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Scientific Article

Lumbosacral Plexopathy After Carbon-ion Radiation Therapy for Postoperative Pelvic Recurrence of Rectal Cancer: Subanalysis of a Prospective Observational Study (GUNMA 0801)

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Purpose: Data are lacking on the risk factors for radiation-induced lumbosacral plexopathy (RILSP) after carbon-ion radiation therapy (CIRT) for pelvic tumors, such as postoperative recurrence of rectal cancer. We investigated the incidence of RILSP and the associated dosimetric parameters using data from a prospective study of CIRT for postoperative pelvic recurrence of rectal cancer (GUNMA 0801).

Methods and Materials: The GUNMA 0801 study included 28 patients, of which we analyzed 20 without lumbosacral plexopathy prior to CIRT. The total dose of CIRT was 73.6 Gy (relative biological effectiveness [RBE]) in 16 fractions. The incidence of RILSP and parameters of the dose-volume histogram were evaluated for the lumbosacral plexuses. RILSP was graded according to the Common Terminology Criteria for Adverse Events version 4.0.

Results: Median follow-up was 24 months. The incidence of all RILSP (grades 1 and 2) and grade 2 RILSP was 22.5% (9/40) and 10% (4/40) of 40 lumbosacral plexuses in 20 patients, respectively, and no grade ≥ 3 toxicity was observed. Throughout the dose range, the volumes of the irradiated lumbosacral plexuses were significantly higher in patients with RILSP than in patients without RILSP ($P < .001$ for Dmax, D0.5 cm^3 − D2 cm^3, V20 Gy(RBE) − V70 Gy(RBE)). D2 cm^3 and V50 Gy(RBE) were considered useful for receiver operating characteristic analysis. Cutoff values for RILSP were 73.82 Gy(RBE) and 33.2% for D2 cm^3 and V50 Gy(RBE), respectively.

Conclusions: We demonstrated the incidence and predictive dosimetric parameters for RILSP after CIRT and showed that D2 $cm^3 \geq 73.82$ Gy(RBE) and V50 Gy(RBE) = 33.2% are cutoff values for predicting RILSP. These results would improve treatment plans using CIRT for patients with pelvic recurrences of rectal cancer.

Introduction

Surgery with preoperative chemotherapy or chemoradiation therapy is the most effective method for treating naïve, resectable rectal cancer. Although local recurrence rates have decreased in this era of robotic-assisted surgery,

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The analyzed data sets generated during the study are available from the corresponding author upon reasonable request.

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2% to 5% rates have been reported.[1,2] After local recurrence, pelvic exenteration is the most likely treatment modality for postoperative pelvic recurrence of rectal cancer, but the R0 resection rate is 55% to 80%.[3-5] Many patients with local recurrence are unsuitable for curative resection, which is often highly invasive in terms of loss of function, complications, and old age. For patients with unresectable pelvic recurrence of rectal cancer, treatment options include X-ray radiation therapy (RT), including stereotactic body RT (SBRT). However, clinical outcomes of X-ray RT, including SBRT, were 16% to 41% in 5-year overall survival and 56% to 74% in 4- and 5-year local control, respectively, which are unsatisfactory.[6-8] Although rare, adverse events, such as grade 4 intestinal tract perforation and grade 3 neuropathy, have been reported.[6,8] Furthermore, a report on proton beam therapy for postoperative rectal cancer recurrence showed 3-year local control and overall survival rates of 80.2% and 71.3%, respectively, with no grade 3 or higher adverse events, although case numbers remain limited.[9]

In the last decade, clinical outcomes of patients with pelvic recurrence of rectal cancer treated with carbon-ion RT (CIRT), which has physical and biological advantages over x-rays, have been favorable, with 3-year local control and overall survival rates of 85% to 93% and 73% to 92%, respectively.[10-12] By contrast, 2% to 7% of the patients developed grade $\geq$ 3 toxicity after CIRT, and 5% to 14% of the patients developed grade 2 lumbosacral plexopathy.[10-13] Although grade 2 lumbosacral plexopathy is not life-threatening, it should be avoided because it reduces patient quality of life. Dose-volume histogram analyses with or without dose constraints have been reported on the gastrointestinal tract, skin, and bone; however, little is known about the dose constraints of lumbosacral plexopathy in CIRT.[14-16]

We have conducted a prospective clinical trial (GUNMA 0801) of CIRT for pelvic recurrence of rectal cancer.[11] Additionally, we performed dose-volume histogram analysis for radiation-induced lumbosacral plexopathy (RILSP) in this prospective cohort to clarify dose constraints.

