b]	55	*20.8*[b]	203	*24.9*[b]	
Annual no. patients/Linac	393.2[d]		244.3[d]		339.1[a]		118.0[d]		266.9[d]		9.8[a]
Particle	3		0		3		0		6		
Microtoron	6		2		3		4		15		
Telecobalt (actual use)	2 (0)		2 (0)		3 (1)		8 (7)		15 (9)		
Gamma knife	3		2		32		9		46		
Other accelerator	2		1		1		1		5		
Other external irradiation device	4		2		1		0		6		
New type ^{60}Co RALS (actual use)	4 (4)	5.7[e] (5.7)	1 (1)	1.4[e] (1.4)	9 (9)	3.2[e] (3.2)	2 (1)	0.7[e] (0.4)	16 (15)	2.3[e] (2.1)	
Old type ^{60}Co RALS (actual use)	2 (2)	2.9[e] (2.9)	2 (1)	2.9[e] (1.4)	14 (11)	5.0[e] (3.9)	4 (0)	1.4[e] (0.0)	22 (14)	3.1[e] (2.0)	
^{192}Ir RALS (actual use)	60 (60)	85.7[e] (85.7)	32 (31)	45.7[e] (44.3)	37 (37)	13.2[e] (13.2)	4 (2)	1.4[e] (0.7)	133 (130)	19.0[e] (18.6)	
^{137}Cs RALS (actual use)	1 (0)		0 (0)		1 (1)		0 (0)		2 (2)		

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.

[a]Rate of increase compared with the data of 2007. Calculating formula: $\frac{data\ of\ 2009\ (n) - data\ of\ 2007\ (n)}{data\ of\ 2007\ (n)} \times 100\ (\%)$

[b]Percentage calculated from the number of systems using this function and the total number of linear accelerator systems.

[c]Comparison with the data of 2007. Calculating formula: *data of* 2009 (%) − *data of* 2007 (%)

[d]The number of patients over the number of linear accelerators; institutions without linear accelerators excluded from calculation.

[e]Rate of institutions that have this equipment (≥2 pieces of equipment per institution).

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

RT planning and other equipment	A1 ($n=70$)		A2 ($n=70$)		B1 ($n=280$)		B2 ($n=280$)		Total ($n=700$)		Comparison with data of 2007[b] (%)
	n	%[a]	*n*	%[a]	*n*	%[a]	*n*	%[a]	*n*	%[a]	
X-ray simulator	55	74.3	41	55.7	130	46.1	135	48.2	361	50.7	−10.2
CT simulator	74	95.7	61	84.3	235	78.6	205	69.3	575	77.1	11.5
RTP computer (two or more)	340 (63)	100 (90.0)	167 (35)	100 (50.0)	461 (99)	97.5 (35.4)	303 (37)	92.5 (13.2)	1271 (234)	96.0 (33.4)	0.7 (10.1)
MRI (two or more)	201 (60)	95.7 (85.7)	151 (56)	98.6 (80.0)	504 (184)	97.5 (65.7)	364 (86)	97.9 (30.7)	1220 (386)	97.6 (55.1)	1.8 (3.8)
for RT only	2	2.9	2	2.9	9	2.9	3	1.1	16	2.1	0.6
Computer use for RT recording	64	91.4	65	92.9	264	94.3	238	85.0	631	90.1	1.3

CT = computed tomography; RTP = radiotherapy planning; MRI = magnetic resonance imaging; other abbreviations as in Table 2.
[a]Ratio of institutions that have equipment (≥2 pieces of equipment per institution).
[b]Comparison with the data of 2007. Calculating formula: *data of* 2009 (%) − *data of* 2007 (%).

FTE RO was 13.7% compared with 2007 (6). In Japan, 42.6 % of the institutions providing RT have their own designated beds, where ROs must also take care of their in-patients. The percentage distribution of institutions by patient load per FTE RO shown in Fig. 1a indicates that the largest number of facilities featured a patient/FTE staff level in the 101–150 range, and in the 151–200 range for the second largest number. The blue areas of the bars show that 47.7% of the institutions (334/700) had less than one FTE RO. Compared with 2007 [6], the patient load has increased even more.

A similar trend was observed for RT technologists and their patient load by institutional stratification with the percentage distribution of institutions by patient load per radiation technologist displayed in Fig. 1b. The largest number of facilities had a patient-per-radiotherapy technologist level in the 101–120 range, with the second largest number showing a range of 81–100 and the third largest a range of 121–140. There were 113.1 FTE medical physicists, 113.1FTE radiotherapy quality assurance (QA) staff and 1836FTE radiotherapists. For this survey, personnel numbers were checked for duplicate reporting by identification of individuals on staffing data and these data were analyzed in detail in another report [7]. Finally, there were 621.2 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 the breast, followed by the lung/bronchus/mediastinum and genito-urinary region. In Japan, the number of patients with prostate cancer undergoing RT was 17 919 in 2009, showing an increase of 10.4% over 2007 [6]. By disease site, the rate of increase compared with 2007 was the highest for prostate cancer at 10.4%, the second highest for breast cancer at 9.6% and the third highest for head and neck cancer at 9.3%. The stratification of institutions indicates that the rate of increase for lung cancer was notable for A1 institutions and the rates for prostate cancer were high for all categories, ranging from 8.0–20.3%. On the other hand, the rate for breast cancer was the lowest (–0.7%) for A2, while those for B1 and B2 ranged from 11.8–18.8%, and the rates for head and neck cancer were high for A2 (17.7%) and B1 (21.4%).

Table 6 shows the distribution of use 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, IMRT and hyperthermia increased by 23.3%, 14.5%, 4.9%, 34.8% and 15%, respectively, compared with 2007 [6]. On the other hand, the use of intraoperative RT decreased significantly by –31.1%. Institutional stratification shows that there was a dramatic increase of 454.1% in the use of IMRT in B2 [5]. In 2009,

Table 4: Structure and personnel by PCS institutional stratification

	Structure and personnel					
	A1 (n = 70)	**A2 (n = 70)**	**B1 (n = 280)**	**B2 (n = 280)**	**Total (n = 700)**	**Comparison with data of 2007 [a] (%)**
Institutions/total institutions (%)	10.0	10.0	40.0	40.0	100	-
Institutions with RT bed (n)	59 (84.3)	37 (52.9)	124 (44.3)	78 (27.9)	298 (42.6)	6.0 (3.6 [b])
Average RT beds/institution (n)	11.2	3.3	3.1	1.5	3.3	6.5
Number of ROs (full time + part time)	369 + 64	151 + 35	372 + 216	193 + 245	1085 + 560	6.7
JASTRO-certified RO (full time)	214	73	192	52	531	11.3
Average JASTRO-certified RO/institution (n)	3.1	1.0	0.7	0.2	0.8	14.2
Total (full-time and part-time) RO FTE*	321.1	110.7	350.1	157.5	939.4	13.7
Average FTE ROs/institution	4.6	1.6	1.3	0.6	1.3	18.2
Patient load/FTE RO	193.5	205.2	290.6	198.4	231.9	-6.7
Number of RT technologists (full time + part time)	492 + 22	280 + 13	1133 + 33	825 + 2	2730 + 70	4.4
Total (full-time and part-time) RT technologist FTE	434.3	206.8	758.6	436.2	1836.0	12.4
Average FTE RT technologists/institution	6.2	3.0	2.7	1.6	2.6	13.0
Patient load/FTE RT technologist	143.0	109.9	134.1	71.7	118.6	-5.5
Number of full-time nurse (full time + part time)	114 + 26	74 + 13	270 + 82	125 + 50	583 + 171	-37.1
Total (full-time and part-time) nurse FTE	135.4	68.7	290.4	126.8	621.2	25.6
Number of medical physicists (full time + part time)	70 + 5	27 + 2	125 + 10	65 + 5	287 + 22	10.8
Total (full-time and part-time) medical physicist FTE	32.3	8.7	54.4	22.0	117.6	71.9
Number of RT QA staffs (full time + part time)	79 + 0	52 + 0	174 + 3	85 + 3	390 + 6	-26.1
Total (full-time and part-time) RT QA staff FTE	25.8	15.2	50.3	25.0	116.3	9.1

JASTRO = Japanese Society of Therapeutic Radiation Oncology; RO = radiation oncologist; FTE = full-time equivalent (40 h/wk only for RT practice); QA = quality assurance; other abbreviations as in Table 2. RT QA staff: Japanese Organization of RT Quality Management has certified RT quality managers from RT technologist since 2005 mainly by educational session.Data in parentheses are percentages.

