Peer Review File

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Reviewer A

This is an interesting study, however I think there are several topics that the authors may want to address. For patients with life expectancy <3 months, one could argue that only a single fraction of RT vs multifraction RT should be offered, or perhaps no radiation at all in this population with very limited life expectancy, and this is not mentioned anywhere.

Reviewer A response(1):

We would like to thank Reviewer A for your time and efforts in reviewing our manuscript and for providing comments, which have considerably helped us improve our manuscript. We have made revisions based on your comments and have provided our point-by-point responses below. We hope that our responses and revisions appropriately address your comments.

Regarding this limitation, Reviewer B also made a similar point. As you have pointed out, the number of fractions and the pros and cons of single-fraction irradiation for patients with a life expectancy <3 months are very sensitive issues. Lines 137 in the document have been changed from "The patients were not indicated for surgical intervention and received palliative RT except the single fraction for painful spinal metastases." to "The patients were not indicated for surgical intervention and received best palliative RT for painful spinal metastases. However, patients who received a single-fraction of irradiation were excluded from the study, as non-completion of palliative irradiation was the main focus." (Lines 117-119)

Also, there are many publications in the literature on estimating survival for patients with bone metastases that the authors do not reference, including a recent systematic review for patients with spinal metastases ie (doi.org/10.1186/s12885-019-6385-7; doi.org/10.1007/s00586-017-5320-3). This systematic review did not find pre-TLC to be significant predictor, so perhaps the authors can comment on this.

Reviewer A response(2):

We have noted these suggestions and referred to them. The first study you have referenced is highly interesting; in particular, we are surprised that they did not use the Charlson Comorbidity Index or the age-adjusted Charlson Comorbidity Index. Regarding the systematic review, we have now added to the main text that the primary tumor, PS, and ASA classification were strongly correlated with survival and are factors that can predict survival in patients with spinal metastases. and further commented on this.

Lines 281–285 "Bollen et al. (34) reported that PS is a strong prognostic predictor of survival in patients with spinal metastases, which is contrary to our study findings, as PS was not found to be a strong prognostic predictor. Furthermore, although the white blood cell count used in the nomogram created by the Skeletal Oncology Research Group should be a prognostic factor, to the best of our knowledge, no study has clarified its potential as a prognostic factor for pre-TLC."

Line 298 " For radiation oncologists who plan RT and perform CT for positioning of irradiation sites, measuring PMI

on CT images is a very common method of predicting prognosis". I have not heard of this before, can the authors provide a reference?

Reviewer A response(3):

Based on your comment, the relevant text (Lines 254–255) has been changed as follows: "For radiation oncologists who plan RT and perform CT to localize the radiation site, measuring PMI on CT images is not difficult."

One of the main limitations of this study is the small sample size (n=67), 58 who completed and 9 patients who did not complete a course of palliative RT. One can argue that any variables found to be significant may not be clinically relevant.

Reviewer A response(4):

Regarding this limitation, Reviewer F also made a similar point. As stated in the text, the results obtained in our retrospective series cannot be considered conclusive due to the small and heterogeneous sample and the limited power of the associated statistical analyses. However, this study demonstrated the efficacy and good tolerability of RT in the entire cohort of patients with or without completion of palliative RT, regardless of pre-RT TLC values. Therefore, studies similar to this one should be conducted with a larger number of patients. This limitation has been mentioned on Lines 287.

Reviewer B

The authors describe a novel relationship between pre-RT TLC and noncompletion of palliative RT for spinal metastases in cancer patients. They do a sufficient job in discussing the context of why these data are important in the care of patients with cancer. They may consider discussing more on how these data may be used going forward, including the current data supporting the use of single fraction RT and typical duration of its effects. I recommend acceptance of this manuscript with minor revisions. Suggested revisions are below.

line 95: consider describing more of why single fraction may not be given (patients with single fraction RT are more likely to need reirradiation so those who are expected to have long term survival may need a more fractionated course.)

Reviewer B response(1):

We would like to thank Reviewer B for your time and efforts in reviewing our manuscript and for providing comments, which have considerably helped us improve our manuscript. We have made revisions based on your comments and have provided our point-by-point responses below. We hope that our responses and revisions appropriately address your comments.