Methods and Materials

Study design

We have conducted a prospective observational study (GUNMA 0801) for postoperative recurrence of rectal cancer. We used data from cases enrolled in GUNMA 0801 for this dosimetric analysis of lumbosacral plexopathy. We excluded patients with lumbosacral plexopathy prior to CIRT or tumors distant from the lumbosacral plexus. The study was approved by the institutional review board of Gunma University Hospital and registered with the University Hospital Medical Information Network in Japan (UMIN; ID, 000009719; prospectively registered on January 8, 2013). Written informed consent for participation was obtained from all the participants.

The eligibility criteria for GUNMA 0801 were as follows: patients (1) had pelvic recurrence of rectal cancer without distant metastasis, confirmed by histology or diagnostic imaging; (2) had curative resection of primary disease and regional lymph nodes, without gross or microscopic residual disease; (3) had radiographically measurable tumors; (4) had Eastern Cooperative Oncology Group performance status $\leq$ 2; and (5) were aged between 20 and 80 years. Patients with direct invasion of the bladder and/or gastrointestinal tract, chemotherapy within 4 weeks, prior RT to the target area, intractable infections in the target area, or another active malignancy were excluded.[11]

The protocol for GUNMA 0801 included a 3-year follow-up period from the start of CIRT. Pelvic magnetic resonance imaging scans were taken at 3 and 6 months after starting CIRT, and then every 6 months up to 36 months. Thoracic and abdominal computed tomography scans were performed at 6 and 12 months after starting CIRT, and then annually until 36 months. On recurrence, protocol testing was discontinued. All patients were examined every 3 months and taken thoracic and abdominal computed tomography scans every 6 months at our hospital unless a recurrence occurred.

CIRT

C-ion beams were generated using a synchrotron at Gunma University Heavy Ion Medical Center. Passive scattering was used to treat pelvic recurrence of rectal cancer. Beam energy was 290, 380, or 400 MeV/u based on tumor depth. At our facility, radiation dose was calculated using XiO-N—an XiO (Elekta)-based software that incorporates a dose engine for ion-beam RT (K2dose)—developed by the National Institute of Radiological Sciences, with interfaces of Mitsubishi Electric.[17] The dose of CIRT was expressed in Gy (relative biological effectiveness [RBE]), defined as the physical dose multiplied by the RBE of C-ion beams.[18]

Target delineation and treatment planning

Preparation for CIRT, target delineation, treatment planning, and evaluation during follow-up were performed as described.[11] Patients received CIRT once daily, 4 days a week (Tuesday to Friday). CIRT was performed with 73.6 Gy(RBE) in 16 fractions for 4 weeks (4.6 Gy [RBE] per fraction). Dose constraints were defined as mean dose (D_{mean}) < 50 Gy(RBE) and maximum

dose (D_{max}) < 60 Gy(RBE) to the intestinal tract and dose delivered to 1 cm^3 volume of the bladder (D1 cm^3) < 60 Gy(RBE). No dose constraints were defined for the peripheral nerves.

Assessment of RILSP

Patients were followed up for 1 month after CIRT and every 3 months thereafter. RILSP was evaluated based on symptoms of neuralgia or peripheral motor or sensory neuropathy of the lower extremities, according to the Common Terminology Criteria for Adverse Events, version 4.0. Grades 1, 2, and 3 are defined as "asymptomatic, clinical or diagnostic observations only, intervention not indicated"; "moderate symptoms, limiting instrumental activities of daily living"; and "severe symptoms, limiting self-care activities of daily living, assistive device indicated," respectively. To ensure that pelvic recurrence did not influence RILSP, we censored the analysis at the time of pelvic recurrence.

Contouring and dose-volume analysis of the lumbosacral plexus

The bilateral lumbosacral plexus was delineated following the contouring protocol developed by Yi et al (Fig. 1).[19] Briefly, the lumbosacral plexus was delineated from the L4 to L5 interspace to the level of the superior-most portion of the femoral neck with reference to the pelvic musculature, iliac vessels, and vertebral and pelvic bones. Dose-volume analysis of the lumbosacral plexus was performed using XiO-N (Elekta). DX was the minimum dose in the most irradiated tissue volume of X cm^3 and VY indicating the percentage of each side of the lumbosacral plexus irradiated with Y Gy(RBE). We assessed Dmax, Dmean, D0.5 cm^3, D1 cm^3, D2 cm^3, V20 Gy (RBE), V30 Gy(RBE), V40 Gy(RBE), V50 Gy(RBE), V60 Gy(RBE), and V70 Gy(RBE) for the lumbosacral plexus.

