Reviewer's report

Title: MRI to Assess Chemoprevention in Transgenic Adenocarcinoma of Mouse Prostate (TRAMP)

Version: 1 Date: 16 October 2011

Reviewer: Robert Kirschner

Reviewer's report:

The authors investigate whether in vivo MRI without contrast agent can be used to follow the effect of chemoprevention of carcinoma of prostate using a 3 T clinical MRI system. The investigations were carried out applying transgenic mouse model of carcinoma of prostate (TRAMP). The authors determine the volume of seminal vesicle and prostate gland before, during and after treatment, investigating the efficacy of a chemopreventive agent, CDDO in prostate cancer in contrast to current method which is based on extraction and weighing the prostate at different time points or by immunohistochemistry analysis. The researchers also try to track the tumor mass indirectly using T2 weighted imaging and a postprocessing method.

In general, the topic is interesting for the reader of the journal and is of clinical interest. However, there are some major issues, which have to be sorted out before considering publication:

- Major Compulsory Revisions

Treatment protocol

Identity of animals during MRI sessions was not tracked. See “Treatment protocol” paragraph in “Materials and Methods” section: “identity of individual animals was not tracked during imaging”. This impedes the correct comparison of the measurement of prostate/seminal gland volume/mass (MRI vs. pathology) with two different methods.

Statistical analysis

The statistical analysis of the data is not correct.

1. It is not shown whether the variables follow the normal (Gaussian) distribution. The equality of variances is not tested, either. These would be the prerequisites of the use of parametric methods. Otherwise, non-parametric analogue tests should be used.

2. Taking into account of the experimental design, application of Students t-test is insufficient, even if the variables fulfill the above detailed conditions. There are at least two factors for every variable. For example, two-way analysis of variance should be used for the statistical analysis of SI variable and two factors should be considered:
a) treatment (treated, control)
b) time points (week 5, week 12, week 25)

If an overall significance (P<0.05) is established for rejecting the null hypothesis that the six groups are not different, pairwise differences between the groups should be assessed (Holm-Sidak or Bonferroni correction etc). Additional variables should be analyzed similarly.

3. After the correct statistical analysis, the figures must be redesigned in order to fit to the results.
4. Figure 3.b uses different dimensions (volume and mass) within one graph.
5. The data of prostate/seminal gland volume/mass with two different methods are not reported. Bland-Altman’s plot and overall bias are not announced.

Discussion

The theoretical basis of the changes in signal intensity on T2 weighted MRI images with different TE is not fully elaborated. The cited paper [25] in the “Discussion” section does not support the hypothesis that “high TE images usually produce differential signal intensity from a tissue/organ based on the differential relaxation or T2 parameters”. A new paragraph should be written which elucidates the signal intensity changes on differential images using the theoretical formula between SI vs. T2 values of the normal/cancer prostate tissues and the different TE values. The other solution for the problem is to find a previous paper which contains the explanation.

The data and statistical analysis supporting the hypothesis that higher grade of cancer involves higher mean signal intensity changes on differential images are also lacking.

-Minor Essential Revisions

The “DLP” acronym is not defined (first mentioned at “CDDO slows down the progression of prostate carcinoma in TRAMP mice” paragraph).

Which software has been used for the image analysis?

-Discretionary Revisions

The sentence “in future, tumor specific or non-specific MRI contrast agents will be used to determine the exact location of tumors in our ongoing studies” in the conclusion paragraph does not fit to the context. It makes the reader rather feel that the authors are not sure the feasibility of the reported methods.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published
Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests.

Robert Kirschner MD, PhD