Based on your comment, we have now added our reasoning for excluding patients receiving single-fraction RT from this study on Lines 117–119.

"The patients were not indicated for surgical intervention and received palliative RT except the single fraction for painful spinal metastases." to "The patients were not indicated for surgical intervention and received best palliative RT for painful spinal metastases. However, patients who received a single-fraction of irradiation were excluded from the study, as non-completion of palliative irradiation was the main focus."

line 101: “not all the” to “not all of the”

Reviewer B response(2):

Accordingly, we have made this change on Lines 86–87.

Thank you for your comment. line 138-138: odd wording of first sentence. consider “ Patients with pre-RT surgical management at the same vertebral level and those who received single fraction RT were excluded.”

Reviewer B response(3):

Regarding this limitation, Reviewer A also made a similar point. The text in question (Lines 117–1119) has been changed as follows:

“The patients were not indicated for surgical intervention and received palliative RT except the single fraction for painful spinal metastases.” to “The patients were not indicated for surgical intervention and received best palliative RT for painful spinal metastases. However, patients who received a single-fraction of irradiation were excluded from the study, as non-completion of palliative irradiation was the main focus.”

line 138-144: please explain how social reasons were determined. including “loss of motivation to fight the disease” is a difficult variable as some could argue you are not able to fully determine all who meet this in a retrospective review. Also please consider different wording from “loss of motivation to FIGHT the disease.” Patient advocates have asked us to avoid as it implies a person is losing the fight.

Reviewer B response(4):

Based on your comment, the text in question (Lines 120–124) has been changed as follows: “Patients who could not complete RT owing to social reasons, such as transfer to another hospital or refusal to receive radiotherapy for financial reasons, or owing to medical reasons, such as treatment discontinuation determined at an in-hospital conference with radiation oncologists certified by the Japanese Society for Radiation Oncology, were excluded from the incomplete group, as quantitative evaluation of factors that lead to the non-completion of palliative RT is difficult.”

line 165: can say that <7 is stable while ≥7 includes potentially unstable and stable line 232: can you separate lung into NSCLC and SCLC. if it is only NSCLC, can you please specify

line 233: “double cancer” to two separate primary diagnoses

line 276-277: very strong statement.

Reviewer B response(5):

Accordingly, “<7 or ≥7” has been rewritten as “≥7”(Line 137) in the manuscript.

Reviewer B response(6):

Kindly note that we did not consider NSCLC and SCLC separately in this separately.

Reviewer B response(7):

Based on your comment, the term “double cancer” has been rewritten to “synchronous cancer” (Line 193).

Reviewer B response(8):

Based on your comment, we have modified the text on lines 233–234 to “Patients with terminal cancer are likely to experience rapid deterioration causing worsening of their general condition and death within 1–2 days.”

Include citation General comment: Your study only includes patients who have an OS <3 months after RT.
Some would argue that these patients who have this short OS should have been treated with single fraction RT. Any thoughts on why they weren’t?
In the results section, consider reporting the number that lived <3 months that were excluded due to having a single fraction. This may add credibility as readers will be wondering why some weren’t treated with this technique.
Especially given this is a single institution study, this will advise readers on what your institutional practice is as interpreting these data will be very different if readers perceive that these patients were given longer fractionation schemes because (perhaps) your team expected these patients to live long enough to benefit from them.
Also consider addressing in the discussion on how patients who did not complete RT may have benefited from single fraction RT and the current literature supporting single fraction RT’s use

Reviewer B response(9):

Reviewer A made a similar point. As you have pointed out, the number of fractions and the pros and cons of single-fraction irradiation for patients with a life expectancy <3 months are very sensitive issues. Lines 137 in the document have been changed from “The patients were not indicated for surgical intervention and received palliative RT except the single fraction for painful spinal metastases.” to “The patients were not indicated for surgical intervention and received best palliative RT for painful spinal metastases. However, patients who received a single-fraction of irradiation were excluded from the study, as non-completion of palliative irradiation was the main focus.” (Lines 117-119)

Figure 3: typo in figure legend. Call it PSS Table 1: you put “%” behind the first two rows then not again. Consider changing so that you present n (%), mean ± SD, and median [IQR]. Using brackets further separates percentage from IQR.

Reviewer B response(10):

We apologize for this overlook and have now corrected the typo in Figure 3 that you have pointed out.
We have added the following text to Figure 3: “Complete group: n=58, mean ± SD; -10.3 ± 8.8, median IQR; -10.0 [-20.0, 0.0]; and incomplete group: n=9, mean ± SD; -26.7 ± 16.6, median IQR; -30.0 [-40.0, -10.0].”.

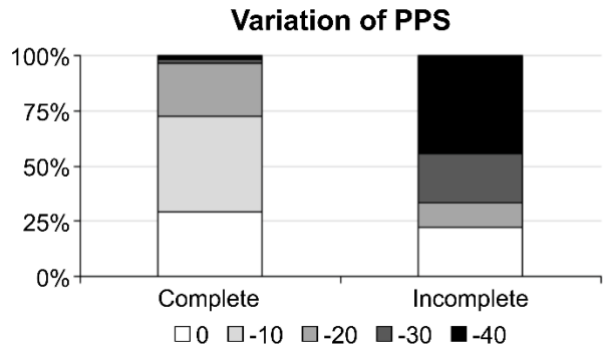

Figure 3. The variations in the PPS scores of the patients in the complete and incomplete groups. Compared with the complete group, the incomplete group included many patients whose PPS scores decreased rapidly by 30%–40% points from baseline.

Reviewer C

First of all I'd like to make my compliments for your good effort and you worth work.

The only suggestion I'd like to you is:

- Reduce just some abbreviation so to make the manuscript more readable;
- Implement discussion paragraph also including these article:

1. https://pubmed.ncbi.nlm.nih.gov/35395371/
2. https://pubmed.ncbi.nlm.nih.gov/36786970/
3. https://pubmed.ncbi.nlm.nih.gov/24511047/
4. https://pubmed.ncbi.nlm.nih.gov/37510078/
5. https://pubmed.ncbi.nlm.nih.gov/33815186/

I think a good, wealthy and up-to-date reference list is essential in order to complete your great effort.

Reviewer C response(1):

We would like to thank Reviewer C for your time and efforts in reviewing our manuscript and for providing comments, which have considerably helped us improve our manuscript. We have made revisions based on your comments and have provided our point-by-point responses below. We hope that our responses and revisions appropriately address your comments.

Based on your comment, we have reduced the number of abbreviations by removing any abbreviations/acronyms that were not used more than three times throughout the text.

Reviewer C response(2):

We have reviewed your suggestions, but we did not find any of these studies to be relevant enough to enhance our discussion and warrant their inclusion in the cited literature.

Reviewer D

I have only two questions:

1) Were all patients treated on the same number of vertebrae? I assume that a larger spinal involvement may negatively affect the completion of RT as a surrogate of a worse clinical condition.

Reviewer D response(1):

We would like to thank Reviewer D for your time and efforts in reviewing our manuscript and for providing comments, which have considerably helped us improve our manuscript. We have made revisions based on your comments and have provided our point-by-point responses below. We hope that our responses and revisions appropriately address your comments.

Kindly note that the irradiation range covered 1–2 vertebrae in most cases in this study.

2) Even if you indicated a comparable SINS score between the completed and non-completed cohorts, I wonder if among the non-completed group there were more patients suffering of procedural pain, i.e. that related to the daily setup procedure, which may discourage the patient compliance.

Reviewer D response(2):

In addition to our research, we consider this aspect in our daily operations. For instance, if a patient experiences severe pain, we administer opioids or NSAIDs one hour prior to starting irradiation. Once the pain has subsided, we initiate the treatment.

These two points should be clarified in the manuscript.

Moreover, I would appreciate if you'll decide to cite PMID: 35455062 as pertinent reference at the end of first sentence of the introduction and PMID: 33402511 as pertinent reference for “Older patients have a high risk for undernutrition, sarcopenic frailty, and multiple complications owing to aging”.

Reviewer D response(3):

Based in your suggestion, we have added these references where you have indicated.