Statistical analysis

The cumulative incidence of RILSP was evaluated using the Kaplan-Meier method and measured from the date of CIRT initiation to the date of occurrence of RILSP or the most recent follow-up. Additionally, cases of pelvic recurrence after CIRT were terminated on the date of pelvic recurrence in the observation of RILSP because the recurrent tumor might cause neurological symptoms. Patient-related predictive factors for RILSP were examined using univariate analysis using the Cox proportional hazards model.

Cutoff values for V_X for classifying RILSP were determined using receiver operating characteristic (ROC) curve analysis. Differences in values between 2 groups were examined using the Mann-Whitney *U* test. Pearson's chi-square test was used to test the association between 2 categorical variables. *P* values < .05 were considered statistically significant. Statistical analysis was performed using SPSS (version 28; SPSS Inc).

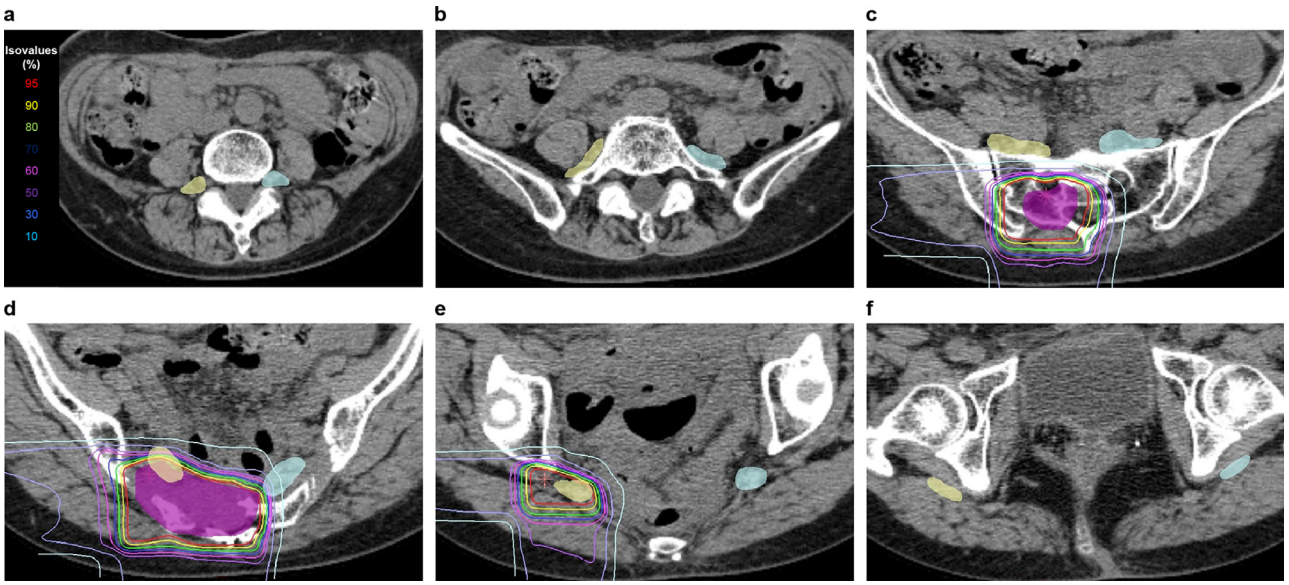

Figure 1 Axial images of the lumbosacral plexus. (a) L5 vertebral body level. (b) L5/S1 level. (c) S2 level. (d) S3 level. (e) S4 level. (f) S5 level. The clinical target volume is shown in magenta. The right and left lumbosacral plexuses are displayed in yellow and blue, respectively. Dose distribution on an axial CT image. Highlighted areas represent 95% (red), 90% (yellow), 80% (green), 70% (dark blue), 60% (magenta), 50% (purple), 30% (blue), and 10% (light blue) isodose curves (100% is 73.6 Gy [RBE]). *Abbreviations:* CT = computed tomography; RBE = relative biological effectiveness.

Results

Patients

The GUNMA 0801 study included 28 patients between October 2011 and July 2017. We excluded 8 patients because of unsuitability and analyzed 20 patients with 40 lumbosacral plexuses (Fig. E1). Patient characteristics of all and those separated by the presence of RILSP after CIRT are summarized in Table 1. The follow-up rate was 95% (19/20). Eleven cases were followed up at our hospital through 36 months, while other cases were followed up at external hospitals, with information sent to our hospital.