[a]Rate of increase compared with the data of 2007. Calculating formula: $\frac{data\ of\ 2009\ (n) - data\ of\ 2007\ (n)}{data\ of\ 2007\ (n)} \times 100\ (\%)$

[b]Comparison with the data of 2007. Calculating formula: *data of* 2009 (%) − *data of* 2007 (%)

101 institutions (14.4%) actually utilized IMRT, which was significantly lower than the 337 Linacs with IMRT function (41.3%) as shown in Table 2. Figure 2 lists the numbers of patients treated with SRT and IMRT for each survey year. Approximately 12 000 patients were treated with SRT for the brain in each survey year and this number has remained stable. On the other hand, the number treated with SRT for the rest of the body has been increasing gradually and exceeded 2000 in 2009. The corresponding number of patients for IMRT has been increasing more rapidly and exceeds 4000, or about 2% of all RT-treated patients in 2009.

Table 7 shows the number of patients with brain or bone metastasis treated with radiation according to the same institutional stratification. More patients with brain metastasis (12.2% of all patients) were treated at B1 than at the other types of institutions, while use of radiation for bone

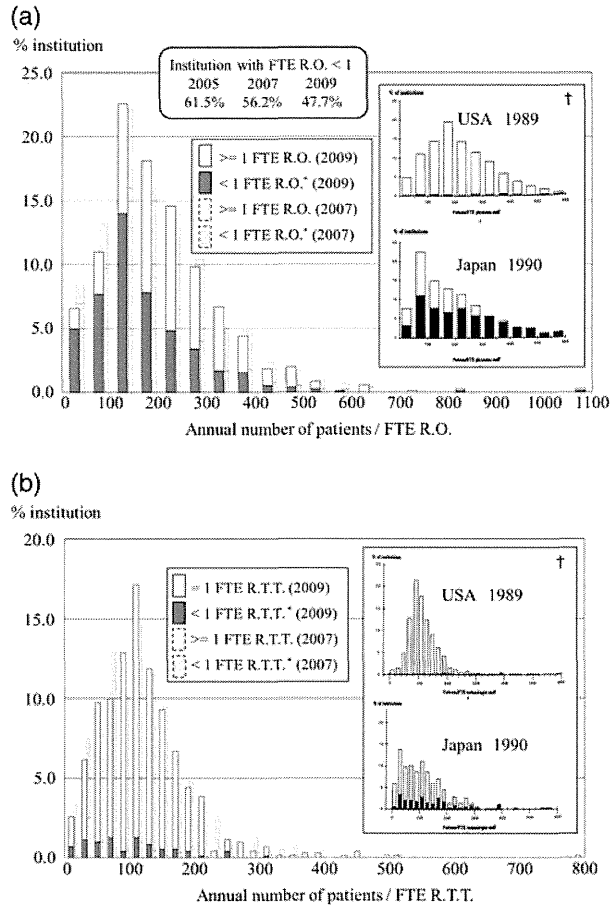

Fig. 1. (**a**) Percentage distribution by institution for patient load/full-time equivalent (FTE) radiation oncologists (ROs) in Japan; (**b**) corresponding percentage distribution for patient load/full-time equivalent (FTE) radiotherapy technologists in Japan (a) Spacing of the bars represents intervals of 50 patients/FTE radiation oncologist. Open bars represent institutions with one or more FTE staff member, and solid bars represent institutions with less than one FTE radiation oncologist. The number of FTEs for institutions with less than one FTE staff member was calculated as the equivalent of one FTE to avoid overestimating patient load per FTE RO or staff. (b) *Spacing of the bars represents intervals of 20 patients/FTE staff. †Corresponding data for the USA and Japan are shown for reference [3]. Originally published in Int. J. Radiat. Oncol. Biol. Phys. 34(1): 235–242.

metastasis ranged from 10.4% for A2 to 15.7% for B2. Overall, more patients with bone metastasis were treated with radiation at non-academic than at academic institutions. The number of patients with brain metastasis decreased slightly by –4.7% compared with 2007 [6].

Geographic patterns

Figure 3 shows the geographic distributions for 47 prefectures of the annual number of patients (new plus repeat) per 1000 population arranged in increasing order of the number of JASTRO-certified ROs per 1 000 000 population [20]. There were significant differences in the use of RT, from 1.1 patients per 1000 population (Saitama) to 2.3 (Tokyo). The average number of cancer patients per 1000 population per quarter ranged from 1.57 to 1.80 ($P = 0.1585$). 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. Similar trends were clearly observed in 2005 [5] and 2007 [6]. Compared with 2005 and 2007, the utilization rate of RT increased in every prefecture in 2009. However, the rates in 2007 and 2009 were not related to prefectural population density as was also observed in the data for 1990 [3].

DISCUSSION

In 1990, there were fewer facilities for radiation treatment and fewer patients treated with radiation in Japan than in the USA. Over the next 19 years, however, the number of patients in Japan increased significantly by a factor of 3.2 [3]. On the other hand, the utilization rate of radiation for new cancer patients remained at 27.6%, less than half that recorded in the USA and European countries, although the rate increased slightly by 0.75% per year between 2007 [6] and 2009. For implementation of the Cancer Control Act, comparative data of the structure of radiation oncology in Japan and in the USA as well as relevant PCS data proved to be very helpful.

Compared with 1990, the number of Linac systems increased significantly by a factor of 2.62 and increased by 1.1% over 2007 [6], while the number of systems using telecobalt decreased to only nine and remained stable. Furthermore, the use of various functions of Linac, such as dual energy, 3DCRT (MLC width <1 cm) and IMRT, improved significantly. The number of high dose rate (HDR) RALS in use has increased and ^{60}Co RALS has been largely replaced with ^{192}Ir RALS. In 2009, CT simulators had been installed in 82.1% of institutions throughout the country for a 15.7% increase over 2007 [6] and exceeded the number of X-ray simulators (51.6%). Radiotherapy planning systems (RTPs) were used at 96.0% of institutions for an increase in the number of RTPs of 6.59 times compared with 1990 [3]. Maturity of the functions of Linac and installation rates of CT simulators and systems using ^{192} Ir RALS also improved further compared with 2007 [6], but were still closely correlated with the PCS institutional stratification, which could therefore aid accurate differentiation between structural maturity and immaturity and the identification of structural targets for improvement.

The staffing patterns in Japan also improved in terms of numbers. However, institutions with less than one FTE radiation oncologist on their staff still account for 47.7% nationwide, although this represents an 8% decrease

Table 5. Primary sites of cancer treatment with RT in 2009 by PCS institutional stratification for new patients

