Reviewer's report

Title: Prognostic Factors and Multidisciplinary Treatment Modalities of Brain Metastases from Colorectal Cancer: Analysis of 93 Patients

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Reviewer: Filippo Ruggieri Grillo-Ruggieri

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Major Compulsory Revision
Authors have evaluated only overall survival as parameter to compare different treatment options. No mentions are made of response rate and local control, toxicity, complications of treatments and quality of life. These are essential when dealing with brain metastasis with very short expected life, while overall survival is so dependent on such a large number of conditions that it cannot be enough specific for such comparison.

They show radiation doses that apparently are lower, 2000 cGy in 20 fractions, for patients with higher PS while higher dose, 3000 cGy in 10 fractions, are associated to lower PS. If this is true this can adversely affect radiation treatment results. No details on SRS are provided while the dose range appears to be low also with possible influence on results.

Authors perform statistical procedures, choosing significance level of $p=0.10$, that is quite unusual, with univariate and multivariate analysis without considering treatment options, and they correctly conclude that number of brain metastasis and extra cranial metastasis are independent significant variables. However, they subsequently start a survival analysis with Kaplan Meier curves, comparing treatments, that is completely unrelated to the previous statistical parameters and analysis. There is no indication of the power of the test, no data on the number of patients remaining at the end of the curves where they diverge and very small difference in survival between the few remaining patients can dramatically, even if artificially, affect the significance of the curves and not even confidence intervals are mentioned. In other words, the clinical meaning and significance of the Kaplan Meier curves shown are, at the moment, much questionable because they compare, as stated by the Authors themselves, small subgroups of patients with heterogeneous clinical and demographics conditions including primary and so called salvage treatments.

In fact, the major drawback of this paper is the fact that Authors clearly state and demonstrate that patients population is strongly biased for treatment selection because single brain lesion and fit conditions are requisite for surgery, even if they operate some patients with multiple lesions and are so bound to treat them also with other modalities (SRS, WBRT) increasing heterogeneity.

Notwithstanding this major problem, they draw the firm and unjustified conclusion that surgery can prolong survival while the reverse holds true from their data: the patient with fewer lesions and more fit, possibly bound to longer survival, are
selected for surgery, while the others are treated with radiation modalities. Instead, nowadays, in major cancer center where quality of life and limited invasiveness of palliative treatment are considered essential for patients with short life expectancy, as those included in this study, modern selective radiation techniques as radio surgery and stereotactic radiotherapy are preferred limiting surgery to highly selected cases with hemorrhage, large lesion, ventricular compression.

Authors should better include treatment options into univariate and multivariate analysis and try to reduce, if possible, evident treatment selection bias influence existing in this retrospective review, to draw possible different and sound conclusions.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interest