Incidence of RILSP

With a median follow-up of 24 months (range, 2-100 months), grade 1 and grade 2 RILSP were observed in 25% (5/20) and 20% (4/20) patients, respectively. No grade $\geq$ 3 RILSP was observed. No case had bilateral RILSP. When lumbosacral plexuses on both sides were analyzed separately, all RILSP (grades 1 and 2) and grade 2 RILSP were observed in 23% (9/40) and 10% (4/40) lumbosacral plexuses in 20 patients, respectively. The median interval from initiation of CIRT to developing RILSP was 11 months (range, 2-25 months). The 2-year cumulative incidence of grades 1 to 2 and 2 RILSP was 46% and 26% for 20 patients and 25% and 13% for 40 lumbosacral plexuses, respectively (Fig. 2).

Dose-volume histogram analysis of RILSP

To identify the dosimetric parameters associated with RILSP after CIRT, we performed dose-volume analysis for the lumbosacral plexus. The volume of the lumbosacral plexus irradiated with C-ions was significantly higher

Table 1 Patient characteristics

		RILSP		
Characteristic	**All (n = 20)**	**positive (n = 9)**	**negative (n = 11)**	***P* value**
Age (y)				.230
Median (range)	62 (47-76)	67 (47-74)	58 (51-76)	
Gender				.175
Male	11	3	8	
Female	9	6	3	
CTV volume (cc)				.941
Median (range)	132.7 (24.1-690.9)	135.0 (33.4-690.9)	130.5 (24.1-352.9)	
Location of recurrence				0.403
Sidewall	14	7	7	
Presacral region	4	2	2	
Perineum	2	0	2	
Diabetes mellites				1.000
Yes	2	1	1	
No	18	8	10	
Chemotherapy after surgery before CIRT				1.000
Yes	9	4	5	
No	11	5	6	
Chemotherapy after CIRT				.285
Yes	4	3	1	
No	16	6	10	
Platinum-containing drug				.769
Yes	6	3	3	
No	14	6	8	

Abbreviations: CTV = clinical target volume; CIRT = carbon-ion radiation therapy; LSP = lumbosacral plexus; RILSP = radiation-induced lumbosacral plexopathy.

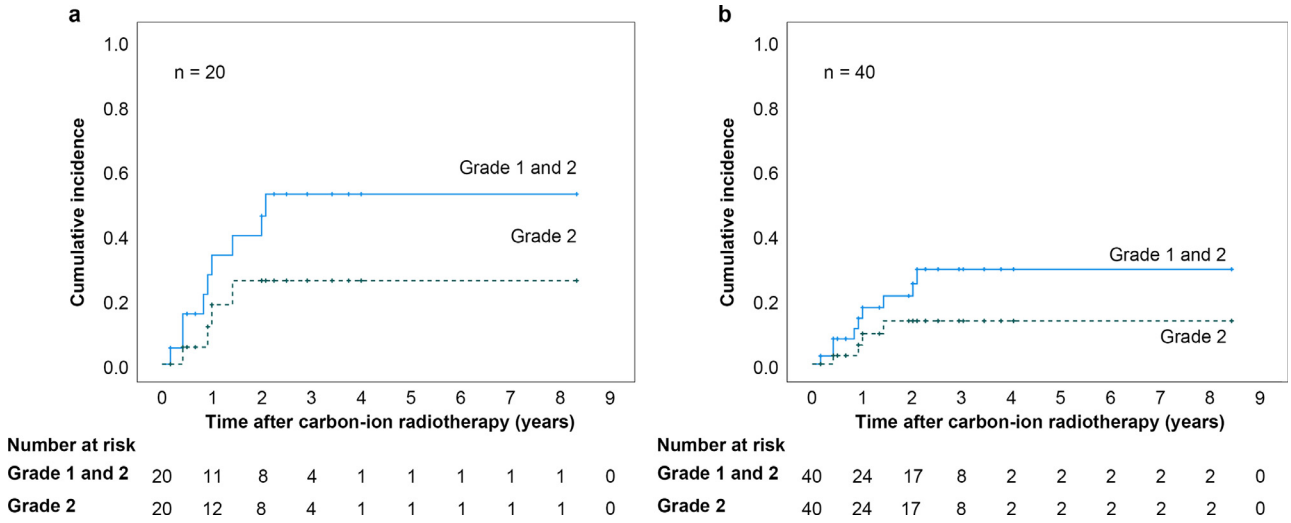

Figure 2 Cumulative incidence of grade 1 or 2 radiation-induced lumbosacral plexopathy (RILSP) after carbon-ion radiation therapy (CIRT) in patients with recurrence of postoperative rectal cancer. We examined (a) 20 patients and (b) 40 lumbosacral plexuses in 20 patients.

