Reviewer’s report

Title: The diagnostic performance of $^{18}$F-FAMT PET and $^{18}$F-FDG PET for malignancy detection: A meta-analysis

Version: 0 Date: 10 Aug 2017

Reviewer: Monica Shokeen

Reviewer’s report:

In the manuscript titled, "Diagnostic performance of $^{18}$F-FAMT PET for malignancy detection: Meta-analysis of diagnostic accuracy in comparison to $^{18}$F-FDG PET” Achmad et al performed meta-analysis to evaluate the diagnostic accuracy of L-3-$^{18}$F-$\alpha$-methyl tyrosine ($^{18}$F-FAMT) PET in malignancy detection in comparison with that of 2-deoxy-2-[$^{18}$F]fluoro-D-glucose ($^{18}$F-FDG) PET.

Background: While FDG is a widely used PET tracer for oncologic imaging, this tracer has limitations in slow growing tumors, tumors with low metabolism and in tumors residing in tissues that are inherently metabolically active such as brain and liver. Alternative tracers such as $^{18}$F-FAMT that target amino acid metabolism might be better than $^{18}$F-FDG for imaging certain types of tumors. FAMT is taken up by cells primarily via the L-type amino acid transporter 1 (LAT-1). LAT-1 is upregulated in several cancer types.

The study design used the current recommendations for systematic review of diagnostic test accuracy studies by the Cochrane Collaboration.

The meta-analysis involved visual assessment and by diagnostic cut-off values. Contingency table was constructed to include true positives, false positives, true negatives, and false negatives. Meta-analysis was performed using the 'mada' (Meta-Analysis of Diagnostic Accuracy) package in R statistical software version 3.2.2.

Six studies with a total of 278 patients were included.

Weaknesses.

What was the reasoning behind the use of Cochrane Collaboration over other methods? A rationale for using these recommendations should be described in some detail.

For the extraction method, it would have been appropriate to use the last author's name along with the first author's name as the last author is generally the corresponding author with most expertise.

Line 6-8: The sentence "Overall, the methodological…..was good" should be removed or edited to include objectivity such as significance level.
The conclusion statement is not fully supported by the results.

A major concern is that the dynamic data with FAMT especially at the early 5-10 minute time point is not available. This makes it hard to correlate with the biology of the tracer uptake as the washout of amino acid based tracers occurs at early time points.

Another major limitation of the study is that all the authors are part of the same institution where 18F-FAMT was produced. All six studies included in the analysis are also part of the same single institution.

To enhance the value of using FAMT tracer for certain cancer types, authors should tabulate the tumor type and then compare with FDG. Discussion as written does not provide a "trend" in tumor types or location favoring FAMT over FDG. While there is some data supporting this, this is not summarized in the 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.

No

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

No

**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.

I recommend additional statistical review

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