Reviewer E

This is a single center, retrospective analysis to identify potential predictors of RT non-completion among advanced cancer patients that received >1 fraction to the spine for pain. Varied laboratory, demographic, and anatomic data (i.e. psoas muscle index) were collected before and after palliative RT.

58 patients were eligible for this analysis, specifically that they died within 3 months after RT and received >1 fraction spine RT. Perhaps not surprisingly, those that did not complete RT had a lower survival compared to those that completed their intended RT course.

The authors found that pre-TLC was lower among patients that did not complete their RT course; however other laboratory values and/or metrics were similar between those who did and did not complete the RT course, including albumin, LDH, performance status, and palliative performance status (PPS).

In fact, the mean pre-PPS was higher within the incomplete group.

Many studies have sought to identify predictors for shorter survival and/or non-completion of RT, with hopes to better

tailor our RT dose/fractionation schemes to a patient's life expectancy. TLC has been associated with outcomes among cancer patients and represents an attractive predictor given that it is readily measured. Typically, performance status is one of the strongest predictors for survival amongst these advanced cancer patients and is attractive as it is readily assessed in the clinic.

It is interesting that here, performance status was not different between the two groups and as mentioned earlier, PPS was higher in the non-completion group. This study adds to the growing literature of what predictors radiation oncologists may use, though I think there are several limitations of this study (please see below) that should be addressed for it to be more applicable to clinical practice.

Abstract

• Background: I would consider modifying the first sentence. The goal is not to identify predictors of non-completion to "determine the optimal RT dose" but instead to better tailor recommended RT dose/fractionation schemes for patients.

Reviewer E response(1):

We would like to thank Reviewer E for your time and efforts in reviewing our manuscript and for providing comments, which have considerably helped us improve our manuscript. We have made revisions based on your comments and have provided our point-by-point responses below. We hope that our responses and revisions appropriately address your comments.

Based on your comment, "Radiation oncologists should accurately predict the prognosis in patients with terminal cancer for determining the appropriate dose and fractionation of RT for each patient." has been rewritten to "To better tailor the recommended RT dose/fractionation schemes, radiation oncologists should accurately predict prognosis in patients with terminal cancer." (Lines 91-92)

Methods

• I think it is important to include those patients that could not complete RT due to social or medical reasons, as arguably, these should be incorporated into our clinical decision making process. The medical reasons for treatment discontinuation may be related to disease progression, which appears to be a main driver of non-completion in the incomplete group.

• Please comment on how data was handled if patients were received concurrent systemic therapy during RT (e.g. anti-cancer treatment was received <2 weeks before RT). Also, why was a 2 week threshold picked? Return of lymphocyte count may take longer than 2 weeks (e.g. on the order of months). Does TLC instead reflect how heavily pre-treated a patient may be?

Reviewer E response(2):

This patient cohort excluded patients who received concurrent systemic therapy during RT. We have added this to the description of the exclusion criteria. In addition, the description of the data (Line 145–146) has been changed to: "we used data collected ≥2 weeks after the latest anticancer treatment (surgery, chemotherapy, hormone therapy, or immunotherapy)."

• The authors describe that PMI was determined based on CT images 1-3 months prior to, images for CT simulation, and images 1-3 months after RT. The assumption is that pre-PMI was based on CT images 1-3 months before RT and post-PMI was based on CT images 1-3 months after RT. However, what were the measurements obtained at CT sim used for? (pre versus post-PMI)

Reviewer E response(3):

Kindly note that the measured values obtained by CT simulation were treated as reference values for pre-PMI.

• Please clarify whether spine RT was for uncomplicated versus complicated bone lesions. One may argue that for uncomplicated bone lesions, there is very strong data that a single fraction of RT is equivalent with respect to pain relief to multi-fraction (i.e. the optimal dose is a single fraction). If there were included patients with complicated bone lesions, what proportion were for impending/pathologic fracture, cord compression, prior surgery/RT, etc?

Reviewer E response(4):

Reviewer D made a similar same point. In this study, the irradiation range covered 1–2 vertebrae in most cases, and no complicated bone lesions were involved.

• Please include within your methods the definition of "variation of PPS"? When was the second measurement of PPS obtained? Is this during RT? 1 week after RT, etc?

Reviewer E response(5):

The second measurement of PPS was conducted approximately 2 weeks after the end of RT.

Results

• Page 7, line 255: The word "and" may be missing between "Alb (p=0.036) TLC (P=0.018)".

Reviewer E response(6):

Based on your comment, we have corrected the errors that you pointed out.

• I would consider moving Figure 3 from the discussion into the results as it is less standard to present new data within the discussion.

Reviewer E response(7):

We have moved Figure 3 from the Discussion to the Results and added the following text on lines 205–206 "Compared with the complete group, the incomplete group included several patients whose PPS scores rapidly decreased by 30–40 points from the baseline (Figure 3)." Further, the text on lines 265 in the Discussion has been changed to "The most likely reason for the results shown in Figure 3 is rapid and unpredictable disease progression."

• Table 1: Please clarify when the measurements for Alb, CRP, LDH, TLC, PS taken? For example, presumably, pre-

Alb was taken >2 weeks before RT; was Alb during RT?

Reviewer E response(8):

Based on your comment, we have specified when the measurements were taken in Table 1.

The pre-XX measurements were taken >1 week before radiotherapy, the post-YY measurements were taken <1 week after radiotherapy, and the Alb, LDH, and CRP measurements were taken during radiotherapy

Table 1. Characteristics of the patients in the complete and incomplete groups

	n	Complete group	n	Incomplete group	P-value (Uni)	P-value (Multi)	OR (95% CI)
Sex	58		9		>0.999†		
Male; n (%)		41(70.7%)		6 (66.7%)			
Female; n (%)		17 (29.3%)		3 (33.3%)			
SINS	58		9		0.295†		
<7; n (%)		25 (43.1)		2 (22.2)			
≥7; n (%)		33 (56.9)		7 (77.8)			
Fraction times	58		9		0.700§		
≥ 2 to < 10; n (%)		20 (34.5)		2 (22.2)			
10; n (%)		34 (58.6)		7 (77.8)			
>10; n (%)		4 (6.9)		0 (0.0)			
Type of the malignant tumor	58		9		0.693†		
Lung cancer; n (%)		15 (25.9)		3 (33.3)			
Other cancer; n (%)		43 (74.1)		6 (66.7)			
Other metastatic lesions; n (%)	58	50 (86.2)	9	6 (66.7)	0.159†		
Bone-modifying agent; n (%)	58	40 (69.0)	9	6 (66.7)	>0.999†		

Type of bone metastasis	58			9			0.368†		
Osteolysis; n (%)		39 (67.2)			6 (66.7)				
Mixture; n (%)		6 (10.3)			2 (22.2)				
Osteoblast; n (%)		9 (15.5)			0 (0.0)				
Trabeculae; n (%)		4 (6.9)			1 (11.1)				
CCI	58			9			>0.999†		
<7; n (%)		26 (44.8)			4 (44.4)				
≥7; n (%)		32 (55.2)			5 (55.6)				
aCCI	58			9			0.437†		
<10; n (%)		13 (22.4)			3 (33.3)				
≥10; n (%)		45 (77.6)			6 (66.7)				
Age (years)	58	70.8	± 10.2	9	68.8	± 13.6	0.598‡		
pre-PMI	58	4.2	(3.4, 5.0)	9	2.9	(2.6, 5.1)	0.282§		
post-PMI	58	3.9	(3.2, 5.0)	9	2.5	(2.2, 4.7)	0.044*§	n.e.	n.e.
pre-Alb	56	3.3	± 0.6	9	3.4	± 0.6	0.681‡		
Alb	57	3.1	± 0.6	9	2.8	± 0.7	0.276‡		
pre-CRP	54	1.6	(0.5, 6.4)	8	1.9	(0.3, 3.0)	0.793§		
CRP	53	3.8	(1.3, 6.5)	9	5.4	(2.5, 10.1)	0.285§		