Primary site	A1 ($n = 69$)		Comparison with data of 2007[a] (%)	A2 ($n = 66$)		Comparison with data of 2007[a] (%)	B1 ($n = 256$)		Comparison with data of 2007[a] (%)	B2 ($n = 253$)		Comparison with data of 2007[a] (%)	Total ($n = 644$)		Comparison with data of 2007[a] (%)
	n	%		*n*	%		*n*	%		*n*	%		*n*	%	
Cerebrospinal	1906	3.8	–5.7	994	5.4	38.1	4812	6.2	–13.6	1349	5.4	–3.4	9061	5.3	–6.6
Head and neck (including thyroid)	6444	12.8	–1.2	2500	13.6	17.7	7601	9.8	21.4	1560	6.3	–5.7	18 105	10.6	9.3
Esophagus	3247	6.5	–5.8	1196	6.5	1.4	3735	4.8	–8.2	1416	5.7	–3.9	9594	5.6	–5.7
Lung, trachea and mediastinum	7880	15.7	5.6	2771	15.0	–2.8	15 855	20.4	–5.7	5801	23.3	–0.7	32 307	18.9	–2.0
Lung	7335	14.6	8.0	2438	13.2	–0.6	14 358	18.5	–1.3	5060	20.4	–6.2	29 191	17.0	0.0
Breast	10 869	21.7	5.2	3637	19.7	–0.7	19 373	24.9	11.8	5955	24.0	18.8	39 834	23.3	9.6
Liver, biliary tract, pancreas	1948	3.9	1.0	806	4.4	19.6	2907	3.7	3.6	980	3.9	–4.2	6641	3.9	3.2
Gastric, small intestine, colorectal	2167	4.3	4.4	945	5.1	–6.9	3783	4.9	–6.2	1384	5.6	–7.6	8279	4.8	–4.0
Gynecologic	3430	6.8	3.5	1135	6.2	7.3	2914	3.7	–4.7	737	3.0	–5.6	8216	4.8	0.0
Urogenital	7167	14.3	5.8	2470	13.4	–1.1	10 019	12.9	2.8	3394	13.7	13.4	23 050	13.5	4.7
Prostate	5926	11.8	9.9	1888	10.2	8.0	7618	9.8	8.6	2487	10.0	20.3	17 919	10.5	10.4
Hematopoietic and lymphatic	2639	5.3	1.9	963	5.2	7.0	3264	4.2	–10.1	1083	4.4	15.8	7949	4.6	–1.3
Skin, bone and soft tissue	1269	2.5	–12.8	496	2.7	2.5	1590	2.0	–15.4	738	3.0	–1.7	4093	2.4	–10.4
Other (malignant)	541	1.1	–39.5	241	1.3	1.7	852	1.1	–5.0	307	1.2	5.1	1941	1.1	–16.3
Benign tumors	675	1.3	–31.7	278	1.5	4.5	1112	1.4	–13.7	155	0.6	–16.7	2220	1.3	–18.6
Pediatric <15 y (included in totals above)	461	0.9	4.8	145	0.8	25.0	349	0.4	–6.7	137	0.6	8.7	1092	0.6	3.4
Total	50 182	100	0.8	18 432	100	4.3	77 817	100	0.6	24 859	100.0	4.3	171 290	100	1.5

Abbreviations as in Table 2.

[a]Rate of increase compared with the data of 2007. Calculating formula: $\frac{data\ of\ 2009\ (n) - data\ of\ 2007\ (n)}{data\ of\ 2007\ (n)} \times 100\ (\%)$

[b]Total number of new patients different with these data, because no data on primary sites were reported by some institutions.

Table 6: Distribution of specific treatments and numbers of patients treated with these modalities by PCS stratification of institutions

Specific therapy	A1 ($n = 70$)		A2 ($n = 70$)		B1 ($n = 280$)		B2 ($n = 280$)		Total ($n = 700$)		Comparison with data of 2007[a] (%)
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	
Intracavitary RT											
Treatment facilities	64	91.4	28	40.0	58	20.7	1	0.4	151	21.6	
Cases	1864		421		848		6		3139		–3.0
Interstitial RT											
Treatment facilities	55	78.6	20	28.6	32	11.4	2	0.7	109	15.6	
Cases	2482		550		993		45		4070		23.3
Radioactive iodine therapy for prostate											
Treatment facilities	50	71.4	16	22.9	29	10.4	1	0.4	96	13.7	
Cases	1842		360		856		22		3080		14.5
Total body RT											
Treatment facilities	63	90.0	31	44.3	65	23.2	21	7.5	180	25.7	
Cases	798		235		620		137		1790		4.9
Intraoperative RT											
Treatment facilities	15	21.4	6	8.6	4	1.4	3	1.1	28	4.0	
Cases	135		21		9		8		173		–31.1
Stereotactic brain RT											
Treatment facilities	43	61.4	26	37.1	94	33.6	39	13.9	202	25.8	
Cases	1660		658		9671		1866		13 855		10.4
Stereotactic body RT											
Treatment facilities	51	72.9	26	37.1	71	25.4	17	6.1	165	23.6	
Cases	1087		185		1125		140		2537		1.9
IMRT											
Treatment facilities	47	67.1	10	14.3	36	12.9	8	2.9	101	14.4	
Cases	1855		94		1961		386		4296		34.8
Thermoradiotherapy											
Treatment facilities	7	10.0	5	7.1	4	1.4	4	1.4	20	2.9	
Cases	185		38		137		31		391		15.0

PCS = Patterns of Care Study; RT = radiotherapy; IMRT = intensity-modulated radiotherapy.

[a]Rate of increase compared with the data of 2007. Calculating formula: $\frac{data\ of\ 2009\ (n) - data\ of\ 2007\ (n)}{data\ of\ 2007\ (n)} \times 100\ (\%)$

compared with 2007 [6]. In other words, nearly half the institutions in Japan still rely on part-time radiation oncologists. There are two reasons for this. First, although the number of FTE radiation oncologists grew by 13.7 % over the last 2 years, the number of cancer patients who require radiation has also increased by 10% over the same period. Second, specialist fees for radiation oncologists in academic institutions are not covered by the Japanese medical care insurance system, which is strictly controlled by the government. Therefore, most radiation or other oncologists at academic institutions must work part-time at affiliated hospitals in the B1 and B2 groups to earn a living. To reduce the number of institutions that rely on part-time radiation oncologists and thus may encounter problems with their quality of care, a reform of Japan's current medical care system based on treatment outcome is required, especially as it applies to staff at academic institutions. However, great care is needed to ensure that the long-term success of radiation oncology in Japan and patient benefits are well balanced with costs. For this reason, personal identification of ROs in both A and B institutions was included and recorded in the 2007 and 2009 surveys for further detailed analysis of patient load and real cost [7]. There were significant differences in the average practice index for patients between ROs working mainly in main university hospitals and in affiliated hospitals (1.07 vs 0.71: $P < 0.0001$). Under the current Japanese national medical system, patterns of work by ROs at academic facilities appear to be problematic for fostering true specialization of ROs. On the other hand, according to the increase in the number of cancer patients who require RT, B1 institutions are gradually offering full-time positions for ROs. However, the speed of offers for second or third positions are slow in individual institutions due to tight budgets in most B1 institutions. Therefore, monitoring these structural data is necessary to convince local government to improve working environments for ROs. Even under these conditions, however, the number of FTE ROs increased by 2.57 times compared with 1990 [3], and by 13.7% over 2007 [6]. On the other hand, patient load per FTE RO also increased by 1.35 times to 231.9 during the same period 1990–2009, but registered a –0.67% decrease compared

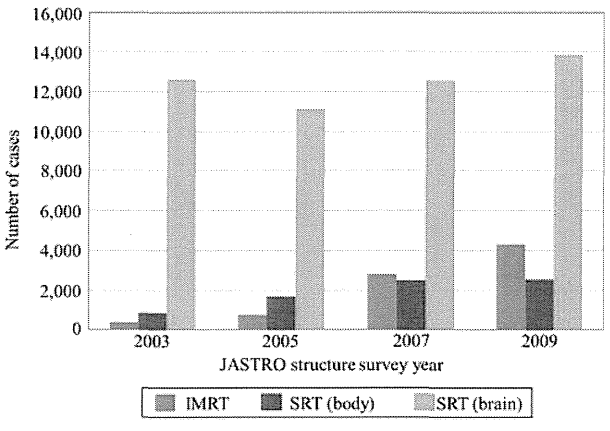

Fig. 2. Trends in numbers of patients treated with SRT for brain, SRT for body and IMRT by survey year

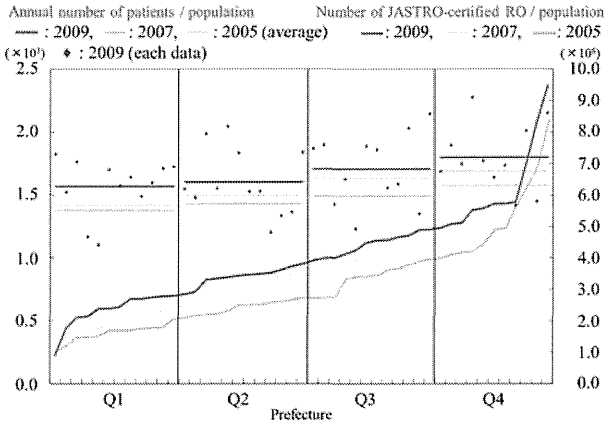

Fig. 3. Geographic distribution for 47 prefectures of annual numbers of patients (new plus repeat) per 1000 population in increasing order for JASTRO-certified radiation oncologists (RO)/ 1 000 000 population by prefecture Q1, 0–25%; Q2, 26–50%; Q3, 51–75%; and Q4, 76–100%. Horizontal lines show average annual number of patients (new plus repeat) per 1000 prefectural population per quarter.

