



The role of palliative radiation therapy in treating pleural or peritoneal disseminated tumors: 22 cases and a review of the literature

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Background: Local radiation therapy (RT) can provide pain relief and reduce bleeding resulting from pleural or peritoneal dissemination of primary tumors. However, the optimal RT exposure dose for such tumors is unclear and the response rate is unknown. In this study, we examined the effectiveness of palliative RT for pleural or peritoneal disseminated tumors to determine the optimal dose in these patients.

Methods: The data of 22 patients with pleural- or peritoneal-disseminated tumors who were treated with local RT at our institution between 2011 and 2019 were retrospectively reviewed.

Results: Among these patients, 9 (40.9%) had pleural tumors, 13 (59.1%) had peritoneal tumors and 2 had tumors in the peritoneum and umbilicus. The most common primary tumors were lung (22.8%) and pancreatic cancer (18.2%). RT was mainly administered for pain alleviation (72.7%). Three patients (13.6%) received RT for hemostasis. Thirteen patients (59.1%) received a regimen of 30 Gy/10 fractions (fr), with the total dosage for all patients ranging from 27 to 56 Gy. No grade 2 or higher RT-related adverse events occurred. Three and four patients obtained complete and partial responses, respectively. The timing of the measurement of response to pain relief ranged from 0 to 232 (median, 21) days upon completion of RT. Overall response to pain relief occurred in nine of 16 patients (56.3%) with pain before RT. Hemostasis was confirmed in 2 of the 3 patients (66.7%) with bleeding before RT. Twelve of 20 (60%) patients with symptoms before RT responded to RT. Disease-specific survival (DSS) time after RT ranged from 1 to 656 (median, 106) days.

Conclusions: Prompt palliative administration of RT to patients with advanced disease to alleviate pain from disseminated tumors may achieve therapeutic efficacy.

Keywords: Radiation therapy (RT); pleural dissemination; peritoneal dissemination

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Introduction

Pleural or peritoneal dissemination from malignant tumors can occasionally induce tumorigenesis, and the resultant tumors may invade the surrounding tissues and cause pain or bleeding. If such tumors are identified by imaging approaches such as computed tomography, local radiation therapy (RT) may be selected to alleviate symptoms. However, few reports have focused on the effects of palliative RT or the optimal irradiation dose for pleural or peritoneal disseminated tumors. We assessed the significance of RT by investigating the purpose, effect, and dose of RT in patients who received palliative RT for pleural or peritoneal disseminated tumors arising from malignant tumors at our hospital between 2011 and 2019. We present the following article in accordance with the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/apm-19-495>).

Methods

We retrospectively reviewed the data of 22 patients with pleural or peritoneal disseminated tumors treated with local RT between 2011 and 2019. The Kaplan-Meier method was used to determine the probability of disease-specific survival (DSS) from the date of completion of RT. This study was approved by our institutional review board of Nihon University Itabashi Hospital (Ref No. RK-191008-8). Informed consent was obtained from all patients and the study was performed in accordance with the Declaration of Helsinki (as revised in 2013).

Results

The clinical data of all 22 patients are summarized in *Table 1*. Thirteen patients (59.1%) were men and 9 (40.9%) were women. The age at initiation of RT ranged from 47 to 80 (median, 67) years.

Regarding the irradiated disseminated tumor location, tumors in the pleura occurred in 9 (40.9%) patients, peritoneum in 13 (59.1%) and 2 tumor occurred in peritoneum and umbilicus. Regarding the primary tumor, the most common tumor type was lung cancer, which was identified in 5 patients (22.8%) and all were irradiated for pleural disseminated tumors. Pancreatic cancer was the second most common cancer type and was diagnosed in 4 patients (18.2%). Two patients were irradiated for peritoneum and umbilical tumors.

Concurrent metastasis of irradiated disseminated tumors at RT was observed in all but three patients. The most common purpose of RT was pain relief in 16 patients (72.7%). The second most common purpose was hemostasis in three patients (13.6%); specifically, RT was administered to stop direct bleeding from tumors in two patients and to treat hematuria due to bleeding from a tumor invading the bladder in one patient (1). The two patients without concurrent metastasis with irradiated disseminated tumors at RT were asymptomatic and were treated with RT for local control. *Figure 1* shows RT dosimetry for peritoneum and abdominal wall disseminated tumors from pancreatic cancer with refractory pain. The most common RT regimen was 30 Gy/10 fractions (fr) in 13 patients (59.1%), and the total RT dose ranged widely, from 27 to 56 Gy. No grade 2 or higher RT-related toxicities (National Cancer Institute Common Terminology Criteria for Adverse Events 4.03) (2) were observed. The categories of bone metastases (3) were used to substitute for the categories of pain relief. Based on scores on a 0–10 numerical rating scale and the extent of analgesic use, complete and partial responses were achieved in four and four patients, respectively. Indeterminate responses were obtained in one patient. The timing of the measurement of response to pain relief ranged from 0 to 232 days with a median time of 21 days after RT completion. Overall response to pain relief was observed in 9 of 16 patients (56.3%) with pain before RT. Hemostasis or reduced bleeding was confirmed in 2 of 3 patients (66.7%) with bleeding before RT. In one patient with pre-existing superior vena cava (SVC) syndrome before RT, SVC syndrome resolved. Of 20 patients who had some symptoms before RT, 12 patients (60%) responded to RT. Survival time after RT completion ranged from 1 to 656 days with a median of 106 days (*Figure 2*).

