

Peer Review File

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Reviewer Comments

Introduction with lack of information. Comments are available in the document to explain more clearly. Table 3 misreferenced. Bt and EBRT concepts mixed up. Division of MRI concept in EBRT and BT is recommended.

(See the documentation for details)

Reply: Thank you for your comments and suggestions in the attached document. We acknowledge that a clearer distinction between the concepts of external beam radiotherapy (EBRT) and brachytherapy (BT) should be made in some parts of the review. This review aims to predominantly focus on EBRT, with only brief references to BT as part of the standard cervical cancer treatment. Please see below for how we have addressed each comment to reinforce the overall aim.

Comment 1: I will add references from ABS and GEC eSTRO recommendations of IGABT and EMBRACE results. Also, some references of the importance of MRI imaging for brachytherapy, therefore it's also important for contouring and planning in EBRT. Lack of background in the introduction.

Reply 1: Thank you for your comment. We agree with the importance of providing more context at the beginning of this manuscript to introduce how MRI fits in the current guidelines.

Changes in the text: We have added lines 66-71 (page 4) to incorporate GEC ESTRO-ABS recommendations and EMBRACE results into the introduction in a succinct way.

Comment 2: The reference is GEC ESTRO-ABS guidelines for CT contouring in BT!!!! not in EBRT. Should not be referred here.

Reply 2: Thank for your comment in identifying the error in referencing the relevant literature (EBRT vs BT). We agree that this should be amended for the purpose of drawing clear distinction between EBRT and BT.

Changes in the text: We have changed the reference to an EBRT based paper (see page 4, line 74).

Comment 3: For contouring and treatment planning,

Reply 3: Thank you for your comment to suggest alternative phrasing to include the concept of contouring.

Changes in the text: We have modified the text as advised (see page 4, line 75).

Comment 4: Uterus is not an organ at risk

Reply 4: Thank you for identifying the error in including uterus as an organ at risk.

Changes in the text: We have corrected this part to provide accurate information on organs at risk (see page 4, line 76).

Comment 5: YOU SHOULD INTRODUCE IMRT

Reply 5: Thank you for your suggestion on introducing IMRT, which is an important part of clinical practice in MRI-guided radiotherapy.

Changes in the text: We have added information in lines 83-84 (page 4) to discuss IMRT as one of the strategies to optimise the irradiated treatment field, also as advised in **Comment 8** below.

Comment 6: Specify which image. Not clear this sentence.

Reply 6: Thank you for seeking clarification on the nature of imaging for target volume (TV) definition.

Changes in the text: We have modified the text improve clarity to the information that TV is defined based on the images, acquired at the time of treatment planning (see page 4, lines 74-78).

Comment 7: MRI at diagnosis in treatment position is important to define target volumes,

Reply 7: Thank you for your suggestion on alternative phrasing of the text.

Changes in the text: We have modified the text as advised (see page 4, line 75-76).

Comment 8: You should explain which strategies we have to avoid this situation: ITV, pTV, filling protocol and daily IGRT that improve accuracy of field placement.

Reply 8: Thank you for your suggestion on introducing strategies to minimise geographical miss of the target and OAR irradiation. We agree that this will serve to gather the individual concepts such as ITV, IMRT or ART into one coherent topic of discussion (i.e. improving accuracy of the irradiated field).

Changes in the text: We have modified the text to elaborate on the suggested strategies (see page 4, lines 81-85). ART is further discussed in the following paragraph (see page 4, line 87).

Comment 9: brief introduction of ART: IGRT, offline, plan of the day and anatomy of the day. CT based and MRI based.

Reply 9: Thank you for your suggestion on elaborating on the concept of ART to aid better understanding of the review.

Changes in the text: We have modified the text with additional information to address ART (see page 4, line 87 to page 5, line 92).

Comment 10: YOU SHOULD REFER THE ORIGINAL ARTICLES, NOT OTHER REVIEW.

Reply 10: Thank you for your suggestion on using an alternative reference to support the text.

Changes in the text: We have changed the reference to a primary study (see page 5, line 90).

Comment 11: nO EVIDENCE OF IMPROVEMENT OF OUTCOMES, BUT REDUCING TOXICITY

Reply 11: Thank you for your comment.