Table 7: brain metastasis or bone metastasis patients treated with RT in 2007 by PCS institutional stratification

Metastasis	Patients										Comparison with data of 2007[a] (%)
	A1 ($n = 70$)		A2 ($n = 70$)		B1 ($n = 280$)		B2 ($n = 280$)		Total ($n = 700$)		
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	
Brain	3534	5.2	1363	6.0	12 394	12.2	3043	9.7	20 334	9.3	–4.3
Bone	6948	11.2	2419	10.6	12 618	12.4	4921	15.7	26 906	12.4	–3.8

Data presented as number of patients, with percentages in parentheses.
[a]Rate of increase compared with the data of 2007. Calculating formula: $\frac{data\ of\ 2009\ (n) - data\ of\ 2007\ (n)}{data\ of\ 2007\ (n)} \times 100\ (\%)$

with 2007 [6]. This may reflect the growing popularity of RT due to an increase in the elderly population and recent advances in technology and improvement in clinical results. The caseload ratio in Japan has therefore already exceeded the limit of the Blue Book guidelines of 200 patients per radiation oncologist and improved only slightly in 2009 [21, 22]. The percentage distribution of institutions by patient load per RO showed a slightly high percentage for smaller patient load/RO than that in the USA in 1989 [3], but also showed a major shift to a larger size in 2009 compared with 1990. In Japan, the patterns are now becoming similar to those of the USA in 1989 [3], indicating that Japanese radiation oncology is catching up quickly with western systems and growing steadily in spite of limited resources. Furthermore, additional recruiting and education of ROs continue to be top priorities for JASTRO. The distribution of patient load per RT technologist shows that only 17.3% of institutions met the narrow guideline range (100–120 patient per RT technologist) and the rest showed a dense distribution around the peak level. Compared with the distribution in the USA in 1989, nearly 18% of institutions in Japan had a relatively low caseload of 10–60, because there are still a large number of smaller B2-type institutions, which account for nearly 40% of institutions that do not attain the range specified by the guidelines. As for medical physicists, an analysis of patient load for FTE staff similar to that for RT technologists remains difficult, because the number of the former was very small and they were working mainly in metropolitan areas. However, RT technologists in Japan have been acting partly as medical physicists. Their training duration has changed from 3 to 4 years over the last decade, and graduate and postgraduate courses have been introduced. Currently, RT technologists who have obtained a master's degree or those with enough clinical experience can take the examination for qualification as a medical physicist, as can those with a master's degree in science or engineering like in the USA or Europe. A unique, hybrid education system for medical physicists has thus been developed in Japan since the Cancer Control Act actively started to support improvement in quality assurance and quality control (QA/QC) specialization for RT. However, the validity of this education and training system remains to be proven, not only for QA/QC but also for unique research and developmental activities. The discrepancy between FTE medical physicists and the number of registered medical physicists in Japan reflects the fact that their role in the clinic is not recognized as a full-time position only for medical physics services.

Analysis of the distribution of primary sites for RT showed that the number of lung cancer patients at A1-type institutions increased by 8% compared with 2007. On the other hand, more head and neck cancer patients were treated at A1-, A2- or B1-type institutions, but the rates of increase compared with 2007 were high for A2 and B1 institutions. The increase in the number of lung cancer patients at A1 institutions in 2009 was noteworthy and the same goes for that of prostate cancer patients or breast cancer patients at A1-, A2-, B1- and B2-type institutions. This suggests that stereotactic body RT (SBRT) for lung cancer at A1 and 3DCRT for prostate cancer or breast-conserving therapy for breast cancer (BCT) at A1, A2, B1 and B2 were used more frequently in 2009. Especially in B2-type institutions, breast cancer patients (18.8%) and prostate cancer patients (20.3%) increased at two of the highest rates. This indicates that treatments such as 3DCRT and BCT were disseminated widely to B2-type institutions as a standard. The number of patients with brain or bone metastasis did not increase compared with 2007 [6]. The use of specific treatments and the number of patients treated with these modalities were significantly affected by institutional stratification, with more specific treatments being performed at academic institutions. These findings indicate that significant differences in patterns of care, as reflected in structure, process and possibly outcome for cancer patients continued to be prevalent in Japan in 2009. However, these differences point to opportunities for improvement. The Japanese PCS group published structural guidelines based on PCS data [22] and we are using the structural data obtained in 2009 to revise the Japanese structural guidelines for radiation oncology in the near future. The use of intraoperative RT decreased significantly from 2005 to 2007 and showed a similar rate of decrease (35%) between 2007 and 2009, while that of thermoradiotherapy increased slightly by 15% compared with 2007 [6]. These two modalities are thus not considered mainstay treatments in Japan. The numbers of patients with bone metastasis or brain metastasis in 2009 decreased, compared with those in 2007. Within the limited resources of departments of radiation oncology, more efforts may be made, focusing on radical treatment than palliative ones. Also general treatments such as bisphosphonates or narcotic drugs such as opioids for bone metastasis may relatively reduce the candidates for RT. The reason for the reduction in use of RT for brain metastasis is unknown.

Geographic patterns showed that there were significant differences among prefectures in the use of RT, and the number of JASTRO-certified physicians per population was associated with the utilization of RT in 2005 [5], 2007 [6] and 2009, so that a shortage of radiation oncologists or medical physicists on a regional basis will remain a major concern in Japan. Compared with 2005 [5] and 2007 [6], however, the utilization rate of radiation for new cancer patients in 2009 showed further increase. JASTRO has been making every effort to recruit and educate radiation oncologists and medical physicists through public relations, to establish and conduct training courses at academic

institutions, to become involved in the national examination for physicians and to seek an increase in the coverage of fees for ROs by the government-controlled insurance scheme.

In conclusion, the Japanese structure of radiation oncology has clearly and steadily improved over the past 19 years in terms of installation and use of equipment and its functions, but shortages of man power and differences in maturity depending on type of institution and caseload remain. Structural immaturity is an immediate target for improvement, while for improvements in process and outcome, the PCS or National Cancer Database (NCDB), which are currently operational and the subject of close examination, can be expected to perform an important function in the future of radiation oncology in Japan.

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ORIGINAL ARTICLE

Long-term outcomes of intraluminal brachytherapy in combination with external beam radiotherapy for superficial esophageal cancer

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Abstract
Background The aim of this study was to assess the long-term outcomes of combining high-dose-rate intraluminal brachytherapy (IBT) with external beam radiotherapy (EBRT) for superficial esophageal cancer (SEC).
Methods From 1992 to 2002, 87 patients with T1N0M0 thoracic esophageal cancer received IBT in combination with EBRT. Of these, 44 had mucosal cancer and 43 had submucosal cancer. For patients with tumor invasion within the lamina propria mucosa, IBT alone was performed ($n = 27$). IBT boost following EBRT was performed for patients with tumor invasion in the muscularis mucosa or deeper ($n = 60$). No patient received chemotherapy.
Results The median follow-up time was 94 months. For mucosal cancer, the 5-year locoregional control (LRC), cause-specific survival (CSS) and overall survival (OS) rates were 75, 97 and 84%, respectively, and 49, 55 and 31%, respectively, for submucosal cancer. Tumor depth was a significant factor associated with LRC ($p = 0.02$), CSS ($p < 0.001$) and OS ($p < 0.001$) by univariate analysis. Multivariate analysis revealed that tumor depth was the only significant predictor for OS ($p = 0.003$). Late toxicities of grade 3 or higher in esophagus, pneumonitis, pleural effusion and pericardial effusion were observed in 5, 0, 0 and 1 patients, respectively. Grade ≥ 3 events of cardiac ischemia and heart failure after radiotherapy were observed in 9 patients, and history of heart disease before radiotherapy was the only significant factor ($p = 0.002$).
Conclusion There was a clear difference in outcomes of IBT combined with EBRT between mucosal and submucosal esophageal cancers. More intensive treatment should be considered for submucosal cancer.