Discussion

RT is widely known to have a role in preventing dissemination; hemithorax RT is administered after surgery for malignant mesothelioma and whole abdominal RT after surgery for ovarian cancer (4–7). However, local RT for pleural or peritoneal disseminated tumors has been described in only a few case reports. There have been no reports, to date, on its effects and the optimal radiation dose. Our literature search identified nine case reports of RT for peritoneal disseminated tumors. In five of these, RT was administered for pain relief, hemostasis, or symptom

Table 1 Characteristics of patients treated with irradiation for pleural or peritoneal disseminated tumors and their clinical responses

Characteristics	N (%) (n=22)
Age at the time of RT, median years [range]	67 [47–80]
Gender	
Male	13 (59.1)
Female	9 (40.9)
Disseminated tumor location	
Pleura	9 (40.9)
Peritoneum	13 (59.1)
Primary tumor site	
Larynx	1 (4.5)
Thyroid	1 (4.5)
Lung	5 (22.8)
Thymoma	1 (4.5)
Stomach	1 (4.5)
Pancreas	4 (18.2)
Gallbladder	1 (4.5)
Bile duct	1 (4.5)
Jejunum	1 (4.5)
Appendix	1 (4.5)
Colon	2 (9.1)
Ovary	2 (9.1)
Uterine body	1 (4.5)
Concurrent metastasis at RT	
Yes	19 (86.4)
No	3 (13.6)
Purpose of RT	
Pain relief	16 (72.7)
Hemostasis	3 (13.6)
SVC syndrome release	1 (4.5)
No symptom	2 (9.1)
RT regimen (dose/fractions)	
56 Gy/28 fr	1 (4.5)
50.4 Gy/28 fr	1 (4.5)
45 Gy/15 fr	1 (4.5)

Table 1 (continued)**Table 1** (continued)

Characteristics	N (%) (n=22)
45 Gy/25 fr	1 (4.5)
39 Gy/13 fr	1 (4.5)
38 Gy/19 fr	1 (4.5)
36 Gy/12 fr	1 (4.5)
30 Gy/10 fr	13 (59.1)
28 Gy/7 fr	1 (4.5)
27 Gy/9 fr	1 (4.5)
Response*	
Yes	12 (60.0)
No	8 (40.0)
Survival time after RT, median days [range]	106 [1–656]

*, response rate in 20 cases with symptoms. RT, radiation therapy; SVC, superior vena cava.

alleviation (*Table 2*). We also previously reported a case in which hemostasis was achieved with hemostatic-intent RT for hematuria caused by a peritoneal disseminated tumor invading the bladder (1). In all five reported cases, symptoms were successfully alleviated; however, the actual response rate to RT for symptom alleviation is unknown. The RT regimens described in the case reports widely ranged from 20 Gy/5 fr to 50 Gy/25 fr. The irradiation doses tended to be higher in patients without concurrent metastasis with irradiated disseminated tumors at RT. Meanwhile, no reports were identified concerning RT administration to alleviate symptoms associated with pleural disseminated tumors. Regarding RT for symptom alleviation, the role of RT in relieving pain due to bone metastasis has been established. For example, meta-analyses have shown an overall pain response rate of RT ranging from 58.7% to 62.1% and a complete pain response rate ranging from 23% to 34% (16–18). In our present study, the overall pain response was observed in 56.3% of patients with pain, with our therapeutic effect being slightly inferior to that for pain due to bone metastasis. This may be explained by the difference in the timing of the measurement of response rates. Previous studies involving patients with bone metastasis measured patients' response rates at 3–6 weeks after RT completion (19–21). However, the response rate in our patients with pain was measured at a median of 21 days

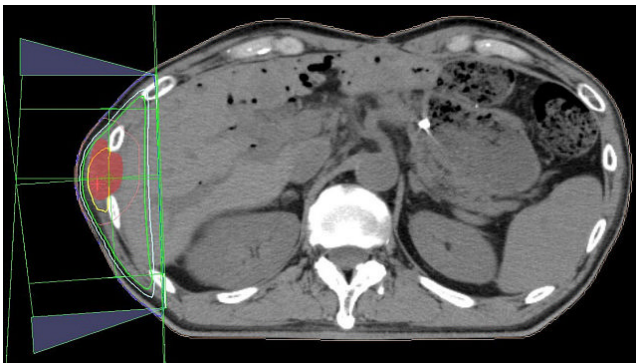


Figure 1 Computed tomography scan with RT dosimetry for a peritoneum disseminated tumor from pancreatic cancer. The gross tumor volume (red color fill) and clinical target volume (light red line) was well covered by the prescribed isodose: 100% isodose line is yellow, 95% is green, 90% is light cyan, and 50% is blue. RT, radiation therapy.