in the RILSP-positive group than the RILSP-negative group ($P < .001$ for V20 Gy(RBE), V30 Gy(RBE), V40 Gy (RBE), V50 Gy(RBE), V60 Gy(RBE), and V70 Gy(RBE); Fig. 3 and Table 2). Therefore, D0.5 cm^3, D1 cm^3, D2 cm^3, Dmax, and Dmean delivered to lumbosacral plexuses were significantly higher in the RILSP-positive group than the RILSP-negative group (Table 2).

To evaluate cutoff values associated with RILSP development, ROC curve analysis was performed using dose-volume data for the lumbosacral plexus. Cutoff values in high doses for RILSP were 74.44, 73.98, 73.88, and 73.82 Gy for Dmax, D0.5 cm^3, D1 cm^3, and D2 cm^3, respectively. Area under the curve (AUC) values were 0.930, 0.934, 0.953, and 0.969 for Dmax, D0.5 cm^3, D1 cm^3, and D2 cm^3, respectively. We focused on D2 cm^3 because it had the largest AUC values. Cutoff values in volume for RILSP were 45.6%, 44.4%, 42.8%, 33.2%, 28.5%, and 15.8%, and AUC values were 0.907, 0.903, 0.910, 0.953, 0.961, and 0.953 for V20 Gy(RBE), V30 Gy(RBE), V40 Gy(RBE), V50 Gy(RBE), V60 Gy(RBE), and V70 Gy (RBE), respectively. In addition, we focused on V50 Gy (RBE) – V70 Gy(RBE) because of the large AUC values.

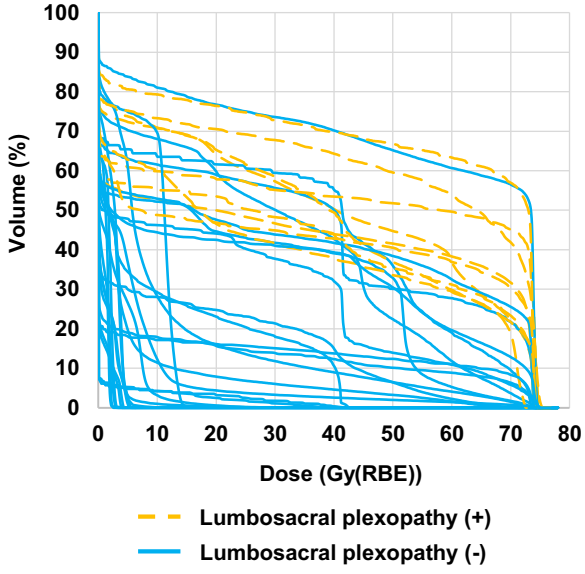

Figure 3 Cumulative dose-volume histograms for the lumbosacral plexus in patients with recurrences of postoperative rectal cancer treated with carbon-ion radiation therapy (CIRT). Yellow and blue lines indicate radiation-induced lumbosacral plexopathy (RILSP)-positive (n = 11) and -negative (n = 29) lumbosacral plexuses, respectively.