Keywords Esophageal cancer · Superficial esophageal cancer · Squamous cell carcinoma · Radiotherapy · Brachytherapy

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Introduction

Advances in endoscopic equipment have enabled the treatment of increasing numbers of patients with superficial esophageal cancer (SEC) [1–3], which can be divided into mucosal and submucosal cancers. In SEC patients treated by surgery, pathological analyses have shown significant differences in rates of lymph node (LN) metastasis according to tumor depth: 0–6% in the mucosa and 38–53% in the submucosa [4–9]. Among mucosal cancer patients, when tumor cells were found within the lamina propria mucosa there was almost no LN metastasis (0–1.4%), whereas in patients with tumors invading to the muscularis mucosa, a ratio of LN metastases of more than 10% was reported [4]. Endoscopic resection is generally indicated for patients with tumors invading within the lamina propria mucosa. For patients with tumors invading the muscularis mucosa or deeper, esophagectomy with systematic LN dissection is the main treatment. However, due to the extent of surgery, the alternative of radiotherapy (RT) is often selected for patients in poor medical condition or advanced age, and its efficacy has been reported by several authors [10–14].

Brachytherapy is a RT technique that can deliver a high dose to local tumors while sparing exposure to the surrounding normal tissues. Intraluminal brachytherapy (IBT) has been used mainly for SEC in Japan, while in Western countries IBT has been used with palliative intent for malignant esophageal strictures. The efficacy of IBT combined with external beam radiotherapy (EBRT) for SEC has been reported [15–19], and this method was considered an effective treatment in Japan in the 1990s. We performed IBT combined with EBRT for SEC patients until 2002, following the introduction in 1991 of the high-dose-rate iridium-192 remote afterloading system (micro-Selectron HDR from Nucletron, Netherlands). Subsequently, the protocol was changed and chemoradiotherapy (CRT) was introduced for SEC. In this study, the long-term outcomes of IBT combined with EBRT for SEC were evaluated.

Patients and methods

Patient and tumor characteristics

Patient and tumor characteristics are listed in Table 1. There were 87 patients eligible for this study with T1N0M0 (International Union Against Cancer TNM system, 1997) thoracic esophageal cancer who received IBT combined with EBRT between 1992 and 2002. The median age was 70 years (range 43–89), with 80 males and 7 females. Sixty-nine patients had Karnofsky performance status (KPS) of 90 or more. RT was selected in 54 patients who were judged medically inoperable and in 33 patients who declined surgery. Medically inoperable factors included concurrent illnesses, advanced age and coexisting malignancies. Main concurrent illnesses included heart disease in 14, hepatic disease in 18 and pulmonary disease in 9. Coexisting malignancies were observed in 28 patients, and 16 had malignancies within 5 years before the diagnosis of esophageal cancer. Among them, 12 had active malignancies. Taken together, these malignancies were distributed as follows: gastric cancer in 11, head and neck cancer in 10, hepatocellular carcinoma in 4, colorectal cancer in 3 and lung cancer in 2. Histologically, 86 patients had squamous cell carcinoma and one had adenocarcinoma. Tumor sites were upper thoracic in 8 patients, middle thoracic in 65 and lower thoracic in 14. Forty-four had mucosal cancer and 43 had submucosal cancer. Of the 44 mucosal cancer patients, 25 received incomplete endoscopic mucosal resection (EMR) for tumors within the lamina propria mucosa, i.e., positive margin or partial resection of multiple or large lesions for the purpose of diagnosing tumor depth.

Table 1 Patient and tumor characteristics

Characteristics	No. of patients (%)
Age (years)	
Range	43–89
Median	70
Gender	
Male	80 (92)
Female	7 (8)
KPS	
90–100	69 (79)
60–80	18 (21)
Reasons for selecting RT	
Medically inoperable	54 (62)
Patient refused surgery	33 (38)
Double cancer	
All	28 (32)
Within 5 years	16 (18)
Histology	
Squamous cell	86 (99)
Adenocarcinoma	1 (1)
Tumor sites	
Upper thoracic	8 (9)
Middle thoracic	65 (75)
Lower thoracic	14 (16)
Tumor depth	
Mucosal	44 (51)
Submucosal	43 (49)

KPS Karnofsky performance status, *RT* radiotherapy

Treatment

Intraluminal brachytherapy was performed using the high-dose-rate iridium-192 remote afterloading system. The double-balloon applicator was used for IBT. The outer diameter of the applicator was either 16 or 20 mm, and the latter was mainly used. A prescribed dose was calculated at a depth of 5 mm from the surface of the esophageal mucosa.

EBRT was administered with 6 or 18 MV X-rays. After irradiation with 45–46 Gy using a fractional dose of 1.8–2.0 Gy to the primary tumor and regional LN area with anterior–posterior opposed beams, a planned dose was delivered to the primary tumor with oblique opposed beams to spare the spinal cord.

For patients with tumors within the lamina propria mucosa who had almost no risk of LN metastases, IBT alone was performed ($n = 27$). IBT was performed 5 days per week and irradiation doses were 35 Gy/14 fractions in 15 patients, 36 Gy/18 fractions in 9, 30 Gy/15 fractions in 2 and 25 Gy/5 fractions in 1.

Intraluminal brachytherapy boost following EBRT was performed for patients with tumors in the muscularis mucosa or deeper who had risk of LN metastases ($n = 60$). Irradiation doses of EBRT were 50–58 Gy/25–29 fractions (median 54 Gy) in cases of tumors in the muscularis mucosa or inner one-third of the submucosa and 54–61 Gy/27–33 fractions (median 60 Gy) in cases of tumors in the outer two-thirds of the submucosa. The IBT boost was generally performed immediately after EBRT using a schedule of 5 days per week. IBT boost doses were 10 Gy/4 fractions in 29, 10 Gy/5 fractions in 25, 10 Gy/2 fractions in 3, 7.5 Gy/3 fractions in 1, and 15 Gy/3 fractions in 1.

In this study, no patient received chemotherapy.

Analysis

The data were updated in June 2009. The median follow-up time for survivors was 94 months (range 28–187) and for all patients 64 months (range 2–187). There were 3 patients who were lost to follow-up within 60 months from RT. The follow-up periods of these 3 patients were 28, 56 and 57 months. Complete response (CR) was defined as the disappearance of the primary tumor by endoscopic biopsy. Overall survival (OS) was defined as the time from the initiation of RT to death from any cause. Cause-specific survival (CSS) was defined as the time from the initiation of RT to death due to esophageal cancer. Locoregional control (LRC) was calculated from the initiation of RT to the earliest events of recurrences in esophageal primary site, esophageal metachronous cancers and regional LN metastases. OS, CSS and LRC rates were calculated using the Kaplan–Meier method. Comparison of data was analyzed by Fisher's exact test. Univariate (UVA) and multivariate analyses (MVA) were performed using the log-rank test and the Cox proportional hazards test. A p value of <0.05 was considered significant. Toxicities were assessed using the Common Terminology Criteria for Adverse Events (CTCAE) v3.0.

