Author’s response to reviews

Title: Identification of breast cancer patients with a high risk of developing brain metastases: A single-institutional retrospective analysis.

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We would like to thank the reviewers for their helpful comments.

Following the recommendations of the reviewers, we added the following paragraphs in the section “Discussion”:

Reviewer: Michael Chan
1. Factors associated with the development of brain metastases & 2. Greater affinity to develop brain metastasis:

“The biology underlying the development of brain metastases from breast cancer is only partially understood. The hormone receptor status appears to be associated with the development of brain metastases as well as with the control of extracranial disease. In addition, it has been shown that the hormonal receptor status is associated with the risk of recurrence of brain metastases after radiosurgery [44]. However, there is a body of evidence suggesting that interactions of metastatic tumour cells with the blood brain barrier and brain microenvironment are also involved in the colonization process [45].”

3. Seeding of brain metastases after PCI:

“The time to the development of brain metastases varies between the patients and it cannot be excluded that in selected patients the seeding of tumors cells in the brain may occur after a prophylactic whole brain irradiation.”

4. Limitations of the study AND Reviewer: John Henson, why some known risk factors were not borne out:

“Limitations of our study are related to the retrospective study design and moderate patient numbers. The observed lack of a statistically significant impact of a young age at diagnosis and advanced disease stage on the brain
metastasis-free survival ($p = 0.10$) may be explained by a possible insufficient statistical power of our study. A selection bias cannot be fully excluded and results should be confirmed by future prospective studies."