pre-LDH	55	285.0	(220.0, 359.0)		9	285.0	(225.5, 511.5)		0.582§		
LDH	57	313.0	(241.0, 501.0)		9	364.0	(297.0, 636.5)		0.182§		
pre-TLC	52	1080.0	(727.5, 1410.0)		9	590.0	(331.0, 869.8)		0.013*§	0.048*§	0.998 (0.996-1.00)
TLC	55	870.0	(480.0, 1310.0)		9	510.0	(321.5, 929.6)		0.153§		
pre-PS	58	1.4	±	0.7	9	1.4	±	0.5	0.904‡		
PS	58	1.9	±	1.0	9	2.4	±	1.0	0.109‡		
pre-PPS	58	67.8	±	12.4	9	78.9	±	7.8	0.012*‡	0.039*‡	1.097 (1.005-1.198)
PPS	58	57.4	±	14.1	9	52.2	±	21.1	0.342‡		
SINS	58	6.7	±	2.6	9	6.8	±	1.8	0.953‡		
CCI	58	7.0	(6.0, 7.5)		9	7.0	(6.0, 9.0)		0.899§		
aCCI	58	10.4	±	1.7	9	10.7	±	2.9	0.748‡		

Data are presented as n, %; mean ± SD; and median (IQR); *, P-value < 0.05; †, Fisher's exact test; ‡, unpaired t-test; §, Mann–Whitney U-test.

The pre-XX measurements were taken >1 week before radiotherapy, the post-YY measurements were taken <1 week after radiotherapy, and the Alb, LDH, and CRP measurements were taken during radiotherapy.

OR, odds ratio; CI, confidence interval; IQR, interquartile range; SINS, spinal instability neoplastic score; CCI, Charlson comorbidity index; aCCI, age-adjusted Charlson comorbidity index; PMI, psoas muscle index; Alb, albumin; CRP, C-reactive protein; LDH, lactate dehydrogenase; TLC, total lymphocyte count; PS, performance status (Eastern Cooperative Oncology Group); PPS, palliative performance scale; n.e., not entered

Reviewer F

- Could the authors state in the Intro whether other groups have looked into this issue in the past?

Reviewer F response(1):

We would like to thank Reviewer F for your time and efforts in reviewing our manuscript and for providing comments, which have considerably helped us improve our manuscript. We have made revisions based on your comments and have provided our point-by-point responses below. We hope that our responses and revisions appropriately address your comments.

Based on your comment, we have added the following text on Lines 97–98: "Therefore, we investigated prognostic factors influencing non-completion of palliative RT, which have rarely been reported to date."

- The introduction makes the reader think the underlying research question is more about anticipating prognosis, rather than examining a more global picture of all factors (beyond limited survival) that can lead to a course of multiple fraction XRT being interrupted.
- Patients for the study were identified from being registered on the tumor board - does this board include all patients with terminal cancer treated at the centre?

Reviewer F response(2):

Kindly note that this cancer board manages data on almost all of our center's patients with terminal bone metastases.

- I don't understand why the authors would only examine patients with spinal metastases, and why they would only examine patients that survived <=3mo. If the underlying research question truly is trying to figure out why patients might not complete a course of radiotherapy, why would you exclude somebody that lived 6mo but did not complete the course?

Reviewer F response(3):

The reason for this has been presented in Lines 120–124 in the "Methods" section.

Patients who did not complete the course of RT because of social reasons, logistical travel reasons, other medical reasons, were excluded from this analysis. Respectfully, saying that they were excluded because evaluating these factors is 'difficult' misses out on an important source of data that can contribute to answering your underlying research questions. And why were those without CT images or those with tumors infiltrating the psoas muscle excluded? I understand the desire to incorporate PMI into your model, but it seems too awkward to do that within this study. All of these factors are contributing to a denominator of patients that arguably has very limited external validity for a centre's overall patient population.

Reviewer F response(4):

As you have pointed out, there are pros and cons to how data should be handled when a patient refuses treatment for social or logistical reasons. However, measuring the PMI using CT is relatively easy and can be performed quickly.

This was used for this study.

- The overall number of patients on whom the authors were able to run their analyses were small - only 9 in the incomplete group. I think this severely limits both interpretation of the data and conclusions that can stem from those interpretations.

