Reviewer's report

Title: pO2 Polarography, Contrast Enhanced Color Duplex Sonography (CDS), [18F] Fluoromisonidazole and [18F] Fluorodeoxyglucose Positron Emission Tomography: Validated Methods for the Evaluation of Therapy-Relevant Tumor Oxygenation or only Bricks in the Puzzle of Tumor Hypoxia?

Version: 3 Date: 16 March 2007

Reviewer: Susanne Keding

Reviewer's report:

General

>1. Is the question posed by the authors new and well defined?
*I'm not an expert on ultrasonography but the comparison of pO2 measurements and the PET measurements is not new, but nevertheless interesting. Furthermore, the authors still do not specify a hypothesis.* 

>2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
*The procedures of the pO2, FDG PET and FMISO PET are each described ok. However, I still can't figure out how the tumours can be defined on the PET images for correlation analyses without co-registration of the images. The authors still do not tell us how many of the tumour nodules seen on CT, can be seen independently by either of the two PET methods. Specifically, I don't understand how tumour nodules with SUV values in the lower range of the values reported can be seen on the FMISO images without knowledge of the results of the CT- or FDG PET results? Furthermore, I still can't figure out how the pO2-measurements were guided by CT and how this could be used to ensure that the measurements were representative for the same volume as seen by the PET measurements.*

3. Are the data sound and well controlled? *Sorry, I don't think so, please see above.*

>4. Does the manuscript adhere to the relevant standards for reporting and data deposition? *Sorry, no. **I still feel uneasy with such multiple correlation analyses, even if the authors adjust the statistical method for multiple comparisons. Furthermore how can such correlation analyses be justified in view of the lack of proper co-registrations of the images?*

>5. Are the discussion and conclusions well balanced and adequately supported by the data? *Sorry, no.*

>6. Do the title and abstract accurately convey what has been found? *Sorry, no. Specifically the title "Evaluation of Therapy-Relevant Tumor Oxygenation" indicate that therapy-relevance is evaluated which is not the case. The authors only quote that other authors have shown that pO2 values have prognostic information... which is true. But the authors do not evaluate this issue in the present manuscript.*

>7. Is the writing acceptable? *Sorry, no.*

In reviewing the revised manuscript, please consider whether the authors have answered your points sufficiently well to allow their manuscript to be published. As before, we would like you to divide your comments into the following three categories:
* In my first referee report, I did my best to be thorough and constructive ... I tried to give the authors some good advice to improve their manuscript. Unfortunately the authors have not replied to each of my comments or questions...and not provided a thorough point-to-point reply. They have not indicated specifically in the revised manuscript where they have changed the text... and if not, why not. Therefore I don't feel that I should go through the revised manuscript ... and probably repeat most of my comments and questions. Sorry!*
Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)