Results

Response and failures

Treatment outcomes are shown in Table 2. Initial response was evaluated 8–181 days (median 31 days) after RT. Two patients were not evaluated because one died in a traffic accident soon after treatment, and concurrent illness

Table 2 Treatment outcomes

Outcomes	No. of patients (%)		
	Mucosal ($n = 44$)	Submucosal ($n = 41$)	Total ($n = 85$)
Initial response (evaluable cases)			
Complete response	43 (98)	40 (98)	83 (98)
Partial response	1 (2)	1 (2)	2 (2)
Recurrences			
Locoregional	14 (32)	19 (46)	30 (39)
Esophagus—primary site	5 (11)	8 (20)	13 (15)
Esophagus—metachronous	8 (18)	4 (10)	12 (14)
Lymph node—in EBRT field	0 (0)	1 (2)	1 (1)
Lymph node—out of EBRT field	1 (2)	4 (10)	5 (6)
Distant	0 (0)	1 (2)	1 (1)
Unknown	1 (2)	1 (2)	2 (2)

EBRT external beam radiotherapy, *RT* radiotherapy

progressed after treatment in the other patient. In 85 evaluable patients, 83 (98%) achieved CR and residual cancer cells were confirmed in 2 patients. Failures were observed in 33: locoregional failures in 30, distant metastasis (malignant pleural effusion) in 1 and unspecified in 2. Among the 30 patients with locoregional failures, one had failure at the primary esophageal site and regional LN metastasis concurrently. Esophageal failures were observed in 25 patients: 13 were primary tumor failures and 12 were metachronous esophageal cancers. There were no differences according to tumor depth in the occurrence rate of all esophageal failures, primary site failures and metachronous esophageal cancers. Regional LN metastases were observed in 6 patients. Although submucosal cancer patients showed a high rate of regional LN metastasis compared with mucosal cancer patients, the difference lacked significance (2% in mucosal and 12% in submucosal cancer, $p = 0.10$). Furthermore, 5 failures were not in the EBRT field and one was in the EBRT field.

Among the 33 patients with failures, an early stage failure detected as a superficial esophageal lesion was observed in 15 patients and an advanced stage failure was observed in 18. According to the depth of tumor, the occurrence rate of advanced stage failures was significantly higher in submucosal cancer patients (7% in mucosal and 37% in submucosal cancer, $p < 0.01$). Regarding salvage treatments for 15 patients with early stage failures, 14 patients were salvaged by esophagectomy or endoscopic resection. For 18 patients with advanced stage failures, only one patient who received lymphadenectomy with adjuvant CRT for LN metastasis out of the EBRT field was salvaged.

Survival rates and prognostic factor

At the time of last follow-up, 49 of 87 patients had died. Seventeen patients had esophageal cancer deaths including one treatment-related death; 2 in mucosal and 15 in submucosal cancer patients. Submucosal cancer patients showed a higher rate of esophageal cancer deaths compared with mucosal cancer patients ($p < 0.01$). Eleven patients died of other malignancies: lung cancer in 3, hepatocellular carcinoma in 3, head and neck cancer in 2, and single cases each of malignant lymphoma, bile duct carcinoma and bladder sarcoma. Among these 11 patients, 3 had esophageal metachronous cancers and 1 had LN recurrence, however, all of them were controlled by salvage treatments. Twenty-one patients died of intercurrent diseases: pulmonary infection in 9, heart disease in 4, hepatic failure in 2, unknown cause in 2 and single cases each of renal failure, suicide, senility and cerebral thrombosis.

The 5-year OS, CSS and LRC for all patients were 58% [95% confidence intervals (CI) 48–69%], 78% (95% CI 69–88%) and 63% (95% CI 52–75%), respectively (Fig. 1). According to the depth of tumors, the 5-year OS, CSS and LRC for mucosal and submucosal cancers were 84% (95% CI 73–95%) and 31% (95% CI 17–46%), 97% (95% CI 92–100%) and 55% (95% CI 38–73%), and 75% (95% CI 62–89%) and 49% (95% CI 36–67%), respectively (Fig. 2a–c). There were significant differences in OS, CSS and LRC between mucosal and submucosal cancer ($p < 0.01$, $p < 0.01$ and $p = 0.02$, respectively). Prognostic factors according to UVA are summarized in Table 3. The significant factors for LRC were tumor depth ($p = 0.02$) and tumor length ($p = 0.01$), those for CSS were tumor depth ($p < 0.01$) and tumor length ($p = 0.02$), and those for OS were KPS ($p = 0.04$), operability ($p = 0.02$), double cancer within 5 years ($p < 0.01$) and tumor depth ($p < 0.01$). MVA for OS revealed that tumor depth was the only significant prognostic factor ($p < 0.01$).

Toxicity

Toxicities are summarized in Table 4. Grade ≥3 acute toxicities of esophagitis, leucopenia and thrombocytopenia occurred in 2, 1 and 0 patients, respectively. Grade ≥3 late toxicities of esophageal ulcers, pneumonitis, pleural effusion and pericardial effusion were observed in 5, 0, 0 and 1 patients, respectively. Details of Grade ≥3 late toxicities of the esophageal ulcers are shown in Table 5. All of them received IBT boost following EBRT and 3 patients developed esophago-mediastinal fistulas concurrently. One needed bypass surgery (Grade 4) and another died of mediastinitis (Grade 5). The other 3 patients recovered by conservative treatment. The lone patient with Grade 3 pericardial effusion, who was the same patient with Grade 3 esophago-mediastinal fistula, developed Grade 2 pleural effusion concurrently. Both pericardial and pleural effusion decreased after recovery from the fistula. Regarding

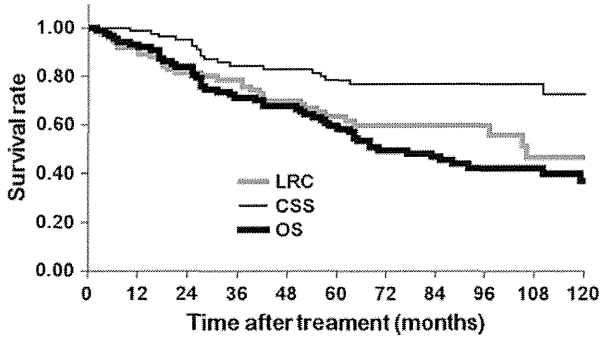

Fig. 1 Curves for overall survival (*OS*), cause-specific survival (*CSS*) and locoregional control (*LRC*) rates for all patients. The 5-year OS, CSS and LRC were 58% (95% CI 48–69%), 78% (95% CI 69–88%) and 63% (95% CI 52–75%), respectively

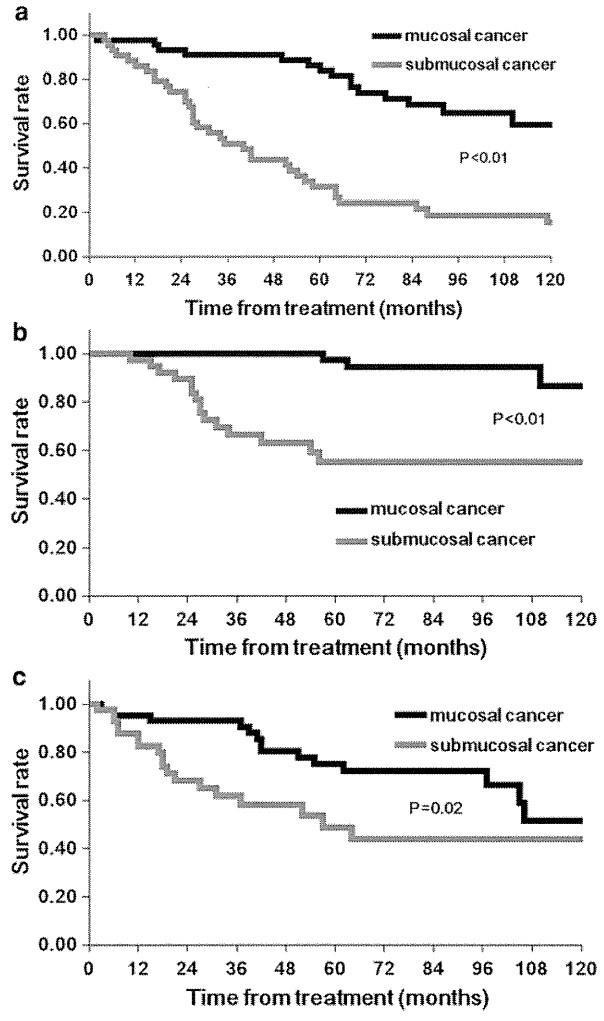

Fig. 2 **a** Curves for OS according to tumor depth. The 5-year OS for mucosal and submucosal cancer were 84% (95% CI 73–95%) and 31% (95% CI 17–46%), respectively ($p < 0.01$). **b** Curves for CSS according to tumor depth. The 5-year CSS for mucosal and submucosal cancer were 97% (95% CI 92–100%) and 55% (95% CI 38–73%), respectively ($p < 0.01$). **c** Curves for LRC according to tumor depth. The 5-year LRC for mucosal and submucosal cancer were 75% (95% CI 62–89%) and 49% (95% CI 36–67%), respectively ($p = 0.02$)

occurrence of Grade ≥3 esophageal ulcers, no significant factor emerged.

