Author's response to reviews

Title: Long-term follow-up results of simultaneous integrated or late course accelerated boost with external beam radiotherapy to vaginal cuff for high risk cervical cancer patients after radical hysterectomy

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Author's response to reviews: see over
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Editorial Office of BMC Cancer
Dear editor:

I am enclosing here with a manuscript entitled “Long-term follow-up results of simultaneous integrated or late course accelerated boost with external beam radiotherapy to vaginal cuff for high risk cervical cancer patients after radical hysterectomy” for publication in “BMC Cancer” for possible evaluation. This manuscript (MS: 1634619058145903) was submitted to “BMC Cancer” a couple of months ago. We received the comments of editor and reviewers, and are allowed to submit a new manuscript after addressing all the concerns. According to these comments, we revised the manuscript very carefully, now we submit it again and explain the revisions we have made.

The revisions according to the comments are listed as follows:

1. **Editor’s Comments:** This is an interesting article on the prevention of vaginal cuff relapse after radical hysterectomy for high risk cervical cancer. Among the comments of the reviewers, I want to underline that the choice to include in this study a great proportion of patients with parametrial involvement (FIGO stage IIB) should be clearly justified, as standard treatment for these patients is not radical surgery but concomitant radio-chemotherapy. Without this explanation the work risks to be scientifically unsound.
R: Thanks for the constructive comments. We have explained the justification of patients with stage IIB disease in method. Patients in this retrospective study had undergone adjuvant EBRT boost to vaginal cuff after radical hysterectomy with pelvic lymphadenectomy for a clinical stage IB-IIA cervical cancer, or stage IIB that were resectable after neoadjuvant chemotherapy but did not achieve complete pathological responses to the neoadjuvant treatment.

2. **Referee 1-1:** It appears from manuscript and table 1, that 15 patients in Arm A (out of total patients of 42) and 17 patients of Arm B (out of total patients of 38) were in Stage IIB who underwent radical surgery. As Stage IIB Ca cervix Patients involves parametrium- Radical Surgery is not indicated.

**R:** Thanks for the constructive comments. As mentioned above, we have explained the justification of patients with stage IIB in method.

3. **Referee 1-2:** It appears from manuscript and table 2, that in both arms some patients received no chemotherapy, some neoadjuvant chemotherapy while those patients who had received concurrent chemotherapy-regimens differ. In such facts and circumstances, it may not be justifiable to reflect proper locoregional control, disease-free survival, overall survival and complications.

**R:** Thanks for the valuable comments. The purpose of this study is to report the safety and efficacy of using the adjuvant external beam radiotherapy (EBRT) boost to vaginal cuff with two techniques, and make the comparison between
these two EBRT boost techniques. According to NCCN guideline, pelvic radiation is recommended (category 1) with (or without) concurrent cisplatin-based chemotherapy (category 2B for chemotherapy) for patients with stage IA2,IB1, or II A1 disease who have negative lymph nodes after surgery but have other high risk factors. There were 6 patients in arm-A and 4 patients in arm-B who were eligible for these criteria and didn’t receive any chemotherapy, respectively. The other patients (36 patients in arm-A and 34 patients in arm-B) received adjuvant cisplatin-based chemotherapy. 16 and 19 patients with stage II in arm-A and B underwent neoadjuvant chemotherapy, respectively. And all of these patients achieved tumor shrinkage and then received radical hysterectomy with pelvic lymphadenectomy. One weakness of this retrospective study is the lack of standardization in the chemotherapy. And it is also very difficult to standardize the chemotherapy to all the patients in a retrospective study. We have added the limitation of this study in discussion.

4. Referee 2- Major Compulsory Revisions: define follow up time; add a paragraph or a few sentences in your discussion on the limitations of your study.

R: Thanks for the valuable comments. We have defined the follow up time in the method, and have added a paragraph on the limitations of our study in discussion.

5. Referee 2- Minor Essential Revisions.
R: Thanks for the constructive comments. We have revised all the contents and corrected the language very carefully according to the comments.

6. Referee 2- Discretionary Revisions: had a paragraph on the comparison of your outcomes to that of outcomes with brachytherapy.

R: Thanks for the valuable suggestion. We have added the comparison of our outcomes to that of outcomes with brachytherapy in discussion.

Submitted manuscript is an Original Article about evaluating the safety and efficacy of adjuvant external beam radiotherapy boost to vaginal cuff, and comparing two boost techniques (simultaneous integrated (SIB) and late course accelerated boost (LCAB)) in postoperative cervical cancer patient with high risk factors. And our results of long-term follow-up indicate that both SIB and LCAB to vaginal cuff are associated with excellent survival, local control and low toxicity; and can be an alternative to brachytherapy in certain circumstances when vaginal brachytherapy could not be feasible.

The study was approved by the institutional review board. With the submission of this manuscript, I would like to undertake that the above mentioned manuscript has not been published previously, accepted for publication elsewhere or under editorial review for publication elsewhere. The abstract of this manuscript was accepted as a poster presentation by the 2014 ASTRO (American Society for Radiation Oncology) 56th annual meeting. We confirm all authors have read and approved the manuscript. We declare that there is no conflict of interest. And we also confirm that if accepted, this manuscript will
not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright-holder.

All authors have made significant contributions to this work. Each author's contribution to this work can be quantified.

Please direct all correspondence with respect to this paper to me.

Thanks a lot in advance for your editorial services.

Yours sincerely

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