Peer Review File

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Reviewer A

I detected no particular issues in your manuscript, which I deem very interesting and important.

- Thank you for your feedback and interest in this topic.

I suggest only minor revision:

- Both in the introduction and in the discussion section, you used long sentences without suited references. See for example from line 86 to 92 and from 190 to 193. You could enrich the text by adding some relevant references.
  - Citations 4-6 have been added for lines 86-91
  - Citations 4-6 have been added for lines 190-192
  - Citation 42 has been added for lines 192-193
- In line 107, where "focal therapies such as stereotactic radiosurgery (SRS)" is, you can add "or hypofractionated courses" and cite PMID: 35347003.
  - Lines 107-108 now includes mention of hypofractionated courses to account for FSRT.
  - Citation 20 (PMID: 35347003) has been added to line 108
- I would be pleased if you'll cite PMID: 36186686 as reflecting the Italian practice for palliative radiotherapy, including that for brain metastases.
  - A section discussing Italian and German practice pattern surveys has been added to lines 255-263: “Despite a greater representation of European countries, only one to two centers from each country were sampled which may be insufficient to represent the entire region. Prior surveys of Italian and German centers have revealed more complete country-specific data than could be collected here. (56, 57) In the Italian survey, the majority (>90%) of brain metastases treated with palliative intent utilized non-IMRT and non-SRT which is congruent with our findings; however, the survey revealed larger variations in dose regimens (range: 4-45 Gy).(57) In the German study, high-volume centers more frequently used targeted radiation over WBRT and employed more IMRT relative to low-volume centers.(56) The participating high-volume center in the present study used SIB approaches 78% of the time, confirming this survey’s findings of frequent IMRT-based WBRT in this region. However, potential differences among high and low-volume centers were unable to be assessed.”
  - PMID: 36186686 (Italian study) and PMID: 33620657 (German study) have been added as citations 56-57 and cited in the above added paragraph.
- Please, specify that the dose constraint you provided in line 111 (V12 < 10 cc) is suitable only for SRS, not for fractionated courses. Moreover, it's valid per each metastasis treated; this could be not clear to the reader.
  - There was absolutely room for misinterpretation in the way it was written; thank you for pointing out this potential for confusion.
  - Line 110-112 has been corrected; the specific dose constraint for SRS was removed. As there are a variety of dose constraints for different FSRT regimens, specific values were

removed. The sentence is now more generalized and reads as follows: “As is stands today, it is generally deemed safe to treat up to fifteen small brain metastases with SRT, either as single-fraction SRS or fractionated stereotactic radiotherapy (FSRT), in efforts to avoid irradiation of healthy brain tissue. (22, 23).” These sources can provide more specific information if desired by readers.

Reviewer B

This is an important topic that I am grateful the authors are exploring. Their findings are clearly written and easy to understand.

- Thank you for your feedback and interest in this topic.

Authors conclude that patients are being appropriately selected for WBRT as noted by their low median survival but that is not the entire story. We would need to know the OS of patients treated with SRS/GK for comparison or at least acknowledge this as a weakness of that conclusion. It could be that there are a number of patients getting non-WBRT to the brain that should instead be getting WBRT or even supportive care.

- We agree patients are likely being inappropriately selected for SRT regimens given its now widespread accessibility and believe this warrants investigation. Unfortunately, we do not have this data readily available.
- A section has been added to lines 270-273: “Data regarding all institutional SRT use and resulting survival was not consistently available among centers which limits our ability to comment on whether patients are being appropriately selected for focal palliation of brain metastases. As SRT continues to become more accessible and offers the potential for neurocognitive protection, exploring palliative SRT trends and survival outcomes is deserving of future investigation.”

Are there any relevant patient characteristics to help guide rad oncs in their decision to offer palliative RT or not? Did you calculate GPA or prognostics for these patients to determine if their survival correlated? Would be much more useful demonstrate certain patient characteristics or to demonstrate continued validity of this prognostic tools in this era rather than to suggest rad oncs carefully consider risks and benefits.

- At our institution, GPA scores and other prognostic models are used per provider preference and rarely documented. Therefore, this data was not available for review.
- Other than a subjective gestalt approach and provider experience, there are certain characteristics predictive of 30-day mortality. A section discussing several indicators predictive of 30-day mortality specifically in patients receiving palliative radiation was added to lines 238-241: “Certain patient factors have also been significantly associated with 30-day mortality including those receiving palliative treatment to multiple locations, primary site melanoma, mesothelioma, and hepatobiliary cancers, presence of liver metastases, inpatient status, and an eastern cooperative oncology group (ECOG) performance status of 3-4. (55)”

In addition to prognostic scores, would be useful to touch on other patient characteristics which may

inform deciding between SRS and WBRT and WBRT and supportive care namely, number of prior lines of prior therapy and hemorrhagic mets, respectively, to name a few.

- A section was added outlining contraindications for SRT to lines 222-224: "Although SRT may be appealing from a logistical perspective due to fewer fractions, such advanced techniques are not suitable for patients with numerous or bulky metastases, hemorrhagic metastases, uncontrolled systemic disease, poor performance status, or limited access to surveillance imaging. (36, 37, 43)"

Would be useful to cite the QUARTZ trial.

- The QUARTZ trial is referenced as citation 32 but was not specifically discussed.
- A section discussing this trial was added to lines 231-233: "With nearly a quarter of patients (22%) receiving WBRT within the last month of life, there is potential to better select patients for WBRT; maximal supportive care over WBRT has shown QOL and OS non-inferiority among those with multiple non-small cell lung cancer brain metastases ineligible for SRT or surgery, with both groups surviving a median of approximately nine weeks. (32)"