We also investigated cardiac ischemia and heart failure after RT (Grade ≥3 according to CTCAE v3.0) (Table 6). Cardiac ischemia occurred in 5 patients. Two patients died of acute myocardial infarction, at 2 and 6 months after RT. One had a history of angina and the other patient had a history of brain infarction and KPS of 60. The time to onset of the other 3 patients was 22, 76 and 151 months after RT. They received stent placement and were alive 65, 24 and 13 months later, respectively. Four patients suffered heart failure. One died of heart failure at 64 months after RT; he had a history of dilated cardiomyopathy. The time to onset of the other 3 patients was 42, 46 and 124 months. They received pacemaker placement; one of them died of malignant lymphoma 9 months later; the other 2 patients were alive 18 and 47 months later. Investigation of significant factors associated with cardiac ischemia and heart failure revealed that a history of heart disease before RT was the only significant factor ($p = 0.002$) (Table 7).

Discussion

With advances in endoscopic equipment, the number of SECs treated has increased. According to the report of the Registry of Esophageal Carcinomas in Japan, SEC accounted for 8.5% of esophageal cancer patients treated in 1979–1982 and 28% in 1998–1999 [1, 2]. In the data of the Japanese Patterns of Care Study, 21% of the esophageal cancer patients who were treated with RT in 1999–2001 had SEC [3].

In our study, there was a clear difference in treatment results depending on the depth of tumor invasion. Tumor depth was a significant factor for OS, CSS and LRC by UVA. Furthermore, tumor depth was the only significant factor for OS by MVA. Favorable treatment outcomes in mucosal cancer were achieved in this study. The CR rate was 98% and the 5-year OS, CSS and LRC were 84, 97 and 75%, respectively. These results were almost equivalent to that reported for surgery [4–9]. Most of the mucosal cancers in this study were large or multiple lesions that were difficult to completely resect by EMR or had margin-positive lesions after EMR. In the 1990s, surgery or radiotherapy was often considered for these lesions. However, remarkable progress in endoscopic techniques has resulted in significant changes. Recently, endoscopic submucosal dissection (ESD) has been increasingly used as a new technique of endoscopic resection. ESD facilitates en-bloc resection even in large lesions where piecemeal resection was needed by EMR. Takahashi et al. [20] reported that ESD reduced the local recurrence rate (0.9% in the ESD group and 9.8% in the EMR group) significantly and that the disease-free survival rate was significantly better with ESD than with EMR. Most mucosal cancers can now be cured by endoscopic treatment alone due to advances in the technique of endoscopic resection. Thus, surgery and RT in the treatment of mucosal cancer have been relegated to a limited role.

Initial response for submucosal cancer was considered equally good as that achieved for mucosal cancer. CR rate was 98% and high long-term LRC and survival rates were anticipated. However, the 5-year OS, CSS and LRC were 31, 55 and 49%, respectively. These results were obviously inferior to those of mucosal cancer, and little difference

Table 3 Prognostic factors

Patient characteristics	*n*	LRC		CSS		OS		
		5-year rate (%)	UVA	5-year rate (%)	UVA	5-year rate (%)	UVA	MVA
Age (years)								
≤70	49	61	n.s.	84	n.s.	65	n.s.	–
>70	38	67		72		51		
Gender								
Male	80	62	n.s.	77	n.s.	58	n.s.	–
Female	7	86		100		57		
KPS								
90–100	71	61	n.s.	79	n.s.	64	0.04	0.222
60–80	16	74		73		37		
Operability								
Operable	33	63	n.s.	86	n.s.	72	0.010	0.076
Inoperable	54	63		73		50		
Double cancer within 5 years								
Yes	16	69	n.s.	90	n.s.	64	0.007	0.485
No	71	63		77		31		
Tumor depth								
Mucosal	44	75	0.023	97	<0.001	84	<0.001	0.003
Submucosal	43	49		55		31		
Tumor length (cm)								
≤3.0	63	72	0.012	85	0.026	63	n.s.	–
>3.0	24	38		63		45		
Circumferential extent								
≤1/2	70	65	n.s.	79	n.s.	60	n.s.	–
>1/2	17	57		78		51		
Multiple Lugol-voiding regions								
Yes	59	58	n.s.	78	n.s.	58	n.s.	–
No	28	74		81		60		
Multiple cancer in esophagus								
Yes	21	69	n.s.	81	n.s.	52	n.s.	–
No	66	62		78		60		

KPS Karnofsky performance status, *LRC* locoregional control rate, *CSS* cause-specific survival rate, *OS* overall survival rate, *UVA* univariate analysis, *MVA* multivariate analysis, *n.s.* not significant

Table 4 Toxicity

	G2	G3	G4	G5	≥G3 (%)
Acute					
Esophagitis	22	2	0	0	2 (2%)
Leukopenia	3	1	0	0	1 (1%)
Thrombocytopenia	1	0	0	0	0 (0%)
Late					
Esophagus	3	3	1	1	5 (6%)
Pneumonitis	2	0	0	0	0 (0%)
Pleural effusion	3	0	0	0	0 (0%)
Pericardial effusion	–	1	0	0	1 (1%)

G grade

was seen when compared with previous reports of RT alone [10–16]. The main pattern of failures was locoregional failures (18 of 19 patients with failures). These outcomes suggest that treatment needs to be intensified to improve the locoregional control rate for submucosal cancer patients.

Table 5 Details of patients with esophageal ulcer (≥Grade 3)

	Depth	Treatment	Complication	Grade	Support
1	Mucosal	EBRT + IBT	Ulcer + perforation	3	TPN
2	Submucosal	EBRT + IBT	Ulcer	3	TPN
3	Submucosal	EBRT + IBT	Ulcer	3	TPN
4	Submucosal	EBRT + IBT	Ulcer + perforation	4	Bypass surgery
5	Submucosal	EBRT + IBT	Ulcer + perforation	5	Death

EBRT external beam radiotherapy, *IBT* intraluminal brachytherapy, *TPN* total parental nutrition

Table 6 Details of patients with heart disease (≥Grade 3)

	Sex	Age	History of HD	Tumor site	Treatment	Complication	Onset (months)	Outcome (months)	
1	Male	69	Angina	Mt	IBT	CI	2	Dead with AMI	2
2	Male	78	–	Mt	EBRT + IBT	CI	5	Dead with AMI	6
3	Male	61	–	Mt	EBRT + IBT	CI	22	Alive	87
4	Male	70	–	Mt	EBRT + IBT	CI	76	Alive	100
5	Male	73	AR	Mt	EBRT + IBT	CI	151	Alive	164
6	Male	84	–	Lt	EBRT + IBT	HF	42	Dead with ML	51
7	Male	65	DCM	Lt	EBRT + IBT	HF	50	Dead with HD	64
8	Male	71	OMI	Mt	EBRT + IBT	HF	46	Alive	64
9	Male	55	AF	Mt	EBRT + IBT	HF	124	Alive	171

