Reviewer's report

Title: Predictive Value of Metabolic 18FDG-PET Response on Outcomes in Patients with Locally Advanced Pancreatic Carcinoma Treated with Definitive Concurrent Chemoradiotherapy

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Reviewer: Devin Schellenberg

Reviewer's report:

I had the pleasure of reviewing your recent paper regarding the predictive value of PET in pancreas cancer. We have made little progress in the field of pancreas cancer so I wish you the best with your continued studies. Below are my comments regarding the manuscript.

Major Revisions:

1) I believe the most significant issue I have with the manuscript is one that is difficult to fully address in the setting of pancreas cancer where early progression is common. The authors use an arbitrary cutoff of SUVmax reduction above (n=21) and below (n=11) the mean to create 2 comparative groups at the time of the 12 week follow up scan. In the lesser responsive group 6 of the 11 patients show local progression by the 12 week scan. The authors are essentially then comparing a group of non-progressors (n=21) to a group which contains those that have already progressed (n=6) and a minority (n=5) of patients that have not progressed. The finding of a difference in local control, progression free and overall survival is therefore not surprising.

2) Also, the timing of gemcitabine post chemoradiation is not definitively addressed. How many cycles of gemcitabine did patients receive prior to the 12 week scan? Was there a difference among patients?

3) The change in SUV is deemed significant on multivariate analysis but the other factors analyzed on multivariate analysis are never mentioned. Did they include age, sex, original SUV, tumor volume, ECOG, tumor location, stage…?

4) In general I felt that the lengthy references to FDG-PET as a tool for delineating malignant from benign pancreatic masses, as well as the benefit of FDG-PET for GTV delineation where tangential to the main thrust of the manuscript and I feel the 2nd paragraph of the introduction, and the 1st 3 paragraphs of the discussion where off point.

5) The 3rd paragraph of the introduction omits several studies outlining the utility of PET in predicting clinical outcomes in pancreatic cancer including those by Lee, SM; Schellenberg, D and Okumato, K, nor does it stress a very similar study by Choi, M (reference 26) that used a 50% decrease in SUV post chemotherapy as a cutoff to evaluate prognosis.

6) The stated conclusions were not the focus of this study. For example, other
studies have noted extremely low rates of regional failures in pancreas cancer. To conclude that FDG-PET-CT reduces geographical misses versus CT alone without any direct comparison of the two in the current study is misleading.

Minor revisions

1) In the results section of the abstract it is unclear how the groups of greater versus lesser SUVmax change are defined (this is stated only later in the manuscript)
2) Background, 1st paragraph, end of second sentence reads “chemotherapeutics and/or sufficient doses…” perhaps specifying that they are referring to radiation doses versus chemotherapy doses with “chemotherapeutics and/or sufficient RADIATION doses…”
3) Background, 2nd paragraph, end of 1st sentence...”and systemic extend of disease in tumor sites…” I think it should read “and systemic extend of disease in MANY tumor sites” or “SEVERAL tumor sites”...
4) Results, 1st paragraph, ~7th sentence “Sixteen patients developed in field recurrences, 3 of which were isolated and 13 were distant relapses” should be changed to “Sixteen patients developed in field recurrences, 3 of which were isolated and 13 were CONCOMITANT WITH distant relapses”
5) Discussion, 4th paragraph. I disagree with the sentence “Gemcitabine, with its strong radiosensitizing properties, is promising, but its utility remains to be investigated.” Studies by Brade, Murphy and others have combined gemcitabine with radiation effectively.
6) In table 1 and 2 the Y axis is “Survival (%))” but the demarcations of the Y axis are 0,2 to 1,0 (the 0,8 demarcation is missing the comma). These should be changed to 20-100 to be concordant with the (%) symbol.

Discretionary revisions

1) Emphasizing how SUVmax changes effect prognosis could be accomplished by reporting the differences in overall survival between “responders and non-responders” groups differentiated by the median SUVmax change or a strict 50% reduction in SUVmax as Choi et al. report. This might at strength to the authors’ conclusions.
2) The median SUVmax seems high versus previous pancreas studies. I’m not sure this needs to be addressed but could be compared with other studies.
3) Why was the 12 weeks post CRT chosen as the time to evaluate response?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests