Reviewer’s report

Title: Adjuvant chemoradiation in pancreatic cancer: impact of radiotherapy dose on survival

Version: 0 Date: 29 Mar 2019

Reviewer: Michael Back

Reviewer's report:

This is a well structured manuscript originating from a large longstanding international database collaboration in pancreatic cancer. The data that is provided gives further evidence towards radiation dose response, and potential survival advantages of dose escalation above 45Gy, and potentially to beyond 55Gy. There is a well defined population, results are presented with clarity and the discussion provides a sound overview of issues relating to adjuvant therapy.

The manuscript is likely to be eventually suitable for publication but should be improved by addressing the following aspects with further analysis from their database.

1. The timeframe of the study extend from 1995-2008 over which period staging investigations and more conformal RT techniques improved significantly. The more recently managed patients may have not only been more likely to receive doses beyond 55Gy but also may have had more effective staging procedures excluding the presence of previously occult metastatic disease. The authors should provide the RT doses in relation to year of treatment. The year of treatment can also be include in statistical analysis to determine whether it is an independent prognostic factor.

2. The favorable dose response described in multivariate analysis is related to 45Gy dose level. As a dose of 50.4Gy is now become more standard the results could detail the analysis performed on the dose level of 55Gy as the reference dose, especially at 2 year survival. The numbers of patients in this >55Gy cohort should be adequate for this calculation, especially against the 50-55Gy cohort.

3. The discussion can be broadened by describing some of the issues related to potential morbidity from dose escalation, especially in relation to current protocols that deliver neoadjuvant chemotherapy prior to surgical procedures. Will the morbidity of 55Gy be heightened significantly when patients have more extensive definitive management? Perhaps the paper by Morganti, referred to in the text( reference 35) could be expanded upon in the discussion.

4. The proportion of patients receiving chemotherapy was far greater in the >55Gy subgroup. However chemotherapy presumably was not associated with survival on multivariate analysis. This could be more detailed in the results and discussion.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

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