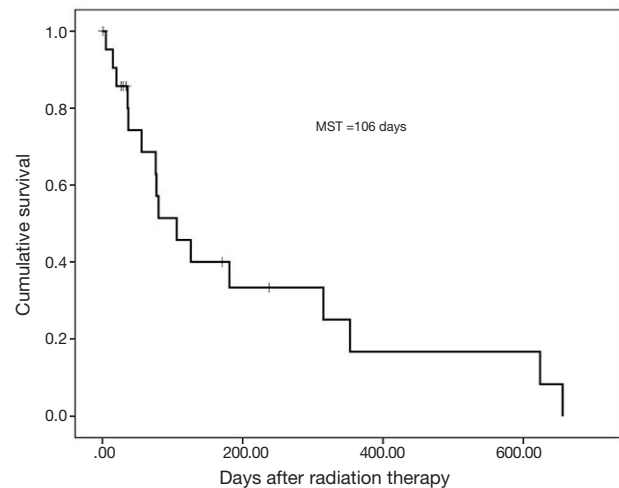


Figure 2 Kaplan-Meier DSS curves. The MST after RT completion was 106 days. DSS, disease-specific survival; MST, median survival time; RT, radiation therapy.

Table 2 Reported cases of peritoneal disseminated tumors treated with RT

Patient	Age* (years)	Gender	Disseminated tumor location	Primary tumor site	Concurrent metastasis at RT	Purpose of RT	RT regimen (dose/fractions)	Response	Reference
1	64	Male	Peritoneum	Stomach	Yes	Hemostasis	30 Gy/10 fr	Yes	(1)
2	65	Male	Abdominal wall	Liver	No	No symptom	Not mentioned	Yes	(8)
3	49	Male	Abdominal wall	Pancreas	Yes	Pain relief	40 Gy (total dose only)	Yes	(9)
4	65	Male	Peritoneum	Duodenum	No	No symptom	50 Gy/25 fr	No	(10)
5	82	Male	Peritoneum	Stomach	No	Dyschezia release	40 Gy/20 fr	Yes	(11)
6	79	Male	Abdominal wall	Bile duct	Yes	No symptom	30 Gy/10 fr	Not mentioned	(12)
7	52	Female	Umbilicus	Uterine cervix	Yes	Hemostasis	20 Gy/5 fr	Yes	(13)
8	69	Male	Peritoneum	Stomach	No	No symptom	50 Gy/25 fr	Yes	(14)
9	82	Male	Peritoneum	Pancreas	No	Pain relief	30 Gy/10 fr	Yes	(15)

*, age at first visit and not at RT. RT, radiation therapy.

after RT completion. However, as the survival time after RT completion was short, pain response in five patients was measured at 0 or 1 day after RT completion. It seems that if RT is administered in the early stages to alleviate pain due to disseminated tumors, patients may survive until therapeutic efficacy can be attained.

In our present study, 30 Gy/10 fr, a RT regimen

commonly used for bone metastasis, was delivered, but the median survival time (MST) after RT completion was as short as 106 days. Although short-term irradiation such as RT of 8 Gy in a single fraction for bone metastasis could also be considered, attention should be paid to RT doses that would be delivered to the surrounding gastrointestinal tract in cases with peritoneal disseminated tumors.

Regarding the association between disseminated tumors and prognosis, the survival time after umbilical metastasis from various primary tumor sites, which is conventionally known as Sister Mary Joseph's nodule, reportedly range from 1 week to 36 months, and the MST after umbilical metastasis from ovarian or uterine tube carcinoma is 26 months (22,23). Furthermore, a literature review of cutaneous metastases from pancreatic cancer, including umbilical metastasis, indicated that the survival time after cutaneous metastasis ranged from a few days to 19 months with a MST of 5 months (24). In this review, the survival time was significantly more improved in patients receiving any therapy including RT than in those receiving no therapy. In the current study, the MST after RT completion was 106 days. The association between RT and prognosis of disseminated tumors may differ depending on the primary tumor site or concurrent metastasis at RT. We will perform further studies to investigate the significance of RT for disseminated tumors from malignant tumors in terms of survival time by comparing patients receiving RT with those receiving no therapy.

Conclusions

Our findings indicate that if RT is administered in the early stages of cancer to alleviate pain due to disseminated tumors, patients may survive until therapeutic efficacy can be attained.

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Footnote

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of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by our institutional review board of Nihon University Itabashi Hospital (Ref No. RK-191008-8). Informed consent was obtained from all patients and the study was performed in accordance with the Declaration of Helsinki (as revised in 2013).

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