Table 2 DVH parameters

Parameter	All (n = 40) Median (range)	RILSP		
		Positive (n = 9) Median (range)	Negative (n = 31) Median (range)	*P* value
LSP volume (cc)	39.9 (25.4-58.3)	37.2 (26.7-53.5)	42.4 (25.4-58.3)	.425
Dmax (Gy[RBE])	72.3 (0.7-75.7)	74.7 (72.7-75.7)	42.7 (0.7-75.2)	<.001
Dmean (Gy[RBE])	10.8 (0.5-52.1)	36.8 (29.6-51.8)	5.3 (0.5-52.1)	<.001
D0.5 cm^3 (Gy[RBE])	68.5 (2.2-75.1)	74.3 (72.3-75.1)	40.9 (2.2-74.6)	<.001
D1 cm^3 (Gy[RBE])	59.9 (2.0-74.9)	74.2 (72.0-74.9)	35.9 (2.0-74.5)	<.001
D2 cm^3 (Gy[RBE])	48.9 (1.9-74.7)	74.1 (71.6-74.7)	24.8 (1.9-74.0)	<.001
V70 Gy(%)	1.1 (0-57.0)	30.2 (18.8-57.0)	0 (0-56.5)	<.001
V60 Gy(%)	3.2 (0-63.3)	36.9 (29.3-63.3)	0 (0-60.7)	<.001
V50 Gy(%)	6.5 (0-66.9)	41.6 (33.6-66.9)	0 (0-65.2)	<.001
V40 Gy(%)	11.5 (0-70.2)	49.4 (38.0-69.7)	1.5 (0-70.2)	<.001
V30 Gy(%)	14.5 (0-73.6)	55.1 (41.7-72.8)	3.3 (0-73.6)	<.001
V20 Gy(%)	16.1 (0-76.7)	57.9 (46.6-76.4)	4.4 (0-76.7)	<.001
length > 70 Gy (cm)	1.1 (0-8.6)	5.4 (3.0-8.6)	0 (0-6.2)	<.001

Abbreviations: DVH = dose-volume histogram. LSP = lumbosacral plexus; RBE = relative biological effectiveness; RILSP = radiation-induced lumbosacral plexopathy.

Analysis with Fisher's exact test showed significant differences for RILSP in D2 cm^3, V50 Gy(RBE), V60 Gy(RBE), and V70 Gy(RBE) (Table 3). Kaplan-Meier analysis showed that the 2-year cumulative incidence of RILSP for the lumbosacral plexus with D2 $cm^3 \geq 73.82$ Gy, V50 Gy (RBE) $\geq$ 33.2%, V60 Gy(RBE) $\geq$ 28.5%, and V70 Gy (RBE) $\geq$ 15.8% was 80.0%, 66.7%, 72.7%, and 66.7%, respectively, whereas that for patients with D2 cm^3 < 73.82 Gy, V50 Gy(RBE) < 33.2%, V60 Gy(RBE) < 28.5%, and V70 Gy(RBE) < 15.8% was 0% (log-rank test, $P < 0.001$; Fig. 4).

Discussion

In this study, we showed that the incidence of grades 1 and 2 RILSP in CIRT for patients with postoperative pelvic recurrence of rectal cancer was 45% in 20 patients, and no patient developed grade $\geq$ 3 RILSP. Additionally, the parameters to evaluate the high-dose area and volume of the irradiated lumbosacral plexus have high predictive value for patients with RILSP (Dmax, D0.5 cm^3 − D2 cm^3, and V20 Gy(RBE) − V70 Gy(RBE)). To our knowledge, our study is the first to identify the risk factors for RILSP after CIRT for postoperative pelvic recurrence of rectal cancer. Our results can be useful in optimizing a treatment plan for preventing RILSP after CIRT.

Imai et al[20] reported that for sacral chordoma, length > 10 cm and total dose > 70 Gy(RBE) were risk factors for severe neuropathy after CIRT. The study of Imai et al[20] included large pelvic bone tumors (median clinical target volume 345 cm^3) and patients with RILSP before CIRT. These patient characteristics are different from our study, in which there were no cases of lumbosacral plexopathy > 10 cm irradiated with > 70 Gy(RBE). However, both studies showed a significant correlation between RILSP occurrence and high dose (70 Gy[RBE]). Therefore, it is important to avoid hot spots in the lumbosacral plexus area that exceed 70 Gy(RBE).

Studies on dose evaluation of RILSP after X-ray RT are limited. Yi et al[19] reported that in cases of RILSP, mean maximal and mean average doses to the lumbosacral plexus were 53.7 Gy and 42.1 Gy, respectively, in Intensity-modulated-radiotherapy (IMRT)-treated patients with rectal or anal cancer. Tunio et al[21] demonstrated that mean dose >45 Gy, V40 Gy > 55%, V50 Gy > 30%, V55 Gy > 5%, and V60 Gy > 0.5% for the lumbosacral plexus were significant risk factors for RILSP in IMRT for cervical cancer. They focused on delineation levels from the inferior part of the sacroiliac joint to the ischial spine/acetabulum.[22] Although our study showed similar cutoff volumes at 50 Gy(RBE) compared with the study of Tunio et al[21], comparing the 2 treatment modalities is challenging because we used hypofractionated CIRT and Tunio et al[21] used concurrent chemotherapy. Our study used a relatively higher dose (73.6 Gy[RBE]) for target volume, and dose constraints were defined as mean dose (Dmean) < 50 Gy(RBE) and maximum dose (Dmax) < 60 Gy (RBE) to the intestinal tract. Thus, we believed that optimization of dose-volume histogram parameters, such as

