

Peer Review File

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Reviewer A

Comment 1:

You have written a solid review of the literature.

I have one minor remark:

line 179 If no risk factors for peptic ulcer are present (eg NSAIDs, history of ulcer...), the effectiveness of adding a proton pump inhibitor is unknown.

Reply: modified text as advised. Line 179 referenced in the old manuscript is now line 208

Changes in text: statement added. See page 9, lines 210-211

Reviewer B

Overall, a thoughtful and well-organized review of metastatic spinal cord compression. The review covers diagnostic imaging, and management with steroids, surgery and radiation, highlighting hybrid therapy as an emerging treatment modality. Figures are clear and relevant.

Major issues:

Comment 1) The review does not include any discussion or literature regarding survival and prognosis. As this is an important clinical element, a common outcome measure for trials of MSCC, and an element of the proposed treatment algorithm (figure 4), it ought to be addressed with a dedicated section in the review. Additionally, there is no guidance regarding how to assess prognosis and determine whether an individual has ‘poor’ or ‘intermediate to favourable’ prognosis, making it difficult to employ the algorithm.

Reply: Modified text as advised. We have added a new section which makes a statement on the median overall survival data from randomized clinical trials as well as the reported ranges. Then we have summarized the key features of a published prognostication tool. Additionally we have presented subgroup analysis from a randomized clinical trial which suggests factors associated with overall survival in the context of cord compression . This section is now 1.5 with the section “Management of Cord Compression” following (previously section 1.5, now management is 1.6)

Changes in text: This new section is now section 1.5, page 7-8, lines 167-195.

Comment 2) Would include some element of QOL/improved pain control as a goal and measured study outcome with treatment of MSCC.

Reply: Modified text as advised. We have added statement commenting on pain and narcotic reduction from randomized clinical trials addressing radiotherapy to treat cord compression We

have also presented findings from a recent clinical trial (SCORAD trial) which formally assessed quality life and was reported in their supplementary data.

Changes in text: statements added in the section 1.6.4, page 12, lines 292-301

Comment 3) In section 1.5.5, some of the statistics related to local control with SRS need to be presented more accurately or with more context so that they are not misleading. For example, in line 263/4 it says, ‘the use of adjuvant SABR for MSCC demonstrates excellent 1 year local control rates of 95.9%’ yet the study reported a local failure rate of 4.1%, and >50% of subjects died before 1 year. Presenting this as a 95.9% local control rate is misleading. Similarly, in the Redmond study (Ref 12; line 268), the local control rate of 90% was ‘per protocol’ yet 19 of the 35 subjects died before 12 months.

Reply: Modified text as advised. We have removed local control, and have instead used the study’s term of local progression and presented those rates instead in the first study being referenced in the comment. For both studies we have described the percentage of patients who have died in less than a year.

Changes in text: statements modified and added in now section 1.6.5, pages 12-13, lines 313-239