Reviewer's report

Title: Dynamic [18F]-Fluoromisonidazole PET Predicts Radiation Treatment Outcome in Head-and-Neck Cancer

Version: 1 Date: 28 August 2005

Reviewer: marianne Nordsmark

Reviewer's report:

General
This study describes pre-treatment functional imaging of hypoxia using 18Fmiso in 16 patients with head and neck cancer. The authors present two aims;

a) To develop a kinetic model in order to understand the spatial and temporal distribution of 18Fmiso in the tumor tissue. They study the time course of tracer accumulation and generated patient specific value for perfusion, kinetic constants and concentration of tracer retaining cells. This question is new, highly relevant to refine the technique and explore the diversity in the results obtained by 18Fmiso PET.

b) To investigate the relation between the PET derived parameters and treatment outcome studying progression free survival in 16 patients only. This number of patients is far to low to perform an outcome analysis and the data do not allow the conclusions drawn here due to lack of statistical power.

The methods are appropriate and well described, and sufficient details are provided to replicate the work. The data are sound and well controlled. The manuscript adheres to the relevant standards for reporting and data deposition?

The discussion and conclusions well balanced and adequately supported by the data?

The title needs rephrased emphasizing the modelling approach, which is unique and thereby the title will not be misleading.

The writing is acceptable.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The relation between the PET derived parameters and treatment outcome using Kaplan Meier analysis is not valid due to the low number of patients. Further accrual is needed before the analysis can provide a result that is statistically sound. This is the only real major criticism to this otherwise interesting study with excellent data analyses. It is suggested to leave out figures 2 and 3 and postpone the Kalan Meier outcome analysis until the number of patients is high enough to meet the statistical requirements. A power calculation is useful taking into account the number needed to allow further stratification for treatment, as some had chemo, some had not.

The current analysis and modelling will allow the authors to decide which biological PET hypoxia parameter they will use in the future outcome analysis looking for relevant predictive markers.
Patients
Specify how pre-treatment tumor volume was measured. This measure is used in the results. Is it possible to co-localize the imaging assessment and PET Fmiso?

Fmiso Data Acquisition
If MRI or CT scans are available for delineation of tumor volume in addition to the FDG PET this would raise the data quality considerably as the regions of interest for dose painting is both those with and those without hypoxia signalling, and it is well known that FDG is not tumor volume-specific.

Results
Figure 2 and 3, log-rank test-values in table 2 and the equivalent text should be omitted.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
NONE
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Discretionary Revisions (which the author can choose to ignore)

Page 2 line 20-23. The argumentation is not logic, but it is true that the prognostic and predictive values of Fmiso SUV's are not described.

What next?: Accept after minor essential revisions

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

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests' below