Author’s response to reviews

Title: Diagnostic accuracy of 18F-FDG PET/CT and MR imaging in patients with adenoid cystic carcinoma

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Author’s response to reviews:

Thank you for reviewing our manuscript entitled “Diagnostic accuracy of 18F-FDG PET/CT and MR imaging in patients with adenoid cystic carcinoma” and for the very valuable comments. We have tried to address the criticism raised and revised the paper accordingly.

Reviewer #1 (Gerhard Huber):

Ruhlmann et al. Performed an interesting retrospective study on the diagnostic value of PET-CT in addition to routine MRI (sometimes CT) regarding diagnosis and follow up of patients with adenoid cystic carcinoma. The study is scientifically sound, the English satisfactory, the conclusions comprehensible.
However, there are some points of criticism:

Although mentioned in the discussion section that there are different subtypes of ACC as well mucoepidermoid Carcinoma, they didn't discriminate between the three different subgroups of ACC (cribriform, tubular, solid). It would be of interest whether there are differences in the FDG uptake (SUV) in the three subtypes.

-->This is a very interesting point raised by the reviewer and reviewed our data accordingly. All tumors were ACC and none of the patients had a mucoepidermoid carcinoma. The corresponding histopathologies of the ACC tumors were: 18% cribriform, 4% solid, 30 % mixed tubular, solid and cribriform and in the remaining 48 % of the cases the histopathology was not further specified. The latter is due to the fact that many patients were referred from all over Germany resulting in non-standardized histopathological reports. Based on the data available, further analysis of the FDG uptake depending on the histopathological subtype seemed not feasible. In addition, even with more detailed histopathological information, the size of our sample is too small for obtaining reliable results.

However, as we agree that the proposed analysis considering the differences in the FDG uptake (SUV) depending on subtypes is of high interest and should be included in further prospective investigations with a larger patient cohort. We also intend to establish reference pathology. To address this aspect we added the following sentence: (page 11, line 24-25): “The small sample size did not permit an analysis of the FDG uptake depending on the histopathological ACC subtypes (cribriform, solid and tubular).”.

It would also be of interest whether the additional PET-CT (or in the future PET-MRI) would be cost-effective, since despite best treatments of local, regional and distant disease, survival and quality of life seem not the be much affected by earlier diagnosis. I would expect a comment on that.

-->Thank you for stressing this very important aspect. It is indeed debatable whether a diagnostic test should be expected to impact outcome (it is not a therapy but just a test). Most recently many health authorities accepted impact on management instead of impact on outcome as a valid endpoint for diagnostic tests. Nevertheless, the question of cost-effectiveness is a highly important and relevant topic. However, the sample size of our present study is definitively too small for creating a substantial health-economic analysis. We strongly believe that our data convey that PET/CT (or in future PET/MRI) are useful for staging ACC patients. Moreover, the whole-body imaging approach enables the early detection of distant metastases giving a better understanding of the natural history of this mostly slowly progressing disease. We were surprised to realize that at the time of diagnosis about 11% of the patients already showed distant
metastases in the lung. Additionally, we found in three patients secondary carcinomas by PET/CT allowing duly therapeutic interventions. This high incidence of secondary cancer in ACC patients has not yet been reported by other authors. PET/CT imaging allow to support the individual therapy management in a rare type of cancer with a complex course of metastatic disease.

Last but not least, the relevant literature is included, however seems almost too extensive.

--> As suggested by the reviewer we reduced the included literature by deleting 5 citations.

Line 6. With the risk of incomplete resection and (late) local recurrences (2-4). Here I would add also (late) distant recurrences.

--> According to the reviewer’s suggestion, we´ve added the requested changes in the above-mentioned sentence in the background section (page 3, line 6).