Author's response to reviews

**Title:** Prognostic implication of intratumoral metabolic heterogeneity in invasive ductal breast cancer patients

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To the Editor of *BMC Cancer*, Professor Steve Povoski:

We wish to submit our manuscript entitled ‘Prognostic implication of intratumoral metabolic heterogeneity in invasive ductal breast cancer patients’ for consideration for publication in *BMC Cancer*. This work comprises a more detailed prognostication and metabolic profiling using $^{18}$F-FDG PET/CT in patients with invasive ductal breast cancer. This manuscript was previously submitted to Breast Cancer Research, and the editor of the journal recommended transfer of the manuscript to *BMC cancer* for publication. It has not been submitted for publication to any other primary scientific journal while under consideration for publication in *BMC Cancer*.

In this manuscript, we report that intratumoral metabolic heterogeneity on pretreatment $^{18}$F-FDG PET/CT was predictive of overall survival in patients with invasive ductal breast cancer. To date, several studies regarding the biologic mechanisms involved in the intratumoral heterogeneous distribution of $^{18}$F-FDG have been reported; and, previous studies have demonstrated an association of the heterogeneous $^{18}$F-FDG distribution within a tumor on PET scan with the heterogeneity of histopathologic features in variable malignancy. Intratumoral heterogeneity of $^{18}$F-FDG uptake has also been found to show significant correlation with patient outcome in several cancers. However, the intratumoral heterogeneity of FDG uptake has not been evaluated and assessed as a prognostic PET parameter for breast cancer. In the current study, we report for the first time that intratumoral metabolic heterogeneity on pretreatment $^{18}$F-FDG PET/CT can predict overall survival in patients with invasive ductal breast cancer and is the strongest prognostic PET parameter. Our results suggest that patients with a more heterogeneous tumor can be considered as candidates for an aggressive neo- or adjuvant therapeutic plan to reduce mortality rates and should be followed up with caution.
Each author contributed to review of clinical records, and participated in writing the manuscript and all agreed to responsibility for the accuracy of the content of the paper. The paper has been written according to the guidelines provided by *BMC Cancer*.

We are hopeful that this manuscript will be considered for publication in *BMC Cancer* and look forward to receiving a positive response.

Best regards,

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