Peer Review File

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Minor Revision:

Comment 1: In line 74, the authors introduced the mechanism of radiofrequency ablation in the treatment of metastatic tumor pain. “after radiofrequency ablation causes tumor cells to die, a large number of cytokines, such as TNF - α, substance P and interleukin, can be produced to stimulate sensitive nerves;” My understanding is that the release of those cytokines from dead tumor cells causes pain, instead of relieving pain. Please clarify it.

Reply 1: we have clarified our text as advised (see line 97-99).

Changes in the text: “(c) the death of tumor cells caused by radiofrequency ablation can reduce the production and release of a large number of cytokines, such as TNF - α, substance P and interleukin, which can be produced to stimulate sensitive nerves”.

Comment 2: The authors also briefly introduced other ablation methods including percutaneous cryoablation and microwave ablation (MWA). I did not see much comparison with RFA. They are not much relevant as
well. This section can be removed in order to focus on RFA discussion.

Reply 2: considering the Reviewer’s suggestion, we removed this part of content.

Changes in the text: we delete the paragraph of “COMPARISON OF DIFFERENT ABLATION METHODS”

Comment 3: The authors mentioned the combination of RFA with vertebroplasty could create synergistic effect. But I did not see any articles that reported synergistic effect. Are there any articles that reported better treatment effect of the combination treatment as compared with RFA or vertebroplasty alone?

Reply 3: there are some controversy about the synergistic effect of combination of RFA with vertebroplasty. As we analyzed in the paper, in theory, RFA alone can effectively relieve the pain of spinal metastasis, but it can not achieve the effect of vertebral body strengthening and reconstruction stability brought by vertebroplasty. Some studies reported the synergistic effect of combined RFA and vertebroplasty on pain management (see reference 15-18). But these studies are single-arm observational studies. There is no direct evidence shows better treatment effect of the combination treatment as compared with RFA or vertebroplasty alone. A comparative analysis of multicenter with large sample study is essential.

Changes in the text:

Line 121-122: “In view of the above analysis, it is generally considered that the combined application of the two has certain synergistic effect” was modified as “In view of the above theoretical analysis, it is generally considered that the combined application of the two has certain synergistic effect.”

Line 124: “The combination of the two has a certain synergistic effect” was deleted.

Line 142-144: “There is no direct evidence shows better treatment effect of the combination treatment as compared with RFA or vertebroplasty alone. A comparative analysis of multicenter with large sample study is essential” was added.

Comment 4: This review articles focused on the RFA treatment in spinal metastasis. It seems there was only a brief introduction regarding the history of RFA and its clinical outcome. Instead, the authors gave a relatively more detailed introduction regarding the combination of RFA with vertebroplasty. It is better to give more detailed introduction regarding the history of RFA itself and its use in the treatment of spinal metastasis.

Reply 4: Considering the reviewer’s suggestion, we have added more introduction regarding the history of RFA and its use in the treatment of spinal metastasis, and we updated the latest reference literature.

Changes in the text:

Line 83-87: “This technique was first used as a target therapy in the treatment of liver and lung tumors. In 1992, Rosenthal et al. successfully used RFA to treat osteoid

osteoma with effective pain relieving result (4). Since then, RFA had been widely used in the management of osseous lesions, including bony metastases, but not used on vertebral lesions because of the potential risk of spinal cord or never root heating injury by RFA" was added.

Line 97-101: "In 2002, Grönemeyer et al. reported 21 spinal lesions with an average relative pain reduction of 74% after RFA treatment in a single center retrospective study (6). Anchala et al. published the retrospective results of 92 patients with 128 lesions who received RFA, reporting significantly decreased average VAS pain scores from 7.51 per-operative to 1.73 at 1 week, 2.25 at 1 month, and 1.75 at 6 months post-operative in 2014 (8)" was added.