Reviewer F response(5):

Regarding this limitation, Reviewer A made a similar same point. As stated in the text, the results obtained in our retrospective series cannot be considered conclusive due to the small and heterogeneous sample and the limited power of the associated statistical analyses. However, this study demonstrated the efficacy and good tolerability of RT in the entire cohort of patients with or without completion of palliative RT, regardless of pre-RT TLC values. Therefore, studies similar to this one should be conducted with a larger number of patients. This limitation has been mentioned on Line 287.

Reviewer G

This retrospective study of palliative patients undergoing RT for symptomatic spinal lesions is interesting in that it provides a potential new marker for predicting patients who will not finish treatment. This might help guide treatment decisions near end of life. The decision to give palliative radiation at all and with what fractionation is a difficult one and it has been studied extensively. As such, there should be more discussion of known prognostic indices either in the introduction or the discussion, including TEACHH, Chow and PACS, specifically.

Reviewer G response(1):

We would like to thank Reviewer G for your time and efforts in reviewing our manuscript and for providing comments, which have considerably helped us improve our manuscript. We have made revisions based on your comments and have provided our point-by-point responses below. We hope that our responses and revisions appropriately address your comments.

Based on your comment, we have added the following text on lines 229–232: “TEACHH (21), Chow (22), and palliative home care setting (23) are prognostic models that were developed for patients with metastatic cancer being treated with palliative RT. These models may help clinicians provide quality palliative care to their patients with advanced cancer and their families. However, detailed examination items such as pre-TLC values and PMI, which were used in the present study, were not included in these models.”

The methods and results are practical and clearly presented.

As mentioned before, the discussion could benefit from more inclusion of the current literature including the prognostic indices listed above. Additionally, there seemed to be a focus on treatment completion when this data could also be useful when deciding whether to treat at all. Given over 75% of the patients passed away within 1 month in the incomplete arm, it begs the question of whether these patients ever saw a benefit from their radiation, given it was incomplete and a response to palliative RT can take weeks. This topic should be addressed at least briefly.

Reviewer G response(2):

Unfortunately, many patients who did not complete the procedure did not receive the benefit of palliative RT.

Limitations are clear and reasonable.

In the conclusion, in addition to stating the identified predictors can be used to set the number of fractions for palliative RT, as mentioned before, authors should consider adding that it may also be useful when deciding whether to treat at all.

Reviewer G response(3):

In order to determine whether this prognostic factor, as you pointed out, can be used when determining treatment strategies, it is necessary to accumulate and study more cases in the future.

There are a few grammatic/linguistic issues. For instance, line 236: I believe “double cancer” should be changed to “multiple cancer diagnoses.” “Double cancer” does not sound grammatically or linguistically correct.

Reviewer G response(4):

This is noted, and the manuscript has been checked accordingly. In particular, the term “double cancer” has been revised as “synchronous cancer”.

here are a few inconsistencies including the following on line 285: The authors state they collected hematologic test data such as ECOG PS, which is not hematologic. Additionally, on line 289, the authors specify low vs high for Alb, CRP and LDH but don’t specify whether low or high TLC is associated with poor prognosis.

Reviewer G response(5):

Accordingly, we have modified the text in question to (Lines 242–248): “We retrospectively collected various data that are predictors of prognosis, such as Eastern Cooperative Oncology Group PS, PPS, PMI, CCI, and aCCI, and analyzed the changes in their values. Since biochemistry and blood count data are abnormal during the terminal stage of cancer (10), some data obtained from blood samples are used to calculate scores for predicting the prognoses of patients with terminal cancer (11,12). Low TLC (11), low Alb levels (13), high C-reactive protein levels (14), and high lactate dehydrogenase levels (15) have been associated with poor prognosis in patients with various solid cancers. In previous studies, PPS scores (9) showed rapid decline during the 4 weeks before death (25).”

We have also added the following point that there are no reports yet that have clarified the possibility of “pre-TLC” as a prognostic factor (Lines 281–285): “Bollen et al. (34) reported that PS is a strong prognostic predictor of survival in patients with spinal metastases, which is contrary to our study findings, as PS was not found to be a strong prognostic predictor. Furthermore, although the white blood cell count used in the nomogram created by the Skeletal Oncology Research Group should be a prognostic factor, to the best of our knowledge, no study has clarified its potential as a prognostic factor for pre-TLC.”