Author's response to reviews

Title: Gamma knife radiosurgery for elderly patients with brain metastases: evaluation of scoring systems that predict survival

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Author's response to reviews: see over
Dear Editor-in-chief,

I’d like to thank the editor and reviewers of the ‘BMC Cancer’ for taking time to review our article (MS 2037813039144210). I have made some corrections and clarifications in the manuscript after going over your comments. The changes are summarized below.

**Answers for Reviewer #1’s comments:**

This is a well conducted study on a not small number of patients.

**Answer** We added this reference, as you recommended.

2) The Authors’ effort in addressing prognostic factors in the elderly population is noteworthy, especially considering increasing age and the socioeconomic impact of cancer in the overall population in our countries. I would like to see further developed in the discussion part the Authors’ opinion regarding how aggressive we can be in treating this subgroup of patients. I think this is a fundamental question to be answered. Especially important since little is add to what is already known and previously reported i.e. that K.P.S. (general clinical conditions) and extracranial metastases (degree of control of primary cancer) are some of the most important factors in predicting survival. This holds true for the oncologic patient per se, either young or old.  
**Answer** Many oncologists or neurosurgeons may hesitate to perform the aggressive treatment for brain metastasis in old-aged cancer patients. However, some papers revealed the efficacy of stereotactic radiosurgery for brain metastasis in old-aged cancer patients. The results of these studies, including ours, suggest that the majority of old-aged patients have outcomes similar to those of younger patients, with good neurological and general conditions. We inserted some sentences to clarify this point in discussion.

3) Potential bias: vast majority of patients considered in good conditions: high K.P.S. (median 84), small number of cranial metastases (median 2).  
**Answer** High KPS or low number of brain metastasis can be a selection bias in our study. However, the patient with good neurological performance and relatively less-numbered
intracranial metastasis are considered as a candidate for stereotactic radiosurgery, rather than whole brain radiotherapy. In the previous paper [Kim SH, Weil RJ, Chao ST, Toms SA, Angelov L, Vogelbaum MA, Suh JH, Barnett GH: Stereotactic radiosurgical treatment of brain metastases in older patients. Cancer 2008, 113(4):834-840.], median KPS of enrolled patients was 80 and around 60% of the patients was classified as good performance state (over 80 in KPS). The majority of the patients had single brain lesion (70.5%). In another paper [Minniti G, Esposito V, Clarke E, Scaringi C, Bozzao A, Lanzetta G, De Sanctis V, Valeriani M, Osti M, Enrici RM: Stereotactic radiosurgery in elderly patients with brain metastases. J Neurooncol 2013, 111(3):319-325.], majority of the patients (78%) showed good performance state (over 80 in KPS). In the aspect of number of intracranial metastasis, 42% of the patients was treated for a single lesion. The remaining patients had multiple lesions, less than 4. That is, for brain metastasis in the elderly, aggressive treatment (radiosurgery or open resection) was applied for the better conditioned patients, compared to whole brain radiotherapy. In addition to that, previous studies, including ours, did not compare the outcome based on the different treatment modalities but postulated the prognostic factors only in the patients treated with radiosurgery.

Answers for Reviewer #2’s comments:

This manuscript covered an important issue about the decision making for the treatment of the elderly patients with brain metastasis. The authors analyzed the prognostic factors of these patients treated with Gamma Knife radiosurgery (GKRS) and evaluated which scoring system would be the most suitable for the prediction of prognosis and helpful for treatment decision. This manuscript is well analyzed and well written. However, it needs some minor revisions.

1). There have been already many papers about the prognostic factors for the patients with brain metastases after radiosurgery. As authors pointed out, the purpose and merit of this study is to determine most appropriate scoring system. Therefore, authors should decrease the simple analysis for prognostic factors and focus on evaluation of scoring system.

Answer) We shortened the several paragraphs, as you recommended.

2). This manuscript is too long, especially result section. The authors made very detailed and lengthy tables, and so should not repeat same description in the context. Based on Table 2, 3, and
4, the "Patients' characteristics" and Overall survival and prognostic factors" paragraphs should be shortened and summarized, and only important points could be emphasized.

**Answer** We deleted and shortened the several paragraphs, as you recommended.

3). The Table 5 is not necessary and should be deleted. The brief mention about the negative results in the context is enough. The role of chemotherapy is not the main topic of this manuscript. The sentence about chemotherapy in results of abstract should be deleted. And, the final sentence of discussion about the suggestion of concurrent use of chemotherapy and GKRS should be also deleted. That sentence is so random.

**Answer** We deleted table and shorted the some sentences, as you recommended.

4). A few minor errors about spelling and the location of reference number in context (for example, Kim et al. [29] found~). The reference number 5 should be checked again. The final sentence of methods of abstract should be revised.

**Answer** We fixed some mistakes and revised the sentence, as you recommended.

In addition, we organized the references without marking in detail and fixed a lot of errors (as recommended English-Editing Service).

Hopefully the revised manuscript will better meet the requirements of the ‘BMC Cancer’ for publication. I’d like to thank you again for the constructive comments by reviewers.

Sincerely yours,

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A specialist editor with suitable professional knowledge (M.Sc. or Ph.D./M.D.) reviewed and corrected the English. An English language specialist subsequently checked the paper again. The first language of both editors is English.

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