Changes in the text: We have removed this text given a similar point has been conveyed in the preceding sentence (see page 5, lines 90-92) and to avoid confusion.

Comment 12: ct WITH BLADDER FILLING PRPTOCOL AND mri IN TREATMENT POSITION SHOULD BE PERFORMED.

Reply 12: Thank you for your suggestion to clarify the current recommendation for treatment planning.

Changes in the text: We have modified the text as advised (see page 6, lines 127-128).

Comment 13: Lim et al. RTOG consensus guidelines in cervical cancer. EMBRACE II protocol

Reply 13: Thank you for the suggested study to reference the current guideline for radiotherapy planning.

Changes in the text: We have included the reference to support the relevant text (see page 6, lines 127-128).

Comment 14: IGABT with MRI is the golg standard. If you are refereing to your country or region, you should specify it at some poitn in the article.

Reply 14: Thank you for seeking clarification in the current recommendation for IGABT. We agree that despite the evidence, the practices may vary depending on the region/country.

Changes in the text: We have removed the text as this information was considered redundant and may potentially cause confusion regarding the use of different imaging modalities for treatment planning (see page 6, line 128).

Comment 15: reference based in IGABT with CT

Reply 15: Thank you for identifying the error in referencing BT papers in discussing intrafraction motion in EBRT.

Changes in the text: We have referenced alternative studies which are more appropriate for the text (see page 6, line 142).

Comment 16: reference on BT (9 and 10) and you are talking about EBRT.

Reply 16: Thank you for identifying the error in referencing BT papers in discussing uterus displacement during EBRT fractions.

Changes in the text: We have referenced a study which focuses on EBRT as opposed to BT (see page 7, line 148).

Comment 17: not clear

Reply 17: Thank you for seeking clarification on the results of the study described in this text. The study evaluated the degree of tumour regression in two treatment groups: one group with patients undergoing RT (EBRT + BT) alone, the other group with patients undergoing concurrent chemoradiotherapy (CCRT). The results showed that tumour regression was significant in both groups, with numerical values included in the text.

Changes in the text: We have modified the text to better differentiate the two groups of patients studied in the article (see page 8, lines 185-187).

Comment 18: Not clear what you mean in this paragraph. Are you talking about BT?

Reply 18: Thank you for seeking clarification on this paragraph, which aims to discuss different patterns of residual disease after the completion of CCRT (i.e. at the time of commencing BT) and how this would influence target dosimetry during BT. We acknowledge that the discussion in this paragraph extends to the domain of BT and therefore may no longer be appropriate for the aim of this review.

Changes in the text: We have removed this paragraph to improve the relevance of the discussion to the overall aim of this manuscript (see page 8, line 197).

Comment 19: 3D or IMRT?

Reply 19: Thank you for seeking clarification on the nature of imaging. In this study, they used volumetric modulated arc therapy (VMAT) to study organ geometry in subsequent fractions of EBRT.

Changes in the text: We have modified the text to define the imaging modality (see page 8, lines 199-200).

Comment 20: I will not add here the BT. There is protocol fillings and prefraction control and planning.

Reply 20: Thank you for your suggestion on drawing distinction between EBRT and BT.

Changes in the text: We have modified the text to focus on EBRT (see page 8, line 203).

Comment 21: daily IGRT is already established in the clinical practice.

Reply 21: Thank you for your comment to

Changes in the text:

Comment 22: explain HOW to use it in the treatment

Reply 22: Thank you for seeking clarification the utility of MRI in the assessment of interfraction organ motion in EBRT. In this paragraph, we aimed to provide a comprehensive

statement that, in summary, the superior visualisation of disease status and organ motion through MRI can improve target dosimetry and coverage, as demonstrated in the studies. We acknowledge that this could be phrased differently to clearly indicate that optimal target coverage and minimal OAR irradiation are the main outcomes we expect to achieve through MRI guidance.

Changes in the text: We have modified the text as advised (see page 9, lines 210-213).

Comment 23: misreferenced:

Reply 23: Thank you for identifying the error in referencing in Table 4.

Changes in the text: We have updated the reference to the correct study (see page 5, reference 33).