HD heart disease, *EBRT* external beam radiotherapy, *IBT* intraluminal brachytherapy, *CI* cardiac ischemia, *HF* heart failure, *AR* aortic regurgitation, *DCM* dilated cardiomyopathy, *OMI* old myocardial infarction, *AF* atrial fibrillation, *AMI* acute myocardial infarction, *ML* malignant lymphoma, *Mt* middle thoracic esophagus, *Lt* lower thoracic esophagus

Intraluminal brachytherapy is a RT method that can deliver an isolated high dose to local tumors while sparing the surrounding normal tissues. Its efficacy for SEC has been reported by several authors [13–19]. However, a significant advantage of IBT in the treatment of esophageal cancer remains to be demonstrated. The Study Group of the Japanese Society of Therapeutic Radiology and Oncology reported no advantage when IBT was compared with EBRT alone [11]. Recently, some promising results of IBT combined with EBRT for submucosal cancer were reported by Ishikawa et al. [19] from Gunma University. Their study showed a significant difference in the 5-year CSS between the IBT + EBRT group and EBRT alone (86 vs. 62%, $p = 0.04$). However, there were no significant differences in LRC, OS and recurrence-free survival. Furthermore, according to the Japanese Patterns of Care Study, the performance rate of IBT in the treatment of esophageal cancer in Japan has been decreasing [3]. Concurrent CRT has become the standard therapy as a non-surgical treatment for locally advanced esophageal cancer, because randomized controlled trials revealed the efficacy of CRT [21–23]. Recently, the efficacy of CRT for SEC has been studied. Yamada et al. [24] reported that the 5-year OS of CRT for stage I esophageal cancer was 66.4%. Kato et al. reported the outcome of a phase II trial of CRT in patients with stage I esophageal cancer. In their study, the 4-year OS was 80.5% [25]. The survival rates from these studies were equivalent to those of surgery. There has thus been a shift from RT alone to CRT in the RT methods for SEC.

In this study, 13 primary site recurrences and 12 metachronous esophageal cancers were observed. Fifteen of these 25 lesions were detected as superficial lesions and 14 of these were successfully salvaged. Meanwhile, most of the patients who developed advanced recurrences died of esophageal cancer. This suggests that detection of esophageal failures or metachronous cancers as a superficial lesion by periodic endoscopy is very important.

In treating with IBT, avoiding the toxicity of treatment-related esophageal ulcer is of critical importance. Nemoto et al. [10] recommended that the IBT fractional dose should not exceed 5 Gy to prevent esophageal ulcers. Akagi et al. [26] have also recommended a small fractional dose of 2.0 or 2.5 Gy in high-dose-rate IBT to minimize esophageal complications. In our study, Grade ≥3 esophageal ulcer occurred in 5 patients (6%). This incidence rate was comparatively low; however, Grade 4 and 5 ulcers

Table 7 Late toxicities: heart disease

Characteristics	*n*	Heart disease	
		n (%)	*p* value
Age (years)			
≤70	49	5 (10)	n.s.
>70	38	6 (16)	
Gender			
Male	80	9 (11)	n.s.
Female	7	2 (29)	
KPS			
90–100	71	7 (10)	n.s.
60–80	16	4 (25)	
Operability			
Operable	33	2 (6)	n.s.
Inoperable	54	9 (17)	
Tumor depth			
Mucosal	44	6 (14)	n.s.
Submucosal	43	5 (12)	
Tumor length (cm)			
≤3.0	63	7 (11)	n.s.
>3.0	24	4 (17)	
Treatment			
IBT alone	27	2 (7)	n.s.
IBT + EBRT	60	9 (15)	
Diabetes mellitus			
Yes	14	2 (14)	n.s.
No	73	9 (12)	
Heart disease history			
Yes	14	6 (43)	0.002
No	73	5 (7)	
Hypertension			
Yes	15	2 (13)	n.s.
No	72	9 (13)	
Alcoholic drinking			
Yes	64	7 (11)	n.s.
No	23	4 (17)	
Tobacco smoking			
Yes	66	7 (11)	n.s.
No	21	4 (19)	

KPS Karnofsky performance status, *n.s.* not significant

occurred in patients treated with IBT fractional doses of 2.0 and 2.5 Gy. We need to be aware of the occurrence of severe esophageal ulcer even when we perform IBT with a low fractional dose.

In our study, Grade ≥3 pneumonitis, pleural effusion and pericardial effusion developed in 0, 0 and one patient, respectively. This result suggests that RT without chemotherapy was safe regarding these toxicities. We also investigated cardiac ischemia and heart failure after treatment. Nine patients suffered Grade ≥3 events. Two died of AMI and one died of heart failure. Five of them had a history of heart disease, and a history of heart disease was the only significant factor associated with developing events of cardiac ischemia and heart failure after RT ($p = 0.002$). Radiation-induced heart disease is one of the complications after thoracic RT. The effects on various portions of heart, such as pericardium, myocardium or coronary artery, due to RT have been reported [27–29]. In CRT of esophageal cancer, cardiopulmonary toxicities became problems to be solved after the report by Ishikura et al. [30]. We are not sure whether all events of cardiac ischemia and heart failure in this study occurred due to irradiation. However, in the RT for esophageal cancer, irradiation to the heart cannot be avoided. Therefore, efforts should be made to decrease the irradiation dose to the heart as much as possible using the newest technique. Furthermore, follow-up with attention to development of heart disease is important.

As mentioned previously, the role of IBT has been limited in the treatment of SEC. However, we consider that IBT can be a treatment option for mucosal cancer patients who have multiple or large legions that have a risk of severe esophageal stenosis by endoscopic resection and for submucosal cancer patients who have difficulties in receiving surgery or concurrent chemotherapy because of high age or concurrent illnesses.

In conclusion, there was a clear difference in treatment results depending on tumor depth. The outcomes of IBT combined with EBRT for submucosal cancer were not satisfactory and more intensive treatment should be considered. In our institution, CRT was introduced for submucosal cancer after 2002 and the efficacy and safety of CRT are currently under investigation.

Conflict of interest No author has any conflict of interest.

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Computerized estimation of patient setup errors in portal images based on localized pelvic templates for prostate cancer radiotherapy

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We have developed a computerized method for estimating patient setup errors in portal images based on localized pelvic templates for prostate cancer radiotherapy. The patient setup errors were estimated based on a template-matching technique that compared the portal image and a localized pelvic template image with a clinical target volume produced from a digitally reconstructed radiography (DRR) image of each patient. We evaluated the proposed method by calculating the residual error between the patient setup error obtained by the proposed method and the gold standard setup error determined by consensus between two radiation oncologists. Eleven training cases with prostate cancer were used for development of the proposed method, and then we applied the method to 10 test cases as a validation test. As a result, the residual errors in the anterior–posterior, superior–inferior and left–right directions were smaller than 2 mm for the validation test. The mean residual error was 2.65 ± 1.21 mm in the Euclidean distance for training cases, and 3.10 ± 1.49 mm for the validation test. There was no statistically significant difference in the residual error between the test for training cases and the validation test ($P = 0.438$). The proposed method appears to be robust for detecting patient setup error in the treatment of prostate cancer radiotherapy.

Keywords: Computerized method; patient setup error; prostate cancer; portal image; digitally reconstructed radiography; template matching technique

INTRODUCTION

The incidence of prostate cancer has increased throughout the world, even in Japan [1] and other Asian countries that historically have had a low incidence of prostate cancer. This trend has led to a growing number of patients receiving radiation therapy as a definitive treatment for prostate cancer. Recently, high-precision radiotherapies such as conformal radiotherapy (CRT) and intensity-modulated radiation therapy (IMRT) have been routinely employed for dose escalation to the whole prostate and/or reduction of rectal toxicity [2]. Accurate patient setup is essential in high-precision radiotherapy for prostate cancer, because deviations in the delivered beam geometry may result in decreased tumor control and increased complications in the surrounding normal tissue. However, the majority of clinical facilities do not have an automatic setup system, and thus the radiation oncologists or radiological technologists