Reviewer's report

Title: The impact of 18F-FDOPA-PET/MRI image fusion in detecting liver metastasis in patients with neuroendocrine tumors of the gastrointestinal tract

Version: 0 Date: 23 Sep 2019

Reviewer: Anders Sundin

Reviewer's report:

This is an interesting study with noteworthy data and therefore is a pity that these are not presented clearly by the authors. Before publication is considered this manuscript therefore requires major revision.

Page 6, line 22: Not only are neuroendocrine neoplasms divided into well and poorly differentiated tumours. Importantly, they are additionally graded according to their proliferation, usually based on their ki-67 index, into G1, G2 and G3 tumours. This is of interest when the authors further on in the paper are discussing appropriate PET-tracers. Please add.

Page 6, line 47: "poor prognosis". Well, worse than situation when there are no metastases or only regional spread but not necessarily poor when you consider other types of cancer in general oncology. I suggest a change to "worse prognosis".

Page 7, line 32: Regionally, in some parts of Europe 18FDOPA is used as frequently as 68Ga-DOTA-somatostatin analogues but on the whole the latter are more common and should be reflected in the text. I therefore suggest that 68Ga-DOTA-somatostatin analogues and 18FDG are described before 18FDOPA.

Page 7, line 45: "characterize". Isn’t lesion depiction the most important task!? I suggest rephrasing of this sentence.

Page 7, line 54: "18Ffluorodeoxyglucose (18F-FDG), which depicts poorly differentiated NENs with a high proliferation rate, and the somatostatin analogues 68Ga-DOTATATE, 68Ga-DOTATOC, and 68Ga-DOTANOC, which visualize well-differentiated NENs"
In the end of the sentence the authors need to ad "….with low proliferation rate",

Also, they need to ad that this is "generally" the case but that it is in the clinical setting a huge overlap in this regard.

Page 8, line 2: "serotonin secreting". Do they really need to be actively secreting serotonin? Isn´t it enough if they are APUDOMAs!? Please elaborate!

Page 9, line 13 & 29: It is unclear-contradictory (difficult to understand) whether MRI was acquired in the early arterial contrast-enhancement phase to depict hypervascular liver metastases. This phase is mandatory to perform in NET patients!

Page 9: 8mm slice thickness seems a little too thick! We do 5 mm. Please comment!

Page 9, line 51 and Page 10, line 2: Have the authors developed their own imaging protocol or has it been adapted from that in another centre where it has been developed? It seems to be a short interval between tracer injection and scanning (30 minutes). Is the highest tumour uptake and/or tumour-to-normal tissue contrast reached at 30 minutes? Please provide information why this time interval was chosen and if possible e reference!

Similarly, 1,25 min/bed is a very short emission. Please provide information why this scanning time was chosen and if possible e reference!

Page 10, line 17: This paper is based on the comparison of the PET/MRI-fusion with other imaging. Yet, the authors do not present which software the used for this fusion! Please add!

Page 10, line 39: ".previously published criteria." Please provide reference(s)!

Page 10, line 55: ".previously published characteristic parameters."

Perhaps the lesions were rather characterised by the radiologist!?
If the characterisation indeed relied on literature data, please provide reference(s)!

Page 10, line 61: "similar appearance" On what? Imaging? Histopathology?

Page 10, line 55 & Page 11, line 0: How long was the follow-up and by what? CT? MRI? PET/CT?

Page 11, Statistical Analysis: Significance level?

Page 12, line 10: "axial" means along the axis of the body. Transaxial or transverse is correct.

Page 12, line 15: The authors state that they performed both a patient-based and a lesion-based analysis and they need to clearly indicate in the manuscript which one is which when they present the data.

Page 12, line 46: Why do the authors suddenly shift from describing sensitivity to stating detection rate?

Page 12, line 53: "or" Should this be "and"?

Page 13: Discussion. The first paragraph until "[25]" does not add anything to this manuscript.
I think that the authors can start by stating the main results of their study and then continue with the last sentence in the first paragraph, which needs to be supported by reference(s).

Page 13, line 41: Inflammatory uptake of 68Ga-DOTA-SSA is very rarely high enough to cause any diagnostic problems! For FDG it is. Please rephrase!
Page 13, line 57: "meta-analysis" Supply reference!

Page 13, line 59: "…should be limited to poorly differentiated tumours." This is incorrect!

As previously pointed out (comment regarding Page 7, line 54), there is a huge overlap regarding low-high ki-67 index and high-low FDG-uptake and low-high 68Ga-DOTA-SSA uptake and some centres with resources therefore subject all their NEN G2,G3 and NEC patients to PET/CT with both tracers. Also, some centres regard the information on FDG avidity important because it provides prognostic information.

Also the rest of the discussion needs to be rewritten

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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.

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 am able to assess the statistics

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