Table 3 Fisher's exact test for risk factors of RILSP

		RILSP		
Parameter	**All (n = 40)**	**Positive (n = 9)**	**Negative (n = 31)**	***P* value**
D2 cm^3				
< 73.82 Gy	30	0	30	< .001
≥ 73.82 Gy	10	9	1	
V70 Gy(RBE)				
< 15.8%	28	0	28	<.001
≥ 15.8%	12	9	3	
V60 Gy(RBE)				
< 28.5%	29	0	29	< .001
≥ 28.5%	11	9	2	
V50 Gy(RBE)				
< 33.2%	28	0	28	< .001
≥ 33.2%	12	9	3	
Age (y)				
< Median	20	3	17	.451
≥ Median	20	6	14	
Gender				
Male	22	3	19	.253
Female	18	6	12	
Distance from GTV (cm)				
< 1	16	9	10	< .001
≥ 1	21	0	21	
Tumor location				
Sidewall	28	7	21	.697
*Others	12	2	10	
Chemotherapy before CIRT				
No	22	5	17	1.000
Yes	18	4	14	
Chemotherapy after CIRT				
No	32	6	26	.348
Yes	8	3	5	
Platinum-containing drug				
No	28	6	22	1.000
Yes	12	3	9	

Abbreviations: CIRT = carbon-ion radiation therapy; GTV = gross tumor volume; RILSP = radiation-induced lumbosacral plexopathy.
*presacral region and perineum.

D2 cm^3, V50 Gy(RBE), and V60 Gy(RBE), for the lumbosacral plexus area in the treatment plan, would help avoid RILSP, and studies on the effect of the dose-response relationship on the development of RILSP in CIRT are warranted.

Our findings reveal that the median interval from initiation of CIRT to occurrence of RILSP was 11 months, with 89% (8/9) of RILSP occurring within 24 months of CIRT initiation. In photon therapy, studies on the time of RILSP occurrence are limited. Yi et al[19] reported that in patients with rectal or anal cancer, the initial onset of RILSP after IMRT was 13 to 22 months.[19] Tunio et al[21] reported that in patients with cervical cancer, the initial onset of RILSP after IMRT concurrent with cisplatin was

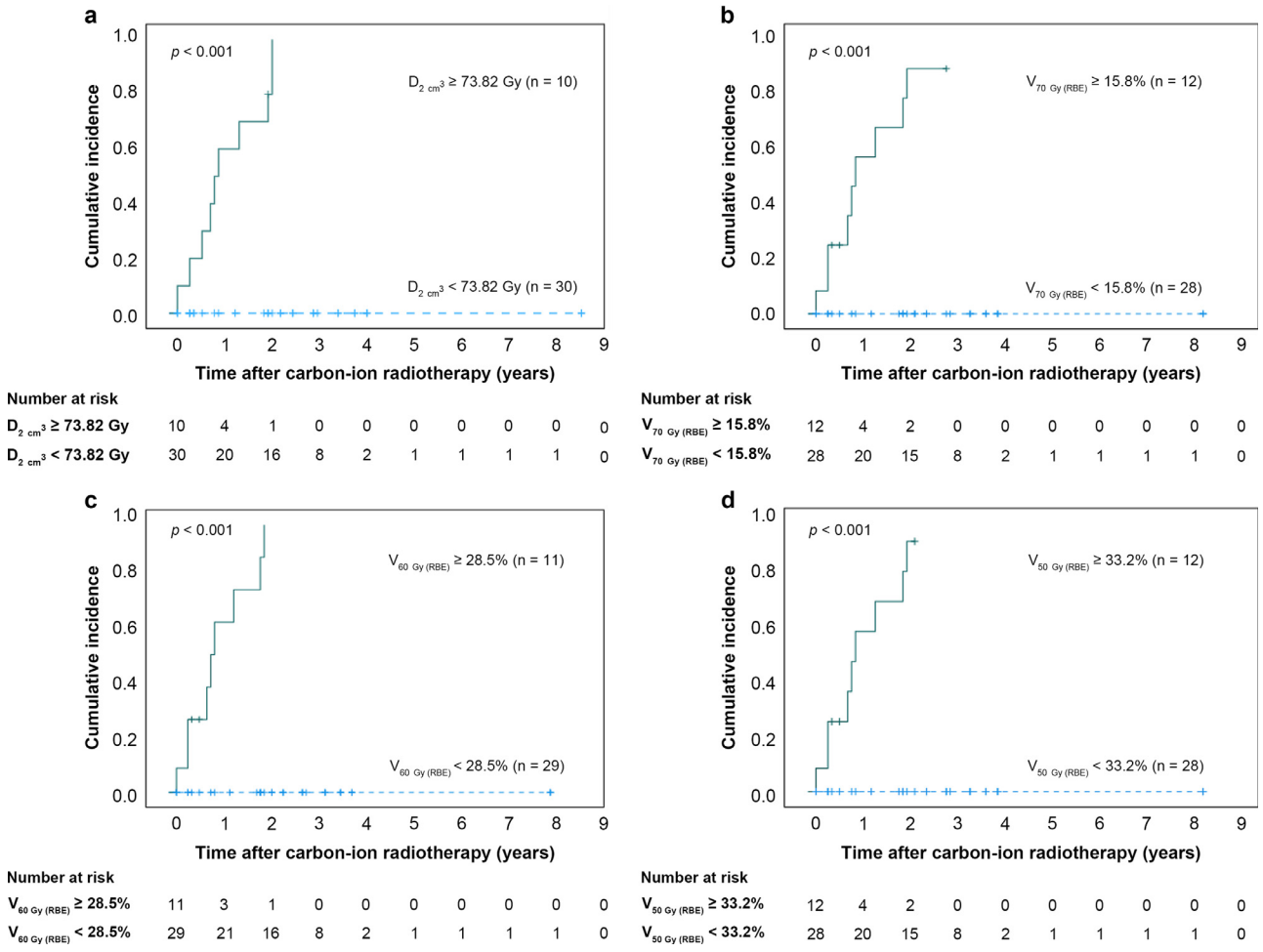

Figure 4 Cumulative incidence of grade ≥ 1 radiation-induced lumbosacral plexopathy (RILSP) stratified by (a) D2 cm^3 = 73.82 Gy, (b) V70 Gy(RBE) = 15.8%, (c) V60 Gy(RBE) = 28.5%, and (d) V50 Gy(RBE) = 33.2%. *P* value calculated using a log-rank test.

20 to 52 months. Stubblefield et al[22] reported that RILSP symptoms can arise 4 to 32 months after SBRT. The timing of RILSP onset varies across reports, and factors influencing it need further investigation regarding radiation type, dose fractionation, and combined therapy.

Our study has some limitations. First, it was unclear whether chemotherapy before and/or after CIRT affected RILSP because the GUNMA 0801 protocol did not exclude systemic chemotherapy before and after CIRT. Therefore, patient backgrounds regarding chemotherapy vary. Although there was no significant difference in the development of RILSP between the presence and absence of chemotherapy before and after CIRT in our analysis, careful evaluation with a larger cohort is needed to confirm the impact of chemotherapy. Second, we used the method of Yi et al[19]. to perform lumbosacral plexus contouring, which is controversial. According to Min et al[23], when delineating the lumbosacral plexus, the proximal components of the nerves, such as nerve roots within the spinal canal, should be included. In our study, no patient received nerve root irradiation; therefore, we followed the contouring protocol of Yi et al[19]. If sacral tumors are irradiated, the contouring method of Yi et al[19] may not be sufficient, because nerve roots are more likely to be irradiated. Third, while the observation period of this study was relatively short at 24 months, new RILSP cases may emerge with long-term follow-up. However, no studies have indicated neurological damage caused by CIRT, and previous X-ray RT reports have shown RILSP occurring after observation periods of 13 to 22, 20 to 52, and 4 to 32 months. Therefore, we conclude that the present study holds considerable value. Moreover, the linear energy transfer (LET) distribution in LSP was not verified in our study because radiotherapy treatment planning system (RTPS) in our facility is XiO-N, which cannot show the LET distribution. It is believed that LET distribution may also affect the occurrence of adverse events; therefore, future research is required.

In conclusion, we showed dosimetric parameters that predict RILSP, and the median interval from initiation of

CIRT to development of RILSP was 11 months. Our results provide useful information for optimizing the treatment plan of CIRT for pelvic recurrences of postoperative rectal cancer to prevent RILSP.

Disclosures

Tatsuya Ohno has potential financial conflicts of interest because of research funding from Hitachi Ltd. The other authors have nothing to disclose.

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Declaration of AI and AI-Assisted Technologies in the Writing Process

None.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.adro.2024.101711.

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