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Comment on "Repeated HyperArc radiosurgery for recurrent intracranial metastases and dosimetric analysis of recurrence pattern to account for diffuse dose effect on microscopical disease"

We read with great attention the article by Nicosia et al. [1]. In this study on repeated radiosurgery (SRS) for recurrent brain metastases, the authors found that 95 % of new brain metastases occurred in brain tissue receiving 7 Gy or less. They hypothesize that diffuse low radiation dose to the surrounding brain might control microscopic disease, acting as a virtual clinical target volume. In this context, they consider the idea of combining low-dose whole-brain radiotherapy (WBRT) with SRS as a way to deliver ablative doses to active brain metastases while controlling microscopic disease. However, some reservations must be presented regarding this hypothesis:

(1) Limited volume of the 7 Gy isodose:
The study population mainly consists of patients with a limited number of small metastases (i.e., median metastases treated per cycle: 3; median metastasis volume: 0.1 cc). In this context, the 7 Gy isodose volume is expected to be relatively small compared to the total brain volume. The fact that the vast majority of recurrences occur outside this isodose could simply be due to its limited volume rather than an inherent ability of a dose as low as 7 Gy to control microscopic disease. It would be interesting to know the ratio between the 7 Gy isodose volume within the brain and the total brain volume for the patients analyzed.

(2) Significant distant brain failure risk after standard dose WBRT:
In a meta-analysis of phase 3 trials of SRS with or without WBRT (30 Gy in 10–12 fractions) in patients with 1–4 brain metastases, distant brain failure risk after WBRT was 34 % [2]. It can be hypothesized that this risk would be even greater with low-dose WBRT.

(3) Potential cognitive toxicity of low radiation doses:
Preclinical studies have shown that radiation dose as low as 2 Gy may result in dysfunction of neural precursor cells [3]. Parallel to that, in patients with benign or low-grade brain tumors, a dose greater than 7.3 Gy to 40 % of the hippocampi was shown to be associated with neurocognitive function impairment [4]. This potential side effect must be carefully weighed against the benefits, especially considering the aim of improving overall quality of life and survival without significantly impairing cognitive function.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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