Reviewer’s report

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

Version: 2
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Reviewer: Michael Chan

Reviewer’s report:

The authors present an interesting manuscript identifying factors in patients with primary breast cancers that predict for the development of brain metastases. The manuscript is well written and makes several important points that will be of interest to the readership of this journal. I have made some suggestions as to MINOR ESSENTIAL REVISIONS to help improve this manuscript.

1) The general theme of the factors that predict for development of brain metastases are those that would predict for decreased likelihood of control of extracranial disease (such as ER/PR negative, and particularly triple negative tumors). This should probably be acknowledged. There is also recently published data to suggest that for brain metastases treated with radiosurgery, the likelihood of distant brain failure is related to the ER/PR/Her2 status of the primary breast cancer (Vern-Gross et al, Journal of Neuro-Oncology 2012). This data may be worth citing as it relates to the theme of systemic control based on efficacy of available treatments preventing seeding of the brain.

2) In relation to comment #1, an existing theory to the likelihood of developing brain metastases is that some tumors (or tumor subtypes) may have a greater affinity to development of brain metastases. The authors also should probably acknowledge this in the discussion section as well, even though there data would suggest that the first theory is more likely to be true.

3) The concern I have for PCI in the setting of breast cancer is that it is unclear when during the natural history of metastatic breast cancer that the brain is seeded. Looking at Figure 1 in the manuscript, it appears that most of the brain failures occur between 24 and 48 months. It is unclear if these metastases would be present for 2-3 years prior to becoming symptomatic. As such, the use of PCI prior to the time of seeding the brain may in fact be counterproductive because it uses one of the definitive treatment options for brain metastases possibly prior to the presence of metastases. This issue should be acknowledged in the discussion section.

4) the authors should acknowledge the limitations of their study: retrospective with limited numbers. Limited patient population that may or may not be generalizable to other populations.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.